OPeRA-HF study design (Risk Arm): an **O**bservational study to assess and **Pre**dict the in-patient course, risk of **R**e-**A**dmission and mortality for patients hospitalised for or with **H**eart **F**ailure

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Background:

Heart failure (HF) is a complex syndrome, the final common pathway of many different pathological processes and usually accompanied by other serious co-morbid conditions. It is a common reason for urgent hospitalisation. The subsequent health trajectory of such patients discharged after an admission for HF is variable. Identifying those patients at high risk of re-admission or death and understanding the causes could improve discharge planning and the targeting of monitoring and community support. At present, there is no robust model for clinical practice.

Previous risk models of HF re-admission or death have usually been derived from registries or clinical trial data; have shown limited predictive accuracy and their results have not been reproduced. They have also focused on clinical and demographic variables with little attention to the effects of frailty, cognitive function, mood, social network, deprivation and lifestyle. Very few models have made use of repeated measurements during an admission. Designing or identifying a model that can characterise patients with HF in order to predict those at highest risk of (cardiovascular) re-admission and death could make a substantial difference to care by facilitating management tailored to the individual patient.

Study design:

A prospective observational study collecting demographic, clinical and psycho-social data during hospital admission, in-patient stay and pre discharge timeframes. The study consists of two components: in-patient monitoring (see separate poster) and risk stratification (this poster).

PANEL A: Study aims (Risk stratification arm)

(1) To establish the causes of admission or re-admission of patients with HF to the Hull & East Yorkshire Hospitals NHS Trust and classify them according to primary and contributory causes, severity, urgency and whether they were avoidable or appropriate.

(2) To identify the primary reason and contributory factors to death within the first 6 months after discharge, including the events leading up to death and the place of death

(3) To develop one or more risk stratification models to identify patients with HF at high risk of early death and re-admission, who are in need of intensive support and early hospitalisation and to identify those at very low risk who could be discharged early. Importantly, unlike conventional prognostic models of HF, information on measures of patient-frailty, cognition and social support network will be collected. This will create a holistic picture of the challenges facing patients with HF and the services required to support them.

(4) To use the data captured in this study to validate previously published risk models.

Measurement	Enrolment*	Pre-Discharge	Discharge
Demographics and socio-economic status	X		
Clinical and family history	X		
HF related symptoms (e.g. breathlessness, orthopnoea, nocturnal dyspnoea, chest pain, etc)	X		
Lifestyle	X		
Quality of sleep	X		
Mood and cognitive function	X		
Medication and devices e.g. CRT, ICD	X		
Social deprivation and support	X		
Admission procedures performed / discharge details	X		X
Results of ECG, Echo (if available)	X		X
Frailty test result (if available)	X		
Prediction of outcome (clinician/patient perceived)	X		X
Mobility tests – 50m corridor walk test	X	X	
Vital signs: Blood pressure lying/standing, heart rate, height and weight, presence of lung and peripheral oedema jugular venous pressure, transcutaneous arterial oxygen saturation, lung function	X	X	
Routine haematology/biochemistry blood tests	X	X	X
Charlson co-morbidity index score (where recorded)	X		
Questionnaires: Berlin Sleep, Hospital Anxiety & Depression Scale, HF Knowledge, Dutch HF Knowledge and EQ-5D	X		
Bio-impedance	X	X	

*(3-7 days after admission)

Table 1: Measurement schedule

PANEL B: Inclusion and exclusion criteria

Inclusion criteria: (a) Age > 18 years; (b) In hospital; (c) Usual residence is in the catchment region for Hull & East Yorkshire Hospitals NHS Trust; (d) Either treated with loop diuretics or with a clinical diagnosis of HF (prior research has shown that patients treated with loop diuretics have a similar prognosis to patients with HF, suggesting that the diagnosis of HF may often be over-looked.); (e) Willing and able to consent.

Exclusion criteria: Unable to understand and comply with the protocol or to give informed consent

Study design (continued):

Patients with a confirmed diagnosis of HF will be invited to take part in both parts of the study. Patients can choose just to enrol in the risk stratification element only as this is less intensive. Patient written consent will be obtained by a doctor or research nurse. Ethics approval was sought and granted in October 2012.

The study aims are shown in ***Panel A*** and the inclusion and exclusion criteria in ***Panel B***.

Study methods:

Data Collection:

Patients will be enrolled into the study in the post-acute phase of their care, generally 3-7 day after admission. Data will be collected at enrolment and on or close to the day of discharge. A summary of the data to be collected at enrolment, prior to discharge and at discharge is shown in ***Table 1***.

The primary end-points for model development will be death or re-admission for (a) any reason, (b) cardiovascular disease (c) worsening HF at (i) 30-days, (ii) 6-months and (iii) 1-year.

Patient follow-up:

Patients will be followed according to their consultant's instructions. They may be discharged back to their General Practitioner or followed up in a medical, cardiology or HF clinic. Follow up will be for up to ten years after the last patient is enrolled.

The information collected will be used to investigate the utility of previously published models to determine the incremental value of a new model derived from these data. Existing models that may be validated are shown in ***Table 2.***

Study / Data set used / End-point	Model type & Variables in model
Fonarow (2005) / ADHERE / In-hospital mortality	Logistic regression model: *BUN, systolic BP, heart rate, age* // CART model: *BUN, systolic BP, creatinine*
O'Connor (2012) / PROTECT / Combined death, WHF, or re-hospitalization for HF within 7 days of index admission	Cox-regression model: *BUN, respiratory rate, systolic BP, heart rate, albumin, cholesterol, diabetes, prior HF hospitalisation*
O'Connor (2008) / OPTIMIZE-HF / All-cause mortality after discharge	Cox regression model: *Admission: systolic BP, age, weight, reactive airway disease, depression, sodium, creatinine, liver disease, lower-limb oedema; Discharge: statin, beta-blocker, creatinine, systolic BP*
Combined mortality or re-hospitalisation after discharge	Logistic regression model: *Admission: systolic BP, creatinine, haemoglobin, taking a nitrate/digoxin/diuretic, history of COPD, prior CVA/TIA, HF hospitalisation in last 6 months ;During admission: coronary angiography / mechanical ventilation / ICD implant; Discharge: statin/ACEi/ARB*
Pocock (2006) / CHARM / All-cause mortality	Cox regression model: *Age, LVEF, diabetes, BMI, female, NYHA, current smoker, BBB, cariomegaly, prior HF hospitalisation <6-months, diastolic BP, diagnosis of HF >2years, prior MI, dependent oedema, heart rate, pulmonary crackles, pulmonary oedema, AF, resting dyspnoea, candesartan (vs placebo).*
Combined mortality & re-hospitalisation	Cox-regression model: *Age, diabetes, LVEF, prior HF hospitalisation <6-month, cardiomegaly, diagnosis of HF >2 years, NYHA class, diastolic BP, BBB, heart rate, candesartan (vs placebo), dependent oedema, pulmonary crackles, female, AF, BMI, mitral regurgitation, previous MI, pulmonary oedema, current smoker*
Felker (2004) / OPTIME-CHF / 60-day mortality	Logistic regression model: *Age, NYHA, systolic BP, BUN, sodium*
Combined 60-day mortality or re-hospitalisation	Logistic regression model: *Prior HF admission <12-months, systolic BP, BUN, haemoglobin, history of PCI*
Chin & Goldman (1997) / Routine clinic / 60-day mortality	Cox regression model: *diabetes, admission systolic BP, non-sinus rhythm*
Combined 60-day mortality or re-hospitalisation	Cox regression model: *Admission systolic BP, no ST wave changes, Charlson's co-morbidity score (22 conditions), single*
Krumholz (2000) / Routine clinic / All-cause re-admission	Cox regression model: *Creatinine, hospitalisation in last year, HF admission history, diabetes*
Keenan (2008) / CMS Medical / 30-day all-cause re-admission	Logistic regression: *Gender, age, history of CABG, plus 34 co-morbidities from CMS medical hierarchical condition categories*

Table 2: Some of the risk models to be validated using the OPERA-HF study data

	Valid n	N (%) Median [25th – 75th]
Age (years)	42	74 [65 – 80]
Male (%)	43	33 (77%)
Clinical History		
Myocardial Infarction	42	13 (31 %)
CVA/TIA	40	2 (5%)
Peripheral vascular disease	38	1 (2.6%)
Device (ICD, PPM, CRT, CRT-D)	42	9 (21.4%)
Lung disease (COPD, Asthma, etc)	42	14 (33.3%)
Diabetes	42	16 (38.2%)
Chronic kidney disease	42	9 (21.4 %)
Liver disease	42	3 (7.1 %)
Gastro-intestinal disease	42	3 (7.1 %)
Joint or connective tissue disease	42	6 (14.3 %)
Cancer (inc. leukaemia lymphoma)	42	3 (7.1 %)
Examination		
Main presenting symptom	43	
Acute SOB		27 (63%)
Breathless on slight exertion		8 (19%)
Chest pain - cardiac		6 (14%)
Severe oedema		2 (5%)
Heart rate (bpm)	41	92 [76 - 117]
Heart Rhythm	42	
Sinus Rhythm		18 (42.9 %)
Atrial fibrillation		18 (42.9 %)
Other rhythm		6 (14.3 %)
Diastolic BP (mmHg)	43	75 [64 - 84]
Systolic BP (mmHg)	43	124 [109 - 133]
Worst NYHA in last 7-days	39	
Class II		3 (7.7 %)
Class III		24 (61.5 %)
Class IV		12 (30.8 %)
HF Medication		
ACE-inhibitor	39	17 (43.6 %)
Beta-blocker	39	20 (51.3 %)
Aldosterone Receptor Antagonist	38	8 (21.1 %)
Loop diuretic	39	22 (56.4 %)
Thiazide	37	2 (5.4)
Digitalis	39	8 (20.5 %)
LV-Impairment*	36	
None / Trivial		5 (14%)
Mild / Mild-to-mod / Moderate		11 (31%)
Mod-to-Sever / Severe		20 (56%)
NT-proBNP (ng/L)*	36	5862 [3303 – 11831]

Table 3: Admission characteristics of patients recruited

Results:

Forty three patients have so far been recruited. A limited set of admission characteristics for these patients are shown in ***Table 3***. Data are presented as number (percentage) for categorical variables, median (interquartile range) for continuous variables.

Conclusion:

This study will provide insight into the factors which influence re-admission after hospitalisation for HF. The data collected will result in a risk stratification model enabling the identification of patients at most risk of 30-day re-admission or death. It is envisaged that such a model will facilitate an improved discharge-planning pathway.

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