BMJ Open

Primary care Adherence To Heart Failure guidelines In Diagnosis, Evaluation & Routine management (PATHFINDER): a randomised controlled trial protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-063656
Article Type:	Protocol
Date Submitted by the Author:	29-Apr-2022
Complete List of Authors:	Dai, Liying; Curtin University, School of Allied Health Dorje, Tashi; Fiona Stanley Hospital, Department of Cardiology Gootjes, Jan ; Fiona Stanley Hospital, Department of Cardiology Shah, Amit; Fiona Stanley Hospital, Department of Cardiology Dembo, Lawrence ; Fiona Stanley Hospital, Department of Cardiology Rankin, Jamie ; Fiona Stanley Hospital, Department of Cardiology Hillis, Graham; Royal Perth Hospital, Department of Cardiology ; The University of Western Australia, Medical School Robinson, Suzanne; Curtin University, School of Population Health Atherton, John ; Royal Brisbane and Women's Hospital, Department of Cardiology; The University of Queensland, Faculty of Medicine Jacques, Angela; Curtin University, Curtin School of Allied Health Reid, Christopher; Curtin University, School of Population Health Maiorana, Andrew; Curtin University, School of Allied Health; Fiona Stanley Hospital, Department of Allied Health
Keywords:	Heart failure < CARDIOLOGY, PRIMARY CARE, Clinical trials < THERAPEUTICS

Title page

Primary care **A**dherence **T**o **H**eart **F**ailure guidelines **I**n **D**iagnosis, **E**valuation & **R**outine management (PATHFINDER): a randomised controlled trial protocol

Word count: 4231

Corresponding author:
Andrew Maiorana, Curtin School of Allied Health, Kent Street, Bentley, Western Australia, 6102, Australia and Allied Health Department, Fiona Stanley Hospital, Perth, Australia A.Maiorana@curtin.edu.au

All contributing authors (a name, email, institution):
Liying Dai, liying.dai@postgrad.curtin.edu.au, Curtin School of Allied Health, Curtin University, Perth, Australia;

Dr Tashi Dorje, tashi.dorje@health.wa.gov.au , Department of Cardiology, Fiona Stanley Hospital, Perth, Australia;

Jan Gootjes, jan.gootjes@health.wa.gov.au , Department of Cardiology, Fiona Stanley Hospital, Perth, Australia;

Dr Amit Shah, Amit.Shah@health.wa.gov.au , Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital, Perth, Australia;

Dr Lawrence Dembo, Lawrence.Dembo@health.wa.gov.au , Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital, Perth, Australia;

Dr Jamie Rankin, James.Rankin@health.wa.gov.au , Department of Cardiology, Fiona Stanley Hospital, Perth, Australia;

Prof Graham S. Hillis, Graham.Hillis@health.wa.gov.au , Department of Cardiology, Royal Perth Hospital, and Medical School, University of Western Australia, Perth, Australia;

Prof Suzanne Robinson, Suzanne.robinson@curtin.edu.au School of Population Health, Curtin University, Perth, Australia;

Prof John J Atherton, John_Atherton@health.qld.gov.au , Department of Cardiology, Royal Brisbane and Women's Hospital and Faculty of Medicine, University of Queensland, Brisbane, Australia;

Dr Angela Jacques, angela.jacques@curtin.edu.au, Curtin School of Allied Health, Curtin University, Perth, Australia;

Prof Christopher M Reid, christopher.reid@curtin.edu.au, School of Population Health, Curtin University, Perth, Australia;

Prof Andrew Maiorana, A.Maiorana@curtin.edu.au , Curtin School of Allied Health, Curtin University, Perth, Australia and Department of Allied Health, Fiona Stanley Hospital, Perth, Australia.

Keywords: heart failure with reduced ejection fraction, guideline adherence, primary care

ABSTRACT

Introduction
General practitioners (GPs) routinely provide care for patients with heart failure (HF), however adherence to management guidelines, including titrating medication to optimal dose, can be challenging in this setting. This study will evaluate the effectiveness of a multifaceted intervention to support adherence to HF management guidelines in primary care.
Methods and analysis
We will undertake a multi-centre, parallel-group, randomised controlled trial of 200 participants with HF with reduced ejection fraction. Participants will be recruited during a hospital admission due to HF. Following hospital discharge, the intervention group will have follow-up with their GP scheduled at 1week, 4 weeks and 3 months with the provision of a medication titration plan approved by a specialist HF cardiologist. The control group will receive usual care. The primary endpoint, assessed at 6 months, will be the difference between groups in the proportion of participants being prescribed five guideline-recommended treatments; i) ACEI/ARB/ARNI at least 50% of target dose, ii) beta blocker at least 50% of target dose, iii) mineralocorticoid receptor antagonist at any dose, iv) anticoagulation for patients diagnosed with atrial fibrillation, iv) referral to cardiac rehabilitation. Secondary outcomes will include functional capacity (six-minute walk test); quality of life (Kansas City Cardiomyopathy Questionnaire); depressive symptoms (Patient Health Questionnaire-2); self-care behaviour (Self-Care of Heart Failure Index). Resource utilisation will also be assessed.
Ethics and dissemination Ethical approval was granted by the South Metropolitan Health Service Ethics Committee (RGS3531), reciprocal approval at Curtin University (HRE2020-0322). Results will be disseminated via peer-reviewed publications and conferences.
Trial registration number ACTRN12620001069943, prospectively registered.

Strengths and limitations of this study

- This study will evaluate the effectiveness of a novel multifaceted intervention to assess guideline adherence and assess feasibility for future large-scale clinical trials to evaluate clinical outcomes.
- The primary and secondary outcome measures will test the effect of the intervention on clinical practice and patient physical and psychosocial health.
- The intervention is highly translatable to routine practice to improve care coordination between hospital and primary care sectors.
- The study will be conducted in a single state health jurisdiction and may not translate to other jurisdictions.
- The study will evaluate costs associated with resource utilisation across the control and intervention groups
- The current study is not statistically powered to evaluate clinical outcomes such as mortality or rehospitalisation rates.

Introduction

Heart failure (HF) is a complex condition affecting over 60 million people worldwide and associated with high mortality and hospitalisation rates,[1 2] placing a heavy burden on patients and healthcare systems.[3] In Australia, the prevalence of HF is estimated to be 1% to 2%, resulting in hospitalisations costing approximately $2.7 billion annually.[4] Due to the ageing population, and improved treatment of acute cardiovascular events, the prevalence of HF is expected to increase over the next decade.[2]

Guideline-advocated pharmacotherapy and non-pharmacological treatment, such as cardiac rehabilitation (CR), are core components for the effective treatment of patients with HF with reduced ejection fraction (HFrEF) to improve clinical outcomes, functional capacity, and quality of life.[5 6] However, despite these established benefits, guideline adherence is often suboptimal.[7] This is

especially pertinent in primary care. General practitioners (GPs) play an essential role in managing patients with HF;[8 9] patients can be holistically monitored, cared for by the same team members, and reviewed regularly.[10] However, despite progress in the adoption of guideline-advocated HF treatment in primary care,[11] barriers remain for the delivery of best-practice management[12] at the patient[13], provider[14 15] and system-level.[16 17] For example, HF medication titration is a well-documented challenge in general practice,[12 18] resulting in HF medications often not being titrated to the target dose.[11 19] Compounding this issue is that access and referral of patients to cardiac rehabilitation and community-based HF programs, which support the role of GPs in the management and surveillance of patients with HF, is not ubiquitous.[9 20]

Multifaceted interventions with two or more combined strategies have been found to be more effective than isolated processes for instigating changes in practice among health providers.[21] In outpatient cardiology practice, the *Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting* (IMPROVE-HF) study, which included clinical decision support tools and chart audits with feedback, and the *Get With The Guidelines-Heart Failure* (GWTG-HF) program which provided education, webinars, and quality improvement conferences to support clinical decision making, were both associated with increased use of guideline-recommended therapies.[22-24]. However, the limited research which has reported the effectiveness of multifaceted interventions to support guideline-advocated management of HF in primary care, have been less successful. Neither the combined strategies of an educational train-the-trainer course with a pharmacotherapy feedback[25] nor guideline summary dissemination, performance audit with feedback, patient-specific chart reminders, and patient activation mailings[26] resulted in improvement in the prescription of angiotensin converting enzyme inhibitors (ACEIs) at any dose. In the *Swedish Intervention study, Guideline and NT-pro-BNP analysis in Heart Failure* (SIGNAL-HF), GPs received an education program and applied N-terminal pro-B-type natriuretic peptide (NT-pro-BNP)-guided therapy, but there were no statistically significant dose increases of ACEIs/angiotensin receptor blockers (ARBs) or beta-blockers (BBs) between the intervention and control groups at 9-month follow-up.[27]

In Australia, Nurse Practitioners (NP) have advanced scope of practice which includes medication titration and ordering blood tests in response to changing clinical status.[28] Accordingly, they are well credentialed to apply case management for patients with HF. We have recently reported that a NP -led HF clinic can improve self-care behaviour and quality of life, and reduce hospital admissions,[29] highlighting the efficacy of heart failure models of care involving NPs.

We propose a multifaceted intervention to improve the provision of guideline-advocated management of HFrEF in primary care. The intervention will be facilitated by a Nurse Practitioner specializing in HF management, who will provide care support pre- and post-discharge. The study's primary objective is to evaluate the effectiveness of the multifaceted intervention for improving **P**rimary care **A**dherence **T**o **H**eart **F**ailure guidelines **In D**iagnosis, **E**valuation & **R**outine management (PATHFINDER).

METHOD

Study design

This will be a prospective, multi-centre, parallel-group, randomised controlled trial with blinded assessment of study outcomes conducted between February 2021 and September 2022. Two hundred eligible patients will be randomly assigned to either the intervention or a usual care control group at a 1:1 ratio. The intervention group will receive multifaceted support involving pre- and post-hospital discharge components. Pre-discharge elements of the PATHFINDER intervention will include HF self-management education, the provision of a discharge plan that includes scheduled GP follow-up appointments, cardiac rehabilitation referral, and feedback to the supervising hospital physician. Post-discharge, the intervention will involve letters to participants to remind them to book a GP appointment at 1 week, 4 weeks and 3 months, for review of their HF management. Prior to each appointment, the participant will be provided with a HF medication titration plan, approved by a

cardiologist, to take to the appointment, which will include the telephone number of a support line for GPs to contact in the event that they require HF management advice (provided through a specialist HF service). The overall schedule of the trial is outlined in Table 1, and the study flow chart is presented in Figure 1. Both groups will be followed-up over six months.

Recruitment

Patients with HF with reduced ejection fraction (HFrEF) will be recruited from two tertiary hospitals in Western Australia (WA). A research nurse will identify potential participants from the echocardiogram reporting system and electronic medical records of patients in the cardiology and general medical wards, and a daily list of patients with an admission diagnosis of HF will be generated. The study will also be advertised by posting study flyers in the hospitals' cardiology and general medical wards and the study will be promoted to clinicians at departmental meetings. Patients will be required to provide written informed consent prior to enrolling in the study. [Appendix1]

Table 1.	**Data collection points**					
Outcome	**Assessment**	**Baseline**	**1w**	**4w**	**3m**	**6m**
Primary						
Overall guideline adherence	Proportion of patients prescribed five out of five HF quality metrics[#]					*
Secondary						
Medication adherence	Proportion of eligible patients prescribed ACEIs/ARBs/ARNIs, BBs, MRAs at any dose		*	*	*	*
	Proportion of eligible patients prescribed ACEI/ ARB/ARNI, BB, or MRA at ≥50% of the target dose or maximum tolerated dose		*	*	*	*
	Proportion of eligible patients prescribed ACEI/ARB/ARNI, BB, or MRA at the target dose or maximum tolerated dose					*
	Proportion of eligible patients prescribed an anticoagulant if diagnosed with atrial fibrillation					*
Cardiac rehabilitation	Proportion of patients referred to an exercise training program or cardiac rehabilitation program					*
	Proportion of patients attending 16 sessions of cardiac rehabilitation					*
Functional capacity	6 minute walk test distance	*				*
	PROMIS physical function short form 4a					*

Patients' medication adherence	MMAS-8	*	*
Depressive symptoms	Patient Questionnaire-2	*	*
Health status	KCCQ-12	*	*
Self-care	SCHFI V7.2		*
Health care resource utilisation	Visits to physician, hospitalisations, days of admission.		*

HF, heart failure; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor neprilysin inhibitor; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; PROMIS, Patient-Reported Outcomes Measurement Information System; MMAS-8, Patients' medication adherence measured by the Morisky Medication Adherence Measure Scale-8; KCCQ-12, quality of life measured by the Kansas City Cardiomyopathy Questionnaire-Short Version; SCHFI V7.2 , Self-care behaviour measured by the Self-Care of Heart Failure Index version 7.2. [#]or 4 out of four if 5 are not indicated

Participants

Inclusion criteria

(1) Patients hospitalised with signs and symptoms of HF (dyspnoea at rest or on exertion, plus at least one of the following: raised jugular venous pressure, peripheral oedema, third heart sound, or pulmonary congestion); or a left ventricular ejection fraction (LVEF) <40%; or a LVEF 41-49% and fulfilling the diagnostic criteria for HF according to the Australian Clinical Guidelines for the Management of Heart Failure 2018[5].

i.e. displaying signs of HF, brain natriuretic peptides (BNP) >100ng/L or NT-proBNP >300 ng/L or objective evidence of high filling pressure as indicated by at least three of the following echocardiography measures: i) mitral annular velocity septal e' of less than 7 cm/ s or lateral e' of less than 10-cm/s; ii) average mitral valve early wave inflow velocity to mitral annular velocity (E/e') ratio of more than 14; iii) left atrial volume index of more than 34 mL/m^2; 4) tricuspid valve regurgitation velocity of more than 2.8 m/s;

(2) Able to nominate a personal GP.

(3) >18 years of age;

Exclusion criteria:

(1) Patients currently under the management of a specialist HF service; (2) Receiving palliative care or with a life expectancy less than six months for conditions other than HF; (3) Nursing home/assisted living residents; (4) Impaired cognitive function; (5) Non-English speaking; (6) End-stage renal failure (eGFR < 15ml/min per 1.73 m^2).

Randomisation and blinding

Randomisation will be performed via a web-based program to generate a block randomisation sequence with a 1:1 allocation ratio. The randomisation list will be generated by an independent researcher not involved in the study. The HF NP will enrol participants and the independent researcher will assign the participants' allocation group to the HF NP by email following consent. Due to the nature of the intervention, it will not be possible to blind either the participants or the practitioner delivering the intervention. The study statistician will be blinded to group allocation when analysing the study outcomes. It's possible that participants being managed by the same GP may be allocated to different arms within the trial, resulting in the potential for contamination, however we anticipate the likelihood of this is low.

Control Group

The control group will receive usual care as provided by their treating cardiologist or general physician while an inpatient, and their GP post-discharge. The "Living Well with Heart Failure, information to help you feel better" (third edition 2020, National Heart Foundation of Australia) will be provided to all control participants prior to hospital discharge.

Intervention Group

In addition to usual care, as outlined for the control group, the intervention group will receive the following components:

Inpatient education

A 30 minute, one-on-one HF education session provided by a HF NP. The education will complement topics in the "Living Well with Heart Failure" and include self-management strategies and information on the value of adherence to HF medications to maintain optimal health.

Post-discharge plan

1) A *PATHFINDER Envelope* will be provided to participants to take to an appointment with their GP at approximately 1 week, 4 weeks, and 3 months after discharge; 2) referral to cardiac rehabilitation; 3) Feedback to the hospital clinical team if the patient is not prescribed an ACEI/ARB/angiotensin receptor neprilysin inhibitor(ARNI), BB or mineralocorticoid receptor antagonist (MRA) despite being eligible, or if there is deviation from the HF medication titration plan (outlined below).

The PATHFINDER Envelope, will contain a cover letter to the GP detailing the study [Appendix 2] and the PATHFINDER Study Follow-up Form. The Follow-up Form will be individualised to the patient and provide details of dry weight at discharge, current dose and target dose of ACEI/ARB/ARNI, BB, and MRA approved by a cardiologist specialising in HF. It will serve as both a clinical support and a data collection tool. The form will include the following components: (1) clinical assessment by the GP;(2) HF medication titration plan: (3) details of any further treatment action required;(4) HF medication titration problem-solving guide; (5) Heart Failure Helpline, which will be available 8am to 4pm Monday to Friday for further guidance with medication titration or enacting an action plan for the patient. The HF NP will be the first to respond to calls to the Helpline. If the case is out of the HF NP's scope of practice, or clinically complex, it will be escalated to a specialist HF cardiologist to action.

Participants will receive reminders (phone call or text message) to support their adherence in attending the scheduled GP appointments. The HF NP will give the first PATHFINDER Envelope directly to the patient during hospitalisation for the 1-week post-discharge GP follow-up and mail the envelopes for the 4-week and 3-month post-discharge GP follow-ups. The HF NP will also phone the patient 4 months after discharge. If the patient is not prescribed 50% of the target dose of HF medications at that point without clinical justification, an additional GP visit will be encouraged. If participants miss a scheduled GP follow-up they will be encouraged to visit their GP by the HF NP as soon as possible thereafter. Participants who are referred to a specialist HF service following their enrolment in the trial will continue in the trial consistent with intention to treat.

The role of the GP

Participants' GPs will be asked to complete the PATHFINDER Study Follow-up Forms at the 1week, 4 week and 3 month appointments. Each follow-up will involve documenting participants' current weight, heart rate, blood pressure and any HF symptoms. The form will also guide GPs in titrating HF medications as recommended by a cardiologist and in accordance with guidelines.[5] At the conclusion of the appointment, the GP will record the current dose or provide justification for not titrating the medication and return the form by fax or email to the HF NP. If the research team does not receive the form despite two reminder calls to the practice, HF medications will be collected by patient-report and cross-checked with medical records.

Outcomes

Primary outcome

The primary outcome will be the difference between groups in the proportion of patients receiving HF guideline-recommended treatment at six months after an index hospital admission for HF based on five quality metrics for HF management:

(1) Either prescribed at least 50% of the recommended dose for an ACEI/ARB/ARNI or documentation that such a dose was not tolerated or otherwise inappropriate for eligible patients;[30]

(2) Either prescribed at least 50% of the recommended dose for a beta-blocker or documentation that such a dose was not tolerated or otherwise inappropriate for eligible patients;[30]

(3) Prescribed a MRA at any dose for eligible patients;[5]

(4) Prescribed anticoagulation for eligible patients with atrial fibrillation;[5]

(5) Referral to an exercise training program or cardiac rehabilitation program.[5]

The criteria for adherence to the HF guideline-recommended treatment will be defined as participants receiving 5 out of 5 of the HF quality metrics.[31] Medications and dosage prescribed to participants will be based on documentation on the PATHFINDER Study Follow-up Form for the experimental group and by patient-report in the control group and cross-checked with electronic records or pharmacy medication profiles. Referral to cardiac rehabilitation programs will be measured by patient-reported participation and cross-checked with documentation in medical records. If one or more treatments is not indicated, participants will be assessed based on the number of HF quality metrics they are eligible to receive. The recommended dose is based on the target dose of Guideline-Directed Medical Therapies (GDMT) in the 2020 ACC/AHA clinical performance and quality measures for adults with HF.[30]

Secondary outcomes

The secondary endpoints related to HF guideline-recommended care will include the difference between groups in the proportion of eligible patients receiving the following guideline-advocated treatment:

i) ACEI/ARB/ARNI, beta-blocker, and MRA at the target dose, or maximum tolerated dose at six months;
ii) ACEI/ARB/ARNI, beta-blocker, and MRA at any dose at six months;
iii) At least 50% of the target dose or maximum tolerated dose of each of ACEI/ARB/ARNI, beta-blocker and MRA at six months;
iv) Anticoagulation if diagnosed with atrial fibrillation at six month;
v) Any dose of each of ACEI/ARB/ARNI, beta-blocker, MRA at 1 week, 4 weeks, 3 months and 6 months;
vi) At least 50% of the target dose of each of ACEI/ARB/ARNI, beta-blocker and MRA at 1 week, 4 weeks, 3 months and 6 months;
vii) Referral to an exercise training program or cardiac rehabilitation program by six months;
viii) Attendance at 16 sessions of an exercise training program or cardiac rehabilitation program at six months.

Additional outcomes will be:

i) Functional capacity measured by six-minute walk test distance;[32]
ii) Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function Short Form 4a;[33]
iii) Quality of life measured by the Kansas City Cardiomyopathy Questionnaire-Short Version (KCCQ12);[34]

iv) Depression symptoms measured by the Patient Health Questionnaire (PHQ-2);[35]
v) Self-care behaviour measured by the Self-Care of Heart Failure Index (SCHFI) v7.2;[36]
vi) Patients' medication adherence measured by the Morisky Medication Adherence Measure Scale (MMAS-8).[37]

The timeline for outcome collection is described in Table 1.

Resource use

Health care utilisation will include the number of visits to physicians, cardiovascular-related hospitalisation and HF-related hospitalisation, number of cardiovascular-related procedures, days of admission, and use of specialised care. Given the feasibility of obtaining health administrative data within the study time frame, we will adapt a validated patient cost questionnaire to obtain self-reported health care utilisation data[38] and this will be cross-checked with medical records. Whilst we recognise the potential for recall bias, there is evidence to suggest that this is a valid method of collecting data on healthcare resource utilization, especially when administrative data is not easily available.[39]

Safety assessment

An adverse event will be defined as any undesirable experience resulting in a participant's death, hospitalisation, prolongation of hospitalisation, or disability. All AEs will be recorded over the six month follow up period of the study. The research investigators will determine whether there was any AE occurrence by asking the participant and cross-checking with medical records.

Process measures

The Reach, Efficacy, Adoption, Implementation and Maintenance (RE-AIM) evaluation model[40] will be used to perform a process evaluation. Reach will be assessed using patient-level measures of participation. The recruitment rate, completion rate and reasons for exclusion and dropping out of the study will be determined. Efficacy will be assessed according to the effectiveness of the intervention on influencing GP practice i.e. the global adherence indicator (GAI-3).[41] GPs' satisfaction with the intervention will be measured by a survey administered at the conclusion of the 6 month follow-up period for a participant under their care [Appendix 3]. Adoption will be assessed at the participant and GP level. Participant adoption will be based on the proportion of patients visiting their GP at approximately 1 week, 4 weeks, 3 month post discharge and the proportion of participants attending at least one session of cardiac rehab training. Reasons for participants not visiting their GP and not attending cardiac rehabilitation will be explored. GP adoption will be assessed based on the proportion of GPs completing and returning the follow up forms at the 1 week, 4 week, and 3 month time-points and the usage of the helpline. Implementation will be assessed based on the extent that the GP delivers the intervention as intended. The proportion of GPs starting, increasing, decreasing, ceasing, and not changing ACEIs/ARBs/ARNIs, BBs, and MRAs will be measured at 1 week, 4 week, and 3 months. Reasons for lower dose or medication cessation at 3 months compared with the baseline will be examined. Maintenance will be assessed based on whether the titration of HF medication in primary care, at the levels achieved during the trial, is maintained at 6 months following the conclusion of the trial. [Table 2]

Table 2 RE-AIM framework of process evaluation

RE-AIM dimension	**Definition**	**Data sources**
Reach	The recruitment rate, completion rate and reasons for exclusion and dropping out of the study	Recruitment record; participant's check-in sheet

Efficacy	GAI-3; GP's satisfaction with the intervention arm	Patient-reported Medication; case report form; survey
Adoption	The proportion of patients visiting GP at 1 week, 4 week, 3month, reasons for not visiting GP; The proportion of GPs faxing back follow up form at 1 week, 4 week, 3 month; The proportion of patient participating in ≥ one session of cardiac rehab; reasons for not attending cardiac rehab; use of the helpline and information requested	PATHFINDER follow-up forms; case report form; field notes; electronic medical records; patient-reported
Implementation	The proportion of GP starting, increasing, decreasing, ceasing, and not changing ACEI/ARB/ARNI, BB, or MRA medication at 1 week, 4 week, and 3 months; reasons for lower dose or medication cessation at 3 month compared with the baseline	PATHFINDER follow-up forms; case report form; field notes; electronic medical records; patient-reported
Maintenance	The proportion of patients prescribed ACEI/ARB/ARNI, BB, or MRA at the same or higher dose, lower dose or ceased at 6 months compared with 3 month; reasons for lower dose and medication cessation	PATHFINDER follow-up forms; case report form; field notes; electronic medical records; patient-reported

RE-AIM, Reach, Efficacy-Adoption, Implementation and Maintenance; GAI-3, global adherence indicator; GP, general practitioner; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor neprilysin inhibitor; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; PATHFIDNER, **P**rimary care **A**dherence **T**o **H**eart **F**ailure guidelines **In D**iagnosis, **E**valuation & **R**outine management.

Data collection and Management

Six month follow-up assessments will be conducted in person where possible, however patients who live remotely from the hospital will be assessed via phone and return the questionnaires by mail. A follow-up six-minute walk test will not be performed in these participants. Participants who withdraw from the intervention protocol will be contacted for the six month follow-up assessment for primary, secondary and additional outcomes either in person or via phone (intention to treat). Data will be documented in case report forms and entered into a Research Electronic Data Capture (REDCap) database. Patient data will be deidentified and saved as a unique trial participant number to assure data confidentiality. Only authorised members of the researcher team will have access to the dataset.

Sample size

A recent Australian audit of HF management observed that 53 % of patients were prescribed an ACEI/ARB and beta-blocker at ≥50 % of the target dose.[7] Furthermore, the prescribing rate of MRAs and anticoagulants with atrial fibrillation was 38% and over 90% respectively.[7] Data from the GWTG-HF Registry showed that only 12% of patients with HFrEF were referred to CR at discharge, although additional patients may be referred subsequently.[43] It is likely that the proportion of patients treated with ≥50 % of the target doses of ACEIs/ARBs together with ≥50 % of the target doses of beta-blockers, receiving MRAs and cardiac rehabilitation referral by six months after discharge in combination will be even lower. Based on these assumptions we estimate that 20% of patients receive 5 out of 5 HF guideline-recommended treatments by six months after discharge in usual care. We

expect to observe an absolute 20% improvement in the intervention group (20% in the usual care group, 40% in the intervention group) 6 months after discharge. With 80% power (type I error=5%, two-sided test), we would require a total sample size of 182, increasing to 220, to account for a potential 20% loss to follow-up.

Statistics

The intention to treat principle will be applied, and patients will be analysed according to the group to which they are allocated. Descriptive summaries of patient clinical and selected outcome data will include means and standard deviations or medians and interquartile ranges for continuous data and frequency distributions for categorical data. Univariate group comparisons between groups will be performed using t tests or Mann-Whitney U tests for continuous data and Chi squared tests for categorical data. Primary adherence outcomes will be expressed as binary indicator variables. Proportional differences in adherence will be compared between groups at six-month post-discharge using Chi squared tests and modelled using logistic regression models. Models will be adjusted for relevant patient and clinical factors. Results will be summarised as odds ratios (OR) and 95% confidence intervals (CI). Secondary outcomes collected at baseline (during admission) and at six-month post-discharge will be modelled using generalised linear mixed models (GLMM), with appropriate link functions depending on data distributions, random subject effects and group-time interaction effects in order to compare differences between groups over time. All models will be adjusted for baseline and relevant patient and clinical factors. Model results will be summarised as estimated marginal mean differences and 95% CIs. Secondary outcome counts of health resource utilisation will be compared between groups using Poisson or negative binomial regression models. Model results will be summarised as estimated marginal mean differences and 95% CIs. Significance levels will be set at alpha=0.05 and Stata version 17.0 will be used for data analysis.

Patient and Public Involvement

Before designing the intervention, focus groups and interviews with patients with HF, clinicians and administrators in tertiary care and primary care were held to explore barriers and facilitators to post-discharge HF management. Patients were not involved in the recruitment to and conduct of the study. The findings of the study will be disseminated to study participants with a narrative summary. The burden of the intervention was not assessed by patients themselves. The research team also consulted the GP liaison officers of the two hospitals involved in the project to discuss the project methodology, including design of the PATHFINDER Study Follow-up Form.

DISCUSSION AND CONCLUSION

Effective management of HF in primary care practice remains challenging for many clinicians.[42] Despite the availability of evidence-based treatment guidelines, translating these into practice can be complicated by the clinical characteristics of many patients (including hypotension, bradycardia, renal impairment and hyperkalaemia) as well as socioeconomic and behavioural factors relevant to patients.[43-47] Limited access to specialist care,[48] general practitioners not aware of recent guideline-recommended therapies or contraindications to prescribing medications, nor the importance of achieving the target dose, and concerns about adverse effects all contribute to suboptimal HF treatment.[47 49] Moreover, effective systems to support care coordination are often lacking.[12 50] Accordingly, strategies to support general practice in the delivery of evidence-based HF management are required.

Hospital discharge planning plays a vital role in the transition of care from hospital to general practice.[51] This includes initiating a medication regimen that can be modified over time.[52 53] Following discharge, a structured medication titration plan can lead to greater responsibility for medication titration by primary care physicians,[54] with point-of-care reminders involving specific guidance having been found to improve medication prescription in accordance with guidelines.[55] However,

these studies were limited in their size or trial design, hence the need for a well conducted RCT. Furthermore, providing patients with self-care education during admission can further improve clinical outcomes,[56] and patients who schedule regular follow-up appointments have been found to experience fewer readmissions than those who do not.[56]

The PATHFINDER study will incorporate these aspects into a multifaceted intervention to support HF management in primary care. A strength of the PATHFINDER intervention will be that it will include components across multiple levels of the health system. The intervention will commence during the inpatient period, involving patient education and medication initiation. A HF NP will subsequently act as a health navigator for the patient, liaising between the patients GP and a cardiologist. Due to their advanced scope of practice, which includes prescribing and titrating medications, ordering and interpreting pathology and radiology tests and initiating referral to other health professionals,[5 28] NPs are well-credentialed to coordinate the management of patients with HF[57] and to support transitional care between the tertiary and primary health care sectors.[58 59] The NP will facilitate the Follow-up Forms and helpline, which will serve as a bridge between the primary and tertiary care sectors, providing clinical decision support and reinforcement of guideline-advocated treatment. Importantly, we anticipate the intervention will help formalise care goals through improved guideline adherence. Improved referral to and uptake of cardiac rehabilitation will provide stronger multidisciplinary support through ongoing patient education, exercise prescription and clinical surveillance.

There are several limitations to this trial. Firstly, due to the nature of the intervention, it will not be possible to blind either the patient, GP, or HF NP to group allocation. Second, because the HF NP will only be employed Monday to Friday, participants admitted to hospital later in the week may be discharged over the weekend before there is an opportunity to review, consent and undertake baseline assessments and self-management education. Third, COVID-19 may impact the opportunity for patients to attend the scheduled GP appointments at the proposed time or face to face, and it's unclear how virtual clinics will impact GPs willingness to titrate medication. Given that randomisation will occur at the participant level, there is a risk that contamination may occur, whereby the same GP might have a patient enrolled in the intervention and usual care arms of the study, but we anticipate this will occur very rarely.

In conclusion, this study will be a prospective, multi-centre, parallel-group, randomised controlled trial with blinded assessment of study outcomes to explore the effectiveness of a multifaceted intervention for guideline implementation in the GP practice. It will determine the feasibility of future large-scale clinical trials aiming to improve primary care physicians' adherence to HF guideline-advocated treatment.

Ethics and dissemination

Ethical approval has been obtained through the South Metropolitan Health Service (RGS3531) with reciprocal approval at Curtin University (HRE2020-0322).Written informed consent will be obtained from all the participants. The project will be conducted in adherence to the Australian National Health and Medical Research Council National Statement for Ethical Research. The current protocol version is version 3.1 dated 4 April 2022. Major modifications during the trial will require a formal amendment to the protocol. Results will be disseminated via peer-reviewed publications and conference presentations.

Acknowledgements We would like to acknowledge ethics committee for granting us permission to conduct the study. We would like to express our gratitude to physicians in Fiona Stanley Hospital, as well as Royal Perth Hospital for engaging participants to enrol. We would also like to thank patients, clinicians and administrators to participate in focus groups and interviews and thank study participants for their willingness to participate in this study.

Contributors AM and CR had the original idea for the study. LD, AM, TD and JG were involved in study design and protocol development. LD and AS contributed to the design of the statistical analysis approach. AM and GH are site PI engaged in providing a critical review of the manuscript. All authors read and approved the final manuscript.

Funding This work is funded by the Medical Research Future Fund (MRFF) Rapid Applied Research Translation (RART) Grants from the Western Australia Health Translation Network (WAHTN, grant number N/A). LD is funded by a postgraduate research scholarship funded by Curtin University. CMR is funded through a NHMRC Principal Research Fellowship (GNT 1136372).

Competing interests None declared.

Ethics approval The South Metropolitan Health Service Human Research Ethics Committee; reciprocal approval from the Curtin University Human Research Ethics Committee

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

ORCID IDs

Liying Dai http://orcid.org/0000-0002-7843-6344

Andrew Maiorana https://orcid.org/0000-0002-0681-1707

Christopher M Reid https://orcid.org/0000-0001-9173-3944

Graham Hillis https://orcid.org/0000-0003-2417-4673

Suzanne Robinson https://orcid.org/0000-0001-5703-6475

John J Atherton https://orcid.org/0000-0003-2271-578X

Angela Jacques https://orcid.org/0000-0002-0461-681X

References

1. Groenewegen A, Rutten FH, Mosterd A, et al. Epidemiology of heart failure. *European Journal of Heart Failure* 2020;22(8):1342-56. doi: 10.1002/ejhf.1858
2. Metra M, Teerlink JR. Heart failure. *Lancet* 2017;390(10106):1981-95. doi: 10.1016/s0140-6736(17)31071-1 [published Online First: 2017/05/04]
3. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Cardiac failure review* 2017;3(1):7-11. doi: http://dx.doi.org/10.15420/cfr.2016:25:2
4. Chan YK, Tuttle C, Ball J, et al. Current and projected burden of heart failure in the Australian adult population: a substantive but still ill-defined major health issue. *BMC Health Serv Res* 2016;16(1):501. doi: 10.1186/s12913-016-1748-0 [published Online First: 2016/09/23]
5. Atherton JJ, Sindone A, De Pasquale CG, et al. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the management of heart failure 2018. *Med J Aust* 2018;209(8):363-69. doi: 10.5694/mja18.00647 [published Online First: 2018/08/02]
6. Komajda M, Cowie MR, Tavazzi L, et al. Physicians' guideline adherence is associated with better prognosis in outpatients with heart failure with reduced ejection fraction: the QUALIFY international registry. *Eur J Heart Fail* 2017;19(11):1414-23. doi: 10.1002/ejhf.887 [published Online First: 2017/05/04]
7. Chin KL, Skiba M, Tonkin A, et al. The treatment gap in patients with chronic systolic heart failure: a systematic review of evidence-based prescribing in practice. *Heart Fail Rev* 2016;21(6):675-97. doi: 10.1007/s10741-016-9575-2 [published Online First: 2016/10/28]
8. Page K, Marwick TH, Lee R, et al. A systematic approach to chronic heart failure care: a consensus statement. *Medical Journal of Australia* 2014;201(3):146-50. doi: 10.5694/mja14.00032
9. Scott I, Jackson C. Chronic heart failure management in Australia -- time for general practice centred models of care? *Aust Fam Physician* 2013;42(5):343-6. [published Online First: 2013/06/20]
10. Weenink JW, van Lieshout J, Jung HP, et al. Patient Care Teams in treatment of diabetes and chronic heart failure in primary care: an observational networks study. *Implement Sci* 2011;6:66. doi: 10.1186/1748-5908-6-66 [published Online First: 2011/07/05]
11. Hirt MN, Muttardi A, Helms TM, et al. General practitioners' adherence to chronic heart failure guidelines regarding medication: the GP-HF study. *Clin Res Cardiol* 2016;105(5):441-50. doi: 10.1007/s00392-015-0939-8 [published Online First: 2015/11/11]
12. Smeets M, Van Roy S, Aertgeerts B, et al. Improving care for heart failure patients in primary care, GPs' perceptions: a qualitative evidence synthesis. *Bmj Open* 2016;6(11):12. doi: 10.1136/bmjopen-2016-013459
13. Calvin JE, Shanbhag S, Avery E, et al. Adherence to evidence-based guidelines for heart failure in physicians and their patients: lessons from the Heart Failure Adherence Retention Trial (HART). *Congest Heart Fail* 2012;18(2):73-8. doi: 10.1111/j.1751-7133.2011.00263.x [published Online First: 2012/03/22]
14. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *Jama* 1999;282(15):1458-65. doi: 10.1001/jama.282.15.1458 [published Online First: 1999/10/27]
15. Khunti K, Hearnshaw H, Baker R, et al. Heart failure in primary care: qualitative study of current management and perceived obstacles to evidence-based diagnosis and management by general practitioners. *Eur J Heart Fail* 2002;4(6):771-7. doi: 10.1016/s1388-9842(02)00119-8 [published Online First: 2002/11/28]

16. Verhestraeten C, Heggermont WA, Maris M. Clinical inertia in the treatment of heart failure: a major issue to tackle. *Heart Fail Rev* 2020 doi: 10.1007/s10741-020-09979-z [published Online First: 2020/06/01]
17. Aujoulat I, Jacquemin P, Rietzschel E, et al. Factors associated with clinical inertia: an integrative review. *Adv Med Educ Pract* 2014;5:141-7. doi: 10.2147/amep.S59022 [published Online First: 2014/05/29]
18. Giezeman M, Arne M, Theander K. Adherence to guidelines in patients with chronic heart failure in primary health care. *Scandinavian Journal of Primary Health Care* 2017;35(4):336-43. doi: 10.1080/02813432.2017.1397253
19. Cleland JG, Cohen-Solal A, Aguilar JC, et al. Management of heart failure in primary care (the IMPROVEMENT of Heart Failure Programme): an international survey. *Lancet* 2002;360(9346):1631-9. doi: 10.1016/s0140-6736(02)11601-1 [published Online First: 2002/11/30]
20. Huynh Q, Negishi K, De Pasquale C, et al. Effects of post-discharge management on rates of early re-admission and death after hospitalisation for heart failure. *Med J Aust* 2018;208(11):485-91. doi: 10.5694/mja17.00809 [published Online First: 2018/05/12]
21. Bero LA, Grilli R, Grimshaw JM, et al. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. *Bmj* 1998;317(7156):465-8. doi: 10.1136/bmj.317.7156.465 [published Online First: 1998/08/14]
22. Fonarow GC, Albert NM, Curtis AB, et al. Improving evidence-based care for heart failure in outpatient cardiology practices: primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). *Circulation* 2010;122(6):585-96. doi: 10.1161/circulationaha.109.934471 [published Online First: 2010/07/28]
23. Ellrodt AG, Fonarow GC, Schwamm LH, et al. Synthesizing lessons learned from get with the guidelines: the value of disease-based registries in improving quality and outcomes. *Circulation* 2013;128(22):2447-60. doi: 10.1161/01.cir.0000435779.48007.5c [published Online First: 20131028]
24. Heidenreich PA, Lewis WR, LaBresh KA, et al. Hospital performance recognition with the Get With The Guidelines Program and mortality for acute myocardial infarction and heart failure. *Am Heart J* 2009;158(4):546-53. doi: 10.1016/j.ahj.2009.07.031
25. Peters-Klimm F, Müller-Tasch T, Remppis A, et al. Improved guideline adherence to pharmacotherapy of chronic systolic heart failure in general practice--results from a cluster-randomized controlled trial of implementation of a clinical practice guideline. *J Eval Clin Pract* 2008;14(5):823-9. doi: 10.1111/j.1365-2753.2008.01060.x [published Online First: 2008/11/21]
26. Goff DC, Jr., Massing MW, Bertoni AG, et al. Enhancing quality of heart failure care in managed Medicare and Medicaid in North Carolina: results of the North Carolina Achieving Cardiac Excellence (NC ACE) Project. *Am Heart J* 2005;150(4):717-24. doi: 10.1016/j.ahj.2004.12.025 [published Online First: 2005/10/08]
27. Persson H, Erntell H, Eriksson B, et al. Improved pharmacological therapy of chronic heart failure in primary care: a randomized Study of NT-proBNP Guided Management of Heart Failure - SIGNAL-HF (Swedish Intervention study - Guidelines and NT-proBNP AnaLysis in Heart Failure). *European Journal of Heart Failure* 2010;12(12):1300-08. doi: 10.1093/eurjhf/hfq169
28. . https://www.nursingmidwiferyboard.gov.au/Codes-Guidelines-Statements/Professional-standards/registered-nurse-standards-for-practice.aspx Date accessed: 2 Dec 2021.
29. Chen SH, Boyd J, Randall S, et al. Association between community-based nurse practitioner support, self-care behaviour and quality of life in patients with chronic heart

failure. *Australian Journal of Advanced Nursing* 2021;38(3):25-32. doi: 10.37464/2020.383.147
30. Heidenreich PA, Fonarow GC, Breathett K, et al. 2020 ACC/AHA Clinical Performance and Quality Measures for Adults With Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol* 2020;76(21):2527-64. doi: 10.1016/j.jacc.2020.07.023 [published Online First: 2020/11/07]
31. Chow CK, Thiagalingam A, Santo K, et al. TEXT messages to improve MEDication adherence and Secondary prevention (TEXTMEDS) after acute coronary syndrome: a randomised clinical trial protocol. *BMJ Open* 2018;8(1):e019463. doi: 10.1136/bmjopen-2017-019463 [published Online First: 2018/01/29]
32. Rostagno C, Olivo G, Comeglio M, et al. Prognostic value of 6-minute walk corridor test in patients with mild to moderate heart failure: comparison with other methods of functional evaluation. *European Journal of Heart Failure* 2003;5(3):247-52. doi: 10.1016/s1388-9842(02)00244-1
33. DeWalt DA, Rothrock N, Yount S, et al. Evaluation of item candidates - The PROMIS qualitative item review. *Medical Care* 2007;45(5):S12-S21. doi: 10.1097/01.mlr.0000254567.79743.e2
34. Spertus JA, Jones PG. Development and Validation of a Short Version of the Kansas City Cardiomyopathy Questionnaire. *Circulation-Cardiovascular Quality and Outcomes* 2015;8(5):469-76. doi: 10.1161/circoutcomes.115.001958
35. Lowe B, Kroenke K, Grafe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *Journal of Psychosomatic Research* 2005;58(2):163-71. doi: 10.1016/j.jpsychores.2004.09.006
36. Barbaranelli C, Lee CS, Vellone E, et al. Dimensionality and Reliability of the Self-Care of Heart Failure Index Scales: Further Evidence From Confirmatory Factor Analysis. *Research in Nursing & Health* 2014;37(6):524-37. doi: 10.1002/nur.21623
37. Morisky DE, Ang A, Krousel-Wood M, et al. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. *Journal of Clinical Hypertension* 2008;10(5):348-54. doi: 10.1111/j.1751-7176.2008.07572.x
38. van den Brink M, van den Hout WB, Stiggelbout AM, et al. Self-reports of health-care utilization: diary or questionnaire? *Int J Technol Assess Health Care* 2005;21(3):298-304. doi: 10.1017/s0266462305050397
39. Leggett LE, Khadaroo RG, Holroyd-Leduc J, et al. Measuring Resource Utilization: A Systematic Review of Validated Self-Reported Questionnaires. *Medicine (Baltimore)* 2016;95(10):e2759. doi: 10.1097/md.0000000000002759
40. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health* 1999;89(9):1322-7. doi: 10.2105/ajph.89.9.1322 [published Online First: 1999/09/04]
41. Komajda M, Lapuerta P, Hermans N, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. *European Heart Journal* 2005;26(16):1653-59. doi: 10.1093/eurheartj/ehi251
42. Taylor CJ, Valenti L, Britt H, et al. Management of chronic heart failure in general practice in Australia. *Aust Fam Physician* 2016;45(11):734-39. [published Online First: 2016/11/03]
43. Komajda M, Anker SD, Cowie MR, et al. Physicians' adherence to guideline-recommended medications in heart failure with reduced ejection fraction: data from the QUALIFY global survey. *European Journal of Heart Failure* 2016;18(5):514-22. doi: 10.1002/ejhf.510

44. Crespo-Leiro MG, Segovia-Cubero J, Gonzalez-Costello J, et al. Adherence to the ESC Heart Failure Treatment Guidelines in Spain: ESC Heart Failure Long-term Registry. *Revista Espanola De Cardiologia* 2015;68(9):785-93. doi: 10.1016/j.rec.2015.03.008
45. Chang HY, Wang CC, Wei J, et al. Gap between guidelines and clinical practice in heart failure with reduced ejection fraction: Results from TSOC-HFrEF registry. *Journal of the Chinese Medical Association* 2017;80(12):750-57. doi: 10.1016/j.jcma.2017.04.011
46. Ouwerkerk W, Voors AA, Anker SD, et al. Determinants and clinical outcome of uptitration of ACE-inhibitors and beta-blockers in patients with heart failure: a prospective European study. *European Heart Journal* 2017;38(24):1883-+. doi: 10.1093/eurheartj/ehx026
47. Greene SJ, Tan X, Yeh YC, et al. Factors associated with non-use and sub-target dosing of medical therapy for heart failure with reduced ejection fraction. *Heart Fail Rev* 2021 doi: 10.1007/s10741-021-10077-x [published Online First: 2021/01/21]
48. Savarese G, Carrero JJ, Pitt B, et al. Factors associated with underuse of mineralocorticoid receptor antagonists in heart failure with reduced ejection fraction: an analysis of 11 215 patients from the Swedish Heart Failure Registry. *Eur J Heart Fail* 2018;20(9):1326-34. doi: 10.1002/ejhf.1182 [published Online First: 20180326]
49. Hirt MN, Muttardi A, Helms TM, et al. General practitioners' adherence to chronic heart failure guidelines regarding medication: the GP-HF study. *Clinical Research in Cardiology* 2016;105(5):441-50. doi: 10.1007/s00392-015-0939-8
50. Verhestraeten C, Heggermont WA, Maris M. Clinical inertia in the treatment of heart failure: a major issue to tackle. *Heart Fail Rev* 2021;26(6):1359-70. doi: 10.1007/s10741-020-09979-z [published Online First: 2020/06/01]
51. Rosano GMC, Moura B, Metra M, et al. Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2021;23(6):872-81. doi: 10.1002/ejhf.2206 [published Online First: 20210520]
52. Bitar S, Agrinier N, Alla F, et al. Adherence to ESC guideline-recommended medications over a 36-month follow-up period after hospitalization for heart failure: Results from the EPICAL2 cohort study. *Pharmacoepidemiol Drug Saf* 2019;28(11):1489-500. doi: 10.1002/pds.4868 [published Online First: 2019/07/25]
53. Rørth R, Fosbøl EL, Mogensen UM, et al. Evidence-Based Therapy and Its Association With Workforce Detachment After First Hospitalization for Heart Failure. *JACC Heart Fail* 2018;6(1):41-48. doi: 10.1016/j.jchf.2017.09.019 [published Online First: 2017/12/12]
54. Hickey A, Suna J, Marquart L, et al. Improving medication titration in heart failure by embedding a structured medication titration plan. *International Journal of Cardiology* 2016;224:99-106. doi: 10.1016/j.ijcard.2016.09.001
55. Shanbhag D, Graham ID, Harlos K, et al. Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review. *BMJ Open* 2018;8(3) doi: http://dx.doi.org/10.1136/bmjopen-2017-017765
56. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *European Heart Journal* 2016;37(27):2129-U130. doi: 10.1093/eurheartj/ehw128
57. Chen Y, Zhu L, Xu F, et al. Discharge planning for heart failure patients in a tertiary hospital in Shanghai: a best practice implementation project. *JBI Database System Rev Implement Rep* 2016;14(2):322-36. doi: 10.11124/jbisrir-2016-2510 [published Online First: 2016/08/19]
58. Vedel I, Khanassov V. Transitional Care for Patients With Congestive Heart Failure: A Systematic Review and Meta-Analysis. *Ann Fam Med* 2015;13(6):562-71. doi: 10.1370/afm.1844

59. Phillips CO, Singa RM, Rubin HR, et al. Complexity of program and clinical outcomes of heart failure disease management incorporating specialist nurse-led heart failure clinics. A meta-regression analysis. *Eur J Heart Fail* 2005;7(3):333-41. doi: 10.1016/j.ejheart.2005.01.011

HF, heart failure; NP, nurse practitioner; GP, general practitioner; PATHFINDER, Primary care Adherence To Heart Failure guidelines IN Diagnosis, Evaluation and Routine management
Figure 1. Study flow chart

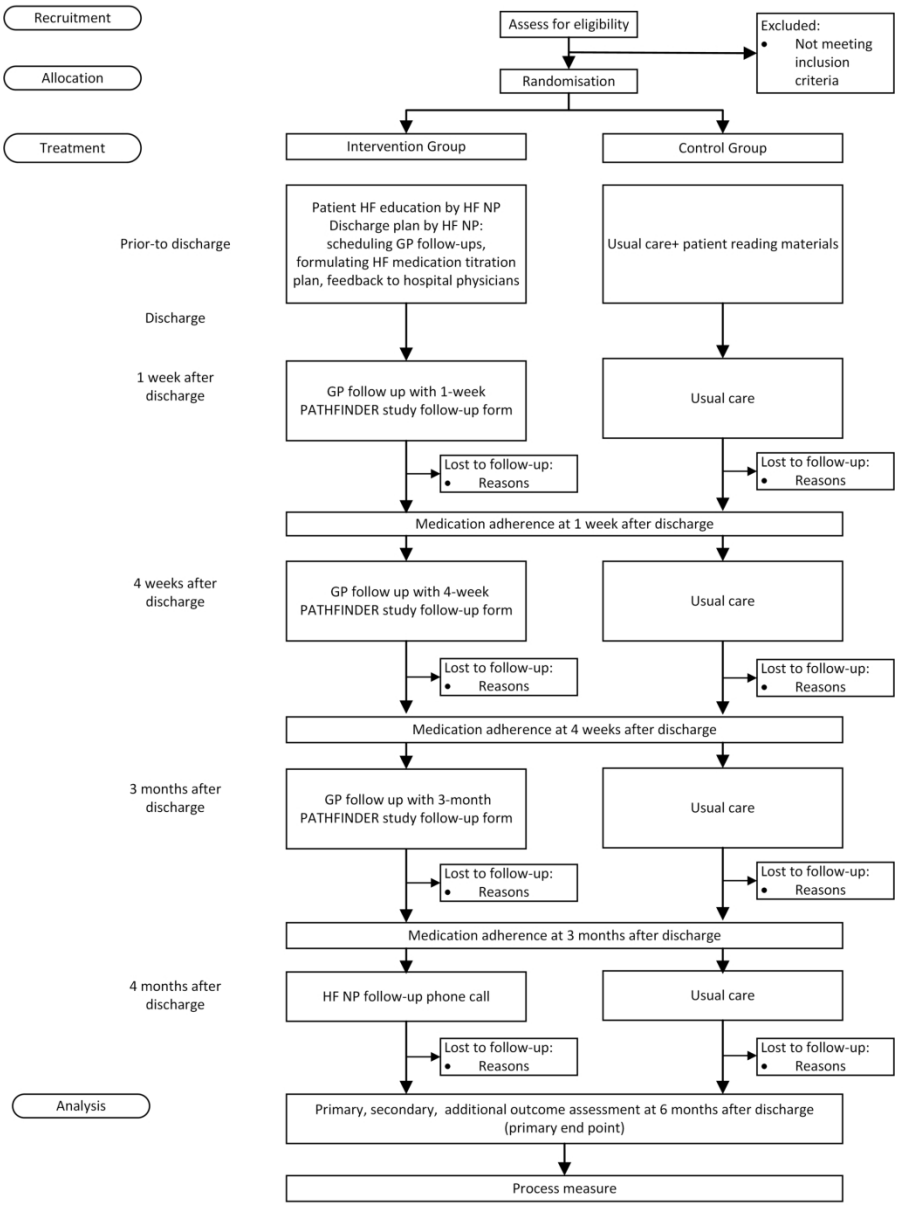

Figure 1. Study flow chart HF, heart failure; NP, nurse practitioner ; GP, general practitioner; PATHFINDER, Primary care Adherence To Heart Failure guidelines IN Diagnosis, Evaluation and Routine management

165x222mm (300 x 300 DPI)

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PARTICIPANT INFORMATION SHEET

Primary care adherence to heart failure guidelines in the diagnosis, evaluation & routine management (PATHFINDER) of heart failure Study.

Principal Investigator: Associate Professor Andrew Maiorana, Allied Health Dept. and Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital

Fiona Stanley Hospital, Royal Perth Hospital and Curtin University are undertaking research to evaluate and improve the level of adherence to published guidelines for the management of people who have been admitted to hospital with heart failure, a medical condition in which the heart doesn't pump as strongly as it should. The following information describes what will be involved should you decide to participate in this research project. Please read the information about this study carefully and ask any questions you might have. You may also wish to discuss the study with a relative or friend.

BACKGROUND

Heart failure is a common cause of hospital admissions in Australia. However, many of these admissions are preventable with better adherence to published guidelines about heart failure management, such as increased use of appropriate medication, and clear advice to patients on healthy lifestyle (including physical activity) and self-management.

WHAT IS THE PURPOSE OF THE STUDY?

The aim of this study is to evaluate the effects of providing a Heart Health Plan to patients who have been admitted to hospital with heart failure. The Heart Health Plan will involve providing specific information to patients and their nominated GP to support the management of heart failure. This research has been funded by WA Health Translation Network (Rapid Applied Research Translation Grant) through funds provide by the Medical Research Future Fund.

WHAT WILL HAPPEN?

Patients who have been admitted to hospital will be randomly allocated to receive the Heart Health Plan or medical management following standard processes (usual care).

If you agree to take part in the study, you will be asked to complete a walking test prior to leaving hospital. This test involves walking for six minutes as quickly as you're able to, up and down a hospital corridor. In some cases we may ask you to come back to the hospital shortly after you have been discharged to perform the test if you're not able to perform it while in hospital. At the time of each walking test we will also measure your height and weight.

You will also be asked to complete several questionnaires. These should take approximately 20 minutes to complete. We will ask you to repeat these questionnaires when you return for your repeat walking tests.

The questionnaires are:

i. Kansas City Cardiomyopathy Questionnaire-short version (KCCQ12) – questions about your heart condition and how it affects your life.
ii. PROMIS Physical Function Short Form 4a, Patient Health Questionnaire (PHQ-2) – questions about how you heart condition affects your ability to do manual chores and physical activity.
iii. Patient Health Questionnaire (PHQ-2) - two questions about how you heart condition has affected the way you feel over the past 2 weeks.
iv. Self-care of Heart Failure Index – questions about the behaviours you use to manage your heart condition.
v. Medication Compliance Questionnaire - questions about your use of medication.

This walking test and questionnaires will be repeated at Fiona Stanley Hospital following 6 months. You will be reimbursed for parking to attend these visits.

If you are randomised to receive the Heart Health Plan you will be given specific information before you leave hospital about self-management of heart failure by a specialist nurse (a Heart Failure Nurse Practitioner), including information about undertaking physical activity suited to your level of fitness. In addition, you will be provided with a form to take to your GP at 7 days, 28 days, 3 months following discharge from hospital to help adjust your medications. If after 3 months post-discharge, you are still having problems with your medications more follow-ups by your GP may be recommended. Your GP will also be given the phone number of heart failure helpline to contact in the event that they need to seek advice (the Nurse Practitioner will work with a Cardiologist in providing this advice).

Patients who are randomised to the usual care group, will receive all the standard care provided to patients following an admission with heart failure at Fiona Stanley Hospital, but won't receive the Heart Health Plan. You will be contacted by phone approximately 7 days, 28 days and 3 months after you leave hospital to confirm your heart medications, and the dose and frequency that you take them every day.

We are seeking your permission to review your hospital records to document your medical history and demographic information. If there is some relevant information missing we may need to ask you some questions directly. We also wish to monitor your health into the future, including hospital admissions and if you pass away, so are also seeking your permission to collect this information.

TIME COMMITMENT

The education that will be part of the Heart Health Plan will also take approximately 30 minutes.

The walking test and associated measurements will take less than 30 minutes and the questionnaires will take you around 20-30 minutes to complete. The walking test will be undertaken on two occasions; while you're still in hospital (or soon after you're discharged) and 6 months after you're discharged from hospital. People who live in country areas and are unable to attend the hospital will be mailed the questionnaires but won't need to repeat the walking tests. The questionnaires will be undertaken at hospital and 6 months after you're discharged. If you are randomised to the usual care group, each follow up phone calls will take about 5-10 minutes.

WHAT ARE THE POSSIBLE DISADVANTAGES AND RISK OF TAKING PART?

This is a low risk study. Some people may feel self-conscious about answering some of the questions in the questionnaires. However, your responses won't be available to anyone outside the research team and we will use a participant ID code rather than your name so your identity won't appear on your responses.

POSSIBLE BENEFITS

We cannot guarantee that you will receive any benefits from this research; however, we anticipate that findings from the study will help inform better management of patients with heart failure into the future.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Participation in this study is voluntary. You do not have to participate and, if you decide to participate, you can stop at any time without explanation. Your decision to participate or not, or to later withdraw from the study, will in no way affect your current or future care at Fiona Stanley Hospital.

WHAT ARE THE COSTS OF BEING IN THIS STUDY?

There are no financial costs associated with participating in the study. You will not be paid for participation, however expenses you incur associated with parking will be reimbursed.

PRIVACY AND CONFIDENTIALITY

The information gathered about you by the investigator or obtained during this study will be held by the investigator in strict confidence. All the people who handle your information will adhere to traditional standards of confidentiality and will also comply with the Privacy Act 1988. If the results of the trial are published in a medical journal, as is intended, no reader will be able to identify individual patients.

WHAT IF SOMETHING GOES WRONG?

In the event that you suffer an expected or unexpected side effect or medical accident during this study that arises from your participation, you will be offered all full and necessary treatment by Fiona Stanley Hospital.

WHAT HAPPENS WHEN THE RESEARCH PROJECT ENDS?

You will be provided with a narrative summary of the results by letter in 6 months when the research project is completed.

WHAT WILL HAPPEN TO INFORMATION ABOUT ME?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. 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. Only authorised researchers will have access to the data. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

The study data will be retained a minimum of seven years after completion of the project or publication. Disposal of research data and primary materials will be in accordance with the Information Management Policy of Curtin University.

CONTACT INFORMATION

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

If you have questions about this study, please contact Associate Professor Maiorana on (08) 61521692 or alternatively Zoe Dai on 0413349200.

This study has been submitted to the South Metropolitan Health Service Human Research Ethics and Governance Committee.

Reviewing HREC approving this research:

South Metropolitan Health Service Human Research Ethics Committee
Contact person: Ethics Coordinator Phone: 08 6152 2064.
Email: smhs.hrec@health.wa.gov.au

If you have any concerns about the conduct of the study or your rights as a research participant, please let us know. We will be very glad to answer your queries.
For matters relating to research at the site at which you are participating, the details of the local site complaints person are: Manager, South Metropolitan Health Service Research Support and Development Unit by email SMHS.RGO@health.wa.gov.au or phone 08 6152 3214.

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

CONSENT FORM

Primary care adherence to heart failure guidelines in the diagnosis, evaluation & routine management (PATHFINDER) of heart failure Study.

Principal Investigator: Associate Professor Andrew Maiorana, Allied Health Dept. and Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital

I, …….. agree to participate in the above study. I have read and understood the attached information sheet and I have retained a copy of the signed document. I have been given the opportunity to ask questions about the study by the Investigator. I understand that I may withdraw from the study at any time without affecting any future medical treatment, or the treatment of the condition which is the subject of the study.

Signed _____ **Date** _____

Signature _____ **Date** _____

of person obtaining consent

Name _____

of person obtaining consent

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

GPs address

Dear Dr.

Re: **P**rimary care **A**dherence **T**o **H**eart **F**ailure guidelines **IN D**iagnosis, **E**valuation and **R**outine management (PATHFINDER) Research Project

Patient details – name, DOB, address, URMN

The above patient under your care has recently consented to participate in the PATHFINDER Research Project being undertaken by Fiona Stanley Hospital (FSH) and has been allocated to the intervention group.

What is the PATHFINDER project? The aim of PATHFINDER is to support GPs in the delivery of guideline advocated management for patients with heart failure.

What is involved for patients? Patients hospitalised with heart failure will be encouraged to book 3 follow-up appointments with their GP over 3 months, as part of their routine care (reminders will be provided by the research team).

What is involved for GPs? At each appointment the patient will provide the GP with a form to help guide heart failure follow up care involving clinical assessment, medication titration, and further management actions. These appointments will be undertaken under the GP's normal consultation items and can be done by telehealth if required. Please fax the form back to FSH on the number below.

What support is provided for GPs? A Heart Failure Medication Titration Problem Solving Guide is provided on the rear of the follow-up form. The PATHFINDER Project also provides a helpline (**0480111493,** Mon – Fri, 8am-4pm) for GPs to contact if they are seeking guidance related to heart failure management. The helpline is staffed by a Specialist Heart Failure Nurse Practitioner supported by a Cardiologist from the Advanced Heart Failure Service at FSH.

We would be grateful if you could incorporate the attached PATHFINDER follow-up form into this appointment by completing the actions in yellow and return the form by fax to 61524888.

Thank you for your support of this important initiative.

Yours sincerely,

Dr Amit Shah, Cardiologist
Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital

Helpline: 0480111493 (Mon-Fri, 8am-4pm) Fax: 61524888

PATHFINDER

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PATHFINDER Study Follow-up Form

[Sticker]

GP Visit: 1 week Post Discharge

Please complete the sections in yellow and return this form to:
Fax: 61524888 or Email: fsh.ahfcts@health.wa.gov.au

See overleaf for Heart Failure Medication Titration Problem Solving guide.

Dial 0480111493 if you require further guidance with medication titration or enacting an action plan for this patient.

A. Assessment

Dry weight (at discharge)	Weight	HR	BP	Symptom:
kg	_____kg	_____bpm	_____mmHg	□ NA □ Dyspnoea □ Dizziness □ Fatigue Other _____.

B. Please titrate HF Medications

Drug Class	Medication Name	Current dose	Target dose#	Guideline-recommended medication titration plan	Dose after the current appointment
ACEI/ ARB/ ARNI*				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
Beta-blocker				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
MRA*				Commence with 25mg daily. Up-titrate in 4 to 8 weeks aiming for target dose for 50mg.	□ _____ mg □ OD □ BD □ Cease medication
Diuretics			Variable dose with no target	Adjust according to clinical assessment.	□ _____ mg □ OD □ BD □ Cease medication

#Target dose approved by PATHFINDER Cardiologist:

Name: ..... **Signature:** .....

* Kidney function test and electrolytes should be checked 1 week after commencing or titrating dose of ACEI/ARB/ARNI/MRA

C. Further actions

Is any further action required for this patient at this time?

☐ No further action needed

☐ GP review within a week

☐ Refer to Emergency Department

☐ Refer to a Cardiologist

☐ Refer to Allied Health Professional (i.e. Chronic Disease Management Plan)

☐ Other: _____.

GP Name: ..... **Signature:** ..... **Date:** .....

PATHFINDER

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

Heart Failure Medication Titration Problem Solving Guide

NSAIDS or COX-2 inhibitors are contraindicated in patients with heart failure. Avoid negatively inotropic calcium channel blockers (verapamil, diltiazem) in patients with heart failure with reduced ejection fraction (HFrEF).

Hypotension

- **Asymptomatic hypotension** does not usually require any change in therapy (systolic BP 90–100 mmHg)
- **Symptomatic hypotension** (dizziness, light-headedness and/or confusion):

I. Stop or reduce calcium - channel blockers and/or other vasodilators unless essential e.g. for angina

II. Consider reducing diuretic dose if there are no signs or symptoms of congestion

III. Temporarily reduce ACEI / ARB / ARNI or beta-blocker dose if above measures do not work

IV. Review patient as clinically appropriate within one week and seek specialist advice if the above measures do not work

Severe symptomatic hypotension or shock requires immediate referral to an emergency department

Worsening renal function

- ACEI /ARB are generally well tolerated even in patients with renal impairment (eGFR less than 30mL/min). Use ARNI with caution in patients with eGFR less than 30mL/min.
- Heart failure patients are more vulnerable to acute renal failure following a destabilising event such as a dehydrating illness or over-diuresis or addition of nephrotoxic medications.
  NB. Advise patients experiencing such an event to seek urgent medical attention and to stop the ACEI / ARB / ARNI until clinically reviewed and blood chemistry is checked.
- Some rise in urea, creatinine and serum K+ is expected after commencing an ACEI / ARB / ARNI. Blood chemistry must be checked one week after commencing or titrating dose and monitored closely there after to ensure kidney function is not worsening.
- An eGFR decrease of up to 30% is acceptable provided it stabilises within 2 weeks. Check serum K+, creatinine and urea within 48 hours if required.
- If the eGFR declines more than 30%, the patient should be reviewed urgently for clinical assessment of volume status and review of nephrotoxic medications. Seek specialist advice regarding the safety of continuing therapy.

Caution: eGFR may over estimate renal function in low body weight individuals and does not reflect accurate renal function in individuals with fluctuating creatinine levels.

Hyperkalaemia

Careful serum K+ monitoring is required with ACEI / ARB / ARNI and MRA. Urgently check serum K+, creatinine and urea if patient is dehydrated or septic. If serum K+ rises to:

I. 5.0–5.5 mmol/L, review and reduce K+ supplements or retaining agents (e.g. amiloride, spironolactone, eplerenone)

II. 5.6–5.9 mmol/L, cease all K+ supplements or retaining agents

III. 6 mmol/L or greater, immediately seek specialist advice

Bradycardia

- Where heart rate is less than 50 beats per minute, and the patient is on a beta-blocker, review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist; and arrange ECG to exclude heart block
- Consider reduction of beta-blocker where there is marked fatigue or symptomatic bradycardia

Congestion or peripheral oedema

Suggested actions when congestion or peripheral oedema is worsening:

- Increase the diuretic dose and then consider halving the dose of beta-blocker
- Liaise with the heart failure service and review the patient daily or weekly (as appropriate)
- Seek specialist advice if symptoms do not improve; and, if there is severe deterioration, refer patient to an emergency department immediately.

Angioedema and cough

I. Angioedema, although rare, can occur at any time when using ACEI / ARB / ARNI. Actions include:

- Stop ACEI / ARB / ARNI immediately
- Seek specialist advice where angioedema occurs with an ACEI before trialling ARB due to possible cross-sensitivity
- Avoid ARNI where angioedema is due to ACEI / ARB

II. Cough is common in patients with heart failure. Actions include:

- Exclude pulmonary oedema as a cause if cough is new or worsening
- Consider if cough is caused by ACEI or other drugs and only discontinue drug if cough is not tolerable
- Consider substituting ACEI with an ARB if the cough is troublesome or interferes with sleep

Reference: Qld Health HF Medication Titration Plan, https://www.health.qld.gov.au/__data/assets/pdf_file/0018/428121/Medn_Titration.pdf (Last accessed date: 04-Feb-2021)

The current Australian Heart Failure Management Guidelines are available at:
https://www.heartlungcirc.org/article/S1443-9506(18)31777-3/fulltext

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PATHFINDER Study Follow-up Form

[Sticker]

GP Visit: 4 week Post Discharge

Please complete the sections in yellow and return this form to:
Fax: 61524888 or Email: fsh.ahfcts@health.wa.gov.au

See overleaf for Heart Failure Medication Titration Problem Solving guide.

Dial 0480111493 if you require further guidance with medication titration or enacting an action plan for this patient.

D. Assessment

Dry weight (at discharge) _____kg	Weight _____kg	HR _____bpm	BP _____mmHg	Symptom: □ NA □ Dyspnoea □ Dizziness □ Fatigue Other _____.

E. Please titrate HF Medications

Drug Class	Medication Name	Current dose	Target dose#	Guideline-recommended medication titration plan	Dose after the current appointment
ACEI/ ARB/ ARNI*				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
Beta-blocker				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
MRA*				Commence with 25mg daily. Up-titrate in 4 to 8 weeks aiming for target dose for 50mg.	□ _____ mg □ OD □ BD □ Cease medication
Diuretics			Variable dose with no target	Adjust according to clinical assessment.	□ _____ mg □ OD □ BD □ Cease medication

#Target dose approved by PATHFINDER Cardiologist:

Name: ..... **Signature:** .....

* Kidney function test and electrolytes to be checked 1 week after commencing or titrating dose of ACEI/ARB/ARNI/MRA

F. Further actions

Is any further action required for this patient at this time?

☐ No further action needed

☐ GP Review within a week

☐ Refer to Emergency department

☐ Refer to a Cardiologist

☐ Refer to Allied Health Professional (i.e. Chronic Disease Management Plan)

☐ Other: _____.

GP Name: ..... **Signature:** ..... **Date:** .....

PATHFINDER

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

Heart Failure Medication Titration Problem Solving Guide

NSAIDS or COX-2 inhibitors are contraindicated in patients with heart failure. Avoid negatively inotropic calcium channel blockers (verapamil, diltiazem) in patients with heart failure with reduced ejection fraction (HFrEF).

Hypotension

- **Asymptomatic hypotension** does not usually require any change in therapy (systolic BP 90–100 mmHg)
- **Symptomatic hypotension** (dizziness, light-headedness and/or confusion):

I. Stop or reduce calcium - channel blockers and/or other vasodilators unless essential e.g. for angina

II. Consider reducing diuretic dose if there are no signs or symptoms of congestion

III. Temporarily reduce ACEI / ARB / ARNI or beta-blocker dose if above measures do not work

IV. Review patient as clinically appropriate within one week and seek specialist advice if the above measures do not work

Severe symptomatic hypotension or shock requires immediate referral to an emergency department

Worsening renal function

- ACEI /ARB are generally well tolerated even in patients with renal impairment (eGFR less than 30mL/min). Use ARNI with caution in patients with eGFR less than 30mL/min.
- Heart failure patients are more vulnerable to acute renal failure following a destabilising event such as a dehydrating illness or over-diuresis or addition of nephrotoxic medications.
  NB. Advise patients experiencing such an event to seek urgent medical attention and to stop the ACEI / ARB / ARNI until clinically reviewed and blood chemistry is checked.
- Some rise in urea, creatinine and serum K+ is expected after commencing an ACEI / ARB / ARNI. Blood chemistry must be checked one week after commencing or titrating dose and monitored closely there after to ensure kidney function is not worsening.
- An eGFR decrease of up to 30% is acceptable provided it stabilises within 2 weeks. Check serum K+, creatinine and urea within 48 hours if required.
- If the eGFR declines more than 30%, the patient should be reviewed urgently for clinical assessment of volume status and review of nephrotoxic medications. Seek specialist advice regarding the safety of continuing therapy.

Caution: eGFR may over estimate renal function in low body weight individuals and does not reflect accurate renal function in individuals with fluctuating creatinine levels.

Hyperkalaemia

Careful serum K+ monitoring is required with ACEI / ARB / ARNI and MRA. Urgently check serum K+, creatinine and urea if patient is dehydrated or septic. If serum K+ rises to:

I. 5.0–5.5 mmol/L, review and reduce K+ supplements or retaining agents (e.g. amiloride, spironolactone, eplerenone)

II. 5.6–5.9 mmol/L, cease all K+ supplements or retaining agents

III. 6 mmol/L or greater, immediately seek specialist advice

Bradycardia

- Where heart rate is less than 50 beats per minute, and the patient is on a beta-blocker, review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist; and arrange ECG to exclude heart block
- Consider reduction of beta-blocker where there is marked fatigue or symptomatic bradycardia

Congestion or peripheral oedema

Suggested actions when congestion or peripheral oedema is worsening:

- Increase the diuretic dose and then consider halving the dose of beta-blocker
- Liaise with the heart failure service and review the patient daily or weekly (as appropriate)
- Seek specialist advice if symptoms do not improve; and, if there is severe deterioration, refer patient to an emergency department immediately.

Angioedema and cough

I. Angioedema, although rare, can occur at any time when using ACEI / ARB / ARNI. Actions include:

- Stop ACEI / ARB / ARNI immediately
- Seek specialist advice where angioedema occurs with an ACEI before trialling ARB due to possible cross-sensitivity
- Avoid ARNI where angioedema is due to ACEI / ARB

II. Cough is common in patients with heart failure. Actions include:

- Exclude pulmonary oedema as a cause if cough is new or worsening
- Consider if cough is caused by ACEI or other drugs and only discontinue drug if cough is not tolerable
- Consider substituting ACEI with an ARB if the cough is troublesome or interferes with sleep

Reference: Qld Health HF Medication Titration Plan, https://www.health.qld.gov.au/__data/assets/pdf_file/0018/428121/Medn_Titration.pdf (Last accessed date: 04-Feb-2021).

The current Australian Heart Failure Management Guidelines are available at:
https://www.heartlungcirc.org/article/S1443-9506(18)31777-3/fulltext

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PATHFINDER Study Follow-up Form

[Sticker]

GP Visit: 3 month Post Discharge

Please complete the sections in yellow and return this form to:
Fax: 61524888 or Email: fsh.ahfcts@health.wa.gov.au

See overleaf for Heart Failure Medication Titration Problem Solving guide.

Dial 0480111493 if you require further guidance with medication titration or enacting an action plan for this patient.

G. Assessment

Dry weight (at discharge) _____kg	Weight _____kg	HR _____bpm	BP _____mmHg	Symptom: □ NA □ Dyspnoea □ Dizziness □ Fatigue Other _____.

H. Please titrate HF Medications

Drug Class	Medication Name	Current dose	Target dose#	Dose recommended by PATHFINDER cardiologist#	Dose after the current appointment
ACEI/ ARB/ ARNI*					□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
Beta-blocker					□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
MRA*					□ _____ mg □ OD □ BD □ Cease medication
Diuretics			Variable dose with no target	Adjust according to clinical assessment.	□ _____ mg □ OD □ BD □ Cease medication

 # Target dose and recommended dose approved by PATHFINDER Cardiologist:

Name: ..... **Signature:** .....

* Kidney function test and electrolytes to be checked 1 week after commencing or titrating dose of ACEI/ARB/ARNI/MRA

I. Further actions

Is any further action required for this patient at this time?

☐ No further action needed

☐ GP Review within a week

☐ Refer to Emergency department

☐ Refer to a Cardiologist

☐ Refer to Allied Health Professional (i.e. Chronic Disease Management Plan)

☐ Other: _____.

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

Heart Failure Medication Titration Problem Solving Guide

NSAIDS or COX-2 inhibitors are contraindicated in patients with heart failure. Avoid negatively inotropic calcium channel blockers (verapamil, diltiazem) in patients with heart failure with reduced ejection fraction (HFrEF).

Hypotension

- **Asymptomatic hypotension** does not usually require any change in therapy (systolic BP 90–100 mmHg)
- **Symptomatic hypotension** (dizziness, light-headedness and/or confusion):

I. Stop or reduce calcium - channel blockers and/or other vasodilators unless essential e.g. for angina

II. Consider reducing diuretic dose if there are no signs or symptoms of congestion

III. Temporarily reduce ACEI / ARB / ARNI or beta-blocker dose if above measures do not work

IV. Review patient as clinically appropriate within one week and seek specialist advice if the above measures do not work

Severe symptomatic hypotension or shock requires immediate referral to an emergency department

Worsening renal function

- ACEI /ARB are generally well tolerated even in patients with renal impairment (eGFR less than 30mL/min). Use ARNI with caution in patients with eGFR less than 30mL/min.
- Heart failure patients are more vulnerable to acute renal failure following a destabilising event such as a dehydrating illness or over-diuresis or addition of nephrotoxic medications.
  NB. Advise patients experiencing such an event to seek urgent medical attention and to stop the ACEI / ARB / ARNI until clinically reviewed and blood chemistry is checked.
- Some rise in urea, creatinine and serum K+ is expected after commencing an ACEI / ARB / ARNI. Blood chemistry must be checked one week after commencing or titrating dose and monitored closely there after to ensure kidney function is not worsening.
- An eGFR decrease of up to 30% is acceptable provided it stabilises within 2 weeks. Check serum K+, creatinine and urea within 48 hours if required.
- If the eGFR declines more than 30%, the patient should be reviewed urgently for clinical assessment of volume status and review of nephrotoxic medications. Seek specialist advice regarding the safety of continuing therapy.

Caution: eGFR may over estimate renal function in low body weight individuals and does not reflect accurate renal function in individuals with fluctuating creatinine levels.

Hyperkalaemia

Careful serum K+ monitoring is required with ACEI / ARB / ARNI and MRA. Urgently check serum K+, creatinine and urea if patient is dehydrated or septic. If serum K+ rises to:

I. 5.0–5.5 mmol/L, review and reduce K+ supplements or retaining agents (e.g. amiloride, spironolactone, eplerenone)

II. 5.6–5.9 mmol/L, cease all K+ supplements or retaining agents

III. 6 mmol/L or greater, immediately seek specialist advice

Bradycardia

- Where heart rate is less than 50 beats per minute, and the patient is on a beta-blocker, review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist; and arrange ECG to exclude heart block
- Consider reduction of beta-blocker where there is marked fatigue or symptomatic bradycardia

Congestion or peripheral oedema

Suggested actions when congestion or peripheral oedema is worsening:

- Increase the diuretic dose and then consider halving the dose of beta-blocker
- Liaise with the heart failure service and review the patient daily or weekly (as appropriate)
- Seek specialist advice if symptoms do not improve; and, if there is severe deterioration, refer patient to an emergency department immediately.

Angioedema and cough

I. Angioedema, although rare, can occur at any time when using ACEI / ARB / ARNI. Actions include:

- Stop ACEI / ARB / ARNI immediately
- Seek specialist advice where angioedema occurs with an ACEI before trialling ARB due to possible cross-sensitivity
- Avoid ARNI where angioedema is due to ACEI / ARB

II. Cough is common in patients with heart failure. Actions include:

- Exclude pulmonary oedema as a cause if cough is new or worsening
- Consider if cough is caused by ACEI or other drugs and only discontinue drug if cough is not tolerable
- Consider substituting ACEI with an ARB if the cough is troublesome or interferes with sleep

Reference: Qld Health HF Medication Titration Plan, https://www.health.qld.gov.au/__data/assets/pdf_file/0018/428121/Medn_Titration.pdf (Last accessed date: 04-Feb-2021)

The current Australian Heart Failure Management Guidelines are available at:
https://www.heartlungcirc.org/article/S1443-9506(18)31777-3/fulltext

Please return the form by fax to 61524888.

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet	2

		registered, name of intended registry	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	11
Funding	#4	Sources and types of financial, material, and other support	11
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 11
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a, no sponsor
Roles and responsibilities: sponsor and funder	#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	n/a, no sponsor
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data	n/a

		management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
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	2,3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3
Objectives	#7	Specific objectives or hypotheses	3
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, non-inferiority, exploratory)	3
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community	3

		clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	
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)	5
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5,6
Interventions: modifications	#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)	6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	6
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5,6
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric	6-8

		(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	
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)	3,4
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	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	3
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers),	5

generation		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	
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	5
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	5
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a, open-blinded to participants and the practitioner delivering the intervention
Methods: Data collection,			

management, and analysis			
Data collection plan	#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	6,9
Data collection plan: retention	#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	9
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	9
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where	9

		other details of the statistical analysis plan can be found, if not in the protocol	
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	n/a
Statistics: analysis population and missing data	#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)	9
Methods: **Monitoring**			
Data monitoring: formal committee	#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	n/a, open-blinded, small sample size, intervention component is evidence-based and not invasive, short study duration
Data monitoring: interim analysis	#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	n/a, open-blinded, small sample size, intervention component is evidence-based and not invasive, short

			study duration
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	7
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a, audit by the ethic committee or governance
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11
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)	11
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological	n/a

		specimens in ancillary studies, if 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	9
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	11
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9
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	n/a
Dissemination policy: trial results	#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	11
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a, no plan for use of professional writers

Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Reference to appendix
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	n/a

BMJ Open

Primary care Adherence To Heart Failure guidelines In Diagnosis, Evaluation & Routine management (PATHFINDER): a randomised controlled trial protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-063656.R1
Article Type:	Protocol
Date Submitted by the Author:	28-Dec-2022
Complete List of Authors:	Dai, Liying; Curtin University, School of Allied Health Dorje, Tashi; Mount Hospital, Department of Cardiology Gootjes, Jan ; WA Cardiology Shah, Amit; Fiona Stanley Hospital, Department of Cardiology Dembo, Lawrence ; Fiona Stanley Hospital, Department of Cardiology Rankin, Jamie ; Fiona Stanley Hospital, Department of Cardiology Hillis, Graham; Royal Perth Hospital, Department of Cardiology ; The University of Western Australia, Medical School Robinson, Suzanne; Curtin University, School of Population Health Atherton, John ; Royal Brisbane and Women's Hospital, Department of Cardiology; The University of Queensland, Faculty of Medicine Jacques, Angela; Curtin University, Curtin School of Allied Health Reid, Christopher; Curtin University, School of Population Health Maiorana, Andrew; Curtin University, School of Allied Health; Fiona Stanley Hospital, Department of Allied Health
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, PRIMARY CARE, Clinical trials < THERAPEUTICS

Title page

Primary care **A**dherence **T**o **H**eart **F**ailure guidelines **In** **D**iagnosis, **E**valuation & **R**outine management (PATHFINDER): a randomised controlled trial protocol

Word count: 4280

Corresponding author:
Andrew Maiorana, Curtin School of Allied Health, Kent Street, Bentley, Western Australia, 6102, Australia and Allied Health Department, Fiona Stanley Hospital, Perth, Australia A.Maiorana@curtin.edu.au

All contributing authors (a name, email, institution):
Liying Dai, liying.dai@postgrad.curtin.edu.au, Curtin School of Allied Health, Curtin University, Perth, Australia;

Dr Tashi Dorje, woshiyak@gmail.com , Department of Cardiology, Mount Hospital, Perth, Australia;

Jan Gootjes , jang@wacardiology.com.au, WA Cardiology , Perth, Australia;

Dr Amit Shah, Amit.Shah@health.wa.gov.au , Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital, Perth, Australia;

Dr Lawrence Dembo, Lawrence.Dembo@health.wa.gov.au , Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital, Perth, Australia;

Dr Jamie Rankin, James.Rankin@health.wa.gov.au , Department of Cardiology, Fiona Stanley Hospital, Perth, Australia;

Prof Graham S. Hillis, Graham.Hillis@health.wa.gov.au , Department of Cardiology, Royal Perth Hospital, and Medical School, University of Western Australia, Perth, Australia;

Prof Suzanne Robinson, Suzanne.robinson@curtin.edu.au School of Population Health, Curtin University, Perth, Australia;

Prof John J Atherton, John_Atherton@health.qld.gov.au , Department of Cardiology, Royal Brisbane and Women's Hospital and Faculty of Medicine, University of Queensland, Brisbane, Australia;

Dr Angela Jacques, angela.jacques@curtin.edu.au, Curtin School of Allied Health, Curtin University, Perth, Australia;

Prof Christopher M Reid, christopher.reid@curtin.edu.au, School of Population Health, Curtin University, Perth, Australia;

Prof Andrew Maiorana, A.Maiorana@curtin.edu.au , Curtin School of Allied Health, Curtin University, Perth, Australia and Department of Allied Health, Fiona Stanley Hospital, Perth, Australia.

Keywords: heart failure with reduced ejection fraction, guideline adherence, primary care

ABSTRACT

Introduction
General practitioners (GPs) routinely provide care for patients with heart failure (HF), however adherence to management guidelines, including titrating medication to optimal dose, can be challenging in this setting. This study will evaluate the effectiveness of a multifaceted intervention to support adherence to HF management guidelines in primary care.
Methods and analysis
We will undertake a multi-centre, parallel-group, randomised controlled trial of 200 participants with HF with reduced ejection fraction. Participants will be recruited during a hospital admission due to HF. Following hospital discharge, the intervention group will have follow-up with their GP scheduled at 1week, 4 weeks and 3 months with the provision of a medication titration plan approved by a specialist HF cardiologist. The control group will receive usual care. The primary endpoint, assessed at 6 months, will be the difference between groups in the proportion of participants being prescribed five guideline-recommended treatments; i) ACEI/ARB/ARNI at least 50% of target dose, ii) beta blocker at least 50% of target dose, iii) mineralocorticoid receptor antagonist at any dose, iv) anticoagulation for patients diagnosed with atrial fibrillation, iv) referral to cardiac rehabilitation. Secondary outcomes will include functional capacity (six-minute walk test); quality of life (Kansas City Cardiomyopathy Questionnaire); depressive symptoms (Patient Health Questionnaire-2); self-care behaviour (Self-Care of Heart Failure Index). Resource utilisation will also be assessed.
Ethics and dissemination Ethical approval was granted by the South Metropolitan Health Service Ethics Committee (RGS3531), reciprocal approval at Curtin University (HRE2020-0322). Results will be disseminated via peer-reviewed publications and conferences.
Trial registration number ACTRN12620001069943, prospectively registered.

Strengths and limitations of this study

- This study evaluates the effectiveness of a novel multifaceted intervention (involving pre- and post-hospital discharge components) to support HF guideline adherence in primary care.
- The intervention involves a model whereby GPs are responsible for enacting guideline advocated care, with prompts and guidance through hospital-based support.
- The model provides an opportunity for experiential learning that can be applied to the management of other patients with HF under the GPs care.
- The intervention is highly translatable to routine practice.
- The study will be conducted in a single state health jurisdiction and may not translate to other jurisdictions.

Introduction

Heart failure (HF) is a complex condition affecting over 60 million people worldwide and associated with high mortality and hospitalisation rates,[1 2] placing a heavy burden on patients and healthcare systems.[3] In Australia, the prevalence of HF is estimated to be 1% to 2%, resulting in hospitalisations costing approximately $2.7 billion annually.[4] Due to the ageing population, and improved treatment of acute cardiovascular events, the prevalence of HF is expected to increase over the next decade.[2]

Guideline-advocated pharmacotherapy and non-pharmacological treatment, such as cardiac rehabilitation (CR), are core components for the effective treatment of patients with HF with reduced ejection fraction (HFrEF) to improve clinical outcomes, functional capacity, and quality of life.[5 6]

However, despite these established benefits, guideline adherence is often suboptimal.[7-9] This is especially pertinent in primary care.[10] General practitioners (GPs) play an essential role in managing patients with HF;[11 12] patients can be holistically monitored, cared for by the same team members, and reviewed regularly.[13] However, despite progress in the adoption of guideline-advocated HF treatment in primary care,[14] barriers remain for the delivery of best-practice management[15] at the patient[16], provider[17 18] and system-level.[19 20] For example, HF medication titration is a well-documented challenge in general practice,[15 21] resulting in HF medications often not being titrated to the target dose.[14 22] Compounding this issue is that access and referral of patients to cardiac rehabilitation and community-based HF programs, which support the role of GPs in the management and surveillance of patients with HF, is not ubiquitous.[12 23]

Multifaceted interventions with two or more combined strategies have been found to be more effective than isolated processes for instigating changes in practice among health providers.[24] In outpatient cardiology practice, the *Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting* (IMPROVE-HF) study, which included clinical decision support tools and chart audits with feedback, and the *Get With The Guidelines-Heart Failure* (GWTG-HF) program which provided education, webinars, and quality improvement conferences to support clinical decision making, were both associated with increased use of guideline-recommended therapies.[25-27]. However, the limited research which has reported the effectiveness of multifaceted interventions to support guideline-advocated management of HF in primary care, have been less successful. Neither the combined strategies of an educational train-the-trainer course with a pharmacotherapy feedback[28] nor guideline summary dissemination, performance audit with feedback, patient-specific chart reminders, and patient activation mailings[29] resulted in improvement in the prescription of angiotensin converting enzyme inhibitors (ACEIs) at any dose. In the *Swedish Intervention study, Guideline and NT-pro-BNP analysis in Heart Failure* (SIGNAL-HF), GPs received an education program and applied N-terminal pro-B-type natriuretic peptide (NT-pro-BNP)-guided therapy, but there were no statistically significant dose increases of ACEIs/angiotensin receptor blockers (ARBs) or beta-blockers (BBs) between the intervention and control groups at 9-month follow-up.[30]

In Australia, Nurse Practitioners (NP) have advanced scope of practice which includes medication titration and ordering blood tests in response to changing clinical status.[31] Accordingly, they are well credentialed to apply case management for patients with HF. We have recently reported that a NP -led HF clinic can improve self-care behaviour and quality of life, and reduce hospital admissions,[32] highlighting the efficacy of heart failure models of care involving NPs.

We propose a multifaceted intervention to improve the provision of guideline-advocated management of HFrEF in primary care. The intervention will be facilitated by a Nurse Practitioner specializing in HF management, who will provide care support pre- and post-discharge. The study's primary objective is to evaluate the effectiveness of the multifaceted intervention for improving **P**rimary care **A**dherence **T**o **H**eart **F**ailure guidelines **In D**iagnosis, **E**valuation & **R**outine management (PATHFINDER).

METHOD

Study design

This will be a prospective, multi-centre, parallel-group, randomised controlled trial with blinded assessment of study outcomes conducted between February 2021 and September 2022. Two hundred eligible patients will be randomly assigned to either the intervention or a usual care control group at a 1:1 ratio. The intervention group will receive multifaceted support involving pre- and post-hospital discharge components. Pre-discharge elements of the PATHFINDER intervention will include HF self-management education, the provision of a discharge plan that includes scheduled GP follow-up appointments, cardiac rehabilitation referral, and feedback to the supervising hospital physician. Post-discharge, the intervention will involve letters to participants to remind them to book a GP appointment at 1 week, 4 weeks and 3 months, for review of their HF management. Prior to each

appointment, the participant will be provided with a HF medication titration plan, approved by a cardiologist, to take to the appointment, which will include the telephone number of a support line for GPs to contact in the event that they require HF management advice (provided through a specialist HF service). The overall schedule of the trial is outlined in Table 1, and the study flow chart is presented in Figure 1. Both groups will be followed-up over six months.

Recruitment

Patients with HF with reduced ejection fraction (HFrEF) will be recruited from two tertiary hospitals in Western Australia (WA). A research nurse will identify potential participants from the echocardiogram reporting system and electronic medical records of patients in the cardiology and general medical wards, and a daily list of patients with an admission diagnosis of HF will be generated. The study will also be advertised by posting study flyers in the hospitals' cardiology and general medical wards and the study will be promoted to clinicians at departmental meetings. Patients will be required to provide written informed consent prior to enrolling in the study. [Appendix1] For patients enrolling in the trial, baseline clinical characteristics and prescribed medication will be documented.

Table 1.	**Data collection points**					
Outcome	**Assessment**	**Baseline**	**1w**	**4w**	**3m**	**6m**
Primary						
Overall guideline adherence	Proportion of patients prescribed five out of five HF quality metrics[#]					*
Secondary						
Medication adherence	Proportion of eligible patients prescribed ACEIs/ARBs/ARNIs, BBs, MRAs at any dose		*	*	*	*
	Proportion of eligible patients prescribed ACEI/ ARB/ARNI, BB, or MRA at ≥50% of the target dose or maximum tolerated dose		*	*	*	*
	Proportion of eligible patients prescribed ACEI/ARB/ARNI, BB, or MRA at the target dose or maximum tolerated dose					*
	Proportion of eligible patients prescribed an anticoagulant if diagnosed with atrial fibrillation					*
Cardiac rehabilitation	Proportion of patients referred to an exercise training program or cardiac rehabilitation program					*
	Proportion of patients attending 16 sessions of cardiac rehabilitation					*
Functional capacity	6 minute walk test distance	*				*

	PROMIS physical function short form 4a		*
Patients' medication adherence	MMAS-8	*	*
Depressive symptoms	Patient Questionnaire-2	*	*
Health status	KCCQ-12	*	*
Self-care	SCHFI V7.2		*
Health care resource utilisation	Visits to physician, hospitalisations, days of admission.		*

HF, heart failure; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor neprilysin inhibitor; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; PROMIS, Patient-Reported Outcomes Measurement Information System; MMAS-8, Patients' medication adherence measured by the Morisky Medication Adherence Measure Scale-8; KCCQ-12, quality of life measured by the Kansas City Cardiomyopathy Questionnaire-Short Version; SCHFI V7.2 , Self-care behaviour measured by the Self-Care of Heart Failure Index version 7.2. #or 4 out of four if 5 are not indicated. Baseline medications will be documented upon discharge.

Participants

Inclusion criteria

(1) Patients hospitalised with signs and symptoms of HF (dyspnoea at rest or on exertion, plus at least one of the following: raised jugular venous pressure, peripheral oedema, third heart sound, or pulmonary congestion); or a left ventricular ejection fraction (LVEF) <40%; or a LVEF 41-49% and fulfilling the diagnostic criteria for HF according to the Australian Clinical Guidelines for the Management of Heart Failure 2018[5].

i.e. displaying signs of HF, brain natriuretic peptides (BNP) >100ng/L or NT-proBNP >300 ng/L or objective evidence of high filling pressure as indicated by at least three of the following echocardiography measures: i) mitral annular velocity septal e' of less than 7 cm/ s or lateral e' of less than 10-cm/s; ii) average mitral valve early wave inflow velocity to mitral annular velocity (E/e') ratio of more than 14; iii) left atrial volume index of more than 34 mL/m^2; 4) tricuspid valve regurgitation velocity of more than 2.8 m/s;

(2) Able to nominate a personal GP.

(3) >18 years of age;

Exclusion criteria:

(1) Patients currently under the management of a specialist HF service; (2) Receiving palliative care or with a life expectancy less than six months for conditions other than HF; (3) Nursing home/assisted living residents; (4) Impaired cognitive function; (5) Non-English speaking; (6) End-stage renal failure (eGFR < 15ml/min per 1.73 m^2).

Randomisation and blinding

Randomisation will be performed via a web-based program to generate a block randomisation sequence with a 1:1 allocation ratio. The randomisation list will be generated by an independent researcher not involved in the study. The HF NP will enrol participants and the independent researcher will assign the participants' allocation group to the HF NP by email following consent. Due to the nature of the intervention, it will not be possible to blind either the participants or the practitioner delivering the intervention. The study statistician will be blinded to group allocation when analysing the study outcomes. It's possible that participants being managed by the same GP may be

allocated to different arms within the trial, resulting in the potential for contamination, however we anticipate the likelihood of this is low.

Control Group

The control group will receive usual care as provided by their treating cardiologist or general physician while an inpatient, and their GP post-discharge. The "Living Well with Heart Failure, information to help you feel better" (third edition 2020, National Heart Foundation of Australia) will be provided to all control participants prior to hospital discharge.

Intervention Group

In addition to usual care, as outlined for the control group, the intervention group will receive the following components:

Inpatient education

A 30 minute, one-on-one HF education session provided by a HF NP. The education will complement topics in the "Living Well with Heart Failure" and include self-management strategies and information on the value of adherence to HF medications to maintain optimal health.

Post-discharge plan

1) A *PATHFINDER Envelope* will be provided to participants to take to an appointment with their GP at approximately 1 week, 4 weeks, and 3 months after discharge; 2) referral to cardiac rehabilitation; 3) Feedback to the hospital clinical team if the patient is not prescribed an ACEI/ARB/angiotensin receptor neprilysin inhibitor(ARNI), BB or mineralocorticoid receptor antagonist (MRA) despite being eligible, or if there is deviation from the HF medication titration plan (outlined below).

The PATHFINDER Envelope, will contain a cover letter to the GP detailing the study [Appendix 2] and the PATHFINDER Study Follow-up Form. The Follow-up Form will be individualised to the patient and provide details of dry weight at discharge, current dose and target dose of ACEI/ARB/ARNI, BB, and MRA approved by a cardiologist specialising in HF. It will serve as both a clinical support and a data collection tool. The form will include the following components: (1) clinical assessment by the GP;(2) HF medication titration plan: (3) details of any further treatment action required;(4) HF medication titration problem-solving guide; (5) Heart Failure Helpline, which will be available 8am to 4pm Monday to Friday for further guidance with medication titration or enacting an action plan for the patient. The HF NP will be the first to respond to calls to the Helpline. If the case is out of the HF NP's scope of practice, or clinically complex, it will be escalated to a specialist HF cardiologist to action.

Participants will receive reminders (phone call or text message) to support their adherence in attending the scheduled GP appointments. The HF NP will give the first PATHFINDER Envelope directly to the patient during hospitalisation for the 1-week post-discharge GP follow-up and mail the envelopes for the 4-week and 3-month post-discharge GP follow-ups. The HF NP will also phone the patient 4 months after discharge. If the patient is not prescribed 50% of the target dose of HF medications at that point without clinical justification, an additional GP visit will be encouraged. If participants miss a scheduled GP follow-up they will be encouraged to visit their GP by the HF NP as soon as possible thereafter. Participants who are referred to a specialist HF service following their enrolment in the trial will continue in the trial consistent with intention to treat.

The role of the GP

Participants' GPs will be asked to complete the PATHFINDER Study Follow-up Forms at the 1week, 4 week and 3 month appointments. Each follow-up will involve documenting participants' current weight, heart rate, blood pressure and any HF symptoms. The form will also guide GPs in titrating HF medications as recommended by a cardiologist and in accordance with guidelines.[5] At the conclusion of the appointment, the GP will record the current dose or provide justification for not titrating the medication and return the form by fax or email to the HF NP. If the research team does not receive the

form despite two reminder calls to the practice, HF medications will be collected by patient-report and cross-checked with medical records. Participants in the control group will self-report their medication at the same time-points.

Outcomes

Primary outcome

The primary outcome will be the difference between groups in the proportion of patients receiving HF guideline-recommended treatment at six months after an index hospital admission for HF based on five quality metrics for HF management:

(1) Either prescribed at least 50% of the recommended dose for an ACEI/ARB/ARNI or documentation that such a dose was not tolerated or otherwise inappropriate for eligible patients;[33]

(2) Either prescribed at least 50% of the recommended dose for a beta-blocker or documentation that such a dose was not tolerated or otherwise inappropriate for eligible patients;[33]

(3) Prescribed a MRA at any dose for eligible patients;[5]

(4) Prescribed anticoagulation for eligible patients with atrial fibrillation;[5]

(5) Referral to an exercise training program or cardiac rehabilitation program.[5]

The criteria for adherence to the HF guideline-recommended treatment will be defined as participants receiving 5 out of 5 of the HF quality metrics.[34] Medications and dosage prescribed to participants will be based on documentation on the PATHFINDER Study Follow-up Form for the experimental group and by patient-report in the control group and cross-checked with electronic records or pharmacy medication profiles. Referral to cardiac rehabilitation programs will be measured by patient-reported participation and cross-checked with documentation in medical records. If one or more treatments is not indicated, participants will be assessed based on the number of HF quality metrics they are eligible to receive. The recommended dose is based on the target dose of Guideline-Directed Medical Therapies (GDMT) in the 2020 ACC/AHA clinical performance and quality measures for adults with HF.[33]

Secondary outcomes

The secondary endpoints related to HF guideline-recommended care will include the difference between groups in the proportion of eligible patients receiving the following guideline-advocated treatment:

i) ACEI/ARB/ARNI, beta-blocker, and MRA at the target dose, or maximum tolerated dose at six months;
ii) ACEI/ARB/ARNI, beta-blocker, and MRA at any dose at six months;
iii) At least 50% of the target dose or maximum tolerated dose of each of ACEI/ARB/ARNI, beta-blocker and MRA at six months;
iv) Anticoagulation if diagnosed with atrial fibrillation at six month;
v) Any dose of each of ACEI/ARB/ARNI, beta-blocker, MRA at 1 week, 4 weeks, 3 months and 6 months;
vi) At least 50% of the target dose of each of ACEI/ARB/ARNI, beta-blocker and MRA at 1 week, 4 weeks, 3 months and 6 months;
vii) Referral to an exercise training program or cardiac rehabilitation program by six months;
viii) Attendance at 16 sessions of an exercise training program or cardiac rehabilitation program at six months.

Additional outcomes will be:

i) Functional capacity measured by six-minute walk test distance;[35]
ii) Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function Short Form 4a;[36]
iii) Quality of life measured by the Kansas City Cardiomyopathy Questionnaire-Short Version (KCCQ12);[37]
iv) Depression symptoms measured by the Patient Health Questionnaire (PHQ-2);[38]
v) Self-care behaviour measured by the Self-Care of Heart Failure Index (SCHFI) v7.2;[39]
vi) Patients' medication adherence measured by the Morisky Medication Adherence Measure Scale (MMAS-8).[40]

The timeline for outcome collection is described in Table 1.

Resource use

Health care utilisation will include the number of visits to physicians, cardiovascular-related hospitalisation and HF-related hospitalisation, number of cardiovascular-related procedures, days of admission, and use of specialised care. Given the feasibility of obtaining health administrative data within the study time frame, we will adapt a validated patient cost questionnaire to obtain self-reported health care utilisation data[41] and this will be cross-checked with medical records. Whilst we recognise the potential for recall bias, there is evidence to suggest that this is a valid method of collecting data on healthcare resource utilization, especially when administrative data is not easily available.[42]

Safety assessment

An adverse event (SAE) will be defined as any undesirable experience resulting in a participant's death, hospitalisation, prolongation of hospitalisation, or disability. All AEs will be recorded over the six month follow up period of the study. Adverse events including symptomatic hypotension, hyperkalemia, azotemia will be documented. The research investigators will determine whether there was any AE occurrence by asking the participant and cross-checking with medical records.

Process measures

The Reach, Efficacy, Adoption, Implementation and Maintenance (RE-AIM) evaluation model[43] will be used to perform a process evaluation. Reach will be assessed using patient-level measures of participation. The recruitment rate, completion rate and reasons for exclusion and dropping out of the study will be determined. Efficacy will be assessed according to the effectiveness of the intervention on influencing GP practice i.e. the global adherence indicator (GAI-3).[44] GPs' satisfaction with the intervention will be measured by a survey administered at the conclusion of the 6 month follow-up period for a participant under their care [Appendix 3]. Adoption will be assessed at the participant and GP level. Participant adoption will be based on the proportion of patients visiting their GP at approximately 1 week, 4 weeks, 3 month post discharge and the proportion of participants attending at least one session of cardiac rehab training. Reasons for participants not visiting their GP and not attending cardiac rehabilitation will be explored. GP adoption will be assessed based on the proportion of GPs completing and returning the follow up forms at the 1 week, 4 week, and 3 month time-points and the usage of the helpline. Implementation will be assessed based on the extent that the GP delivers the intervention as intended. The proportion of GPs starting, increasing, decreasing, ceasing, and not changing ACEIs/ARBs/ARNIs, BBs, and MRAs will be measured at 1 week, 4 week, and 3 months. Reasons for lower dose or medication cessation at 3 months compared with the baseline will be examined. Maintenance will be assessed based on whether the titration of HF medication in primary care, at the levels achieved during the trial, is maintained at 6 months following the conclusion of the trial. [Table 2] The number of patients with shared GPs will be reported.

Table 2	RE-AIM framework of process evaluation	
RE-AIM dimension	**Definition**	**Data sources**
Reach	The recruitment rate, completion rate and reasons for exclusion and dropping out of the study	Recruitment record; participant's check-in sheet
Efficacy	GAI-3; GP's satisfaction with the intervention arm	Patient-reported Medication; case report form; survey
Adoption	The proportion of patients visiting GP at 1 week, 4 week, 3month, reasons for not visiting GP; The proportion of GPs faxing back follow up form at 1 week, 4 week, 3 month; The proportion of patient participating in ≥ one session of cardiac rehab; reasons for not attending cardiac rehab; use of the helpline and information requested	PATHFINDER follow-up forms; case report form; field notes; electronic medical records; patient-reported
Implementation	The proportion of GP starting, increasing, decreasing, ceasing, and not changing ACEI/ARB/ARNI, BB, or MRA medication at 1 week, 4 week, and 3 months; reasons for lower dose or medication cessation at 3 month compared with the baseline	PATHFINDER follow-up forms; case report form; field notes; electronic medical records; patient-reported
Maintenance	The proportion of patients prescribed ACEI/ARB/ARNI, BB, or MRA at the same or higher dose, lower dose or ceased at 6 months compared with 3 month; reasons for lower dose and medication cessation	PATHFINDER follow-up forms; case report form; field notes; electronic medical records; patient-reported

RE-AIM, Reach, Efficacy-Adoption, Implementation and Maintenance; GAI-3, global adherence indicator; GP, general practitioner; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor neprilysin inhibitor; BB, beta-blocker; MRA, mineralocorticoid receptor antagonist; PATHFIDNER, **P**rimary care **A**dherence **T**o **H**eart **F**ailure guidelines **In D**iagnosis, **E**valuation & **R**outine management.

Data collection and Management

Six month follow-up assessments will be conducted in person where possible, however patients who live remotely from the hospital will be assessed via phone and return the questionnaires by mail. A follow-up six-minute walk test will not be performed in these participants. Participants who withdraw from the intervention protocol will be contacted for the six month follow-up assessment for primary, secondary and additional outcomes either in person or via phone (intention to treat). Data will be documented in case report forms and entered into a Research Electronic Data Capture (REDCap) database. Patient data will be deidentified and saved as a unique trial participant number to assure data confidentiality. Only authorised members of the researcher team will have access to the dataset.

Sample size

A recent Australian audit of HF management observed that 53 % of patients were prescribed an ACEI/ARB and beta-blocker at ≥50 % of the target dose.[45] Furthermore, the prescribing rate of MRAs

and anticoagulants with atrial fibrillation was 38% and over 90% respectively.[45] Data from the GWTG-HF Registry showed that only 12% of patients with HFrEF were referred to CR at discharge, although additional patients may be referred subsequently.[46] It is likely that the proportion of patients treated with ≥50 % of the target doses of ACEIs/ARBs together with ≥50 % of the target doses of beta-blockers, receiving MRAs and cardiac rehabilitation referral by six months after discharge in combination will be even lower. Based on these assumptions we estimate that 20% of patients receive 5 out of 5 HF guideline-recommended treatments by six months after discharge in usual care. We expect to observe an absolute 20% improvement in the intervention group (20% in the usual care group, 40% in the intervention group) 6 months after discharge. With 80% power (type I error=5%, two-sided test), we would require a total sample size of 182, increasing to 220, to account for a potential 20% loss to follow-up.

Statistics

The intention to treat principle will be applied, and patients will be analysed according to the group to which they are allocated. Descriptive summaries of patient clinical and selected outcome data will include means and standard deviations or medians and interquartile ranges for continuous data and frequency distributions for categorical data. Univariate group comparisons between groups will be performed using t tests or Mann-Whitney U tests for continuous data and Chi squared tests for categorical data. Primary adherence outcomes will be expressed as binary indicator variables. Proportional differences in adherence will be compared between groups at six-month post-discharge using Chi squared tests and modelled using logistic regression models. Models will be adjusted for relevant patient and clinical factors. Results will be summarised as odds ratios (OR) and 95% confidence intervals (CI). Secondary outcomes collected at baseline (during admission) and at six-month post-discharge will be modelled using generalised linear mixed models (GLMM), with appropriate link functions depending on data distributions, random subject effects and group-time interaction effects in order to compare differences between groups over time. All models will be adjusted for baseline and relevant patient and clinical factors. Model results will be summarised as estimated marginal mean differences and 95% CIs. Secondary outcome counts of health resource utilisation will be compared between groups using Poisson or negative binomial regression models. Model results will be summarised as estimated marginal mean differences and 95% CIs. Significance levels will be set at alpha=0.05 and Stata version 17.0 will be used for data analysis.

Patient and Public Involvement

Before designing the intervention, focus groups and interviews with patients with HF, clinicians and administrators in tertiary care and primary care were held to explore barriers and facilitators to post-discharge HF management. Patients were not involved in the recruitment to and conduct of the study. The findings of the study will be disseminated to study participants with a narrative summary. The burden of the intervention was not assessed by patients themselves. The research team also consulted the GP liaison officers of the two hospitals involved in the project to discuss the project methodology, including design of the PATHFINDER Study Follow-up Form.

DISCUSSION AND CONCLUSION

Effective management of HF in primary care practice remains challenging for many clinicians.[47] Despite the availability of evidence-based treatment guidelines, translating these into practice can be complicated by the clinical characteristics of many patients (including hypotension, bradycardia, renal impairment and hyperkalaemia) as well as socioeconomic and behavioural factors relevant to patients.[48-52] Limited access to specialist care,[53] general practitioners not aware of recent guideline-recommended therapies or contraindications to prescribing medications, nor the importance of achieving the target dose, and concerns about adverse effects all contribute to suboptimal HF treatment.[52 54] Moreover, effective systems to support care coordination are often lacking.[15 55]

Accordingly, strategies to support general practice in the delivery of evidence-based HF management are required.

Hospital discharge planning plays a vital role in the transition of care from hospital to general practice.[56] This includes initiating a medication regimen that can be modified over time.[57 58] Following discharge, a structured medication titration plan can lead to greater responsibility for medication titration by primary care physicians,[59] with point-of-care reminders involving specific guidance having been found to improve medication prescription in accordance with guidelines.[60] However, these studies were limited in their size or trial design, hence the need for a well conducted RCT. Furthermore, providing patients with self-care education during admission can further improve clinical outcomes,[61] and patients who schedule regular follow-up appointments have been found to experience fewer readmissions than those who do not.[61]

The PATHFINDER study will incorporate these aspects into a multifaceted intervention to support HF management in primary care. A strength of the PATHFINDER intervention will be that it will include components across multiple levels of the health system. The intervention will commence during the inpatient period, involving patient education and medication initiation. A HF NP will subsequently act as a health navigator for the patient, liaising between the patients GP and a cardiologist. Due to their advanced scope of practice, which includes prescribing and titrating medications, ordering and interpreting pathology and radiology tests and initiating referral to other health professionals,[5 31] NPs are well-credentialed to coordinate the management of patients with HF[62] and to support transitional care between the tertiary and primary health care sectors.[63 64] The NP will facilitate the Follow-up Forms and helpline, which will serve as a bridge between the primary and tertiary care sectors, providing clinical decision support and reinforcement of guideline-advocated treatment. Importantly, we anticipate the intervention will help formalise care goals through improved guideline adherence. Improved referral to and uptake of cardiac rehabilitation will provide stronger multidisciplinary support through ongoing patient education, exercise prescription and clinical surveillance.

There are several limitations to this trial. Firstly, due to the nature of the intervention, it will not be possible to blind either the patient, GP, or HF NP to group allocation. Second, because the HF NP will only be employed Monday to Friday, participants admitted to hospital later in the week may be discharged over the weekend before there is an opportunity to review, consent and undertake baseline assessments and self-management education. Third, COVID-19 may impact the opportunity for patients to attend the scheduled GP appointments at the proposed time or face to face, and it's unclear how virtual clinics will impact GPs willingness to titrate medication. Given that randomisation will occur at the participant level, there is a risk that contamination may occur, whereby the same GP might have a patient enrolled in the intervention and usual care arms of the study, but we anticipate this will occur very rarely.

In conclusion, this study will be a prospective, multi-centre, parallel-group, randomised controlled trial with blinded assessment of study outcomes to explore the effectiveness of a multifaceted intervention for guideline implementation in the GP practice. It will determine the feasibility of future large-scale clinical trials aiming to improve primary care physicians' adherence to HF guideline-advocated treatment.

Ethics and dissemination

Ethical approval has been obtained through the South Metropolitan Health Service (RGS3531) with reciprocal approval at Curtin University (HRE2020-0322).Written informed consent will be obtained from all the participants. The project will be conducted in adherence to the Australian National Health and Medical Research Council National Statement for Ethical Research. The current protocol version is version 3.1 dated 4 April 2022. Major modifications during the trial will require a formal

amendment to the protocol. Results will be disseminated via peer-reviewed publications and conference presentations.

Acknowledgements We would like to acknowledge ethics committee for granting us permission to conduct the study. We would like to express our gratitude to physicians in Fiona Stanley Hospital, as well as Royal Perth Hospital for engaging participants to enrol. We would also like to thank patients, clinicians and administrators to participate in focus groups and interviews and thank study participants for their willingness to participate in this study.

Contributors LD contributed to the study design and wrote the protocol. TD contributed to the study design. JG contributed to the study design and provided clinical area expertise. AS provided methodological and clinical area expertise. LD provided methodological and clinical area expertise. JR provided methodological and clinical area expertise. GSH is site PI and provided methodological and clinical area expertise. SR provided methodological area expertise. JJA provided methodological area expertise. AJ provided methodological area expertise. CMR provided the original idea for the study and methodological area expertise. AM is site PI and provided the original idea for the study and methodological and clinical area expertise. All authors read, contributed to and approved the final manuscript.

Funding This work is funded by the Medical Research Future Fund (MRFF) Rapid Applied Research Translation (RART) Grants from the Western Australia Health Translation Network (WAHTN, grant number N/A). LD is funded by a postgraduate research scholarship funded by Curtin University. CMR is funded through a NHMRC Principal Research Fellowship (GNT 1136372).

Competing interests None declared.

Ethics approval The South Metropolitan Health Service Human Research Ethics Committee; reciprocal approval from the Curtin University Human Research Ethics Committee

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

ORCID IDs

Liying Dai http://orcid.org/0000-0002-7843-6344

Andrew Maiorana https://orcid.org/0000-0002-0681-1707

Christopher M Reid https://orcid.org/0000-0001-9173-3944

Graham Hillis https://orcid.org/0000-0003-2417-4673

Suzanne Robinson https://orcid.org/0000-0001-5703-6475

John J Atherton https://orcid.org/0000-0003-2271-578X

Angela Jacques https://orcid.org/0000-0002-0461-681X

References

1. Groenewegen A, Rutten FH, Mosterd A, et al. Epidemiology of heart failure. *European Journal of Heart Failure* 2020;22(8):1342-56. doi: 10.1002/ejhf.1858
2. Metra M, Teerlink JR. Heart failure. *Lancet* 2017;390(10106):1981-95. doi: 10.1016/s0140-6736(17)31071-1 [published Online First: 2017/05/04]
3. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Cardiac failure review* 2017;3(1):7-11. doi: http://dx.doi.org/10.15420/cfr.2016:25:2
4. Chan YK, Tuttle C, Ball J, et al. Current and projected burden of heart failure in the Australian adult population: a substantive but still ill-defined major health issue. *BMC Health Serv Res* 2016;16(1):501. doi: 10.1186/s12913-016-1748-0 [published Online First: 2016/09/23]
5. Atherton JJ, Sindone A, De Pasquale CG, et al. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the management of heart failure 2018. *Med J Aust* 2018;209(8):363-69. doi: 10.5694/mja18.00647 [published Online First: 2018/08/02]
6. Komajda M, Cowie MR, Tavazzi L, et al. Physicians' guideline adherence is associated with better prognosis in outpatients with heart failure with reduced ejection fraction: the QUALIFY international registry. *Eur J Heart Fail* 2017;19(11):1414-23. doi: 10.1002/ejhf.887 [published Online First: 2017/05/04]
7. Stolfo D, Lund LH, Becher PM, et al. Use of evidence-based therapy in heart failure with reduced ejection fraction across age strata. *Eur J Heart Fail* 2022;24(6):1047-62. doi: 10.1002/ejhf.2483 [published Online First: 2022/03/13]
8. Mentz RJ, Lautsch D, Pulungan Z, et al. Medication Trajectory and Treatment Patterns in Medicare Patients With Heart Failure and Reduced Ejection Fraction. *J Card Fail* 2022;28(8):1349-54. doi: 10.1016/j.cardfail.2021.11.013 [published Online First: 2021/12/22]
9. Savarese G, Kishi T, Vardeny O, et al. Heart Failure Drug Treatment-Inertia, Titration, and Discontinuation: A Multinational Observational Study (EVOLUTION HF). *JACC Heart Fail* 2022 doi: 10.1016/j.jchf.2022.08.009 [published Online First: 2022/10/07]
10. Liew D, Audehm RG, Haikerwal D, et al. Epidemiology of heart failure: Study of Heart failure in the Australian Primary carE setting (SHAPE). *ESC heart failure* 2020 doi: http://dx.doi.org/10.1002/ehf2.12979
11. Page K, Marwick TH, Lee R, et al. A systematic approach to chronic heart failure care: a consensus statement. *Medical Journal of Australia* 2014;201(3):146-50. doi: 10.5694/mja14.00032
12. Scott I, Jackson C. Chronic heart failure management in Australia -- time for general practice centred models of care? *Aust Fam Physician* 2013;42(5):343-6. [published Online First: 2013/06/20]
13. Weenink JW, van Lieshout J, Jung HP, et al. Patient Care Teams in treatment of diabetes and chronic heart failure in primary care: an observational networks study. *Implement Sci* 2011;6:66. doi: 10.1186/1748-5908-6-66 [published Online First: 2011/07/05]
14. Hirt MN, Muttardi A, Helms TM, et al. General practitioners' adherence to chronic heart failure guidelines regarding medication: the GP-HF study. *Clin Res Cardiol* 2016;105(5):441-50. doi: 10.1007/s00392-015-0939-8 [published Online First: 2015/11/11]
15. Smeets M, Van Roy S, Aertgeerts B, et al. Improving care for heart failure patients in primary care, GPs' perceptions: a qualitative evidence synthesis. *Bmj Open* 2016;6(11):12. doi: 10.1136/bmjopen-2016-013459
16. Calvin JE, Shanbhag S, Avery E, et al. Adherence to evidence-based guidelines for heart failure in physicians and their patients: lessons from the Heart Failure Adherence Retention

Trial (HART). *Congest Heart Fail* 2012;18(2):73-8. doi: 10.1111/j.1751-7133.2011.00263.x [published Online First: 2012/03/22]
17. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *Jama* 1999;282(15):1458-65. doi: 10.1001/jama.282.15.1458 [published Online First: 1999/10/27]
18. Khunti K, Hearnshaw H, Baker R, et al. Heart failure in primary care: qualitative study of current management and perceived obstacles to evidence-based diagnosis and management by general practitioners. *Eur J Heart Fail* 2002;4(6):771-7. doi: 10.1016/s1388-9842(02)00119-8 [published Online First: 2002/11/28]
19. Verhestraeten C, Heggermont WA, Maris M. Clinical inertia in the treatment of heart failure: a major issue to tackle. *Heart Fail Rev* 2020 doi: 10.1007/s10741-020-09979-z [published Online First: 2020/06/01]
20. Aujoulat I, Jacquemin P, Rietzschel E, et al. Factors associated with clinical inertia: an integrative review. *Adv Med Educ Pract* 2014;5:141-7. doi: 10.2147/amep.S59022 [published Online First: 2014/05/29]
21. Giezeman M, Arne M, Theander K. Adherence to guidelines in patients with chronic heart failure in primary health care. *Scandinavian Journal of Primary Health Care* 2017;35(4):336-43. doi: 10.1080/02813432.2017.1397253
22. Cleland JG, Cohen-Solal A, Aguilar JC, et al. Management of heart failure in primary care (the IMPROVEMENT of Heart Failure Programme): an international survey. *Lancet* 2002;360(9346):1631-9. doi: 10.1016/s0140-6736(02)11601-1 [published Online First: 2002/11/30]
23. Huynh Q, Negishi K, De Pasquale C, et al. Effects of post-discharge management on rates of early re-admission and death after hospitalisation for heart failure. *Med J Aust* 2018;208(11):485-91. doi: 10.5694/mja17.00809 [published Online First: 2018/05/12]
24. Bero LA, Grilli R, Grimshaw JM, et al. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. *Bmj* 1998;317(7156):465-8. doi: 10.1136/bmj.317.7156.465 [published Online First: 1998/08/14]
25. Fonarow GC, Albert NM, Curtis AB, et al. Improving evidence-based care for heart failure in outpatient cardiology practices: primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). *Circulation* 2010;122(6):585-96. doi: 10.1161/circulationaha.109.934471 [published Online First: 2010/07/28]
26. Ellrodt AG, Fonarow GC, Schwamm LH, et al. Synthesizing lessons learned from get with the guidelines: the value of disease-based registries in improving quality and outcomes. *Circulation* 2013;128(22):2447-60. doi: 10.1161/01.cir.0000435779.48007.5c [published Online First: 20131028]
27. Heidenreich PA, Lewis WR, LaBresh KA, et al. Hospital performance recognition with the Get With The Guidelines Program and mortality for acute myocardial infarction and heart failure. *Am Heart J* 2009;158(4):546-53. doi: 10.1016/j.ahj.2009.07.031
28. Peters-Klimm F, Müller-Tasch T, Remppis A, et al. Improved guideline adherence to pharmacotherapy of chronic systolic heart failure in general practice--results from a cluster-randomized controlled trial of implementation of a clinical practice guideline. *J Eval Clin Pract* 2008;14(5):823-9. doi: 10.1111/j.1365-2753.2008.01060.x [published Online First: 2008/11/21]
29. Goff DC, Jr., Massing MW, Bertoni AG, et al. Enhancing quality of heart failure care in managed Medicare and Medicaid in North Carolina: results of the North Carolina Achieving Cardiac Excellence (NC ACE) Project. *Am Heart J* 2005;150(4):717-24. doi: 10.1016/j.ahj.2004.12.025 [published Online First: 2005/10/08]

30. Persson H, Erntell H, Eriksson B, et al. Improved pharmacological therapy of chronic heart failure in primary care: a randomized Study of NT-proBNP Guided Management of Heart Failure - SIGNAL-HF (Swedish Intervention study - Guidelines and NT-proBNP AnaLysis in Heart Failure). *European Journal of Heart Failure* 2010;12(12):1300-08. doi: 10.1093/eurjhf/hfq169
31. . https://www.nursingmidwiferyboard.gov.au/Codes-Guidelines-Statements/Professional-standards/registered-nurse-standards-for-practice.aspx Date accessed: 2 Dec 2021.
32. Chen SH, Boyd J, Randall S, et al. Association between community-based nurse practitioner support, self-care behaviour and quality of life in patients with chronic heart failure. *Australian Journal of Advanced Nursing* 2021;38(3):25-32. doi: 10.37464/2020.383.147
33. Heidenreich PA, Fonarow GC, Breathett K, et al. 2020 ACC/AHA Clinical Performance and Quality Measures for Adults With Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol* 2020;76(21):2527-64. doi: 10.1016/j.jacc.2020.07.023 [published Online First: 2020/11/07]
34. Chow CK, Thiagalingam A, Santo K, et al. TEXT messages to improve MEDication adherence and Secondary prevention (TEXTMEDS) after acute coronary syndrome: a randomised clinical trial protocol. *BMJ Open* 2018;8(1):e019463. doi: 10.1136/bmjopen-2017-019463 [published Online First: 2018/01/29]
35. Rostagno C, Olivo G, Comeglio M, et al. Prognostic value of 6-minute walk corridor test in patients with mild to moderate heart failure: comparison with other methods of functional evaluation. *European Journal of Heart Failure* 2003;5(3):247-52. doi: 10.1016/s1388-9842(02)00244-1
36. DeWalt DA, Rothrock N, Yount S, et al. Evaluation of item candidates - The PROMIS qualitative item review. *Medical Care* 2007;45(5):S12-S21. doi: 10.1097/01.mlr.0000254567.79743.e2
37. Spertus JA, Jones PG. Development and Validation of a Short Version of the Kansas City Cardiomyopathy Questionnaire. *Circulation-Cardiovascular Quality and Outcomes* 2015;8(5):469-76. doi: 10.1161/circoutcomes.115.001958
38. Lowe B, Kroenke K, Grafe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *Journal of Psychosomatic Research* 2005;58(2):163-71. doi: 10.1016/j.jpsychores.2004.09.006
39. Barbaranelli C, Lee CS, Vellone E, et al. Dimensionality and Reliability of the Self-Care of Heart Failure Index Scales: Further Evidence From Confirmatory Factor Analysis. *Research in Nursing & Health* 2014;37(6):524-37. doi: 10.1002/nur.21623
40. Morisky DE, Ang A, Krousel-Wood M, et al. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. *Journal of Clinical Hypertension* 2008;10(5):348-54. doi: 10.1111/j.1751-7176.2008.07572.x
41. van den Brink M, van den Hout WB, Stiggelbout AM, et al. Self-reports of health-care utilization: diary or questionnaire? *Int J Technol Assess Health Care* 2005;21(3):298-304. doi: 10.1017/s0266462305050397
42. Leggett LE, Khadaroo RG, Holroyd-Leduc J, et al. Measuring Resource Utilization: A Systematic Review of Validated Self-Reported Questionnaires. *Medicine (Baltimore)* 2016;95(10):e2759. doi: 10.1097/md.0000000000002759
43. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health* 1999;89(9):1322-7. doi: 10.2105/ajph.89.9.1322 [published Online First: 1999/09/04]

44. Komajda M, Lapuerta P, Hermans N, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. *European Heart Journal* 2005;26(16):1653-59. doi: 10.1093/eurheartj/ehi251
45. Chin KL, Skiba M, Tonkin A, et al. The treatment gap in patients with chronic systolic heart failure: a systematic review of evidence-based prescribing in practice. *Heart Fail Rev* 2016;21(6):675-97. doi: 10.1007/s10741-016-9575-2 [published Online First: 2016/10/28]
46. Golwala H, Pandey A, Ju C, et al. Temporal Trends and Factors Associated With Cardiac Rehabilitation Referral Among Patients Hospitalized With Heart Failure: Findings From Get With The Guidelines-Heart Failure Registry. *J Am Coll Cardiol* 2015;66(8):917-26. doi: 10.1016/j.jacc.2015.06.1089
47. Taylor CJ, Valenti L, Britt H, et al. Management of chronic heart failure in general practice in Australia. *Aust Fam Physician* 2016;45(11):734-39. [published Online First: 2016/11/03]
48. Komajda M, Anker SD, Cowie MR, et al. Physicians' adherence to guideline-recommended medications in heart failure with reduced ejection fraction: data from the QUALIFY global survey. *European Journal of Heart Failure* 2016;18(5):514-22. doi: 10.1002/ejhf.510
49. Crespo-Leiro MG, Segovia-Cubero J, Gonzalez-Costello J, et al. Adherence to the ESC Heart Failure Treatment Guidelines in Spain: ESC Heart Failure Long-term Registry. *Revista Espanola De Cardiologia* 2015;68(9):785-93. doi: 10.1016/j.rec.2015.03.008
50. Chang HY, Wang CC, Wei J, et al. Gap between guidelines and clinical practice in heart failure with reduced ejection fraction: Results from TSOC-HFrEF registry. *Journal of the Chinese Medical Association* 2017;80(12):750-57. doi: 10.1016/j.jcma.2017.04.011
51. Ouwerkerk W, Voors AA, Anker SD, et al. Determinants and clinical outcome of uptitration of ACE-inhibitors and beta-blockers in patients with heart failure: a prospective European study. *European Heart Journal* 2017;38(24):1883-+. doi: 10.1093/eurheartj/ehx026
52. Greene SJ, Tan X, Yeh YC, et al. Factors associated with non-use and sub-target dosing of medical therapy for heart failure with reduced ejection fraction. *Heart Fail Rev* 2021 doi: 10.1007/s10741-021-10077-x [published Online First: 2021/01/21]
53. Savarese G, Carrero JJ, Pitt B, et al. Factors associated with underuse of mineralocorticoid receptor antagonists in heart failure with reduced ejection fraction: an analysis of 11 215 patients from the Swedish Heart Failure Registry. *Eur J Heart Fail* 2018;20(9):1326-34. doi: 10.1002/ejhf.1182 [published Online First: 20180326]
54. Hirt MN, Muttardi A, Helms TM, et al. General practitioners' adherence to chronic heart failure guidelines regarding medication: the GP-HF study. *Clinical Research in Cardiology* 2016;105(5):441-50. doi: 10.1007/s00392-015-0939-8
55. Verhestraeten C, Heggermont WA, Maris M. Clinical inertia in the treatment of heart failure: a major issue to tackle. *Heart Fail Rev* 2021;26(6):1359-70. doi: 10.1007/s10741-020-09979-z [published Online First: 2020/06/01]
56. Rosano GMC, Moura B, Metra M, et al. Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2021;23(6):872-81. doi: 10.1002/ejhf.2206 [published Online First: 2021/05/02]
57. Bitar S, Agrinier N, Alla F, et al. Adherence to ESC guideline-recommended medications over a 36-month follow-up period after hospitalization for heart failure: Results from the EPICAL2 cohort study. *Pharmacoepidemiol Drug Saf* 2019;28(11):1489-500. doi: 10.1002/pds.4868 [published Online First: 2019/07/25]

58. Rørth R, Fosbøl EL, Mogensen UM, et al. Evidence-Based Therapy and Its Association With Workforce Detachment After First Hospitalization for Heart Failure. *JACC Heart Fail* 2018;6(1):41-48. doi: 10.1016/j.jchf.2017.09.019 [published Online First: 2017/12/12]
59. Hickey A, Suna J, Marquart L, et al. Improving medication titration in heart failure by embedding a structured medication titration plan. *International Journal of Cardiology* 2016;224:99-106. doi: 10.1016/j.ijcard.2016.09.001
60. Shanbhag D, Graham ID, Harlos K, et al. Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review. *BMJ Open* 2018;8(3) doi: http://dx.doi.org/10.1136/bmjopen-2017-017765
61. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *European Heart Journal* 2016;37(27):2129-U130. doi: 10.1093/eurheartj/ehw128
62. Chen Y, Zhu L, Xu F, et al. Discharge planning for heart failure patients in a tertiary hospital in Shanghai: a best practice implementation project. *JBI Database System Rev Implement Rep* 2016;14(2):322-36. doi: 10.11124/jbisrir-2016-2510 [published Online First: 2016/08/19]
63. Vedel I, Khanassov V. Transitional Care for Patients With Congestive Heart Failure: A Systematic Review and Meta-Analysis. *Ann Fam Med* 2015;13(6):562-71. doi: 10.1370/afm.1844
64. Phillips CO, Singa RM, Rubin HR, et al. Complexity of program and clinical outcomes of heart failure disease management incorporating specialist nurse-led heart failure clinics. A meta-regression analysis. *Eur J Heart Fail* 2005;7(3):333-41. doi: 10.1016/j.ejheart.2005.01.011 [published Online First: 2005/02/19]

HF, heart failure; NP, nurse practitioner; GP, general practitioner; PATHFINDER, Primary care Adherence To Heart Failure guidelines IN Diagnosis, Evaluation and Routine management
Figure 1. Study flow chart

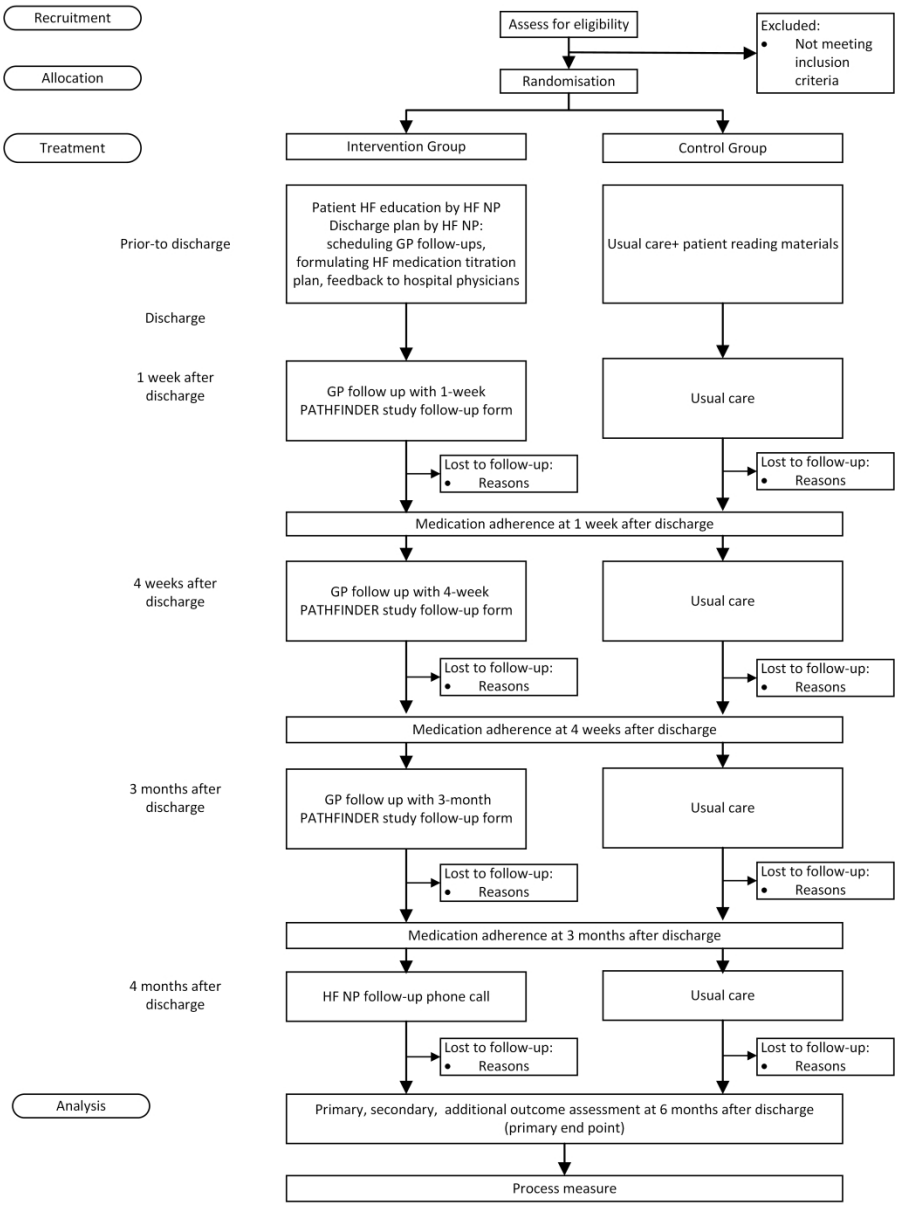

Figure 1. Study flow chart HF, heart failure; NP, nurse practitioner ; GP, general practitioner; PATHFINDER, Primary care Adherence To Heart Failure guidelines IN Diagnosis, Evaluation and Routine management

165x222mm (600 x 600 DPI)

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PARTICIPANT INFORMATION SHEET

Primary care adherence to heart failure guidelines in the diagnosis, evaluation & routine management (PATHFINDER) of heart failure Study.

Principal Investigator: Associate Professor Andrew Maiorana, Allied Health Dept. and Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital

Fiona Stanley Hospital, Royal Perth Hospital and Curtin University are undertaking research to evaluate and improve the level of adherence to published guidelines for the management of people who have been admitted to hospital with heart failure, a medical condition in which the heart doesn't pump as strongly as it should. The following information describes what will be involved should you decide to participate in this research project. Please read the information about this study carefully and ask any questions you might have. You may also wish to discuss the study with a relative or friend.

BACKGROUND

Heart failure is a common cause of hospital admissions in Australia. However, many of these admissions are preventable with better adherence to published guidelines about heart failure management, such as increased use of appropriate medication, and clear advice to patients on healthy lifestyle (including physical activity) and self-management.

WHAT IS THE PURPOSE OF THE STUDY?

The aim of this study is to evaluate the effects of providing a Heart Health Plan to patients who have been admitted to hospital with heart failure. The Heart Health Plan will involve providing specific information to patients and their nominated GP to support the management of heart failure. This research has been funded by WA Health Translation Network (Rapid Applied Research Translation Grant) through funds provide by the Medical Research Future Fund.

WHAT WILL HAPPEN?

Patients who have been admitted to hospital will be randomly allocated to receive the Heart Health Plan or medical management following standard processes (usual care).

If you agree to take part in the study, you will be asked to complete a walking test prior to leaving hospital. This test involves walking for six minutes as quickly as you're able to, up and down a hospital corridor. In some cases we may ask you to come back to the hospital shortly after you have been discharged to perform the test if you're not able to perform it while in hospital. At the time of each walking test we will also measure your height and weight.

You will also be asked to complete several questionnaires. These should take approximately 20 minutes to complete. We will ask you to repeat these questionnaires when you return for your repeat walking tests.

The questionnaires are:

i. Kansas City Cardiomyopathy Questionnaire-short version (KCCQ12) – questions about your heart condition and how it affects your life.
ii. PROMIS Physical Function Short Form 4a, Patient Health Questionnaire (PHQ-2) – questions about how you heart condition affects your ability to do manual chores and physical activity.
iii. Patient Health Questionnaire (PHQ-2) - two questions about how you heart condition has affected the way you feel over the past 2 weeks.
iv. Self-care of Heart Failure Index – questions about the behaviours you use to manage your heart condition.
v. Medication Compliance Questionnaire - questions about your use of medication.

This walking test and questionnaires will be repeated at Fiona Stanley Hospital following 6 months. You will be reimbursed for parking to attend these visits.

If you are randomised to receive the Heart Health Plan you will be given specific information before you leave hospital about self-management of heart failure by a specialist nurse (a Heart Failure Nurse Practitioner), including information about undertaking physical activity suited to your level of fitness. In addition, you will be provided with a form to take to your GP at 7 days, 28 days, 3 months following discharge from hospital to help adjust your medications. If after 3 months post-discharge, you are still having problems with your medications more follow-ups by your GP may be recommended. Your GP will also be given the phone number of heart failure helpline to contact in the event that they need to seek advice (the Nurse Practitioner will work with a Cardiologist in providing this advice).

Patients who are randomised to the usual care group, will receive all the standard care provided to patients following an admission with heart failure at Fiona Stanley Hospital, but won't receive the Heart Health Plan. You will be contacted by phone approximately 7 days, 28 days and 3 months after you leave hospital to confirm your heart medications, and the dose and frequency that you take them every day.

We are seeking your permission to review your hospital records to document your medical history and demographic information. If there is some relevant information missing we may need to ask you some questions directly. We also wish to monitor your health into the future, including hospital admissions and if you pass away, so are also seeking your permission to collect this information.

TIME COMMITMENT

The education that will be part of the Heart Health Plan will also take approximately 30 minutes.

The walking test and associated measurements will take less than 30 minutes and the questionnaires will take you around 20-30 minutes to complete. The walking test will be undertaken on two occasions; while you're still in hospital (or soon after you're discharged) and 6 months after you're discharged from hospital. People who live in country areas and are unable to attend the hospital will be mailed the questionnaires but won't need to repeat the walking tests. The questionnaires will be undertaken at hospital and 6 months after you're discharged. If you are randomised to the usual care group, each follow up phone calls will take about 5-10 minutes.

WHAT ARE THE POSSIBLE DISADVANTAGES AND RISK OF TAKING PART?

This is a low risk study. Some people may feel self-conscious about answering some of the questions in the questionnaires. However, your responses won't be available to anyone outside the research team and we will use a participant ID code rather than your name so your identity won't appear on your responses.

POSSIBLE BENEFITS

We cannot guarantee that you will receive any benefits from this research; however, we anticipate that findings from the study will help inform better management of patients with heart failure into the future.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Participation in this study is voluntary. You do not have to participate and, if you decide to participate, you can stop at any time without explanation. Your decision to participate or not, or to later withdraw from the study, will in no way affect your current or future care at Fiona Stanley Hospital.

WHAT ARE THE COSTS OF BEING IN THIS STUDY?

There are no financial costs associated with participating in the study. You will not be paid for participation, however expenses you incur associated with parking will be reimbursed.

PRIVACY AND CONFIDENTIALITY

The information gathered about you by the investigator or obtained during this study will be held by the investigator in strict confidence. All the people who handle your information will adhere to traditional standards of confidentiality and will also comply with the Privacy Act 1988. If the results of the trial are published in a medical journal, as is intended, no reader will be able to identify individual patients.

WHAT IF SOMETHING GOES WRONG?

In the event that you suffer an expected or unexpected side effect or medical accident during this study that arises from your participation, you will be offered all full and necessary treatment by Fiona Stanley Hospital.

WHAT HAPPENS WHEN THE RESEARCH PROJECT ENDS?

You will be provided with a narrative summary of the results by letter in 6 months when the research project is completed.

WHAT WILL HAPPEN TO INFORMATION ABOUT ME?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. 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. Only authorised researchers will have access to the data. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

The study data will be retained a minimum of seven years after completion of the project or publication. Disposal of research data and primary materials will be in accordance with the Information Management Policy of Curtin University.

CONTACT INFORMATION

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

If you have questions about this study, please contact Associate Professor Maiorana on (08) 61521692 or alternatively Zoe Dai on 0413349200.

This study has been submitted to the South Metropolitan Health Service Human Research Ethics and Governance Committee.

Reviewing HREC approving this research:

South Metropolitan Health Service Human Research Ethics Committee
Contact person: Ethics Coordinator Phone: 08 6152 2064.
Email: smhs.hrec@health.wa.gov.au

If you have any concerns about the conduct of the study or your rights as a research participant, please let us know. We will be very glad to answer your queries.
For matters relating to research at the site at which you are participating, the details of the local site complaints person are: Manager, South Metropolitan Health Service Research Support and Development Unit by email SMHS.RGO@health.wa.gov.au or phone 08 6152 3214.

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

CONSENT FORM

Primary care adherence to heart failure guidelines in the diagnosis, evaluation & routine management (PATHFINDER) of heart failure Study.

Principal Investigator: Associate Professor Andrew Maiorana, Allied Health Dept. and Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital

I, …….. agree to participate in the above study. I have read and understood the attached information sheet and I have retained a copy of the signed document. I have been given the opportunity to ask questions about the study by the Investigator. I understand that I may withdraw from the study at any time without affecting any future medical treatment, or the treatment of the condition which is the subject of the study.

Signed _____ **Date** _____

Signature _____ **Date** _____

of person obtaining consent

Name _____

of person obtaining consent

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

GPs address

Dear Dr.

Re: **P**rimary care **A**dherence **T**o **H**eart **F**ailure guidelines **IN D**iagnosis, **E**valuation and **R**outine management (PATHFINDER) Research Project

Patient details – name, DOB, address, URMN

The above patient under your care has recently consented to participate in the PATHFINDER Research Project being undertaken by Fiona Stanley Hospital (FSH) and has been allocated to the intervention group.

What is the PATHFINDER project? The aim of PATHFINDER is to support GPs in the delivery of guideline advocated management for patients with heart failure.

What is involved for patients? Patients hospitalised with heart failure will be encouraged to book 3 follow-up appointments with their GP over 3 months, as part of their routine care (reminders will be provided by the research team).

What is involved for GPs? At each appointment the patient will provide the GP with a form to help guide heart failure follow up care involving clinical assessment, medication titration, and further management actions. These appointments will be undertaken under the GP's normal consultation items and can be done by telehealth if required. Please fax the form back to FSH on the number below.

What support is provided for GPs? A Heart Failure Medication Titration Problem Solving Guide is provided on the rear of the follow-up form. The PATHFINDER Project also provides a helpline (**0480111493,** Mon – Fri, 8am-4pm) for GPs to contact if they are seeking guidance related to heart failure management. The helpline is staffed by a Specialist Heart Failure Nurse Practitioner supported by a Cardiologist from the Advanced Heart Failure Service at FSH.

We would be grateful if you could incorporate the attached PATHFINDER follow-up form into this appointment by completing the actions in yellow and return the form by fax to 61524888.

Thank you for your support of this important initiative.

Yours sincerely,

Dr Amit Shah, Cardiologist
Advanced Heart Failure and Cardiac Transplant Service, Fiona Stanley Hospital

Helpline: 0480111493 (Mon-Fri, 8am-4pm) Fax: 61524888

PATHFINDER

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PATHFINDER Study Follow-up Form

[Sticker]

GP Visit: 1 week Post Discharge

Please complete the sections in yellow and return this form to:
Fax: 61524888 or Email: fsh.ahfcts@health.wa.gov.au

See overleaf for Heart Failure Medication Titration Problem Solving guide.

Dial 0480111493 if you require further guidance with medication titration or enacting an action plan for this patient.

A. Assessment

Dry weight (at discharge)	Weight	HR	BP	Symptom:
kg	_____kg	_____bpm	_____mmHg	□ NA □ Dyspnoea □ Dizziness □ Fatigue Other _____.

B. Please titrate HF Medications

Drug Class	Medication Name	Current dose	Target dose#	Guideline-recommended medication titration plan	Dose after the current appointment
ACEI/ ARB/ ARNI*				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
Beta-blocker				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
MRA*				Commence with 25mg daily. Up-titrate in 4 to 8 weeks aiming for target dose for 50mg.	□ _____ mg □ OD □ BD □ Cease medication
Diuretics			Variable dose with no target	Adjust according to clinical assessment.	□ _____ mg □ OD □ BD □ Cease medication

#Target dose approved by PATHFINDER Cardiologist:

Name: ..... **Signature:** .....

* Kidney function test and electrolytes should be checked 1 week after commencing or titrating dose of ACEI/ARB/ARNI/MRA

C. Further actions

Is any further action required for this patient at this time?

☐ No further action needed

☐ GP review within a week

☐ Refer to Emergency Department

☐ Refer to a Cardiologist

☐ Refer to Allied Health Professional (i.e. Chronic Disease Management Plan)

☐ Other: _____.

GP Name: ..... **Signature:** ..... **Date:** .....

PATHFINDER

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

Heart Failure Medication Titration Problem Solving Guide

NSAIDS or COX-2 inhibitors are contraindicated in patients with heart failure. Avoid negatively inotropic calcium channel blockers (verapamil, diltiazem) in patients with heart failure with reduced ejection fraction (HFrEF).

Hypotension

- **Asymptomatic hypotension** does not usually require any change in therapy (systolic BP 90–100 mmHg)
- **Symptomatic hypotension** (dizziness, light-headedness and/or confusion):

I. Stop or reduce calcium - channel blockers and/or other vasodilators unless essential e.g. for angina

II. Consider reducing diuretic dose if there are no signs or symptoms of congestion

III. Temporarily reduce ACEI / ARB / ARNI or beta-blocker dose if above measures do not work

IV. Review patient as clinically appropriate within one week and seek specialist advice if the above measures do not work

Severe symptomatic hypotension or shock requires immediate referral to an emergency department

Worsening renal function

- ACEI /ARB are generally well tolerated even in patients with renal impairment (eGFR less than 30mL/min). Use ARNI with caution in patients with eGFR less than 30mL/min.
- Heart failure patients are more vulnerable to acute renal failure following a destabilising event such as a dehydrating illness or over-diuresis or addition of nephrotoxic medications.
  NB. Advise patients experiencing such an event to seek urgent medical attention and to stop the ACEI / ARB / ARNI until clinically reviewed and blood chemistry is checked.
- Some rise in urea, creatinine and serum K+ is expected after commencing an ACEI / ARB / ARNI. Blood chemistry must be checked one week after commencing or titrating dose and monitored closely there after to ensure kidney function is not worsening.
- An eGFR decrease of up to 30% is acceptable provided it stabilises within 2 weeks. Check serum K+, creatinine and urea within 48 hours if required.
- If the eGFR declines more than 30%, the patient should be reviewed urgently for clinical assessment of volume status and review of nephrotoxic medications. Seek specialist advice regarding the safety of continuing therapy.

Caution: eGFR may over estimate renal function in low body weight individuals and does not reflect accurate renal function in individuals with fluctuating creatinine levels.

Hyperkalaemia

Careful serum K+ monitoring is required with ACEI / ARB / ARNI and MRA. Urgently check serum K+, creatinine and urea if patient is dehydrated or septic. If serum K+ rises to:

I. 5.0–5.5 mmol/L, review and reduce K+ supplements or retaining agents (e.g. amiloride, spironolactone, eplerenone)

II. 5.6–5.9 mmol/L, cease all K+ supplements or retaining agents

III. 6 mmol/L or greater, immediately seek specialist advice

Bradycardia

- Where heart rate is less than 50 beats per minute, and the patient is on a beta-blocker, review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist; and arrange ECG to exclude heart block
- Consider reduction of beta-blocker where there is marked fatigue or symptomatic bradycardia

Congestion or peripheral oedema

Suggested actions when congestion or peripheral oedema is worsening:

- Increase the diuretic dose and then consider halving the dose of beta-blocker
- Liaise with the heart failure service and review the patient daily or weekly (as appropriate)
- Seek specialist advice if symptoms do not improve; and, if there is severe deterioration, refer patient to an emergency department immediately.

Angioedema and cough

I. Angioedema, although rare, can occur at any time when using ACEI / ARB / ARNI. Actions include:

- Stop ACEI / ARB / ARNI immediately
- Seek specialist advice where angioedema occurs with an ACEI before trialling ARB due to possible cross-sensitivity
- Avoid ARNI where angioedema is due to ACEI / ARB

II. Cough is common in patients with heart failure. Actions include:

- Exclude pulmonary oedema as a cause if cough is new or worsening
- Consider if cough is caused by ACEI or other drugs and only discontinue drug if cough is not tolerable
- Consider substituting ACEI with an ARB if the cough is troublesome or interferes with sleep

Reference: Qld Health HF Medication Titration Plan, https://www.health.qld.gov.au/__data/assets/pdf_file/0018/428121/Medn_Titration.pdf (Last accessed date: 04-Feb-2021)

The current Australian Heart Failure Management Guidelines are available at:
https://www.heartlungcirc.org/article/S1443-9506(18)31777-3/fulltext

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PATHFINDER Study Follow-up Form

[Sticker]

GP Visit: 4 week Post Discharge

Please complete the sections in yellow and return this form to:
Fax: 61524888 or Email: fsh.ahfcts@health.wa.gov.au

See overleaf for Heart Failure Medication Titration Problem Solving guide.

Dial 0480111493 if you require further guidance with medication titration or enacting an action plan for this patient.

D. Assessment

Dry weight (at discharge) _____kg	Weight _____kg	HR _____bpm	BP _____mmHg	Symptom: □ NA □ Dyspnoea □ Dizziness □ Fatigue Other _____.

E. Please titrate HF Medications

Drug Class	Medication Name	Current dose	Target dose#	Guideline-recommended medication titration plan	Dose after the current appointment
ACEI/ ARB/ ARNI*				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
Beta-blocker				Start at the low dose. Up-titrate by doubling the dose every 2 to 4 weeks.	□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
MRA*				Commence with 25mg daily. Up-titrate in 4 to 8 weeks aiming for target dose for 50mg.	□ _____ mg □ OD □ BD □ Cease medication
Diuretics			Variable dose with no target	Adjust according to clinical assessment.	□ _____ mg □ OD □ BD □ Cease medication

#Target dose approved by PATHFINDER Cardiologist:

Name: ..... **Signature:** .....

* Kidney function test and electrolytes to be checked 1 week after commencing or titrating dose of ACEI/ARB/ARNI/MRA

F. Further actions

Is any further action required for this patient at this time?

☐ No further action needed

☐ GP Review within a week

☐ Refer to Emergency department

☐ Refer to a Cardiologist

☐ Refer to Allied Health Professional (i.e. Chronic Disease Management Plan)

☐ Other: _____.

GP Name: ..... **Signature:** ..... **Date:** .....

PATHFINDER

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

Heart Failure Medication Titration Problem Solving Guide

NSAIDS or COX-2 inhibitors are contraindicated in patients with heart failure. Avoid negatively inotropic calcium channel blockers (verapamil, diltiazem) in patients with heart failure with reduced ejection fraction (HFrEF).

Hypotension

- **Asymptomatic hypotension** does not usually require any change in therapy (systolic BP 90–100 mmHg)
- **Symptomatic hypotension** (dizziness, light-headedness and/or confusion):

I. Stop or reduce calcium - channel blockers and/or other vasodilators unless essential e.g. for angina

II. Consider reducing diuretic dose if there are no signs or symptoms of congestion

III. Temporarily reduce ACEI / ARB / ARNI or beta-blocker dose if above measures do not work

IV. Review patient as clinically appropriate within one week and seek specialist advice if the above measures do not work

Severe symptomatic hypotension or shock requires immediate referral to an emergency department

Worsening renal function

- ACEI /ARB are generally well tolerated even in patients with renal impairment (eGFR less than 30mL/min). Use ARNI with caution in patients with eGFR less than 30mL/min.
- Heart failure patients are more vulnerable to acute renal failure following a destabilising event such as a dehydrating illness or over-diuresis or addition of nephrotoxic medications.
  NB. Advise patients experiencing such an event to seek urgent medical attention and to stop the ACEI / ARB / ARNI until clinically reviewed and blood chemistry is checked.
- Some rise in urea, creatinine and serum K+ is expected after commencing an ACEI / ARB / ARNI. Blood chemistry must be checked one week after commencing or titrating dose and monitored closely there after to ensure kidney function is not worsening.
- An eGFR decrease of up to 30% is acceptable provided it stabilises within 2 weeks. Check serum K+, creatinine and urea within 48 hours if required.
- If the eGFR declines more than 30%, the patient should be reviewed urgently for clinical assessment of volume status and review of nephrotoxic medications. Seek specialist advice regarding the safety of continuing therapy.

Caution: eGFR may over estimate renal function in low body weight individuals and does not reflect accurate renal function in individuals with fluctuating creatinine levels.

Hyperkalaemia

Careful serum K+ monitoring is required with ACEI / ARB / ARNI and MRA. Urgently check serum K+, creatinine and urea if patient is dehydrated or septic. If serum K+ rises to:

I. 5.0–5.5 mmol/L, review and reduce K+ supplements or retaining agents (e.g. amiloride, spironolactone, eplerenone)

II. 5.6–5.9 mmol/L, cease all K+ supplements or retaining agents

III. 6 mmol/L or greater, immediately seek specialist advice

Bradycardia

- Where heart rate is less than 50 beats per minute, and the patient is on a beta-blocker, review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist; and arrange ECG to exclude heart block
- Consider reduction of beta-blocker where there is marked fatigue or symptomatic bradycardia

Congestion or peripheral oedema

Suggested actions when congestion or peripheral oedema is worsening:

- Increase the diuretic dose and then consider halving the dose of beta-blocker
- Liaise with the heart failure service and review the patient daily or weekly (as appropriate)
- Seek specialist advice if symptoms do not improve; and, if there is severe deterioration, refer patient to an emergency department immediately.

Angioedema and cough

I. Angioedema, although rare, can occur at any time when using ACEI / ARB / ARNI. Actions include:

- Stop ACEI / ARB / ARNI immediately
- Seek specialist advice where angioedema occurs with an ACEI before trialling ARB due to possible cross-sensitivity
- Avoid ARNI where angioedema is due to ACEI / ARB

II. Cough is common in patients with heart failure. Actions include:

- Exclude pulmonary oedema as a cause if cough is new or worsening
- Consider if cough is caused by ACEI or other drugs and only discontinue drug if cough is not tolerable
- Consider substituting ACEI with an ARB if the cough is troublesome or interferes with sleep

Reference: Qld Health HF Medication Titration Plan, https://www.health.qld.gov.au/__data/assets/pdf_file/0018/428121/Medn_Titration.pdf (Last accessed date: 04-Feb-2021).

The current Australian Heart Failure Management Guidelines are available at:
https://www.heartlungcirc.org/article/S1443-9506(18)31777-3/fulltext

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

PATHFINDER Study Follow-up Form

[Sticker]

GP Visit: 3 month Post Discharge

Please complete the sections in yellow and return this form to:
Fax: 61524888 or Email: fsh.ahfcts@health.wa.gov.au

See overleaf for Heart Failure Medication Titration Problem Solving guide.

Dial 0480111493 if you require further guidance with medication titration or enacting an action plan for this patient.

G. Assessment

Dry weight (at discharge) _____kg	Weight _____kg	HR _____bpm	BP _____mmHg	Symptom: □ NA □ Dyspnoea □ Dizziness □ Fatigue Other _____.

H. Please titrate HF Medications

Drug Class	Medication Name	Current dose	Target dose#	Dose recommended by PATHFINDER cardiologist#	Dose after the current appointment
ACEI/ ARB/ ARNI*					□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
Beta-blocker					□ _____ mg □ OD □ BD □ Maximum-tolerated □ Cease medication
MRA*					□ _____ mg □ OD □ BD □ Cease medication
Diuretics			Variable dose with no target	Adjust according to clinical assessment.	□ _____ mg □ OD □ BD □ Cease medication

 # Target dose and recommended dose approved by PATHFINDER Cardiologist:

Name: ..... **Signature:** .....

* Kidney function test and electrolytes to be checked 1 week after commencing or titrating dose of ACEI/ARB/ARNI/MRA

I. Further actions

Is any further action required for this patient at this time?

☐ No further action needed

☐ GP Review within a week

☐ Refer to Emergency department

☐ Refer to a Cardiologist

☐ Refer to Allied Health Professional (i.e. Chronic Disease Management Plan)

☐ Other: _____.

Government of **Western Australia**
Department of **Health**

FIONA STANLEY hospital

Heart Failure Medication Titration Problem Solving Guide

NSAIDS or COX-2 inhibitors are contraindicated in patients with heart failure. Avoid negatively inotropic calcium channel blockers (verapamil, diltiazem) in patients with heart failure with reduced ejection fraction (HFrEF).

Hypotension

- **Asymptomatic hypotension** does not usually require any change in therapy (systolic BP 90–100 mmHg)
- **Symptomatic hypotension** (dizziness, light-headedness and/or confusion):

I. Stop or reduce calcium - channel blockers and/or other vasodilators unless essential e.g. for angina

II. Consider reducing diuretic dose if there are no signs or symptoms of congestion

III. Temporarily reduce ACEI / ARB / ARNI or beta-blocker dose if above measures do not work

IV. Review patient as clinically appropriate within one week and seek specialist advice if the above measures do not work

Severe symptomatic hypotension or shock requires immediate referral to an emergency department

Worsening renal function

- ACEI /ARB are generally well tolerated even in patients with renal impairment (eGFR less than 30mL/min). Use ARNI with caution in patients with eGFR less than 30mL/min.
- Heart failure patients are more vulnerable to acute renal failure following a destabilising event such as a dehydrating illness or over-diuresis or addition of nephrotoxic medications.
  NB. Advise patients experiencing such an event to seek urgent medical attention and to stop the ACEI / ARB / ARNI until clinically reviewed and blood chemistry is checked.
- Some rise in urea, creatinine and serum K+ is expected after commencing an ACEI / ARB / ARNI. Blood chemistry must be checked one week after commencing or titrating dose and monitored closely there after to ensure kidney function is not worsening.
- An eGFR decrease of up to 30% is acceptable provided it stabilises within 2 weeks. Check serum K+, creatinine and urea within 48 hours if required.
- If the eGFR declines more than 30%, the patient should be reviewed urgently for clinical assessment of volume status and review of nephrotoxic medications. Seek specialist advice regarding the safety of continuing therapy.

Caution: eGFR may over estimate renal function in low body weight individuals and does not reflect accurate renal function in individuals with fluctuating creatinine levels.

Hyperkalaemia

Careful serum K+ monitoring is required with ACEI / ARB / ARNI and MRA. Urgently check serum K+, creatinine and urea if patient is dehydrated or septic. If serum K+ rises to:

I. 5.0–5.5 mmol/L, review and reduce K+ supplements or retaining agents (e.g. amiloride, spironolactone, eplerenone)

II. 5.6–5.9 mmol/L, cease all K+ supplements or retaining agents

III. 6 mmol/L or greater, immediately seek specialist advice

Bradycardia

- Where heart rate is less than 50 beats per minute, and the patient is on a beta-blocker, review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist; and arrange ECG to exclude heart block
- Consider reduction of beta-blocker where there is marked fatigue or symptomatic bradycardia

Congestion or peripheral oedema

Suggested actions when congestion or peripheral oedema is worsening:

- Increase the diuretic dose and then consider halving the dose of beta-blocker
- Liaise with the heart failure service and review the patient daily or weekly (as appropriate)
- Seek specialist advice if symptoms do not improve; and, if there is severe deterioration, refer patient to an emergency department immediately.

Angioedema and cough

I. Angioedema, although rare, can occur at any time when using ACEI / ARB / ARNI. Actions include:

- Stop ACEI / ARB / ARNI immediately
- Seek specialist advice where angioedema occurs with an ACEI before trialling ARB due to possible cross-sensitivity
- Avoid ARNI where angioedema is due to ACEI / ARB

II. Cough is common in patients with heart failure. Actions include:

- Exclude pulmonary oedema as a cause if cough is new or worsening
- Consider if cough is caused by ACEI or other drugs and only discontinue drug if cough is not tolerable
- Consider substituting ACEI with an ARB if the cough is troublesome or interferes with sleep

Reference: Qld Health HF Medication Titration Plan, https://www.health.qld.gov.au/__data/assets/pdf_file/0018/428121/Medn_Titration.pdf (Last accessed date: 04-Feb-2021)

The current Australian Heart Failure Management Guidelines are available at:
https://www.heartlungcirc.org/article/S1443-9506(18)31777-3/fulltext

Please return the form by fax to 61524888.

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet	2

		registered, name of intended registry	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	11
Funding	#4	Sources and types of financial, material, and other support	11
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 11
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a, no sponsor
Roles and responsibilities: sponsor and funder	#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	n/a, no sponsor
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data	n/a

		management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
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	2,3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3
Objectives	#7	Specific objectives or hypotheses	3
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, non-inferiority, exploratory)	3
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community	3

		clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	
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)	5
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5,6
Interventions: modifications	#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)	6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	6
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	5,6
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric	6-8

		(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	
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)	3,4
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	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	3
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers),	5

generation		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	
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	5
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	5
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a, open-blinded to participants and the practitioner delivering the intervention
Methods: Data collection,			

management, and analysis			
Data collection plan	#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	6,9
Data collection plan: retention	#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	9
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	9
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where	9

		other details of the statistical analysis plan can be found, if not in the protocol	
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	n/a
Statistics: analysis population and missing data	#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)	9
Methods: **Monitoring**			
Data monitoring: formal committee	#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	n/a, open-blinded, small sample size, intervention component is evidence-based and not invasive, short study duration
Data monitoring: interim analysis	#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	n/a, open-blinded, small sample size, intervention component is evidence-based and not invasive, short

			study duration
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	7
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a, audit by the ethic committee or governance
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11
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)	11
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological	n/a

		specimens in ancillary studies, if 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	9
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	11
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	9
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	n/a
Dissemination policy: trial results	#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	11
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a, no plan for use of professional writers

Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Reference to appendix
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	n/a