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Exercise Prescription Considerations for Individuals with Multiple Chronic Diseases: Systematic Review

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Abstract

Background: Although the benefits of exercise are well-known, guidelines often target the general public or individuals living with single pathologies. Currently, there is no systematic exercise prescription approach for individuals with multiple chronic diseases.

Objective: To determine overlapping physiological and subjective markers for use by clinicians to define safe exercise for individuals with multiple chronic diseases.

Methods: Eight databases were used to complete a comprehensive systematic review. Thirty-nine articles met the inclusion criteria for chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD) and type two diabetes mellitus (T2DM). Four reviewers extracted all qualitative and quantitative data.

Results: Findings show that: 1) aerobic and resistance training done 2-3 times per week is beneficial for individuals with chronic diseases, and 2) overlapping ranges of physiological and subjective markers can be used to determine safe exercise prescription. Exercise for the chronic diseases searched is safe with overlapping markers including: systolic and diastolic blood pressure, Borg scale, VO2Max, and heart rate. Each disease state did have unique markers that must be monitored to ensure safety during exercise. Specifically, with COPD SpO2 should be kept above 90%, for CAD exercise heart rate should be kept 10 bpm below causing angina symptoms, and for diabetes blood glucose should be kept between 100-300 mg/dl.

Conclusion: This review shows initial evidence for a multi-system approach to exercise prescription, which suggests screening key physiological markers from various body systems in order to safely prescribe exercise to individuals with multiple chronic diseases.

Keywords: COPD; CAD; Type II Diabetes mellitus; Exercise prescription; Physiological markers; Subjective markers

Introduction

According to the World Health Organization, chronic diseases are the leading causes of death worldwide, and in western countries such as Canada and the United States two-thirds of deaths each year are due to cancer, diabetes, respiratory, and cardiovascular conditions [1-3]. Almost half of all patients have at least one chronic disease, and 6% have 3 or more. Overall, hypertension is the most prevalent chronic disease followed by depression, osteoarthritis, diabetes mellitus, asthma, chronic obstructive pulmonary disease (COPD), and finally coronary artery disease (CAD) [1]. Physical activity (PA) has been shown to improve chronic disease management and function, decrease pain, and reduce morbidity and mortality [3-8]. To take advantage of these benefits, exercise guidelines for the general population, as well as for individuals with specific chronic diseases have been standardized. The aim of this systematic review was to determine specific overlapping physiological and subjective markers that could be used by clinicians to determine safe exercise prescription for individuals with multiple chronic diseases. For the purposes of this review, physiological markers are those that can be objectively measured by a clinician indicating a physiological change in the body, while subjective markers are reported by the individual before, during or after exercise. In this way, a personalized guideline could be determined for people with multi-system involvement in order for clinicians to provide objective and systematic exercise prescription for these individuals.

Numerous exercise guidelines [4,6-14] have repeatedly highlighted the importance of tailoring exercise on an individual basis to ensure a safe and appropriate activity program is implemented. However, none have provided specifics on how this could be done effectively, taking into account the complexity of health conditions experienced by individuals living with chronic diseases. The major recommendation from most guidelines is to see your "physician/ healthcare provider", which assumes that your specific healthcare provider has the appropriate knowledge and training to develop and implement an individually tailored exercise program. However, lack of time and limited knowledge has repeatedly emerged from the literature as barriers for physicians to prescribe exercise to individuals [15-18]. Given that current exercise guidelines are designed for the general/healthy population or geared towards those living with a single pathology, there is limited guidance to ensure safety with exercise prescription for individuals living with more than a single pathology.

Therefore, despite the availability of general physical activity guidelines for individuals with one chronic disease, people with multiple conditions tend to receive exercise prescription based on non-objective measures and clinical reasoning as opposed to standardized protocols [5]. Physiotherapists (PTs) commonly develop exercise protocols for clinical populations, which often include individuals living with chronic conditions. Currently, they acquire medical histories from patients and then develop individualized exercise programs in the absence of disease-specific contraindications. For instance, the recommended exercise guidelines for patients with type 2 diabetes (T2DM) include 30 minutes of aerobic activity, 5 times per week [6-8,10,13]. Contraindications to exercise for patients with type 2 diabetes include severe autonomic neuropathy, severe peripheral neuropathy, and pre or proliferative retinopathy [13]. Similar exercise guidelines exist for patients with coronary artery disease and chronic obstructive pulmonary disease, including recommendations of at least 150 minutes of aerobic exercise per week for patients with CAD [9,11,12,14] and 30-60 minutes of aerobic exercise at least 3 times a week for patients with COPD [19,20]. Contraindications to exercise for patients with CAD include unstable angina, uncontrolled arrhythmias, heart failure, stenotic/uncompensated valves, and hypertrophic obstructive cardiomyopathy [9,21]. Current contraindications to exercise for patients with COPD consist of severe hypertension, hypoxemia with a drop of oxygen saturation below 85%, uncontrolled angina, or congestive heart failure [19]. This review attempts to extrapolate key physiological markers from multiple systems in the body based on leading chronic conditions, in order to begin addressing the how of individualized exercise prescription. If safe ranges of key physiological markers can be identified from each system in the body, clinicians can then begin to have concrete markers they can monitor to ensure safe exercise programs are implemented on an individual basis. Also, a systems-based approach to exercise prescription instead of a single pathology-based guideline might enable tailored programming to individuals with multiple conditions. This is a worthwhile endeavour, given that over half of the population living with a chronic condition have more than one disease [22].

For this review, three of the seven most common chronic diseases were chosen for investigation, from three different body systems: coronary artery disease (cardiovascular system), chronic obstructive pulmonary disease (respiratory system), and type 2 diabetes (endocrine system). These three diseases were chosen in the attempt to identify disease-specific biological markers that could indicate a contraindication to exercise. This systems-based approach can be further developed in the future by extrapolating key markers from many other diseases to enable a more encompassing system for exercise prescription.

Methods

Studies were identified by using the following electronic databases: CINAHL, Pubmed, MEDLINE, EMBASE, SCOPUS, Cochrane, AMED and Pedro. These databases generated MESH terms based on the following keywords: coronary artery disease/CAD, chronic obstructive pulmonary disease/COPD, diabetes mellitus/diabetes, contraindication, adverse, risk, treatment, testing, training, physical activity, exercise, guideline, recommendation. These search terms were entered into the databases using an appropriate combination of "OR" and "AND" (see appendix A for a sample of the search history). In order for the articles to be included in this systematic review, the inclusion and exclusion criteria (Table 1) needed to be satisfied:

Inclusion criteria:	**Exclusion criteria**:
· Participants must be over the age of 18	·Combined chronic conditions (e.g., Cancer and Cerebrovascular Accidents)
· Paper must include the disease searched	Goal: extrapolate key physiological markers per system; combining systems at onset prevents achievement of goal.
· Must be human subjects	·Outcomes of disease processes (e.g., MI and Heart Failure)
· Either aerobic or strengthening exercise was administered to the patient	·Neuromuscular, Neurological, Gastro-intestinal, Psychological, Nephrological and Excretory Conditions, i.e., Not in the upper most prevalent disease states
· Must have an appropriate physiological or biological outcome measure	
· Must be English	
· Must be a guideline, systematic review, meta-analysis or randomized control trial	

Table 1: List of inclusion and exclusion criteria for published articles. The aforementioned inclusion and exclusion criteria were developed in order to obtain the most recent (last ten years), scientifically rigorous (RCTs) evidence. Some of the review articles, commentaries and case-studies that did not satisfy the inclusion criteria were used to inform the introduction and the discussion sections of this paper. The search was conducted from June 1, 2013 to December 1, 2013.

Both COPD and T2DM are the leading causes of death in chronic respiratory and endocrine disease states respectively. T2DM was chosen over type 1 diabetes mellitus (T1DM), because it is more prevalent and it can be controlled with exercise and diet, whereas T1DM must be controlled with insulin injections. The leading cause of death for the cardiovascular system is myocardial infarction, which was not included as it is an outcome of other disease states not a chronic disease in and of itself. As such, coronary artery disease (CAD) was the chronic disease selected for the cardiovascular system.

Outcome Measures

Outcome measures in this review include: 1) physiological markers such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), peripheral capillary oxygen saturation (SpO2) and blood glucose, as well 2) subjective markers such as the rate of perceived exertion (RPE) and the Borg Scale reviewed for each disease state. These markers were chosen as a way to monitor physiological and subjective changes that can occur during exercise.

Data Collection and Analysis

After keyword searches were completed all duplicate articles were eliminated using RefWorks software. Next, the article's titles and abstracts were screened (JK-CAD, DB-COPD, AVV-T2DM, FM-T2DM) based on the inclusion and exclusion criteria. Then, 2 authors independently reviewed full-text articles, and selected papers were compared based on the inclusion/exclusion criteria. Reviewers (JK, AVV) analyzed all COPD and CAD articles and reviewers (DB, FM) analyzed all diabetes articles. Any discrepancy in article selection was decided by a third party (JK, DB). See Figure 1 for full study selection overview.

Remaining articles were then reviewed for data extraction. The following data were extracted from the selected studies: (1) characteristics of the interventions, including the: type, frequency, intensity, and duration; (2) characteristics of the outcomes: physiological or subjective outcome measures. The outcomes of this systematic review can be found in the results section.

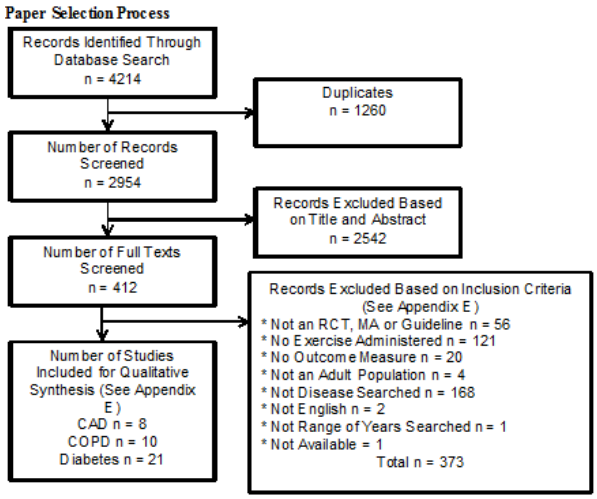

Figure 1: Overview of process for selecting key articles included in systematic review.

Results

Based on the review of the literature, it is recommended that individuals living with chronic diseases should engage in aerobic, resistive or a combination of both of these types of exercises. The corresponding specific exercise recommendations as well as contraindications and/or precautions are summarized below in Tables 2-4.

Recommendations for Aerobic Training (AT)

Aerobic training studies have emerged throughout the extensive research for individuals with various chronic diseases. For individuals with T2DM, multiple studies have shown that accumulating 150 minutes a week of moderate (40% to 60% VO2 maximum) to vigorous (60 to 90% VO2 maximum) physical activity is recommended [7,8,23,24,25,28,30]. For individuals with T2DM who enjoy cycling, it is recommended that they achieve 30 to 40 minutes per day, 5 days a week at an intensity of 75% of their maximum VO2 [23-30]. Araiza et al. in 2011 found that it is safe for an individual with T2DM to walk 10,000 steps per day monitored using a pedometer [24].

Recommendations for individuals with CAD vary between researchers. Briffa, et al. found that aerobic exercise may be performed most days of the week for 30 minutes at a moderate intensity [9]. Similarly Pavy, et al. recommend aerobic exercise 3 to 6 days a week for 30 to 60 minutes, while maintaining a rate of perceived exertion (RPE) between 12 and 14 [11]. In a 2011 systematic review, Cornish, et al. found that individuals with CAD are able to perform aerobic exercise 2 to 5 days a weeks for 30 to 60 minutes at an intensity of 70 to 95% maximum VO2 [31].

Furthermore, research has determined that individuals with COPD are also able to safely participate in aerobic training (AT). Sharma and Singh found that those with COPD are able to participate in AT 2 to 3 times per week for 30 to 60 minutes, working towards a goal of 80% workload on either a treadmill or cycling [20]. These results were similar to those of Nonoyama, et al. who recommended 2 to 3 sessions per week of cycling for 15 minutes at 75% to 80% peak workload [32], while Corbridge, et al. recommended 20 minutes at an intensity that is 60% to 80% of the onset of symptoms (e.g., dyspnea and fatigue) [33]. If the individual with COPD prefers cycling, it is safe to cycle at an intensity of 7 to 34 watts, performed 4 times a week [34].

	Frequency	Intensity	Time	Type
T2DM	Every day		10,000 steps	AT – walking [23]
			150 minutes per week	AT [24]
	5 days per week		30 minutes per day	AT [25]
		1000 Kcal per week		AT [26]
			150 minutes per week	AT – treadmill (7]
	5 days per week		20 to 30 minutes	AT- treadmill [8]
	4 days per week	Moderate	3 miles	AT [27]
	3 days a week	Moderate	50 minutes	AT [28]
	5 days a week	75% VO2 max	30 to 40 minutes	AT – cycling [29]
	3 to 4 days a week	50% to 70% VO2 max	150 minutes per week	AT [30]
CAD	Most to all days of the week	Moderate	30 minutes per day	AT [9]
	3 to 6 days per week	12 to 14 Rating Perceived Exertion	30 to 60 minutes	AT [11]
	2 to 5 days per week	70% to 95% VO2 max	30 to 60 minutes	AT [31]

COPD		60% to 80% of symptom onset	20 minutes	AT [32]
	4 days per week	7 to 34 Watts		AT – cycling [33]
	2 to 3 days per week	75% to 80% peak workload, 40 Watts	2 to 15 minutes	AT – cycling [34]
	2 to 3 days per week	80% maximum workload	30 to 60 minutes	AT [20]

Table 2: Exercise recommendations for aerobic training (AT) for 3 chronic diseases: Type 2 Diabetes (T2DM), Coronary Artery Disease (CAD) and Chronic Obstructive Pulmonary Disease (COPD).

Resistance Training

Compared to research completed on AT or a combination of AT and resistive training (RT) for individuals with chronic diseases, few research studies have been conducted looking at the effect of RT alone for chronic disease (Table 3). For individuals with T2DM it is recommended RT occur 3 days per week, completing 10 repetitions [35].

For individuals with CAD, Bjarnason-Wehrens, et al. recommend 1 to 2 sets with 5 to 15 repetitions per set at an intensity of 30% to 60% maximum voluntary contraction [21]. DeJong, et al. recommend RT at an intensity of 12 to 14 RPE, completing 1 set with 10 repetitions of each of the 8 exercises (i.e., leg press, latissimusdorsi pull down, military press, lateral row, chest press, triceps press, biceps curl, and leg extension) [36].

Recommendations for RT for those with COPD are limited to one study by Costi, et al. [37] who recommended performing upper extremity exercises (e.g., shoulder abduction, deltoid lift in the scapular plane, behind head triceps press, bicep curls at 90 degrees shoulder abduction and bicep curls), with an intensity of 50% of one repetition maximum weight, starting at 3 sets of 10 repetitions.

	Frequency	Intensity	Time	Type
T2DM	3 days per week		10 repetitions	RT [35]
CAD	2 to 3 days per week	30% to 60% maximum voluntary contraction	1 to 2 sets, 5 to 15 repetitions	RT [21]
		12 to 14 Rating perceived exertion	8 exercises, 1 set, 10 repetition	RT [36]
COPD		50% one repetition maximum	3 sets, 10 repetitions, progressing to 3 sets of 15 repetitions	RT [37]

Table 3: Exercise recommendations for resistance training (RT).

When the individual rates the difficulty as 3 on the Borg scale, then the repetitions are increased to 12, then again to 15. Subsequently, once an individual reaches level 3 on the Borg scale while completing 3 sets of 15 repetitions, resistance is increased by 500 grams and the exercise cycle is repeated.

Combined Aerobic and Resistance Training Programs

Research into chronic disease and RT has mostly occurred in combination with AT (Table 4). The majority of the studies investigating T2DM and a combination of AT and RT provided the same recommendations for AT as the studies looking at AT alone: 150 minutes of AT per week at moderate (40% to 60% VO2 maximum) to vigorous intensity (60% to 90% maximum VO2) [6,13,38,39,40,41,42]. Sigal, et al. [13] recommended that in addition to 150 minutes of AT per week, individuals with T2DM should perform RT for 1 to 3 sets of 8 to 15 repetitions at moderate (50% to 74% one repetition maximum) to high intensity (75% or higher one repetition maximum), 3 days per week, similar to the findings of Praet and Van Loon who recommended 3 sets of 8 to 10 repetitions at a weight that cannot be lifted more than 8 to 10 times, 3 days per week, targeting all major muscle groups [40]. Weltman, et al. [43,44] suggest similar RT intensity (moderate to vigorous) and repetitions (8 to 12) but recommend RT 3 to 5 days per week in combination with AT. Whyte [45] recommended that in addition to regular AT, RT should include 3 to 4 sets of 10 to 15 repetitions at moderate to vigorous intensity, 2 days per week, while completing 5 to 10 exercises targeting major muscle groups. Colberg, et al. [6] recommend RT of 10 to 15 repetitions at moderate (50% one repetition maximum) to vigorous (75% to 80% one repetition maximum), 2 days per week, of 5 to 10 exercises targeting major muscle groups, as well as 150 minutes of AT per week.

Other recommendations for individuals with T2DM include AT at 55% to 70% VO2 maximum and RT at 60% one repetition max [38] similar to Hills, et al. [39], who recommended 15 to 75 minutes of AT per day at an intensity of 60% to 85% VO2 maximum, and RT at 60% to 80% of one repetition maximum. Waryasz and McDermott [43] recommended 30 to 90 minutes of AT per day for 5 days per week at an intensity of 40% to 70% VO2 maximum, and RT at 50% to 74% of one repetition maximum. Whereas Stewart, et al. [41] recommended AT 2 days per week, at an intensity of 50% to 79% maximum heart rate, and RT at 30% to 50% of one repetition maximum, with 1 set, 8 to 10 repetitions. In addition, Sukula, et al. [42] recommended AT and RT, 3 days per week. Specifically these authors recommended AT for 40 to 60 minutes at 65% to 85% of heart rate reserve and 6 to 8 repetitions of RT for each of the 8 different exercises (e.g., seated leg press, knee extension, knee flexion, chest press, latissumusdorsi pull-down, overhead press, biceps curls, triceps extension).

There are a limited number of studies providing RT and AT recommendations for people with CAD. Vanhees, et al. [14] recommended AT occurs 3 to 5 days per week for 30 to 60 minutes, at 40% to 60% of heart rate reserve and RT 2 to 3 days per week, at 30% to 70% of one repetition maximum. Perez-Terzic, et al. [12] recommended AT occurs 5 to 7 days per week, for 20 to 60 minutes at 60% to 70% of VO2 maximum and RT 2 to 3 days per week, at 30% to 60% of a single maximum voluntary contraction, completing 1 to 3 sets of 8 to 12 repetitions.

Individuals with COPD can also benefit from a combination of AT and RT. Eves and Davidson [19] recommended AT 3 days per

week at 60% to 80% of maximum work load and RT 2 to 3 days per week, with 1 to 4 sets of 6 to 12 repetitions, at 50% to 80% of one repetition maximum. Finally, Gutpaet al. [46] recommended AT and RT occur 1 to 7 days per week, for 15 to 45 minutes per day, between 50% and maximum tolerable intensity.

	Frequency	Intensity	Time	Type
T2DM		AT – 55% to 70% VO2 max RT- 60% one repetition maximum		AT and RT [38]
	AT – 3 days per week RT- 2 days per week	AT – 40% to 60% VO2 max RT – 50% to 80% one repetition maximum	AT – 150 minutes per week	AT and RT [6]
		AT – 60% to 85% VO2 max or maximum heart rate RT – 60% to 80% one repetition maximum	AT – 15 to 75 minutes per day	AT and RT [39]
	3 days per week	AT – moderate or vigorous RT – weight should not be able to be lifted more than 8 to 10 times	AT – 150 minutes per week RT – 3 sets, 8 to 10 repetitions targeting all major muscle groups	AT and RT [40]
	3 days per week	AT – 40% to 60% VO2 max or 50% to 70% maximum heart rate RT – moderate (50% to 74% one repetition maximum) to high (75% or higher of one repetition maximum)	AT – 150 minutes per week RT – 1 to 3 sets, 8 to 15 repetitions	AT and RT [13]
	2 days per weeks	AT – 50% to 79% maximum heart rate RT – 30% to 50% one repetition maximum	RT – 1 set, 8 to 10 repetitions	AT and RT [41]
	3 days per week	AT – 65% to 85% heart rate reserve	AT – 40 to 60 minutes RT – 6 to 8 repetitions, 8	AT and RT [42]
			different muscle groups	
	5 days per week	AT - 40% to 70% VO2 max RT - 50% to 74% one repetition maximum	30 to 90 minutes per day	AT and RT [43]
	3 to 5 days per week	AT – 40% to 80% heart rate reserve RT – moderate to high	AT – 150 minutes per week RT – 8 to 12 repetitions	AT and RT [44]
	AT – 3 days per week RT – 2 days per week	AT – 40% to 60% VO2 max RT – moderate to vigorous	AT – 150 minutes per week RT – 3 to 4 sets of 5 to 10 exercises, 10 to 15 repetitions	AT and RT [45]
CAD	AT – 5 to 7 days per week RT – 2 to 3 days per week	AT – 60% to 70% VO2 max RT – 30% to 60% maximum voluntary contraction	AT – 20 to 60 minutes per day RT – 1 to 3 sets, 8 to 12 repetitions	AT and RT [12]
	AT – 3 to 5 days per week RT – 2 to 3 days per week	AT – 40% to 60% heart rate reserve RT – 30% to 70% one repetition maximum	AT – 30 to 60 minutes per day	AT and RT [14]
COPD	AT – 3 days per week RT – 2 to 3 days per week	AT – 60% to 80% maximum workload RT – 50% to 80% one repetition maximum	RT – 1 to 4 sets, 6 to 12 repetitions	AT and RT [19]
	1 to 7 days per week	50% maximum to maximum tolerable	15 to 45 minutes per day	AT and RT [46]

Table 4: Exercise recommendations for AT and RT combined.

Physiological Markers to Monitor

When investigating physiological markers and exercise for individuals with chronic disease, there are multiple markers that should be monitored (Table 5). Blood pressure is one that ought to be monitored in those living with T2DM, CAD and COPD. For individuals with T2DM, Riddell and Burr [29] recommended keeping systolic blood pressure less than 260 mmHg and diastolic blood pressure below 155 mmHg, while Sigal, et al. [13] recommended

systolic blood pressure be kept below 200 mmHg for individuals with diabetic neuropathy. Blood glucose level is another marker that needs to be monitored with T2DM. The most common recommendation for blood glucose is to keep it between 100 and 300 mg/dL [6,44], or at least above 100mg/dL [13,30]. Although Misra, et al. recommended staying under a maximum of 300 mg/dL for blood glucose levels, they were the only researchers to recommend that it is also safe to exercise with blood glucose as low as 70 mg/dL [35].

Blood pressure also needs to be monitored in individuals with CAD. Bjarnason-Weherns, et al. [21] recommended that systolic blood pressure be below 160 mmHg and diastolic blood pressure be below 100 mmHg, which is similar to the results of Pavy, et al. [11]. Briffa, et al. [9] recommended systolic blood pressure be between 90 and 180 mmHg, with diastolic pressure between 60 and 100 mmHg. Individuals with CAD should also have their heart rates monitored and it is recommended that the heart beat should not rise higher to any higher rate than 10 beats per minute below an individual's angina threshold [11,12].

Blood pressure is also imperative to monitor for individuals with COPD. Bradley and O'Neill [47] recommended systolic blood pressure be between 195 and 210 mmHg and diastolic blood pressure be between 93 and 101 mmHg, which is similar to Nonoyama, et al. [34]. Several researchers have also noted safe ranges for heart rate for individuals with COPD. Nonoyama, et al. recommend 125 to 130 beats per minute [34], similar to both Bradley and O'Neill (131 to 142 beats per minute) [47] and Zainuldin, et al. (131 to 134 beats per minute [48]). Costi, et al. have the lowest recommendation for heart rate at 79.7 to 93.9 beats per minute [37]. Respiratory rate for individuals with COPD varies, with Costi, et al. [37] recommending between 20.9 and 21.9 breaths per minute, and Nonoyama, et al. [34] recommending 30 to 34 breaths per minute as safe.

	Physiological Marker	Safe Levels
T2DM	Blood Glucose (mg/dL)	100 to 300 [6,44]
		70 to 300 [35]
		> 100 [13, 30]
	Blood Pressure (systolic/diastolic mmHg)	< 260/155 [29]
		Systolic < 200 mmHg if diabetic neuropathy present [13]
CAD	Blood Pressure (systolic/diastolic mmHg)	<160/100 [21]
		90 to 180/60 to 100 [9]
		Systolic < 160 [11]
	Heart Rate (beats per minute)	10 bpm below angina threshold [11,12]
COPD	Heart Rate (beats per minute)	131 to 142 [47]
		79.7 to 93.9 [37]
		125 to 130 [34]
		131 to 134 [48]
	Blood Pressure (systolic/diastolic mmHg)	195 to 210/93 to 101 [47]
		187 to 197/87 to 94 [34]
	Respiratory rate (breaths per minute)	20.9 to 21.9 [37]
		30 to 34 [34]

Table 5: Physiological marker recommendations.

Contraindication to Exercise

In terms of contraindications to exercise in individuals with multiple chronic diseases, each disease has a specific set of indicators that must be monitored for the safety of the individual (See Table 6). With T2DM, exercise is contraindicated and should not be performed in individuals with blood glucose level above 300 mg/dL or below 70 mg/dL [29,35]. Exercise is also contraindicated for individuals with T2DM if they have ketosis29, 44, or severe autonomic or peripheral neuropathy [13]. For individuals with retinopathy due to T2DM vigorous AT or RT is contraindicated [13,41,44]. Individuals with peripheral neuropathy may be able to safely perform non-weight bearing activities like swimming or cycling [35].

Individuals with CAD should not exercise if they have unstable angina, uncontrolled arrhythmias, heart failure, stenosis or uncompensated valves, or hypertrophic obstructive cardiomyopathy [21]. Exercise should be terminated if the individual starts to feel dizziness, discomfort or pain in chest, leg ache that prohibits function, physical inability to continue, palpitations, fatigue, difficulty breathing, nausea and/or excessive sweating [9]. In addition for those individuals with COPD, exercise is contraindicated if they have angina pectoris, recent myocardial infarction, severe pulmonary hypertension, congestive heart failure, inability to exercise due to orthopedic condition, severe exercise-induced hypoxemia not correctable with O2 supplementation, and/or are unwilling to give consent [19,20].

Furthermore, precautions to exercise should also be considered before initiating and during participation in an exercise program (See Table 6). For individuals with T2DM on insulin therapy - to avoid a hypoglycemic event (a drop of blood sugar below 100 mg/dL) - insulin may need to be adjusted [6,30] or carbohydrates may need to be consumed before starting to exercise [6,28,30]. Individuals with T2DM who exercise at an intensity of 6 metabolic equivalents (METS) are at an increased risk of myocardial infarction and need to be monitored closely when exercising. Riddell and Burr recommended that for those individuals at risk for a cardiac event (increased waist circumference, increased triglyceride levels, hypertension, advanced age, a history of smoking and a family history of CAD), a warm up and cool down of 10 minutes each occurs and that they perform 20 to 60 minutes of activity at a lower intensity [29]. For individuals with uncontrolled hypertension (greater than 160mmHg SBP and/or 100mmHg DBP) blood pressure must be controlled before exercise can begin [41]. Marwick, et al. recommended that if there is a temperature elevation of 4°F in an individual's foot when compared to the other, it may be a marker of inflammation and therefore the individual is at increased risk of ulceration [8].

Individuals with CAD need to take precaution when exercising, as the individual should be able to perform at an intensity in which they are able to speak without breathlessness, and exercise should be stopped when the rating of perceived exertion is 17/20 or higher [11,49]. For individuals with COPD, exercise should be stopped when SpO2 drops below 88% or if there is a drop of 2% below the average SpO2 then the exercise session should also be terminated [50].

Therefore individuals with multiple chronic diseases are encouraged to exercise throughout the literature, but careful precautions must be taken to ensure it is done safely. When working with individuals with different chronic diseases, each disease has its own dosage for exercise prescription and markers, as well as overlapping markers for the clinician to use to determine safe and effective exercise.

T2DM	**Contraindications**	Avoid exercise if blood glucose is greater than 300 mg/dl or less than 70 mg/dl [35]
		If fasting blood glucose is greater than 15 mmol/L and ketones are elevated, no vigorous activity until glucose is under control [29]
		Severe autonomic neuropathy, severe peripheral neuropathy, proliferative retinopathy [13]
		If have non or proliferative retinopathy, no lifting heavy weights [41]
		No exercise when patient has ketosis. If retinopathy, no vigorous RT and AT [44]
	Precaution	Patient should be adequately hydrated if glucose levels are 300 mg/dl (16.7 mmol/l). Carbohydrates should be ingested if blood glucose is greater than 100 mg/dl (5.5mmol/l) only if taking insulin [6]
		Temperature elevation of 4°F compared to the opposite foot may be a marker of inflammation and increased risk of ulceration [8]
		If severe peripheral neuropathy, non-weight bearing activities like swimming, bicycling or arm exercises should not be used [35]
		Pay attention to peripheral artery disease or diabetic foot disease before starting exercise. Medication (insulin) needs to be adjusted before starting an exercise program [28]
		Exercising at greater than 6 metabolic equivalents increases the probability of having a myocardial infarction. Vigorous activity needs to be supervised because of an increased risk for a cardiac event. For those at risk for a coronary event: warm up and cool down (10 minutes each) and do 20 to 60 minutes of activity at a lower intensity. Non-weight bearing exercises are suggested for high-risk individuals. [29]
		Moderate to severe hypertension (greater than 160/100) should be controlled before starting exercise [41]
		Prior to exercising, individuals with diabetes taking insulin may need to reduce their insulin doses and consume carbohydrates to prevent hypoglycemia. Glucose should be ingested when blood glucose is less than 100 mg/dl prior to exercising [30]
CAD	**Contraindications**	Unstable angina, uncontrolled arrhythmias, heart failure, stenotic/uncompensated valves, hypertrophic obstructive cardiomyopathy [21]
		Terminate exercise if any of the following signs: dizziness, discomfort/pain in chest, leg ache that prohibits function, physical inability to continue, palpitations, fatigue, difficulty breathing, nausea, excessive sweating [9]
	Precautions	Exercise should be stopped when rating of perceived exertion is 17 or higher [49]
		Individual should be able to speak without breathlessness [11]
COPD	**Contraindications**	Severe hypertension, hypoxemia, uncontrolled angina or congestive heart failure [19]
		Angina pectoris, recent myocardial infarction, severe pulmonary hypertension, congestive heart failure, unstable diabetes, inability to do exercise due to orthopedic conditions, severe exercise-induced hypoxemia, not correctable with O2 supplementation, and unwilling to give consent [20]
	Precautions	Stop exercise if SpO2 drops below 88% or a sudden drop of 2-5% from average [50]

Table 6: Contraindications and precautions to exercise.

Discussion

The results of this review show evidence in support of a systems-based exercise prescription process using overlapping physiological and subjective markers. As demonstrated from various existing exercise guidelines [4,6-14], there is currently only knowledge on exercise prescription for specific individual pathologies. Therefore this lack of integrative information begs the question of how to prescribe exercise when an individual has more than one chronic disease. Furthermore, guidelines often recommend simply for these types of patients to speak to their healthcare provider about a safe exercise regimen, yet a lack of time coupled with limited knowledge and education about exercise prescription are noted barriers to this tailoring approach [15-18]. Instead, in order for individuals with chronic diseases to reap the benefits of physical activity with reduced risk, safe ranges of physiological markers can be identified for clinicians to guide their exercise prescription efforts. This paper focussed on CAD, T2DM and COPD (for the cardiovascular, endocrine and respiratory systems respectively) to outline evidence of overlapping markers that clinicians can use to determine safe exercise limits for individuals with chronic conditions. The most commonly overlapping markers across all three systems included SBP, DBP, RPE and HR.

Each of several disease states existing in the person living with multiple chronic disorders will involve unique contraindications to exercise that must be considered before a clinician refers patients to a program [9,13,19-21,41,44]. This complexity stresses the need for a systematic approach that can simplify the exercise prescription process for busy physicians while also emphasizing the importance of contraindication clearance [51]. Furthermore, the results show from multiple studies that each of the disease states also present with both unique disease markers and overlapping markers for monitoring. For instance, COPD representing the respiratory system has a unique marker of SpO2 that should be kept above 90% in order to know that the body tissues are getting adequate oxygenation [19,34,37,47], while individuals with CAD, representative of the cardiovascular system,

must keep their exercise HR 10 beats per minute below the threshold of angina symptoms [11,12]. And individuals with T2DM, representing the endocrinology system, must maintain their blood glucose levels between 100 and 300 mg/dLin order to prevent any symptoms of hypoglycemia while exercising [6,13,35].

Most importantly, this review portrays an emerging pattern of overlapping physiological and subjective markers that could be used by clinicians to guide safe exercise. Blood pressure has been suggested for assessment and monitoring for T2DM, CAD and COPD. Findings from articles on all three diseases suggest keeping systolic blood pressure (SBP) between 160-260 mmHg and diastolic blood pressure (DBP) between 94-155 mmHg to ensure safety during exercise [21,29,31,47]. Working out at a submaximal percentage of Maximum VO2 (e.g., over 40% but less than 95%) is another physiological marker that was suggested in the literature as a guide for exercise intensity for people living with T2DM and CAD [6,12-14,21,29,30,31,38,39,41,43-45]. The information provided in the Summary Tables of the Results section thus demonstrate that overlapping markers do exist across multiple chronic diseases, alluding to an innovative way for clinicians to prescribe and monitor safe exercise limits for individuals who have more than one condition. See Table 7 for the common physiological markers that this paper suggests should be monitored.

	Cardiovascular System	Respiratory System	Endocrine System
Physiological Markers	HR [11,12] BP [9,11,21] VO2Max [12,14,21,31]	SaO2 [19, 34, 37, 47] BP [34,47] RR [34,37]	Glucose [6,13,29,30,35,44] BP [13,29] VO2Max [6,13,29,30,38,39,41,43-45]

Table 7: Key physiological markers to be monitored for exercise prescription based on a body-systems approach.

An algorithm based on this systematic literature review is proposed for use by clinicians in the future. The application starts with an individual arriving in the clinical setting for an assessment (Figure 2). The clinician takes the medical history. If the individual has any single chronic disease, as determined by the history, the clinician would simply follow the current best-practice guidelines for exercise prescription with regards to the single pathology. If, however, the individual is living with more than one chronic disease (such as T2DM and CAD) then the clinician reviews the disease-specific contraindications to exercise with the individual (such as severe autonomic neuropathy for T2DM and unstable angina for CAD). If the contraindications are cleared, the dosage of safe exercise for that person is then systematically guided by the overlapping physiological and subjective markers for the two diseases. In this way, the clinician can reliably determine safe exercise for that individual as part of the assessment. To take it further, the same overlapping markers could then guide re-assessment during the following treatment sessions for exercise progression or individualized changes in the dosage of physical activity.

This review presents the initial framework for a systems-based approach to exercise prescription for individuals with CAD, COPD and T2DM. The systems approach method used in this systematic review can be applied to many other chronic diseases in the future to create a more encompassing exercise prescription. The next step for this area of research is to examine other chronic diseases such as: hypertension, depression, arthritis and cancer for subjective, biological and physiological markers that will help inform exercise prescription for clinicians. Another area of research that could be explored is physiological markers and T2DM. Having physiological markers to monitor in addition to biological markers would be advantageous for this population. Finally, another approach that can emerge from this initial attempt at systems-based exercise prescription is to analyze each body system in isolation and extrapolate safe ranges of key physiological markers unique to that system. For instance, heart rate is a marker associated with the cardiovascular system, which we have identified as one of the key factors to be monitored when exercising. Glucose, is a biological marker associated with the endocrine system, which we know must remain in a specified range to prevent serious consequence such as hypoglycaemia and in most severe cases death. Thus, future researchers with sufficient resources may want to begin extrapolating markers per system, rather than pathology, so that we can begin to tailor programs for the whole individual regardless of which disease(s) they have, as we would rely on screening all of the key markers from each body system before initiating an exercise program. This approach would truly step away from pathology-driven guidelines and consider the full physiology of the person. The underlying hypothesis would be that if the key marker in each system is within the safe range, then regardless of the pathology a safe and unique exercise program could be developed, implemented, and monitored.

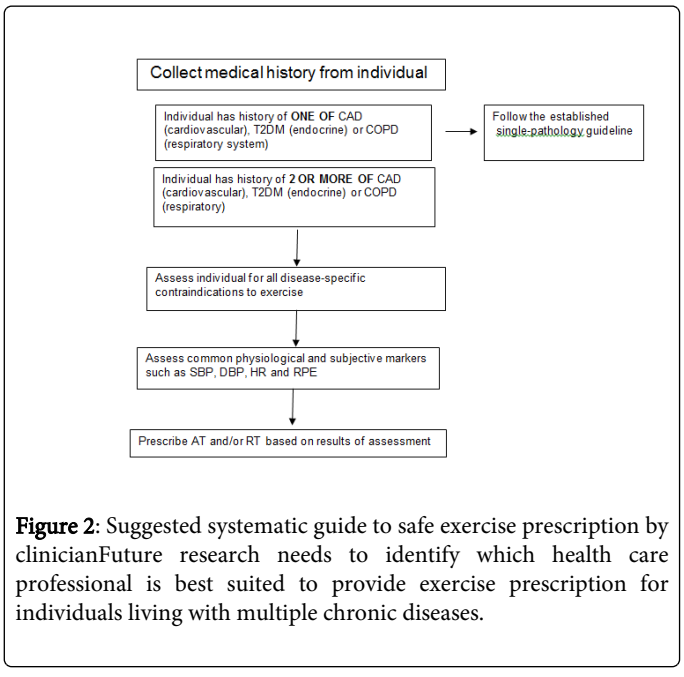

Figure 2: Suggested systematic guide to safe exercise prescription by clinicianFuture research needs to identify which health care professional is best suited to provide exercise prescription for individuals living with multiple chronic diseases.

The current model of "referring to your healthcare provider for a patient-specific exercise program" is not ideal nor necessarily safe for individuals with multiple co-morbidities. This is an inadequate

recommendation because it assumes that the healthcare provider has sufficient knowledge to create and implement a patient-specific exercise program for individuals with multiple chronic diseases. Recent articles have noted that physicians often do not have exercise science training and therefore rely on disease specific guidelines for recommendations [15-18]. This systematic review acts as a stepping-stone for the emergence of safe yet individualized exercise prescription.

Conclusion

This review shows initial evidence for a multi-system approach to exercise prescription. Screening key physiological markers from various body systems in order to safely prescribe exercise to individuals with multiple chronic diseases is not only possible, but highly recommended. Resistance and aerobic training exercise prescription can be safely tailored to individuals with CAD, COPD and T2DM. Disease-specific contraindications and precautions to exercise need to be recognized and discussed within the clinical setting. Upon assessment and throughout treatment, safe ranges of key physiological and biological markers need to be monitored for specific exercise to be prescribed and implemented safely for individuals with or at risk of having chronic disease(s).

References

1. Canadian Institute of Health Information (2014) Chronic Disease Management in Primary Health Care: A Demonstration of EMR Data for Quality and Health System Monitoring.
2. World Health Organization (2011) Global status report on noncommunicable diseases 2010.
3. Public Health Agency of Canada (2013) Preventing Chronic Disease Strategic Plan 2013-2016.
4. Allen K, Anderson M, Balady G, Berry M, Blissmer B (2014) ACSM's Guidelines for Exercise Testing and Prescription. 9th edn. American College of Sports Medicine, Philadelphia, PA.
5. Anemaet WK, Hammerich AS (2014) A framework for exercise prescription. Top Geriatr Rehabil 30: 79-101.
6. Colberg SR, Sigal RJ, Fernhall B, Regensteiner JG, Blissmer BJ, et al. (2010) Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care 33: 147-167.
7. Madden KM (2013) Evidence for the benefit of exercise therapy in patients with type 2 diabetes. Diabetes Metab Syndr Obes 6: 233-239.
8. Marwick TH, Hordern MD, Miller T, Chyun DA, Bertoni AG, et al. (2009) Exercise training for type 2 diabetes mellitus: impact on cardiovascular risk: a scientific statement from the American Heart Association. Circulation 119: 3244-3262.
9. Briffa TG, Maiorana A, Sheerin NJ, Stubbs AG, Oldenburg BF, et al. (2006) Physical activity for people with cardiovascular disease: recommendations of the National Heart Foundation of Australia. Med J Aust 184: 71-75.
10. Canadian Diabetes Association (2014) Physical Activity and Diabetes.
11. Pavy B, Iliou MC, Vergès-Patois B, Brion R, Monpère C, et al. (2012) French Society of Cardiology guidelines for cardiac rehabilitation in adults. Arch Cardiovasc Dis 105: 309-328.
12. Perez-Terzic CM (2012) Exercise in cardiovascular diseases. PM R 4: 867-873.
13. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C (2004) Physical activity/exercise and type 2 diabetes. Diabetes Care 27: 2518-2539.
14. Vanhees L, Rauch B, Piepoli M, van Buuren F, Takken T, et al. (2012) Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular disease (part III). Eur J Prev Cardiol 19: 1333-1356.
15. Garry JP, Diamond JJ, Whitley TW (2002) Physical activity curricula in medical schools. Acad Med 77: 818-820.
16. Hébert ET, Caughy MO, Shuval K (2012) Primary care providers' perceptions of physical activity counselling in a clinical setting: a systematic review. Br J Sports Med 46: 625-631.
17. Lamarche K, Vallance J (2013) Prescription for physical activity a survey of Canadian nurse practitioners. Can Nurse 109: 22-26.
18. Laschinger HK, Grau AL, Finegan J, Wilk P (2010) New graduate nurses' experiences of bullying and burnout in hospital settings. J Adv Nurs 66: 2732-2742.
19. Eves ND, Davidson WJ (2011) Evidence-based risk assessment and recommendations for physical activity clearance: respiratory disease. Appl Physiol NutrMetab 36 Suppl 1: S80-100.
20. Sharma BB, Singh V (2011) Pulmonary rehabilitation: An overview. Lung India 28: 276-284.
21. Bjarnason-Wehrens B, Mayer-Berger W, Meister ER, Baum K, Hambrecht, et al. (2004) Recommendations for resistance exercise in cardiac rehabilitation. Recommendations of the German Federation for Cardiovascular Prevention and Rehabilitation. Eur J Cardiovasc Prev Rehabil 11: 352-361.
22. Sullivan P (2013) Using EMR Data to Understand Multiple Chronic Diseases. Clinical Measures and Outcomes in Primary Health Care. Canadian Institute for Health Information.
23. Araiza P, Hewes H, Gashetewa C, Vella CA, Burge MR (2006) Efficacy of a pedometer-based physical activity program on parameters of diabetes control in type 2 diabetes mellitus. Metabolism 55: 1382-1387.
24. Hayes C, Kriska A (2008) Role of physical activity in diabetes management and prevention. J Am Diet Assoc 108: S19-23.
25. Krousel-Wood MA, Berger L, Jiang X, Blonde L, Myers L, et al. (2008) Does home-based exercise improve body mass index in patients with type 2 diabetes? Results of a feasibility trial. Diabetes Res ClinPract 79: 230-236.
26. Lim JG, Kang HJ, Stewart KJ (2004) Type 2 diabetes in Singapore: the role of exercise training for its prevention and management. Singapore Med J 45: 62-68.
27. Norris L, Zhang X, Avenell A, Gregg E, Schmid CH, et al. (2008) Long-term non-pharmacological weight loss interventions for adults with type 2 diabetes mellitus. Cochrane Database Syst Rev Apr 18: CD005270
28. Nyenwe EA, Jerkins TW, Umpierrez GE, Kitabchi AE (2011) Management of type 2 diabetes: evolving strategies for the treatment of patients with type 2 diabetes. Metabolism 60: 1-23.
29. Riddell MC, Burr J (2011) Evidence-based risk assessment and recommendations for physical activity clearance: diabetes mellitus and related comorbidities. Appl Physiol Nutr Metab 36 Suppl 1: S154-189.
30. Younk LM, Mikeladze M, Tate D, Davis SN (2011) Exercise-related hypoglycemia in diabetes mellitus. Expert Rev EndocrinolMetab 6: 93-108.
31. Cornish AK, Broadbent S, Cheema BS (2011) Interval training for patients with coronary artery disease: a systematic review. Eur J Appl Physiol 111: 579-589.
32. Corbridge S, Wilken L, Kapella MC, Gronkiewicz C (2012) An evidence-based approach to COPD: part 1. Am J Nurs 112: 46-57.
33. Lacasse Y, Goldstein R, Lasserson TJ, Martin S (2006) Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev Oct 18: CD003793.
34. Nonoyama ML, Brooks D, Lacasse Y, Guyatt GH, Goldstein RS (2007) Oxygen therapy during exercise training in chronic obstructive pulmonary disease. Cochrane Database Syst Rev : CD005372.
35. Misra A, Nigam P, Hills AP, Chadha DS, Sharma V, et al. (2012) Consensus physical activity guidelines for Asian Indians. Diabetes Technol Ther 14: 83-98.

36. deJong AT, Womack CJ, Perrine JA, Franklin BA (2006) Hemostatic responses to resistance training in patients with coronary artery disease. J Cardiopulm Rehabil 26: 80-83.
37. Costi S, Crisafulli E, Antoni FD, Beneventi C, Fabbri LM, et al. (2009) Effects of unsupported upper extremity exercise training in patients with COPD: a randomized clinical trial. Chest 136: 387-395.
38. Balducci S, Zanuso S, Cardelli P, Salvi L, Bazuro A, et al. (2012) Effect of high- versus low-intensity supervised aerobic and resistance training on modifiable cardiovascular risk factors in type 2 diabetes; the Italian Diabetes and Exercise Study (IDES). PLoS One 7: e49297.
39. Hills AP, Shultz SP, Soares MJ, Byrne NM, Hunter GR, et al. (2010) Resistance training for obese, type 2 diabetic adults: a review of the evidence. Obes Rev 11: 740-749.
40. Praet SF, van Loon LJ (2009) Exercise therapy in type 2 diabetes. Acta Diabetol 46: 263-278.
41. Stewart KJ (2004) Role of exercise training on cardiovascular disease in persons who have type 2 diabetes and hypertension. Cardiol Clin 22: 569-586.
42. Sukala WR, Page RA, Rowlands DS, Lys I, Krebs JD, et al. (2012) Exercise intervention in New Zealand Polynesian peoples with type 2 diabetes: Cultural considerations and clinical trial recommendations. Australas Med J 5: 429-435.
43. Waryasz GR, McDermott AY (2010) Exercise prescription and the patient with type 2 diabetes: a clinical approach to optimizing patient outcomes. J Am Acad Nurse Pract 22: 217-227.
44. Weltman NY, Saliba SA, Barrett EJ, Weltman A (2009) The use of exercise in the management of type 1 and type 2 diabetes. Clin Sports Med 28: 423-439.
45. Whyte J (2013) Exercise for patients with diabetic peripheral neuropathy: Getting off on the right foot. Consultant 53: 594-600.
46. Gupta D, Agarwal R, Aggarwal AN, Maturu VN, Dhooria S, et al. (2013) Guidelines for diagnosis and management of chronic obstructive pulmonary disease: Joint ICS/NCCP (I) recommendations. Lung India 30: 228-267.
47. Bradley JM, O'Neill B (2005) Short-term ambulatory oxygen for chronic obstructive pulmonary disease. Cochrane Database Syst Rev Oct 19: CD004356.
48. Zainuldin R, Mackey MG, Alison JA (2011) Optimal intensity and type of leg exercise training for people with chronic obstructive pulmonary disease. Cochrane Database Syst Rev : CD008008.
49. Lai S, Kaykha A, Yamazaki T, Goldstein M, Spin JM, et al. (2004) Treadmill scores in elderly men. J Am Coll Cardiol 43: 606-615.
50. Panos RJ, Eschenbacher W (2009) Exertional desaturation in patients with chronic obstructive pulmonary disease. COPD 6: 478-487.
51. Walsh JM, Swangard DM, Davis T, McPhee SJ (1999) Exercise counseling by primary care physicians in the era of managed care. Am J Prev Med 16: 307-313.