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

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### Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disorder</td>
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<tr>
<td>CLE</td>
<td>Constant load exercise</td>
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<tr>
<td>IE</td>
<td>Interval exercise</td>
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<td>WR&lt;sub&gt;peak&lt;/sub&gt;</td>
<td>Work rate peak</td>
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Exercise training in clinical rehabilitation:

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

Continuous versus interval aerobic exercise in COPD:

The acute effects of interval and continuous exercise in COPD patients was recently compared in *The Journal of Physiology* by Louvaris et al., (2020). The authors investigated a single session of constant-load aerobic exercise (CLE) versus interval exercise (IE) on dynamic hyperinflation, blood lactate, muscle oxygenation, exercise endurance (time until exhaustion), work output, and indices of respiratory function and cardiac output. Twelve clinically stable patients (64±10 years, long-term cigarette smokers [>40 packs per year], forced expiratory volume/forced vital capacity volume ratio <0.7) completed three cycle ergometer sessions (one exercise capacity testing session, two exercise sessions). Patients demonstrated resting lung hyperinflation, moderate and mild reductions in carbon monoxide diffusion capacity and arterial oxygen tension, respectively, reduced peak exercise capacity, moderate arterial oxygen desaturation and exercise-induced dynamic hyperinflation. Reduced functional capacity and sedentarism were also noted. Patients with interfering pathological conditions, other
respiratory diseases, clinical signs of acute heart-failure or -disease, long-term oxygen therapy or requirement during exercise, exercise training in the previous 3 months or hospitalisation from COPD exacerbation (≤6 weeks) were excluded. During CLE, which always preceded IE, participants cycled at a sustained 75% peak work rate (WR<sub>peak</sub>) determined from maximal exercise testing during familiarisation. During IE, patients cycled at 100% WR<sub>peak</sub> for 30 seconds interspersed by 30-second bouts at 50% WR<sub>peak</sub>. Both protocols produced the same average work rate per minute and patients were instructed to continue exercising until the limit of tolerance. Time to exhaustion was significantly longer for IE (19.5±4.8 min) compared to CLE (11.4±2.1 min, P=0.0001) and consequently, total work was also higher (IE: 81.3±27.7 kJ, CLE: 48.9±23.8 kJ, P=0.0001). Furthermore, dynamic hyperinflation was lower during IE at the same time point of exercise termination during CLE (P=0.009), but similar at IE termination. The authors concluded that dynamic hyperinflation was the main determinant of exercise tolerance. Additionally, similar trends were observed for subjective evaluations of dyspnoea and leg fatigue (i.e. lower at corresponding timepoints during IE, but similar at exercise termination for both protocols). Minute ventilation, cardiac output and systemic oxygen delivery did not differ between conditions. In contrast, vastus lateralis and intercostal muscle(s) oxygenation were higher at exhaustion (P=0.0002-0.014), and blood lactate lower for IE (4.9±2.4 mmol l<sup>-1</sup> versus 6.4±2.2 mmol l<sup>-1</sup>, P=0.039) compared to CLE. Thus, IE appears to preserve muscle oxygenation and minimise metabolic acidosis. Overall, Louvaris et al., (2020) provide comprehensive insight into acute physiological responses during CLE and IE and demonstrate the likely efficacy of IE in COPD. These results have potential to inform clinical exercise practice. Specifically, they provoke thought into the further possibilities of exercise structure modification in COPD to improve tolerance, perception and physiologic responses. As such, the below discussion seeks to expand upon the idea of utilising interval-like exercise, with specific focus on possible adaption and relevance in resistance training. It also urges consideration for the use of novel resistance training approaches, and effort toward research and application in a plethora of clinical exercise settings where patient benefit is perceived.

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

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

Not dissimilar to the concept high- and low-effort, or rest intervals in aerobic exercise, ‘cluster sets’ implement further additional ‘intra-set’ rest periods (e.g. 6-45 seconds) after short bouts of intense efforts. Importantly, this rest occurs in addition to traditional ‘inter-set’ rest periods, often 1-3 minutes in duration, that typically occur after performing an entire set of continuous repetitions. Common cluster set structures include the intra-set repetition (rest after several repetitions within a set), inter-repetition (rest after each repetition) or rest-redistribution (total rest of continuous method is divided equally between total repetitions) method (Fig 1A). The latter method may have the additional benefit of matching the total session time of a continuous program.
Reduced cardiac parasympathetic withdrawal and lactate production has also been observed using rest-redistribution compared to continuous repetitions (i.e. set of 10) (Rua-Alonso et al., 2020) (Figure 1B for example). Moreover, perception of effort and neuromuscular fatigue is minimised (Figure 1B), and movement velocity and power maintained (Latella et al., 2019). These benefits are important as although Louvaris et al., (2020) showed that aerobic exercise tolerance is limited by dynamic hyperinflation, concomitant or unique physiological factors may underpin resistance exercise capacity. For example, it is possible that dynamic hyperinflation contributes, at least in part, when repeated sets are performed with inadequate inter-set recovery or exacerbated as a result of increased cardio-respiratory and -vascular response to exercise. In particular, metabolic and nociceptive muscle afferent feedback may be increased from working musculature where dysfunction causes greater fatigability and oxygenation becomes compromised during sustained efforts. Thus, cluster sets may serve to reduce afferent feedback and associated autonomic cardio-respiratory and -vascular responses, especially during compound movements that require large working muscle mass (Sheel et al., 1985). Synergistically or independent of afferent feedback, subjective sensation of effort is also reduced. Speculatively, such benefits may be even more apparent in patients with severely reduced function and poorer exercise capacity/tolerance. Although, individual data on pulmonary function and exercise performance were not presented for all patients by Louvaris et al., (2020), it is suggested that this may be an avenue allowing for more targeted, individualised resistance exercise prescription and structure modification accounting for functional capacity in future studies.

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

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

Additional information
Nil

Competing interests
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Figure 1

(A) Typical resistance set-structure

Continuous

Interval-like [cluster-set] resistance set structures

Intra-set rest

Inter-repetition rest

Rest redistribution

E.g. 3 sets of 12 with 120 seconds 
inter-set rest = 240 seconds

Total rest of continuous method calculated and not 
divided evenly between repetitions. (ft e.g. 
Continue until 36 repetitions completed)
Figure 1. (A) displays an example of continuous resistance set structure (top row) and several interval-type structures or ‘cluster-sets’ (bottom three rows) proposed for use in clinical exercise settings. (B) Theoretical depiction of demonstrated responses (across a set or entire session) to continuous or cluster set paradigms. * note, a degree objective/subjective fatigue may already be apparent prior to exercise commencement in clinical settings.