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

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12. Nov. 2024

Online Supplement

Contents

Methods

Full eligibility criteria

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 ESC HF guideline [25]). The amended protocol also allows inclusion of patients with right ventricular impairment (by "eyeball assessment" or 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. 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.

Sample size –this is a pilot study so formal sample size calculation is not required. In the feasibility study, we aimed to recruit 100 patients over 12-24 months to demonstrate feasibility (of recruiting, randomizing) and inform effect size for a multicentre RCT. In the end, after 12 months, 105 patients were contacted about the study and screened, but only 24 patients were consented and randomised, having satisfied all the inclusion and exclusion criteria.

Clinical outcomes

Details regarding the Pre-specified secondary endpoints -

1. Rehospitalisation for HF within 60 days of randomisation - Note that a further readmission for an in-patient would be in addition to their index HF episode, a readmission for an out-patient may be within the initial index episode but after discharge for in-patient care. Thus, the endpoint Days alive out of hospital (DAOH) took care of the complexities of deciding whether a patient "crossed over" or was readmitted.
2. Death from any cause within 60 days of randomisation
3. Cardiovascular death within 60 days of randomisation,
4. Symptom resolution/ oedema reduction to no more than a "trace of ankle oedema" or "back to usual" in patients known to have refractory leg oedema)/achievement of "dry weight" (usual weight when not fluid-overloaded).
5. Duration of diuretic treatment
6. 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) and the Adult State Hope Scale.

7. Cost effectiveness

Cost effectiveness analysis was performed using the Trust's patient level costing models from financial years 2018/19 and 2019/20 to calculate total treatment costs. This takes into account of length of stay, staff time (doctors/nurses/allied healthcare professionals), lab tests, radiology and other diagnostic tests and medicine/device therapy etc. Where patient level costs were unavailable, e.g. for Community visits, we used a national average cost.

The quality of our patient-level costing data is excellent. We received a Cost Assessment Tool score of 86% from NHS Improvement. The Cost Assessment Tool takes into account of a range of metrics including Data Quality, Costing Allocation Methods, Governance and Information Gaps.

£83 per day was the estimated cost of home visits and community centre; £59 for <4 hour utilisation of the hospital "frusemide lounge" (Cardiac Day Ward).

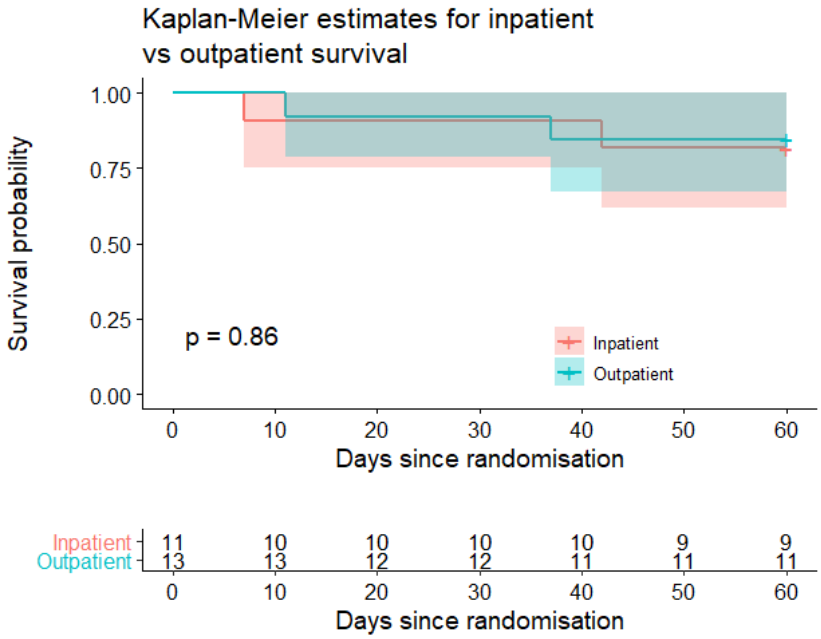
Typically, the cost of medical ward vs cardiology ward vs CCU vs ITU vs HDU (per day) is £214 per day (medical), £162 per day (cardiac), CCU £522 per day, ITU/HDU £787 per day at our Trust. Follow up visit in Cardiac clinic costs £128. £253 is the average cost of an A&E attendance.

Responses to the EQ-5D-5L were mapped to the 3L valuation set [26], 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 with 10,000 replicates was performed to estimate the 95% central ranges (CR) in total costs and QALYs, and their differences [27].

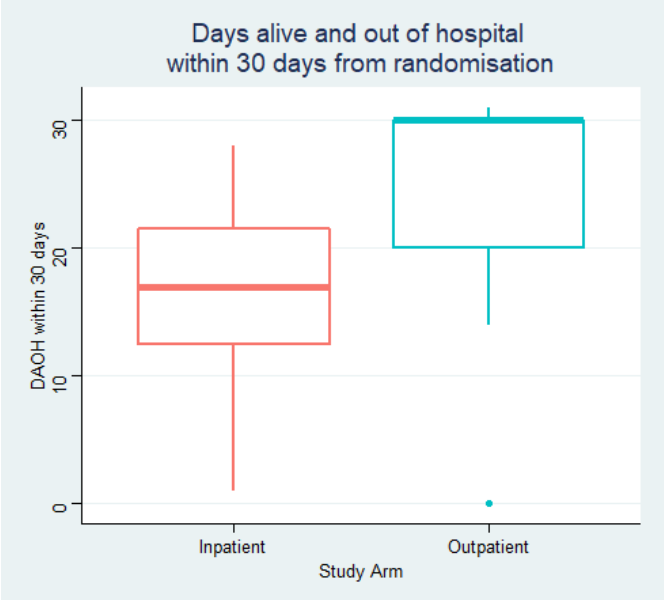
Results [Supplementary Results and Supplementary Figures and tables]

Kaplan-Meier survival analysis assessed the impact of OPM on all-cause mortality. The censor date was at least 60 days after the completion of the last patients' treatment.

Supplementary Figure 1: Out-patient based therapy for AHF was not associated with worse survival (log rank test p=0.86)

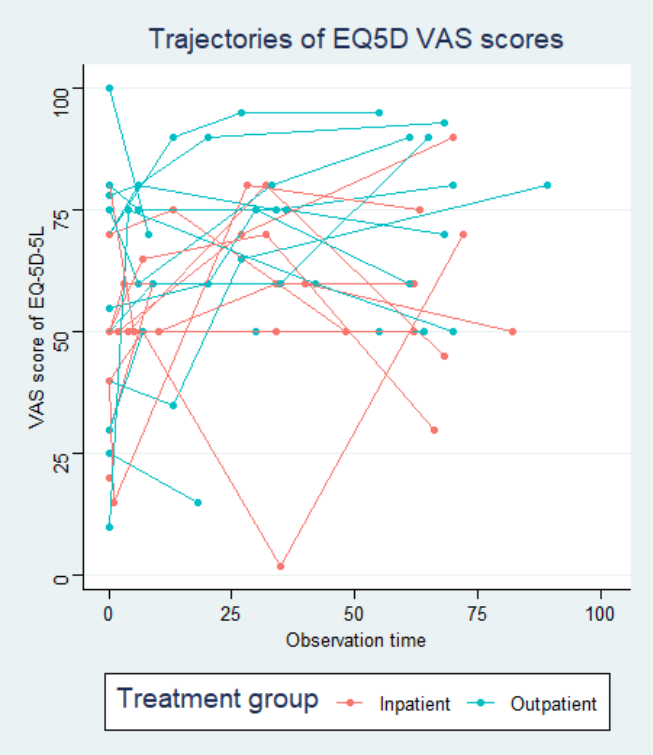


Supplementary Figure 2**: <u>Out-patient based AHF treatment was effective at increasing the number of full days alive out of hospital during 30 day follow-up</u>**

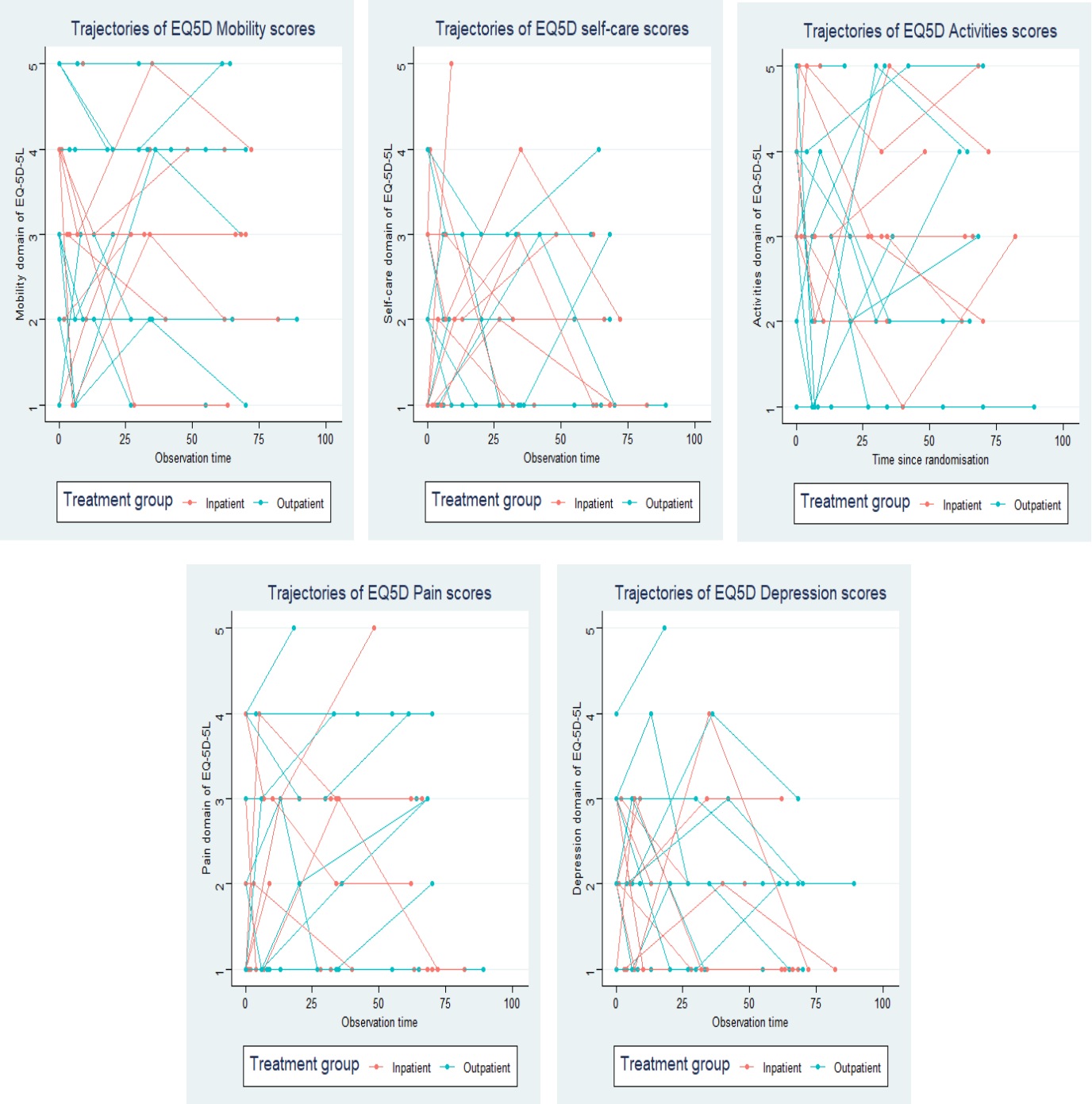


Supplementary Figure 3 [Online Supplement]: **EQ5D Visual Analogue Scale score trajectories across real time**

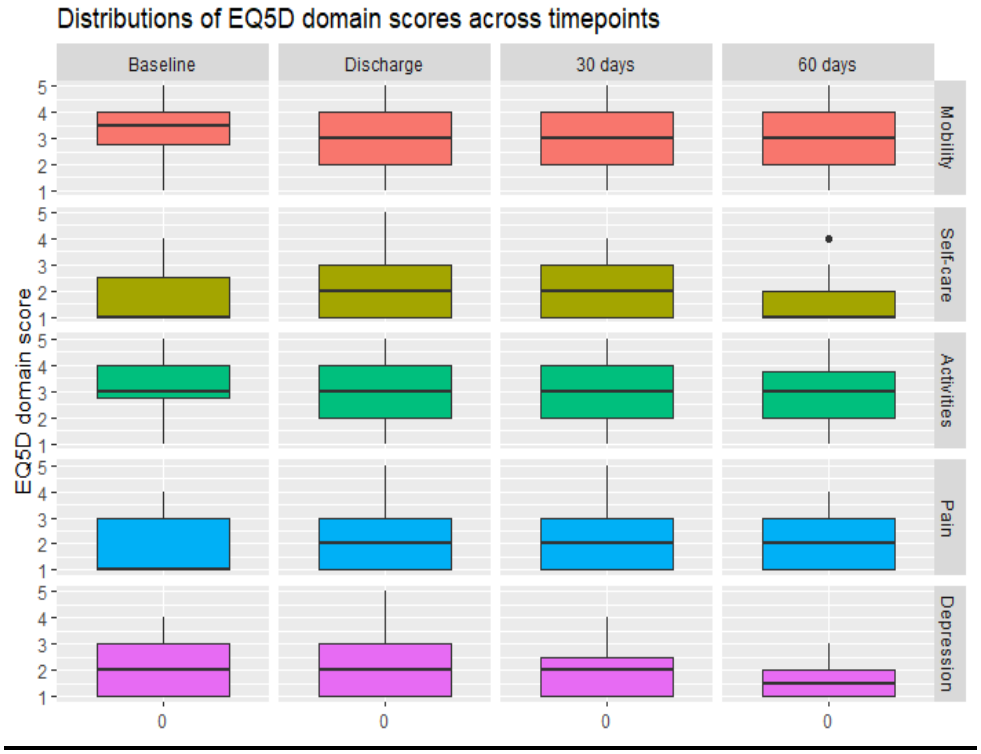
The visual analogue scale scores of the EQ5D plotted per patient across the duration of the study time. The blue trajectories (out-patients) are seen to generally climb more than the red trajectories (in-patients).



Supplementary Figure 4**: EQ5D domain score trajectories across real time**



Supplementary Figure 5**: Distribution of EQ5D domain scores across time points**



The trajectory plots and boxplots of distributions for all 5 individual EQ5D domains show no changes that are statistically significant: Wilcoxon tests of change from baseline to discharge (p=0.23, 0.50, 0.47, 0.51 and 0.81 respectively).

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

	Discharge	30 days	60 days
Patient satisfied			
In-patient (n=10)	10/10	8/8	8/8
Out-patient (n=12)	12/12	10/10	11/11
Patient would choose again			
In-patient (n=10)	9/10	8/8	8/8
Out-patient (n=12)	12/12	10/10	10/11
Carer satisfied			
In-patient (n=7)	3/5	6/6	6/6
Out-patient (n=10)	10/10	6/6	9/9
Carer would choose again			
In-patient (n=7)	3/5	6/6	6/6
Out-patient (n=10)	10/10	6/6	9/9

100% patients in both arms were satisfied according to the "NHS Family and Friends Test" but interestingly 100% would choose OPM again but only 90% would choose Inpatient care. Similarly, 100% carers were satisfied in the OPM arm whilst 60% only were satisfied if the patient is randomised to inpatient care. 100% carers would choose OPM again, vs 60% IPM carers.

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

Hope	Hope (total) score -baseline		Increase in score from baseline to discharge		Increase in score from baseline to 30 days		Increase in score from baseline to 60 days	
In-patient	33 [27,40] (n=11)	P=0.69	0 [-5, 7] (n=9)	p=0.34	2 [-14, 5] (n=9)	p=0.43	6.5 [-4.3, 16] (n=8)	p=0.59
Out-patient	30 [23,42.5] (n=13)		5 [-1.5, 9] (n=12)		6.5 [-5, 8.8] (n=10)		2.5 [-7, 12.3] (n=10)	

Supplementary Table 3 Increases in Visual Analogue Scale scores of EQ5D

Comparing the VAS scores of the EQ5D tool across time points. "Increase in score" is calculated as the simple subtraction of the scores at the two time points, so that a negative result means the score decreased (lower score is indicative of worse overall health).

VAS score	VAS score at baseline		Increase in score from baseline to discharge		Increase in score from baseline to 30 days		Increase in score from baseline to 60 days	
Inpatient	50 [40, 50] (n=11)	P=0.25	2.5 [0, 10] (n=10)	p=0.65	10 [-20, 20] (n=9)	p=0.27	5 [-9, 31] (n=8)	p=0.28
Outpatient	70 [40, 78] (n=13)		10 [-20, 20] (n=12)		20 [6, 24] (n=10)		23 [10,33] (n=11)	

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

Change was calculated as discharge score minus baseline score, so that a positive change represented an increase in score (higher score implies greater wellbeing). Scores were Normally distributed, even in this small sample (Shapiro-Wilk test p>0.23 at all time points) and thus comparisons were made using appropriate t-tests. Scores are presented as mean (SD). Comparisons within time points as well as across time points are shown as outpatients are found to have significantly poorer wellbeing than inpatients at the time of randomisation.

		Inpatients	Outpatients	
Raw scores	**Randomisation** $n_{IN}=10$, $n_{OUT}=12$	25.6 (4.5)	21.0 (5.1)	**p=0.034**
	Discharge $n_{IN}=10$, $n_{OUT}=12$	23.0 (5.2)	24.9 (5.1)	p=0.40
	30 days from rand. $n_{IN}=8$, $n_{OUT}=9$	24.8 (4.9)	27.1 (4.8)	p=0.35
	60 days from rand. $n_{IN}=8$, $n_{OUT}=11$	26.4 (6.1)	24.4 (6.6)	p=0.50
Change from randomisation	**Discharge** $n_{IN}=9$, $n_{OUT}=11$	-1.4 (5.6)	4.4 (4.9)	**p=0.026**
	30 days $n_{IN}=8$, $n_{OUT}=9$	-0.6 (4.2)	6.3 (5.4)	**p=0.010**
	60 days $n_{IN}=8$, $n_{OUT}=10$	0.2 (4.8)	5.3 (5.5)	p=0.053

IPM wellbeing scores at discharge were not significantly different compared with baseline. [25.6 vs 23.0, p=0.46]. OPM wellbeing scores at discharge were significantly increased. [Mean 21.0 vs 24.9, p=0.01].

IPM had higher initial wellbeing scores (25.6 vs 21.0, p=0.034).
On discharge, there was no longer significant difference (23.0 vs 24.9, p=0.40).
Thus, OPM scores increased significantly more than IPM (mean change 4.4 vs -1.4, p=0.026)

Achievement of target weight, oedema and symptom resolution

Diuretic treatment was delivered over 5.8 days (SD 2.8) for in-patients and 8.5 (SD 5.2) days for out-patients. There was no significant difference in target weight achieved (on discharge from treatment) in patients who survived to discharge visit [OPM 9/13 vs IPM 4/10*; P = 0.22 (Fisher's Exact test)]; oedema resolution to no more than a trace/back to normal [OPM 9/13 vs IPM 6/10; P = 0.69]; symptom resolution [OPM 10/13 vs IPM 7/10; P = 1]; composite end-point [i.e. any treatment target met out of the three types: 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. Overall, out-patients lost more weight in this trial, in-patients mostly gained weight, based on only 14 patients (5 from each group had missing data) [Supplementary Table 5 Diuretic Dose and Weight Change].

Supplementary Table 5 Diuretic Dose and Weight Change

		In-patient (n=11)	Out-patient (n=13)	p-value
Weight loss (kg) [difference in weight between randomisation and discharge visit]		-0.2 [-0.7, 2.0]	3.1 [1.2, 7.8]	**0.044**
TOTAL duration of iv diuretic treatment from randomisation to discharge (including "weekend interruption" where no iv treatment was given), days		5.8 (2.8)	8.5 (5.2)	0.117
Median dose of IV diuretic	per day of IV treatment [IQR]	100 [60-123]	103 [80-120]	0.726
No of days of weekend interruption	{% who had weekend interruption in outpatient group}	0 [0-0] {0}	2 [0-2] {8/13, 62%}	-
Total dose of iv frusemide	from randomisation to discharge	720 [240-1160]	640 [400-820]	>0.99
Total dose of bumetanide	over weekend *	-	4 [0-5]	-

* 1 patient had 7.5mg bendofluazide over the weekend in the outpatient group (3 doses of 2.5mg)

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

Appendices [Online Supplement]

Appendix 1

Measures of Hope, Well-being and Quality of Life

The Adult Hope Scale (AHS) relates to Snyder's cognitive model of hope. Snyder sees hope as "a positive motivational state that is based on an interactively derived sense of successful (a) agency (goal-directed energy), and (b) pathways (planning to meet goals)". In essence then, hope stems from being able to see the next step, then having the motivation and the know-how to get there. The Short Warwick-Edinburgh Mental Well-Being Scale (SWEMWBS) measures subjective mental well-being. It has been used to assess the impact of medical interventions on general well-being.

Both measures have been used in a variety of physical health populations, including patients with renal disease, fibromyalgia and amputees. Hope is predictive of subjective well-being and quality of life, which in turn predicts healthcare use and illness management [12].

Importantly, there is evidence suggesting that hope can predict outcome independent of depression. Everson et al. [18] examined the relationship between levels of hopelessness and all-cause and cause-specific mortality, and incidence of myocardial infarction (MI) and cancer in a population-based sample of middle-aged men. The large study included 2428 men, aged 42 to 60, from the Kuopio Ischemic Heart Disease study, a longitudinal study of psychosocial risk factors for ischemic heart disease and other outcomes. In 6 years of follow-up, 174 deaths (87 cardiovascular and 87 non-cardiovascular, including 40 cancer deaths and 29 deaths due to violence or injury), 73 incident cancer cases, and 95 incident MI had occurred. Men were rated low, moderate, or high in hopelessness if they scored in

the lower, middle, or upper 1/3 of scores on a 2-item hopelessness scale. Age-adjusted Cox proportional hazards models identified a dose-response relationship such that moderately and highly hopeless men were at significantly increased risk of all-cause and cause-specific mortality relative to men with low hopelessness scores. Indeed, highly hopeless men were at more than 3-fold increased risk of death from violence or injury compared with the reference group. These relationships were maintained after adjusting for biological, socioeconomic, or behavioural risk factors, perceived health, depression, prevalent disease, or social support. High hopelessness also predicted incident MI, and moderate hopelessness was associated with incident cancer. These findings indicate that hopelessness is a strong predictor of adverse health outcomes, independent of depression and traditional risk factors.

EQ-5D-5L

Consists of five items each with a different domain: mobility, self-care, activities, pain and depression. Each is scored from 1-5 where 5 is the worst (severe limitation/unable to do). According to NICE, the 5-level questionnaire is used because it provides greater sensitivity with smaller "floor and ceiling effect". We have used the 3 level (3L) cross-walk value set for England to calculate the health related QoL index while awaiting validation of the newer 5 level value set.

Value sets are used to transform the health profile into an index value that can be interpreted as a health utility; these range from -0.594 to 1.000 where a value below zero is taken to describe a health state whose quality is perceived to be "worse than death".

The visual analogue scale (VAS) helps us determine patients' perception of their own health, where 100 means the "best health you can imagine" and 0 is the worst.

EQ5D-5L Health Questionnaire: English version for the UK

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY
I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

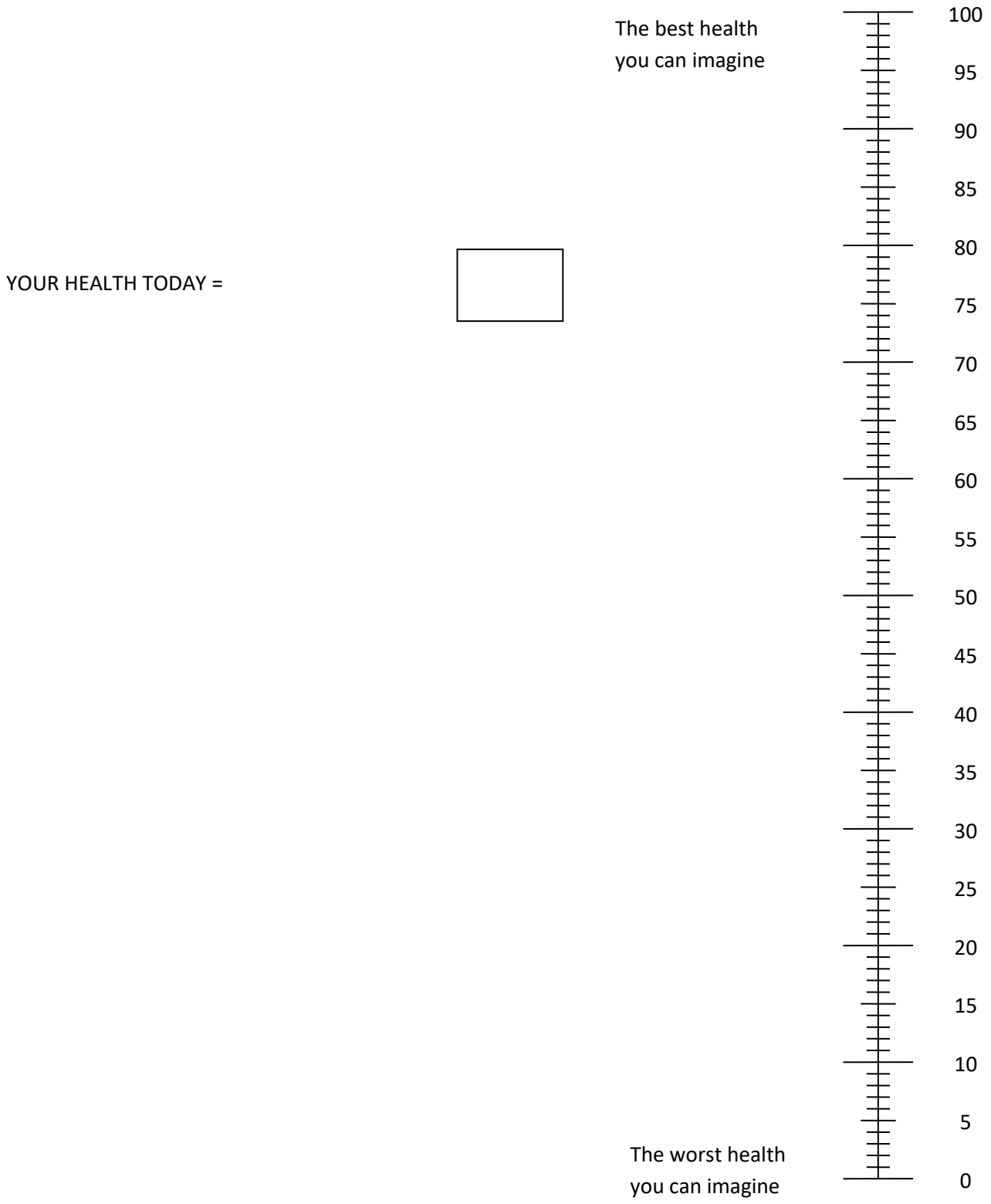
SELF-CARE
I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*
I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION
I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

We would like to know how good or bad your health is TODAY.
This scale is numbered from 0 to 100.
100 means the best health you can imagine.
0 means the worst health you can imagine.
Mark an X on the scale to indicate how your health is TODAY.
Now, please write the number you marked on the scale in the box below.



The Short Warwick-Edinburgh Mental Well-being Scale (SWEMWBS)

Below are some statements about feelings and thoughts.

Please tick the box that best describes your experience of each over the last 2 weeks	None of the time	Rarely	Some of the time	Often	All of the time
STATEMENT					
I've been feeling optimistic about the future	1	2	3	4	5
I've been feeling useful	1	2	3	4	5
I've been feeling relaxed	1	2	3	4	5
I've been dealing with problems well	1	2	3	4	5
I've been thinking clearly	1	2	3	4	5
I've been feeling close to other people	1	2	3	4	5
I've been able to make up my own mind about things	1	2	3	4	5

The Adult State Hope Scale (Snyder et al., 1996)

Read each item carefully.

Using the scale shown below, please select the number that best describes *how you think about yourself right now* and put that number in the blank before each sentence.

Please take a few moments to focus on yourself and what is going on in *your life at this moment.*

Once you have this "here and now " set, go ahead and answer each item according to the following scale:

Definitely False	1
Mostly False	2
Somewhat False	3
Slightly False	4
Slightly True	5
Somewhat True	6
Mostly True	7
Definitely True	8

_____ 1. If I should find myself in a jam, I could think of many ways to get out of it

_____ 2. At the present time, I am energetically pursuing my goals

_____ 3. There are lots of ways around any problem that I am facing now

_____ 4. Right now, I see myself as being pretty successful

_____ 5. I can think of many ways to reach my current goals

_____ 6. At this time, I am meeting the goals that I have set for myself

Scoring information

Pathways subscale score: Add items 1, 3, and 5. Scores on this subscale can range from 3 to 24, with higher scores indicating higher levels of pathways thinking.

Agency subscale score: Add items 2, 4, and 6. Scores on this subscale can range from 3 to 24, with higher scores indicating higher levels of agency thinking.

Total hope score: Add the pathways and Agency subscales together. Scores can range from 6 to 48, with higher scores representing higher hope levels.

Copyright © 1996 by the American Psychological Association. Adapted with permission. The official citation that should be used in referencing this material is Snyder, C. R., Sympson, S. C., Ybasco, F. C., Borders, T. F., Babyak, M. A., & Higgins, R. L. (1996).

Development and validation of the State Hope Scale. Journal of Personality and Social Psychology, 70, 321–335.

Appendix 2

Frailty assessment

The Derby Frailty Index was initially developed as a Frailty identification tool (FIT) in 2013 which does not require additional training for staff. The tool was used to identify suspected frail patients for targeted further comprehensive geriatric assessment and interventions.

Frailty is suggested if one or more of the following criteria were met:

- Age >65 and a care home resident
- >75 with confusion, or falls or reduced mobility
- >84 with >4 co-morbidities.

The Rockwood clinical frailty scale is another simplified screening tool for assessing the degree of frailty. It is a 9-point ordinal scale which takes into account information about cognition, mobility, function and co-morbidities based on the history and physical examination to assign a frailty level from 1 to 9. This method is easier to administer and effectively estimates important outcomes including survival and institutionalisation. A frailty score of 5 or more indicates frailty, as used in other outcome research studies e.g. SENIOR-RITA. Category descriptions are given below:

1 Robust, active, energetic, well-motivated, fit, exercises regularly - Very fit

2 Without active disease but less fit that category 1- Well

3 Disease symptoms are well controlled compared with those in category 4 (Managing well)

4 Not frankly dependent, but commonly complains of being slow or is symptomatic of diseases - Apparently vulnerable

5 Limited dependence on others for IADLs - Mildly frail

6 Needs help for both IADLs and BADLs - Moderately frail

7 Completely dependent for all BADLs and IADLs - Severely frail

8 Completely dependent and approaching end of life,

(could not recover from even a minor illness) - Very severely frail

9 Life expectancy <6 months, but not otherwise frail - Terminally ill

IADLs- instrumental activities of daily living, e.g. banking, transportation, cooking, cleaning, medication management, shopping.

BADLs- basic activities of daily living, e.g. feeding, bathing, dressing, toileting ambulation

Supplementary References

References 1-24 are in the main paper [print version]

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