STUDY PROTOCOL AND ANALYSIS PLAN

Version 5.0

# Feasibility of Cardiac rehabilitation in Patients with Heart Failure at the Moi Teaching and Referral Hospital

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## Study design

This was an observational mixed methods study design involving quantitative and qualitative assessments of study participants enrolled into two different models of cardiac rehabilitation represented by two study arms, namely, institution based cardiac rehabilitation (IBCR), and home based cardiac rehabilitation (HBCR). After tracking a baseline adverse event rate in the study population, the study protocol was modified to incorporate an observational arm (OA) amongst whom there was no intervention beyond usual care.

## Sample size determination

We planned to enroll a total of 100 subjects based on a reasonable estimate of expected subject recruitment over the time frame of the study as well as anticipated facility capacity. Twenty-five participants were enrolled into the IBCR arm and seventy-five participants into the HBCR arm in consideration of the potentially larger population and a wider geographical spread of HBCR.

## Study Population

Patients with heart failure as defined by symptomatic shortness of breath with exertion and documented record of the diagnosis of heart failure in the patient's medical records, were identified from screening of patient records and clinic attendance registers. Study participants were then voluntarily recruited using a convenience sampling approach.

### Inclusion Criteria

1. NYHA Class II or III heart failure
2. Have had an echocardiographic study in the past 5 years
3. Owns a mobile telephone
4. Can participate in exercise
5. Can read/ primary care giver can read in English or Kiswahili
6. Can travel to hospital three times a week

### Exclusion Criteria

1. Recent acute illness requiring hospitalization or initiation of new cardiac medication in the preceding 4 weeks
2. Limitation of activity because of factors other than fatigue or exertional dyspnea, such as arthritis, claudication in the legs, angina, advanced comorbidities
3. Known arrhythmia
4. Heart failure due to congenital heart disease
5. Pregnant patients by patient report or urine pregnancy tests
6. Heart failure due to obstructive cardiomyopathy including mitral stenosis and aortic stenosis
7. Presence of implanted pacemaker

# Procedures

All study procedures were approved by the ethical review boards at Duke University and Moi University

## Initial evaluation, safety screening and enrollment

After giving informed consent, screening logs were used to collect general demographic data and basic medical history. Participant anthropometric measurements were recorded and screening for coronary artery disease was conducted using the Master's two step test. This test served as an additional safety assessment of participant's physical ability to participate in cardiac rehabilitation.

Upon successful completion of the safety screen, participants were enrolled into the study by electing to enter one of two study arms. Entry into either arm was on a rolling basis based on study participant preference. Each study arm would fill up its allotted slots on a "first come first served" basis.

## Establishment of baseline exercise capacity and step rate

Enrolled participants were oriented to the exercise equipment and taught how to rate their perceived exertion using the Borg rate of perceived exertion scale (1). Their aerobic threshold target heart rate was calculated using the Karvonen formula(2,3). Participants were asked to walk on a treadmill starting at a level gradient and speed of 1km/h. The speed was gradually increased by 0.05km/h at three-minute intervals until attainment of their aerobic threshold (AT). AT was measured as the earlier of attainment of target heart rate or attainment of moderate perceived rate of exertion as reflected on the Borg scale. Upon attainment of aerobic threshold, the participants step rate would be computed as the number of steps covered in one minute at the participants AT speed level.

## Exercise prescription

For each participant, an exercise prescription was then generated. The prescription comprised characterization of the exercise type, duration and intensity, tailored to match the participants baseline exercise capacity and their interventional arm.

## Institutional based rehabilitation (IBCR)

IBCR sessions comprised 36 individually tailored rehabilitation sessions of aerobic activity. The exercise intensity was incremental and focused on achievement of the earlier of AT as measured using the Borg scale or target heart rate using Karvonen's formula while exercising on a treadmill or cycle ergometer. During the first 4 weeks target heart rate was set to 50-60% of max HR. During week 5-8 target heart rate was increased to 60-70% of their max HR and during week 8-12, 70- 80% of their max HR. Duration of aerobic exercise was also increased by 5- 10 minutes with each session with a goal of attaining 60 minutes of aerobic exercise by the end of 36 sessions.

## Home based CR (HBCR)

HBCR comprised 12 individualized weekly step targets. Participants were instructed to set aside a daily, convenient time when they would exercise by brisk walking. Participants were taught how to assess moderate exertion based on interval measurements of their heart rates and sensation of moderate exertion as trained during establishment of their baseline step rate. The first weekly step goal was imputed from their step rate at AT multiplied by 140 representing a 20 min target duration of exercise walking for 7 days. Subsequent increments were based on a 10% increment on the preceding week's step goal. Walking distance was measured with the aid of a pedometer issued to participants who were also instructed to log daily readings from the pedometer. Some subjects (see appendix 6.3) received

thrice weekly calls to match contact frequency with participants in the IBCR arm. Participants were evaluated in clinic every 4 weeks for functional capacity and to download data from their pedometers and track their individual logs.

## Observational arm (OA)

A subset of HBCR participants were enrolled into the observational (usual care arm) to characterize the underlying risk profile for heart disease amongst the study population. Participants were informed about the known benefits of exercise, but no weekly exercise targets were prescribed. Participants were given pedometers that track their activity levels and asked to come for a follow up every 4$^{th}$ week for three months in a comparable fashion to participants in the active rehabilitation. During these visits monitoring data from their pedometers was downloaded into a database and functional assessments were conducted.

## Participant questionnaires

Enrolled participants were guided through two standardized questionnaires: the PHQ9 depression screening questionnaire (4,5) and the SF36 quality of life questionnaire (6–8). These were administered at the start of the rehabilitation protocol and at the end of the 3-month follow up period.

## Focus group discussions

Upon completion of the cardiac rehabilitation protocol, participants were invited to participate in focus group. Three groups comprising 4-6 study participants were invited as follows:

- Group 1 – Participants in the institution based cardiac rehabilitation (IBCR) arm who adhered to the study protocol,
- Group 2 – Participants in the home based cardiac rehabilitation (HBCR) arm who adhered to the study protocol, and
- Group 3 – Participants from both IBCR and HBCR arms who did not who adhere to the study protocol

Discussions were led by a moderator using a guide as shown in the appendixes, and audio recordings of the discussion were stored on the study computer. The discussions explored study participant perspectives and understanding of heart failure, their cardiac rehabilitation experience, barriers to participation in cardiac rehabilitation and potential areas for improvement.

# Measures

## Primary outcome measure

Feasibility of cardiac rehabilitation in this study was measured based on ability of participants to adhere to at least 25% of scheduled activities on their cardiac rehabilitation protocol. For participants in the IBCR arm, adherence was measured as a proportion of subjects recruited who participated in at least 9 of 36 prescribed rehabilitation sessions and attained pre-defined exercise targets. In the HBCR arm, this was measured as a proportion of subjects who completed at least 3 of their 12 weekly exercise prescriptions of HBCR. Completion of the exercise prescriptions was self-reported via phone and validated at monthly visits based on data downloaded from pedometer devices.

## Secondary outcome measures

The study also sought to assess other outcome measures including potential benefits of cardiac rehabilitation, that would offer greater insight into feasibility of the intervention. Functional capacity assessment was conducted at enrollment using a six-minute walk time distance test(9). This measure was repeated monthly for all study participants. Depression screening was conducted using a PHQ9 screening questionnaire (5) and repeated at the end of the rehabilitation session. Quality of living was also measured using a SF 36 questionnaire (7,8) at the start and at the end of the rehabilitation protocol.

# Analysis

Study data were collected and managed using REDCap electronic data capture tools hosted at Duke University(10). Summary statistics and analysis of quantitative data was conducted using STATA software V.14. Numeric data were expressed as number (percent), means (standard deviation [SD]) or median (interquartile range [IQR]). For comparisons, we used paired t-tests for continuous variables.

Qualitative data from focus group discussions were manually transcribed and translated into English. Data was entered into a web-based analysis platform, Dedoose V 8.3. Using a deductive constant comparison approach as described by Onuwegbuzie et al (11,12), each focus group discussion transcript was reviewed and codes assigned to excerpts. The codes were then grouped into categories and summarized as themes.

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