

# One-year cost-effectiveness of supervised center-based exercise training in addition to a post-discharge disease management program for patients recently hospitalized with acute heart failure: The EJECTION-HF study

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## ABSTRACT

**Background:** Combining supervised exercise training (ET) and disease management program (DMP) may benefit people with heart failure (HF) but will require additional resources.

**Objectives:** To assess the 1-year cost-effectiveness of a 24-week ET program added to a post-discharge DMP in patients recently hospitalized with HF.

**Methods:** Using randomized controlled trial data, within-trial cost-utility analyses were undertaken in the overall population ( $n = 278$ ), patients aged  $<70$  ( $n = 180$ ), and those aged  $\geq 70$  ( $n = 98$ ). Incremental net monetary benefits (INMB) were calculated based on quality-adjusted life-years (QALY) and healthcare costs from the perspective of a state health department (Queensland, Australia).

**Results:** At the AU\$50,000/QALY threshold, ET showed 29.6% and 1.7% probability of being cost-effective in the overall population (INMB AU\$  $-1,472$ ) and patients aged  $\geq 70$  (INMB AU\$  $-11,469$ ), respectively. In patients aged  $<70$ , ET was potentially cost-effective with 83.6% probability (INMB AU\$4,059).

**Conclusion:** Adding ET to DMP was not cost-effective overall or in patients aged  $\geq 70$  but was relatively cost-effective in those aged  $<70$ .

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## Introduction

Unlike most other cardiac disorders, the prevalence of heart failure (HF) is rising, and treatment advances have only delivered small prolongations in survival.<sup>1</sup> In Australia, nearly one million people are now affected by the syndrome.<sup>2</sup> HF is the most frequent cause for hospital admission among elderly patients,<sup>3</sup> and multiple readmissions are common. HF is attributable to up to 150,000 hospital admissions each year and in excess of one million days in hospital, and the annual direct cost

of managing HF amounts to \$2.7 billion.<sup>2</sup> Given the growing prevalence of HF,<sup>1</sup> the high 5-year mortality rate worse than that of many cancers<sup>4</sup> and the high hospital-activity costs associated with it, cost-effective approaches to improve management are urgently needed.

Disease management programs (DMP) are multidisciplinary interventions incorporating case management, heart failure self-management education, symptom monitoring, and medication counselling and titration in addition to outpatient clinic visits. Multidisciplinary DMPs have been shown to reduce both HF-related and all cause readmissions, and are recommended in clinical practice guidelines.<sup>5</sup> More recently, exercise training (ET) has been studied as another non-pharmacological intervention intended to improve exercise capacity, improve quality of life, and reduce hospital readmissions.<sup>6–9</sup> However, ET is still not widely implemented in practice.<sup>10</sup> The EJECTION-HF randomized controlled trial tested the addition of 24 weeks of supervised centre-based ET in recently

*Abbreviations:* DMP, disease management program; ET, exercise training; HF, heart failure; ICUR, incremental cost-effectiveness ratio; INMB, incremental net monetary benefit; QALY, quality-adjusted life-year

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hospitalized patients with HF participating in a multidisciplinary DMP (i.e. comparing ET+DMP with DMP alone). Combining these two approaches may offer incremental benefits but will require additional resources. Results of the primary effectiveness analysis of the EJECTION-HF trial have been reported elsewhere.<sup>11</sup> The trial did not show a significant reduction in the primary outcome of 12-month all-cause death or readmission, but pre-planned subgroup analysis showed a statistical interaction with age, suggesting greater benefit in participants aged less than 70 years.<sup>11</sup>

Given these results, we aimed to assess the relative cost-effectiveness of supervised exercise training (ET) added to a post-discharge DMP (ET +DMP vs. DMP alone) among all study participants, those aged <70 years, and ≥70 years, to help inform post-discharge HF management practices.

## Methods

A trial-based cost-effectiveness analysis was conducted based on individual patient cost and survival data. The details of the EJECTION-HF randomized controlled trial have been previously published.<sup>12</sup> Briefly, between 2008 and 2013, 278 patients with symptomatic HF willing and able to attend a post-discharge DMP were randomized within 6 weeks of hospital discharge from one of five Australian hospitals (three tertiary metropolitan; two community in metropolitan and regional) into the intervention ( $N = 140$ ) or comparator group ( $N = 138$ ), with follow-up of death and readmissions for 12 months after randomisation.<sup>12</sup> All hospitals offered an existing multidisciplinary DMP to all participants. Both groups received a 12-week DMP including weekly group education sessions, telephone and clinic follow-up, and an individually prescribed home exercise program, aiming for 150 min per week of moderate intensity exercise. Additionally, only the intervention group was offered supervised, centre-based 1-hour ET classes twice weekly for 12 weeks and then weekly for a further 12 weeks (maximum 36 classes over 24 weeks). Classes included aerobic and resistance exercises delivered in a group setting, which were individually prescribed and progressed by a physiotherapist or exercise physiologist with HF expertise and training.

## Cost data

The analyses were conducted from the perspective of a state health department (Queensland, Australia), and only direct health-care costs were included in the analyses. This perspective was chosen because, in Australia, all patients are entitled to public hospital care

**Table 1**

Clinical characteristics of enrolled participants at baseline\*

	All participants $N = 278$	Age <70 years $N = 180$	Age ≥ 70 years $N = 98$
Female, $n$ (%)	71 (25.5)	41 (22.8)	30 (30.6)
NYHA class, $n$ (%)			
I	53 (19.1)	42 (23.3)	11 (11.2)
II	147 (52.9)	89 (49.4)	58 (59.2)
III	47 (16.9)	25 (13.9)	22 (22.4)
IV	31 (11.1)	24 (13.4)	7 (7.1)
Left ventricular ejection fraction, mean (SD)	31.5 (14.8)	27.9 (12.5)	38.4 (16.1)
Co-morbidities, $n$ (%)			
Hypertension	161 (57.9)	94 (52.2)	67 (68.4)
Atrial fibrillation	114 (41.0)	65 (36.1)	49 (50.0)
Previous myocardial infarction	103 (37.1)	56 (31.1)	47 (48.0)
Diabetes	101 (36.5)	60 (33.3)	41 (41.8)
Chronic lung disease	71 (25.5)	44 (24.4)	27 (27.6)
Chronic kidney disease	61 (22.0)	17 (9.5)	44 (44.9)
Cancer	16 (5.8)	11 (6.1)	5 (5.1)
New HF diagnosis, $n$ (%)	154 (55.4)	114 (63.3)	40 (40.8)
Cardiologist inpatient care, $n$ (%)	229 (82.4)	157 (87.3)	72 (73.5)

HF: heart failure, NYHA: New York Heart Association.

\* Baseline is a median of 30 days after hospital discharge.

fully funded by the state government, and most DMPs are delivered through this state-funded health system. Furthermore, healthcare costs for HF are predominantly attributed to hospitalization.<sup>13</sup> Direct health care costs were grouped into three types; hospital costs, non-admitted emergency department costs, and intervention costs. Hospital costs were derived from all-cause admissions identified through state-wide hospital admission databases and based primarily on the Australian Refined Diagnosis Related Groups version 6.0 (AR-DRGs).<sup>14</sup> Non-admitted emergency service costs for any cause were derived from the Emergency Department Information System (EDIS) and based on triage category. Costs of the intervention (ET) were obtained during the trial and constituted personnel and equipment costs required for the ET program additional to the costs of DMP (as both groups received DMP). The personnel costs included a physiotherapist or exercise physiologist and additional nurse, and their full-time equivalent salaries were calculated (see Supplementary Table 1 for details). The breakdown of gymnasium equipment costs is shown in Supplementary Table 2. All costs are reported in 2015 Australian

**Table 2**

Mean costs and resource use measured over 12 months follow-up

	ET+DMP ( $n = 140$ )		DMP alone ( $n = 138$ )		Cost Δ (95% CI)
	Resource use	Cost	Resource use	Cost	
Hospital inpatient admission (frequency) & cost: mean ± SD					
Overall	1.41 ± 1.87	\$13,499 ± 20,233	1.52 ± 2.06	\$13,708 ± 21,335	-210 (-5118; 4699)
Age <70	1.24 ± 1.78	\$11,641 ± 18,273	1.60 ± 2.28	\$14,731 ± 23,151	-3090 (-9233; 3054)
Age ≥70	1.71 ± 1.99	\$16,741 ± 23,100	1.36 ± 1.55	\$11,729 ± 17,348	+5012 (-3234; 13,258)
Emergency visit (frequency) & cost: mean ± SD					
Overall	0.49 ± 1.21	\$799 ± 1497	0.27 ± 0.60	\$623 ± 1244	+176 (-150; 501)
Age <70	0.54 ± 1.41	\$776 ± 1641	0.21 ± 0.46	\$681 ± 1419	+95 (-356; 546)
Age ≥70	0.41 ± 0.75	\$839 ± 1220	0.38 ± 0.80	\$512 ± 808	+328 (-91; 746)
Intervention cost per patient per year					
Intervention		\$2439		0	+2439
Total cost (hospital, emergency, intervention): mean ± SD					
Overall		\$16,737 ± 20,846		\$14,332 ± 22,186	+2405 (-2677; 7487)
Age <70		\$14,856 ± 19,034		\$15,412 ± 24,233	-556 (-6975; 5863)
Age ≥70		\$20,020 ± 23,520		\$12,241 ± 17,613	+7779 (-609; 16,167)

Costs reported in 2015 Australian dollar values.

ET: center-based exercise training, SD: standard deviation, CI: confidence interval.

dollars (AU\$) (AU\$ 1  $\approx$  0.70 US\$ in 2015). The costs and health outcomes were undiscounted as they were accrued within one year.

### Effectiveness data

The follow-up time since the date of randomization until death or the 365th day, whichever occurred earlier, was used as a proxy of life-years. Mortality data was obtained from the state-wide mortality register, with Public Health Act approval. Quality-adjusted Life-years (QALY) were used as the primary effectiveness measure for this analysis. The utility values were derived from Quality of life using the Assessment of Quality of Life (AQoL-4D),<sup>15</sup> which is a utility instrument validated in Australian clinical and nonclinical population samples. Multiple imputations with a randomly-generated seed number was used to replace missing values in the AQoL-4D measurements collected at baseline (missing: 8.9%; 25/278) and 6 months (missing: 30.5%; 85/278). For each missing value, ten possible values were created using multiple linear regression with the covariates of baseline age, gender, Charlson Comorbidity Index,<sup>16</sup> ejection fraction and whether HF was newly-diagnosed or decompensation of known disease. The mean value from the ten data sets were used as the final imputed value. QALYs per patient were then estimated using the area-under-the-curve method from patient-reported utility scores.

### Cost-effectiveness analyses

Cost-effectiveness was assessed by the incremental cost per QALY gained from the intervention. An incremental cost-utility ratio (ICUR) was calculated and the uncertainty surrounding it was quantified<sup>17</sup> as part of a sensitivity analysis. We graphically presented this uncertainty with a 95% confidence ellipse on cost-effectiveness plane and in addition presented the cost-effectiveness acceptability curves (CEAC) to report the probability of ET being cost-effective for a range of willingness-to-pay thresholds per QALY gained.<sup>18</sup> We used a base-case of \$50,000 per QALY gained as it is a commonly-cited threshold in Australian cost-effectiveness analyses.<sup>19–21</sup> As the ICUR can be negative, which has limited interpretability, incremental net monetary benefit (INMB) was also used to facilitate broader understanding of cost-effectiveness.  $INMB = \lambda * \Delta QALY - \Delta Cost$  where  $\lambda$  is the decision maker's maximum willingness to pay for a QALY and  $\Delta$  is the difference between intervention (ET+DMP) and comparator (DMP alone) groups. If INMB is above zero, the intervention is deemed cost-effective at the chosen  $\lambda$ . Three cost-utility analyses were undertaken in the overall population ( $n = 278$ ), patients aged less than 70 ( $n = 180$ ), and patients aged 70 years and older ( $n = 98$ ).

### Sensitivity analysis

One-way sensitivity analyses were conducted to test the robustness of the base-case results to the changes in the assumption about staff capacity and gym occupancy, as these could sway the cost of intervention. The number of patients catered for per centre per year was assumed to be 60 informed by the EJECTION-HF study, and this was varied between 40 and 80 (base-case: 60). In addition, the gym occupied by the HF program was assumed to be 20% of the time representing its usable life, which was tested with 50% and 100% (base-case: 20%). In addition, the uncertainty surrounding ICUR was quantified with 1000 bootstrap simulations and graphically presented as cost-effectiveness plane and CEAC. Statistical analyses were performed using Stata version 14 (Stata Corp). Bootstrapping and the CEAC were conducted with Microsoft Excel.

### Results

The trial enrolled 278 participants (140 ET+DMP and 138 DMP), with vital status, mortality and readmission data available for all

**Table 3**  
Cost-utility analysis over 12 months follow-up

	Cost (mean)	$\Delta$ Cost (mean difference, 95% CI)	Death (n,%)	QALY (mean)	$\Delta$ QALY (mean difference, 95% CI)	ICUR* (\$/QALY, 95% CI)	INMB at $\lambda$ (95% CI)		Probability that ET is cost-effective at $\lambda$	
							\$50,000	\$100,000	\$50,000	\$100,000
Overall	ET+DMP (n = 140) DMP (n = 138)	\$16,737 \$14,332	3 (2.1%) 10 (7.2%)	0.574 0.555	0.02 (-0.04 to 0.08)	\$128,889	\$-1472 (-3,615 to 671)	\$-539 (-1,301 to 223)	29.6%	43.3%
Aged <70	ET+DMP (n = 89) DMP (n = 91)	\$14,856 \$15,412	8 (9.0%) 4 (4.4%)	0.611 0.541	0.07 (0.01 to 0.13)	Dominant	\$4059 (1,757 to 6360)	\$7561 (7,046 to 8077)	83.6%	92.2%
Age $\geq$ 70	ET+DMP (n = 47) DMP (n = 51)	\$20,020 \$12,241	12 (23.5%) 10 (21.3%)	0.510 0.583	-0.07 (-0.13 to -0.01)	Dominated	\$-11,469 (-13,325 to -9613)	\$-15,160 (-16,302 to -14,017)	1.7%	2.0%

Costs reported in 2015 Australian dollar values (undiscounted).

Cost and Effect discounted at 5%. 95% CI: confidence interval, ET: center-based exercise training, ICUR: incremental cost-effectiveness ratio, INMB: incremental net monetary benefit, QALY: quality-adjusted life-year,  $\lambda$ : willingness to pay.  
\* ICURs were bootstrapped.

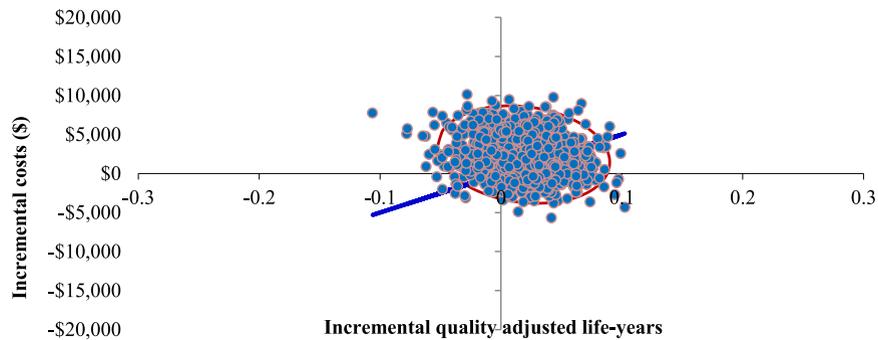
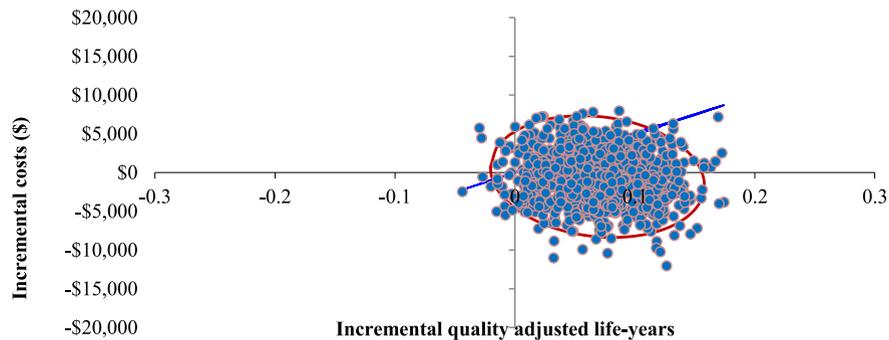
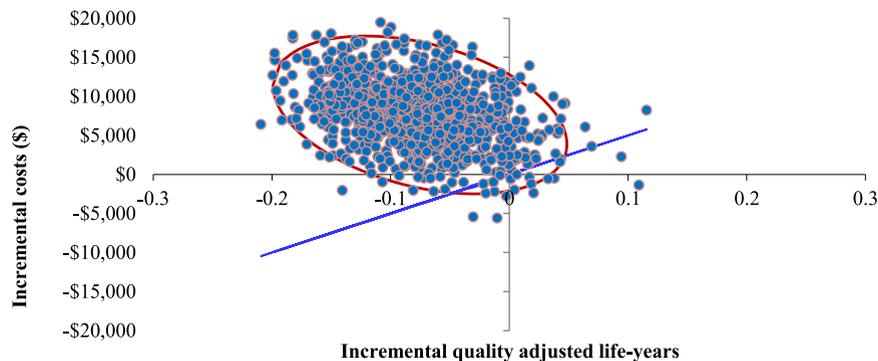
**1a: Overall patients (n=278)****1b: Aged <70 (n=180)****1c: Aged ≥70 (n=98)**

Fig. 1. Cost effectiveness plane (ET+DMP vs. DMP).

participants at 12 months. The flow of participants including reasons for non-participations was previously reported.<sup>11</sup> Briefly, 8/140 patients in the ET+DMP group did not receive allocated intervention (1 died before commencement; 4 did not attend any group session; 3 attended education sessions only), and 23/138 patients in the DMP group did not receive allocated intervention (3 crossed over to ET+DMP; 20 did not attend any group sessions). Further, among 180 patients aged less than 70 (ET+DMP  $n=89$  vs. DMP  $n=91$ ), 165 patients completed the AqoL-4D at baseline (ET+DMP  $n=83$  vs. DMP  $n=82$ ) and 117 patients completed it at 6 months (ET+DMP  $n=60$  vs. DMP  $n=57$ ). Among 98 patients aged older than 70 (ET+DMP  $n=51$  vs. DMP  $n=47$ ), 88 patients completed the AqoL-4D at baseline (ET+DMP  $n=47$  vs. DMP  $n=41$ ) and 76 patients completed it at 6 months (ET+DMP  $n=37$  vs. DMP  $n=39$ ). The quality of life data was unavailable at 6 months for 43 of 140 ET+DMP participants (2 died, 9 too sick/inpatient, 14 declined, 6 moved/returned to work, 10 unable to contact, 2 had incomplete data) and for 42 of 138 DMP-alone participants (5 died, 8 too sick/inpatient, 13 declined, 6 moved/returned to work, 10 unable to contact).

Table 1 shows the clinical characteristics of our study participants by age group. Overall, mean age was 62 years (SD 14), 207 (74.5%) of participants were male, the mean Charlson comorbidity score (unadjusted for age) was 2.8 (SD 1.6), 216 (77.7%) had left ventricular ejection fraction (LVEF) <40% and 154 (55.4%) had newly-diagnosed HF. Participants older than 70 years ( $n=98$ ) were more likely females (30.6% vs 22.8%,  $p=0.15$ ), less likely to have LVEF <40% (59.2% vs 87.8%,  $p<0.001$ ), more likely to have decompensated disease (59.2% vs 36.7%,  $p<0.001$ ) and had higher comorbidity score (3.5 vs 2.5,  $p<0.001$ ). There were no significant differences in participant characteristics, evidence-based medication use, or DMP attendance between ET+DMP and DMP alone overall.<sup>11</sup>

#### Cost

The healthcare costs collected within trial are presented in Table 2. All cost comparisons were statistically non-significant ( $p>0.05$ ). The mean hospital costs and the number of admissions were slightly lower in ET in the overall population (\$-210; -0.11) and those aged <70 (\$-3090; -0.37), while they were higher in ET in those aged  $\geq 70$  (+\$5012; +0.34).

The mean emergency department costs and the number of visits were higher in ET for all groups: overall (+\$176; +0.22), those aged <70 (+\$95; +0.33) and those aged ≥70 (+\$328; +0.03). Hospital admissions accounted for the majority of the total healthcare costs, accounting for 81% (ET +DMP) and 96% (DMP) in the overall population; 78% (ET+DMP) and 96% (DMP) in those aged <70; and 84% (ET+DMP) and 96% (DMP) in those aged ≥70. The marginal cost of the intervention per patient was AU\$2439 in the ET group, which accounted for 15% (overall), 16% (aged <70) and 12% (aged ≥70) of the total costs in the ET group. The mean total costs were higher in ET for the overall population (+\$2405 [95% CI: -2677 to 7487]) and those aged ≥70 (+\$7779 [95%CI: -609 to 16,167]), but lower in ET in those aged <70 (-\$556 [95%CI: -6975 to 5863]).

**Effects**

In the entire population, the mean life-years per patient for ET +DMP and DMP were 0.98 (SD 0.13) and 0.95 (SD 0.18) years, respectively. In patients aged <70, they were 0.99 (SD 0.47) and 0.94 (SD 0.02) years, respectively. In those aged ≥70, they were 0.95 (SD 1.97) and 0.96 (SD 0.15), respectively. Table 3 shows cost-utility analyses and the between-group differences in costs and QALY. In the overall population, the mean QALY per patient was 0.57 for the ET+DMP group and 0.55 years for the DMP group, resulting in 0.02 QALY gain (95% CI: -0.04; 0.08). In patients aged <70, the difference was 0.07 QALY gain (95% CI: 0.01; 0.13), and in those aged ≥70, the difference was 0.07 QALY loss (95% CI: -0.13; -0.01).

**Cost-effectiveness**

As shown in Table 3, in the overall population, the mean ICUR was AU\$128,889 per QALY and the INMB was less than zero (i.e. ET was not cost-effective). In patients aged <70, ET was dominant (less costly, higher QALY) and the INMB was AU\$4059 (95%CI: \$1757 to

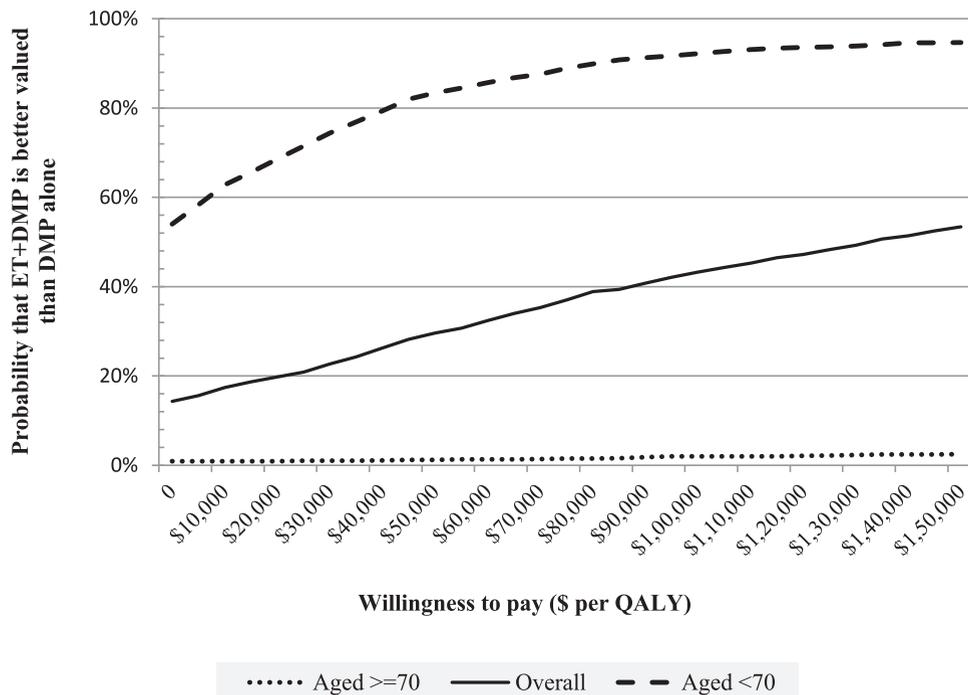
\$6360) at the AU\$50,000/QALY threshold. In patients aged ≥70, ET was dominated by comparator (higher cost, lower QALY) and the INMB was less than zero at the AU\$50,000/QALY threshold.

The bootstrapped cost-effect pairs sampled from the trial data are presented as a scatterplot on the cost-effectiveness plane in three comparisons: the overall population (Fig. 1a), in those aged <70 (Fig. 1b) and those aged ≥70 (Fig. 1c). The horizontal axis represents the difference in QALY (ET+DMP minus DMP). The vertical axis represents the difference in total healthcare costs (ET+DMP minus DMP). The dots in the north-east quadrant indicate that intervention generated a greater number of QALYs while increasing total costs. The position in the south-east quadrant indicates a greater number of QALYs while reducing total costs (dominant), while the north-west quadrant indicates reduced QALYs at higher costs than the comparator (dominated). The red surrounding circle corresponds to a 95% confidence ellipse. The blue angled straight line indicates where the ICUR is AU\$50,000 per QALY.

As Fig. 1a–c shows, the younger group was predominantly represented in the south-east quadrant (Fig. 1b), while the older group was represented mostly in the north-west quadrant (Fig. 1c). A similar trend is seen in CEACs in Fig. 2, which show a probability of cost-effectiveness at varying willingness-to-pay thresholds. At the threshold of AU\$50,000/QALY, there was a 29.6% probability of ET being cost-effective in the overall population, 83.6% in the aged <70, and 1.7% in the aged ≥70.

**Sensitivity analysis**

Table 4 shows different scenarios where the input cost of the intervention was varied according to the number of patients catered for per centre per year and the percentage of the time the gym was used for HF-specific programs. None of these variations materially influenced the ICUR, INMB or the probability of ET being cost-effective. At the AU\$50,000 threshold, the incremental net benefit of ET was negative (INMB <0) under all



Overall patients (n=278); aged <70 (n=180); aged ≥70 (n=98)

**Fig. 2.** Cost effectiveness acceptability curve.

scenarios, suggesting that ET was not cost-effective in the overall population. At the AU\$100,000 threshold, the INMB was marginally positive when staff's catering capacity was assumed to be 400 patients per year. This was an optimistic assumption; even then, the INMB was small ranging from \$47 to \$71. The probability of ET being cost-effective ranged from 18.1% to 37.9% (base-case: 29.6%) at the AU\$50,000 threshold, while it ranged from 33.4% to 50.8% (base-case: 43.3%) at the AU\$100,000 threshold.

**Discussion**

We evaluated the cost-effectiveness of ET as an add-on strategy to a heart failure post-discharge DMP, using data from a multi-centre randomised controlled trial.<sup>11,12</sup> Given the trial primary outcome (12 month all-cause death or readmission) suggesting age as a potential effect modifier, we undertook subgroup analyses in those aged less than 70 years and older participants<sup>11</sup> to explore the impact of age on cost-effectiveness. Over 12 months of complete follow-up, we found that the addition of ET to a DMP was not cost-effective at AU\$50,000/QALY in the entire sample or the older subgroup, but potentially cost-effective in the subgroup aged less than 70 years. At the threshold of AU\$50,000/QALY, there is a 29.6% probability of ET being cost-effective in the overall population, 83.6% in those aged <70, and 1.7% in those aged ≥70

The poor cost-effectiveness seen in the older age group was driven by an increase in hospital readmissions and associated hospital costs. Several reasons may explain this finding. The older subgroup had greater multi-morbidity which may make participation in ET more challenging and reduce the physiological benefits of ET.<sup>22–24</sup> They were also more likely to have HF with preserved ejection fraction, where the evidence for ET effectiveness is poorer,<sup>24</sup> and more likely to be advanced in the disease trajectory rather than newly diagnosed. Patients with multi-morbidity are more likely to have hospital utilisation unrelated to their HF diagnosis, which is unlikely to be impacted by the HF-directed intervention. Indeed, in our primary analysis we reported only 20% of hospital readmissions were due to HF,<sup>11</sup> consistent with large registry findings<sup>25</sup> and reflecting our 'real world' inclusion criteria in this trial. It is also possible that intense follow-up and monitoring within the ET+DMP group may have contributed to the increased hospital readmissions in this older subgroup with more co-morbidities. Importantly, there were no serious adverse event associated with exercise training per se in either subgroup.

The strengths of our study include the pragmatic design of multiple sites involving staff with differing skills and experience, and consideration of a range of real-world settings in sensitivity analyses to facilitate judgements on generalisability. We also recognise several limitations. First, each study centre had its unique resource requirements and there was a moderate between-centre variability, which was reflected in costs. The extent of the between-centre variability may have masked the between-group cost differences, and thus, underestimated the true cost impact of the added ET. Second, comparative information on the use of community care was unavailable, and out-of-hospital costs were not included in our analyses. Even in studies where such costs were included, however, the majority of healthcare costs tends to be represented by hospital-based costs (85–89%),<sup>13</sup> thus, it is unlikely that inclusion of these costs would have substantially changed the findings. Third, despite broad eligibility criteria, only 11% of screened patients were recruited,<sup>11</sup> who tended to be younger and with fewer comorbidities than reported in HF registry studies,<sup>25</sup> and may have been more motivated than the general HF population. Nevertheless, this selectivity likely reflects the type of patients who would engage with this intervention in the real world. Fourth, the DMP included a well-supported home exercise program (unsupervised) for participants in both groups, which may not be a typical service, highlighting the importance of considering contextual factors and the role of co-interventions in designing future studies.

**Table 4**  
Sensitivity analysis by varying staff capacity and gym occupancy (Overall, N = 278)

Staff capacity* (# patients per year)	Cost of intervention /person/year	Δ Total Cost (95% CI)	Δ QALY (95% CI)	ICUR (\$/QALY)	INMB at λ			Probability that ET is cost-effective at λ	
					λ=\$50,000		λ=\$100,000	λ=\$50,000	λ=\$100,000
					INMB	95% CI	INMB	Probability	Probability
Gym occupancy 20%	200 300 (Base-case)	\$3624 (-1423 to 8671) \$2405 (-2642 to 7452)	Same as base case 0.02 (-0.04 to 0.28)	\$194,216 \$128,889	\$-2691 \$-1472	\$-1758 \$-539	20.6% 29.6%	33.4% 43.3%	
Gym occupancy† 50%	400 300	\$1795 (-3252 to 6842) \$3642 (-1405 to 8689)	Same as base case Same as base case	\$96,199 \$195,181	\$-862 \$-2709	\$71 \$-1776	37.7% 18.1%	50.4% 33.6%	
Gym occupancy‡ 100%	200 300 400	\$2417 (-2630 to 7464) \$1804 (-3243 to 6851) \$3671 (-1376 to 8718)	Same as base case	\$129,532 \$96,681 \$196,735	\$-1484 \$-871 \$-2738	\$-551 \$62 \$-1805	33.6% 36.7% 19.3%	45.8% 48.2% 35.3%	
	200 300 400	\$2436 (-2611 to 7483) \$1819 (-3228 to 6866)	Same as base case	\$130,550 \$97,485	\$-1503 \$-886	\$-570 \$47	29.7% 37.9%	43.7% 50.8%	

Costs reported in 2015 Australian dollar values. \*Total cost\* includes hospital costs, non-admitted emergency department costs, and intervention costs. CI: confidence interval; ICUR: incremental cost-effectiveness ratio, INMB (incremental net monetary benefit): if INMB>0, ET is cost-effective at λ (willingness to pay). † The number of patients catered for per year (5 centres). ‡ To make the estimates conservative, the lower limit was set to 200 and we used 300 as the base-case (60 × 5). † Gym occupancy:% of use by the heart failure exercise training.

Finally, although our subgroup analysis was pre-specified, the sample size was relatively small, and caution should be taken when interpreting the results.

## Conclusion

In summary, adding a 24-week structured ET program to a heart failure post-discharge DMP was not cost-effective overall and in those aged 70 or older, but it was relatively cost-effective in patients aged less than 70. Better understanding of the exercise rehabilitation needs and potential of older patients, and exploration of different models of participant selection and intervention delivery may be needed for ET to broadly benefit HF patients who are receiving a DMP.

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## Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2019.03.003.

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