Does exercise 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.

PYMER, S., NICHOLS, S., PROSSER, J., BIRKETT, S., CARROLL, S. and INGLE, L.

2020

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.

Sean Pymer[1]

Simon Nichols[2*]

Jonathon Prosser[3]

Stefan Birkett[4]

Sean Carroll[5]

Lee Ingle[5]

Corresponding Author: ***Dr Simon Nichols, Centre for Sport and Exercise Science, Sheffield Hallam University, Sheffield, UK (S.J.Nichols@shu.ac.uk)

Institutions:

[1]Academic Vascular Surgical Unit Hull York Medical School, Hull, UK.

[2]Centre for Sport and Exercise Science, Sheffield Hallam University, Sheffield, UK

[3]Atrium Health, Centre for Exercise and Health, Coventry, UK

[4]School of Sport & Wellbeing, University of Central Lancashire, Preston, UK

[5]Department of Sport, Health & Exercise Science, University of Hull, Hull, UK.

Funding – Sean Pymer is funded by a University of Hull PhD scholarship.

Word Count 3,128 (excluding abstract, tables, figures, references).

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 $kg \cdot m^{-2}$ [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.

Introduction

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

The prescribed dose of exercise can be influenced by manipulating exercise frequency, duration, type/mode, and/or intensity [exercise dose].(10) In the United Kingdom (UK), current long-term exercise training guidelines for patients undertaking CR, recommend exercise training intensities between 40-70% heart rate reserve (HRR), oxygen uptake reserve (VO_2R), or a Borg rating of perceived exertion (RPE) between 11-14.(11, 12) Both continuous and interval training at an objective physiological threshold has been shown to have a beneficial impact by improving VO_2peak.(13) Training at or above the ventilatory anaerobic threshold (VAT), often referred to as the first ventilatory threshold (VT1), indicates the point above which, further increments in work rate are increasingly supplemented through anaerobic metabolism.(14-17) Despite being associated with mild metabolic perturbations,(16, 17) regular exercise bouts conducted at work rates equivalent to VAT are well tolerated,(18) and induce physiological adaptation leading to improved 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. VO_{2peak} was reported in absolute values ($L{\cdot}min^{-1}$) and standardised to each patient's body mass ($ml{\cdot}kg^{-1}{\cdot}min^{-1}$). 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 $L{\cdot}min^{-1}$ and $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ and expressed as a percentage of directly-determined and predicted VO_{2peak}.(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 x age)) – resting heart rate (-30 beats per min if taking beta-blockers)

To characterise where a patients 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; η_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 ± 20.42bpm) (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; η_p^2=0.002), or relative to body mass (*P*=0.359; η_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; η_p^2=0.08) and measured VO_{2peak} (*P*<0.001; η_p^2=0.151), and HRR (*P*<0.001; η_p^2=0.132) in patients exercising on the treadmill. Measured HRR (*P*=0.012; η_p^2=0.056), and HR at VAT (*P*=0.016; η_p^2=0.052) were significantly higher in the treadmill group. There was a significant between-group difference for predicted HRmax adjusted for β-blockade (*P*=0.003; Table 4). However, there was no difference in predicted HRR (*P*=0.863 η_p^2=<0.001) or VO_{2peak} between groups (*P*=0.815, η_p^2<0.001). Figures 2a and 2b highlight individual case studies which demonstrate how the predicted HRR method can either over- or under- estimate individualised exercise prescription versus directly determined HRR and VAT.

Discussion

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

When considering baseline cardiorespiratory fitness, the proportion of patients whose VAT occurred outside the guidelines increased. 57% of low-fit patients achieving VAT at <40% HRR, and 30% of high-fit patients achieving VAT at >70% HRR, confirming that VAT occurs later with increasing CRF in cardiac patients.(31) For those who achieved VAT at <40% HRR, their exercise prescription may overly exceed VAT and prove too challenging, whilst for those that achieve VAT >70%HRR, their prescription is unlikely to induce a training stimulus and prove too easy. We speculate that this may contribute to the 23% attrition rate recently reported in UK CR,(32) as some patients overly exceed their training stimulus (i.e. low fit patients), which may be uncomfortable, whilst some do not reach it, thus providing minimal benefit (i.e. high fit patients), both of which may cause patients to discontinue CR.

Therefore, a *one size fits all* approach, relying on predictive methods for maximal HR and estimated HRR to prescribe exercise appears ineffective. Exercise prescription within cardiac rehabilitation settings needs to be more accurate, patient specific and fine-tuned, ideally based on ventilatory markers, actual HRR and baseline fitness category determined via CPET.(33) One option could be to shift from 'range-based' to 'threshold-based' CR exercise prescription, with moderate-high intensity exercise, corresponding to work rates between VAT and critical power, being recommended.(17) Based on the current data, CPET would aid prescription to ensure that *all* patients achieved VAT during CR, whilst also ensuring it is not overly exceeded. This is important given that certain cardiac patients, namely those who may be more deconditioned, often perform activities of daily living at levels of VO_2 that exceed VAT.(34) Therefore, exercising in steady-state conditions above VAT is vital for these patients, but may not be possible if it is exceeded. In the late 1970s, limitations in the relative percent method (i.e %HRR) for prescribing exercise intensity were identified, with a study by Katch *et al* showing this method failed to consider individual metabolic differences,(35) yet it is still a recommended approach today.(8,10) More recent investigations have proposed a more individualised exercise prescription based on ventilatory thresholds to personalise individualised training load based on metabolic responses.(36, 37) Recently, Weatherwax *et al* reported that in sedentary adults, 12 weeks of aerobic exercise training based on an individualised exercise prescription using VAT had a greater effect on the incidence of training response compared to a standardised approach using HRR. While the exact mechanisms are still not entirely understood, it is believed that exercise intensity prescribed with the use of ventilatory thresholds takes into consideration individual metabolic characteristics which are overlooked when using relative percent methods.(38)

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

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

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

To be able to confidently prescribe an individualised exercise programme in a safe and effective manner can be challenging in a cardiac population. The healthcare professional must be able to account for medication usage, presence of non-CV co-morbidities, and for example, adverse events during exercise testing. Hansen and colleagues [46] showed significant inter-clinician variance in prescribing exercise for patients with different CVDs, highlighting the challenges posed. Further training and education is key, however, digital resources are available to assist practitioner decision-making processes. For example, the European Association of Preventive Cardiology recently developed the Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool.[47] The EXPERT tool is an interactive, digital training and decision support system that assists healthcare professionals in prescribing clinically effective and medically safe exercise training programmes for CVD patients. The adoption of tools such as EXPERT should be more widely encouraged and facilitated to support decision making processes around exercise prescription in cardiac populations. The impact of their utility within clinical practice could then be audited to determine changes in efficacy.

Limitations

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

Conclusion

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

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

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest

The authors declare that there is no conflict of interest.

Author contributions

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

References:

1. Abell B, Glasziou P, Hoffmann T. The Contribution of Individual Exercise Training Components to Clinical Outcomes in Randomised Controlled Trials of Cardiac Rehabilitation: A Systematic Review and Meta-regression. Sports Medicine Open. 2017;3(1):19.
2. Anderson L, Oldridge N, Thompson DR, Zwisler A-D, Rees K, Martin N, et al. Exercise-Based Cardiac Rehabilitation for Coronary Heart DiseaseCochrane Systematic Review and Meta-Analysis. Journal of the American College of Cardiology. 2016;67(1):1-12.
3. Heran BS, Chen J, Ebrahim S, Moxham T, Oldridge N, Rees K, et al. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev. 2011;7.
4. Taylor RS, Unal B, Critchley JA, Capewell S. Mortality reductions in patients receiving exercise-based cardiac rehabilitation: how much can be attributed to cardiovascular risk factor improvements? European Journal of Cardiovascular Prevention & Rehabilitation. 2006;13(3):369-74.
5. Vanhees L, Fagard R, Thijs L, Amery A. Prognostic value of training-induced change in peak exercise capacity in patients with myocardial infarcts and patients with coronary bypass surgery. The American journal of cardiology. 1995;76(14):1014-9.
6. Kokkinos P, Manolis A, Pittaras A, Doumas M, Giannelou A, Panagiotakos DB, et al. Exercise Capacity and Mortality in Hypertensive Men With and Without Additional Risk Factors. Hypertension. 2009;53(3):494-9.
7. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise Capacity and Mortality among Men Referred for Exercise Testing. New England Journal of Medicine. 2002;346(11):793-801.
8. Pattyn N, Coeckelberghs E, Buys R, Cornelissen VA, Vanhees L. Aerobic interval training vs. moderate continuous training in coronary artery disease patients: a systematic review and meta-analysis. Sports medicine. 2014;44(5):687-700.
9. Weston KS, Wisløff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. Br J Sports Med. 2014;48(16):1227-34.
10. ACSM. ACSM's Guidelines for Exercise Testing and Prescription. 9th ed. Baltimore: Lippincott, Williams, & Wilkins.; 2014.
11. Borg GA. Borg's Rating of Perceived Exertion and Pain Scales. Champaign, IL: Human Kinetics; 1998.
12. ACPICR. Standards for physical activity and exercise in the cardiovascular population. 3rd ed. Heather P, Helen B, Samantha B, John B, Laura Burgess, Keri G, et al., editors: Association of Chartered Physiotherapists in Cardiac Rehabilitation 2015.
13. Ghosh AK. Anaerobic Threshold: Its Concept and Role in Endurance Sport. Malays J Med Sci. 2004 Jan; 11(1): 24–36.
4. Beaver WL, Wasserman K, Whipp BJ. A new method for detecting anaerobic threshold by gas exchange. J Appl Physiol. 1986;60(6):2020-7.
15. Nichols S, Taylor C, Ingle L. A clinician's guide to cardiopulmonary exercise testing 2: test interpretation. Br J Hosp Med (Lond). 2015;76(5):281-9.
16. Ghosh AK. Anaerobic Threshold: Its Concept and Role in Endurance Sport. The Malaysian Journal of Medical Sciences : MJMS. 2004;11(1):24-36.
17. Mezzani A, Hamm LF, Jones AM, McBride PE, Moholdt T, Stone JA, et al. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the

American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. Eur J Prev Cardiol. 2013;20(3):442-67.
18. Ekkekakis P, Hall EE, Petruzzello SJ. Practical markers of the transition from aerobic to anaerobic metabolism during exercise: rationale and a case for affect-based exercise prescription. Preventive medicine. 2004;38(2):149-59.
19. Zheng H, Luo M, Shen Y, Ma Y, Kang W. Effects of 6 months exercise training on ventricular remodelling and autonomic tone in patients with acute myocardial infarction and percutaneous coronary intervention. Journal of rehabilitation medicine. 2008;40(9):776-9.
20. Seki E, Watanabe Y, Shimada K, Sunayama S, Onishi T, Kawakami K, et al. Effects of a phase III cardiac rehabilitation program on physical status and lipid profiles in elderly patients with coronary artery disease: Juntendo Cardiac Rehabilitation Program (J-CARP). Circulation journal : official journal of the Japanese Circulation Society. 2008;72(8):1230-4.
21. Tan SJJ, Allen JC, Tan SY. Determination of ideal target exercise heart rate for cardiac patients suitable for rehabilitation. Clinical cardiology. 2017;40(11):1008-12.
22. Nichols S, Nation F, Goodman T, Clark A, Carroll S, Ingle L. CARE CR-Cardiovascular and cardiorespiratory Adaptations to Routine Exercise-based Cardiac Rehabilitation; A study protocol for a community-based control study with criterion methods. BMJ Open. 2017.
23. Nichols S, Gleadall-Siddall D, Antony R, Clark A, Cleland J, Carroll S, et al. Estimated peak functional capacity: an accurate method for assessing change in peak oxygen consumption after cardiac rehabilitation? Clinical physiology and functional imaging. 2017.
24. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. Am Heart J. 1973;85(4):546-62.
25. American Thoracic Society. ATS/ACCP statement on cardiopulmonary exercise testing. American journal of respiratory and critical care medicine. 2003;167(2):211.
26. Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF, et al. Clinician's Guide to Cardiopulmonary Exercise Testing in Adults: A Scientific Statement From the American Heart Association. Circulation. 2010;122(2):191-225.
27. Mezzani A, Agostoni P, Cohen-Solal A, Corra U, Jegier A, Kouidi E, et al. Standards for the use of cardiopulmonary exercise testing for the functional evaluation of cardiac patients: a report from the Exercise Physiology Section of the European Association for Cardiovascular Prevention and Rehabilitation. European Journal of Cardiovascular Prevention & Rehabilitation. 2009;16(3):249-67.
28. Hansen J, Sue D, Wasserman K. Predicted values for clinical exercise testing. The American review of respiratory disease. 1984;129(2 Pt 2):S49-55.
29. Taylor C, Tsakirides C, Moxon J, Moxon JW, Dudfield M, Witte KK, et al. Submaximal fitness and mortality risk reduction in coronary heart disease: a retrospective cohort study of community-based exercise rehabilitation. BMJ Open. 2016;6(6):e011125.
30. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. ed. Hillsdale, N.J. :: L. Erlbaum Associates; 1988.
31. Xie B, Yan X, Cai X, Li J. Effects of high-intensity interval training on aerobic capacity in cardiac patients: a systematic review with meta-analysis. BioMed research international. 2017;2017.
32. Doherty P, Petre C, Onion N, Harrison A, Hemingway J, Cardy K, et al. National Audit of Cardiac Rehabilitation (NACR): Annual Statistical Report 2017. 2018.
33. Ingle L, Carroll S. Cardiac rehabilitation and exercise training. Heart. 2013;99:1298.
34. Mezzani A, Corra U, Giordano A, Colombo S, Psaroudaki M, Giannuzzi P. Upper intensity limit for prolonged aerobic exercise in chronic heart failure. Med Sci Sports Exerc. 2010;42(4):633-9.

35. Katch V, Weltman A, Sady S, Freedson P. Validity of the relative percent concept for equating training intensity. European journal of applied physiology and occupational physiology. 1978;39(4):219-27.

36. Dalleck LC, Haney DE, Buchanan CA, Weatherwax RM. Does a personalised exercise prescription enhance training efficacy and limit training unresponsiveness? A randomised controlled trial. Journal of Fitness Research. 2016;5(3).

37. Wolpern AE, Burgos DJ, Janot JM, Dalleck LC. Is a threshold-based model a superior method to the relative percent concept for establishing individual exercise intensity? a randomized controlled trial. BMC Sports Science, Medicine and Rehabilitation. 2015;7(1):16.

38. Weatherwax RM, Harris NK, Kilding AE, Dalleck LC. Incidence of VO2max Responders to Personalized vs Standardized Exercise Prescription. Medicine and science in sports and exercise. 2018.

39. Beckers PJ, Possemiers NM, Van Craenenbroeck EM, Van Berendoncks AM, Wuyts K, Vrints CJ, et al. Impact of exercise testing mode on exercise parameters in patients with chronic heart failure. European journal of preventive cardiology. 2012;19(3):389-95.

40. Hansen D, Dendale P, Berger J, Meeusen R. Low agreement of ventilatory threshold between training modes in cardiac patients. Eur J Appl Physiol. 2007;101(5):547-54.

41. Chatterjee S, Sengupta S, Nag M. Cardiopulmonary exercise testing: a review of techniques and applications. J Anesth Clin Res. 2013;4:340.

42. Piepoli MF, Corra U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, et al. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. Eur J Cardiovasc Prev Rehabil. 2010;17(1):1-17.

43. Sandercock G, Hurtado V, Cardoso F. Changes in cardiorespiratory fitness in cardiac rehabilitation patients: a meta-analysis. Int J Cardiol. 2013;167(3):894-902.

44. Ekkekakis P, Hall EE, Petruzzello SJ. Practical markers of the transition from aerobic to anaerobic metabolism during exercise: rationale and a case for affect-based exercise prescription. Preventive medicine. 2004;38(2):149-59.

45. McConnell TR, Clark III BA, Conlin NC, Haas JH. Gas exchange anaerobic threshold: implications for prescribing exercise in cardiac rehabilitation. Journal of Cardiopulmonary Rehabilitation and Prevention. 1993;13(1):31-6.

46. Hansen D, Rovelo Ruiz G, Doherty P, Iliou MC, Vromen T, Hinton S, et al. Do clinicians prescribe exercise similarly in patients with different cardiovascular diseases? Findings from the EAPC EXPERT working group survey. Eur J Prev Cardiol. 2018; 25(7):682-691.

47. Hansen D, Dendale P, Coninx K, Vanhees L, Piepoli MF, Niebauer J, et al. The European Association of Preventive Cardiology Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool: A digital training and decision support system for optimized exercise prescription in cardiovascular disease. Concept, definitions and construction methodology. Eur J Prev Cardiol. 2017; 24(10):1017-1031.

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****	[redacted]

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 $\log_{10}$ 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	[redacted]
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*****	[redacted]
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***	[redacted]
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 log_{10} transformation and reported as arithmetic mean for meaningful interpretation.

Table 4

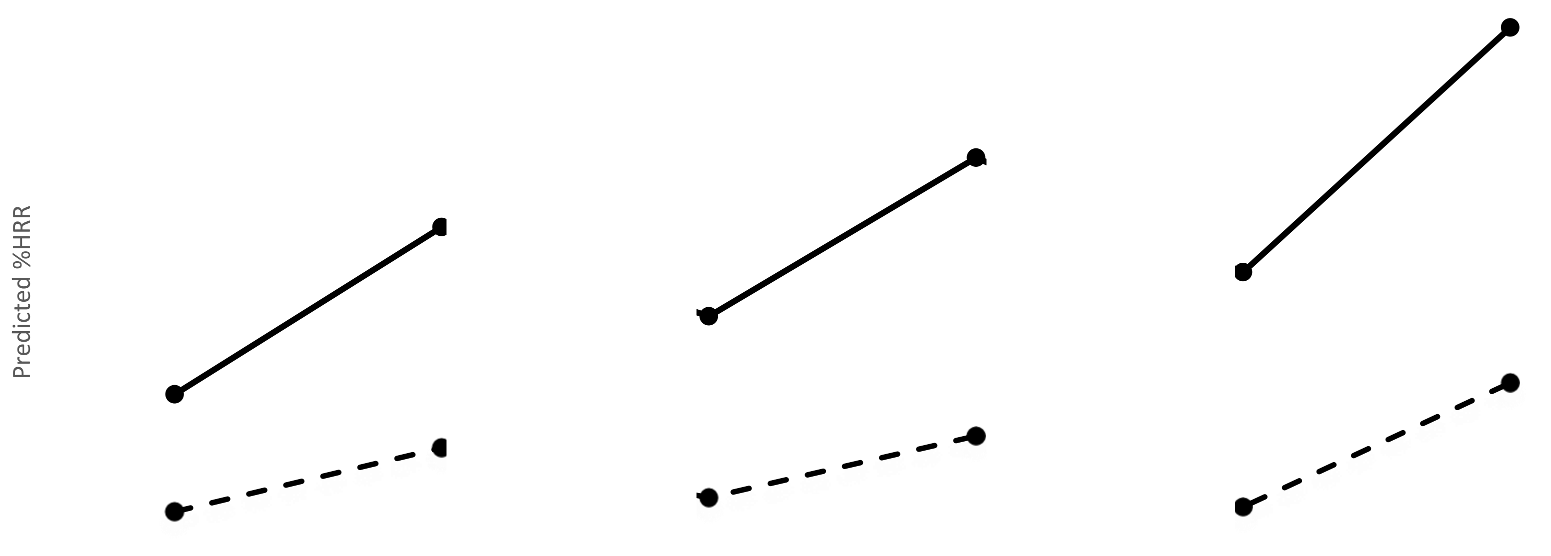
Table 4. Relation between predicted and measured variables stratified by mode of exercise

	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****	[redacted]
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***	[redacted]
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



	Low Fit		Mod Fit		High Fit	
Treadmill	25.9	48.6	40	61.3	51.7	78.3
Cycle	21.6	35.7	24.7	38.3	22.7	50

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}.

Figures 2a and b

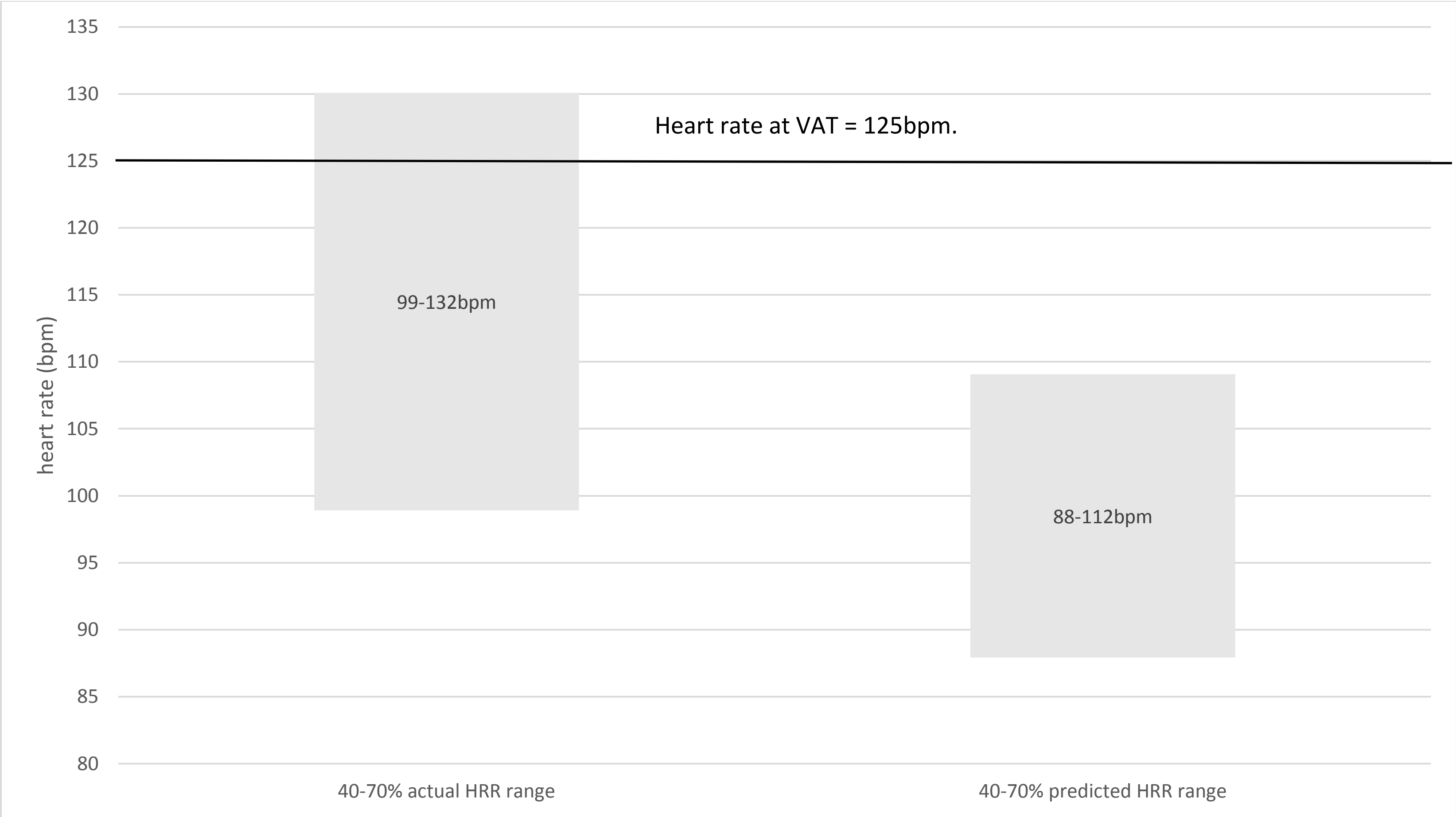


Figure 2a. A case study highlighting how the 40-70% HRR prediction equation may under-estimate individualised exercise prescription. A 58 year-old male taking beta-blockers with a BMI of 24.8, VO_2peak of 35.28 ml·kg^{-1}·min^{-1} in the high fitness category. CPET was conducted on a treadmill. Solid line corresponds to heart rate at ventilatory anaerobic threshold, which is 125bpm.

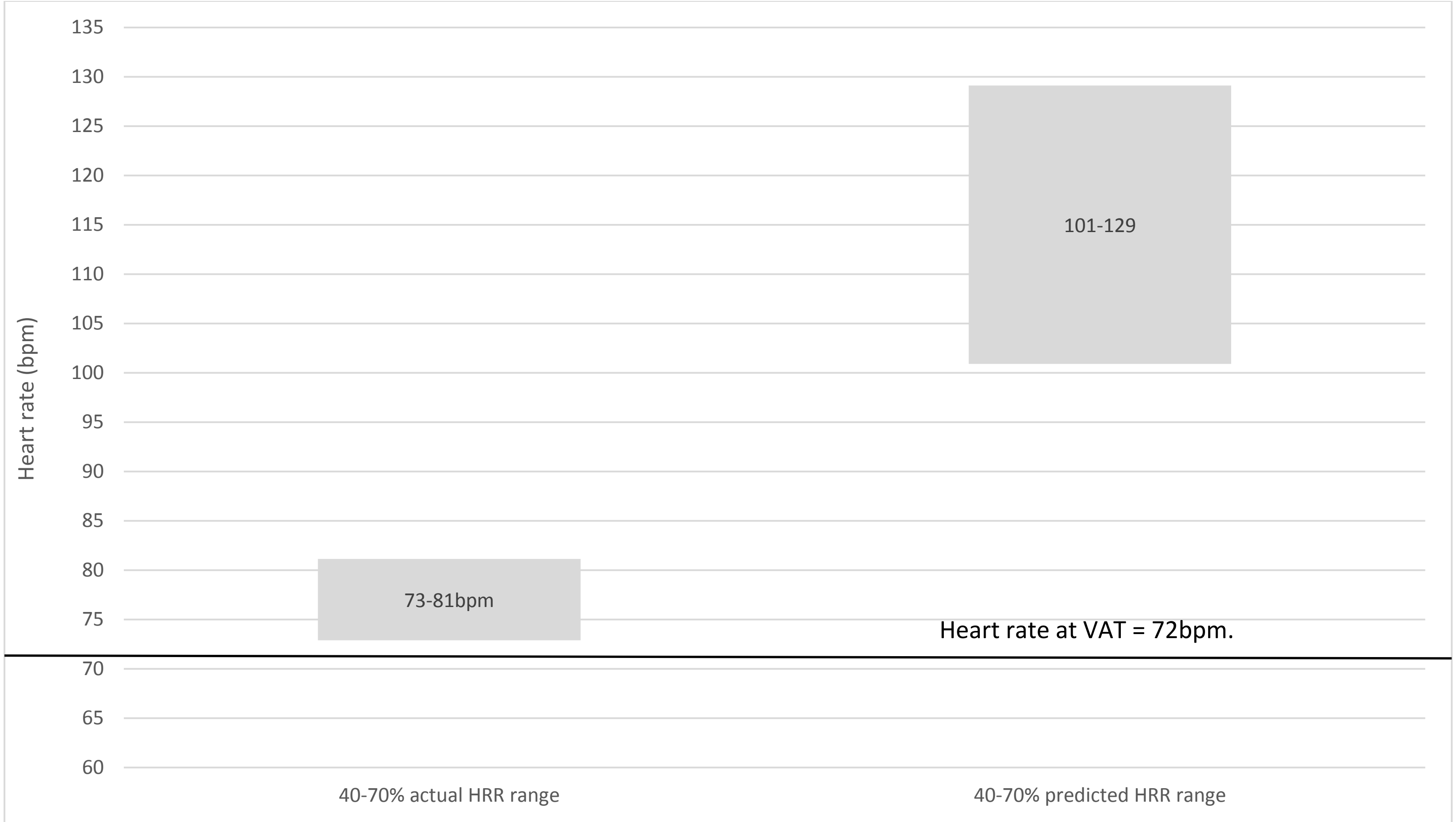


Figure 2b. A case study highlighting how the 40-70% HRR prediction equation may over-estimate individualised exercise prescription. A 71 year-old male not taking beta-blockers with a BMI of 25.8, VO2peak of 13.82 ml·kg^{-1}·min^{-1} in the low fitness category. CPET was conducted on a cycle. Solid line corresponds to heart rate at ventilatory anaerobic threshold, which is 72bpm.