Effects of Aerobic Exercise on Asthma Quality of Life: A Pilot study

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A Thesis

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ABSTRACT

Exercise and Asthma Quality of Life

Alicia Wright

Quality of life (QOL) in chronic disease populations is becoming increasingly important. Exercise is beneficial in many chronic disease populations and improves QOL. A paucity of studies has evaluated the impact of aerobic exercise in adults with asthma. This pilot study examined the efficacy of a 12-week aerobic exercise intervention on quality of life in sedentary adults with asthma. Four adults with asthma were recruited into this pilot study and completed the Asthma Quality of Life Questionnaire (AQLQ) prior to and after completing the exercise intervention. Repeated measure analyses of variance (ANOVA)-type models using general linear models were conducted using SAS. Following the exercise intervention, participants demonstrated clinically significant improvements in total AQLQ (4.27 ± 0.72 to 5.49 ± 0.96), but these changes were not statistically significant ($F=4.63$, $p=.120$). However, participants did demonstrate statistically significant improvements in the symptom domain of the AQLQ (3.75 ± 0.59 to 5.31 ± 1.09; $F=10.96$, $p=.045$), as well as in levels of asthma control as assessed by the Asthma Control Questionnaire (2.54 ± 0.74 to 0.82 ± 0.52; $F=36.03$, $p=.009$) and the Asthma Control Test (13.25 ± 3.30 to 21 ± 1.83; $F=23.44$, $p=.017$). Results suggest that exercise may play an important role in asthma care and should be considered in addition to traditional asthma treatment due to the impact it has on asthma control and asthma quality of life. Further larger efficacy studies are needed, and potential mechanisms of this relationship should be explored.

Acknowledgements

Two and a half years later, I am finally finished! I can see the light at the end of the tunnel! I never expected, nor hoped to reach this level of education, but I am ecstatic that I made the leap.

Simon is responsible for planting the "research" seed. I never had any desire to go this route. I remember when he just started at Concordia; Mr. Panenic (uncle, lol) introduced us. I felt comfortable enough to find myself in his office every now and again. I would ask him questions about what he did and how he got to where he was. Then one day he said (or something really close): "I have a pilot study that has just been funded and I would need someone to run it, have you ever thought of doing a Master's degree?" He continued to explain what research and MSc meant, because I really had no clue. By the end of it he had me interested and by summer 2007 I was on board with our research team and the idea of being MSc student. I thank you Simon for planting that seed, pushing me to go to conferences and other forums, for asking me difficult questions, not always giving me answers and for giving me that TOUGH love. You taught me how to just figure some things out for myself. Self-reliance! Thanks for assuring me that I was competent to do this because I really did lack the confidence initially, but now I have a pretty good idea of what I'm capable of.

I want to thank Amanda Rizk, Jen Robinson, Guillaume Lacoste, Nicole Rutamucero, Chantal Daigneault, and Maryann Joseph for being solid rocks. Thank you all for listening to my wining, complaining, worries and for always being there to pick up the pieces. I love you guys. Kim, you were not always physically there but when you were, you were absolutely instrumental in helping me write and channel my thoughts the right way. I'll never forget the few hours you spent with me reworking the introduction to my

article; you really ripped it apart and helped me make it something beautiful. Thanks! Amanda Rossi, although I only had the pleasure of getting to know you at the end of this road, you helped me so much with that extra information you always seemed to have on everything I needed! Nicole Robertson and Andrew Henry, you guys really helped me out tons, though you may not know it. Nicole you've spent hours explaining to me all the rules and regulations of writing in English (though I should know this because it's my first language!). Faculty and staff, you know who you are, the ones who've been there for me through the BSc and MSc, always answering my million and one questions, and watching me have panic attacks about my work. You were always there to reassure me that everything would be fine (and in the end it always was!). Love you all!

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My Dad and extended family (Gail, Leslie, Auntie and Uncle), although we are all separated and scattered around North America, you've all helped me in some way or the other. Enquiring about my progress, trying to understand exactly what I was doing and just being there to listen. Love you all dearly!

Finally, my Mom! I love you! You're always there for me, by the grace of God you've been my solid rock! You've really helped me have faith in my ability to start what I finish. You were always there to guide me and to hold my hand through the rough times and to give me a pat on the back when I did well! You've helped me see the light at the end of the long tunnel and you've always been there to push me just a step further. Thanks forever and always Mom.

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Abbreviations

QOL: Quality of life

COPD: Chronic Obstructive Pulmonary Disease

PAQLQ: Paediatric Asthma Quality of Life Questionnaire

AQLQ: Asthma Quality of Life Questionnaire

ACQ: Asthma Control Questionnaire

ACT: Asthma Control Test

CI: Confidence Interval

Preface

This thesis follows the *Thesis Preparation and Thesis Examination Regulations* provided by the *School of Graduate Studies* at Concordia University, using the format guidelines for the manuscript-based thesis. It includes a manuscript which is the focus of the thesis and answers the research question. The manuscript is being prepared for submission to the *Journal of Asthma.* A combined list of references is included at the end of the thesis. All figures and tables will appear in the text; however this is not standard for a manuscript. Due to the inclusion of the manuscript, there will be some overlap and redundancy between the manuscript and the introduction and literature of the thesis.

Thesis Composition

The following is a brief overview of the layout and description of each chapter of this manuscript-based thesis.

Chapter 1 is an introduction to the current situation in Canadians with asthma. It introduces the concept of quality of life, the benefits of exercise and its impact in clinical populations. Finally, the research question, objectives, and hypotheses are introduced.

Chapter 2 is a review of the literature of asthma and exercise. It provides background knowledge about asthma and its characteristics. Moreover, it includes a review of studies that have looked at how exercise impacts quality of life, asthma control, medication use, and lung function in people with asthma. Although the focus of this pilot study is an adult population, we felt it necessary to include all studies and not just those with adult cohorts.

Chapters 3 & 4 include the detailed rationale and objectives for this pilot study. They highlight the problems in the current literature in the area of exercise and asthma and explain the necessity for this pilot study as well as provide more detailed objectives and hypotheses.

Chapter 5 is the manuscript. In the manuscript there is a less extensive introduction, however, there is overlap between this and Chapters 2 and 3. It also comprises a methods description, results, discussion, and conclusion.

Author Contributions for the Manuscript

Alicia Wright is the primary author who was responsible for the manuscript composition, the literature review search, and the assembling of the entire manuscript. Ms. Wright was directly responsible for the operation of the pilot study, including recruitment, data collection, intervention delivery, and interpretation of the results.

Dr. Simon L. Bacon was the main supervisor of the primary author and oversaw the assembly of the manuscript. He was also responsible for data analysis and provided assistance in data interpretation. Dr. Bacon helped decide appropriate result display and detail. Dr. Bacon was also the primary editor of the manuscript ensuring that it was clear and contained the appropriated information.

Dr. Kim L. Lavoie assessed readability, clarity, and general comprehensiveness of the manuscript.

Dr. Manon Labrecque, a pneumologist, was the medical director for the pilot study and was responsible for overseeing the welfare of all participants. In addition, Dr. Labrecque helped in the recruitment of patients.

Chapter 1: Introduction

Quality of life (QOL) is an increasingly important outcome in clinical populations. QOL is a term that is broadly used and has not been clearly defined, though it is generally referred to as one's level of satisfaction with one's life and the ability to enjoy life (1-3). Asthma is a chronic respiratory condition, which is characterized by chronic inflammation, with symptoms such persistent cough and shortness of breath (4). Asthma prevalence is on the rise in Canada, such that 2.3 million people reported physician-diagnosed asthma in 2008 (up from 2.2 million in 2007) (5, 6). Unfortunately, people with asthma have been shown to have worse QOL than people without asthma (7).

Exercise is beneficial to general health status as well as to a diversity of clinical populations. It improves cardiorespiratory and cardiovascular health, and general well-being (8). Exercise can also decreases morbidity of numerous conditions such as obesity, type II diabetes, and hypertension (9). Exercise has been used as an adjunct treatment in cardiac, cancer, and chronic obstructive pulmonary disease (COPD) populations with much improvement in clinical status (10, 11).

Exercise in respiratory disease populations such as COPD has proven to be important to increase physical function and QOL. However little is known about how exercise impacts asthma QOL in adults with asthma. Studies examining the impact of exercise interventions in children with asthma have shown that not only are these interventions safe, but they have several positive outcomes including significant improvements in asthma QOL (12, 13). Unfortunately, most exercise intervention studies among adults included QOL measures that were not specific to asthma thus not allowing us to capture aspects of QOL that are specific to asthma. Moreover, in the literature, overall levels asthma symptom control and short-acting bronchodilator (rescue medication) use in particular have been suggested as potential mechanisms underlying changes in asthma QOL (14, 15). However, to our knowledge, no study has evaluated asthma control in adults following an exercise intervention. Finally, intervention studies that evaluated medication use did not specify medication type (i.e., did not differentiate between bronchodilators, which are short-acting rescue medications that are taken to *treat* acute attacks, and inhaled corticosteroids, which are controller medications that are taken daily to *prevent* asthma attacks and treat inflammation), thus providing no information on how exercise can impact bronchodilator use, which is an important measure of asthma control. Overall, the paucity of studies on the impact of exercise interventions on QOL in adults with asthma has been confirmed in a recent systematic review of physical activity and asthma (16).

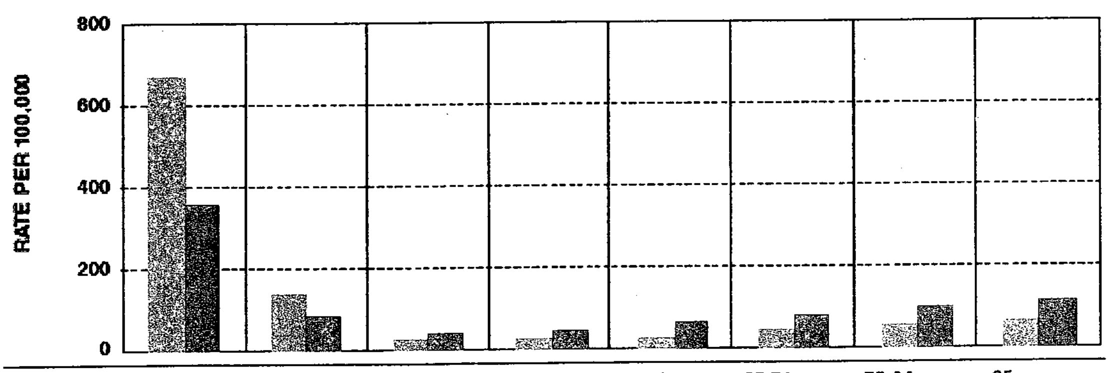
The objective of this pilot study was to determine whether a 12-week aerobic exercise intervention in adults with asthma could improve asthma QOL, asthma control and bronchodilator use. In addition we evaluated if changes in asthma QOL were correlated with changes in asthma control and bronchodilator use. We hypothesized that a 12-week aerobic exercise intervention would significantly improve asthma QOL, and that these improvements would be correlated with improvements in asthma control and bronchodilator use.

Chapter 2: Review of Literature

2a. Asthma in Canada

Asthma is a chronic respiratory condition of the lungs characterized by reversible airway obstruction, airway hyperresponsiveness, and chronic airway inflammation in response to stimuli such as dust, pollen, cigarette smoke and exercise. Symptoms of asthma include: shortness of breath, wheezing, and persistent cough (4). According to the World Health Organization, (WHO; (17)) approximately 300 million people have asthma and 255,000 mortalities were caused by asthma in 2005. According to Statistics Canada, 8% of the population over the age of 12 (over 2.2 million people) were diagnosed with asthma in 2005 (6). Symptoms and attacks can become so severe that many individuals with asthma require hospitalization. Approximately 80,000 Canadians were hospitalized for asthma in the short three-year span between April 1998 and March 2001 (18). Figure 1 represents the hospitalization rate in Canada between 2004 and 2005(19).

Figure 1 Asthma hospitalization rates (per 100, 000) by age group and sex, in Canada



	0-4 years	5-14 years	15-24 years	25-44 years	45-64 years	65-74 years	75-84 years	85+ years
Men	664	134	22	19	22	42	56	60
Women	350	83	39	42	56	75	99	108

Source: Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, using data from Hospital Morbidity File (acute and chronic), Canadian Institute for Health Information.

In general, asthma is directly related to increased work and school absences, an inability to perform household chores, a restriction of social activities (20) and a general decrease in QOL (21-23). In terms of health services, data from the National Population Health Survey (NPHS) (24) (a Canadian survey that looked at general health in 1996), revealed that 60% of people with asthma visited a physician, with 17% visiting a physician four or more times. In addition, 18% of Canadians visited an emergency department, and over 5% required hospitalization. The NPHS also found that 56% of all patients with asthma had an attack which corroborates the results of a separate survey of asthmatics in which more than 50% of adults said they had uncontrolled asthma (25); thus depicting the poor level of asthma control in Canada. The health burden caused by poor asthma control comes with high costs. Based on resource utilization, including emergency department visits in 2000-2001, the total cost of uncontrolled asthma in Canada in 2004 was estimated to be approximately $162 million (26).

2b. Pathophysiology

As previously mentioned, asthma is a complex disease and is characterized by airway obstruction (usually partially or completely reversible), airway hyperresponsiveness in response to stimuli, and chronic inflammation (27, 28). These characteristics are used to diagnose and differentiate asthma from other respiratory diseases such as COPD.

2b.1 Airway obstruction

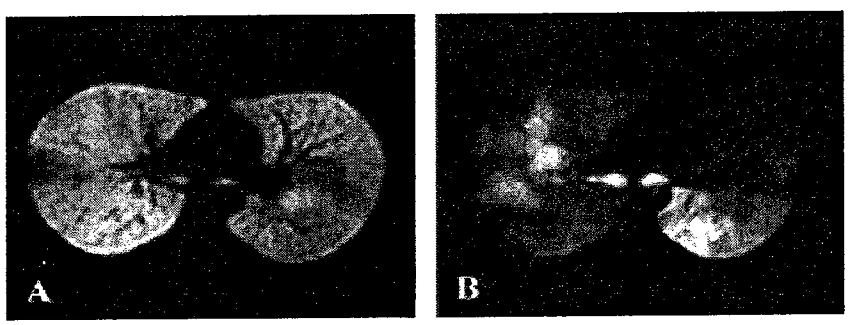
To diagnose asthma, it is necessary to have an objective measure of airway obstruction (28) in addition to a complete patient history and symptom report. Forced expiratory volume in one second (FEV_1) (28), forced vital capacity (FVC), and peak expiratory flow (PEF) are the most commonly used spirometric tests to obtain measures of airway obstruction (29). FEV_1 is the volume of air expired during the first second of a forced expiratory manoeuvre (30). FVC is the maximal volume of air that can be forcefully expired. The FEV_1 and FVC manoeuvres are done following a maximal inhalation. The normal values of these measures are predicted from the age, sex, height and weight based on various population studies. FEV_1 can be represented as an absolute value or as the FEV_1% of the predicted value for a person's age, sex, height and weight. The degree of obstruction is classified as: mild >80%, moderate 60-80%, severe <60% of predicted FEV_1 (31). Airway obstruction reversibility, generally defined as a rapid change in FEV_1, is determined if FEV_1increases by ≥12% and 200ml compared to baseline FEV_1 after the administration of a short-acting bronchodilator (28, 29, 32). Due to the fact that a number of other respiratory conditions may impact FEV_1 (e.g. COPD), and that a person with asthma may have a normal FEV_1 when they are not having an exacerbation (30), the ratio of FEV_1 to FVC becomes useful in properly assessing the degree of airway obstruction. An asymptomatic individual with asthma may have an abnormal FEV_1/FVC with normal ratio ranges being from 0.75-0.90 (29). A ratio of 0.75 means that 75% of the total expired air is expired in the first second. PEF, which is the maximum rate of expiration, is highest when there is minimal obstruction, and lowest during an exacerbation. Although PEF meters are relatively inexpensive and portable, because they may underestimate airway obstruction, they should not be used over spirometric measures of FEV_1 to assess airway obstruction, but rather used as a means of tracking patient progress over time (29).

2b.2 Airway Hyperresponsiveness

In individuals with asthma symptoms and borderline lung function, defined by normal FEV_1 FEV_1/FVC, further testing is often necessary to confirm or exclude asthma (33). The next step would be to test for airway hyperresponsiveness (AHR) which is characterized as maximal airway narrowing in response to a stimulus (34).

Bronchoprovocation tests use provocative agents such as metacholine, histamine, mannitol, or exercise challenge (28, 33) to assess AHR. Most frequently, metacholine challenges are employed, requiring patients to inhale increasing concentrations of metacholine until there is a 20% decrease in FEV_1. The test is considered negative for AHR if FEV_1 does not drop by 20% following the administration of 8mg/ml of metacholine (30). After coming into contact with a trigger in an environmental setting, AHR is responsible for the onset of symptoms as well as the variation in airway obstruction (29). The initial AHR response is due to bronchoconstriction, which is the contraction of the smooth muscle surrounding the bronchi causing airway narrowing (35) (Figure 2 (36)). However, there is also a latent long-term response which is driven by inflammation.

Figure 2 Pre-/Post-bronchoconstriction



Axial chest hyperpolarized helium magnetic resonance scan of a patient with mild asthma before (A) and after (B), demonstrating acute bronchoconstriction and ventilation defects. (36)

2b.3 Inflammation

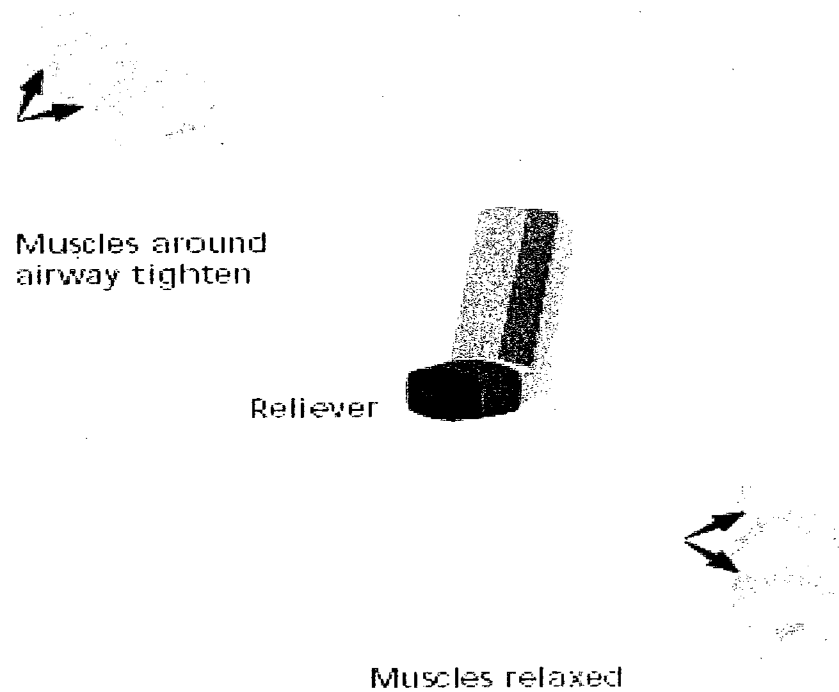
The main component of asthma is inflammation (which occurs about 3 hours after contact (37)), provoked by a trigger, and any diagnosis of asthma should be confirmed by evidence of inflammation (29). The chronic inflammatory nature of asthma remains poorly understood, however, it is believed that the predominant expression of T-2 helper over the T-1 helper cytokines may predict the durability of the chronicity and the severity of asthma (38). Mast cells, eosinophils, T lymphocytes, dendritic cells, macrophages, and neutrophils are inflammatory cells found in the airways of individuals with asthma and key mediators of asthma include cytokines, histamine, chemokines, nitric oxide (NO), and prostaglandin D2 (29, 39).

Although the involvement of many inflammatory cells makes this process complex, a simplistic model of asthma would be the following: When an attack is triggered, bronchoconstriction occurs, coughing and shortness of breath begins, excess mucous is produced, and the inflammatory process is elicited. The increased mucous production further narrows the airways, making it much more difficult for air to reach the lungs. Wheezing may begin as other symptoms such as coughing and shortness of breath continue to worsen. The repeated trigger exposure results in the recurrence of this inflammatory cascade in which inflammatory markers (those mentioned above) are released. While bronchoconstriction is the first immediate response to a trigger, it may only last minutes in contrast to the inflammatory response, which can last for several hours or days after initial contact with a trigger (37).

2c. Medication

Asthma medication is used to control the underlying inflammation as well as control manifestations of the disease. There are two types of medications used for asthma treatment, reliever and controller medication (40). When asthma symptoms develop, an individual with asthma would require the use of their reliever medication. The reliever is an inhaled short-acting bronchodilator that is used to reverse bronchoconstriction and increase airway diameter (29). Figure 3 (41) depicts the effect of the reliever medication on the smooth muscle surrounding the airway. This medication is only used during an asthma exacerbation and does not treat the underlying inflammation. Although inhaled short-acting β_2-agonist are commonly prescribed, there exist numerous other relievers such as short-acting theophylline, inhaled anticholinergics, and short-acting oral β_2-agonist (29, 42). A sign of asthma control deterioration is when use of the reliever medication is increased, and at this point, asthma treatment should be reassessed (29). Common side effects of these medications included restlessness, trembling, and tachycardia (29).

Figure 3 Effect of reliever on constricted muscles surrounding the airway



Top left is during airway constriction and bottom right is after reliever medication is taken, airway diameter is increased.

Controller medication is taken every day and is used to treat the underlying inflammation, whether asthma symptoms are present or not. Inhaled corticosteroids

(ICS) are very effective in asthma control maintenance and are used as standard treatment for asthma (43). ICS have been demonstrated to not only be effective for the treatment of inflammation, but also for overall symptom and AHR reduction, as well as improved lung function and QOL (44). Side effects of long-term high ICS doses include oropharyngeal disorders (45), decreased bone mineral density, and skin bruising (46). As valuable as they are as anti-inflammatories, there exists a variety of other controller medications on the market including oral glucocorticosteroids, leukotrienes, and long-acting inhaled β_2-agonist (40). However, none of these medications cure asthma, and if they are discontinued asthma control deteriorates within weeks to months (47, 48).

2d. Asthma Control and Severity

Asthma control and asthma severity are often confused; however these two phenomena are different. Asthma control refers to the extent to which the manifestations and symptoms of the disease are present or absent (49).These manifestations include day and nocturnal symptoms, activity limitations, use of short-acting bronchodilators, and lung function (29). In contrast, asthma severity defines the severity of the underlying disease, characterized by the level of inflammation, as well as its responsiveness to treatment (29, 33). Asthma severity can be classified into four categories; mild intermittent, mild persistent, moderate persistent, and severe persistent. These four categories are based on the frequency of certain symptoms, the degree of airway obstruction and variability, and the dose of controller medication prescribed (50). Overlapping classification features for both control and severity include: daily and nocturnal symptoms, and lung function (29). Despite this overlap, previous research has shown that these two phenomena assess different processes in patients with asthma (51). In addition, it must be understood that a person can have severe asthma and good control, while another person can have mild asthma but very poor control.

Taking into account the number of hospitalizations, emergency room visits, and asthma exacerbations experienced by individuals with asthma, it is apparent that asthma remains shockingly poorly controlled in Canada. With more than 50% of Canadians having a deplorable level of asthma control (25), there results a negative cycle of increased number of hospital visits, medication use, and symptoms severity, with simultaneous decreases in QOL.

2e. Quality of Life

QOL is a broad term that has not been limited to one distinctive definition (1, 3) and has been evaluated in numerous studies without being defined (2). In addition, some authors have used the terms QOL and health status interchangeably, however, it has been shown that these are two different constructs (52). Gill et al. (2) defined QOL as "a reflection of the way that patients perceive and react to their health status and to other non-medical aspects of their lives". QOL can be divided into: general QOL, health related QOL, and disease-specific QOL. The Center for Disease Control in the USA defines general QOL as: "overall sense of well-being with a strong relation to a person's health perception and ability to function (53)." General QOL is a multidimensional construct that can be subdivided into various domains which influence one's perception of their general QOL such as: financial status, occupational environments, relationships, and health (54). Health-related QOL is predominantly influenced by a person's health status and clinical treatment and is a subset of one's general QOL (54). The most influential domains of health-related QOL appear to be: physical functioning, social functioning, and mental status (52). Different diseases and their treatment interventions (i.e. cancer versus asthma), affect a person's perception of their QOL in a variety of ways, thus leading to the term disease-specific QOL, which assess the QOL of specific clinical populations.

It is important to recognize that a variety of questionnaires have been created to evaluate general QOL, health-related QOL, and disease-specific QOL. General QOL encompasses various domains; therefore measures evaluating general QOL are not heavily dependent on health status but will look at the many factors that influence QOL. In contrast, disease-specific QOL questionnaires focus on aspects of QOL that are affected by the specific disease of interest (i.e. asthma). Characteristics specific to asthma such as night awakening and weekly symptoms have a negative impact on mental health which is a subset of QOL (7), thus contributing to the fact that individuals with asthma have decreased QOL compared to their non-asthma peers (7).

2g. Aerobic Exercise and Asthma

Exercise is defined as activities that are planned and structured, and done to improve or maintain components of physical fitness and health (55, 56). Aerobic exercises are activities that require the use of oxygen in the energy producing system, such as playing a soccer game, in contrast to anaerobic exercise, like weight lifting, that require the use of an energy producing system that is not heavily reliant on oxygen. Aerobic exercise has numerous benefits in healthy populations, such as, improved cardiovascular and cardiorespiratory capacity, as well as improved QOL (8). Similarly, aerobic exercise programmes are favourable for populations with various health conditions, such as coronary artery disease (10), other cardiovascular diseases (57), and COPD (11). Collectively, the evidence suggests that aerobic exercise may also have a positive impact on asthma morbidity such as medication use, and QOL in patients with asthma. However, the majority of the studies were conducted in children or used QOL questionnaires that were non-specific to asthma, thus resulting in a lack of knowledge about the positive effects of aerobic exercise on asthma QOL in adults.

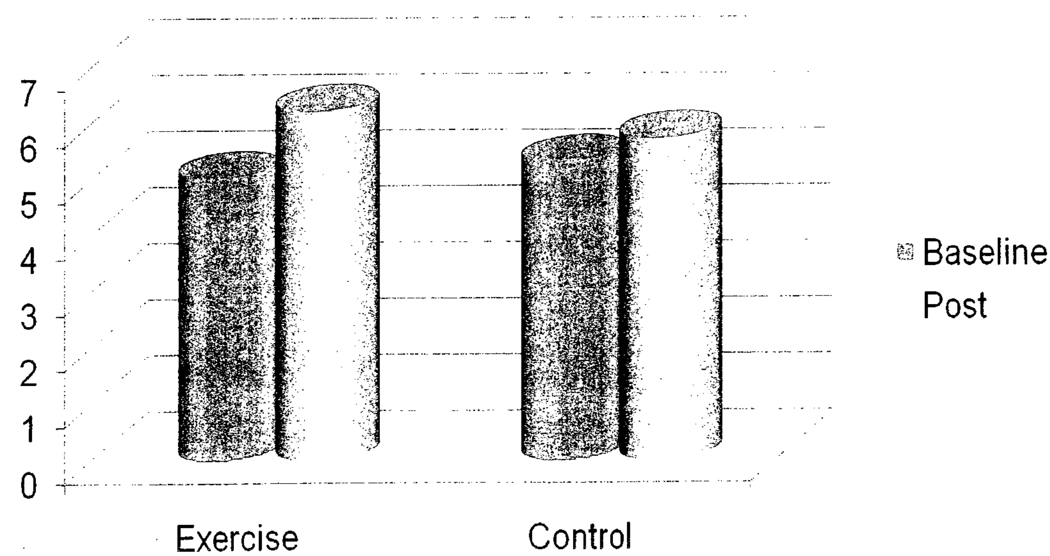
2h. Impact of Exercise on Quality of Life

Studies conducted in other clinical populations found improvements in QOL after exercise training programmes. For example, a meta-analysis of the effects of exercise on QOL in women with or who survived breast cancer revealed that 3 of the 14 studies that provided adequate data of QOL found a significant in improvement in two QOL questionnaires following an exercise programme (58). The two QOL measures were Functional Assessment of Cancer Therapy-General (4.58, 95%CI 0.35 to 8.8) and the Functional Assessment of Cancer Therapy-Breast (6.62, 95% CI 1.21 to 12.03) (58). Two of these interventions were comprised of only aerobic exercise, with the other combining both aerobic and resistance training. Exercise interventions were a minimum of 6 weeks long, 2-5x/week (the duration of the sessions were not mentioned). Similar studies have been done using aerobic training and/or resistance training in populations such as coronary artery disease, with similar improvements in QOL (57, 59-61).

Although there are a limited number of studies done looking primarily at the effects of aerobic exercise on asthma QOL in adults (see Table 1.), in general, it appears that individuals with asthma and other respiratory diseases have an improved QOL following participation in an exercise intervention. For example, in a study done by Basaran et al. (13) children with mild-moderate asthma were randomized to an exercise intervention or a control group. All sessions included a 15-minute warm-up and callisthenics, 30-35 minutes of submaximal basketball training, and a 10-minute cool-down, which included flexibility exercise. When comparing pre- and post- exercise training, the exercisers scores' on the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) increased from

5.03 ±0.7 to 6.23 ±0.4 ($p<.001$) (13). Exercisers also had significant improvements on each subscale of the PAQLQ (activity $p<.001$, symptoms $p<.001$, emotions $p<.001$). A significant difference in QOL scores was also noted when comparing the exercise group to the control group post-training, with the exercisers scoring 1.09 times higher than the controls ($p=.01$) (13). However, as depicted by pre- and post-intervention measures in Figure 4 (13), both exercise and control groups had improvements in QOL. The strength of this study is that they found an improvement in QOL, as measured by an asthma-specific questionnaire. However, this study was done in children, so although there was an improvement in QOL, we do not know how these results may translate to adults with asthma. In addition, information regarding participants' previous levels of physical activity was not measured or reported. This prevents us from determining the magnitude of change due to physical activity. There was also no mention of exercise intensity level, thus we do not know if children training at higher intensities improved more than those who trained at lower intensities, which could affect the mean overall change in QOL.

Figure 4 Total PAQLQ change in children



Baseline and post-intervention changes in PAQLQ in the exercise and control group.

Table 1 Comparison of studies looking at quality of life changes post-exercise intervention in asthma and other clinical populations

Author	Population	Intervention	QOL measurement tool	Results (% change in QOL)
Basaran et al.(13)	N=58 children with asthma (n=30E, n=28C)	Basketball training; 3 days/week/60mins, 8 wks	PAQLQ	24% ↑E, 8% ↑C
Weisgerber et al. (62)	N=28 children with asthma	Swimming lessons and vigorous swimming 3days/week/60mins, 9 wks	PAQLQ	8% ↑** (change combined with that of golfers)
	N=17 children with asthma	Golf 3days/week/60mins, 9wks	PAQLQ	8% ↑** (change combined with that of swimmers)
Fanelli et al.(12)	N=38 children with asthma (n=21E, n=17C)	Aerobic and muscular endurance exercise; 2 days/week/90mins; 16wks	PAQLQ	*Cannot report
Cambach et al.(63)	N=43 adults with asthma	Aerobic exercise (RC,CR); 3 days/week/90mins, 3months	CRDQ	68%↑ RC, 80% ↑ CR

	N=23 adults with COPD			77% ↑ RC, 84% ↑ CR
Haave et al. (64)	N=92 adults with asthma	4 weeks of physical exercise outdoors, gymnasium and pool	PQoL	2%↑
	N=40 adults with COPD			1%↑
Foglio et al. (65)	N=36 adults with asthma	Aerobic exercise (bike), total body weight training, education, and nutrition and counselling	SGRQ	29% ↑
	N=26 adults with COPD			17%↑
Emtner el al.(8)	N=22 adults with asthma	Aerobic exercise (in pool); 2days/week/45mins, 10wks	VAS	14%↑
Hung et al.(57)	N=18 elderly CAD women (n=9AT)	Aerobic exercise; 3 days/week/30mins; 8 wks total	Health-Related QOL	9% ↑

Swank et al.(59)	N=18 CHF adult men	Aerobic and strength training; 3 days/week/30min AT; 2 days/week ST; 8 weeks total	MLHFQ	14% ↑
Cheema et al.(60)	N=27 breast cancer survivors	Aerobic and strength training; 3 days/week/AT; 2 days/week ST; 8 wks total	WHOQOL-BREF	9% ↑

RC=rehabilitation (3months), control (3 months), COPD=Chronic Obstructive Pulmonary Disease; E=exercise group, C=control group; CAD=coronary heart disease; CHF= congestive heart failure; AT=aerobic training, ST=strength training; CRDQ= Chronic Respiratory Disease Questionnaire; SGRQ = St-George's Respiratory Questionnaire; VAS= Visual Analog Scale; PQoL= Perceived Quality of Life Scale; PAQLQ= Paediatric Asthma Quality of Life Questionnaire; MLHFQ= Minnesota Living with Hearth Failure Questionnaire; WHOQOL-BREF= World Health Organization Quality of life Assessment-Abbreviated Version

* Cannot be reported because author did not provide the pre-intervention measures in the paper.** This is the change for both groups (golfers and swimmers) combined.

Weisgerber et al. (62) evaluated the effects of two intensities exercise on QOL in children with asthma. Children between the ages of 7-14 were randomized to either swimming or golf exercise intervention, both lasting 9-weeks. For both programmes, there were 27 sessions, each lasting 1 hour. The swimming intervention was chosen as the high intensity exercise and the golf intervention was chosen as the moderate intensity intervention. The swimming intervention contained two components, each lasting 30 minutes. The first component was swimming lessons that were done at participants' swimming levels. The second component (Swim Team) was comprised of four phases: interval training, endurance training, relay races and water games. The golf intervention included three components: teaching and review, time to practice skills, and group games taking 10, 30 and 20 minutes respectively. Authors evaluated QOL before and after the interventions using Juniper's PAQLQ. Analysis of the swimmers and golfers revealed a statistically significant improvement in PAQLQ score (p=0.02), however this improvement of 0.4 was not clinically significant. These results are the combined results of both groups due to the fact that they did not recruit the minimum number of participants to make group comparisons (62). A drawback of this study it that the authors did not provide any information on the participants' prior physical activity level, which may be one reason why we did not observe any clinical significant changes in PAQLQ (66). Also, participants in both groups attended less than 75% of the sessions, with some attending as low as 10% of the sessions which could have also affected the results (62). Although they used an asthma-specific QOL measurement tool, due to the fact that this was done in children we have no notion of how these results apply to adults with asthma.

The study done by Fanelli et al. (12) is also among the limited number of studies conducted looking at the effects of exercise training on QOL in children with asthma.

This study evaluated children, aged 7-15, with asthma. Prior to group randomization (exercise or control), there was a two-week run-in period for the purpose of confirming disease stability. During this time, all the children received two, weekly educational classes lasting 2 hours each (12). The core of the classes were based on a videotape of the asthma 'ABCs' (which are informational tapes about asthma), and also included lessons on asthma pathophysiology and medication use. Moreover, classes discussed how to use a written action plan, which is a guide written by the patient's physician describing how to monitor symptoms and adjust medication if asthma control worsens (67). Exercise sessions consisted of a 15-minute warm-up including stretching, 30-minutes of aerobic training (treadmill and/or cycle), 30 minutes of upper-body, lower-body and abdominal endurance exercises, and a 15 minute cool-down, stretching and relaxation period all under supervision. At the end of the study, children in the training group had a significant improvement in QOL measured by the PAQLQ compared to the controls. Improvements were seen in the total score ($p<0.04$) as well as all subscales (activity $p<0.04$, symptom $p<0.02$, emotional function $p<0.03$). Although children had not been participating in any regular exercise programme at the time of study entry, we do not know to what extent children were physically active, nor was physical activity defined. Again, level of physical activity prior to study entry could have impacted outcome measures (66). The strength of this study, like the Basaran et al, is the use of an asthma-specific questionnaire to assess QOL changes in both groups and provides evidence that exercise can positively impact QOL in children with asthma; however this may not translate directly to an adult population.

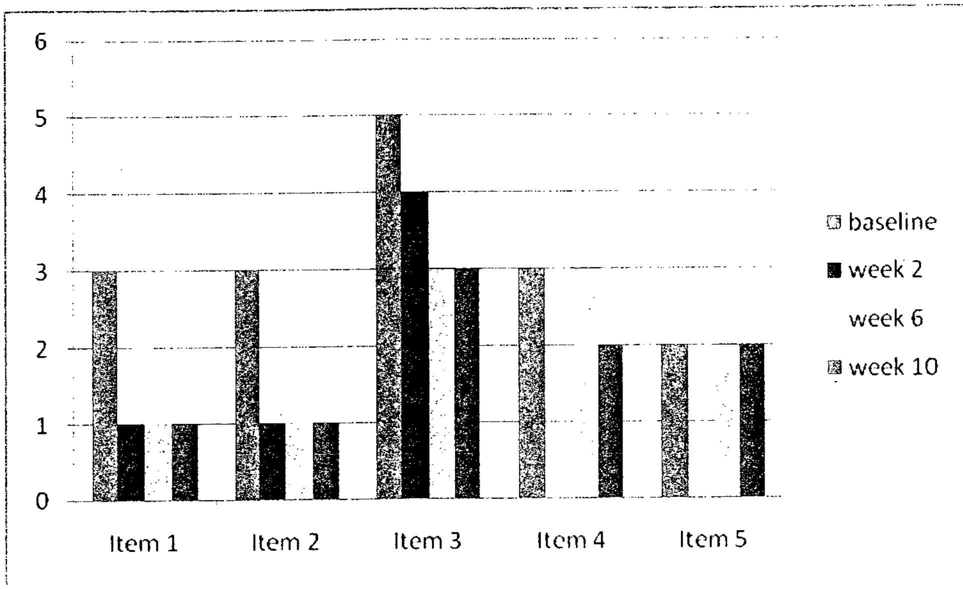
In one of the few adult studies in this area, Cambach et al. (63) assessed QOL changes in response to an exercise programme. This study was composed of asthma and COPD patients. Participants were randomized to either rehabilitation (exercise plus drug treatment) or a control condition (drug treatment only), for a duration of three months, and then switched conditions (crossed-over) for the remaining three months. Exercise training consisted of 2, 90-minute sessions per week of aerobic exercise (cycle ergometer, rowing, and stair walking), and 1, 45-minute session per week of recreational activities (e.g. hockey, etc.). There was a significant improvement in QOL in all participants when the rehabilitation period was compared to the control period (63). Asthma participants who completed the exercise intervention first still showed an improved QOL (compared to at baseline) after three months of exercise cessation. This suggests that there is a residual effect of exercise on QOL even three months after exercise cessation, which could provide evidence of long-term effects of aerobic exercise on asthma. Nonetheless, there was a decline in QOL 3 months post-intervention. Although this study used a respiratory questionnaire to assess QOL, it was not asthma-specific, so it may not capture certain aspects of QOL that are unique to asthma. In addition, the use of recreational activities, which may have been more ecologically valid, indicates that it was impossible to verify if the participants were achieving the desired level of exercise intensity (60% of max heart rate). Nevertheless, to our knowledge, this is the first study evaluating QOL in adults with asthma after completing only an exercise intervention. So although this study used a non-specific measurement tool, it captured the fact that there is a potential for QOL improvement following this type of intervention in adults with asthma.

Haave et al. (64) conducted a pulmonary rehabilitation programme (PRP) in a group of adults with asthma and COPD. The programme included educational lectures, social sharing with other participants, lifestyle change support and physical exercise. No specific details of these planned activities were included in the study methods. Sessions of education or exercise were done 3-4 times per week for 45 minutes. QOL, assessed by the Perceived Quality of Life Scale, improved significantly after the PRP, however, after 6 months, the improvements diminished (64). Although there was an improvement in QOL, due to the multidimensional nature of the PRP, we do not know how exercise alone impacted QOL in the patients with asthma. As this study was a mixed (COPD and asthma) group of adults, it was not possible to use an asthma-specific questionnaire. This again presents the same problem as with the Cambach et al. study, in that the specific impact of exercise on asthma QOL cannot be assessed.

Foglio et al. (65) evaluated the effects of a PRP on QOL in adults with asthma and COPD. The training programme consisted of four components: upper, lower and abdominal muscle exercises, education sessions for both patients and families, nutritional programmes and psychosocial counselling, and exercise. The entire programme lasted for 8-10 weeks, and included 3, 3-hour sessions per week. The exercise component was supervised, with patients doing increments until they reached 30-mins of cycling continuously at 50-70% of the maximal load. This intensity was determined from the incremental cycle ergometer test done prior to programme entry. QOL was evaluated using the St-George's Respiratory Questionnaire (SGRQ). They found a significant improvement in QOL at the end of the programme as well as 12-months after finishing the programme. However, it is difficult to assess which component of the PRP most influenced QOL. On the SGRQ, a change of >4 is clinically significant and asthma participants went from a total SGRQ of 41±15 to 29±16 12-months post-training (65). The authors also did a follow-up study where all participants were randomized to either PRP2 or control condition. They found that there was no significant difference in SGRQ score in either group following PRP2; however both groups had maintained a better SGRQ score than at baseline. Due to the mixed cohort, they could not use an asthma-specific measurement of QOL. Also, we are unable to disentangle the degree of improvement in QOL due to exercise alone due to the multidisciplinary nature of the intervention. Although this method of QOL assessment was not specific to asthma and the intervention included several components, this does highlight that changes in QOL due to a PRP (including exercise) can have positive long-term residual effects on QOL.

In a study conducted by Emtner et al. (8) aspects of QOL were measured using a visual analog scale (VAS). The VAS was created to examine "feelings" related to asthma symptoms and its impact on the ability to carry out physical and occupational activities. However, "feelings" were not defined in this study, making this an ambiguous measure. The programme was a 10-week programme consisting of 2-5 days/week of swimming interval training at a target heart rate of 80-90% of their maximum predicted heart rate. Training included a 12-minute warm-up period followed by 5 sets of interval training. The intervals consisted of large muscle movements, for which 1 set included 2 minutes of intensive and 1.5 minutes of mild movements. The sessions concluded with a 7-minute cool-down period and 10 minutes of stretching. The VAS was given before, at 2, 6, and after the 10-week programme (Figure 5 (8)). At the end of the programme, participants had an improvement in their feelings in regards to exercise. Although this study had some strengths, including the fact that it was one of the few looking at exercise training in adults with asthma and that they demonstrated that asthma does not prevent people from doing high intensity exercise, it was also limited due to the fact that it did not directly measure QOL, nor all aspects of QOL that are affected by asthma (e.g. environment).

Figure 5 Comparing VAS values at start, 2, 6, and 10 weeks



The answers to questions 4 and 5 were not analyzed at 2 weeks. Questions: 1. I am able to exercise at maximal intensity (always-never). 2. I am afraid of experiencing breathlessness when exercising (never-always). 3. I have asthma symptoms (never-always). 4. I can cope with my job/studies (without restrictions-not at all). 5. I am able to leave home for more than 24h (always-never)

Despite these encouraging results, few studies have evaluated the effects of an aerobic exercise intervention on asthma-specific QOL in adults, (see Table 1) thus (as pointed out above) not allowing the determination of how results in children may translate to adults. If, as suggested above, there is a benefit of aerobic exercise on QOL in adults, this raises the question of what mechanisms might lead to such an improvement. It has been suggested that changes in asthma control, bronchodilator use are correlated to QOL thus may play a role in potential improvements in QOL (68, 69).

2i. Asthma Control

As previously mentioned, asthma control is an important aspect of asthma, and is a separate construct from asthma severity. More than half of Canadians with asthma have poor control (24), making the focus of asthma treatment achieving optimal levels of asthma control. This is extremely important due to the fact that poor asthma control has a negative impact on individuals with asthma, particularly on asthma QOL, as well as on the healthcare system and society.

2i.1 Impact of Exercise on Asthma Control

To our knowledge, no studies have examined the impact of an exercise intervention on asthma control in adults. A study done by Sly et al. (70) evaluated the effects of an exercise intervention on children with asthma. Twenty-six children, aged 9-13 years old, were assigned to either general exercise and breathing exercise intervention or the control condition. Sessions took place 3x /week, 2 hours each, for 13 weeks, and consisted of a variety of exercises: running, abdominal strengthening, callisthenics, wall ladder, rope climbing, tumbling and parallel bars, as well as breathing control swimming and swimming skills. Furthermore, children were given a home exercise programme which included breathing exercises, trunk strengthening exercises, relaxation and stretching. Sly et al. (70) assessed number of wheeze days and found a significant difference between the exercise and control groups such that the exercise group had a significant decrease in number of wheeze days (mean: 31.3 pre-exercise to 5.7 during exercise), though there was a significant difference between the groups at baseline (i.e. exercisers had a higher number of wheeze days than the controls (70)). Although wheeze was significantly improved in the exercise group, it is not possible to determine how much of this effect resulted from exercise alone due to the fact the inclusion of breathing exercises in the intervention.

Huang et al. (71) also assessed number of wheeze days and asthma attacks in children following an exercise programme. This programme was a community-based, city-wide swimming program for children in Baltimore, Maryland. It was designed to take place twice a year, two months each time. Sessions were done 3x /week, for an hour per session. The 45 children ranged from 6-12 years old and were compared to a group of age, sex and asthma severity-matched controls. Data on number of wheeze days and asthma attacks was collected for a duration of 12-months prior to starting the programme as well as during 12-months following programme completion. Huang et al. (71) found that there was a statistically significant decrease in number of wheeze days per patient (↓66%), number of wheeze days per patient per month (↓67%), number of attacks (↓78%) and number of attacks per patient (↓79%) 12 months after the exercise programme compared to their baseline data. These results were also statistically significant when compared to the control group. Although this only partially represents asthma control, it is an important finding because it demonstrates that there is a residual effect of exercise on asthma in children.

Szentágothai et al. (72) evaluated the effectiveness of a community-based exercise programme in children with asthma. The programme consisted of 3 exercise components: teaching swimming, swim training, and complete exercise programme. The first was to teach 5-6 year olds how to do the backstroke and sessions took place 5x /week for 4 weeks, for an hour each session. The second consisted of swim competition between children (individual or team), ending each session with a ball game. This took place for one hour, 2x /week. The third was a complete programme that included swimming, gymnasium exercises, and running exercises. Pool sessions were done 2x / week for one hour, with one gymnasium exercise (e.g. relay races, etc.) and one running exercise (gradually increasing the running distance) (72). Children's asthma was classified based on number of wheeze days: <20 days= mild, 21-60 days=moderate and >60=severe. At the end of the first year of the programme, 121 children with asthma were assessed via questionnaires sent to their parents. The exercise programme improved asthma classification such that many children changed classification (i.e. from severe to moderate, etc.) In addition, the number of hospitalizations decreased from 27 to 12 following the first year (72). This demonstrates that exercise in children with asthma can have a positive impact on symptoms such as wheezing, and suggests that we may have similar improvements in adults.

The Basaran study (13) also evaluated symptom scores in children 31 children with asthma after 8-weeks of basketball training (described in section 2h). Symptom scores were assessed on a 4-point scale, from 0-3; specifically 0=no symptoms and 3= severe symptoms. Prior to starting the programme, children in the exercise group had a significantly higher symptom score (Mean ± SD: 0.74±0.5) than those in the control group (p=0.02). Following the 8-week programme, the exercisers had a significantly lower symptom score (Mean ± SD: 0.20 ± 0.8) when compared to baseline (p<0.01). Although this is only one component of asthma control, it gives an excellent insight of the impact of an exercise intervention in children with asthma; however we do not know how these results translate to adults.

Weisgerber et al. evaluated the change in symptoms in 45 children with asthma (described in section 2h) (62). Symptoms were assessed using the symptom subscale of the PAQLQ. Parents' assessment of their children's symptoms was evaluated using the Living with Asthma Questionnaire Index (LWAQ). Following the 9-week intervention (swimming or golf), children had a clinically and statistically significant decrease in both asthma symptom measures, (PAQLQ, p=.01; LWAQ, p<.001). In addition, participants, on average, had fewer emergency consultations to the clinic due to exacerbations during the intervention when compared to 2-months prior to starting the intervention (62).

Although symptoms and average number of clinic visits due to exacerbations decreased, these only represent components of asthma control, and only give us a glimpse of the potential benefit exercise could have on asthma control.

Other non-intervention studies have evaluated the relationship between components of asthma control (or asthma control directly) and exercise status. In a longitudinal study by Garcia-Aymerich et al. (73), a higher level of physical activity was associated to a lower likelihood of having an asthma exacerbation in older women with asthma. This study was a prospective study, where women provided medical and personal information every 2 years starting in 1976. Physical activity assessments were done as of 1998 using a validated 7-day physical activity diary. Type and time spent per week on various activities was used to calculate metabolic equivalent (MET) hours/week. Information about symptoms in the last four weeks, number of days kept from work because of symptoms, and medication in the last 12 months was collected. Asthma exacerbations were defined as emergency room visits, hospitalisations or urgent medical consultations, during a period of 12 months in 1999 and 2000. In addition, exacerbations during a 12-month period (1997-1998), were recorded to determine baseline status. Although this was not an intervention study, it gives an insight about the potential relationship between exercise and asthma control.

Westermann et al. (74) evaluated the relationship between level of physical activity and asthma control in adults. Asthma control was measured using the Asthma Control Questionnaire (ACQ), designed by Juniper. The Paffenbarger Physical Activity and Exercise Index were used to assess level of physical activity and exercise. Additional questions including participation in any sports were asked. Using this information participants were grouped according to exercise status. Doing any exercise, meeting exercise guidelines, moderate- and vigorous-intensity exercise, and exercising 3 or more days per week were defined as exercise habits. Analyses revealed that people who exercised were more likely to have better asthma control, however this did not remain significant in the multivariate analysis making high body mass index the strongest variable associated with exercise habits. Nevertheless, obesity has been related to worse asthma (74) as part of a vicious cycle (75): physical inactivity leads to obesity which leads to worse asthma negatively influence QOL.

2i.2 Asthma Control and Quality of Life

There are a number of studies that have shown a correlation between asthma control and asthma QOL such that people with poor asthma control have impaired QOL compared to those with better control (14). Axelsson et al. (14) evaluated if personality traits in adults were related to health-related QOL and asthma control. The Asthma Control Test (ACT) was used to assess level of asthma control. The Short-Form-8 Health Survey (SF-8) was used to evaluate health-related QOL. Upon analysis they found that asthma control and health-related QOL were correlated.

A retrospective study evaluating asthma symptoms and QOL found that adults with no asthma symptoms reported better asthma QOL (76). Szabó et al. assessed adults over the age of 30 who had had a diagnosis of asthma during childhood. QOL was assessed via the AQLQ and asthma symptoms were assessed via a few questions concerning their current asthma symptoms (76). Adults who had no asthma symptoms scored higher in the AQLQ than adults who were symptomatic, 6.8 and 5.28 respectively. This study highlights the impact of symptoms on asthma QOL in adults.

Also, Erickson et al. (15) found that symptom-derived severity greatly influenced asthma QOL. Data on asthma QOL and asthma were collected from 603 adults with asthma. Symptom-derived severity classified symptoms in four categories: mild intermittent, mild persistent, moderate persistent and severe persistent. These classifications were based on increasing frequency of symptoms and exacerbations (15). Asthma QOL was assessed using AQLQ and general QOL was assessed via the SF-36. Both measures of QOL were significantly related to symptom-derived severity, denoting the link between asthma symptoms and asthma QOL.

Bloomberg et al. (69) conducted a study to evaluate factors that were related to level of asthma control in children with asthma. Asthma control was assessed in terms of frequency of daytime symptoms and albuterol use (a bronchodilator), as well as physical activity limitations in the past two weeks. Asthma exacerbation history (i.e. oral steroids and emergency department visits) was also included in the assessment of asthma control. Asthma QOL was assessed using the PAQLQ. The PAQLQ was significantly related to asthma control such that children with well-controlled, partially controlled, and poorly controlled asthma scored 6.5 ± 0.5, 6.2 ± 0.9, 5.4 ± 1.3, respectively.

In summary, aspects of asthma control such as wheeze and symptoms have been shown to improve following exercise interventions (13, 70-72). In addition, asthma control and components of it (i.e. daytime symptoms) have been shown to be correlated with QOL, such that if they improve, so does QOL (14, 69). Unfortunately, no analysis of overall asthma control has been done following the completion of an exercise intervention in adults with asthma, leaving us with inconclusive data that exercise can improve asthma control. Also, as symptoms tend to result in use of bronchodilators, it would be interesting to specifically examine how bronchodilator use would be affected following an exercise intervention.

2j. Bronchodilator Use

As described previously, bronchodilators (i.e., short-acting β_2 agonists) are used at symptom onset, and relax the smooth muscle surrounding the airway. There is evidence to suggest that frequent bronchodilator use (i.e. which is a sign of frequent asthma symptoms) is an important indicator of asthma control and may impact QOL in individuals with asthma (15).

2j.1 Impact of Exercise on Bronchodilator Use

Improvements in asthma control have been correlated with better QOL in children with asthma (68, 69). One aspect of asthma control is the frequency of symptoms and bronchodilator use. Studies done looking at the effects of exercise on asthma medication use indicate that exercise improves medication use, though the specific details of these changes in medication use have been ambiguous (72). For example, Neder et al. (77) assessed the impact of a 2-month indoor aerobic training programme (using a cycle ergometer) on change in medication score in 26 children with asthma. The training sessions were 3 times a week, an hour each. The authors assessed medication use using a medication score. The medication score was calculated on a scale from 0-4, where a score of 0 represented someone taking no medication and a score of 4 represented someone taking systemic steroids, high-doses of inhaled steroids and bronchodilators on demand (78). At the time of the initial evaluation, 22 of the 26 children had medication scores >3 consisting of bronchodilator use, daily ICS use, and oral corticosteroid use. At the final evaluation, the number of children with a medication score >3 decreased to 15 (77). Due to the fact that medication score included both ICS and bronchodilator use it is impossible to draw conclusions about the effects of exercise on bronchodilator use alone. This important distinction needs to be made because increased ICS use reflects improved adherence (resulting in positive disease outcomes), whereas increased bronchodilator use reflects poor control.

Basaran et al. (13) measured both ICS and bronchodilator use using the Modified Asthma Medication Score (MAMS), on a scale from 0 to 7 where 0 = no medication and 7 = oral steroids > 20mg. On the MAMS, lower scores represent only bronchodilator use and higher scores include bronchodilator and ICS use. Thirty of the 58 children with mild-moderate asthma were randomized to the exercise intervention group. As stated in section 2h., the exercise intervention was comprised of basketball sessions 3x/week, an hour each, for 8 weeks. Within the exercise group, there was a significant change in the MAMS from 4.93 ± 2.5 to 3.53 ± 2.1 ($p<0.001$) (13). Due to the fact that this score was only measuring whether or not a patient was taking medication for their asthma, we cannot say how bronchodilator use changed. The MAMS more likely assessed asthma severity. Therefore, this lack of precision regarding bronchodilator use frequency weakens the suggestive implication of the positive effect of exercise on frequency of bronchodilator use.

In contrast, some studies did not find improvements in medication use following exercise. Hallstrand et al.'s (79) intervention consisted of step aerobics 3x/week for 10 weeks. In a sub-analysis of a sample of 10 adult participants (5 participants with and 5 without asthma) who were asked to keep a medication diary before and after an exercise intervention, Hallstrand et al. (79) found that the participants with asthma did not exhibit significant changes in bronchodilator use. The type of medication use in the non-asthma participants was not reported. Bronchodilator use was a tertiary analysis, thus there was no detailed information about change in frequency of bronchodilator use.

Robinson et al. (80) evaluated the effects of a circuit training programme in 8 adults with asthma. The exercise circuit included seven exercises: sit-ups, leg extensions, dumbbell punch and lateral dumbbell raise, cross country ski machine, cycling and treadmill running. Each exercise was done for 50 seconds with a minimum rest period of 30 seconds in between each exercise. Participants completed the circuit 1-4 times per session, for 12 weeks and were instructed to aim for 3x /week. Included among the many outcome measures was a diary of bronchodilator use for the duration of the training intervention. Authors found no change in bronchodilator use over the time of the training program (80). Due to the fact that bronchodilator use was not the main outcome measure, no detailed information on bronchodilator use was given.

In summary, there is evidence that supports the notion that exercise can improve medication use in individuals with asthma, such that there can be changes in ICS and/or bronchodilator use and symptom frequency post-intervention. Two studies found decreased medication scores (13, 77), however, bronchodilator use was not properly defined nor treated separately from ICS use, thus limiting the interpretability of these results. Additionally, these studies included patients who were not sedentary prior to beginning the exercise intervention, (77) rendering it impossible to ascertain that any medication improvements were solely due to beginning an exercise programme. Inconsistencies remain regarding the impact of exercise on medication use, specifically bronchodilator use, with studies reporting no change in bronchodilator use following an exercise (79, 80). Thus, the impact of an exercise intervention on bronchodilator use needs to be explored further, especially since we know that bronchodilator use (a result of symptoms) can affect QOL (68, 69, 76).

2k. Impact of Exercise on Lung Function

A systematic review of all RCT studies that conducted aerobic exercise interventions with individuals with asthma eight years of age and older found no impact of exercise on lung function (16). In short, 13 studies were included in this review; all studies had aerobic exercise intervention lasting a minimum of 4 weeks, 20-30 minutes per session, 2-3x/ week. Nine studies evaluated FEV_1 and FVC and found no significant changes in either measure of lung function following the exercise interventions. Although the majority of the research suggests that exercise interventions in people with asthma do not improve lung function, there are a few studies that did find otherwise. One can speculate that the type of exercise, intensity, duration and programme may be a reason why there are inconsistencies in the literature. One study suggested that improvement in lung function may have been due to optimization of medical treatment (66).

2l. Summary

There have been a number of studies evaluating the effects of exercise on children with asthma. These studies have used a variety of outcome measures, including lung function, symptom frequency, cardiovascular benefits, as well as QOL. Notwithstanding, very few studies have been conducted evaluating the effects of exercise, and specifically aerobic exercise, on QOL in an adult population of asthmatics. As detailed above, of the studies that have been conducted assessing the impact of exercise on QOL, they have all suffered from various limitations. For example, including participants who were physically active prior to being included in the study (81), giving educational sessions as part of the intervention (8, 66), and using a variety of questionnaires to assess QOL, none of which were asthma specific ((63); see Table 1). These limitations are important because they do not allow us to evaluate patients who are likely to benefit the most from an exercise intervention (i.e., sedentary patients); the specific or unique effects of exercise on asthma; or assess domains of QOL that are specific to people with asthma.

Chapter 3: Rationale

Although effective treatments for asthma are widely available, many patients with asthma remain poorly controlled and, as a result, have a poor QOL. Exercise training has been shown to have a therapeutic effect in other medical conditions such as heart disease (59) and breast cancer (60). Among the studies that have evaluated the effects of exercise on asthma, most have focused on outcome measures such as lung function and exercise capacity. However, very few have assessed the impact of aerobic exercise on asthma QOL, and none have assessed asthma QOL in adults, which is a clinically significant measure that is often of great importance to the patient. This pilot study was necessary to increase researchers understanding of the potential benefit that an aerobic training programme may have on QOL in adult patients with asthma. In addition, few studies have looked specifically at asthma control and bronchodilator use which have been correlated with QOL. This pilot study will also provide clinicians more evidence of the effects of aerobic exercise on their patients' QOL and may potentially aid in the promotion of more exercise protocols as an adjunct treatment. The results of this pilot study could also be the catalyst for future projects, e.g., a full-scale trial or the evaluation of various modes of exercise (for example resistance training).

Chapter 4: Objectives and Hypotheses

This pilot study aimed to assess the effects of a 12-week aerobic exercise programme on asthma QOL, asthma control and bronchodilator use in adults with asthma. This pilot study also served to provide data for power calculations for the design of a future full-scale randomised controlled trial.

4a. Primary Objective

1) **To evaluate changes in asthma quality of life in sedentary adults diagnosed with asthma following a 12-week aerobic exercise intervention.**

Hypothesis

It was hypothesized that after completing a 12-week aerobic exercise intervention, previously sedentary participants with asthma would report statistically and clinically significant improvements in quality of life according to scores on the Asthma Quality of Life Questionnaire, reflecting a reduction in the limitations caused by their asthma.

4b. Secondary Objective

1) **To assess the effects of a 12-week aerobic exercise intervention on asthma control in a sample of sedentary adult asthmatics**

Hypothesis

Following the 12-week aerobic exercise intervention, participants would demonstrate a significant improvement in asthma control as measured by the Asthma Control Test and the Asthma Control Questionnaire, two questionnaires that have been validated to assess asthma control. This improvement would also be strongly correlated with improvements in asthma quality of life.

2) **To assess the effects of a 12-week aerobic exercise intervention on the frequency of bronchodilator use in a sample of sedentary adult asthmatics**

Hypothesis

Following a 12-week aerobic exercise intervention, participants would exhibit a significant decrease in the frequency of bronchodilator use in the week following the end of the intervention relative to the week prior to study entry as assessed by a one-week diary. This improvement would be correlated with improvements in quality of life.

Chapter 5: Manuscript

Asthma Quality of Life in Adults after 12 weeks of Aerobic Exercise

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5a. Abstract

Quality of life in chronic disease populations is becoming increasingly important. There is a paucity of studies evaluating the impact of aerobic exercise on quality of life in adults with asthma. This pilot study examined the efficacy of a 12-week aerobic exercise intervention on quality of life in sedentary adults with asthma. Four adults with asthma were recruited for the pilot project and completed the Asthma Quality of Life Questionnaire (AQLQ) prior to and after completing the exercise intervention. Following the intervention, participants demonstrated a clinically significant improvement in total asthma quality of life, which was not statistically significant ($\Delta 1.22 \pm 1.13$ $F = 4.63$, $p = .12$). However, participants demonstrated statistically significant improvements in the symptoms domain of the AQLQ (3.75 ± 0.59 to 5.31 ± 1.09; $F= 10.96$, $p=.045$). Participants also demonstrated statistically significant improvements in asthma control, as assessed by the Asthma Control Questionnaire (ACQ) (2.54 ± 0.74 to 0.82 ± 0.52; $F= 36.03$, $p=.009$) and the Asthma Control Test (ACT) (13.25 ± 3.30 to 21 ± 1.83; $F= 23.44$, $p= .017$). No significant changes were found for bronchodilator use, FEV_1, or FEV_1/FVC, VO_2max. Consistent with the results obtained in other clinical populations, results of this pilot study suggest that aerobic exercise in adults with asthma may improve quality of life and clinically important aspects of asthma such as asthma control.

Shortened Title: Exercise and Asthma Quality of Life

Keywords: asthma, quality of life, adults, aerobic exercise, asthma control

5b. Introduction

Quality of life (QOL) is an important concern among clinical populations. Generally defined as one's ability to function optimally and enjoy life, QOL can be affected by financial status, occupational environment, and health (52). In terms of health, disease-specific QOL measures the impact of a disease on one's ability to function in daily life (53, 54). In 2005, 8% of the Canadian population over the age of 12 (~2.2 million people) were diagnosed with asthma (6). Asthma has been directly related to increased work and school absences, an inability to perform household chores, a restriction of social activities (20), and a general decrease in QOL (21-23), making it a major health and societal concern in Canada. However, in addition to its prevalence, the control of asthma in Canadians is generally poor with more than 50% of Canadians having poor control of their asthma (25). Defined as one's ability to control or manage manifestations of the disease, asthma control can negatively affect the QOL of patients suffering from this chronic inflammatory disease.

Exercise has been shown to be beneficial to overall health and more specifically, has been shown to reduce morbidity associated with obesity, type II diabetes, and hypertension (9). Exercise has numerous benefits in healthy populations, including improved cardiovascular and cardiorespiratory capacity, as well as improved QOL (82, 83). In respiratory diseases such as chronic obstructive pulmonary disease (COPD), exercise has been shown to improve outcome measures such as exercise tolerance and QOL (11). Studies conducted in other clinical populations, such as coronary artery disease, have also found improvements in QOL after participating in exercise programmes. (10).

Previous studies have evaluated how exercise improves QOL in patients with asthma. However, most of these studies were conducted in paediatric populations. Among these are studies by Basaran et al. (13) and Fanelli et al. (12) which found that children with asthma who completed an exercise programme demonstrated improvements in asthma QOL compared to baseline, as measured by the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) (12, 13). In addition, Cambach et al. (63) found improvements in post-exercise intervention measures of health-related QOL in adults with asthma. However, this study did not use an asthma-specific measurement tool to assess QOL. To our knowledge, no exercise intervention studies have evaluated disease-specific QOL changes in adults with asthma. Thus, the primary objective of this pilot study was to determine whether 12 weeks of aerobic exercise could improve asthma QOL in sedentary adults with asthma. We hypothesized observing a statistically and clinically significant improvement in asthma QOL following the completion of the exercise intervention.

5c. Methods

5c.1 Participant recruitment and screening

Participants were recruited from the asthma tertiary care clinic at l'Hôpital du Sacré-Coeur de Montréal (HSCM) between January 2008 and June 2009. All participants provided signed informed consent prior to data collection. Participants were included if they were 18 years and older, sedentary (i.e., engaged in less than 60 minutes of planned physical activity per week), had physician-diagnosed asthma (i.e. airway reversibility/metacholine $PC20 \leq 16mg/ml$) for which they were prescribed a minimum dose of inhaled corticosteroids (ICS) of 250mg per day, and had mild to moderate asthma symptoms. Mild to moderate symptoms were defined as using bronchodilator medication 2-4 times per week and/or having night awakenings 1-2 times per week.

Participants who were unable to communicate in English or French, had a co-morbid disease that was more serious than asthma (e.g., COPD), or a co-morbid disease for which they had previously established exercise guidelines (e.g., cardiac rehabilitation programme) were excluded from the study. The study was approved by the research ethic boards of both HSCM and Concordia University and all participants provided written informed consent.

5c.2 Screening Procedure

Patients who were referred by a physician were contacted by telephone by a research assistant and were given a brief overview of the study and eligibility criteria were verified. The research assistant briefly explained the project and asked questions including: "do you exercise regularly" and "how many times have you used your bronchodilator medication in the past week", etc. If patients were sedentary, had been using their bronchodilator medication regularly, and were interested in participating in the project, they were invited to participate in an in-person screening interview. Patients who were seen at the clinic and were interested in participating in the study either had their screening interview during the clinic visit or were scheduled for an interview approximately one week later. During the screening interview, the Asthma Control Questionnaire (ACQ) was used to screen participants for eligibility. Participants with a mean score less than 1.5 were considered to be well controlled and were excluded. Next, participants completed a medical history and socio-demographic questionnaire. This questionnaire contained self-report information about weight and height, current asthma medication, health behaviours such as current levels of physical activity, smoking status and medication adherence. It also included a brief medical history of conditions other than asthma and information about their family's medical history. For additional screening purposes, participants were given a one-week diary where they indicated the frequency of bronchodilator medication use, the activity triggering the use of their bronchodilator medication, the symptom severity, and whether or not they had any nocturnal waking asthma symptoms the night before. Baseline assessments were conducted on those patients that met all eligibility criteria.

5c.3 Baseline and Post-intervention Measures

Measures included administration of the ACQ, Asthma Control Test (ACT) and Asthma Quality of Life Questionnaire (AQLQ). Objective testing included standard lung function testing by full body plethysmography and graded-exercise test on a cycle ergometer. These assessments were also repeated following the completion of the exercise programme.

5c.3.1 Quality of Life Assessment

Assessment of QOL was done using the disease-specific AQLQ developed by Juniper (84). This questionnaire assesses the extent to which asthma limits an asthmatic's life or interferes with his or her ability to do and/or enjoy daily activities. This questionnaire includes 32 items, rated on a 7-point scale (i.e., 1= a great deal of limitations to 7= no limitations at all) and has a two-week recall. The AQLQ is scored using the mean score of the questionnaire, with a higher score indicating better QOL. The AQLQ is divided into subscales that measure four aspects of life typically affected by asthma: activity limitations (how asthma limits the ability to carry out daily activities), symptoms (nature and frequency of symptoms), environment (level of difficulty for patients to manage or avoid environmental asthma triggers), and emotional distress (the degree of emotional stress caused by the disease). The AQLQ has high intra-class correlation coefficients

(0.95) and good construct, cross-sectional, and longitudinal validity (85-87). A change or difference of ≥ 0.5 in the AQLQ has been shown to be clinically significant (88).

5c.3.2 Asthma Control Assessments

Asthma control was assessed using the ACQ also developed by Juniper (89). It is a self-report instrument consisting of 7 questions relating to the level of asthma control in the past week. This questionnaire asks patients to recall the frequency and intensity of their asthma symptoms and bronchodilator use over the last week. The seventh additional question is concerning objective lung function values and may also be included in the score, and is completed by the respiratory technician who conducted lung function tests (90). Scores range from 0 (complete asthma control) to 6 (poor asthma control) (90), with a lower score indicating good control. The level of control is calculated by taking the mean score of the questionnaire. The ACQ has an intra-class correlation coefficient 0.90, good construct, cross-sectional and longitudinal validity (89, 90). A change of ≥ 0.5 in the ACQ has been shown to be clinically significant (54).

The ACT is another questionnaire that evaluates level of asthma control. The ACT, designed by Nathan, consists of 5 items rated on a 5-point scale (91). This questionnaire has a four week recall and requires participants to recall symptom frequency, bronchodilator use, etc. (similar to the ACQ), however does not include objective lung function. Scoring ranges from 5 (poor asthma control) to 25 (completely controlled). The questionnaire score is based on the sum total score; with a sum score ≥20 indicating good control. The ACT has good internal consistency reliability (0.84) and a test-retest reliability of 0.77 (91, 92). It has also been shown to be responsive to change in asthma control over time. Although the ACT was more recently developed, it has also been widely used, though there is less validation data available than the ACQ (93). The exclusion of the objective measure of lung function makes this questionnaire easy to use and practical for clinical use. Even without the lung function measure the ACT remains highly correlated with changes in ACQ (r=-0.81, p<.001) (92).

5c.3.3 Lung Function

As per standard protocols for lung function testing, bronchodilator medication was withheld for at least 4 hours prior to the assessment. The tests consisted of diffusion capacities, lung volumes and spirometry using the Vmax encore plethysmograph (Sensormedics, Yorba Linda, CA). Spirometry included forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). Patients were assessed before and 15 minutes after the administration of 200 µg of salbutamol using a metered-dose inhaler or 500 µg terbutaline using a Turbuhaler®. All results were compared to standard normal values (94-98).

5c.3.4 Exercise Capacity

Participants were required to undergo a standard fitness evaluation as recommended by the American Thoracic Society (99). This was done using an electrically braked cycle ergometer (Ergometrics 800, Sensormedics, Yorba Linda, CA), applying the Jones stage 1 exercise protocol. The Jones stage 1 protocol required participants to pedal on the cycle ergometer at 60 revolutions per minute with no resistance or with mild resistance (20 Watts) if the participant was in moderate physical condition. The resistance was increased every minute by 15 Watts and the participants were instructed to exercise to exhaustion (until leg fatigue, shortness of breath). Heart rate, blood pressure, minute ventilation, carbon dioxide (CO_2) excretion and oxygen (O_2) uptake were recorded during the test and active recovery. As per standard practice, (100, 101) minute ventilation

(VE), oxygen uptake (VO_2) and CO_2 excretion (VCO_2) was analyzed on a breath-by-breath basis.

5c.4 Exercise Intervention

The intervention was comprised of 36 sessions at a frequency of 3 sessions per week on non-consecutive days for 12 weeks. Each session consisted of a 10-min warm-up, 40-min aerobic exercise using the participants' choice of equipment (elliptical trainer, treadmill, or stationary bicycle), followed by a 10-min cool-down. Participants were not obliged to continue for 40 minutes on one piece of equipment; rather they had the option to do 3 blocks of exercise for a total of 40 minutes. For the first 4 weeks, participants were required to work at 50-75% of their heart rate reserve (defined from the initial maximal exercise test). During the remaining 8-weeks, the intensity increased to 70-85% of their heart rate reserve. Their exercise intensity was calculated using the Karvonen method (102). Heart rate was verified at random times during each session, using a heart rate monitor, to assure that participants were exercising at the appropriate intensity level. To reduce the risk of having an exercise-induced bronchospasm all participants were obligated to pre-medicate with their bronchodilator prior to each session, which has been shown to be an effective preventative measure (103-106).

5c.5 Statistical Analysis

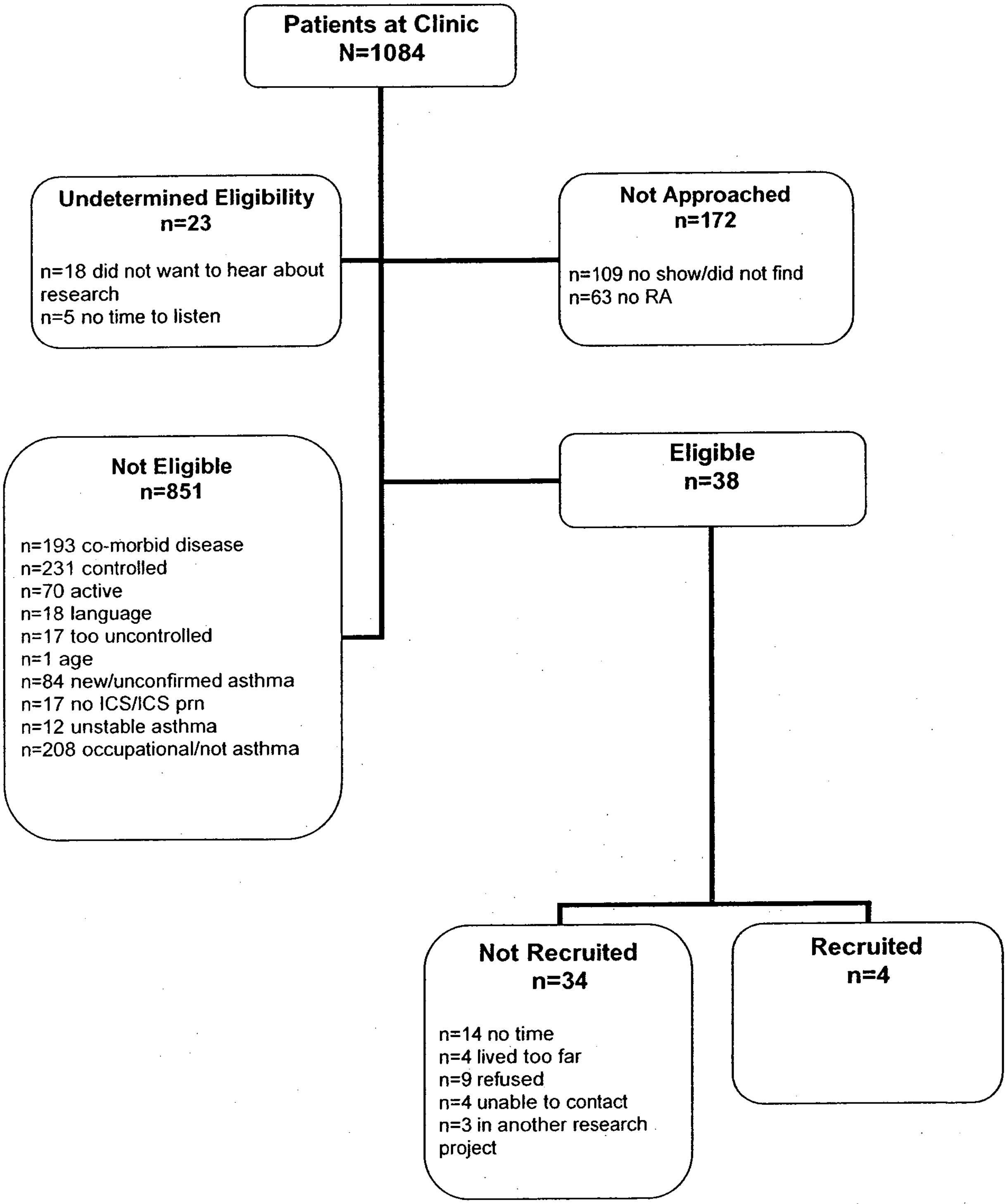
Data analysis was done using SAS version 9.1 (SAS, Durham, NC). A series of repeated measures general linear models were conducted to compare the pre and post- values of the AQLQ (total and subscale scores), ACQ, and ACT and bronchodilator use. In addition, analyses were conducted to compare pre- and post- values of FEV_1 and VO_2max. All analyses were two-sided. One participant did not complete their post-intervention spirometry assessments. To compensate for the lost data, and in line with intention-to-treat principles, we used a last value brought forward procedure to replace the missing values (107). To identify potential mechanisms of any effect, a series of Pearson correlation analyses were used to assess the relationships between AQLQ scores (total and each subscale) and the following variables: ACQ change, ACT change, bronchodilator change, FEV_1 change, FEV_1/FVC change, and VO_2max change. Significance (alpha) was set at .05 for all analyses. Due to the small sample size and repeated measures structure of the analyses, we did not include any covariates in the analyses.

5d. Results

5d.1 Recruitment Details

A total of 4 adults with asthma participated in the study. Figure 6 depicts the recruitment flowchart for patients who presented to the HSCM clinic. A total 1084 participants presented to the HSCM clinic between January 2008 and June 2009. A total of 851 patients, including 356 who were approached, were excluded; 23 patients' had undetermined eligibility; 172 were not approached. Of the 38 patients who were eligible, 4 were recruited. Participant demographics can be found in Table 2.

Figure 6 Flowchart of recruitment between January 2008 and June 2009



Patients at clinic represent the total number of patients who presented to the external asthma clinic at HSCM.

Table 2 Participant demographic

	N/ Mean ± standard deviation	Range
N	4	
Sex (# of females)	3	
Age (years)	41.6 ± 16.5	27.1 – 61.5
Years with asthma	17.3 ± 6.8	12.0-25.0
ICS dose (mg) (including combined beta 2)	875.0 ± 478.7	500.0-1500.0
# of times bronchodilator (in past week)	6.3 ± 1.5	5.0-8.0
# of times bronchodilator (avg. per week)	4.2 ± 2.4	1.5-6
Past smokers	2	
Never-smokers	2	
Gina Severity		
Moderate persistent	2	
Severe persistent	2	

5d.2 Participant Adherence

All participants attended more than 75% of the exercise classes with an average attendance of 82% of the classes. Participants missed sessions due to illness, work/school conflict, etc. During the Christmas holiday season, training was suspended for one week, but all participants completed 12 weeks of exercise.

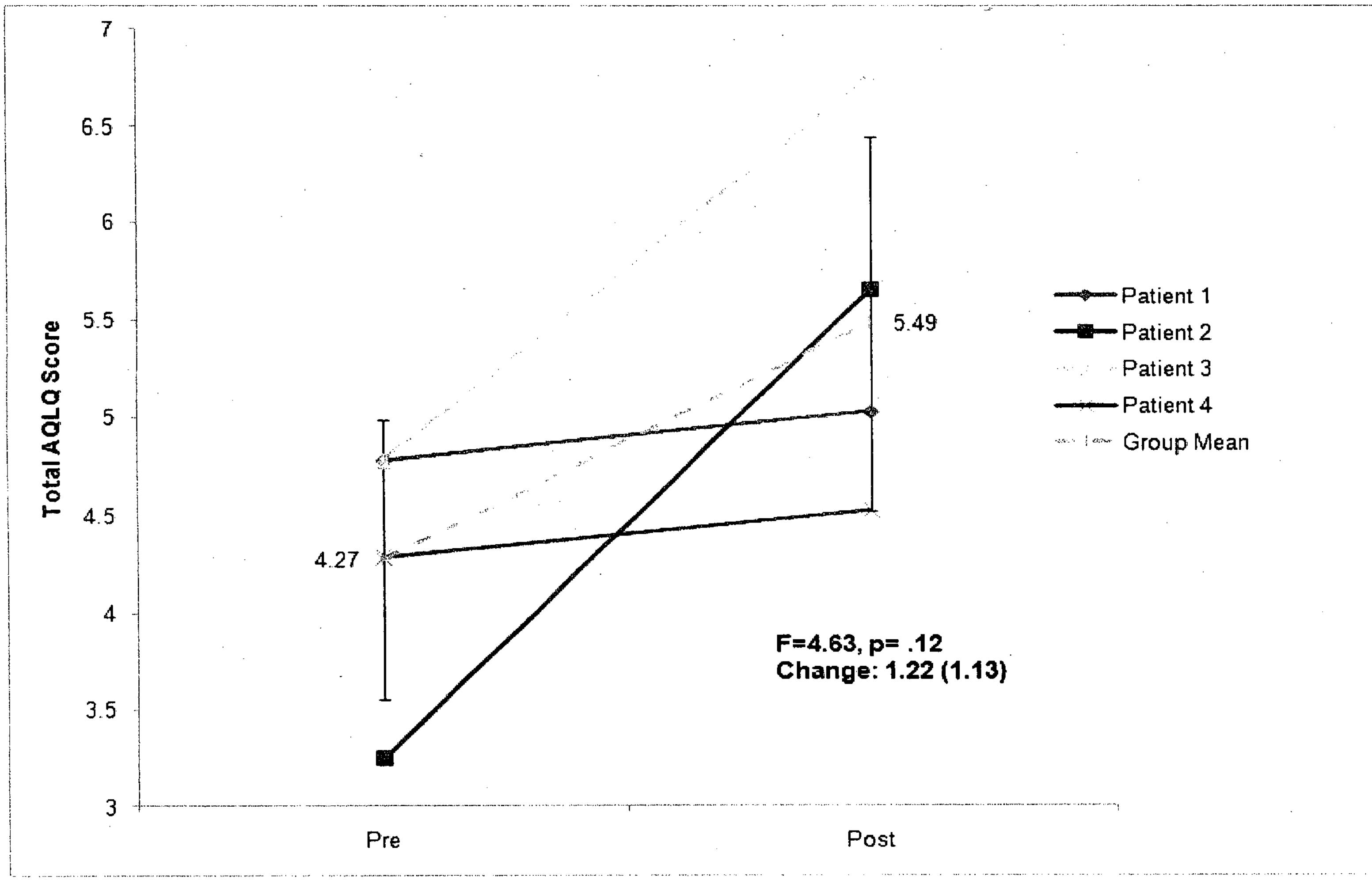
5d.3 Asthma Quality of Life

As seen in Figure 7, after completing the exercise intervention, participants demonstrated clinically significant improvements in the mean total AQLQ, with an increase of 1.22 ± 1.13, which was surprisingly not statistically significant. This represented a 29% improvement in AQLQ. The mean change of each subscale was: 1.56 ± 0.94 (symptoms); 0.95 ± 1.26 (emotions); 0.63 ± 2.11 (environment) and 1.19 ± 1.19 (activity limitations). Table 3 depicts the group mean of each subscale of the AQLQ and other outcome measures pre- and post-intervention.

5d.4 Asthma Control

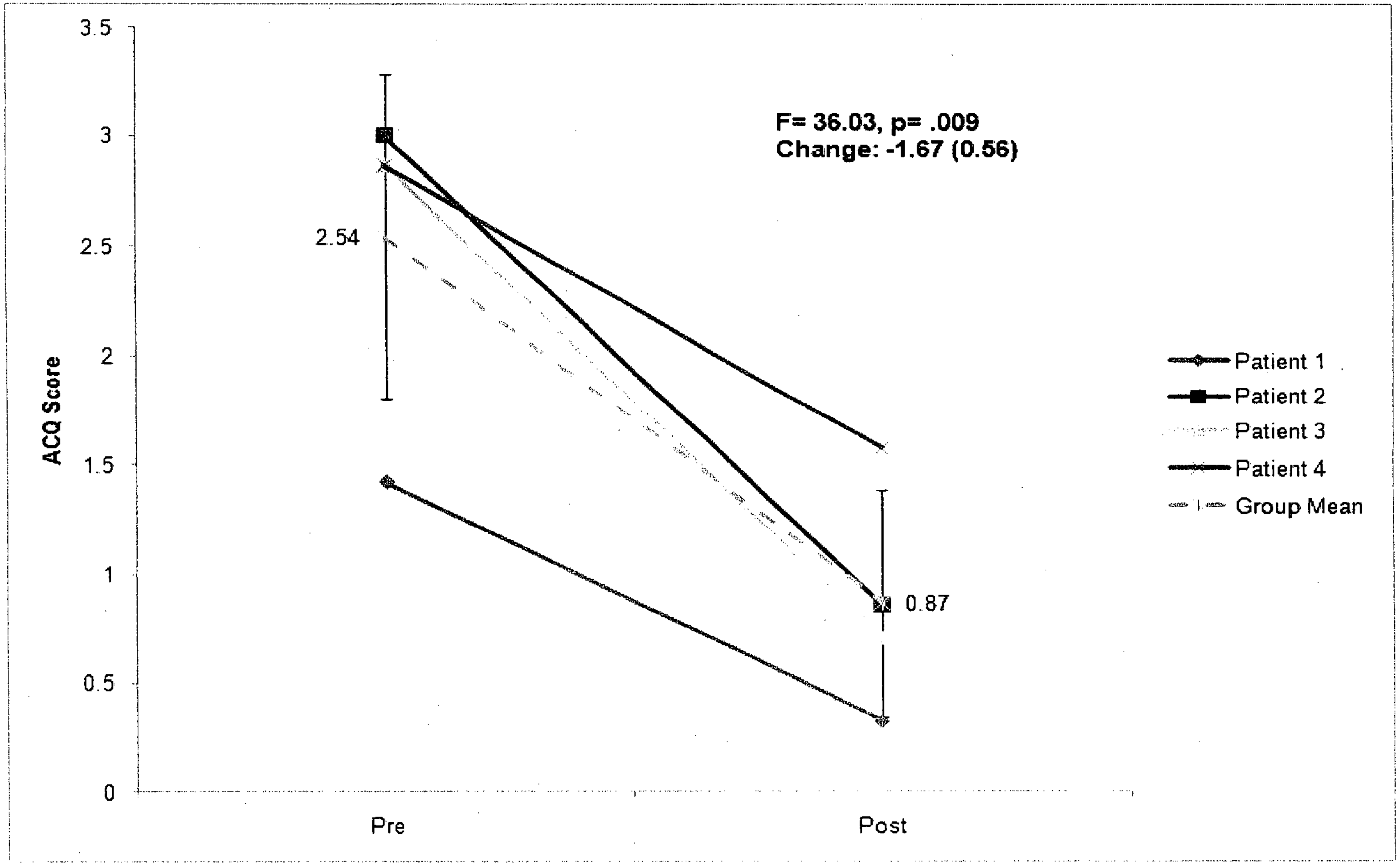
Participants demonstrated both statistically and clinically significant improvements in asthma control measured by both the ACQ and the ACT following the intervention, with a mean -1.67 ± 0.56 changes in ACQ (Figure 8) and the mean 7.75 ± 3.20 changes in ACT of (Figure 9). As represented by both measures, our group started out poorly controlled (ACQ > 1.5 and ACT < 20). However, most participants went from uncontrolled to controlled following the exercise intervention, with the exception of one participant who was borderline (ACT score=19). Changes of 0.5 represent clinically significant changes in asthma control measured by the ACQ (54), and our participants as a group showed three times this increase, denoting the magnitude of change in our participants.

Figure 7 Participants change in Total AQLQ pre- and post-intervention



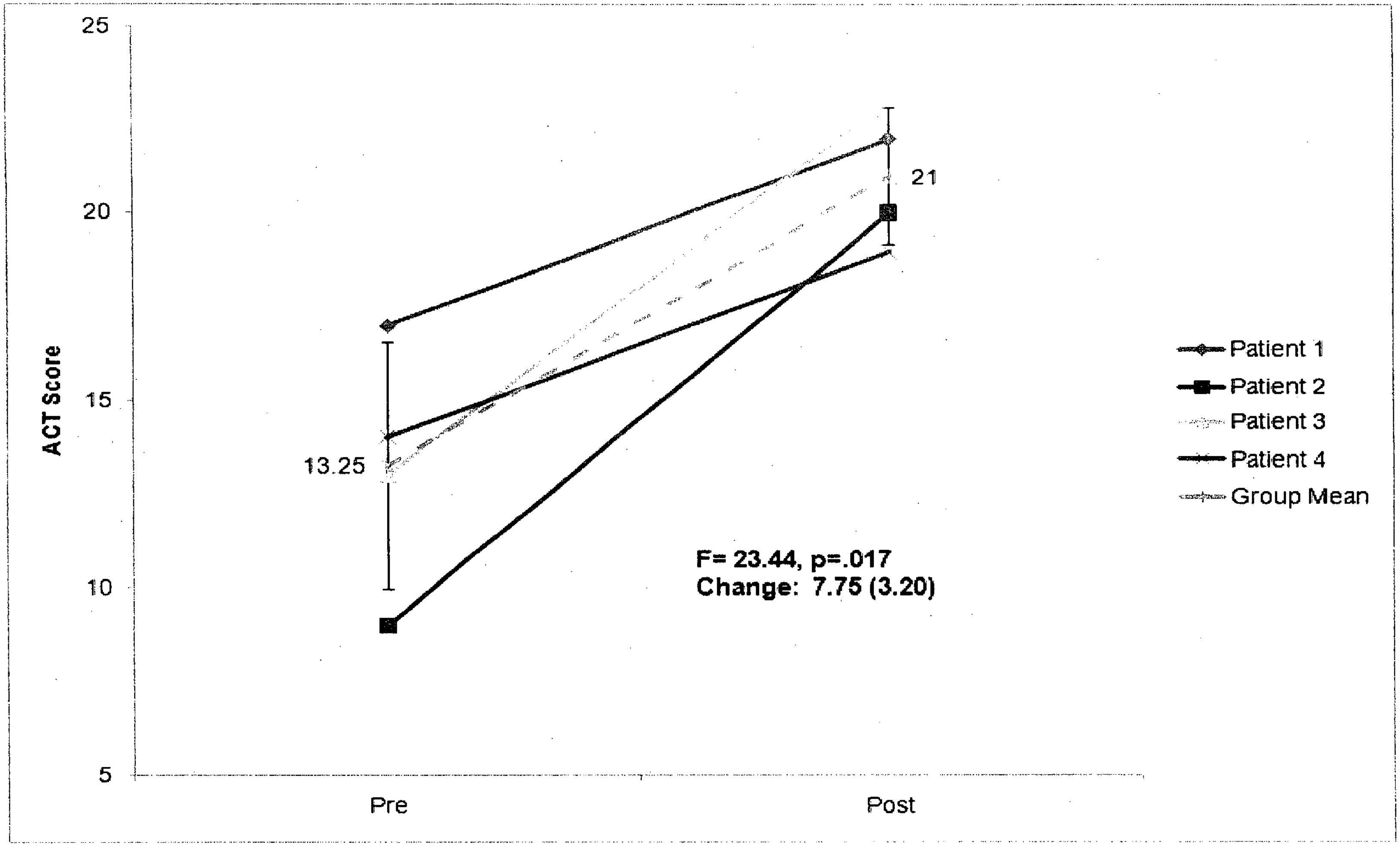
Each participants and group score on the Asthma Quality of Life Questionnaire pre-intervention and post-intervention.

Figure 8 Participants change in ACQ pre- and post-intervention



Each participants and group score on the Asthma Control Questionnaire pre-intervention and post-intervention.

Figure 9 Participants change in ACT pre- and post-intervention



Each participants and group score on the Asthma Control Test pre-intervention and post-intervention.

5d.5 Bronchodilator Use

Although participants did demonstrate important improvements (reductions) in bronchodilator use (Table 3) following the intervention, this change was not statistically significant.

5d.6 Lung Function and Exercise Capacity

Participants did not demonstrate any significant changes in FEV_1 ($F=6.04$, $p=.09$), FEV_1/FVC ($F=6.52$, $p=.08$), or absolute VO_2max ($F=0.01$, $p=.94$) (Table 3) following the intervention.

5d.7 Correlation Analyses

As seen in Table 4, correlation analyses revealed that changes in asthma control (both ACQ and ACT) predicted changes in total AQLQ. In addition, changes in asthma control correlated with changes in all 4 of the AQLQ subscales; however this was only statistically significant between the ACT and the emotions subscale (Table 5). Change in bronchodilator use was significantly related to change in the emotions subscale for the AQLQ. Changes in FEV_1, FEV_1/FVC, and VO_2max did not predict changes in total AQLQ or any of the AQLQ subscales (Table 5).

Table 3 Pre- and post-intervention outcome measures

	Pre (Mean ± SD)	Post (Mean ± SD)	F	p
AQLQ Subscales				
Symptoms	3.75 ± 0.59	5.31 ± 1.09	10.96	.045
Emotions	5.05 ± 0 .85	6.00 ± 1.02	2.28	.228
Environment	4.06 ± 1.03	4.69 ± 1.65	0.35	.595
Activity limitations	4.57 ± 1.09	5.76 ± 0.58	4.00	.139
Weekly bronchodilator use	8.75 ± 7.32	3.25 ± 1.89	1.84	.268
FEV_1 predicted (pre-bronchodilator) (%)	71.83 ± 16.06	79.11 ± 12.43	6.04	.091
FEV_1/FVC predicted (pre-bronchodilator (%)	64.20 ± 18.86	69.61 ± 17.04	6.52	.084
VO_2max (L/min)	1.54 ± 0.51	1.54 ± 0.60	0.01	.939

Pre: group mean of measurements taken prior to starting the exercise intervention. Post: group mean of measurements taken following the exercise intervention.

F: difference between the group means. p: the significance of the pre-/post-intervention change.

Table 4 Correlation between change in total AQLQ and change in asthma control and related asthma measures

Change	Total AQLQ	
	r	p
ACQ	-0.98	.022
ACT	1.00	<.001
FEV_1	0.01	.994
FEV_1/FVC	0.19	.809
VO_2max	-0.49	.514
Weekly bronchodilator use	0.92	.084

r : Pearson's correlation coefficient, p: significance of the correlation.

Table 5 Correlation between changes in AQLQ subscales and changes in asthma control and asthma related measures

Change	Symptoms		Emotion		Environment		Activity Limitations	
	r	p	*r*	p	*r*	p	*r*	p
ACQ	-0.89	.112	-0.94	.055	-0.92	.084	-0.88	.121
ACT	0.94	.055	0.99	.011	0.93	.067	0.86	.139
FEV_1	-0.29	.708	-0.08	.919	-0.16	.838	0.40	.604
FEV_1/FVC	-0.15	.854	0.16	.842	-0.14	.866	0.65	.351
VO_2max	-0.70	.300	-0.45	.547	-0.78	.218	-0.21	.979
Broncho*	-0.92	.079	-0.96	.042	-0.82	.185	-0.75	.254

* Broncho = weekly bronchodilator, *r* : Pearson's correlation coefficient, p: significance of the correlation.

5e. Discussion

The current study found that a 12-week aerobic exercise intervention in adults with asthma produced a clinically important improvement in the total AQLQ score, which did not reach statistical significance. Assessment of each AQLQ subscale showed a statistically important improvement only in the symptoms subscale. Asthma control, measured by the ACQ and ACT, demonstrated both clinical and statistical improvements following the exercise programme. In addition, we found significant correlations between both measures of asthma control and total AQLQ and found a significant correlation between the ACT and emotions subscale. We also observed that on average, there was more than a 50% decrease in bronchodilator use in the week following the exercise programme compared to the week prior to starting. However, this improvement did not reach statistical significance. Change in bronchodilator use was also significantly related to changes in the emotions subscale of the AQLQ.

5e.1 Asthma Quality of Life

Some of our results are consistent with studies that have assessed asthma-specific QOL following an exercise intervention. For example, Fanelli et al. (12) found that children with asthma had significant improvements in QOL following a 16-week exercise programme and Basaran et al (13) also found improvements in QOL of children with asthma after an 8-week exercise programme. While Basaran reported a 24% improvement in total PAQLQ scores, similar to our findings, Fanelli reported a 75% improvement in total PAQLQ scores, which is almost three times the magnitude of change we observed. However, this could be in part explained by the extremely low baseline PAQLQ scores and the inclusion of education classes for children prior to starting the exercise intervention. Similar to our study, both Basaran and Fanelli also found improvements on all subscales of the PAQLQ. These studies also found no correlation between QOL and exercise capacity and lung function (12, 13), which is consistent with our findings that suggest that the improvements in AQLQ appeared to be independent of changes in FEV_1, FEV_1/FVC and VO_2max. In addition, our results are also consistent with two exercise interventions conducted in adults. Cambach (63) found that after 3-months of exercise, adults with asthma showed significant improvements in QOL measured by the Chronic Respiratory Disease Questionnaire (CRDQ). The two groups, RC (exercise condition then control) and CR (control condition then exercise) demonstrated a 68% and 80% improvement in QOL, a magnitude that was more than two times greater than what was observed in the present study. Cambach also, found no significant correlation between changes in exercise tolerance (endurance time, submaximal exercise and walking distance) and QOL (63). Emtner (8) also found 3 out of 5 Visual Analog Scale (VAS) items improved significantly following the 10-week exercise intervention in adults. Although the VAS was not specifically designed to assess QOL, the items included aspects that are related QOL (e.g., I am afraid of experiencing breathlessness when I exercise) (8).

5e.2 Asthma Control

To our knowledge, there have not been any interventional studies that specifically evaluated the impact of an exercise intervention on asthma control (i.e., using the ACQ) among adult asthmatics. However, some intervention studies examined components of asthma control and their outcomes following an exercise programme. One study found that following a swimming programme, children with asthma reported less wheeze days when compared to baseline (71). Other observational studies have looked at components of asthma control such as the frequency of asthma exacerbations, and its relationship to physical activity. A prospective longitudinal study of physical activity and rates of asthma exacerbations found that women who were regularly physically active had a lower risk of having an asthma exacerbation than those who were less physically active (73). Also, a study done in children related more TV-time (more sedentary behaviour) with an increased risk of asthma symptoms (108). Taken together, these studies suggest that a more physically active lifestyle can lead to better asthma control which is in line with the present findings. Another study found that people who had well-controlled asthma were more likely to participate in vigorous-intensity exercise (74). Although the latter study used the ACQ to measure asthma control, due to its cross-sectional nature, we cannot interpret whether the reverse is true, i.e. do patients have good control because they exercise? Nevertheless, it is difficult to compare our study to these studies, due to the fact that they employed different designs (i.e., cohort studies versus an intervention).

5e.3 Bronchodilator Use

Our findings in regards to bronchodilator use is consistent with those of Hallstrand's (79) who did not observe any change in bronchodilator use frequency following a 10-week step aerobic exercise intervention. In contrast to our study other studies have found changes in asthma medication use following an exercise intervention, demonstrating that exercise may influence medication use (13, 77); however type of medication was not specified nor treated independently. Basaran (13) and Neder (77) both reported reduced medication scores following exercise interventions in children with asthma. However, these medication scores assessed not only bronchodilator use but ICS use, which does not allow us to interpret changes in bronchodilator use alone in response to the interventions.

5e.4 Potential Mechanisms

There may be a few potential mechanisms to explain the clinical improvements seen in QOL in our study. Previous studies have shown that there is a relationship between asthma control and asthma QOL (14) such that poor control tends to impair QOL. Assessment of asthma control (ACQ and ACT) focuses on bronchodilator use, symptom frequency and severity. The AQLQ involves questions that assess how symptoms affect QOL. Therefore, with such a significant improvement in asthma control, we would expect there to be similar improvements in the total AQLQ score, and, unsurprisingly, in the symptoms subscale, given that it assesses the impact of asthma symptoms (i.e., asthma control) on quality of life. Subsequently changes in asthma control could be a result of change in inflammatory profile. A study conducted in mice found that 4 weeks of treadmill exercise resulted in a decrease in airway inflammation (109). Due to the fact that airway inflammation is the cornerstone of asthma, this may likely influence asthma control and consequently QOL.

Studies have shown that exercise can positively impact psychological health (e.g. mood, anxiety, and stress) (110, 111). For example, a review of studies looking at the effects of exercise on depression, anxiety, and other mood states found that exercise, which was predominantly aerobic exercise, positively impacted these psychological states (111). In addition, it has been shown that psychological health may be correlated with asthma QOL, such that patients with asthma with psychiatric disorders have decreased QOL (112). It is possible that the exercise intervention in our study led to an improvement in psychological status, which in turn led to increased QOL. However we did not find any change in the emotions subscale of the AQLQ, suggesting that our intervention may not have had any impact on psychological health.

Finally, exercise has been shown to improve functional capacity (13). This was demonstrated in a study done in children after completing a basketball program and also in adults with asthma and COPD following an aerobic exercise intervention (13, 63). Although functional capacity may be a mechanism for improvement in QOL we did not observe any changes in the activity limitation subscale of the AQLQ. This could suggest that our intervention was not effective in decreasing the impact that asthma had on our participants' activities of daily living (i.e. their ability to function).

5e.5 Manipulation Tests

5e.5.1 Lung Function

In contrast to a few studies (8, 66) where improvements in FEV_1 and FEV_1% post-exercise intervention were found, we found no such changes in any measure of lung function (i.e. FEV_1, FEV_1/FVC) following exercise, which is consistent with numerous studies in asthma populations (16, 113). A systematic review of exercise and asthma revealed that 9 of 13 studies that assessed lung function (FEV_1 and FVC) found no changes following the interventions (16). All studies included in the review had to have interventions that were at least 4 weeks long, 20-30 sessions done 2-3 times per week, thus covering a wide range of exercise interventions.

5e.5.2 VO_2max

None of our participants demonstrated changes in absolute VO_2max, which is inconsistent with previous literature in adults. In the same review of exercise and asthma, 7 of the 13 studies that evaluated VO_2max found improvements (Δ5.4ml/kg/min 95% CI= 4.24 to 6.61). The negative findings observed in the present study may be due to the different equipment used for the VO2 assessment and during training. Our participants had the option of using a variety of equipment during the exercise phase; most participants preferred the elliptical trainer and treadmill, and reported less interest in using the bicycle (i.e. finding it 'too tiresome on the legs'). We used a cycle ergometer to do both the baseline and post-intervention testing because this is standard practice in a pulmonary clinic setting (as it is reported to be safer and requires less leg muscle training than treadmill use (114)). Research has shown that specificity is important when assessing VO_2max, such that to maximise improvements in fitness, individuals should be using the same mode of exercise for training and testing (115). Thus the inconsistent modalities between testing and training could have diluted any improvements in fitness.

5e.6 Limitations

The small sample size was the major limiting factor of this pilot study. Many people were excluded due to disease comorbidity, having occupational asthma, or having an unconfirmed case of asthma, leaving us with a small pool of eligible candidates for the study. This factor combined with our self-selection bias, limits our generalizability to patients with asthma. Despite this, a secondary purpose of the current study was to provide pilot data for power calculations for a larger full scale randomised controlled trial, which was achieved. Of note, we performed a post-hoc power analysis on the data which revealed a power of 0.96 with an effect size of 1.7, suggesting that our exercise intervention had no effect on QOL. We also did not have a control group, thus not allowing us to determine whether improvements were due to our intervention or due to participating in a research project (i.e. being followed up more frequently). However the objective of this study was to first determine efficacy of the exercise intervention. Also, we depended on self-reported data for our questionnaires which may have introduced some reporting bias. However they have been validated in this manner (89, 91, 116). Finally, the inconsistent training modality between exercise training and testing potentially diluted any fitness improvements. This contradicts the specificity principle showing that one should employ the same mode of exercise for both testing and training to maximise fitness improvements (115). To avoid this hindrance in future studies, the exercise intervention should be designed to adhere to the specificity principle (114). A limitation of not only ours, but all exercise interventions in asthma, is the lack of consistency in the exercise modality, frequency, and duration used. For example, some studies incorporated resistance training and some included group sports, whilst others used recreational activities. This lack of consistency limits the ability to compare across the studies. In addition, some studies that assessed QOL did not limit themselves to just an exercise intervention but included education classes or breathing and relaxation components (12, 13, 63). The inclusion of these additional components may have addressed other the other aspect of asthma QOL that our programme did not, however this makes our programme unique in that we can evaluate the effect of only exercise on asthma QOL.

5f. Conclusion

In conclusion, our study found that 12-weeks of aerobic exercise in adults with asthma resulted in clinically significant improvements in asthma QOL. The results of this preliminary pilot study suggest that the integration of exercise intervention programmes in the treatment of asthma may be a good adjunct to traditional therapies. Due to the nature of our study, we could not evaluate other potential mechanisms for our findings such as psychological health or attention affects associated with being in a study. Thus, future large-scale randomized control trials are necessary to evaluate other factors that may impact and mediate the relationship between exercise and asthma QOL.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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APPENDIX

A: Assessment Schedule

	Screening	Baseline	Post-Intervention
Demographics			
Exercise History	X		
Medical History	X		
Asthma Control			
ACQ	X	X	X
ACT		X	X
One week diary (bronchodilator use and nocturnal waking)	X		X
Quality of Life			
AQLQ		X	X
Pulmonary Function			
Diffusion Capacity		X	X
Lung Volumes		X	X
Spirometry		X	X
Exercise Capacity			
Bicycle (Jones stage I)		X	X

B: Journal of Asthma: Instructions for Authors

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Journal of Asthma: Advances in the Diagnosis and Management of Allergy and Asthma will provide a unique forum on all aspects of asthma and related conditions. Manuscripts on clinical immunology, allergy, pulmonary physiology, psychosomatics, pharmacology, and any of the clinical health sciences related to asthma will be considered for publication. The journal will contain timely reviews of up-to-date developments from molecular biology to government legislation.

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References

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