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ARNS
Association of Respiratory
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Better lung health for all

Application of intermittent exercise

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Objectives



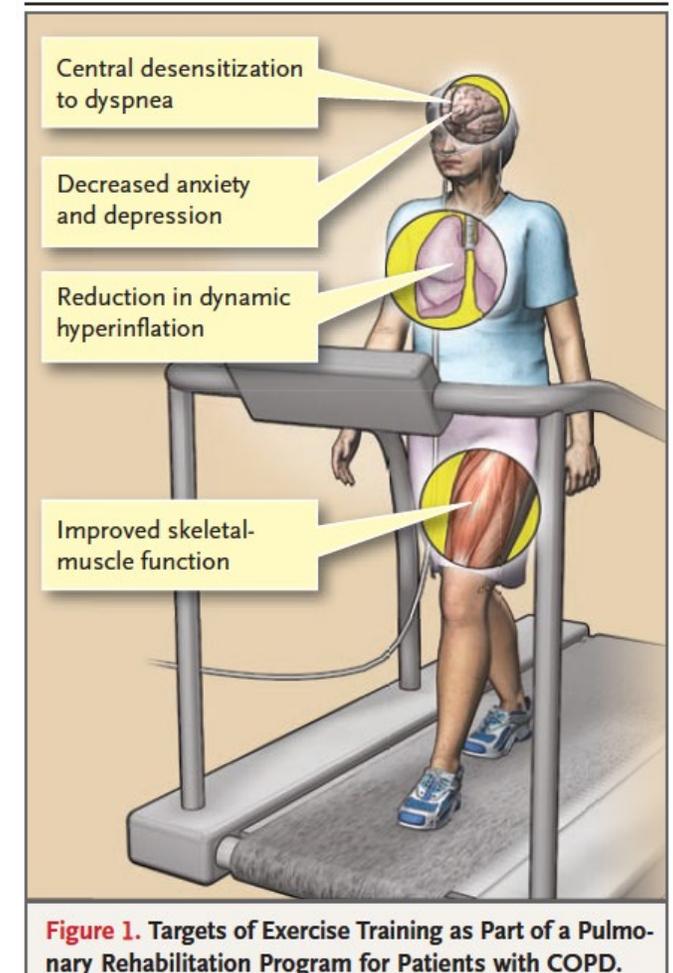
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- Demonstrate the mechanisms by which **acute application** of intermittent compared to continuous exercise lessens exertional symptoms in chronic respiratory diseases
- Review the efficacy of intermittent compared to continuous **exercise training** in patients with chronic respiratory diseases
- Provide practical considerations to implement different intermittent exercise modalities in the pulmonary rehabilitation setting

Pulmonary Rehabilitation: evidence of true physiological training effects

- ↑ Peak work rate
- ↑ Peak oxygen uptake
- ↑ Oxygen uptake @ Lactate threshold
- ↓ Ventilatory requirement and dyspnoea
- ↑ Muscle fiber size
- ↑ Muscle fiber capillarisation
- ↑ Oxidative enzyme activity



Maltais et al. AJRCCM 2014: ATS/ERS Updated Statement on limb muscle dysfunction in COPD

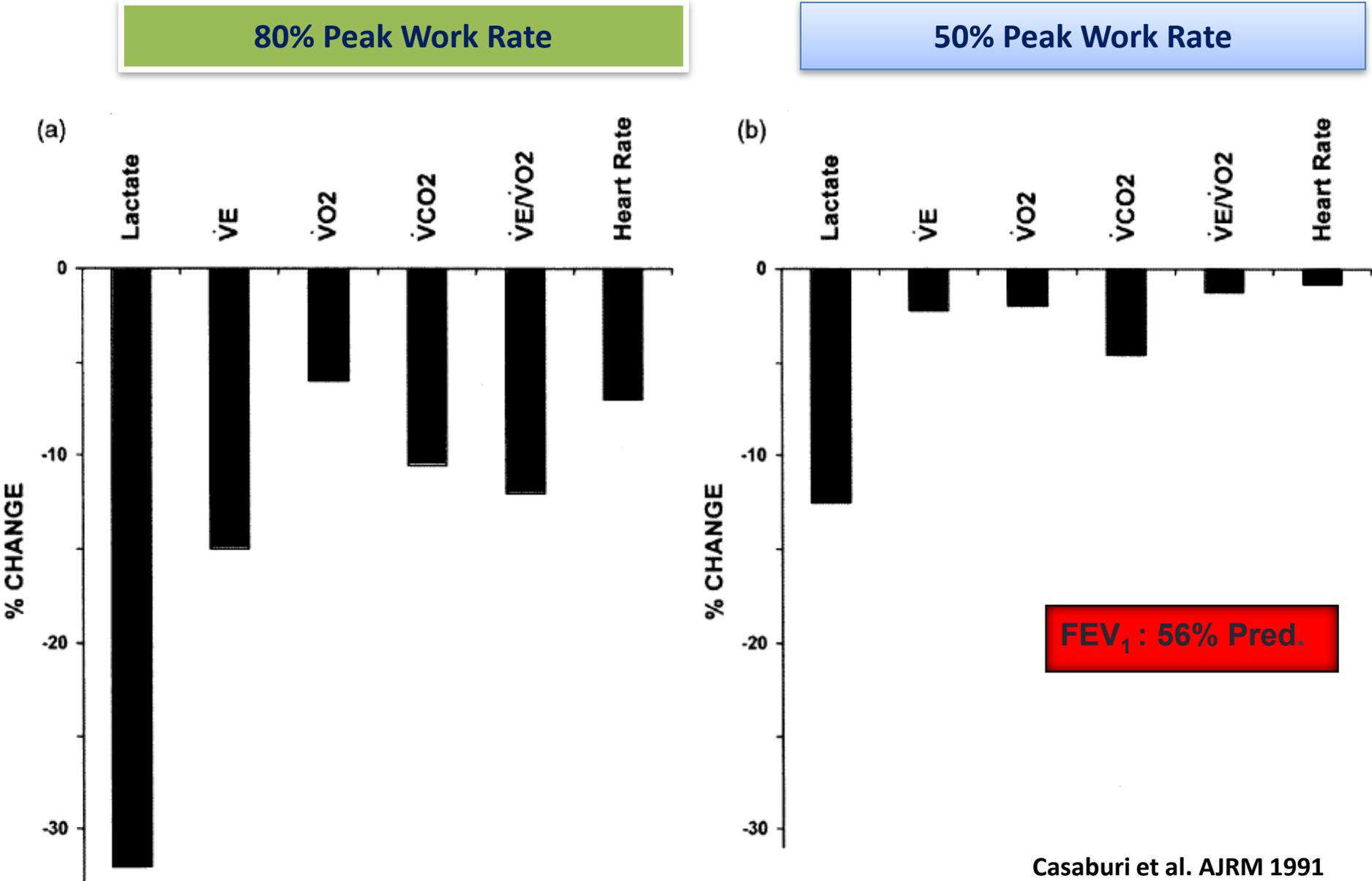
Spruit et al. AJRCCM 2013: ATS/ERS Statement on Pulmonary Rehabilitation

Pulmonary Rehabilitation for Management of Chronic Obstructive Pulmonary Disease

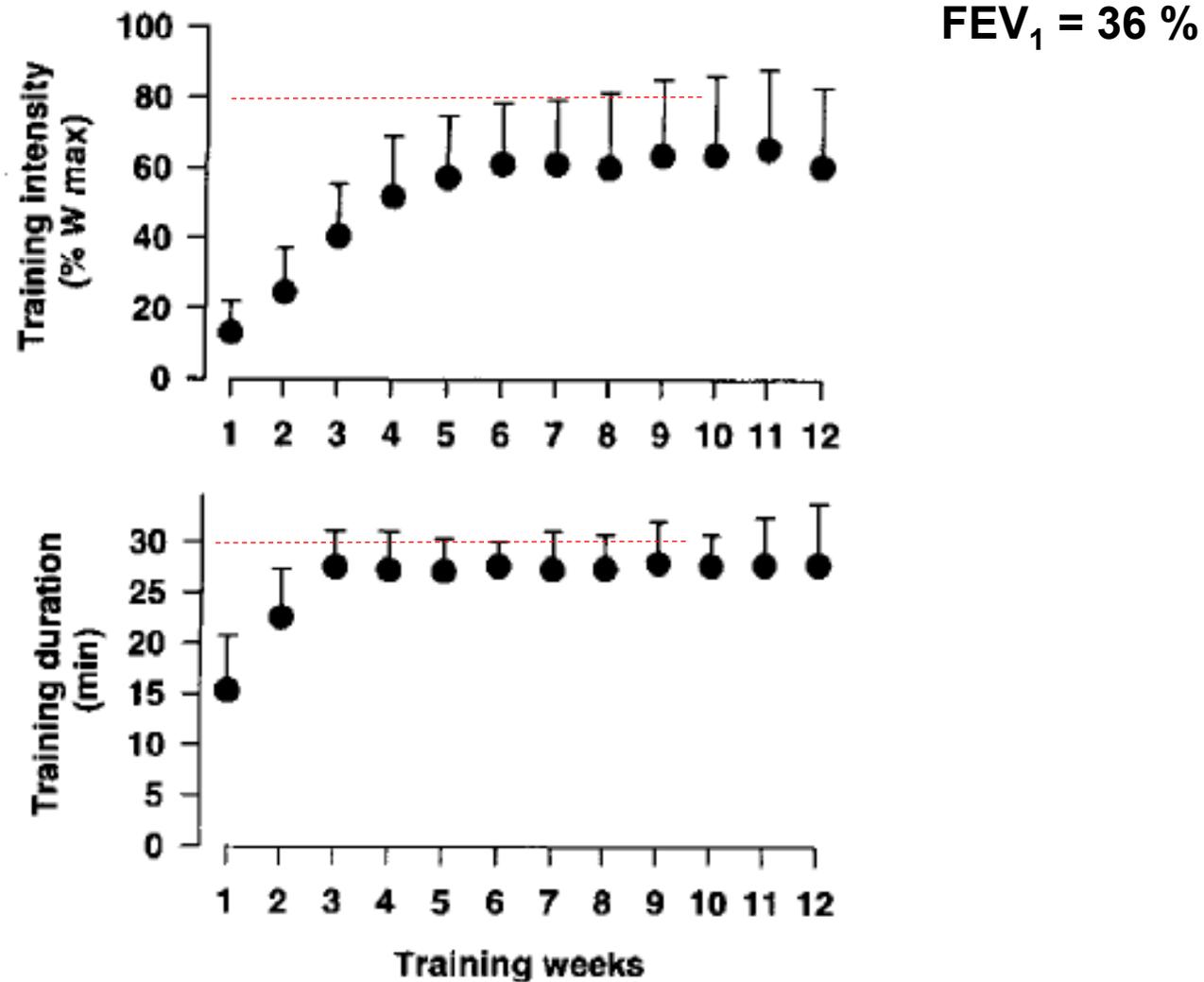
Richard Casaburi, Ph.D., M.D., and Richard ZuWallack, M.D.

N ENGL J MED 360;13 NEJM.ORG MARCH 26, 2009

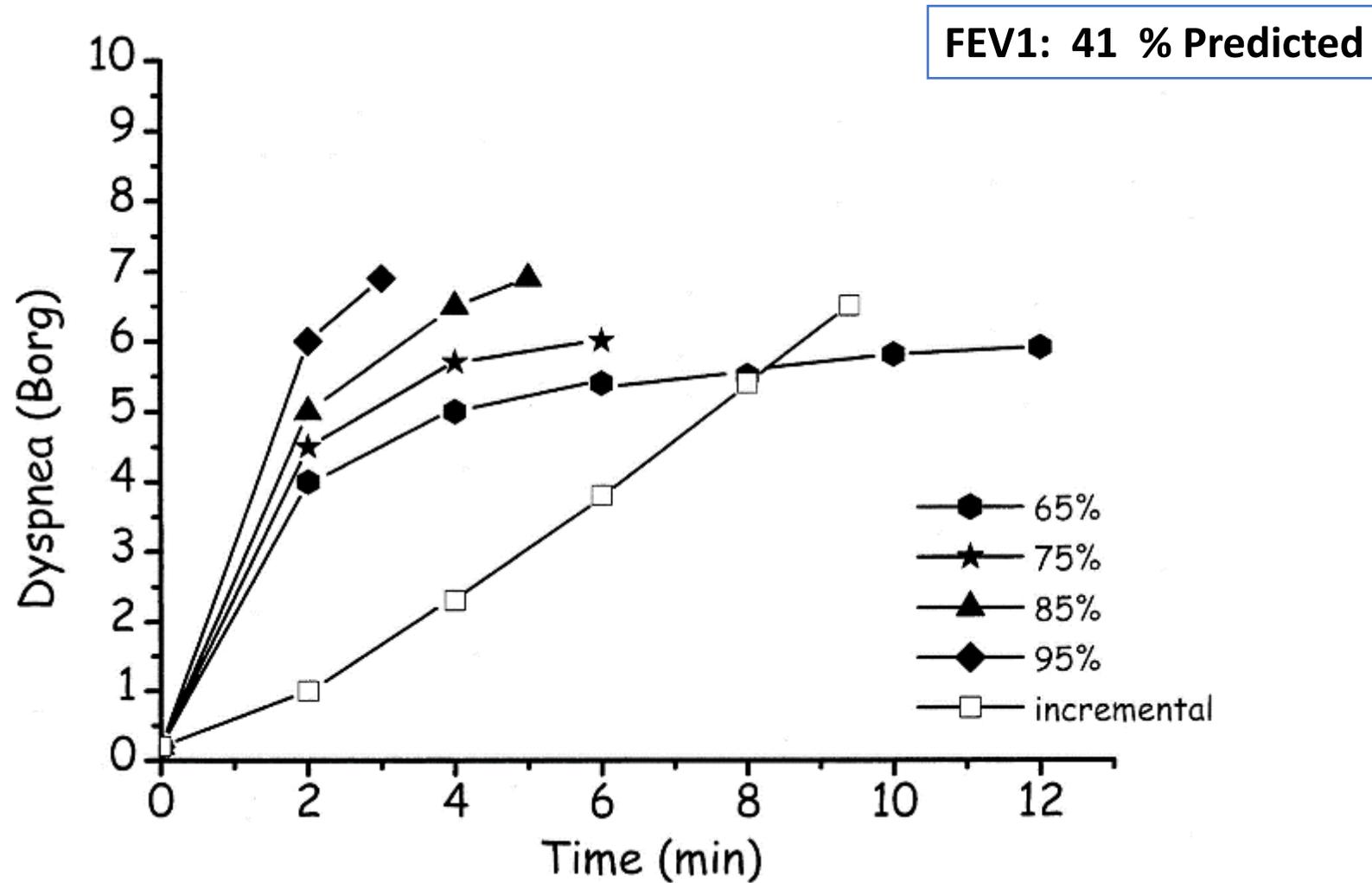
High-intensity constant-load training is superior to moderate intensity training



Severe COPD cannot sustain high intensity constant-load exercise

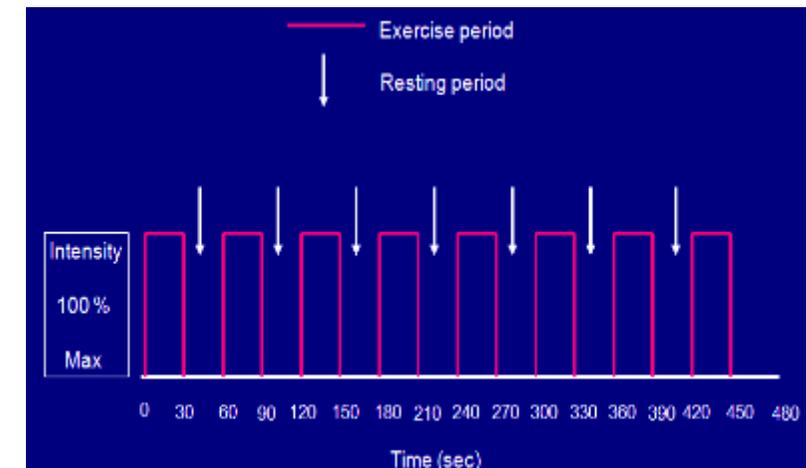
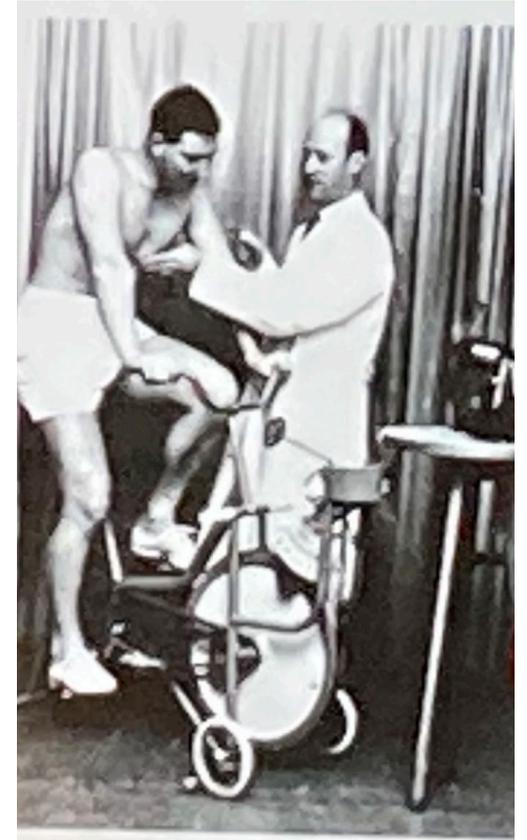


Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease. Maltais et al, [AJRCCM](#). 1997

Dyspnea, Ventilatory Pattern, and Changes in Dynamic Hyperinflation Related to the Intensity of Constant Work Rate Exercise in COPD***Puente-Maestu et al. Chest. 2005**

High Intensity Intermittent Exercise

- When a healthy person sustained high-intensity constant-load cycling work (170 Watts) endurance time was limited to 9 min
- When the same load (170 Watts) was performed intermittently (alternating work and rests of 0.5 min, or 1 min) the individual sustained the load for 1 hour
- It was found that the heavy work was transformed into a submaximal load on respiration and circulation with the shorter work periods of 0.5 and 1 minute.



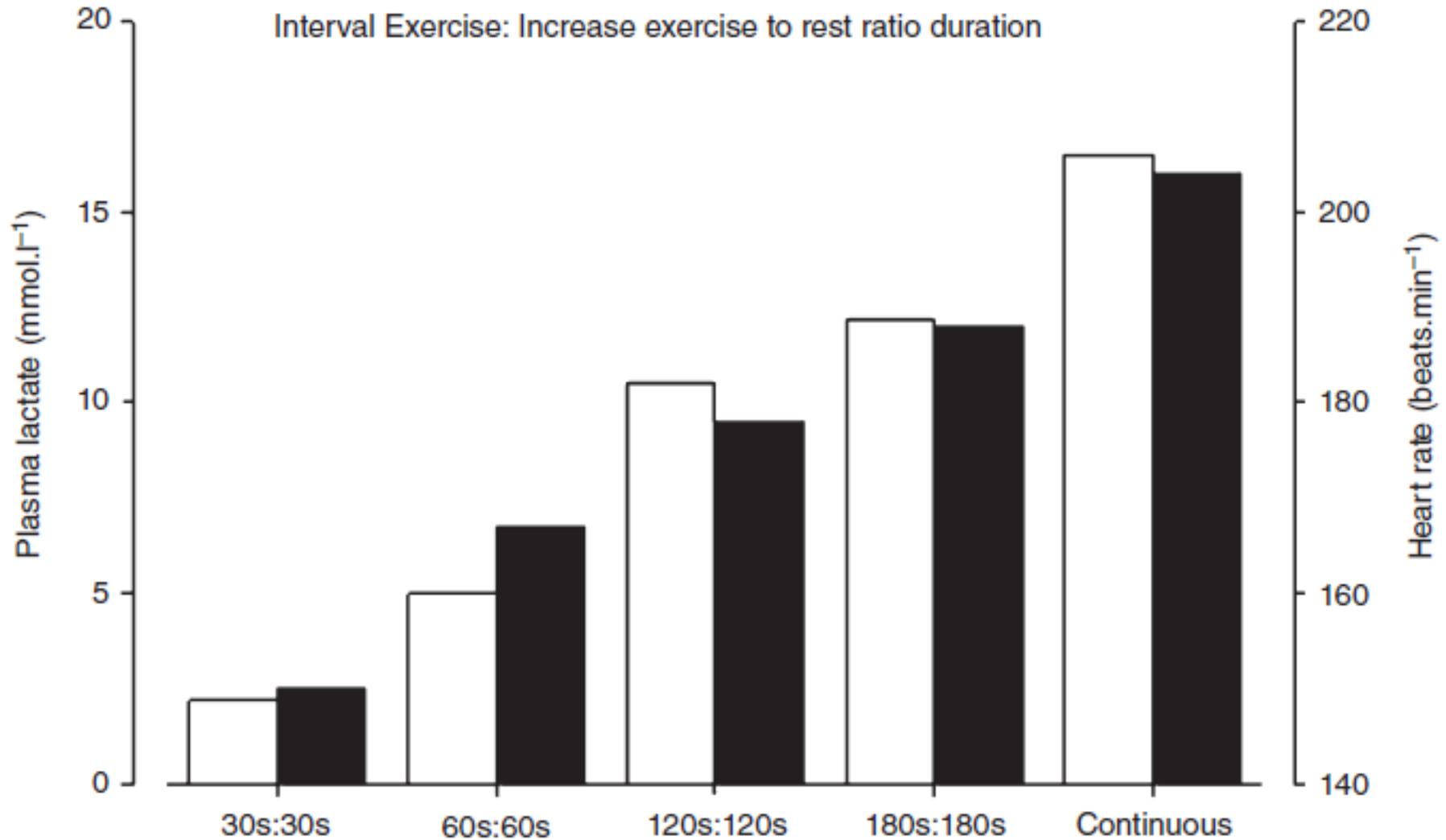
Astrand, I., Astrand, P-O., Christensen, E. H., & Hedman, R. (1960).
Intermittent muscular work. *Acta Physiologica Scandinavica*, 48, 448-453.

Physiological Rationale for intermittent exercise

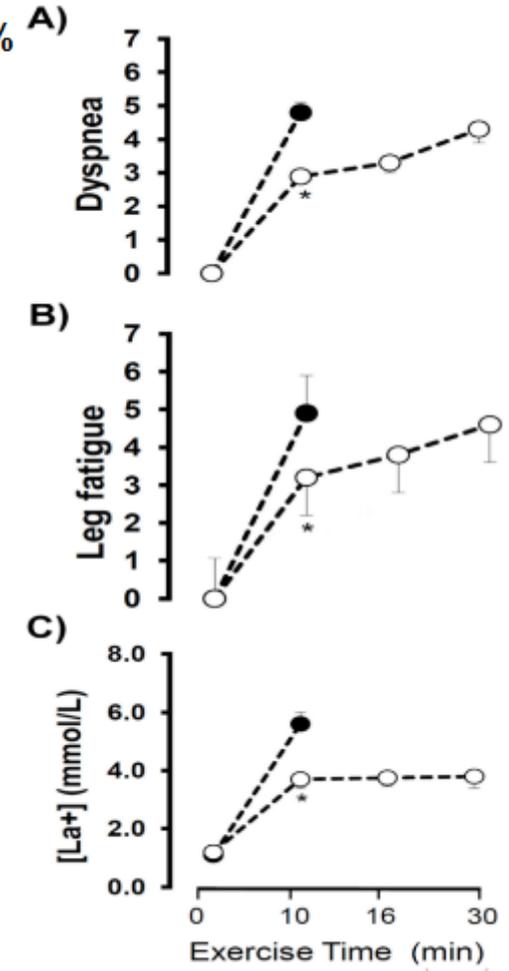
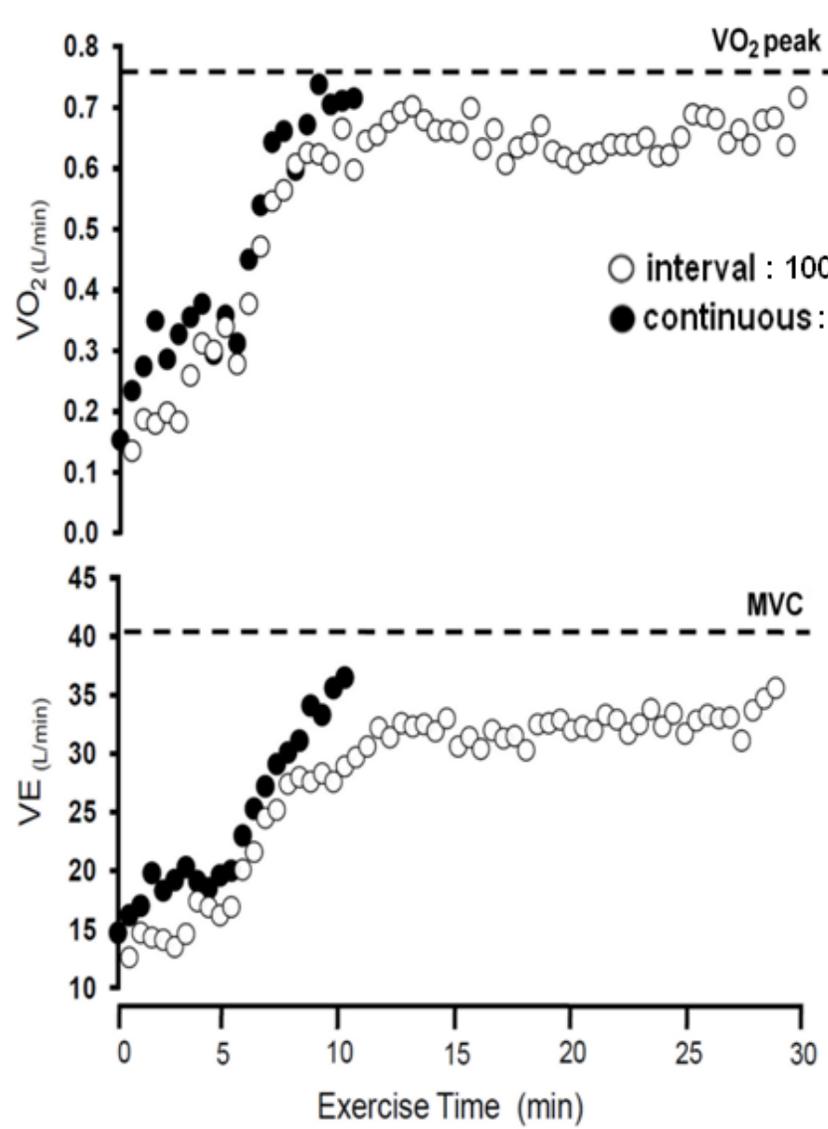
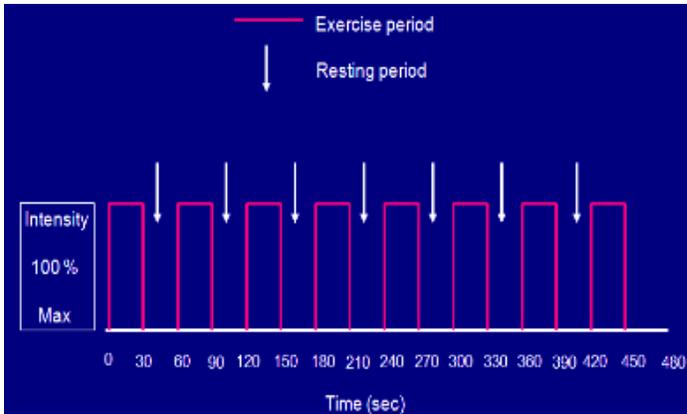
- During the recovery phases there is partial restoration of muscle phosphocreatine levels to rapidly regenerate ATP
- During the recovery phases there is partial reloading of myoglobin stores promoting oxidative degradation of glycogen and lower reliance on anaerobic glycolysis
- Alteration of exercise with rest maintains cardiac output and minute ventilation at relatively constant levels

Astrand, I., Astrand, P-O., Christensen, E. H., & Hedman, R. (1960).
Intermittent muscular work. *Acta Physiologica Scandinavica*, 48, 448-453.

Physiological Rationale for interval training



Application of interval exercise in severe COPD



Vogiatis I. et al. ERJ 2004

High intensity interval exercise in COPD

J Physiol 598.17 (2020) pp 3613–3629

Greater exercise tolerance in COPD during acute interval, compared to equivalent constant-load, cycle exercise: physiological mechanisms

Zafeiris Louvaris^{1,2} , Nikolaos Chynkiamis³, Stavroula Spetsioti¹, Andreas Asimakos¹, Spyros Zakynthinos¹, Peter D. Wagner⁴ and Ioannis Vogiatzis^{1,3}

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Pulmonary function data

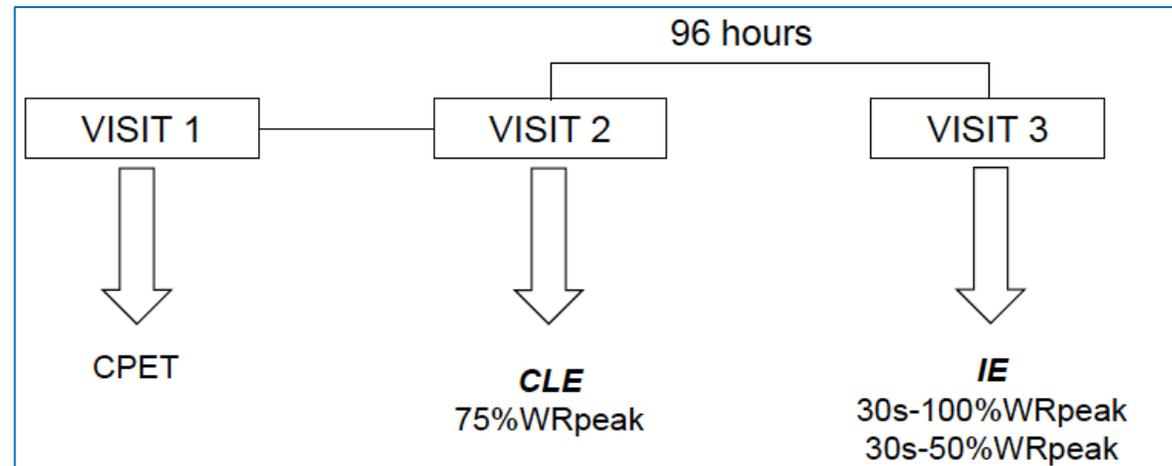
FEV ₁ , % predicted	58.4 ± 17.2
FVC, % predicted	81.6 ± 15.7
FEV ₁ /FVC	52.4 ± 11.1
RV, % predicted	158 ± 33
FRC, % predicted	144 ± 24
TLC, % predicted	112 ± 19
IC, % predicted	74 ± 16
RV/TLC, %	47 ± 6
IC/TLC, %	32 ± 9
TL _{CO} , % predicted	64.6 ± 13.1
MWV, l min ⁻¹	71.5 ± 22.3
SaO ₂ , %	95.3 ± 1.3
Hb, g dl ⁻¹	14.84 ± 0.66
mMRC	2.00 ± 0.71

Patient: COPD

Intervention: Interval exercise (IE)

Comparator: constant load exercise (CLE)

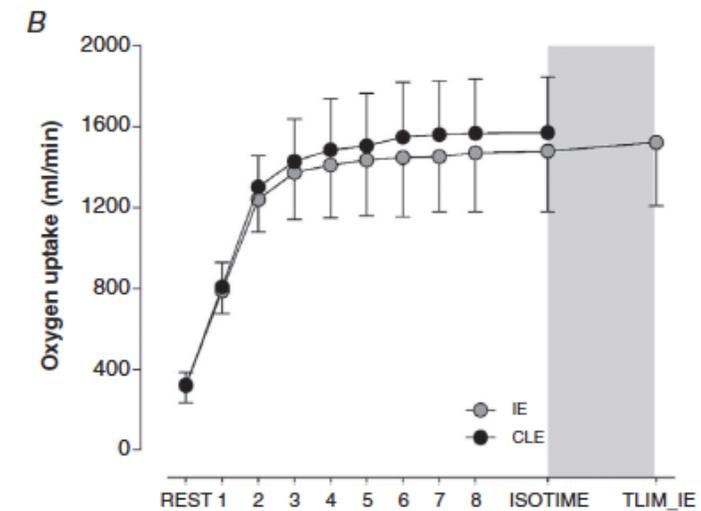
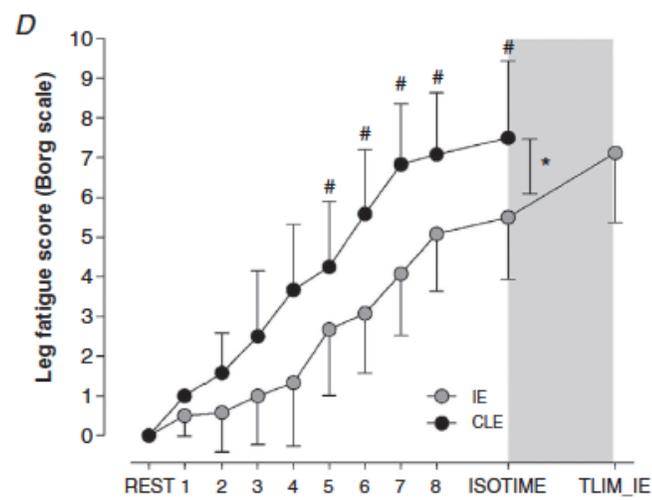
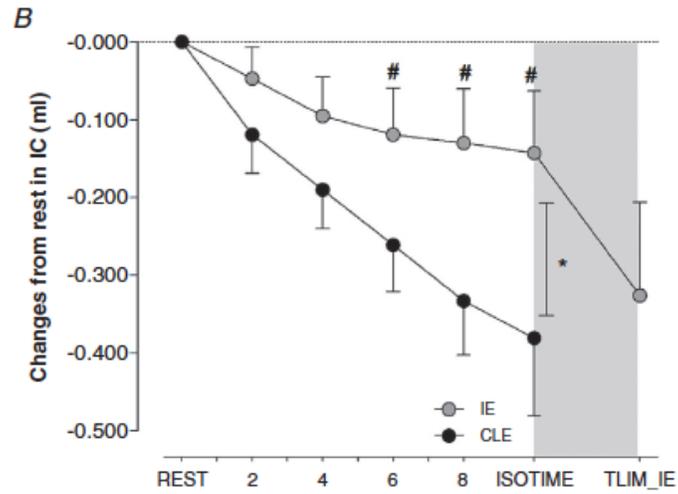
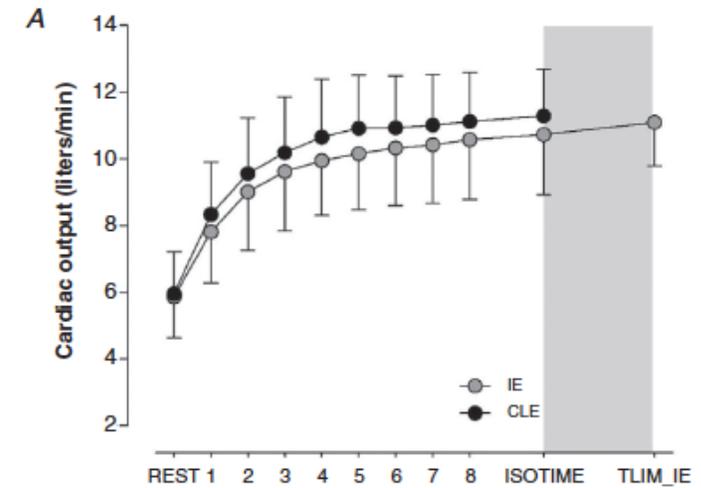
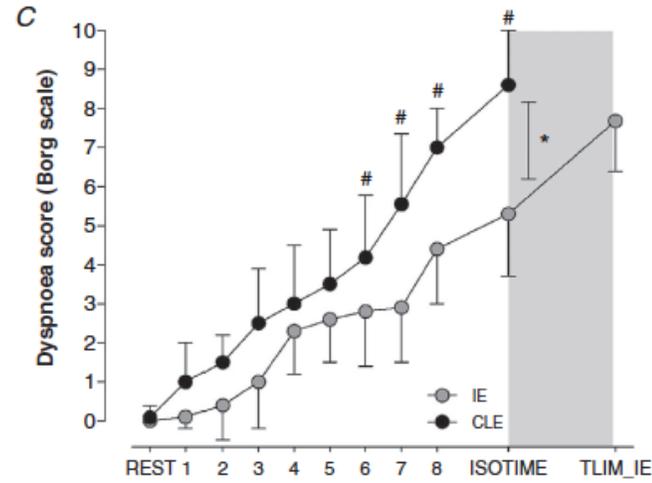
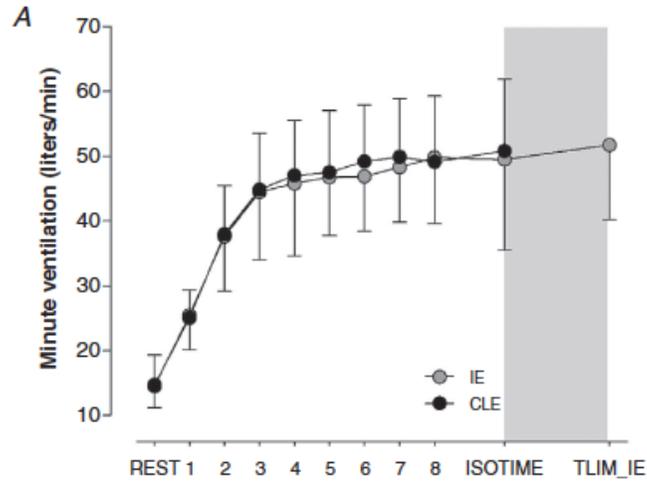
Outcome: exercise tolerance



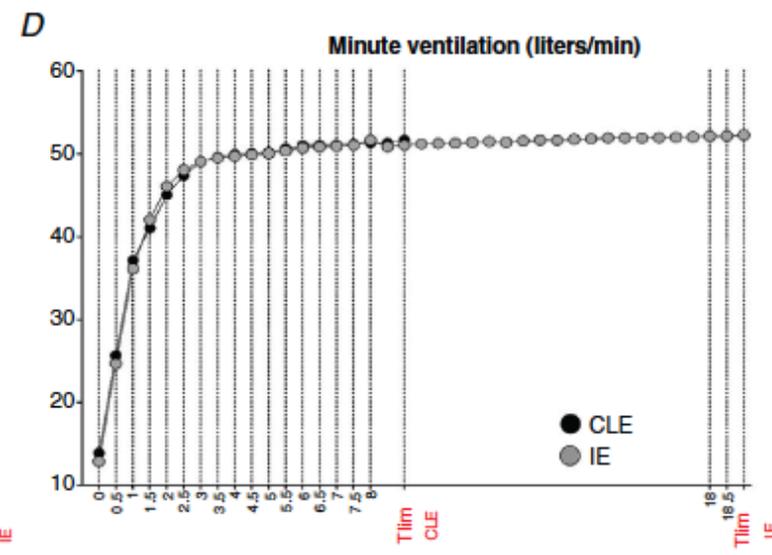
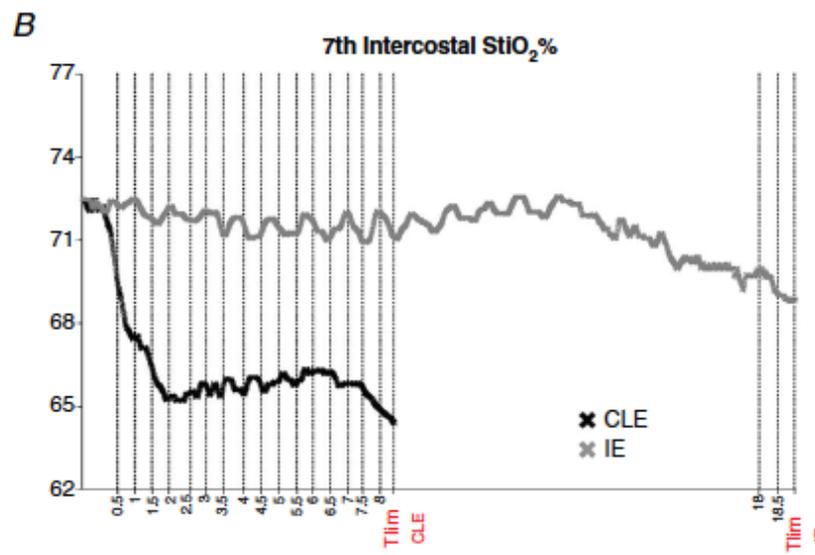
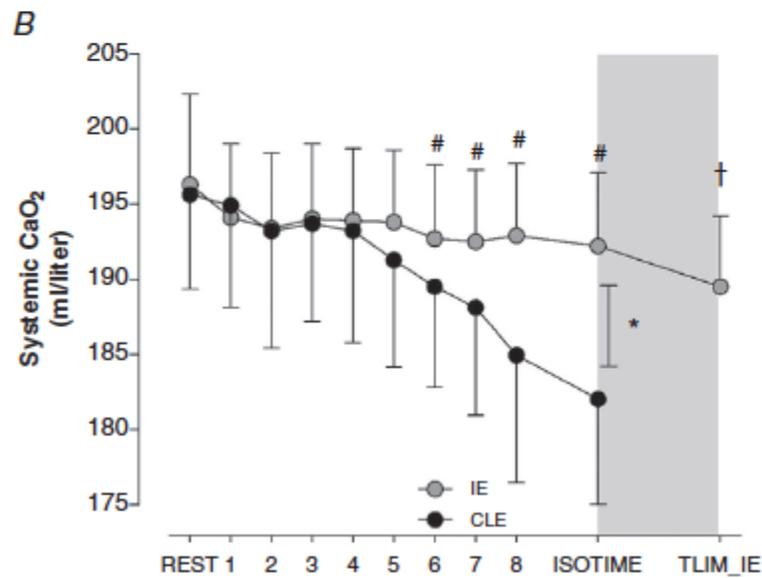
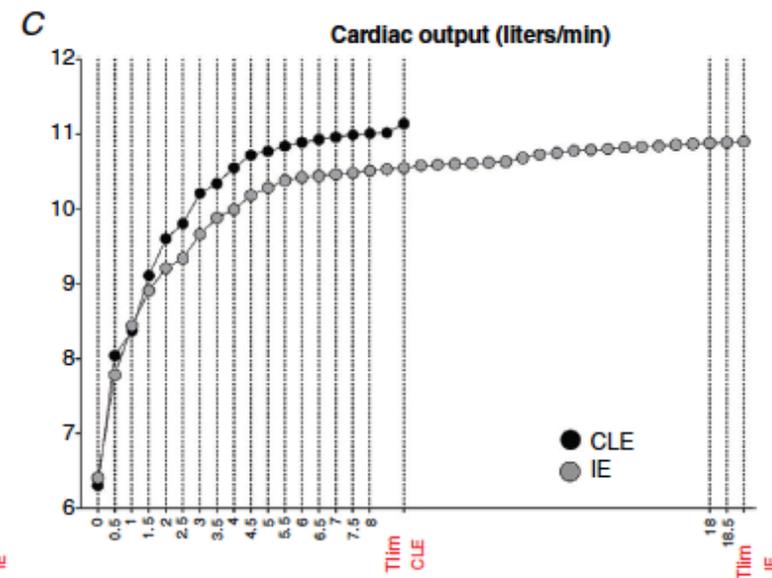
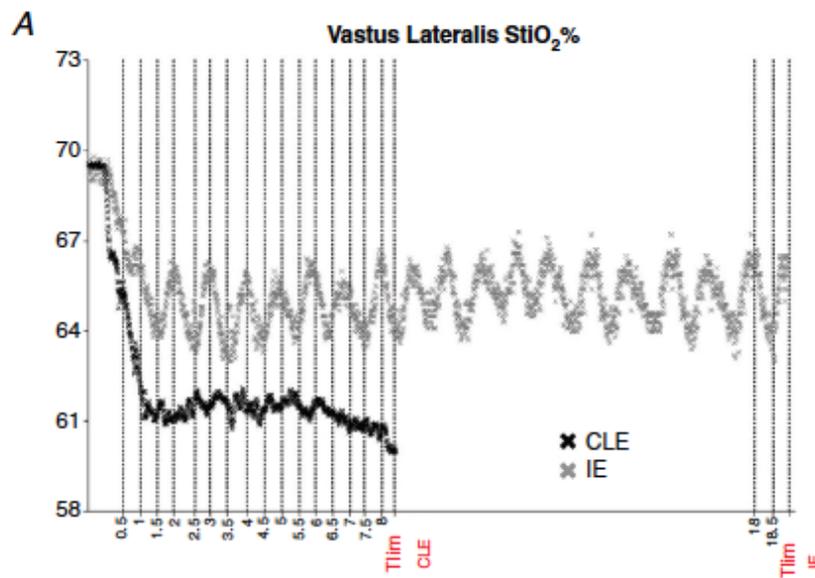
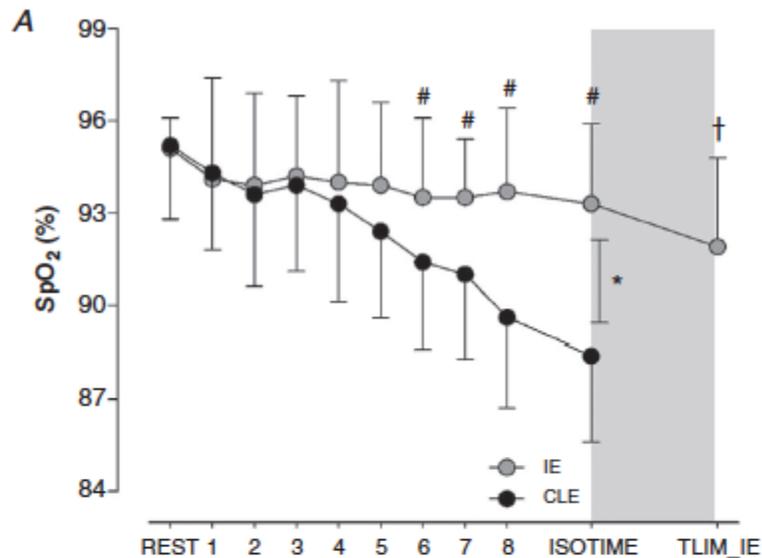
Physiological measures during constant load and interval exercise

	Tlim_CLE	Isotime	Tlim_IE
Cycling responses			
Work rate, W	69.8 ± 18.6	–	69.5 ± 16.6
Cadence, rpm	60 ± 6.9	–	59 ± 6.9
Tlim, min	11.4 ± 2.1	–	19.5 ± 4.8*
Total work, kJ	48.9 ± 23.8	–	81.3 ± 27.7*
Metabolic and ventilatory responses			
E.E., kcals	83 ± 28	81 ± 21	147 ± 44*
VO ₂ , ml min ⁻¹ kg ⁻¹	18.1 ± 4.0	17.2 ± 3.6	17.7 ± 3.6
VCO ₂ , l min ⁻¹	1492 ± 331	1378 ± 355	1449 ± 342
RER	0.95 ± 0.03	0.93 ± 0.03	0.95 ± 0.07
Lactate, mmol l ⁻¹	6.43 ± 2.24	3.96 ± 1.76*	4.87 ± 2.39*
V _E , l min ⁻¹	50.3 ± 10.8	49.5 ± 15.0	51.8 ± 11.5
V _E /MVV, %	70.4 ± 16.9	69.7 ± 15.2	72.8 ± 16.6
V _E /VCO ₂ , %	34.2 ± 6.6	34.5 ± 6.0	35.4 ± 6.6
V _{Tpeak} , l min ⁻¹	1.66 ± 0.29	1.74 ± 0.38*	1.67 ± 0.34
Ti, s	0.78 ± 0.14	0.93 ± 0.17*	0.80 ± 0.26
Ti/Ttot	37.3 ± 5.4	44.4 ± 5.5*	38.0 ± 4.5
Bf, breaths/min	30.6 ± 5.4	28.4 ± 4.9	31.0 ± 5.0
ΔIC, l	-0.381 ± 0.10	-0.143 ± 0.08*	-0.326 ± 0.12
V _T /IC, %	84.3 ± 19.9	78.3 ± 12.9	82.8 ± 18.9

Respiratory, central haemodynamic, metabolic and symptom responses



Arterial and local muscle oxygen saturation



Application of intermittent exercise in COPD

- Acute alteration of maximal and moderate intensity exercise, compared to constant load exercise sustained at the same average power output:
 1. Places comparable loads on respiration and circulation to constant load exercise with lower exertional symptoms
 2. Leads to a two-fold increase in total work output and endurance time
- Interval exercise is deemed safer than constant load exercise as arterial oxygen desaturation is only mild compared with constant load exercise

Intermittent compared to continuous walking in COPD

Original Paper

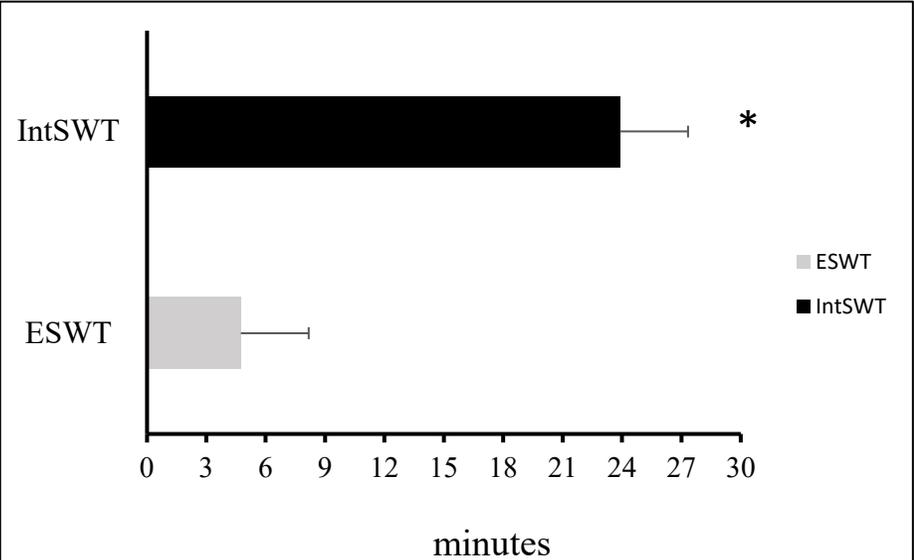
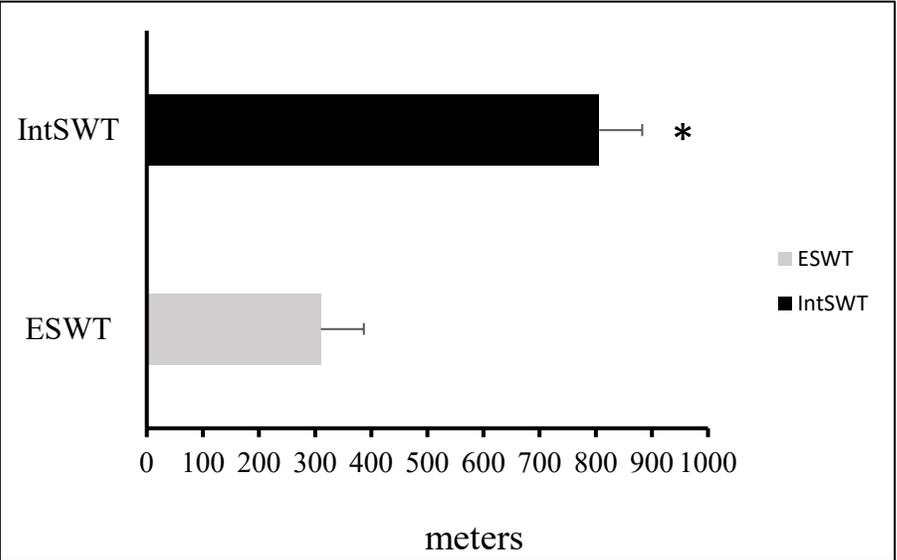
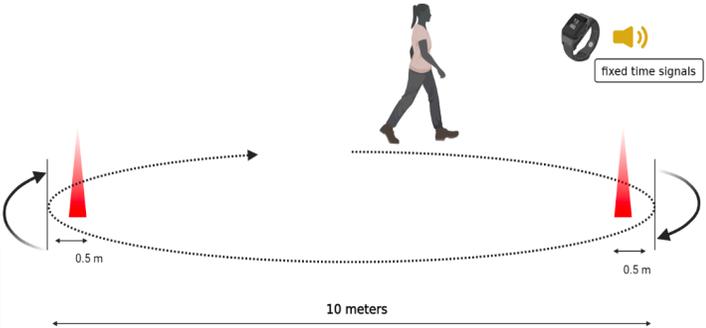


Chronic Respiratory Disease
 Volume 19: 1-11
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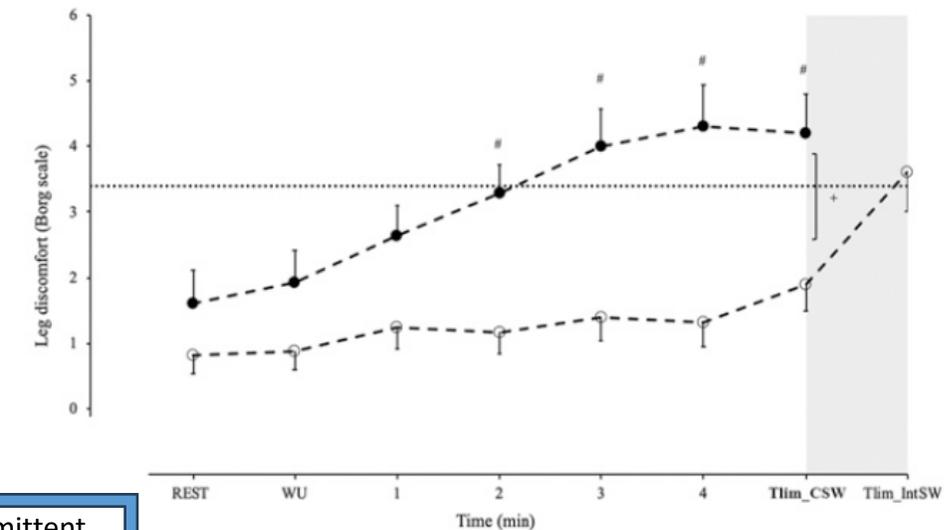
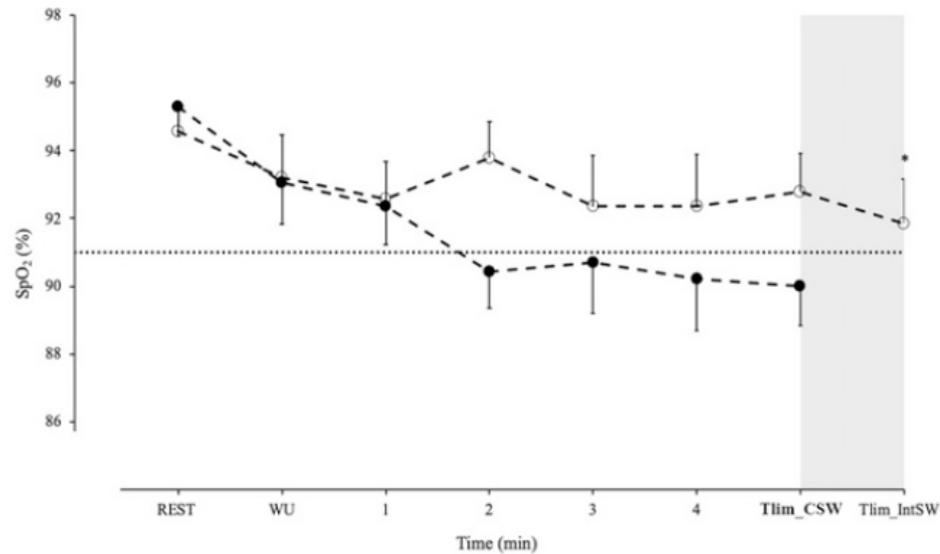
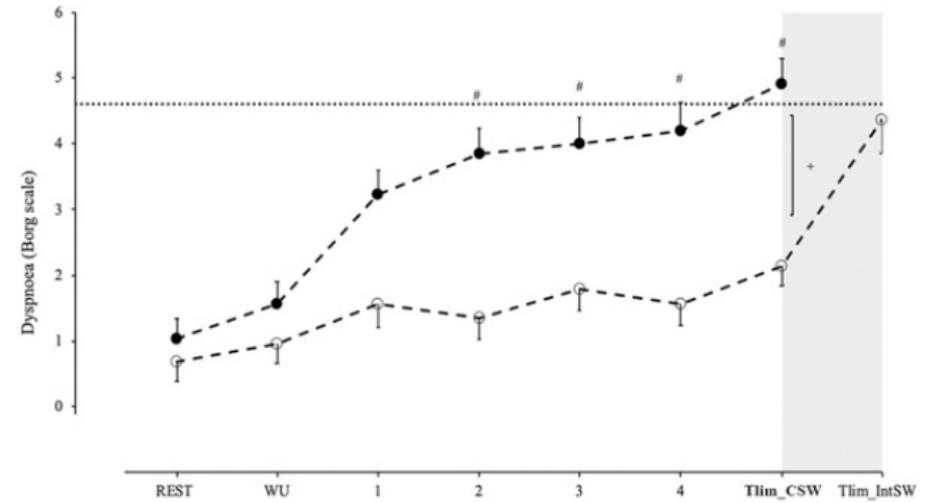
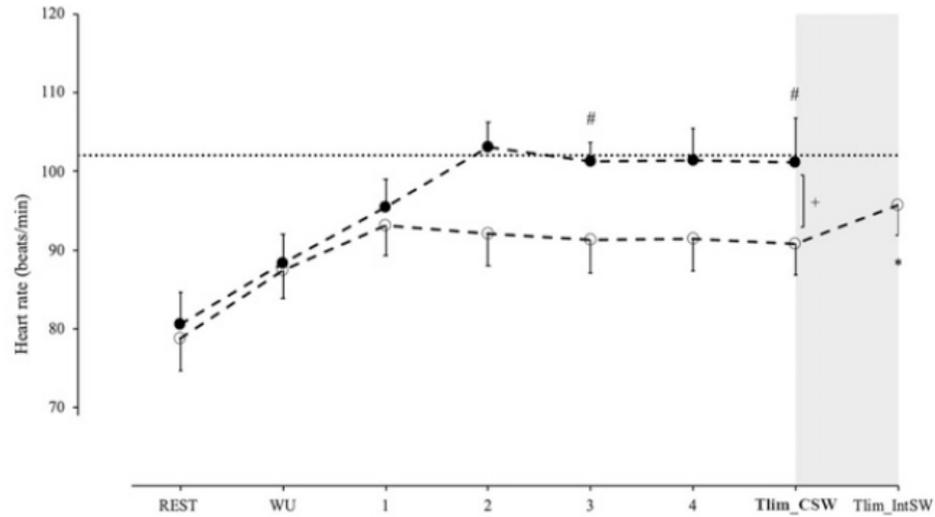
Greater exercise tolerance in COPD during acute intermittent compared to continuous shuttle walking protocols: A proof-of-concept study

Charikleia Alexiou¹, Francesca Chambers², Dimitrios Megaritis¹, Lynsey Wakenshaw², Carlos Echevarria³ and Ioannis Vogiatzis¹

Continuous: ESWT (85% ISWT)
 Intermittent: 1-min at 85% ISWT
 1-min rest



Physiological & symptom responses during continuous and intermittent walking



High intensity interval exercise in Cystic Fibrosis

Contrasting interval to continuous exercise of equivalent work rate

- Continuous exercise at 70% peak work rate (PWR)
- Interval exercise at 100% PWR for 30 sec alternated with 30 sec at 40 % PWR

Respiratory Physiology & Neurobiology 288 (2021) 103643

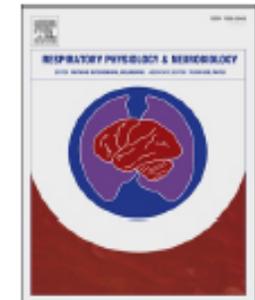


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Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol



<https://doi.org/10.1016/j.resp.2021.103643>

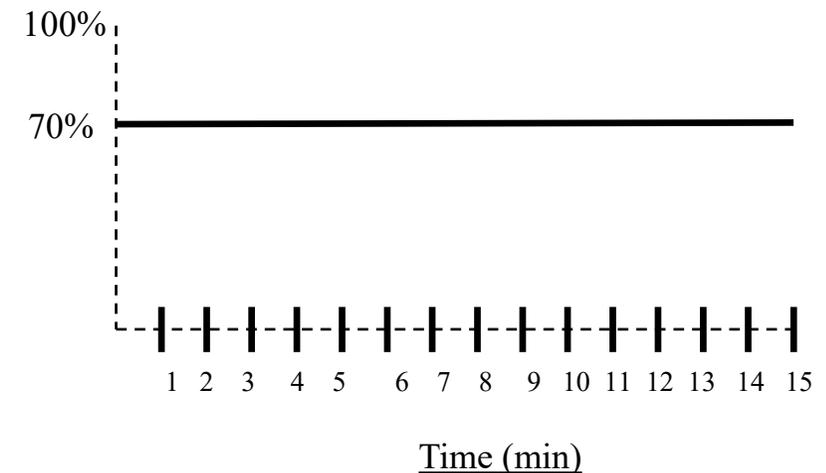


Interval versus constant-load exercise training in adults with Cystic Fibrosis

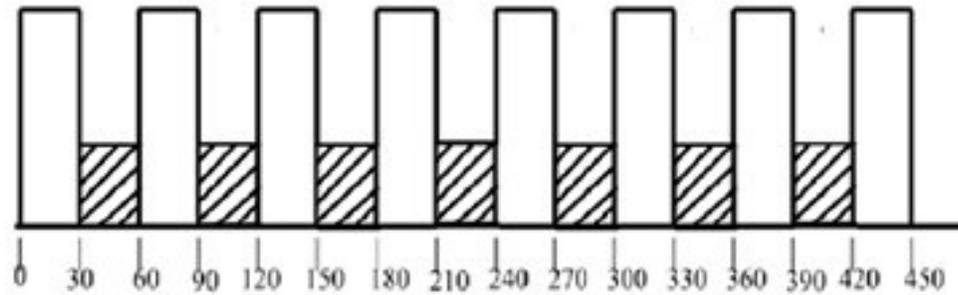
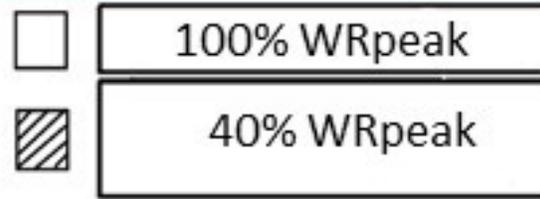
G. Kaltsakas^{a,b,c,1}, N. Chynkiamis^{c,d,e,1}, N. Anastasopoulos^c, P. Zeliou^f, V. Karapatoucha^f,
K. Kotsifas^f, F. Diamantea^f, I. Inglezos^f, N.G. Koulouris^{c,2}, I. Vogiatzis^{c,e,*,2}

Representative case

- 32-year old female with cystic fibrosis
- FEV₁: 45% predicted
- FVC: 64% predicted
- Endurance time at 70% PWR: 15 min
- Exertional dyspnea (1-10 Borg scale): 8



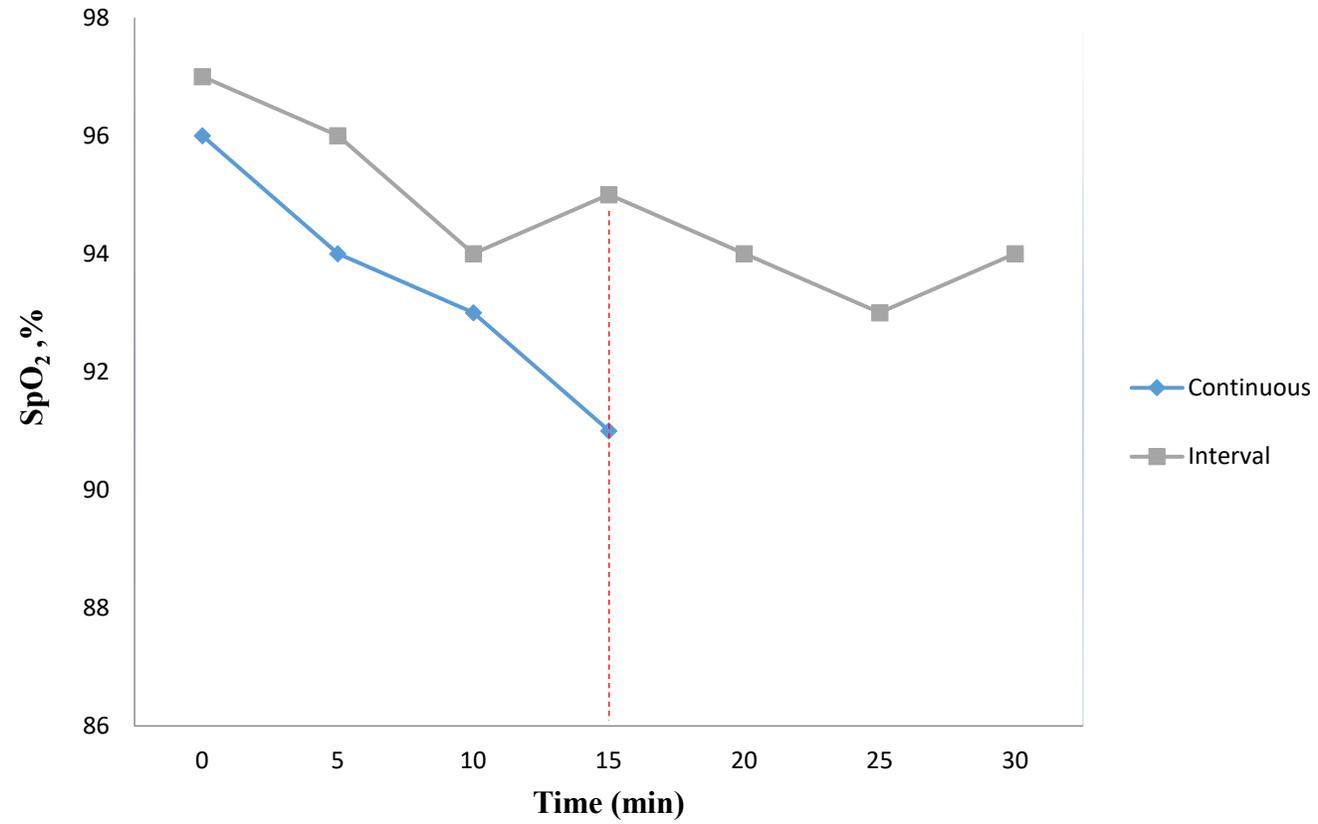
High Intensity Interval Exercise



Time, sec

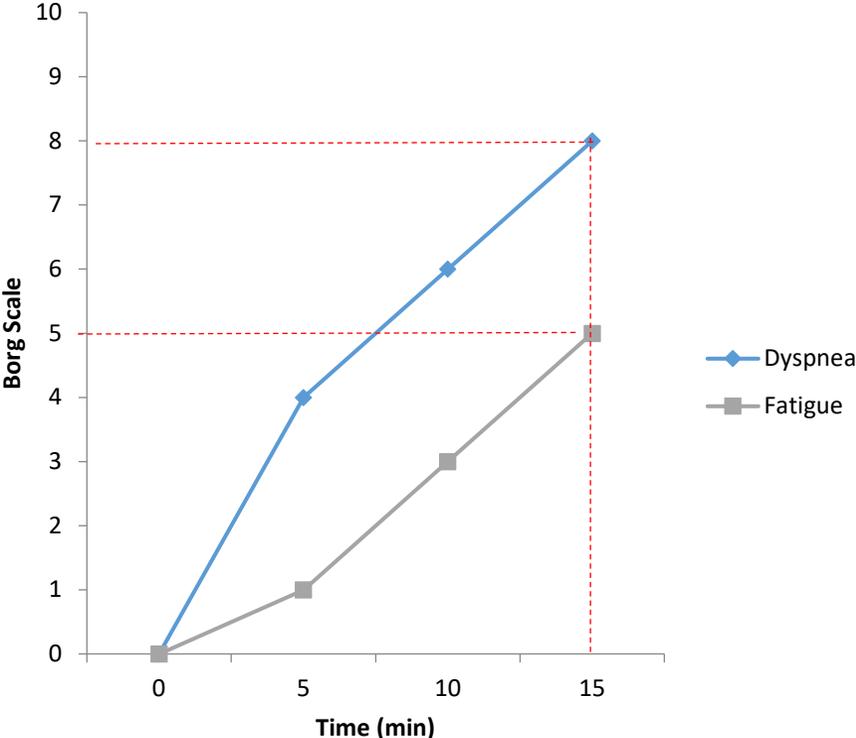
Duration: 30 min

Arterial oxygen saturation in Cystic Fibrosis

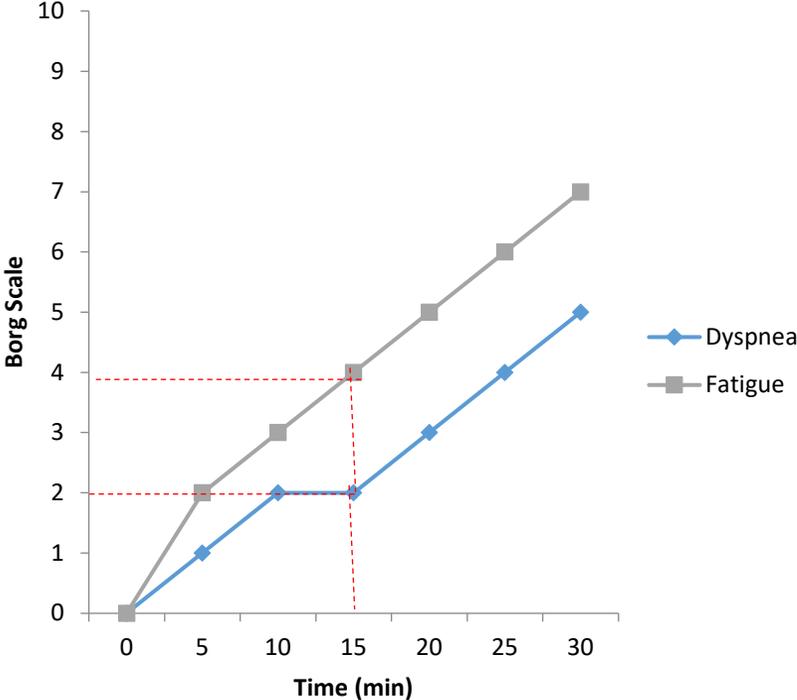


Symptoms during Continuous and Interval Exercise in Cystic Fibrosis

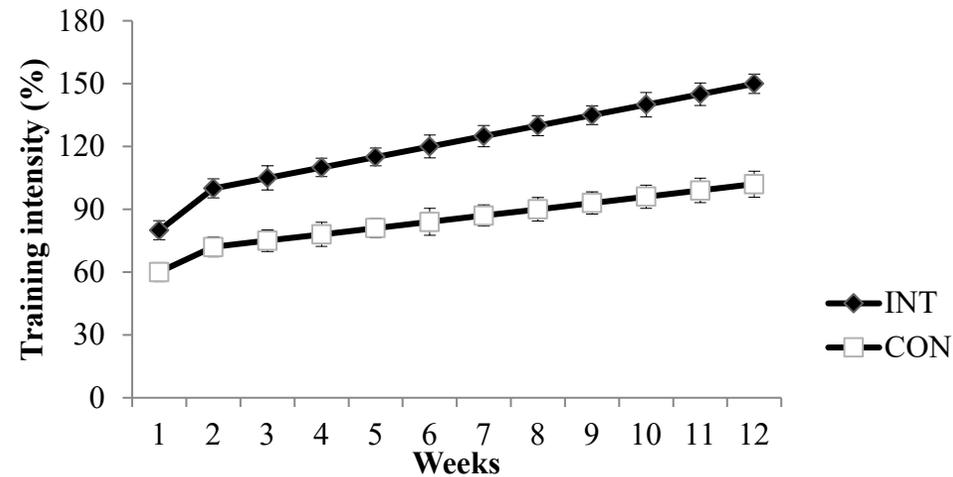
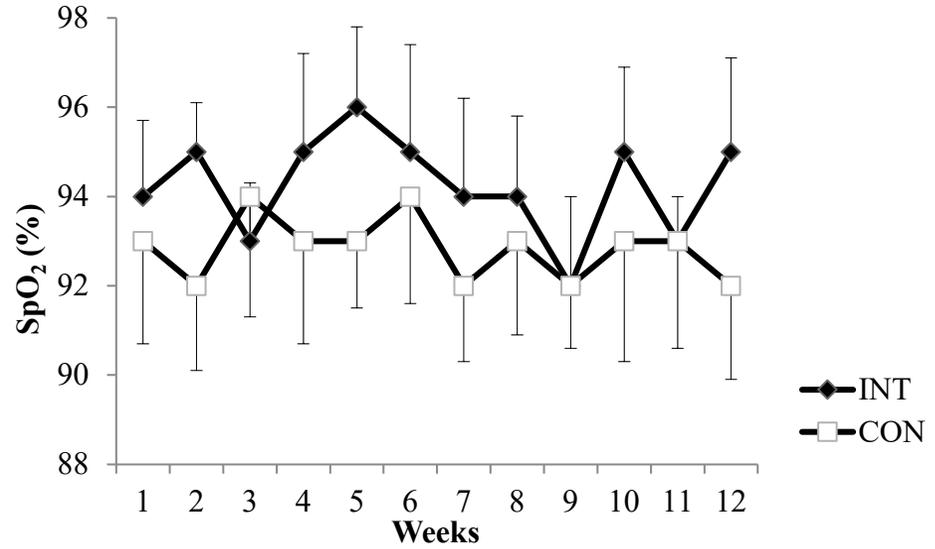
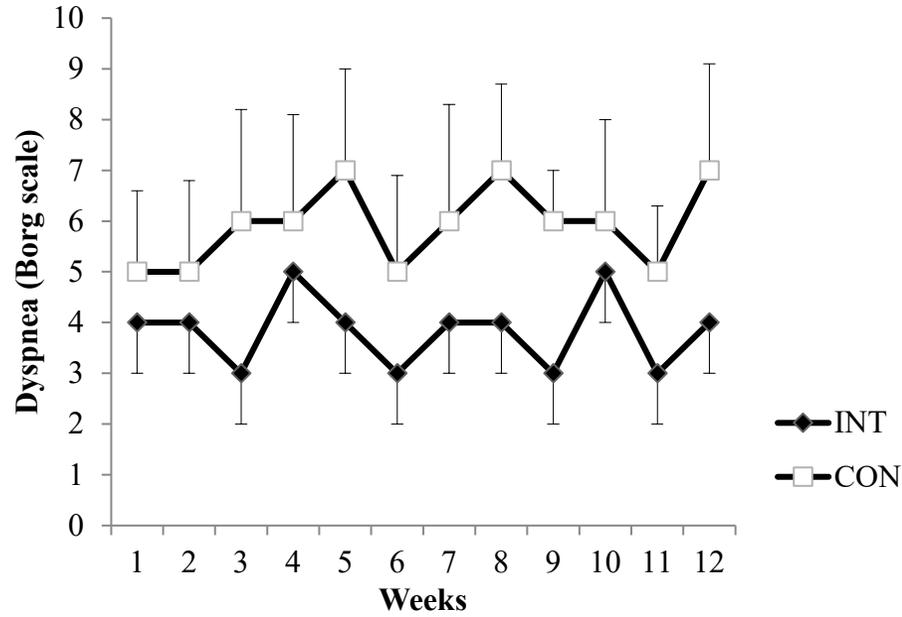
Continuous



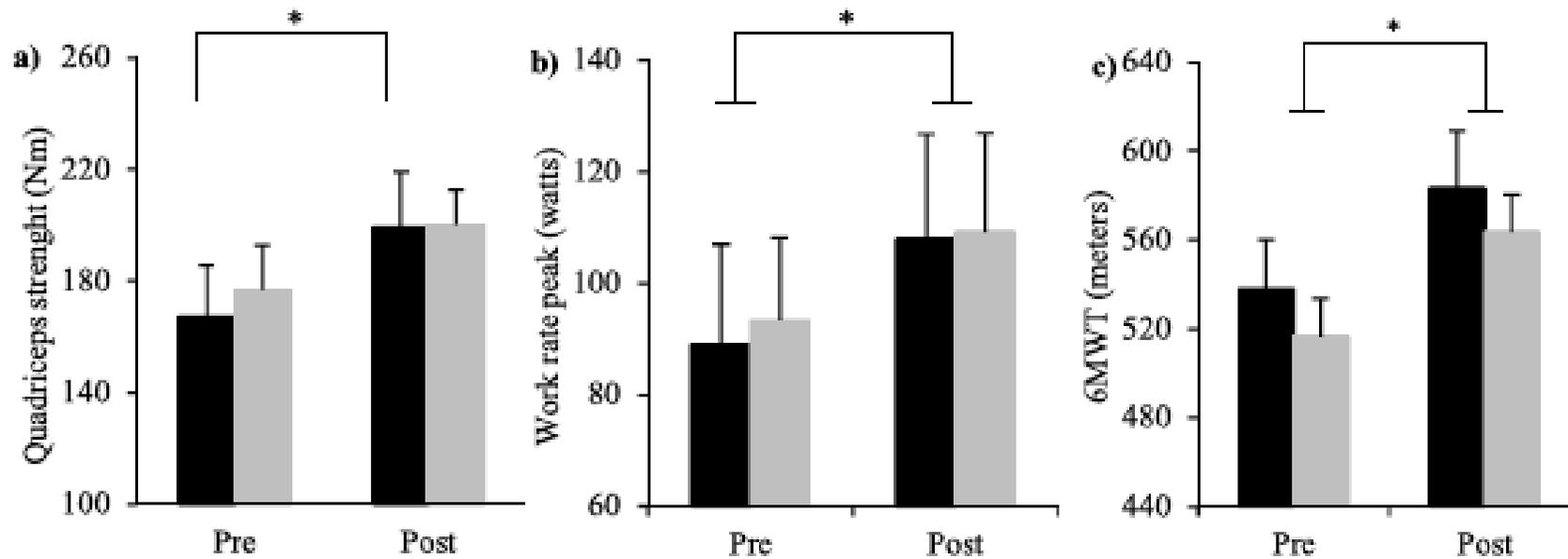
Interval



Application of interval exercise training during Pulmonary Rehabilitation in Cystic Fibrosis



Effects of interval & continuous exercise in CF



Interval exercise
 Continuous exercise

Table 2

Effects of IE and CLE training on physiological outcomes.

	High Intensity IE		Moderate Intensity CLE	
	Pre	Post	Pre	Post
WRpeak (watt)	89 ± 56	108 ± 60*	93 ± 49	109 ± 59*
VO ₂ peak (ml/kg/ min)	24.1 ± 10.7	26.9 ± 11.0*	23.2 ± 8.4	25.7 ± 9.5*
6MWT (meters)	538 ± 70	583 ± 83*	516 ± 57	564 ± 55*
BMI (kg m ⁻²)	21.0 ± 2.1	21.3 ± 1.6	20.2 ± 2.0	20.7 ± 1.9
FFMI (kg m ⁻²)	16.7 ± 1.7	16.8 ± 1.5	16.5 ± 2.0	16.8 ± 1.6
Quadriceps Strength (Nm)	167 ± 58	199 ± 63*	177 ± 54	200 ± 41
PEmax (cmH ₂ O)	121 ± 23	151 ± 30*	100 ± 58	112 ± 58
PImax (cmH ₂ O)	-71 ± 27	-84 ± 16*	-66 ± 33	-73 ± 31

Application of intermittent exercise in Cystic Fibrosis

- Intermittent compared to continuous exercise training:
 1. Is superior in improving locomotor and respiratory muscle strength
 2. It is associated with lower breathlessness and oxygen desaturation during training
- It is deemed safer than constant load exercise as arterial oxygen desaturation is only mild compared with constant load exercise



Interval aerobic exercise in individuals with advanced interstitial lung disease: a feasibility study

Lisa Wickerson, PT, PhD^a, Dina Brooks, PT, PhD^b, John Granton, MD^a, W. Darlene Reid, PT, PhD^c, Dmitry Rozenberg, MD^a, Lianne G. Singer, MD^a, and Sunita Mathur, PT, PhD^d

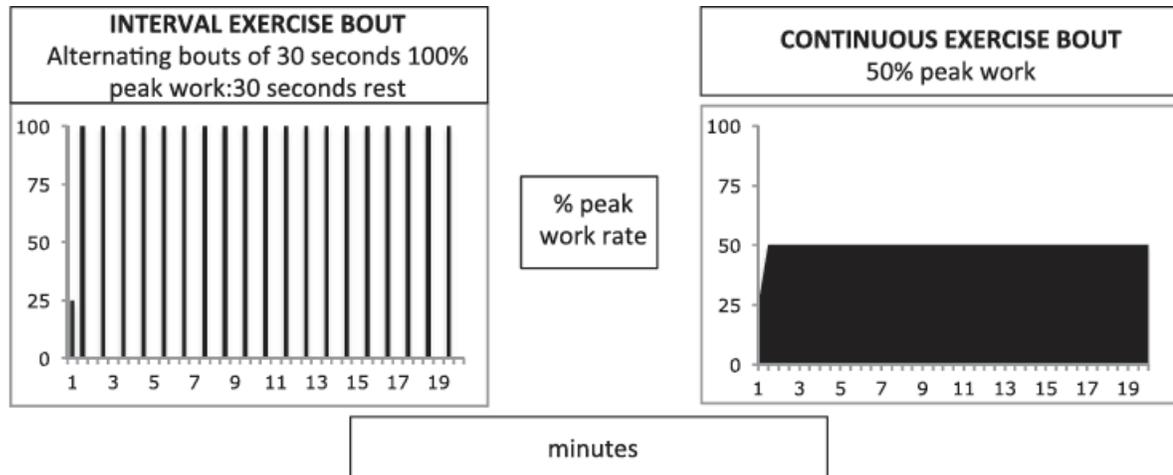


Table 2. Physiological responses to cycling bouts (n = 9), mean (SD).

	Interval	Continuous	p value
Pre-exercise SpO ₂ (%)	100 (0.4)	100 (0.7)	0.99
Nadir SpO ₂ (%)	92 (4)	89 (5)	0.06
Change in SpO ₂ (%)	- 8 (4)	- 11 (5)	0.05
Pre-exercise HR	85 (6)	84 (14)	0.72
Peak HR (bpm)	124 (12)	132 (15)	0.04
Change in HR (bpm)	+ 37 (12)	+ 47 (16)	0.12
Pre-exercise MAP (mmHg)	94 (11)	90 (8)	0.29
End-exercise MAP (mmHg)	110 (16)	112 (17)	0.36
Change in MAP (mmHg)	+ 18 (13)	+ 21 (15)	0.82
Pre-exercise RR (breaths/min)	22 (4)	23 (3)	0.68
End-exercise RR (breaths/min)	37 (5)	37 (8)	0.85
Change in RR (breaths/min)	+ 15 (5)	+ 14 (8)	0.49
Pre-exercise dyspnea	0.7 (0.8)	0.8 (0.6)	0.87
End-exercise dyspnea	4.3 (2)	4.9 (2)	0.21
Change in Borg dyspnea	+ 3.7 (2)	+ 4.1 (2)	0.42
Pre-exercise leg fatigue	0.5 (0.7)	0.7 (0.8)	0.17
End-exercise leg fatigue	3.8 (2)	4.4 (2)	0.05
Change in Borg leg fatigue	+ 3.4 (2)	+ 3.7 (1)	0.19
Pre-exercise lactate (mmol/L)	3.7 (3)	3.3 (3)	0.39
End-exercise lactate (mmol/L)	5.3 (2)	7.3 (5)	0.12
Change in lactate (mmol/L)	+ 1.6 (3)	+ 4.0 (2)	0.07

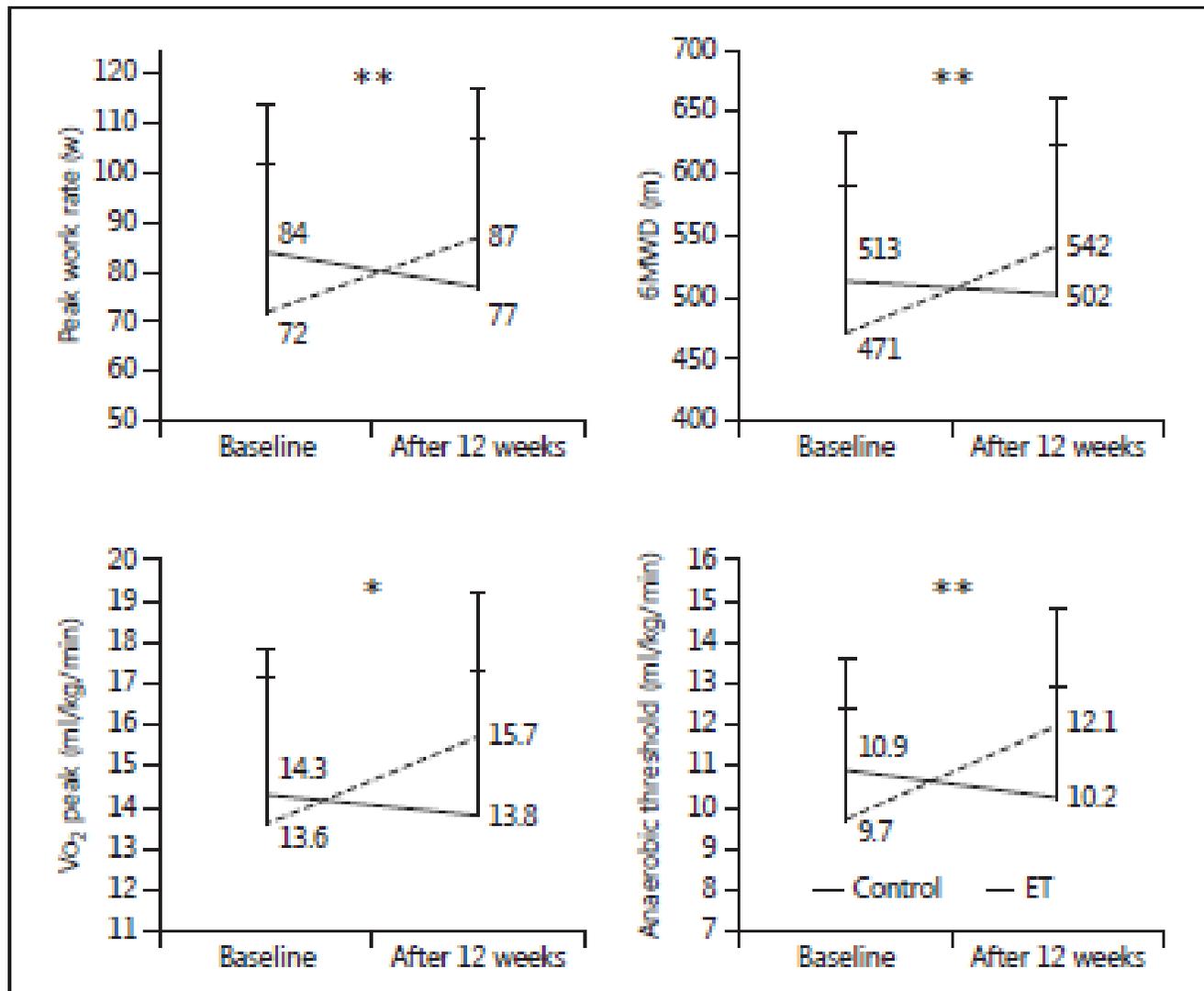
Clinical Investigations

Respiration 2014;88:378–388
DOI: 10.1159/000367899

Received: April 19, 2014
Accepted after revision: July 28
Published online: October 23, 2014

Exercise Training-Based Pulmonary Rehabilitation Program Is Clinically Beneficial for Idiopathic Pulmonary Fibrosis

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Benjamin Daniel Fox^{a,b} Oren Fruchter^{a,b} Mordechai Reuven Kramer^{a,b}



Application of Interval Exercise in Pulmonary Hypertension

Exercise and Respiratory Training Improve Exercise Capacity and Quality of Life in Patients With Severe Chronic Pulmonary Hypertension

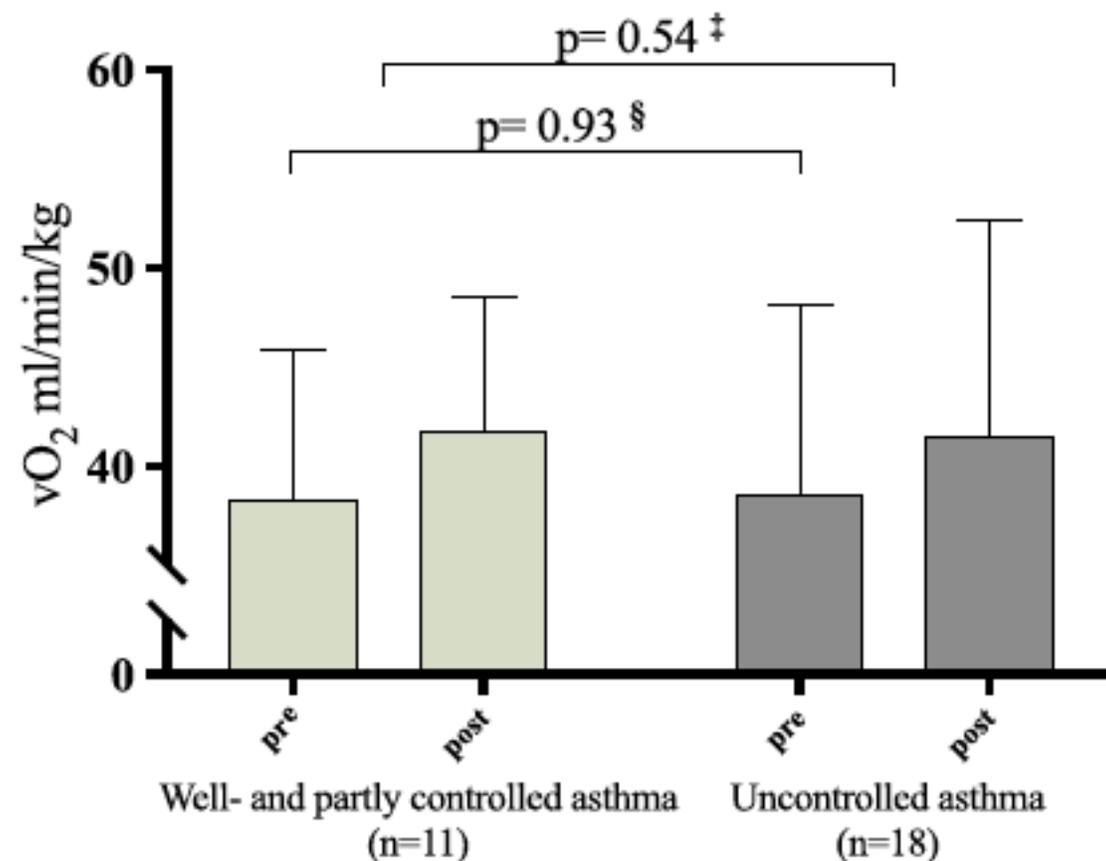
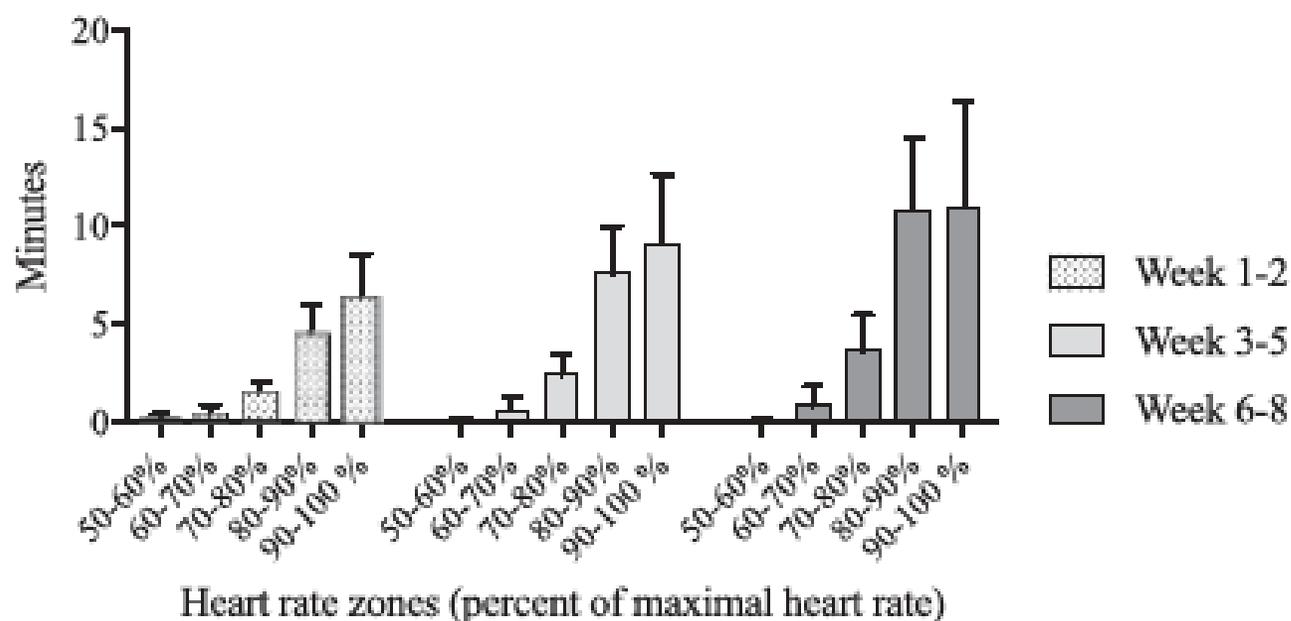
Derliz Mereles, MD*; Nicola Ehlken*; Sandra Kreuzer*; Stefanie Ghofrani, MD; Marius M. Hoeper, MD; Michael Halank, MD; F. Joachim Meyer, MD; Gabriele Karger, MD; Jan Buss, MD; Jana Juenger, MD; Nicole Holzapfel, MA; Christian Opitz, MD; Jörg Winkler, MD; Felix F.J. Herth, MD; Heinrike Wilkens, MD; Hugo A. Katus, MD; Horst Olschewski, MD; Ekkehard Grünig, MD

TABLE 3. Respiratory and Hemodynamic Variables at Baseline and After Intervention

	Control Group (n=15)			Primary Training Group (n=15)		
	Baseline	3 wk	15 wk	Baseline	3 wk	15 wk
Workload _{max} , W	64±22	60±24	67±20	70±17	85±26*†	90±25*†
Borg scale	15±2	15±1	16±1*	15±2	15±2	15±2
HR _{rest} , bpm	71±17	74±11	72±11	72±11	73±11	75±11
HR _{max} , bpm	108±19	107±22	110±20	118±16	125±15*†	132±17*†
VE _{max} , L · min	41.6±14.6	40.5±14.1	43.4±15.3	44.2±13.8	47.1±15.1	48.5±15.1
$\dot{V}O_2$ peak, mL · min ⁻¹ · kg ⁻¹	11.9±3.1	11.6±3.4	11.4±3.3	13.2±3.1	14.5±3.5*†	15.4±3.7*†
$\dot{V}O_2$ % predicted, %	46.3±10.7	45.9±14.6	49.8±12.7	51.6±16.3	56.5±18.6*	60.3±19.6*
Workload at AT, W	35±17	31±16	36±17	45±14	56±21*†	65±19*†
$\dot{V}O_2$ at AT, mL/min	640.7±187.4	613.4±206.6	610.4±200.4	736.6±210.3	802.3±229.8†	865.4±264.7*†

Feasibility of high-intensity training in asthma

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Interval versus continuous training in lung transplant candidates: A randomized trial

J Heart Lung Transplant 2012;31:934–41

Rainer Gloeckl, MSc,^a Martin Halle, MD,^{b,c} and Klaus Kenn, MD^a

- Interval exercise
- Continuous exercise

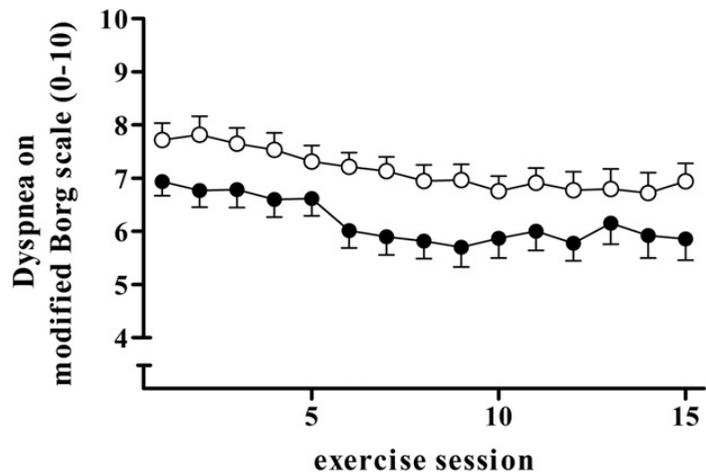


Table 2 Comparison of Treatment Effects of Interval and Continuous Training

Outcome ^a	Per protocol analysis				
	Mean changes from baseline		Difference (95% CI)	p-values	Difference in ITT (95% CI)
	Interval (n = 30)	Continuous (n = 30)			
Primary					
6-MWD, m	35.4 ± 28.9 ^b	35.7 ± 42.2 ^b	0.3 (−18.2 to 18.8)	0.89	1.1 (−15.6 to 17.8)
6-MWD, % pred ^c	14.1 ± 12.7 ^b	15.5 ± 25.1 ^b	1.4 (−8.9 to 11.7)	0.78	1.5 (−7.5 to 10.5)
Secondary					
PWR, W	12.0 ± 8.5 ^b	9.3 ± 10.1 ^b	−2.7 (−7.5 to 2.2)	0.38	−2.0 (−6.5 to 2.5)
FEV ₁ , liters	0.0 ± 0.1	−0.0 ± 0.1	0.0 (−0.1 to 0.0)	0.055	0.1 (−0.1 to 0.0)
FEV ₁ , % pred ^d	0.9 ± 2.9	−0.7 ± 3.8	−1.6 (−3.3 to 0.1)	0.064	−1.4 (−2.8 to 0.1)
FEV ₁ /IVC, % ^d	± 0.1	−0.0 ± 0.1	−0.0 (−0.1 to 0.0)	0.061	−0.0 (−0.0 to 0.0)
Dlco, % pred ^d	0.2 ± 5.3	−2.6 ± 4.4	−2.8 (−6.2 to 0.6)	0.096	−2.4 (−5.2 to 0.4)
Pao ₂ , mm Hg	1.7 ± 5.7	−1.7 ± 6.1	−3.4 (−6.4 to −0.3)	0.60	−2.9 (1.3 to −5.4)
Paco ₂ , mm Hg	−0.6 ± 4.6	−0.6 ± 7.5	−0.0 (−3.2 to 3.1)	0.85	−0.0 (−2.7 to 2.7)
Short-Form 36 SS					
Physical health	2.3 ± 9.5	4.3 ± 6.9 ^b	2.0 (−3.0 to 7.0)	0.43	1.5 (−2.5 to 5.6)
Mental health	9.7 ± 13.0 ^b	2.9 ± 10.9	−6.8 (−14.1 to 0.5)	0.066	−5.5 (−11.5 to 0.4)

Effect of interval compared to continuous exercise training on physiological responses in patients with chronic respiratory diseases: A systematic review and meta-analysis

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Chronic Respiratory Disease

Volume 18: 1–15

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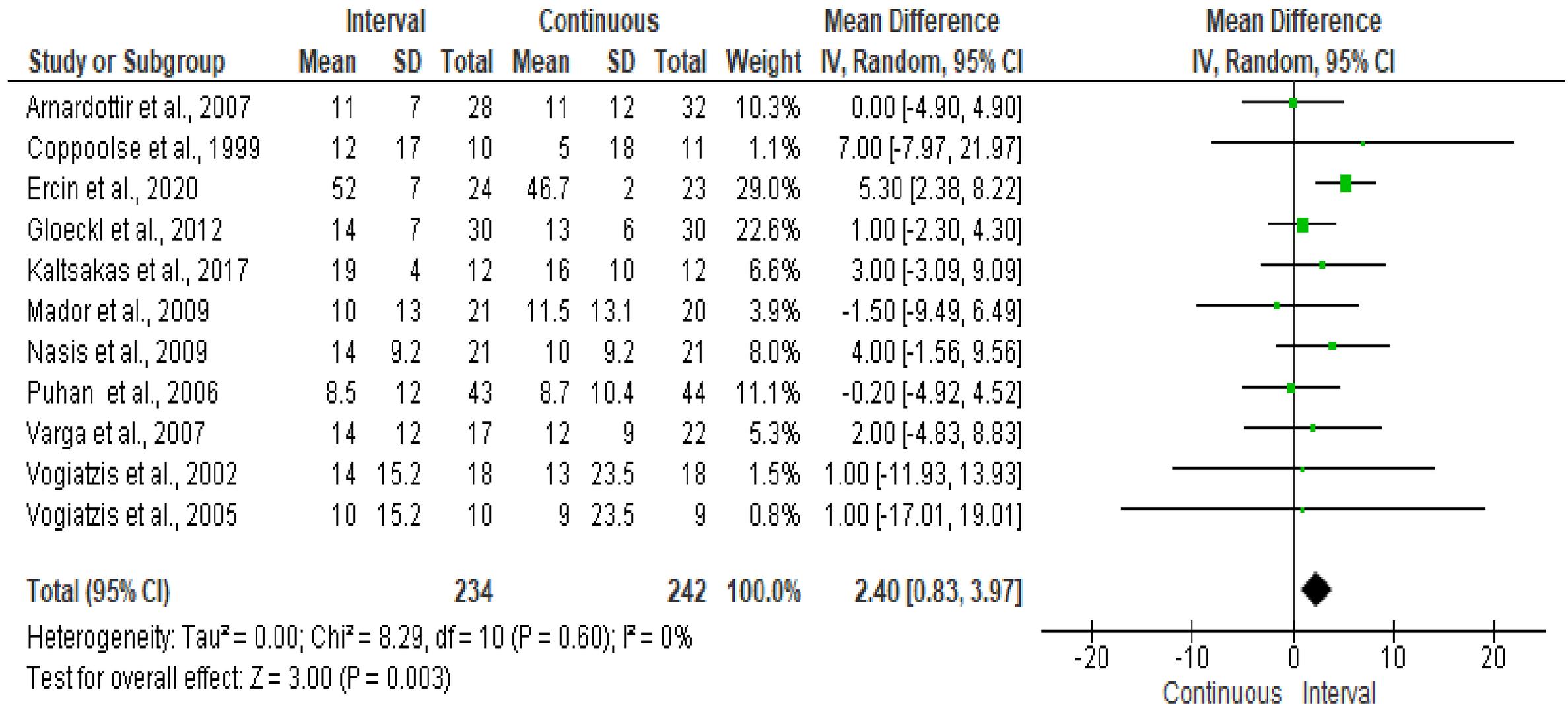
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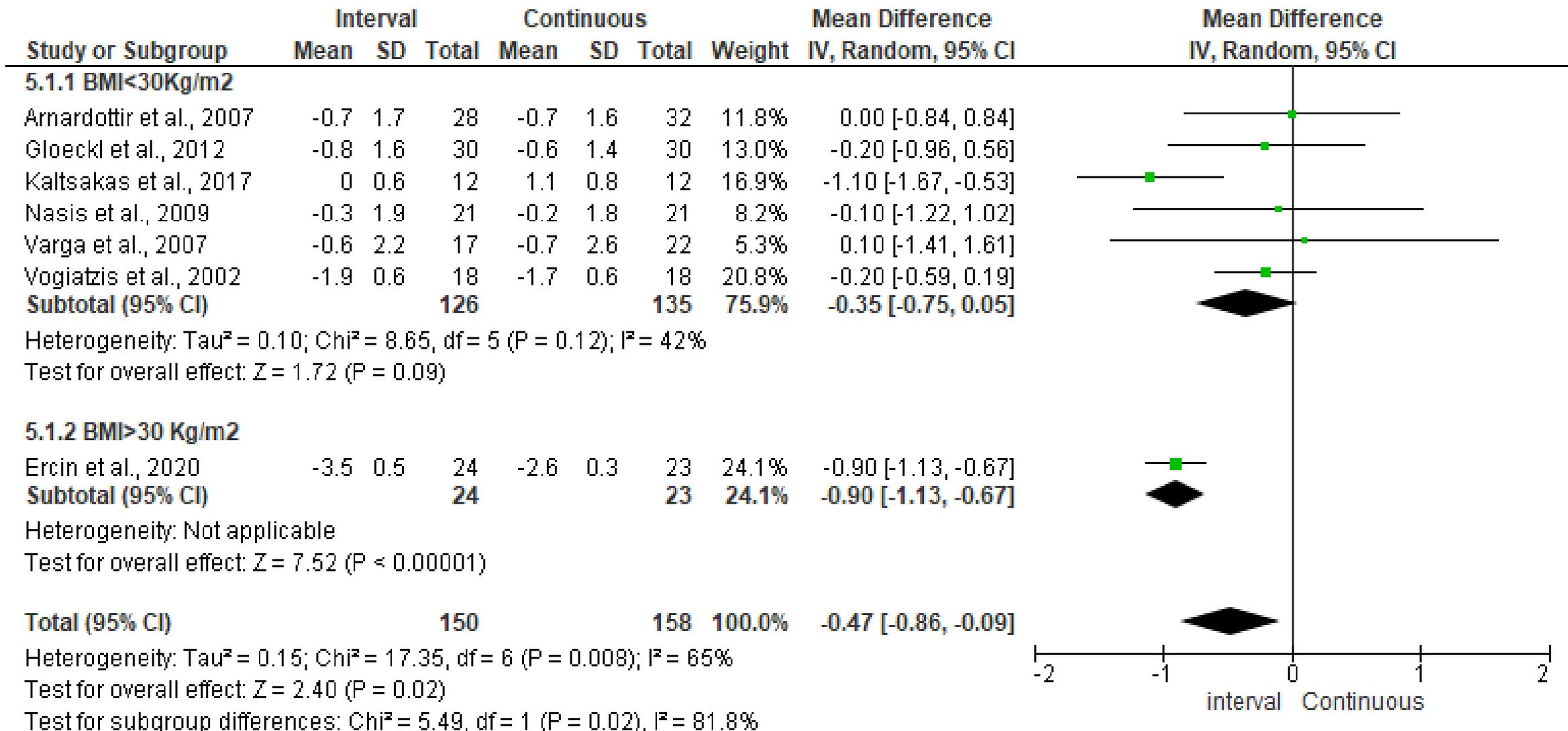
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Comparison of the effect of interval versus continuous exercise on Peak Work Rate (Watts)



Comparison of the effect of interval versus continuous exercise on Dyspnoea (Borg 1-10)



Comparison of the effect of interval versus continuous exercise on leg discomfort (Borg 1-10)

Study or Subgroup	Interval			Continuous			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
6.1.1 BMI<30Kg/m²								
Arnardottir et al., 2007	-0.3	1.4	28	-0.6	1.3	28	18.8%	0.30 [-0.41, 1.01]
Gloeckl et al., 2012	-0.9	1.9	30	-0.7	2.1	30	14.4%	-0.20 [-1.21, 0.81]
Kaltsakas et al., 2017	-1.3	0.1	12	0	0.6	12	24.3%	-1.30 [-1.64, -0.96]
Nasis et al., 2009	0.3	1.4	21	-0.2	3	21	10.0%	0.50 [-0.92, 1.92]
Varga et al., 2007	-0.8	2.4	17	-0.3	3	22	7.8%	-0.50 [-2.20, 1.20]
Subtotal (95% CI)			108			113	75.3%	-0.30 [-1.20, 0.60]

Heterogeneity: Tau² = 0.78; Chi² = 21.95, df = 4 (P = 0.0002); I² = 82%

Test for overall effect: Z = 0.65 (P = 0.52)

6.1.2 BMI>30Kg/m²

Ercin et al., 2020	-3	0.5	24	-2.2	0.6	23	24.7%	-0.80 [-1.12, -0.48]
Subtotal (95% CI)			24			23	24.7%	-0.80 [-1.12, -0.48]

Heterogeneity: Not applicable

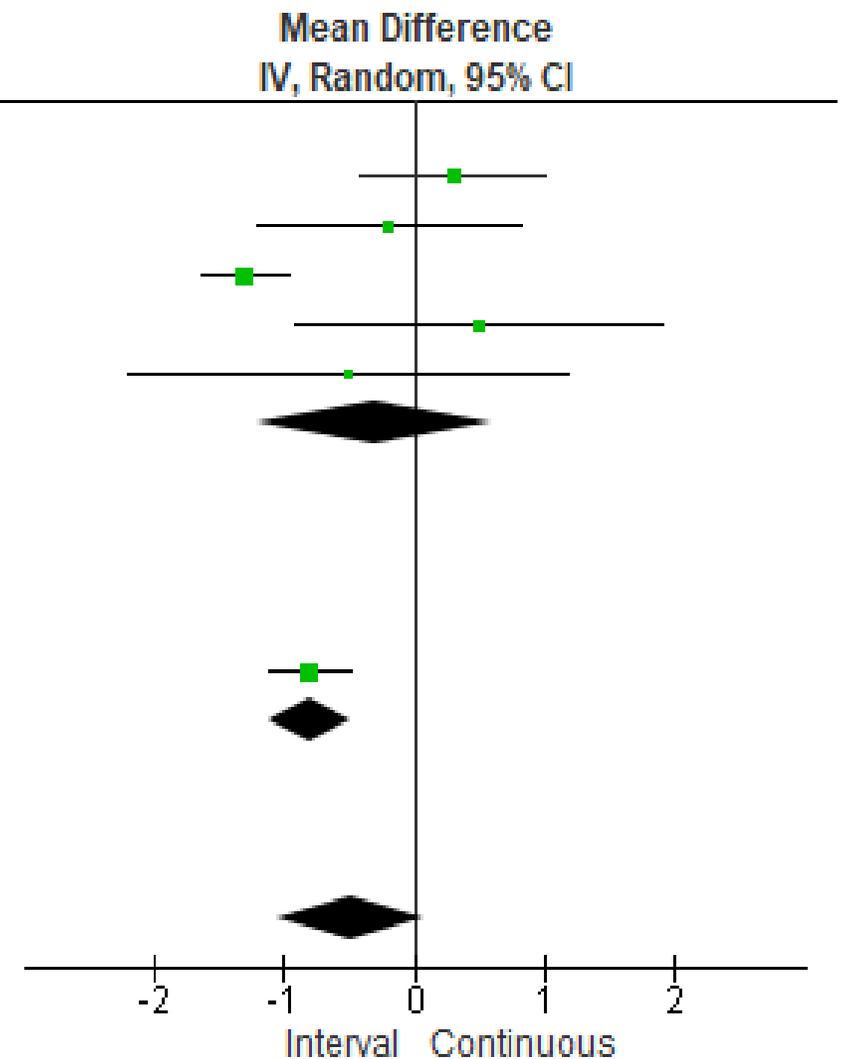
Test for overall effect: Z = 4.95 (P < 0.00001)

Total (95% CI)			132			136	100.0%	-0.48 [-1.04, 0.09]
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Heterogeneity: Tau² = 0.31; Chi² = 22.01, df = 5 (P = 0.0005); I² = 77%

Test for overall effect: Z = 1.65 (P = 0.10)

Test for subgroup differences: Chi² = 1.05, df = 1 (P = 0.30), I² = 5.2%



Conclusions



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Benefits of intermittent versus continuous exercise:

- Prolongs endurance time
- Reduces ventilatory requirement and breathlessness
- *Reduces metabolic acidosis and leg discomfort*
- *Interval exercise affords greater work intensities with reduced symptoms*
- *Implementation of high-intensity interval exercise may maximize the magnitude of the physiological training effects*

BTS Guidelines for Pulmonary Rehabilitation

Interval and continuous aerobic training

- ▶ Interval and continuous training can be applied safely and effectively within the context of pulmonary rehabilitation to patients with COPD. (Grade A)
- ▶ The choice of interval or continuous training will be down to the patient and/or therapist preference. (√)
- ▶ In clinical practice, interval training may require a higher therapist to patient ratio to ensure adequate work rate and rest intervals are achieved compared with continuous training. (√)

Thorax
AN INTERNATIONAL JOURNAL OF RESPIRATORY MEDICINE

BTS Guideline on Pulmonary
Rehabilitation in Adults

British Thoracic Society
Pulmonary Rehabilitation Guideline
Group

September 2013 Volume 68 Supplement 2



BMJ