Effectiveness of out-patient based acute heart failure care: A pilot randomised controlled trial

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Short title: Acute Heart Failure IN or OUT pilot RCT

Wong K.Y.K. MA(Oxon), DM (Oxon), FRCP (Lond), PGCME (HYMS), FHEA, FESC, FACC[1,2],

Hughes D.A. [3] BPharm MSc PhD MRPharmS FFRPS FBPhS FLSW,

Debski M. [1], MD, PhD

Latt N. [1], MBBS, MRCP

Assaf O. [1] MB BCh

Abdelrahman A. [1], MBBS, MRCP

Taylor R. [1], MSc

Allgar V. PhD CStat [4],

McNeill L. [1], BA, CGMA

Howard S. [1], BA, BSc

Wong S.Y.S. [1] MBBS, FRCP,

Jones R.[1], BEd (hons).

Cassidy C. J. [1] MB ChB, FRCP

Seed A. [1] MD

Galasko G. BM BCh MA DM (Oxon) FRCP [1]

Clark A. [4], MA, MD, FRCP

Davis G.K. [6], DGM Dip Card MD MSc (Med Ed) MSc (Med L'dship) FRCP FRACP FESC FSCCT FHEA

Montasem A. [6] MSc, PhD, CPsychol

Lang C.C. BMSc (hons)., MD., FRCP (Edin)., FRCP (Lond)., FACC [7],

Kalra P.R. MA MB BChir MD FRCP [8]

Campbell R. [9], PhD

Lip G.Y.H. [10], MD

Cleland J.G.F. [9] MD, PhD

Correspondence:

Dr Kenneth Wong MA(Oxon), DM (Oxon), FRCP (Lond), PGCME (HYMS), FHEA, FESC, FACC

Department of Cardiology, Lancashire Cardiac Centre,

Blackpool Teaching Hospitals NHS Foundation Trust

Blackpool, United Kingdom

Phone- +44-1253-957783

Dr.Wong@nhs.net

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Author Affiliations

1. Blackpool Teaching Hospitals NHS Foundation Trust
2. Liverpool Centre for Cardiovascular Science, UK
3. Centre for Health Economics and Medicines Evaluation, Bangor University, UK
4. Hull York Medical School
5. Worcerstershire Acute Hospital NHS Trust
6. School of Medicine, University of Central Lancashire, Preston, UK
7. University of Dundee
8. Portsmouth Hospitals University NHS Trust
9. University of Glasgow
10. Liverpool Centre for Cardiovascular Science at University of Liverpool, Liverpool John Moores University and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom; and Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

ABSTRACT

Objectives: Acute heart failure (AHF) hospitalisation is associated with 10% mortality. Outpatient based management (OPM) of AHF appeared effective in observational studies. We conducted a pilot randomised controlled trial (RCT) comparing OPM with standard inpatient care (IPM).

Methods: We randomised patients with AHF, considered to need IV diuretic treatment for ≥2 days, to IPM or OPM. We recorded all-cause mortality, and the number of days alive and out-of-hospital (DAOH). Quality of life, mental well-being and Hope scores were assessed. Mean NHS cost savings and 95% central range (CR) were calculated from bootstrap analysis.

Follow-up: 60 days.

Results: Eleven patients were randomised to IPM and thirteen to OPM. There was no statistically significant difference in all-cause mortality during the index episode (1/11 vs 0/13) and up to 60 days follow-up (2/11 vs 2/13) [p=0.86]. The OPM group accrued more DAOH {47 [36,51] vs 59 [41,60], p=0.13}. Two patients randomised to IPM (vs 6 OPM) were readmitted [p=0.31]. Hope scores increased more with OPM within 30 days but dropped to lower levels than IPM by 60 days. More out-patients had increased total well-being scores by 60 days (p=0.04). OPM was associated with mean cost savings of £2,658 (95% CR 460 - 4,857) per patient.

*Conclusions***:** Patients with acute HF randomised to OPM accrued more days alive out of hospital (albeit not statistically significantly in this small pilot study). OPM is favoured by patients and carers and is associated with improved mental well-being and cost savings.

Introduction

Acute heart failure (AHF) is common and associated with significant morbidity and mortality [1, 2]. The risk of HF hospitalisation is currently augmented by the possibility of COVID-19 exposure. Higher mortality was observed in patients with underlying cardiovascular disease and multi-morbidity after COVID-19 infection. [3] If intravenous (IV) diuretic treatment can be safely delivered at home, and effectively reduce the need for inpatient management, or shorten hospital length of stay, this may also offer patients hope and improved mental wellbeing.

Evidence for the safety of parenteral diuretics out of hospital was suggested by observational studies [4, 5]. In a British Heart Foundation (BHF) sponsored study, involving 96 patients recruited over 2 years in 12 centres, specialist nurses were trained to administer IV diuretics out of hospital, to closely monitor the patients' response to treatment, and adjust dose as necessary. 79% of interventions achieved the desired outcome of avoiding hospital admission but only 63% achieved the target reduction in oedema and/or weight [6,7].

There is also the potential for reduction in hospital bed days with significant cost saving (about £2000 per patient). In addition, there are potential gains in terms of quality of life for patients if given a choice in their place of care, that in turn improves their sense of empowerment and ability to recover [8]. Surprisingly, the BHF observational study reported no deaths. This suggests selection bias, given that expected mortality is 7-11% for patients hospitalised with HF, according to the National HF audit. As such it remains uncertain as to whether these data are relevant for patients typically admitted for IV diuretics.

Our objective was to test the hypothesis that out-patient based management (OPM) has value over inpatient management (IPM) in reducing the number of overnight stays in hospital without compromising patient outcome. We conducted a pilot randomised controlled trial

(RCT) in order to inform the design of a larger multi-centre RCT of in-patient vs out-patient diuretic treatment of AHF.

Methods

Patients- We randomised patients with AHF, peripheral or pulmonary oedema (who no longer had a new requirement of supplementary oxygen) and who were considered to need at least two more days of IV diuretic treatment.

Patients had to have objective evidence of HF including one or all of the following: left ventricular ejection fraction <50% by any imaging modality; plasma brain natriuretic peptide (BNP) >100pg/mL within the previous two years (as per European Society of Cardiology (ESC) HF guideline 2016). The amended protocol (see below) also allows inclusion of patients with right ventricular impairment by "eyeball assessment" or tricuspid annulus plane systolic excursion (TAPSE) <16mm.

Patients were excluded if they had co-morbidities that warranted hospitalisation, e.g. atrial fibrillation with poor ventricular rate control (>140/min), significant bradycardia (<40/min), sepsis, significant anaemia (haemoglobin<80g/L), acute coronary syndrome or haemodynamically significant arrhythmia, symptomatic hypotension/ postural hypotension, creatinine > 250 umol/l, sodium <125 mmol/l, potassium <3 mmol/l, severe aortic stenosis with planned urgent in-patient surgery.

Patients were recruited from a community or inpatient setting.

Protocol amendment- At the beginning of the feasibility study, patients had to be recruited within 72 hours of presenting but we found that not to be feasible with a very low recruitment rate. We thus sought ethical permission to remove this requirement. The minor amendment to the protocol was approved and improved our recruitment rate without affecting our primary objective. The amended protocol also allows inclusion of patients with right ventricular impairment by "eyeball assessment" or tricuspid annulus plane systolic excursion (TAPSE) <16mm.

Patients were randomised to in patient management [(IPM), conventional care] or out-patient management [(OPM), at home, in the community centre or in the hospital "Furosemide lounge"]. Furosemide lounge is an ambulatory care unit within the hospital (Cardiac Day Case Unit), with facilities to administer IV diuretics, and is staffed by nurses and a doctor.

The place of care was selected based on logistical considerations, such as whether the patient could travel to the community centre or hospital "Furosemide lounge". Out-patients were given oral bumetanide to cover the weekends where IV treatment was not feasible, in accordance with the BHF observational study [6,7]. Treatments were allocated in a theoretical 1:1 ratio using mixed block randomisation. Blinding of patients and practitioners was impossible, though all parties were blinded to treatment allocation until after recruitment, consent and randomisation.

The IV furosemide dose was decided by the doctor / HF Nurse specialist. Monitoring of symptoms, blood pressure (BP), fluid status, renal function and electrolytes, medication optimisation and HF education continued as required in both IPM and OPM.

Patient data were collected throughout the index episode (defined as the period from randomisation till hospital discharge for the IPM or from randomisation till the end of the IV diuretic treatment for the OPM) and for 60 days following randomisation. All patients gave fully informed and signed consent to participate in the study which was approved by the North West - Haydock Research Ethics Committee (reference number 17/NW/0645).

Clinical outcomes

The pre-specified primary safety outcome was all-cause mortality within the index episode. The clinical effectiveness outcome was the number of full days alive and out of hospital (DAOH) within 30 days after randomisation. Treatment on the day ward as an out-patient did not count as an in-patient day. DAOH (up to 60 days) was an exploratory effectiveness outcome. [9] DAOH is an endpoint recommended by the United Kingdom (UK) Heart Failure Research Investigator network, which considered this endpoint as more relevant, capturing all episodes of hospitalisation as well as mortality (instead of time to first event). This was also endorsed by the Patient Public Involvement (PPI) group as an endpoint that the PPI group felt to be meaningful. Two or more DAOH were considered to be clinically meaningful (during 30 days follow-up).

Pre-specified secondary endpoints included rehospitalisation for HF, death from any cause, cardiovascular death within 60 days of randomisation, symptom resolution/oedema reduction/achievement of "dry weight". Duration of diuretic treatment was recorded. Costs were assessed from an NHS perspective using the Trust's patient level costing models from

financial years 2018/19 and 2019/20. Where patient level costs were unavailable, e.g. for Community visits, we used a national average cost. [See online supplement for details].

Patient-centred secondary endpoints included patient and carer satisfaction ("family and friend test"), Quality of life assessment, measured using EQ5D-5L, the Short Warwick-Edinburgh Mental Wellbeing scale (SWEMWBS) [10] and the Adult State Hope Scale [11-14] which was validated as accurate in detecting fluctuations in hope.

Statistical methods:

The trial was reported in accordance with the CONSORT statement (http://consort-statement.org/). Analysis was performed on an intention-to-treat basis.

The baseline characteristics of the study cohort were summarised as percentages, mean (SD), or median [IQR], as appropriate. Tests of equivalence of group proportions, means or medians were conducted and considered statistically significant with $p<0.05$: it was understood that the small sample size made it difficult to discern true differences between groups. For categorical values, a chi-squared test was used unless expected cell counts were <5, in which case Fisher's exact test was used. Equivalence of normally-distributed variables was tested using a t-test, and non-normal numeric variables using a Mann-Whitney (Wilcoxon) test.

Responses to the EQ-5D-5L were mapped to the 3L valuation set, and quality-adjusted life years (QALYs) measured based on the trapezium rule. Incremental costs and QALYs were calculated in an exploratory analysis of cost-effectiveness. A bootstrap analysis was performed with 10,000 replications, to estimate the 95% central ranges (CR) in total costs and QALYs, and their differences.

Patient and public involvement (PPI):

The Blackpool Victoria Hospital PPI group was convened after the start of this feasibility RCT. They showed considerable enthusiasm in supporting the study, and unanimously endorsed the meaningfulness of the exploratory clinical effectiveness outcome [number of full days alive and out of hospital (DAOH) within 30 days after randomisation]. Two or more DAOH were considered to be meaningful to members of the PPI group. This informed sample size calculations of the definitive multi-centre RCT. They also preferred 30 rather than 60 days follow-up to allow patients to take part in other interventional HF research studies after the end of their participation in the present study. They were not involved in the recruitment to and conduct of the study, but they will be involved in our plans to disseminate the study results to relevant wider patient communities. A draft of the paper was forwarded to the PPI members and their representative is our patient co-applicant of the NIHR grant for the multi-centre study. He has been given the task of choosing what information/results to share after publication, summarising our key findings in a lay summary in bullet points, and also produce a video to encourage patients to participate in the multi-centre definitive study.

Results

Of 24 patients enrolled, eleven were randomised to in-patient (IPM) and thirteen to out-patient care (OPM). [Figure 1] Baseline characteristics were summarised in Table 1.

During the 30 days following randomisation, patients randomised to IPM accrued a median of 17 (IQR 13 to 22) days alive out of hospital (DAOH) compared to 30 (IQR 20 to30) days for OPM (p=0.018), distribution shown in Online Supplement Figure 2). [Table 2]

There was no statistically significant difference in all-cause mortality during the index episode. Only one patient who was randomised to IPM, died (suddenly). Within 60 days of randomisation, 2 patients from each group died.

Secondary Clinical Endpoints

Two patients randomised to IPM were readmitted compared to 6 patients randomised to OPM within 60 days from randomisation [p=0.31]. Two patients randomised to OPM in the end "crossed over" i.e. did not have IV diuretics outside hospital. One patient was readmitted with HF/multi-organ failure the day after discharge, and deemed inappropriate for further IV diuretic treatment, the other patient crossed over to IPM due to delayed discharge because of subacute limb ischaemia. In OPM, there was one adverse event which was not study-related (day-case nose biopsy of ulcerative lesion). Table 2 summarised details of readmission/SAEs. No patient was readmitted more than once during the first 30 days after randomisation. Beyond 30 days 5 patients randomised to OPM experienced a new SAE (including 3 readmitted with HF) vs 2 IPM (1 HF death and 1 readmission due to HF).

Readmissions were common (3 assigned to OPM required two readmissions within 60 days- one patient had two HF readmissions, one was readmitted for non-HF reasons (NSTEMI and atypical chest pain respectively), one was readmitted for cholecystitis and then HF. Only one patient randomised to IPM required more than one readmission (cellulitis, HF).

Six of 13 (46%) randomised to OPM had serious adverse events (SAE)- delayed discharge, readmission for any reason or death, compared with 5/11 IPM (45%).

Target weight, oedema and symptom resolution

There was no significant difference in the composite end-point of target weight achieved (on discharge from treatment) in patients who survived to discharge visit /oedema

resolution/symptom resolution [OPM 13/13 vs IPM 7/10; P = 0.068]. One in-patient died suddenly before the discharge visit without achieving target weight loss, symptom/oedema resolution. [See online supplement for details].

Patient related outcome measures

All patients who completed the “Family and Friends Test” were satisfied, in both treatment groups, though one in-patient and carer commented that they would not choose the service again. Examples of comments from this validated feedback included "it was helpful to be at home to care for my wife” and “treatment very successful, helped avoid admission to hospital". Carer satisfaction was higher in the out-patient group (100% vs 60% in-patients) by discharge [Supplementary Table 1].

Out-patient Hope scores increased more than in-patient scores (a 5 point increase at discharge for out-patients compared to no change for in-patients, p=0.34, Supplementary Table 2); in-patients’ mental well-being score was higher at baseline but more out-patients had increased total well-being scores by discharge and by the 30-day follow-up visit [Table 3]; and the VAS (visual analogue scale) scores of EQ5D improved more for out-patients than in-patients (Supplementary Table 3, Supplementary Figure 3).

However, by the end of the 60 follow-up, hope scores are increased less for outpatients than inpatients, with a corresponding drop in mental wellbeing scores, despite continued increase in quality of life score (EQ5D-VAS).

Cost-effectiveness (secondary endpoint)

The median length of stay was 3 days in the out-patient group (compared with 13 for in-patients), with no patient admitted to CCU, HDU or ITU or receiving

dialysis/haemofiltration. There was one extra A&E visit. There were no extra GP visits during the index episode for OPM, and the cost of extra visit for consultant /HF clinic (12 extra visits) was factored into the equation (£1536).

Mean total costs of IPM were £5,081 (95% CR 3199 to 6963), compared with £2,423 (95% CR 1394 to 3451) for OPM. OPM thus saved £2,658 (95% CR 460 to 4857) per patient [Figure 2]. OPM was associated with 0.0425 QALYs (95% CR 0.0284 to 0.0566), versus 0.0394 (95% CR 0.0240 to 0.0548) for IPM, a difference of 0.0031 QALYs (95% CR -0.0179 to 0.0242). Given this small and non-significant increment in QALY, this exploratory analysis suggests OPM may be cost-effective, based on cost minimisation.

Discussion

This small pilot RCT demonstrates that patients with AHF randomised to out-patient based therapy accrued significantly more days alive out of hospital (30 vs 17 days for patients randomised to standard in-patient care) without increase in mortality. This was associated with mean cost savings of £2,658 per patient and could lead to significant savings for the NHS if rolled out nationally. Patients with HF are high frequency service users, accounting for 1 million bed days per year and 5% of all adult emergency hospital admissions [1].

In the current COVID-19 pandemic, it can be argued that it may be safer for patients with AHF to be managed at home. [15] Thirteen fewer days in hospital would be appreciated by many patients, as evidenced in the “Family-and-Friends test”/ patient satisfaction survey in the present study. There were no safety signals in terms of excess mortality, but a large multicentre RCT is urgently required to justify large investments in development of out-patient based AHF therapy. Despite the fact that all previous studies examining safety of OPM were observational, there is already significant expansion of such services in the UK.

[16,17] We feel it may be premature for rapid expansion of outpatient based AHF services without definitive evidence of efficacy and safety in a large multi-centre RCT.

Hopelessness, defined as having negative expectations about oneself and the future, is associated with worse prognosis in middle aged men in the Kuopio Ischemic Heart Disease study [18]. Conversely, hope defined as a positive psychology construct, comprises of state hope (which is one's goal directed thinking in any given moment and situation), and trait hope (that is a person's disposition or general way of goal directed thinking and hence more stable). [19] Hope has been linked with positive health outcomes in chronically ill populations [20,21], but there is little research in this regard in cardiovascular disease populations including heart failure. We measured State Hope using the Adult State Hope Scale as we were interested in changes at different time points. There were improvements in the Out-patient group score compared to in-patients at the point of discharge and at the first thirty days. These changes were similar in score to the only other study using the State Hope scale in cardiovascular patients [22] (mean change from 30.6 at baseline to 35.75 at 8 weeks, $p<0.005$). Dunn et al's pilot study in 2018 used an emotional support intervention in patients with ischaemic heart disease [22]. By contrast, the mean hope score for >400 normal students is 37.2 [11] The initial increase in hope in our present feasibility study diminished within 60 days, possibly as a result of increased readmissions. Trait hope was not assessed so the dispositional effects on state Hope cannot be excluded.

The present feasibility study signals that AHF may be successfully treated with IV diuretics on an out-patient basis, and that patients may enjoy a better quality of life and report an increased mental well-being and hope.

Though limited in significance due to a small sample size and imbalance between randomised group characteristics, these results are encouraging and informed the design of a larger, multicentre RCT.

Frailty and its associated high risk of major adverse health outcomes are well documented. The Derby Frailty Index [23] was initially developed as a Frailty identification tool which does not require additional training for staff. The Rockwood clinical frailty scale is another simplified screening tool for assessing the degree of frailty. It takes into account information about cognition, mobility, function and co-morbidities to assign a frailty level from 1 to 9. This method effectively estimates important outcomes including survival and institutionalisation [24]. We found both methods of frailty assessment feasible in the present study. Patients randomised to IPM were slightly more frail, but not clinically or statistically significantly. A mean Rockwood score 5 or 6 suggested mild or moderate frailty which in practice would identify patients as frail indicating comprehensive geriatric assessment so there would be no clinical significance in that difference in score. Further exploration of frailty in a larger RCT may help refine exclusion criteria for OPM. In practice, whilst many of the relatively frail patients might have their preferred place of care in the community, relatives might find the prospect rather daunting and this should be taken into account.

Limitations

The small sample size limits generalisation of this pilot single centre RCT. Nevertheless, even with 24 patients it was possible to demonstrate significantly more DAOH in patients randomised to OPM. We found it was not feasible to ask outpatients to measure their urine output. We also found patients' estimate of dry weight rather inaccurate. However, the use of

the pre-specified composite endpoint of symptom/oedema resolution/target weight achievement helps overcome this limitation.

From an economic evaluation perspective, our study aimed to primarily identify relevant items of resource use associated with each arm, and the feasibility of collecting such data. We collected relevant data associated with each patient in each arm, such as hospitalisation, GP visits. The exploratory cost-effectiveness analysis indicated that OPM might be a cost-effective alternative to IPM based on cost minimisation. A definitive RCT with an integrated economic evaluation would provide a more robust estimate of cost-effectiveness to inform the NHS.

Last but not least, moderate level of hope is prevalent amongst patients with AHF. A recent AHF survey showed <30% have clinical psychology service to support their heart failure service. [25] Only 19% of respondents are aware they have clinical psychology service; whilst 6% are not sure if they have clinical psychology service. Our study highlights the need for business planning for more clinical psychologists who can help us deliver excellent whole person care in patients with HF. More research is urgently required to test other strategies tailored to maintain hope in the longer term beyond 30 days. This pilot RCT provides preliminary evidence that there is benefit to a patient's mental health and quality of life in being able to receive treatment out of hospital.

This small pilot RCT demonstrated that patients with acute HF randomised to OPM accrued significantly more DAOH without increase in mortality. OPM is favoured by patients and carers and is associated with improved mental well-being.

Tables and Figure Legends

Supplementary Table 1 Patient and Carer satisfaction ("NHS Family and Friends Test")

Supplementary Table 2 Does out-patient based therapy increase hope score in patients with acute heart failure?

Supplementary Table 3 EQ5D VAS score comparison

Supplementary Table 4 Comparison of changes in transformed SWEMWBS scores between baseline and discharge

Supplementary Table 5 Diuretic Dose and Weight Change

Supplementary Figure 1 [Online Supplement]: Out-patient based therapy for AHF was not associated with worse survival

Supplementary Figure 2 [Online Supplement]: Out-patient based AHF treatment was effective at increasing the number of full days alive out of hospital during 30 day follow-up

Supplementary Figure 3 [Online Supplement]: Trajectories of EQ5D-VAS scores

Supplementary Figure 4 [Online Supplement]: EQ5D domain score trajectories across real time

Supplementary Figure 5 [Online Supplement]: Distribution of EQ5D domain scores across time points

Figure 1 Participant Flow Diagram

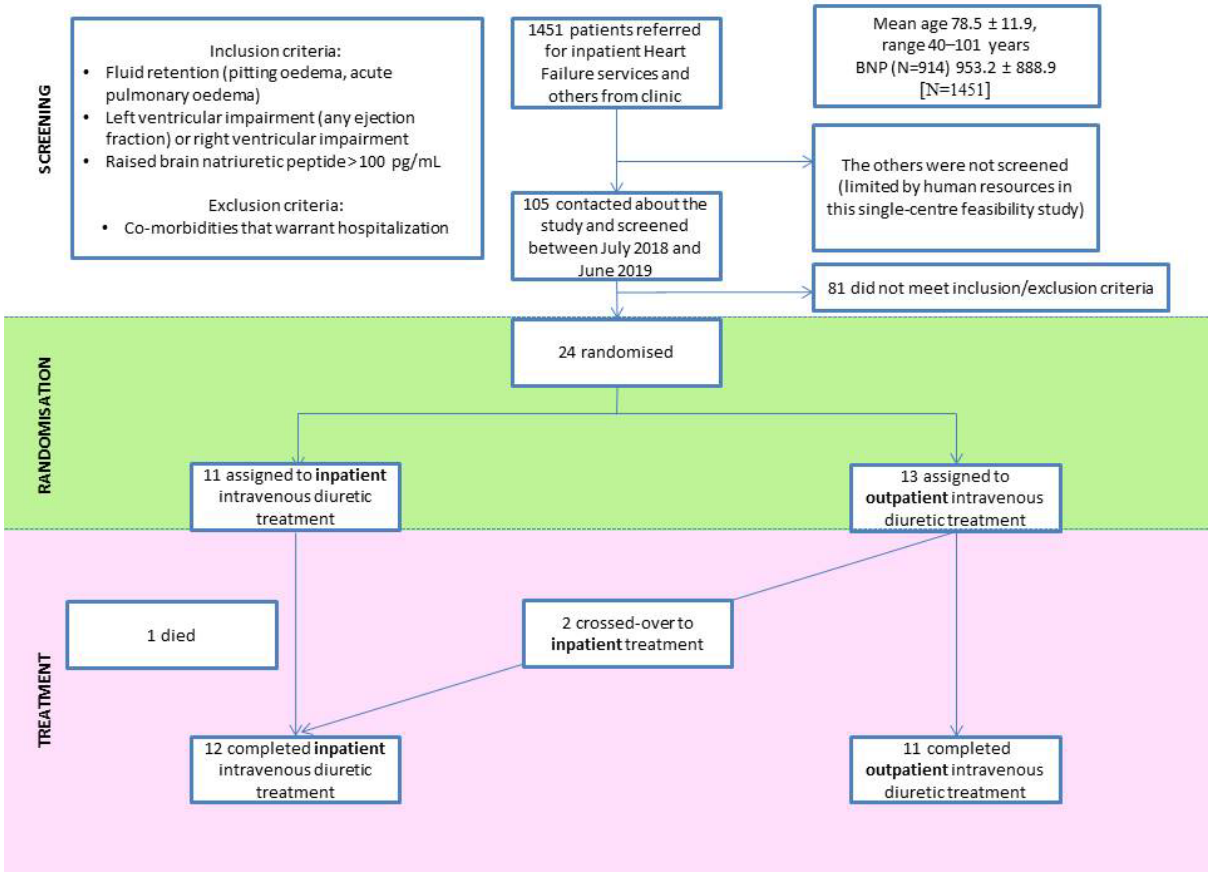

Figure 2 Cost savings with Out-patient based treatment

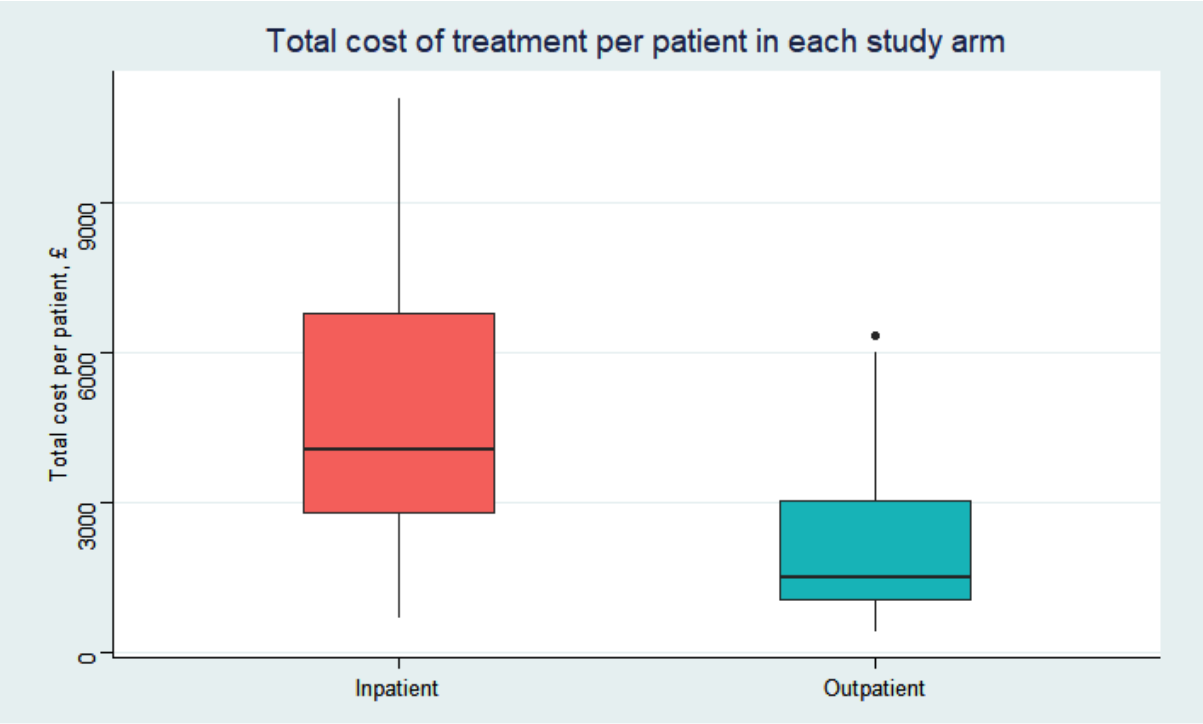

Table 1 Baseline Characteristics

		In-patient (n=11)	Out-patient (n=13)	p
Sex	*Female*	7 (63.6%)	3 (23.1%)	0.095
Age	*at randomisation*	81.8 (10.4)	70 (16.0)	0.052
BMI	*kg/m²*	28 (7)	37.1 (8)	**0.01**
Weight	*kg*	73.6 (20.9)	108.5 (31.9)	**0.005**
HF status	*Peripheral Oedema*	90.9%	92.3%	0.90
	Pulmonary oedema	27.3%	30.77%	0.85
	Both	18.2%	23.1%	0.77
NYHA	*Class II*	0	2 (15.4%)	0.07
	Class III	11 (100%)	8 (61.5%)	
	Class IV	0	3 (23.1%)	
Degree of peripheral oedema	*None*	1 (9%)*	0	
	Mild		2 (15.4%)	0.080
	Moderate	7 (64%)	11 (84.6%)	
	Severe	3 (27%)	0	
BNP	*[missing data-2 from each group]*	357 [251, 470],	360 [264, 699]	>0.99
LV systolic function on echocardiography	*EF 55% or more*	5 (45.5%)	5 (38.5%)	>0.99
	Impaired (<55%)	6 (54.5%)	8 (61.5%)	
IHD Aetiology		18.2%	7.7%	0.44
Arrhythmia		63.6%	23.1%	0.1
DCM		0	7.7%	-
Hypertension		54.54%	46.15%	1
Valvular		45.45%	38.46%	0.68
Number of comorbidities		3.8±2.7	5±2.9	0.3
Rockwood frailty score	at randomisation	5.6 (1.2)	5.4 (1.6)	0.67
Premorbid Rockwood frailty score		5.0 (1.2)	4.8 (1.3)	0.76
Derby frailty index	*Number (%) Frail*	6 (54.5%)	6 (46.2%)	0.99

Receiving “end of life”/palliative care		1 [9.09%] Severe MR - patient did not want surgery.	1 [7.7%] AS deemed not fit for AVR or TAVI by MDT	>0.99
Systolic BP	mmHg	145 (21.2)	137 (25)	0.43
Diastolic BP	mmHg	75 (14)	75 (17.8)	0.96
Hb	g/L	119 (16.7)	119.7 (17.3)	0.92
Albumin	g/L	36 [34,40]	36 [34,39]	0.97
Sodium	mmol/L	138 (2.4)	137.6 (2.8)	0.44
Potassium	mmol/L	4.4 (0.7)	4.1 (0.54)	0.3
Urea	mmol/L	11.35 (4.4)	10.2 (5.1)	0.55
Creatinine	umol/L	119.5 (37)	113.7 (48)	0.75
Already on IV diuretic		6 (54.4%)	10 (76.9%)	0.39
No. of days on IV diuretic pre-randomisation		2.3(3.4)	3.3(3.8)	0.5
ACEi	*(none on ARB in both groups)*	45.45%	23.1%	0.24
Sacubitril / valsartan		0	23.1%	-
Beta blocker		63.6%	76.9%	0.47
MRA		0	30.8%	-
Ivabradine		0	7.7%	-
Digoxin		18.2%	7.7.%	0.43
Iron Deficiency anaemia (IDA)		27.3%	38.46%	0.56
IV replacement therapy for IDA	*(in last 12 months)*	18.2%	15.4%	0.44
Smoker	*Non-smoker*	7 (63.6%)	5 (38.5%)	0.527
	Ex-smoker	3 (27.3%)	6 (46.2%)	
	Smoker	1 (9.1%)	2 (15.4%)	

*pulmonary oedema only

ACEi=Angiotensin Converting Enzyme Inhibitor; ARB= Angiotensin Receptor Blocker; AS= aortic stenosis; BMI=body mass index; BNP=Brain Natriuretic Peptide; BP=blood pressure; DCM=dilated cardiomyopathy; Hb=haemoglobin; HF=heart failure; IDA= Iron Deficiency anaemia; IHD=ischaemic heart disease; IV=intravenous; LV=left ventricular; MR= mitral regurgitation; NYHA=New York Heart Association;

[Descriptive statistics are presented either as: mean (SD), as median [Q1, Q3], or as N (percentage)]

Table 2 Clinical Effectiveness and Safety endpoints

		In-patient (n=11)	Out-patient (n=13)	p-value
Number of full days out of hospital per patient within 30 days of randomisation {min, max}		17 [13,22] min-max {1, 28}	30 [20, 30] min-max {0, 31}	**0.018**
Number of full days out of hospital per patient within 60 days of randomisation {min, max}		47 [36, 51] min-max {1, 58}	59 [41, 60] min-max {0, 61}	0.13
Hospital length of stay per patient during index episode, days		13 [7, 14.5]	3 [2, 7]	**0.004**
Number of patients readmitted within 60 days from randomisation		2	6	0.31
SAE (A&E attendance, delayed discharge, readmission within 60 days , death)	*No.of patients with at least 1 SAE*	5/11	*6/13*	>0.99
	During Index episode ()	2(pacemaker implant delayed discharge , MI leading to death)	*2 (cross-over/ readmitted with HF/multi-organ failure; delay discharge due to subacute limb ischaemia)*	>0.99
	Between discharge and 30 days of randomisation	2(HF; Cellulitis)	*3 (HF X1 , MI , Cholecystitis)*	>0.99
	31-60 days of randomisation	2 (HF readmission, HF Death)	*5 (HFx3 , atypical chest pain, elective leg amputation)*	0.68
	Total SAEs From Index to 60 days of randomisation	6	*10*	N/A
HF Readmissions	*During Index episode*	Not applicable	*1*	
	Between discharge and 30 days of randomisation	1	*1*	>0.99
	31-60 days of randomisation	*1*	*3*	0.71
Total HF admissions *From Index to 60 days of randomisation*		*2*	*5*	0.52
Non-HF readmissions	*During Index episode*	Not applicable	0	
	Between discharge and 30 days of	1 -Joint infection (wrist inflammation/cellulitis)	2 -NSTEMI - cholecystitis	>0.99

	randomisation			
	31-60 days of randomisation	0	2 (atypical chest pain, Elective leg amputation)	0.54
Total Non HF admissions *From Index to 60 days of randomisation*		1	4	0.42
Deaths	*Index episode*	1 (non HF related)	0	0.93
	Between discharge and 30 days of randomisation	0	1 HF death	>0.99
	31-60 days of randomisation	1 HF death	1 HF death	>0.99
Total Deaths *From Index to 60 days of randomisation*		2	2	>0.99

**** Index episode-before inpatient discharge or discharge visit after end of diuretic treatment for outpatients***

HF= heart failure; SAE=Serious Adverse Event

Figures are presented either as: mean (standard deviation), as median [Q1, Q3], or as percentage

Table 3 Mental Well-being (SWEMWBS) score comparison

TRANSFORMED SWEMWBS	In-patient	Out-patient	P value
Mean score at baseline	25.6 (4.46)	21.0 (5.08)	**0.03**
Number of patients whose score increased from baseline to discharge	4	8	0.36
Number of patients whose score increased from baseline to 30 days	3	8	**0.050**
Number of patients whose score increased from baseline to 60 days	3	9	**0.040**

Measurements of the transformed (Normalised) SWEMWBS scores were taken at baseline, discharge and at 30 days and 60 days post randomisation. The table shows the mean score at baseline and the number of patients whose wellbeing levels increased over treatment

REFERENCES

[1.] National Heart Failure audit 2019 Summary data https://www.hqip.org.uk/wp-content/uploads/2019/09/Ref-129-Cardiac-Heart-Failure-Summary-Report-2019-FINAL.pdf (last accessed 20/10/2020)

[2.] Shoaib A, Waleed M, Khan S, Raza A, Zuhair M, Kassianides X, Djahit A, Goode K, Wong K, Rigby A, Clark A, Cleland J. Breathlessness at Rest is Not the Dominant Presentation of Patients Admitted with Heart Failure. European Journal of Heart Failure 2014; 16: 1283–1291. doi:10.1002/ejhf.153

[3.] Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091

[4.] Hebert K, Dias A, Franco E, Tamariz L, Steen D, Arcement LM. Open access to an out-patient intravenous diuresis program in a systolic heart failure disease management program. Congest Heart Fail. 2011;17(6):309–313.

[5.] Ryder M, Murphy NF, McCaffrey D, O'Loughlin C, Ledwidge M, McDonald K. Out-patient intravenous diuretic therapy; potential for marked reduction in hospitalisations for acute decompensated heart failure. Eur J Heart Fail. 2008;10(3):267–272.

[6.] British Heart Foundation. Learning points for the successful introduction of Intravenous diuretics in the community. https://www.bhf.org.uk/informationsupport/publications/healthcare-and-innovations/learning-points-for-the-successful-introduction-of-intravenous-diuretics-in-the-community (last accessed 9/4/19)

[7.] British Heart Foundation. Healthcare professionals – service innovation. Intravenous diuretics in the community. https://www.bhf.org.uk/healthcare-professionals/best-practice/intravenous-diuretics-in-the-community (Last accessed 9/4/2019)

[8.] Cornwell J, Levenson R, Sonola L, Poteliakhoff E. Continuity of care for older hospital patients A call for action. The King's Fund. March 2012.

[9.] Ariti CA, Cleland JGF et al. Days alive and out of hospital and the patient journey in patients with heart failure: Insights from the candesartan in heart failure: assessment of reduction in mortality and morbidity (CHARM) program. Am Heart J. 2011;162(5):900-6.

[10.] Tennant R, Hiller L, Fishwick R, Platt P, Joseph S, Weich S, Parkinson J, Secker J, Stewart-Brown S. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation, Health and Quality of Life Outcome 2007; 5:63.

[11.] Snyder C.R. et al. Development and validation of the State Hope Scale. Journal of personality and social psychology, 1996; 70:321-335.

[12.] Snyder, C.R. Hope theory: Rainbows in the mind. Psychological Inquiry. 2002; 13: 249-275.

[13.] Snyder, C.R. The psychology of hope: You can get there from here. New York: Free Press. 1994

[14.] Snyder, C, Harris, C, Anderson, J, Holleran, S., Irving, L, Sigmon, S, et al. The will and the ways: Development and validation of an individual-differences measure of hope. Journal of Personality and Social Psychology 1991; 60: 570-585.

[15.]Williams S., Barton C. Evaluation of Symptomatic Heart Failure patients as HIGH RISK for COVID-19. https://www.bsh.org.uk/wp-content/uploads/2020/04/Letter-to-NHS-PHE-recognising-HF-patients-as-vulnerable-group-COVID-19.pdf [last accessed 10/4/2020]

[16.] Mohee K, Wong K. Are we ready for out-patient acute heart failure management (frusemide lounges and beyond)?-A nationwide survey of UK acute heart failure practice. Heart Suppl 2016

[17.] Mohee K, Wong KYK. Rapid response to "How to prescribe loop diuretics in oedema". BMJ 2019 (Feb);364:l359. https://www.bmj.com/content/364/bmj.l359/rr-2

[18.] Everson, S, Goldberg, D, Kaplan, G, Cohen R, Pukkala, E, Tuomilehto J, Salonen J. Hopelessness and risk of mortality and incidence of myocardial infarction and cancer. Psychosomatic Medicine 1996; 58: 113-121.

[19.] Snyder, C. R. Handbook of hope: Theory, measures, and applications. San Diego, CA, US:Academic Press. 2000

[20.] Billington E, Simpson J, Unwin J, Bray D, Giles D. Does hope predict adjustment to end-stage renal failure and consequent dialysis?. British journal of health psychology. 2008;13(4):683-99.

[21.] Kortte KB, Stevenson JE, Hosey MM, Castillo R, Wegener ST. Hope predicts positive functional role outcomes in acute rehabilitation populations. Rehabilitation psychology. 2012 Aug;57(3):248.

[22.]Dunn, S. L., DeVon, H. A., & Tintle, N. L. (2018, July). Improving hope in hopeless patients with ischemic heart disease. Podium presentation. Sigma Theta Tau International 2018 Research Congress, Melbourne, Australia

[23.] Sze S, Pellicori P, Zhang J, Weston J, Clark AL. Identification of Frailty in Chronic Heart Failure. JACC Heart Fail. 2019 Apr;7(4):291-302. doi: 10.1016/j.jchf.2018.11.017.

[24.] Sze S, Zhang J, Pellicori P, Morgan D, Hoye A, Clark AL. Prognostic value of simple frailty and malnutrition screening tools in patients with acute heart failure due to left ventricular systolic dysfunction. Clin Res Cardiol. 2017 Jul;106(7):533-541. doi: 10.1007/s00392-017-1082-5.

[25.] Abdullah Abdullah, Suzanne YS Wong, Robbie Jones, Kenneth YK Wong. Outpatient-based acute HF care calls for development of clinical psychology service for whole-person care provision. Br J Cardiol 2022;29:141–4

doi:10.5837/bjc.2022.037

Outpatient-based acute HF care calls for development of clinical psychology service for whole-person care provision (bjcardio.co.uk)

Last accessed 1/12/22

Contributorship Statement

Author Contributions

Wong K.Y.K. [1,2] designed the study, contributed to consent, assessment and management of patients in the trial, data collection, data analysis and interpretation, and writing the paper. He is responsible for the overall content as guarantor.

Hughes D.A.[3] performed the exploratory cost-effectiveness analysis.

Debski M. [1] contributed to consent, assessment and management of patients in the trial, data collection and data analysis and writing.

Latt N. [1] contributed to data collection and data analysis, and submission of abstracts which were published in Heart Suppl 2020.

Assaf O. [1] contributed to data collection for the study, in particular, cost-effectiveness data.

Abdelrahman A. [1] contributed to consent, assessment and management of patients in the trial, and data collection.

Taylor R. [1] performed most of the statistical analysis and writing of the results of the paper.

Allgar V. [4] contributed to the statistical design of the study and generated randomisation schedule blinded to investigators and patients.

McNeill L. [1] contributed to the collection and analysis of the cost-effectiveness data and critically reviewed the manuscript.

Howard S. [1] contributed to the analysis of the cost-effectiveness data and critically reviewed the manuscript.

Wong S.Y.S. [1] contributed to the design of the study and critically reviewed the manuscript.

Jones R.[1] is the patient public involvement group representative and critically reviewed the manuscript.

Cassidy C. J.[1] contributed to the design of the study and is a Safety Committee member.

Seed A. [1] contributed to the design of the study and critically reviewed the manuscript.

Galasko G. [1] contributed to the design of the study and is a Safety Committee member.

Clark A. [4] contributed to the design of the study and critically reviewed the manuscript.

Wilson D. [5] critically reviewed the manuscript.

Davis G.K. [6] critically reviewed the manuscript.

Montasem A [6] critically reviewed the manuscript.

Lang C.C. [7] critically reviewed the manuscript.

Kalra P.R. [8] critically reviewed the manuscript.

Campbell R. [9] critically reviewed the manuscript.

Lip G.Y.H. [2, 10] critically reviewed the manuscript.

Cleland J.G.F. [9] contributed to the design of the study and critically reviewed the manuscript.