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**Lift, stop, rest, repeat: The potential of ‘cluster sets’ as interval  
resistance exercise for COPD**

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**Keywords:** Resistance training; clinical rehabilitation; function; exercise tolerance

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30 **Abbreviations**

31

32 COPD            Chronic obstructive pulmonary disorder

33 CLE             Constant load exercise

34 IE               Interval exercise

35  $WR_{peak}$        Work rate peak

36

37 **Exercise training in clinical rehabilitation:**

38

39 Exercise training is often a focus of clinical rehabilitation programs aimed at  
40 improving patient health, function and decreasing mortality rate. Demonstrated benefits  
41 extend across a plethora of chronic conditions including chronic obstructive pulmonary  
42 disorder (COPD). Briefly, COPD is a progressive chronic inflammatory lung disease  
43 typically resulting from long-term exposure to irritants (e.g. smoking) causing  
44 respiratory issues. Disease progression is often accompanied by peripheral muscle  
45 discomfort, weakness and dysfunction. Intolerable dyspnoea sensations are also  
46 common during exercise. Subsequently, exercise tolerance and health-related quality of  
47 life are severely reduced in COPD patients leading to morbidity and ultimately,  
48 mortality. As such, exercise training is an important tool in pulmonary rehabilitation,  
49 symptomatic control, attenuation of adverse health consequences and to improve patient  
50 function. However, optimal exercise programming strategies producing favourable  
51 acute responses and chronic adaptations in COPD, and across many exercise  
52 rehabilitation settings, are the subject of ongoing debate and exploration. Indeed, even  
53 within exercise modalities alterations in work intensity, rest and structure (e.g.  
54 continuous efforts versus high-intensity intervals) are continually being trialled.

55

56 **Continuous versus interval aerobic exercise in COPD:**

57

58 The acute effects of interval and continuous exercise in COPD patients was recently  
59 compared in *The Journal of Physiology* by Louvaris *et al.*, (2020). The authors  
60 investigated a single session of constant-load aerobic exercise (CLE) versus interval  
61 exercise (IE) on dynamic hyperinflation, blood lactate, muscle oxygenation, exercise  
62 endurance (time until exhaustion), work output, and indices of respiratory function and  
63 cardiac output. Twelve clinically stable patients (64±10 years, long-term cigarette  
64 smokers [ $>40$  packs per year], forced expiratory volume/forced vital capacity volume  
65 ratio  $<0.7$ ) completed three cycle ergometer sessions (one exercise capacity testing  
66 session, two exercise sessions). Patients demonstrated resting lung hyperinflation,  
67 moderate and mild reductions in carbon monoxide diffusion capacity and arterial  
68 oxygen tension, respectively, reduced peak exercise capacity, moderate arterial oxygen  
69 desaturation and exercise-induced dynamic hyperinflation. Reduced functional capacity  
70 and sedentarism were also noted. Patients with interfering pathological conditions, other

71 respiratory diseases, clinical signs of acute heart-failure or -disease, long-term oxygen  
72 therapy or requirement during exercise, exercise training in the previous 3 months or  
73 hospitalisation from COPD exacerbation ( $\leq 6$  weeks) were excluded. During CLE,  
74 which always preceded IE, participants cycled at a sustained 75% peak work rate  
75 ( $WR_{peak}$ ) determined from maximal exercise testing during familiarisation. During IE,  
76 patients cycled at 100%  $WR_{peak}$  for 30 seconds interspersed by 30-second bouts at 50%  
77  $WR_{peak}$ . Both protocols produced the same average work rate per minute and patients  
78 were instructed to continue exercising until the limit of tolerance. Time to exhaustion  
79 was significantly longer for IE ( $19.5 \pm 4.8$  min) compared to CLE ( $11.4 \pm 2.1$  min,  
80  $P=0.0001$ ) and consequently, total work was also higher (IE:  $81.3 \pm 27.7$  kJ, CLE:  
81  $48.9 \pm 23.8$  kJ,  $P=0.0001$ ). Furthermore, dynamic hyperinflation was lower during IE at  
82 the same time point of exercise termination during CLE ( $P=0.009$ ), but similar at IE  
83 termination. The authors concluded that dynamic hyperinflation was the main  
84 determinant of exercise tolerance. Additionally, similar trends were observed for  
85 subjective evaluations of dyspnoea and leg fatigue (i.e. lower at corresponding  
86 timepoints during IE, but similar at exercise termination for both protocols). Minute  
87 ventilation, cardiac output and systemic oxygen delivery did not differ between  
88 conditions. In contrast, vastus lateralis and intercostal muscle(s) oxygenation were  
89 higher at exhaustion ( $P=0.0002-0.014$ ), and blood lactate lower for IE ( $4.9 \pm 2.4$  mmol l<sup>-1</sup>  
90 versus  $6.4 \pm 2.2$  mmol l<sup>-1</sup>,  $P=0.039$ ) compared to CLE. Thus, IE appears to preserve  
91 muscle oxygenation and minimise metabolic acidosis. Overall, Louvaris *et al.*, (2020)  
92 provide comprehensive insight into acute physiological responses during CLE and IE  
93 and demonstrate the likely efficacy of IE in COPD. These results have potential to  
94 inform clinical exercise practice. Specifically, they provoke thought into the further  
95 possibilities of exercise structure modification in COPD to improve tolerance,  
96 perception and physiologic responses. As such, the below discussion seeks to expand  
97 upon the idea of utilising interval-like exercise, with specific focus on possible adaption  
98 and relevance in resistance training. It also urges consideration for the use of novel  
99 resistance training approaches, and effort toward research and application in a plethora  
100 of clinical exercise settings where patient benefit is perceived.

101

102

103 **Can similar concepts be applied in resistance exercise?**

104

105 As expected, aerobic exercise programs demonstrate benefit in COPD. However,  
106 peripheral muscle strength and function are not an inherent focus, nor primary outcome  
107 of aerobic exercise. Thus, it can be argued that these outcomes are not suitably  
108 addressed with such programs. Hence, additional benefits of resistance training in  
109 COPD have also been postulated. In fact, evidence suggests that progressive resistance  
110 training can improve muscle strength, quality of life and exercise capacity in patients  
111 (Vonbank *et al.*, 2012). Moreover, a systematic review reported that substantial  
112 increases in muscle strength occur with short-term (~12 weeks) progressive resistance  
113 training (O'Shea *et al.*, 2009). Of note, the majority of included studies used programs  
114 consisting of 2-4 sets of 8-12 'continuous' repetitions at 30-90% of maximum intensity,  
115 followed by several minutes of '*inter-set*' rest. However, despite common thought, the  
116 notion of breaking down continuous efforts with periods of low work or rest is not  
117 unique to aerobic exercise. For example, the implementation of additional rest (i.e. short  
118 '*intra-set*' rest intervals) within sets is known in resistance training practice as 'cluster-  
119 sets'. Although this concept anecdotally dates to the mid 1900's, cluster-sets have  
120 recently been popularised in acute resistance training literature and practice (Latella *et*  
121 *al.*, 2019). However, despite most work being in healthy individuals, cluster sets show  
122 likely applicability in clinical settings (e.g. COPD) where various factors limit exercise  
123 tolerance/capacity and the ability to sustain muscular work. In a similar fashion to  
124 Louvaris *et al.*, (2020) who demonstrated favourable responses to aerobic IE, cluster-  
125 sets also show ability to evoke unique and favourable responses compared to continuous  
126 repetition efforts.

127

### 128 **Cluster-set resistance exercise: Structure(s) and benefit:**

129

130 Not dissimilar to the concept high- and low-effort, or rest intervals in aerobic exercise,  
131 'cluster sets' implement further additional '*intra-set*' rest periods (e.g. 6-45 seconds)  
132 after short bouts of intense efforts. Importantly, this rest occurs in addition to traditional  
133 '*inter-set*' rest periods, often 1-3 minutes in duration, that typically occur after  
134 performing an entire set of continuous repetitions. Common cluster set structures  
135 include the intra-set repetition (rest after several repetitions within a set), inter-repetition  
136 (rest after each repetition) or rest-redistribution (total rest of continuous method is  
137 divided equally between total repetitions) method (Fig 1A). The latter method may have  
138 the additional benefit of matching the total session time of a continuous program.

139 Reduced cardiac parasympathetic withdrawal and lactate production has also been  
140 observed using rest-redistribution compared to continuous repetitions (i.e. set of 10)  
141 (Rua-Alonso *et al.*, 2020) (Figure 1B for example). Moreover, perception of effort and  
142 neuromuscular fatigue is minimised (Figure 1B), and movement velocity and power  
143 maintained (Latella *et al.*, 2019). These benefits are important as although Louvaris *et*  
144 *al.*, (2020) showed that aerobic exercise tolerance is limited by dynamic hyperinflation,  
145 concomitant or unique physiological factors may underpin resistance exercise capacity.  
146 For example, it is possible that dynamic hyperinflation contributes, at least in part, when  
147 repeated sets are performed with inadequate inter-set recovery or exacerbated as a result  
148 of increased cardio-respiratory and -vascular response to exercise. In particular,  
149 metabolic and nociceptive muscle afferent feedback may be increased from working  
150 musculature where dysfunction causes greater fatigability and oxygenation becomes  
151 compromised during sustained efforts. Thus, cluster sets may serve to reduce afferent  
152 feedback and associated autonomic cardio-respiratory and -vascular responses,  
153 especially during compound movements that require large working muscle mass (Sheel  
154 *et al.*, 1985). Synergistically or independent of afferent feedback, subjective sensation  
155 of effort is also reduced. Speculatively, such benefits may be even more apparent in  
156 patients with severely reduced function and poorer exercise capacity/tolerance.  
157 Although, individual data on pulmonary function and exercise performance were not  
158 presented for all patients by Louvaris *et al.*, (2020), it is suggested that this may be an  
159 avenue allowing for more targeted, individualised resistance exercise prescription and  
160 structure modification accounting for functional capacity in future studies.

161 Furthermore, movement velocity and power are important variables in  
162 functional tasks, locomotion and falls prevention. Cluster sets stimulate similar or  
163 greater strength and power adaptations which is important given the prevalence of  
164 peripheral muscle weakness, dysfunction and reduced functional capacity in COPD. It  
165 can also be reasonably assumed that intolerance leads to poor long-term adherence,  
166 worsening disease progression. Thus, cluster-sets may offer a novel resistance paradigm  
167 addressing peripheral muscle function that compliments existing aerobic pulmonary  
168 rehabilitation programs. It is acknowledged that several physiological parameters  
169 relevant to COPD (e.g. subjective muscle fatigue and dyspnoea), are yet to evaluated  
170 using continuous- and cluster-sets. However, future high-quality disease-specific studies  
171 may advance clinical resistance exercise knowledge and practice.

172



173 <Insert Figure 1A-1B>

174

175 **Cluster-sets: Potential across clinical exercise settings?**

176

177 The insightful work regarding IE by Louvaris *et al.*, (2020) provides precedence  
178 for similar concepts to be adapted into resistance exercise and shows promise across  
179 clinical exercise settings. Besides COPD, numerous conditions exist where muscle  
180 weakness/fatigue, exercise capacity and quality of life are negatively impacted. Such  
181 conditions include ageing, neuromuscular disease and neurological injury, chronic  
182 cardiovascular conditions and cancer, all of which current resistance exercise  
183 prescription has demonstrated positive but often limited success. Partly, this may be due  
184 to limited exercise tolerance and capacity and therefore, a reduced exercise stimulus  
185 being delivered (e.g. mechanical load). Thus, simple low-cost strategies that address  
186 these issues without compromising adaptive potential are promising. It is suggested that  
187 the growing support for cluster-set resistance exercise in healthy individuals is  
188 investigated as a complimentary technique in patient populations.

189

190 **Additional information**

191 Nil

192

193 **Competing interests**

194 The author declares no competing interests.

195

196 **Author contributions**

197 C.L was responsible for the initial concept and manuscript preparation.

198

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201

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204

205

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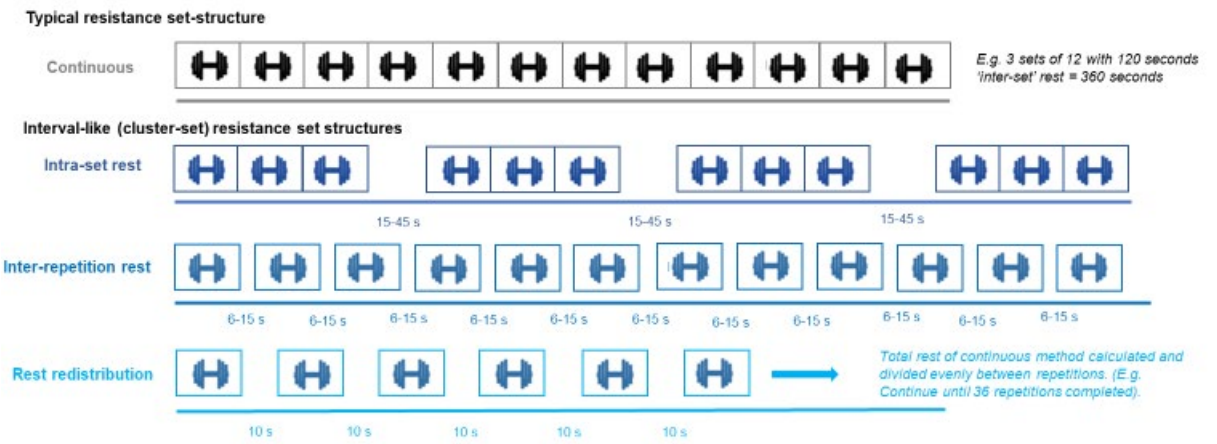
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228

229 **Figure**

230

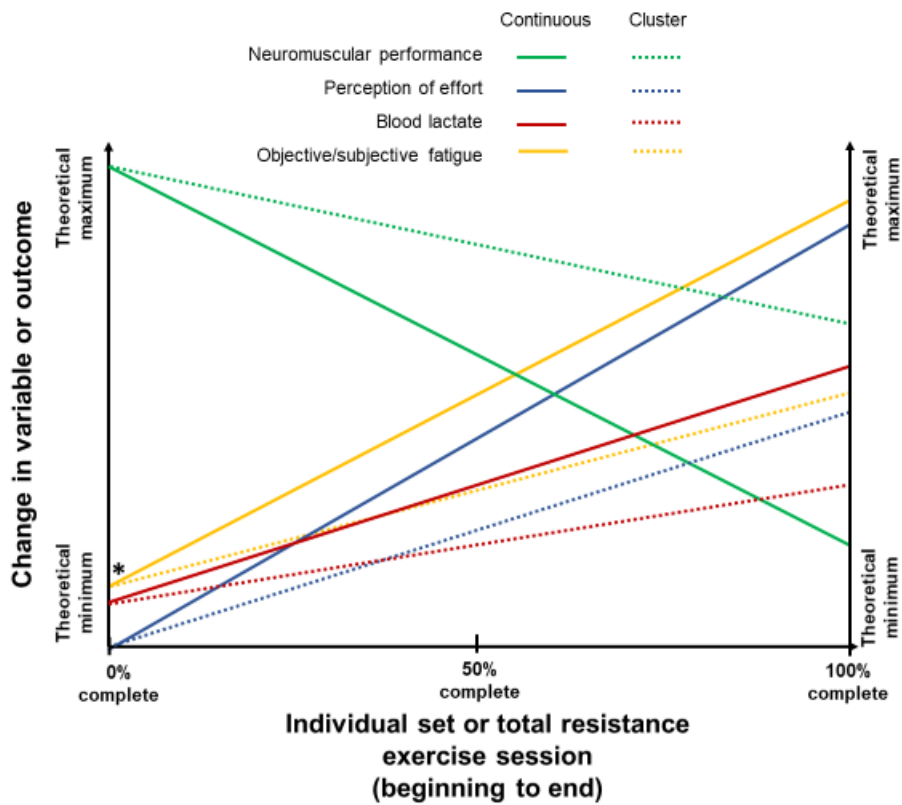
**Figure 1**  
**(A)**



231

232

(B)



233 **Figure 1.** (A) displays an example of continuous resistance set structure (top row) and  
234 several interval-type structures or ‘cluster-sets’ (bottom three rows) proposed for use in  
235 clinical exercise settings. (B) Theoretical depiction of demonstrated responses (across a  
236 set or entire session) to continuous or cluster set paradigms. \* note, a degree  
237 objective/subjective fatigue may already be apparent prior to exercise commencement in  
238 clinical settings.