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Does exercise training prescription based on estimated heart rate training zones exceed the ventilatory anaerobic threshold in patients with coronary heart disease undergoing usual-care cardiovascular rehabilitation?: A United Kingdom perspective.

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Abstract

Background: In the United Kingdom (UK), exercise intensity is prescribed from a fixed percentage range (% heart rate reserve; %HRR) in cardiac rehabilitation (CR) programmes. We aimed to determine the accuracy of this approach by comparing it with an objective, threshold-based approach incorporating the accurate determination of ventilatory anaerobic threshold (VAT). We also aimed to investigate the role of baseline cardiorespiratory fitness status, and exercise testing mode dependency (cycle v treadmill ergometer) on these relationships.

Design/Methods: A maximal cardiopulmonary exercise test was conducted on a cycle ergometer or a treadmill before and following usual-care circuit training from two separate CR programmes from a single region in the UK. The heart rate corresponding to VAT was compared to current heart rate-based exercise prescription guidelines.

Results: We included 112 referred patients (61 years [59-63]; body mass index $29 \text{ kg}\cdot\text{m}^{-2}$ [29-30]; 88% male). There was a significant but relatively weak correlation ($r=0.32$; $P=0.001$) between measured and predicted %HRR, and values were significantly different from each other ($P=0.005$). Within this cohort, we found that 55% of patients had their VAT identified outside of the 40-70% predicted HRR exercise training zone. In the majority of participants (45%), the VAT occurred at an exercise intensity $<40\%$ HRR). Moreover, 57% of patients with low levels of cardiorespiratory achieved VAT at $<40\%$ HRR. Whereas, 30% of patients with higher fitness achieved their VAT at $>70\%$ HRR. VAT was significantly higher on the treadmill than the cycle ergometer ($P<0.001$).

Conclusion: In the UK, current guidelines for prescribing exercise intensity are based on a fixed percentage range. Our findings indicate that this approach may be inaccurate in a large proportion of patients undertaking CR.

Word Count: 274 words

Key words: cardiac rehabilitation, exercise prescription, cardiorespiratory fitness, ventilatory anaerobic threshold.

1 Introduction

2 Cardiovascular rehabilitation (CR) is a multi-disciplinary secondary prevention programme
3 that has been shown to contribute to reduced hospital admissions, and improvements in
4 patient quality of life, following a cardiac event.(1-4) Historically, a 1% improvement in peak
5 oxygen uptake (VO_{2peak}) resulting from exercise-based CR, was thought to confer a 2%
6 reduction in premature mortality.(5) Similarly, every $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ increment in VO_{2peak}
7 has been associated with a 12-13% survival benefit (6, 7) in men referred for exercise
8 testing. Therefore, it is essential that the prescribed dose of exercise is sufficient to
9 stimulate improvements in VO_{2peak} following CR. Recent systematic reviews and meta-
10 analyses have shown that increased exercise intensity is an important factor in achieving
11 superior outcomes in patients with cardiovascular disease.(8, 9)

12 The prescribed dose of exercise can be influenced by manipulating exercise frequency,
13 duration, type/mode, and/or intensity [exercise dose].(10) In the United Kingdom (UK),
14 current long-term exercise training guidelines for patients undertaking CR, recommend
15 exercise training intensities between 40-70% heart rate reserve (HRR), oxygen uptake
16 reserve (VO_{2R}), or a Borg rating of perceived exertion (RPE) between 11-14.(11, 12) Both
17 continuous and interval training at an objective physiological threshold has been shown to have a
18 beneficial impact by improving VO_{2peak} .(13) Training at or above the ventilatory anaerobic
19 threshold (VAT), often referred to as the first ventilatory threshold (VT1), indicates the
20 point above which, further increments in work rate are increasingly supplemented through
21 anaerobic metabolism.(14-17) Despite being associated with mild metabolic
22 perturbations,(16, 17) regular exercise bouts conducted at work rates equivalent to VAT are
23 well tolerated,(18) and induce physiological adaptation leading to improved
24 cardiorespiratory fitness (CRF) and other cardiovascular risk factors.(19, 20) However, whilst

work rates corresponding to VAT may represent a minimum intensity needed to improve CRF, metabolic gas equipment and calibrated ergometers are often not available in a CR setting in the UK. Prescribing exercise as a percentage of measured HRR, or most typically estimated HRR, is often a more practical and realistic alternative in UK cardiac rehabilitation settings.(10)

The 40% HRR threshold is cited as the lowest effective exercise intensity for improving CRF in patients undertaking CR.(10, 12) The individual VAT is widely accepted to occur between 45-65% HRR in healthy and cardiac patients,(8) with lower values reported in patients with a chronic cardiovascular disease.(10) However, the distribution of VAT values, and its relation to exercise capacity, is unclear in patients undertaking CR. How commonly VAT occurs within discrete exercise intensity ranges is also under-reported in patients with coronary artery disease. Tan *et al* (21) showed that the mean VAT was equal to 82% of maximal heart rate (HR), in 19 cardiac patients referred for a cardiopulmonary exercise test (CPET) prior to CR, (21). However, the mode of exercise testing may also influence when an individual's VAT occurs.

In the UK, the mode of exercise testing varies between CR programmes. This means that a patient's exercise prescription could be based on a number of different submaximal exercise tests, including the 6-min walk test, incremental shuttle walk test, step test, or cycle ergometry. The differing metabolic responses to cycling compared with walking may affect a patient's peak oxygen uptake ($\dot{V}O_{2peak}$), and the occurrence of VAT. This, in turn, may significantly affect the accuracy of exercise intensity prescription. These issues have not been addressed sufficiently within UK guidelines for exercise prescription in CR programmes. This information may help practitioners to optimise a patient's initial exercise

prescription and maximise the improvements associated with exercise training programmes. This is especially important when the frequency and duration of CR sessions are finite. We aimed to determine the accuracy of the standard UK approach for prescribing exercise in patients undertaking CR by comparing it with objective measures of exercise prescription, namely $\dot{V}O_{2peak}$ and VAT. Secondary aims were to determine how exercise modality (exercise testing with cycle versus treadmill ergometer), and baseline levels of CRF affected the concordance of VAT and HRR measures.

Methods

Data was collated from the baseline assessment of two separate cohorts who undertook a maximal effort CPET to volitional exhaustion prior to commencing a CR programme. The methods for these studies have previously been reported.(22, 23) Ethical approval was provided by the Yorkshire and Humber – Sheffield National (12/YH/0072) and Humber Bridge NHS (12/YH/0278) Research Ethics Committees. Briefly, patients were recruited following a referral to CR for angina, myocardial infarction (MI), coronary artery bypass graft (CABG), or percutaneous coronary intervention (PCI). Patients attended a baseline study assessment, where written informed consent was obtained. CPET was conducted on a cycle ergometer following a 25W incremental protocol, or on a treadmill following the modified Bruce protocol,(24) adopting previously outlined test termination and maximal effort criteria.(15, 25) Breath-by-breath metabolic gas exchange data were collected using an Innocor (Innovision, Glamsbjerg, Denmark) or Oxycon-Pro metabolic cart (Jaeger, Hoechburg, Germany), respectively, which were calibrated according to manufacturers' instructions and current recommendations.(26) Peak values were averaged over the final 30

seconds of the CPET. $\text{VO}_{2\text{peak}}$ was reported in absolute values ($\text{L}\cdot\text{min}^{-1}$) and standardised to each patient's body mass ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). Individualised VAT was independently determined by two investigators (using the average of the middle five of every seven breaths plotted in the V-slope method, and verified using the ventilatory equivalents.(14, 27) Where investigators reported different VAT values, a third reviewer was consulted and the threshold value agreed by consensus. The VAT was reported in $\text{L}\cdot\text{min}^{-1}$ and $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and expressed as a percentage of directly-determined and predicted $\text{VO}_{2\text{peak}}$.(28) The HR at VAT was then established and reported as a ratio of HRmax and HRR determined from CPET, and as a ratio of predicted HRmax and HRR with relevant adjustment for the effects of beta-blockade on maximal heart rates as follows [10]):

$$((205.8 - (0.685 \times \text{age})) - \text{resting heart rate} (-30 \text{ beats per min if taking beta-blockers}))$$

To characterise where a patient's VAT occurred in relation to established training zones, the VAT values were categorically assigned to exercise intensity groups of <40%, 40-49%, 50-59%, 60-69%, 70%, and >70% of measured, and predicted HRR. Adjustment for β -blockades were made where appropriate,(12). We assessed how many patients had a VAT that occurred within the exercise training intensity ranges recommended by UK CR guidelines, namely 40-70% HRR, or an RPE between 11-14.(11, 12) Patients were sub-categorised according to individual CRF levels as low (<5 METs for women, <6 METs for men), moderate (5<7 METs for women, 6<8 METs for men), and high CRF (≥ 7 METs for women, ≥ 8 METs for men), based on exercise capacity (MET) thresholds derived from the international literature and previously applied to cardiac patients in the UK.(29) These sub-groups were then

categorised based on the HRR zone that the individualised VAT occurred within. We also conducted sub-analyses on patients who undertook their CPET either on a treadmill or cycle ergometer.

Data analysis

Statistical analysis was conducted using SPSS version 24 (IBM, NY, USA). When data was not normally distributed, normalisation of the distribution was attempted using $\log_{10}$ transformation. Logarithmically transformed data was analysed in its transformed state and reported as an arithmetic mean to allow for meaningful interpretation. Normally distributed and transformed data were analysed using a univariate general linear model with significance set at arbitrary level ($P < 0.05$), and is presented as mean (95% confidence intervals), and partial-eta squared (η_p^2) effect sizes, with 0.01, 0.06, and 0.14 denoting small, moderate, and large effects, respectively (30). For non-normally distributed data, a Mann-Whitney U test was conducted with median and range reported. Categorical data was analysed using a Chi-squared test of independence and reported as percentage and frequency. When ≥ 1 cell had an expected value < 5 , the Fisher's exact test was used.

Results

Patient Characteristics

One-hundred and twelve ($n=112$) cardiac patients were included for analysis (61.3 years [59.4-63.1]; 29.3 kg·m⁻² [28.5-30.1]; 88% male). Forty-two patients ($n=42$; 37.5%) undertook their CPET on a cycle ergometer. Patients on a cycle ergometer achieved 79.1% of their predicted HRmax [74.6-83.6%], an RPE of 18 [17-18], and a peak respiratory exchange ratio

(RER) of 1.02 [1.00-1.05). Seventy ($n=70$) patients undertook CPET on a treadmill. Patients conducting CPET on a treadmill achieved 82.3% [79.7-84.9%] of predicted HRmax), an RPE of 17.8 [17.3-18.3], and a peak RER of 1.09 [1.06-1.11]). 77% and 86% of the patients undergoing cycle and treadmill testing, respectively, were prescribed beta-blockers. The majority of patients had a diagnosis of myocardial infarction (MI) with primary (32.5%) or elective (28.9%) PCI. There was a greater prevalence of active smokers ($P=0.017$) in those that conducted a CPET on a cycle ergometer. There were significant between-group differences for age ($P=0.012$; $\eta_p^2=0.054$), and resting HR (mean difference 5.8bpm (95% CI 1.0-10.5bpm) $P=0.032$; Table 1) between the test modality groups. 42 out of 112 patients, were classified within the lower cardiorespiratory fitness group, 50 in the moderate-fit group, and 20 in the high-fit group (Table 2).

VAT, HRR zones, and CRF categories

Measured HRR (72 ± 15 bpm) derived from maximal CPET demonstrated only a modest correlation with predicted HRR (77.99 ± 20.42 bpm) (using current UK CR guidelines ($r=0.32$; $P=0.001$)). However, the directly determined and predicted HRR/peak HR variables were significantly different from each other (mean difference = 6.74bpm (95% CI 2.99-10.49bpm) $P=0.001$). The VAT occurred within 40-70% of directly determined HRR range in 61.6% of patients. In the remaining 38.4% of patients, 33.9% achieved their VAT at <40% HRR, and in 4.5% of patients, their VAT did not occur until >70% HRR. For predicted HRR, VAT occurred within 40-70% HRR in 44.6% of patients. Of the remaining 55.4% of patients, 45.4% achieved VAT at <40% HRR, and 9.8% at >70% HRR (Table 2).

The VAT occurred between 40-70% of predicted HRR in 21.4% of patients undertaking cycling exercise. The majority (76.2%) of patients exceeded the VAT at <40% HRR. For patients undertaking CPET on a treadmill, 58.5% of patients had a VAT that occurred between 40-70% of predicted HRR, and 27.1% had a VAT that occurred at <40% HRR. Interestingly, the VAT occurred between 40-70% of predicted HRR in 35.8% of patients that were categorised as having a low CRF. 57.1% of patients exceeded their VAT at <40% of their HRR. For higher-fit patients, VAT occurred between 40-70% of predicted HRR in 50% of patients, at <40% HRR in 20%, and >70% HRR for the remaining 30% of patients (Table 2).

Figure 1 shows the inter-quartile range for VAT as a percentage of predicted HRR, based on CRF category, and exercise testing modality. The VAT occurred at a higher percentage of VO_{2peak} in patients with a higher CRF. This observation was also evident when CPET was conducted on a treadmill for all CRF categories, but most apparently in the moderate and high-fit groups.

Directly measured compared with predicted cardiorespiratory fitness variables

Mean VO_{2peak} was not significantly different between exercise modality groups in absolute units ($P=0.644$; $\eta_p^2=0.002$), or relative to body mass ($P=0.359$; $\eta_p^2=0.008$) (Table 3).

However, absolute ($P=0.027$) and relative ($P=0.001$) VAT was significantly different across the different CRF groups. VAT occurred at a higher percentage of predicted ($P=0.003$; $\eta_p^2=0.08$) and measured VO_{2peak} ($P<0.001$; $\eta_p^2=0.151$), and HRR ($P<0.001$; $\eta_p^2=0.132$) in

patients exercising on the treadmill. Measured HRR ($P=0.012$; $\eta_p^2=0.056$), and HR at VAT ($P=0.016$; $\eta_p^2=0.052$) were significantly higher in the treadmill group. There was a significant

1 between-group difference for predicted HRmax adjusted for β -blockade ($P=0.003$; Table 4).
2 However, there was no difference in predicted HRR ($P=0.863$, $\eta_p^2<0.001$) or VO_{2peak}
3 between groups ($P=0.815$, $\eta_p^2<0.001$). Figures 2a and 2b highlight individual case studies
4 which demonstrate how the predicted HRR method can either over- or under- estimate
5 individualised exercise prescription versus directly determined HRR and VAT.

7 Discussion

8 This study aimed to determine the accuracy of the standard UK approach for prescribing
9 exercise in patients undertaking CR. This method of determining target heart rates for
10 exercise training in cardiac patients relies largely on predictive methods for determining
11 maximal HR (including patients taking beta-blockade). We sought to compare it with a more
12 objective measure of exercise prescription, namely the VAT derived from respiratory gas
13 exchange during a maximal CPET. Our findings indicate that current UK CR exercise
14 prescription guidelines appear susceptible to substantial inaccuracy with more than half of
15 our cohort achieving a VAT outside the recommended target range of 40-70% HRR. We
16 found that 45% of patients had VAT identified at <40% HRR, and in 9% of patients, VAT was
17 identified at >70% HRR, suggesting that the required exercise intensity spectrum is wider
18 than the recommended 40-70 HRR%.

19 When considering baseline cardiorespiratory fitness, the proportion of patients whose VAT
20 occurred outside the guidelines increased. 57% of low-fit patients achieving VAT at <40%
21 HRR, and 30% of high-fit patients achieving VAT at >70% HRR, confirming that VAT occurs
22 later with increasing CRF in cardiac patients.(31) For those who achieved VAT at <40% HRR,

1 their exercise prescription may overly exceed VAT and prove too challenging, whilst for
2 those that achieve VAT >70%HRR, their prescription is unlikely to induce a training stimulus
3 and prove too easy. We speculate that this may contribute to the 23% attrition rate recently
4 reported in UK CR,(32) as some patients overly exceed their training stimulus (i.e. low fit
5 patients), which may be uncomfortable, whilst some do not reach it, thus providing minimal
6 benefit (i.e. high fit patients), both of which may cause patients to discontinue CR.

7 Therefore, a *one size fits all* approach, relying on predictive methods for maximal HR and
8 estimated HRR to prescribe exercise appears ineffective. Exercise prescription within cardiac
9 rehabilitation settings needs to be more accurate, patient specific and fine-tuned, ideally
10 based on ventilatory markers, actual HRR and baseline fitness category determined via
11 CPET.(33) One option could be to shift from 'range-based' to 'threshold-based' CR exercise
12 prescription, with moderate-high intensity exercise, corresponding to work rates between
13 VAT and critical power, being recommended.(17) Based on the current data, CPET would aid
14 prescription to ensure that *all* patients achieved VAT during CR, whilst also ensuring it is not
15 overly exceeded. This is important given that certain cardiac patients, namely those who
16 may be more deconditioned, often perform activities of daily living at levels of VO_2 that
17 exceed VAT.(34) Therefore, exercising in steady-state conditions above VAT is vital for these
18 patients, but may not be possible if it is exceeded. In the late 1970s, limitations in the
19 relative percent method (i.e %HRR) for prescribing exercise intensity were identified, with a
20 study by Katch *et al* showing this method failed to consider individual metabolic
21 differences,(35) yet it is still a recommended approach today.(8,10) More recent
22 investigations have proposed a more individualised exercise prescription based on
23 ventilatory thresholds to personalise individualised training load based on metabolic
24 responses.(36, 37) Recently, Weatherwax *et al* reported that in sedentary adults, 12 weeks

1 of aerobic exercise training based on an individualised exercise prescription using VAT had a
2 greater effect on the incidence of training response compared to a standardised approach
3 using HRR. While the exact mechanisms are still not entirely understood, it is believed that
4 exercise intensity prescribed with the use of ventilatory thresholds takes into consideration
5 individual metabolic characteristics which are overlooked when using relative percent
6 methods.(38)

7
8 The current data also indicate that VAT is mode-dependant for the overall cohort and across
9 all three CRF categories. Similar to previous suggestions,(17) VAT occurred at around 50%
10 HRR on the treadmill but is 12-15% lower on the cycle. A similar relation has also been
11 observed in patients with chronic heart failure.(39) This mode dependency is also evident in
12 terms of predicted HRR zones, which are adopted in most UK CR centres, with >75% of
13 patients on a cycle ergometer achieving VAT at <40% HRR, compared with just 27% of
14 patients exercising on a treadmill. Previous research has identified a VAT mode dependency
15 in cardiac patients based on VO_2 .(40) The current results differ somewhat as they show a
16 mode dependency for patients who are yet to begin as opposed to those who have finished
17 CR. Furthermore, in the current study this mode dependency is expressed using HRR, which
18 is adopted in most CR centres, rather than VO_2 .

19 UK CR is provided by the state-funded National Health Service, unlike CR operating in other
20 international and EU countries,(15) the integration of CPET equipment is not currently
21 incorporated into most UK centres and may prove to be prohibitive.(41) Another possible
22 solution could be to increase the upper intensity limit of exercise prescription in line with
23 international guidelines at 80% HRR, especially for patients in a higher fit category.(10, 42)

1 Of the 10 patients whose VAT occurred at >70% HRR, 6 achieved VAT at <80% HRR. This
2 suggests that increasing the upper range of exercise prescription guidelines could be helpful
3 to a small cohort of patients, and provide greater scope for training progression in those
4 that could tolerate it; aligning UK guidelines closer to those seen internationally.(43) This
5 does not however, address the issue for those who achieved VAT at <40%. A further
6 alternative to personalise exercise prescription across the whole spectrum would be to
7 identify the HR range corresponding to an RPE of 11-13, given that VAT has been shown to
8 occur around this point (44, 45). Submaximal testing is routinely performed in UK CR and
9 identification and utilisation of the HR between these points during testing could ensure
10 more patients are exercising at or around the VAT. One caveat to such an option is that RPE
11 is a subjective tool, meaning that appropriate anchoring of key values would be required for
12 each patient, and this would need to be applied consistently within and between each CR
13 centre in the UK.

14 To be able to confidently prescribe an individualised exercise programme in a safe and
15 effective manner can be challenging in a cardiac population. The healthcare professional
16 must be able to account for medication usage, presence of non-CV co-morbidities, and for
17 example, adverse events during exercise testing. Hansen and colleagues [46] showed
18 significant inter-clinician variance in prescribing exercise for patients with different CVDs,
19 highlighting the challenges posed. Further training and education is key, however, digital
20 resources are available to assist practitioner decision-making processes. For example, the
21 European Association of Preventive Cardiology recently developed the Exercise Prescription
22 in Everyday Practice and Rehabilitative Training (EXPERT) tool.[47] The EXPERT tool is an
23 interactive, digital training and decision support system that assists healthcare professionals
24 in prescribing clinically effective and medically safe exercise training programmes for CVD

1 patients. The adoption of tools such as EXPERT should be more widely encouraged and
2 facilitated to support decision making processes around exercise prescription in cardiac
3 populations. The impact of their utility within clinical practice could then be audited to
4 determine changes in efficacy.

6 Limitations

7 The key limitation is that the two groups are made up of separate patients who varied on
8 some baseline characteristics. Ideally, all patients would have completed a CPET using both
9 modalities to reduce any individual effect.

11 Conclusion

12 To our knowledge, this is the first study of its kind to explore VAT in terms of prescribed HRR
13 zones for cardiac patients to identify the accuracy of current UK CR exercise prescription
14 guidelines. For a large proportion of patients, the guidelines are inaccurate with many
15 patients achieving VAT at <40% HRR, meaning their exercise prescription may be overly
16 challenging. Conversely, 30% of high-fit patients achieved VAT at >70% HRR, meaning their
17 prescription may be too conservative to provide a stimulus. This under/over-prescription
18 may lead patients to unnecessarily discontinue their CR (see Figures 2a and 2b). Therefore,
19 for UK CR, a *one size fits all* approach is ineffective and a shift from predictive equations and
20 submaximal exercise tests to gold-standard CPET on entry to CR would be required to
21 improve exercise prescription. However, this may not be viable for a number of reasons,
22 meaning that adoption of less conservative guidelines could provide a solution to ensuring
23 that a larger proportion of patients achieve a training stimulus. Furthermore, although

1 $\text{VO}_{2\text{peak}}$ did not demonstrate a mode dependency, VAT did. This suggests that it may be
2 necessary to conduct a CPET using both modalities, or tailor exercise prescription based on
3 the modality used. Future research could confirm this mode dependency for HRR at VAT in
4 cardiac patients by testing the same group of patients twice, once during each modality.

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4 Conflict of interest

5 The authors declare that there is no conflict of interest.

6 Author contributions

7 Both SP and SN have contributed equally to this manuscript, therefore we would like them
8 both to be acknowledged as joint first authors. SN, SC and LI contributed to the design of
9 the work. SN conducted data collection. SN, SB, SP and JP conducted data analysis and
10 drafted the manuscript. SB, JP, SC, LI critically reviewed the manuscript. All gave final approval
11 and agree to be accountable for all aspects of work ensuring integrity and accuracy.

12

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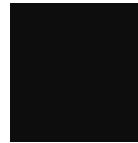
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Table 1

Table 1. Clinical characteristics of patients grouped by exercise modality
Mean (95% CI) † = median and ranges

Variable	Pooled (cycle and treadmill data)	Cycle	Treadmill	P-value	Partial eta- squared
Sex (male/female)	100/14 (87.70% male)	40/4 (90.0% male)	60/10 (85.7% male)	0.411	
Age (years)	61.25 (95% CI; 59.35 to 63.14)	63.13 (95% CI; 60.75 to 65.51)	58.25 (95% CI; 55.21 to 61.29)	0.012*	0.054
BMI (kg/m ²) ^T	29.30 (95% CI; 28.54 to 30.07)	30.1 (95% CI; 28.8 to 31.44)	28.80 (95%CI; 29.74 to 27.90)	0.101	0.024
Resting SBP (mmHg) ^{Tr}	131.55(95% CI; 127.94 to 135.27)	139.57 (95%CI 134.39 to 144.95)	126.74(95% CI; 122.18 to 131.46)	0.001**	0.099
Resting DBP (mmHg) [†]	83 (60 to 149)	85.50 (62 to 104)	82 (60 to 149)	0.09	
LVEF (%)	55.77 (95% CI; 54.34 to 57.20)	57.05 (95%CI; 54.35 to 59.75)	54.99 (95%CI; 53.35 to 56.62)	0.167	0.017

Resting HR (bpm) [†]	60 (42 to 95)	64 (44 to 95)	56 (42 to 91)	0.008**
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BMI, Body mass index. kg·m⁻², kilogram per metre squared. SBP, systolic blood pressure. mmHg, millimetres of mercury. DBP, diastolic blood pressure. LVEF, left ventricular ejection fraction. HR, Heart Rate. Bpm, beats per minute.

P*<0.05, *P*<0.01, ****P*<0.001. †, Variables are reported as median (minimum and maximum) values and analysed using a non-parametric test.

Tr, transformed using log₁₀ transformation and reported as arithmetic mean for meaningful interpretation.

Table 2. The occurrence of VAT in relation to predicted HRR training zones, stratified by exercise modality and baseline CRF levels

Predicted HRR threshold	Number of patients (%)		
	Pooled cycle and treadmill	Cycle	Treadmill
<40% predicted HRR	51 (45.4%)	32 (76.2%)	19 (27.1%)
40-49% predicted HRR	24 (21.4%)	5 (11.9%)	19(27.1%)
50-59% predicted HRR	15 (13.4%)	4 (9.5%)	11 (15.7%)
60-69% predicted HRR	11 (9.8%)	0	11(15.7%)
>70% predicted HRR	11 (9.8%)	1 (2.4%)	10(14.3%)
Total within 40-70% HRR	44.6%	21.4%	58.5%

	Baseline CRF category		
	Low Fit	Mod Fit	High Fit
<40% predicted HRR	24 (57.1%)	23 (46%)	4 (20%)
40-49% predicted HRR	11 (26.2%)	11 (22%)	2 (10%)
50-59% predicted HRR	2 (4.8%)	8 (16%)	5 (25%)
60-69% predicted HRR	2(4.8%)	6 (12%)	3 (15%)
>70% predicted HRR	3 (7.1%)	2(4%)	6 (30%)
Total within 40-70% HRR	35.8%	50%	50%

Predicted heart rate reserve using current guidelines, accounting for beta-blockade. Baseline fitness category based on Taylor et al. (2016); low fit <5 METs for women and <6 METs for men, mod fit = 5<7 METs for women and 6<8 METs for men, high fit ≥7 METs for women, and ≥8 METs for men. VAT, ventilatory anaerobic threshold. HRR, heart rate reserve. MET, metabolic equivalent where 1 MET = 3.5ml·kg⁻¹·min⁻¹.

Table 3

Table 3. Cardiorespiratory data based on maximal CPET in patients using cycle and treadmill exercise modalities

	Pooled	Cycle	Treadmill	P-value	Partial eta-squared
VO _{2peak} (L·min ⁻¹)	2.00 (95% CI; 1.88 to 2.11)	2.03 (95% CI; 1.82 to 2.25)	1.98 (95% CI; 1.83 to 2.12)	0.644	0.002
VO _{2peak} (ml·kg ⁻¹ ·min ⁻¹) Tr	22.12 (95% CI; 19.8 to 24.7)	21.43 (95% CI; 18.0 to 25.5)	22.55 (95%CI; 19.7 to 25.8)	0.359	0.008
HRmax (bpm)†	137 (88 to 181)	131 (88 to 181)	139 (88 to 169)	0.32	
HRR (bpm)	71.5 (95% CI; 67.7 to 75.4)	65.1 (95% CI; 58.9 to 71.3)	75.43 (95% CI; 70.69 to 80.17)	0.009*	0.061
VAT (ml·kg ⁻¹ ·min ⁻¹) †	13.1 (8.2 to 29.7)	13.3 (8.2 to 26.0)	16.6 (8.6 to 30.0)	0.001***	
VAT (L·min ⁻¹) †	1.3 (0.7 to 2.5)	1.15 (0.7 to 2.0)	1.35 (0.7 to 2.5)	0.027*	
HR at VAT (bpm)	94 (95% CI; 91 to 97)	90 (95% CI; 85 to 94)	97 (95%CI; 93 to 101)	0.016*	0.05
VAT (% of VO _{2peak})	67.5 (95%CI; 65 to 70)	61.3 (95%CI; 58 to 65)	71.1 (95%CI; 68 to 74)	<0.001***	0.151
VAT (% of predicted VO _{2peak}) Tr	56.8 (95%CI; 52 to 63)	51.8 (95%CI; 45 to 60)	60.1 (95%CI; 53 to 68)	0.003**	0.08

VAT (% of HRR)	45.90 (95%CI; 43 to 49)	39.45 (95%CI; 35.6 to 43.3)	49.77 (95%CI; 46.5 to 53.0)	<0.001***	0.129
VAT (% of HRmax)	71.58 (95%CI; 70.1 to 73.1)	69.81 (95%CI; 66.9 to 72.7)	72.64 (95%CI; 70.9 to 74.4)	0.072	0.029

CPET, cardiopulmonary exercise test. VO_{2Peak}, Peak oxygen consumption. HRmax, maximum heart rate. Bpm, beats per minute. HRR, heart rate reserve. VAT = ventilatory anaerobic threshold. HR, heart rate. **P*<0.05, ***P*<0.01, ****P*<0.001. †, Variables are reported as median (minimum and maximum) values analysed using a non-parametric test. **Tr**, transformed using log₁₀ transformation and reported as arithmetic mean for meaningful interpretation.

Table 4. Relation between predicted and measured variables stratified by mode of exercise

	Pooled	Cycle	Treadmill	P-value	Partial eta-squared
Predicted HRmax (adjusted for β-blockade; bpm) †	136 (118 to 174)	138 (126 to 174)	134 (118 to 167)	0.009**	
VAT (% of predicted HRmax adjusted for β-blockade)	67.97 (65.86 to 70.07)	62.74 (59.68 to 65.80)	71.10 (68.50 to 73.71)	<0.001* *	0.131
Predicted HRR (adjusted for β-blockade; bpm)	77.85 (95%CI; 75.04 to 80.66)	77.93 (95% CI; 73.19 to 82.68)	77.8 (95%CI; 74.24 to 81.36)	0.965	<0.001
VAT (% of Predicted HRR adjusted for β-blockade)†	40.35 (9.57 to 87.93)	30.49 (9.57 to 69.23)	47.06 (12 to 87.93)	<0.001* **	
Predicted VO _{2Peak} (ml·min ⁻¹)	2272.14 (95% CI; 2184.11 to 2360.17)	2258.79 (95% CI; 2114.05 to 2403.53)	2280.35 (95%CI; 2166.68 to 2394.01)	0.815	<0.001
VO _{2Peak} (% of Predicted VO _{2Peak})	87.85 (95%CI; 84.11 to 91.58)	89.99 (95%CI; 82.64 to 97.35)	86.56 (95% CI; 82.40 to 90.72)	0.380	0.007

HRmax, maximal heart rate. Bpm, beats per minute. VAT, ventilatory anaerobic threshold. HRR, heart rate reserve. VO_{2Peak}, Peak oxygen consumption
*P<0.05, **P<0.01, ***P<0.001. †, Variables are reported as median (minimum and maximum) values and analysed using a non-parametric test.

Figure 1

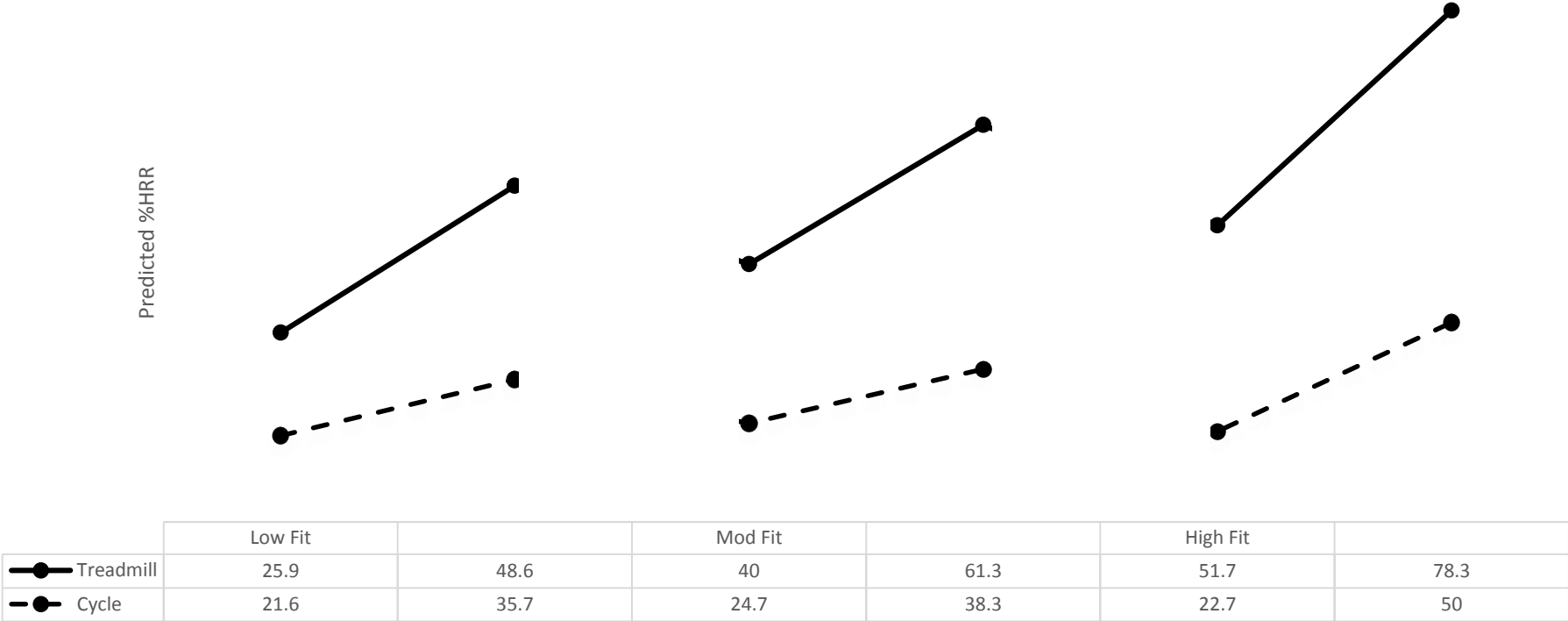


Figure 1. Inter-quartile range of VAT identification based on predicted HRR (% range) in cardiac patients separated by exercise modality and CRF category

Predicted HRR using current guidelines, accounting for beta-blockade. Baseline CRF category based on Taylor et al. (2016); low fit <5 METs for women, and <6 METs for men, mod fit 5<7METs for women, and 6<8 METs for men, high fit ≥7 METs for women, and ≥8 METs for men. VAT, ventilatory anaerobic threshold. HRR, heart rate reserve. MET, metabolic equivalent where 1 MET = 3.5ml·kg⁻¹·min⁻¹.

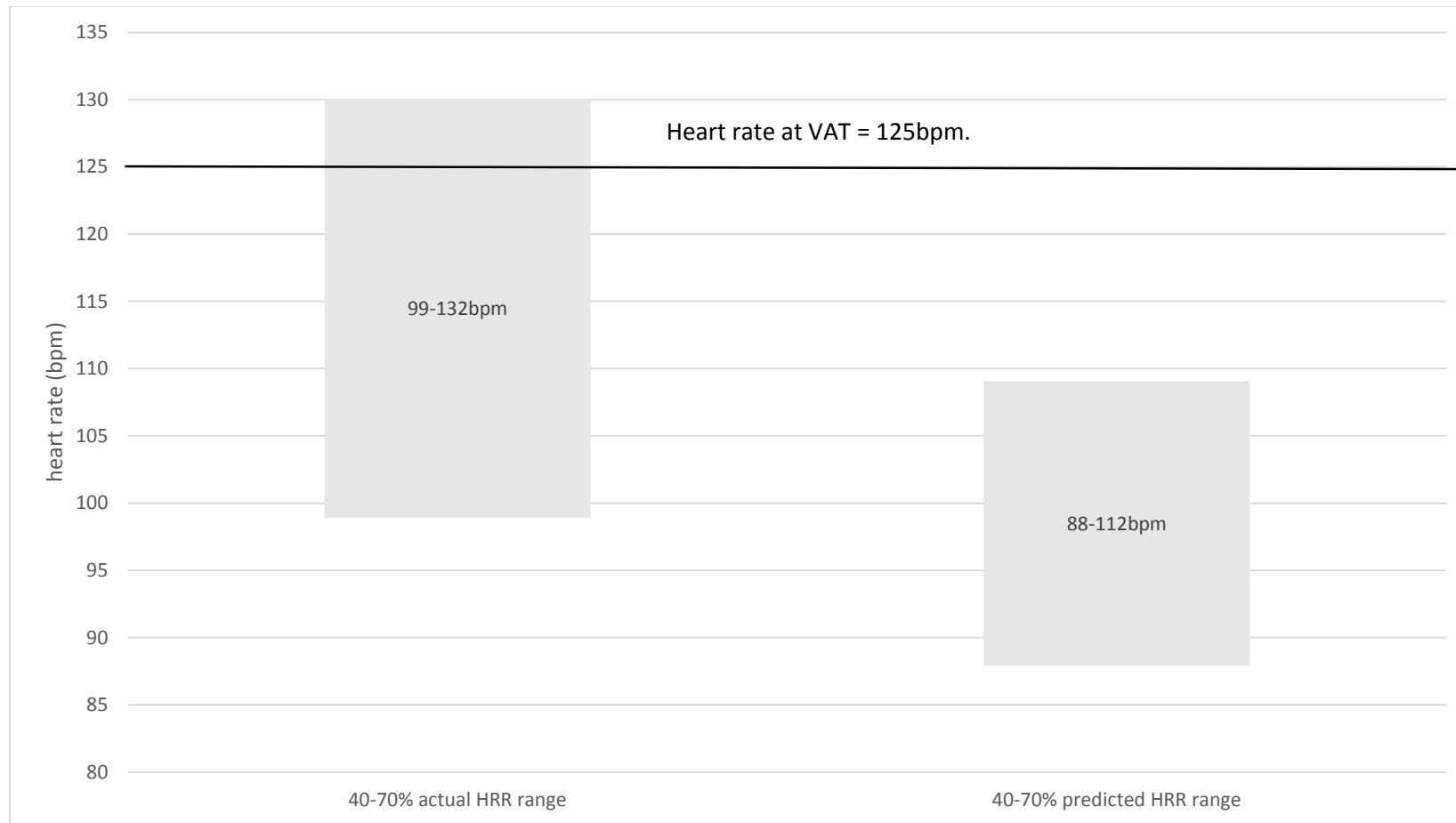


Figure 2a. A case study highlighting how the 40-70% HRR prediction equation may under-estimate individualised exercise prescription. A 58 year-old male taking beta-blockers with a BMI of 24.8, $\text{VO}_{2\text{peak}}$ of $35.28 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ in the high fitness category. CPET was conducted on a treadmill. Solid line corresponds to heart rate at ventilatory anaerobic threshold, which is 125bpm.

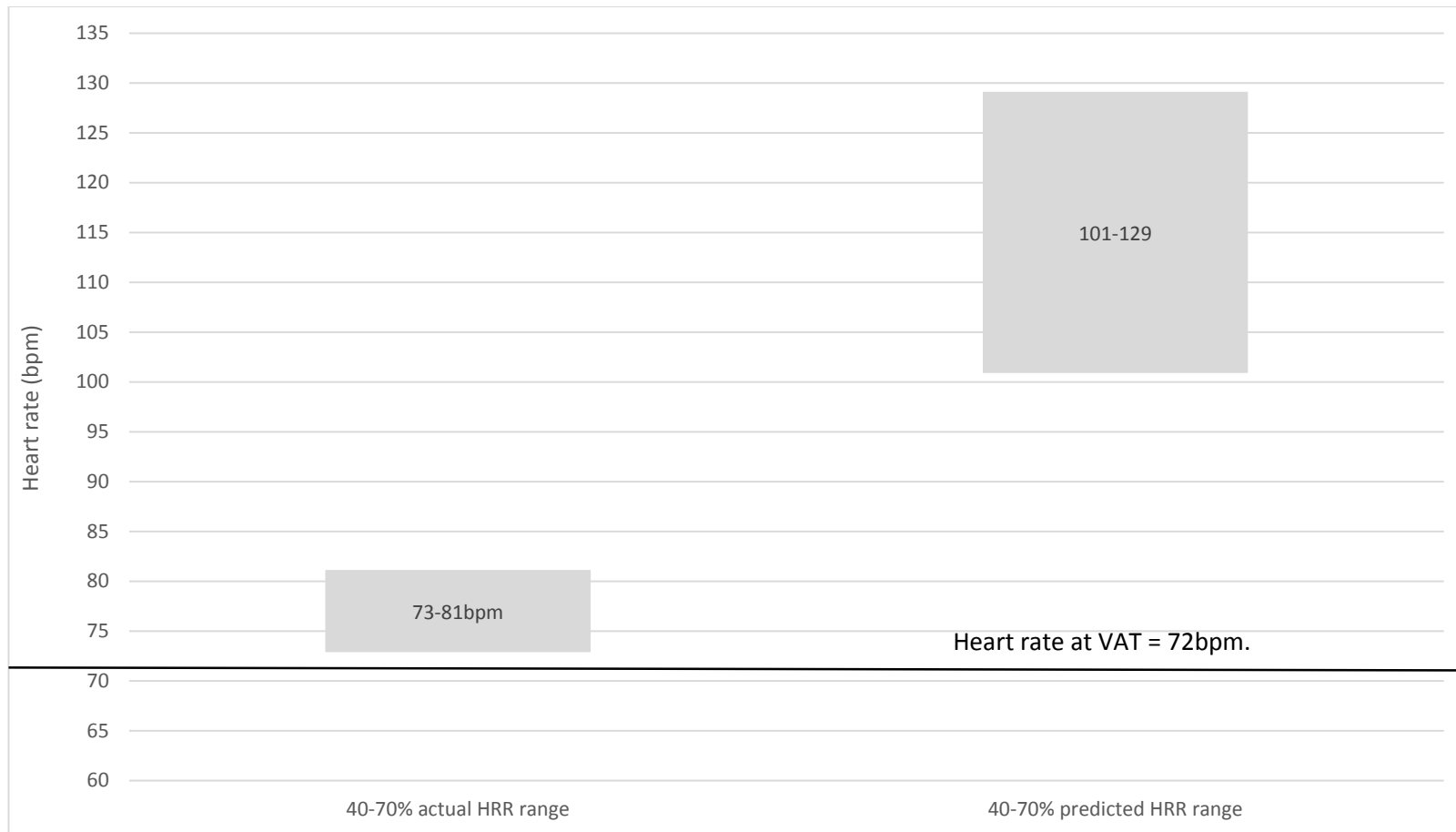


Figure 2b. A case study highlighting how the 40-70% HRR prediction equation may over-estimate individualised exercise prescription. A 71 year-old male not taking beta-blockers with a BMI of 25.8, $\text{VO}_{2\text{peak}}$ of $13.82 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ in the low fitness category. CPET was conducted on a cycle. Solid line corresponds to heart rate at ventilatory anaerobic threshold, which is 72bpm.

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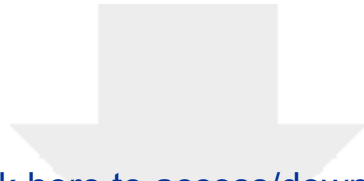
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