Exercise is associated with improved asthma control in adults

Shilpa Dogra M.Sc[1,3], Jennifer L Kuk Ph.D[3], Joseph Baker Ph.D[1,3], Veronica Jamnik Ph.D[2,3]

[1] Lifespan, Health and Performance Laboratory
[2] Human Performance Laboratory
[3] York University, Toronto, ON, Canada

Corresponding Author
Shilpa Dogra
357 Bethune College,
School of Kinesiology and Health Science,
York University,
4700 Keele St, Toronto, ON.
M3J 1P3
Canada.
Email address: shilpad@yorku.ca
Fax number: (416)736-5774

Word Count
Abstract: 199
Text: 2998

Conflicts of Interest:
Shilpa Dogra has no conflicts of interest to disclose.
Dr. Kuk has no conflicts of interest to disclose.
Dr. Baker has no conflicts of interest to disclose.
Dr. Jamnik has no conflicts of interest to disclose.

<u>Abstract:</u>

Background: Asthma control levels are suboptimal. The influence of regular exercise on asthma control is unclear.

Methods: We assessed the effects of a 12-week supervised exercise intervention followed by 12–weeks of self-administered exercise on adults with partly controlled asthma (n=21) compared to matched controls (n=15). Assessments were conducted at baseline and week 12 for both the exercise and control group and again at week 24 for the exercise group.

Results: There was a significant treatment effect in the exercise group for asthma control as measured by the Asthma Control Questionnaire (ACQ) from baseline to week 12 compared to control. A clinically significant improvement (0.5 increase) was observed for asthma quality of life and ACQ in the exercise group from baseline to week 12. There was a significant improvement in aerobic fitness from baseline to week 24 in the exercise group.

Conclusion: In conclusion, a 12-week supervised exercise intervention led to improvements in asthma control and quality of life in partially controlled asthmatics motivated to exercise. These improvements were maintained, while aerobic fitness and perceived asthma control significantly improved over an additional 12 weeks of self-administered exercise. These findings indicate that a structured exercise intervention can improve asthma control.

Key Words: exercise, asthma, quality of life, perceived asthma control, aerobic fitness

Introduction:

There is no known cure for asthma [1,2]; however, pharmacological intervention has been shown to significantly improve symptoms [3-5]. The use of inhaled corticosteroids, long acting ß$_2$-agonists, and a combination of these medications has been shown to improve asthma control [3,4] but compliance rates of greater than 80% are required to maintain this level of control [6]. Unfortunately, compliance to asthma treatment in countries where treatment is readily accessible remains poor [7,8].

Asthma control is determined by the frequency of daytime symptoms, limitation of activities, nocturnal symptoms, need for reliever medication, lung function, and exacerbations [1]. Accordingly, patients are classified as having controlled, partly controlled or uncontrolled asthma. Recent data show that only 23% of asthmatics are controlled [9] and, despite receiving specialist care, 50% are not well controlled [8]. Poor asthma control has been associated with more emergency room visits, physician visits and days spent in hospital [10].

Recent research demonstrates that health care use is higher in physically inactive asthmatics compared to physically active asthmatics [11]. This finding suggests that active asthmatics have better asthma control, if health care use is a proxy of asthma control. Exercise interventions involving adults with asthma have shown improvements in measures such as lung function [12], quality of life [13], breathlessness [14,15], and controller therapy [16] while animal models have shown improvements in airway inflammation [17,18]. A direct association between asthma control and exercise however has not yet been made.

Vollmer et al [19] reported that the activity limitation component, which includes both physical and non-physical activity, is the most powerful contributor to asthma control, suggesting that improvements in aerobic fitness may improve control in partly controlled but physically inactive asthmatics. To date, the benefits of exercise interventions have been demonstrated by medically supervised programs [16,20]. The effects of such programs on future physical activity habits are unclear; furthermore, the effects of self-administered exercise programs remain unknown. Self-administered exercise may be a more cost-effective and readily available therapy for the general population of adults with asthma. If exercise positively impacts asthma control, it may be an important adjunct therapy for adults with partly controlled asthma and poor compliance to prescribed medication.

It is therefore imperative to gain a better understanding of the effect of regular exercise on asthma control and determine whether there is a clinically relevant benefit. The purpose of the current investigation was to determine 1) whether a 12-week supervised exercise program leads to improvements in asthma control levels and aerobic fitness levels in partly controlled adults with asthma compared to a matched control (CON) group and 2) whether the exercise (EX) group would be able to maintain the benefits from the program after an additional 12 weeks of self-administered exercise.

Methods:

Participants:

Participants were recruited from the Greater Toronto Area in Ontario, Canada. Inclusion was limited to male and female adults over the age of 18 years, who were not pregnant, had a current prescription for asthma medication, and were physically inactive

as defined by the Canadian Physical Activity Guidelines[21]. All participants provided informed consent prior to testing, and the study protocol was approved by the Human Participants Review Sub-Committee of the Ethics Committee of York University.

Study Design:

The study was a non-randomized control trial. Placement in the EX group was based on availability to meet with a qualified exercise professional (CSEP-CEP) three times per week for 12 weeks and the ability to exercise uninterrupted for the study duration. All participants in the EX group were recruited in the autumn season and completed the 24 week program by March. The CON group was matched for age and sex and was provided exercise programs upon completing the control period. The CON group was recruited on a rolling intake from the autumn through to spring.

Exercise Program:

Participants in the EX group were assigned to a CSEP-CEP with whom they exercised three times/week for 12-weeks. This was followed by an additional 12-week period of self-administered exercise as prescribed by the CSEP-CEP. The self-administered program was individualized based on the participant's access to equipment, physical activity preferences, and short and long term fitness goals. The CON group was directed to maintain their current lifestyle.

The main focus of the exercise sessions was aerobic training but one set per week of strength exercises targeting the major muscle groups (chest, back, shoulders, triceps, biceps, quadriceps, hamstrings, and abdominals) were also included. The mode of aerobic exercise was based on individual preference but was limited to outdoor jogging, treadmill, recumbent or upright cycling, elliptical or rowing machines. The intensity for

4

aerobic exercise was based on maximum heart rate (HR_{max}) obtained during the aerobic fitness test. Since participants were previously sedentary, the program intensity increased progressively by 5% every three weeks from a minimum of 70% HR_{max} to a minimum of 85% HR_{max}. Participants were required to wear HR monitors (Polar S625x, Finland) during these exercise sessions to ensure that the minimum HR was achieved. They were also shown the Borg Rating of Perceived Exertion [22] scale at each 5-minute interval of exercise so that the participants understood the "feeling" associated with that intensity of exercise; this was particularly important for the self-administered exercise portion of the program. Participants were permitted to use their bronchodilators before or during exercise sessions if necessary.

Self-administered exercise programs provided to the EX group for the second 12-week period included aerobic exercise at 85% HR_{max} and musculoskeletal exercises. Participants were provided with logs which were submitted at the follow-up testing session. They were encouraged to exercise five days of the week.

Testing Sessions:

Participants were given standard instructions to follow before coming to the laboratory: 1) no short acting bronchodilators in the previous 6 hours 2) no caffeine in the previous 6 hours 3) no alcohol or heavy exercise in the previous 24 hours and 4) no smoking in the previous 8 hours. Participants were not instructed to discontinue use of controller medication, as the lung function tests and the exercise test were not intended to be diagnostic tools.

Spirometry: Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured using a handheld spirometer (MicroSpirometer, Micro Medical

Ltd, UK). The pre-bronchodilator FEV_1 was used to determine the percent predicted FEV_1, which was required for the Asthma Control Questionnaire (ACQ) [23]. Participants were asked to take their short-acting bronchodilator to ensure that the exercise test would not be terminated due to exercise-induced asthma symptoms. FEV_1 and FVC were measured 15 minutes after use of the bronchodilator and then again 10 minutes following the aerobic fitness test.

Aerobic Fitness: Participants completed an incremental aerobic fitness test (VO_2max) on a treadmill. The associated measurements (fractional concentrations of oxygen and carbon dioxide plus minute ventilation) were determined directly via the open circuit technique with discrete components (120 Litre Tissot Spirometer, Applied Electrochemistry Oxygen and Carbon Dioxide analyzers). The loading protocol varied depending on the participant's comfort level and ability to run. Participants started with a three minute walking workload and progressed from walking (3.0 - 4.0 mph) to jogging (5.0 -6.0 mph) to running (7.0 - 8.0 mph); subsequent work rates were increased by increasing the incline by 2% per work load. Participants who were unable to run completed a walking protocol that progressed from walking on a low (0-5%) grade which increased by 2% every 2 minutes. The attainment of VO_2max was confirmed when VO_2 plateaued or decreased with progressively increasing work rates. In most instances the criteria for VO_2max was volitional fatigue and therefore the aerobic fitness test did not provide a true maximum but rather a peak (VO_2peak). Peak minute ventilation (V_E) was used to calculate ventilatory reserve or Dyspnea Index (DI; $V_E/(FEV_1 x 35)$) and ventilatory efficiency (Ventilatory Equivalent for Oxygen [V_E/VO_2]) at 75% VO_{2peak} (submaximal) and at peak for each participant. The DI has been used in research related

to chronic obstructive pulmonary conditions as it is a reliable indicator of ventilatory reserve [20, 24].

Questionnaires: The main outcome measure, asthma control, was measured using the ACQ [23] and a single-item perceived asthma control question. The ACQ is a validated questionnaire wherein a score of <0.75 indicates well-controlled asthma, 0.75-1.5 denotes relatively well-controlled asthma and >1.5 indicates poorly controlled asthma. This questionnaire can be used with or without spirometric measures [23]. The single-item perceived asthma control variable was a multiple choice question with the following options for current control levels: 1) Total Control 2) Well Controlled 3) Moderately Controlled 4) Low Control and 5) Poor Control. This variable was included in the study as perceived control is significantly associated with activity restriction in adults with asthma [25]. Quality of life was assessed using the mini-Asthma Quality of Life Questionnaire (mini-AQLQ) [26] wherein higher scores are indicative of better quality of life. Additional information pertaining to demographics, asthma symptoms, and physical activity history was also collected.

Statistical Analyses:

Baseline characteristics between groups were compared using independent sample t-tests and chi squares. ANCOVAs were used to determine treatment differences between groups over the 12-week intervention adjusting for baseline values. Repeated measures ANOVAs were conducted to determine treatment effects over the 24 week period from baseline and week 12 in the EX group. Power calculations were conducted for the primary outcome. All statistics were conducted using SPSS 17.0.

Results:

A total of 66 participants were assessed for eligibility (Figure 1). Eleven were ineligible as they were physically active, while 19 declined to participate in the study. Twenty one participants were placed in the EX and 15 in the CON group. Accounting for drop-outs and loss to follow-up, a total of 18 in the EX and 12 in the CON group were included in the current analyses.

There were no differences in baseline characteristics of the participants between groups (Table 1). Lung function measures, either before or after use of bronchodilator or post-exercise, were similar between groups at baseline (Table 2). There were no changes in lung function measures expressed in terms of FEV_1/FVC or percent predicted FEV_1 after the intervention period or at the follow-up period for the EX group.

The groups differed significantly at baseline for ACQ with spirometry ($p<0.05$). Over the supervised treatment period, ACQ without spirometry significantly improved in the EX group as compared to CON (Table 3). However, ACQ score with spirometry did not improve significantly in the EX group compared to CON. There was a trend for significant improvements for perceived asthma control ($p=0.051$), submaximal V_E/VO_2 ($p=0.078$) and submaximal DI ($p=0.054$) in the EX group. With self-administered EX there was a significant improvement in mini-AQLQ and a trend toward significance ($p=0.073$) for V_E/VO_2 at peak from week 12 to week 24. Further there were significant improvements for ACQ without spirometry, mini-AQLQ, perceived asthma control, VO_2peak and submaximal DI from baseline to week 24 in the EX group. A clinically significant improvement of greater than 0.5 was observed in both the ACQ and mini-AQLQ from baseline to week 12 and was maintained over the follow-up period at week 24.

Adverse Events: One participant experienced an acute attack of asthma that required hospitalization during the self-administered exercise period; this did not occur during an exercise session. The attack was thought to be the result of illness that stemmed from a visit abroad and not due to the exercise program. This participant willingly resumed exercise and attended the follow-up fitness test at week 24. One participant injured her ankle during the self-administered exercise period. Although we cannot say with certainty that this was not a result of the prescribed exercise, the participant claimed to have previous problems with this ankle that became aggravated. No other adverse events were reported. There were no incidents related to exercise-induced asthma over the course of the intervention.

Discussion:

The effect of a 12-week supervised exercise intervention on asthma control was assessed in adults with partly controlled asthma who were interested in beginning an exercise program. Our primary finding is that a 12-week supervised exercise intervention leads to statistically and clinically significant improvements in asthma control compared to a matched control group. This may be attributed to improvements in submaximal measures (at 75%) of aerobic fitness such as V_E/VO_2 and DI. Furthermore, supervised exercise followed by a period of self-administered exercise leads to improvements in VO_2peak, quality of life and maintenance of asthma control.

Our finding that quality of life improved with supervised exercise is consistent with previous research [12,13]. However, the improvement in asthma control with supervised exercise is a novel finding and highlights the importance of encouraging exercise in this population. While previous research has concluded that exercise leads to

improvements in medication use [13], the frequency of exercise-induced asthma [27], and even lung function [12], this study is the first to show that regular exercise participation can lead to a change in overall asthma control. It is important to highlight that there were also clinically relevant improvements in mean ACQ score and mini-AQLQ score from baseline to week 12 in the EX group.

Only one previous study has attempted to assess the association between exercise and asthma control. Fanelli et al [13] conducted a 16-week exercise program in children with asthma for which the children exercised for 90 minutes twice/week. They showed significant improvements in aerobic fitness, improvements in asthma quality of life, and reduction in medication use. Although medication use is a component of asthma control, the authors did not measure overall asthma control. Our analysis fuses a validated asthma control questionnaire (ACQ), as well as perceived asthma control. Previous research has shown that greater perceived control is associated with improved measures of physical and mental health status, better quality of life, and most importantly, fewer days of restricted activity (physical and non-physical) due to asthma [25]. That we observed improvements in both measured and perceived asthma control strengthen our findings and reinforce the importance of regular exercise participation for adults with asthma.

The self-administered exercise was a unique aspect of this study. Participants in the exercise group were provided with an exercise program to execute on their own after week 12. This resulted in significant improvements in quality of life and maintenance of asthma control suggesting that after an initial supervised exercise period, partly controlled adults with asthma can independently perform exercise while maintaining the benefits. These findings are similar to those reported by Emtner et al [12], where a 10

week exercise program in well-controlled asthmatic adults led to improvements in exercise capacity, lung function and asthma severity. Interestingly, 68% of these adults with asthma were still exercising at least once per week three years later, and also had decreased medication use and emergency room visits, both of which are proxy measures of asthma control [28].

It is possible that a greater frequency, duration, or intensity of the exercise intervention was required to induce significant changes in measures of aerobic fitness; however, we believe that it was important to use an exercise intervention that is similar to the guidelines recommended by public health agencies [21,29]. These physical activity guidelines are readily accessible to the public and are easy to interpret by physicians and their patients. It is apparent that the use of these minimum physical activity recommendations as an adjunct therapy for asthma could relieve some of the health care burden associated with asthma [30,31] as well as counter the impact of poor adherence to medication [32]. Lack of significant improvements in measures of aerobic fitness may also be related to power as a sample size of 20 per group (current n = 18) would be required for 80% power at a $p < 0.05$ based on the variability within the EX group [33].

It should be emphasized that all participants in the EX group became physically active, and only two participants in the EX group did not attend 100% of the sessions, but attended over 70% of the sessions. This small increase in exercise levels led to a significant improvement in perceived and measured asthma control. These results are in line with the finding by Vollmer et al [19] indicating that activity restriction (physical and non-physical) is a powerful predictor of asthma control. This is important as poor asthma control is associated with greater healthcare use, and supervised exercise followed with

self-administered exercise may be a sustainable solution to improve asthma control and relieve some of the burden on public healthcare systems.

The results of this study should be interpreted in light of the following limitations: 1) We demonstrate changes in ACQ with the intervention, but the current analysis was underpowered for seeing treatment effects using ACQ with spirometry. Although the use of ACQ without spirometry is a valid method [23], based on previous literature [14], resting spirometric values are not expected to change with regular exercise. Therefore, use of the ACQ without spirometry is perhaps an equivalent measure for longitudinal changes with exercise. 2) We did not have any clinical measures of asthma control or severity such as peak flow variability or exhaled nitric oxide. 3) We did not have objective physical activity monitors and are therefore unable to say what level of physical activity and exercise occurred outside of the supervised sessions 4) We were unable to randomize the sample into intervention groups due to logistics pertaining to gym access and time and 5) The season in which the groups were recruited varied somewhat and may have led to the slight improvements observed in the CON group; however despite this, the EX group had a significant improvement in ACQ compared to CON.

In conclusion, we found that a 12-week supervised exercise intervention led to improvements in asthma control and quality of life in partly controlled adults with asthma who were interested in exercising. Additionally, supervised exercise followed by a period of self-administered exercise maintained the improved asthma control levels and resulted in significant improvements in aerobic fitness and perceived asthma control. These findings indicate that a structured exercise intervention can improve asthma control.

Future research should determine the feasibility of including exercise programs as an essential adjunct to asthma management programs.

Acknowledgements:

References:

1. Global Strategy for Asthma Management and Prevention. GINA Report 2006. Available at: www.ginasthma.org. Accessed on August 12th, 2009.

2. Warner JO, Naspitz CK. Third international pediatric consensus statement on the management of childhood asthma. *Pediatr Pulmonol* 1998;25:1–17.

3. O'Byrne PM, Naya IP, Kallen A, Postma DS, Barnes PJ. Increasing doses of inhaled corticosteroids compared to adding long-acting inhaled beta2-agonists in achieving asthma control. *Chest* 2008;134(6):1192-9.

4. Lalloo UG, Malolepszy J, Kozma D, Krofta K, Ankerst J, Johansen B, Thomson NC. Budesonide and formoterol in a single inhaler improves asthma control compared with increasing the dose of corticosteroid in adults with mild-to-moderate asthma. *Chest* 2003;123(5):1480-7.

5. Foresi A, Morelli MC, Catena E. Low-dose budesonide with the addition of an increased dose during exacerbations is effective in long-term asthma control. On behalf of the Italian study group. *Chest* 2000;117(2):440-6.

6. Lasmar L, Camargos P, Champs NS, Fonseca MT, Fontes MJ, Ibiapina C, Alvim C, Moura JA. Adherence rate to inhaled corticosteroids and their impact on asthma control. *Allergy* 2009;64(5):784-9.

7. Legorreta AP, Christian-Herman J, O'Connor RD, Hasan MM, Evans R, Leung KM. Compliance with national asthma management guidelines and specialty care: a health maintenance organization experience. *Arch Intern Med* 1998;158(5):457-64.

8. Gaga M, Papageorgiou N, Zervas E, Gioulekas D, Konstantopoulos S. Control of asthma under specialist care: is it achieved? *Chest* 2005;128(1):78-84.

9. Chapman KR, Boulet LP, Rea RM, Franssen E. Suboptimal asthma control: prevalence, detection and consequences in general practice. *Eur Respir J* 2008;31(2):320-5.

10. Williams SA, Wagner S, Kannan H, Bolge SC. The association between asthma control and health care utilization, work productivity loss and health-related quality of life. *J Occup Environ Med* 2009;51(7):780-5.

11. Dogra S, Baker J, Ardern CI. The role of physical activity and body mass index in the health care use of adults with asthma. *Ann Allergy Asthma Immunol* 2009;102(6):462-8.

12. Emtner M, Herala M, Stålenheim G. High-intensity physical training in adults with asthma. A 10-week rehabilitation program. *Chest* 1996;109(2):323-30.

13. Fanelli A, Cabral AL, Neder JA, Martins MA, Carvalho CR. Exercise training on disease control and quality of life in asthmatic children. *Med Sci Sports Exerc* 2007;39(9):1474-80.

14. Cochrane LM, Clark CJ. Benefits and problems of a physical training programme for asthmatic patients. *Thorax* 1990;45(5):345-51.

15. Clark CJ. The role of physical training in asthma. *Chest* 1992;101(5 Suppl):293S-298S.

16. Neder JA, Nery LE, Silva AC, Cabral AL, Fernandes AL. Short-term effects of aerobic training in the clinical management of moderate to severe asthma in children. *Thorax* 1999;54(3):202-6.

17. Pastva A, Estell K, Schoeb TR, Atkinson TP, Schwiebert LM. Aerobic exercise attenuates airway inflammatory responses in a mouse model of atopic asthma. *J Immunol* 2004;172(7):4520-6.

18. Vieira RP, Claudino RC, Duarte AC, Santos AB, Perini A, Faria Neto HC, Mauad T, Martins MA, Dolhnikoff M, Carvalho CR. Aerobic exercise decreases chronic allergic lung inflammation and airway remodeling in mice. *Am J Respir Crit Care Med* 2007;176(9):871-7.

19. Voller WM, Markson LE, O'Connor E, Frazier EA, Berger M, Buist AS. Association of asthma control with health care utilization: a prospective evaluation. *Am J Respir Crit Care Med* 2002;165(2):195-9.

20. Hallstrand TS, Bates PW, Schoene RB. Aerobic conditioning in mild asthma decreases the hyperpnea of exercise and improves exercise and ventilatory capacity. *Chest* 2000;118(5):1460-9.

21. Public Health Agency of Canada. Canada's Physical Activity Guide to Healthy Active Living. http://www.phac-aspc.gc.ca/pau-uap/paguide/. Accessed on August 12th, 2009.

22. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14(5):377-81.

23. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;14(4):902-7.

24. Fink G, Moshe S, Goshen J, Klainman E, Lebzelter J, Spitzer S, Kramer MR. Functional evaluation in patients with chronic obstructive pulmonary disease: pulmonary function test versus cardiopulmonary exercise test. *J Occup Environ Med* 2002;44(1):54-8.

25. Calfee CS, Katz PP, Yelin EH, Iribarren C, Eisner MD. The influence of perceived control of asthma on health outcomes. *Chest* 2006;130(5):1312-8.

26. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the mini asthma quality of life questionnaire. *Eur Respir J* 1999;14(1):32-8.

27. Bonsignore MR, La Grutta S, Cibella F et al. Effects of exercise training and montelukast in children with mild asthma. *Med Sci Sports Exerc* 2008;40(3):405-12.

28. Emtner M, Finne M, Stålenheim G. A 3-year follow-up of asthmatic patients participating in a 10-week rehabilitation program with emphasis on physical training. *Arch Phys Med Rehabil* 1998;79(5):539-44.

29. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, Bauman A. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc* 2007;39(8):1423-34.

30. Bahadori K, Doyle-Waters MM, Marra C, Lynd L, Alasaly K, Swiston J, FitzGerald JM. Economic burden of asthma: a systematic review. *BMC Pulm Med* 2009;9:24.

31. Cisternas MG, Blanc PD, Yen IH, Katz PP, Earnest G, Eisner MD, Shiboski S, Yelin EH. A comprehensive study of the direct and indirect costs of adult asthma. *J Allergy Clin Immunol* 2003;111(6):1212-8.

32. Maneechotesuwan K, Essilfie-Quaye S, Kharitonov SA, Adcock IM, Barnes PJ. Loss of control of asthma following inhaled corticosteroid withdrawal is associated with increased sputum interleukin-8 and neutrophils. *Chest* 2007;132(1):98-105.

33. Overall JE, Doyle SR. Estimating sample sizes for repeated measurement designs. *Controlled Clin Trials* 1994; 15:100-123.

Table 1: Baseline characteristics of the Control and Exercise group. Data are presented as mean ± standard error.

	Control Group (n=12)	Exercise Group (n=18)
Age	34.0±3.4	34.2±3.2
Sex (Female)	9	13
BMI	24.4±1.1	25.8±0.9
Prescribed Preventive Medicine	9	11
Prescribed Rescue Medicine	12	16
Presence of EIA	11	14
Presence of Allergies	11	17
Never Smoked	4	12
Pre BD FEV$_1$	2.86±0.18	2.96±0.26

BMI: Body Mass Index; EIA: Exercise Induced Asthma; BD: bronchodilator; FEV$_1$: Forced Expiratory Volume in 1 second.

Table 2: Lung Function parameters by group for each time point of the intervention

	Control Group		Exercise Group		
	Baseline (n=12)	Week 12 (n=11)	Baseline (n=18)	Week 12 (n=18)	Week 24 (n=16)
Pre BD FEV$_1$/FVC	82.6±2.2	80.2±2.1	80.2±2.1	78.5±2.26	78.4±2.8
Post BD FEV$_1$/FVC	84.1±2.5	83.2±2.1	81.8±2.0	82.8±2.0	81.0±2.6
Post Exercise FEV$_1$/FVC	84.9±2.8	84.1±2.7	83.4±2.4	82.7±2.8	81.5±2.9
FEV$_1$ % predicted Pre BD	84.4±4.7	85.5±4.2	84.5±2.8	81.3±3.7	78.6±4.3
FEV$_1$ % predicted Post BD	90.5±4.9	92.1±4.6	88.9±3.7	88.9±2.9	83.6±4.1
FEV$_1$ % predicted Post Exercise	87.8±4.7	87.2±4.2	87.3±3.6	84.2±3.6	80.0±4.7

BD: Bronchodilator; FEV$_1$: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity. All values are presented as percentages.

Table 3: Main Outcome Variables at Baseline and Follow-Up

	Control Group		Exercise Group		
	Baseline **(n=12)**	**Week 12** **(n=11[†])**	**Baseline** **(n=18)**	**Week 12** **(n=18)**	**Week 24** **(n=15[‡])**
ACQ Questionnaire	0.90±0.15	0.99±0.16[†]	1.30±0.19	0.72±0.10[*]	0.72±0.17[‡][***]
ACQ with Spirometry	1.06±0.10[#]	0.80±0.14	1.37±0.21	0.95±0.11	1.02±0.18
Perceived Asthma Control	2.33±0.19	2.25±0.18[†]	2.56±0.15	1.94±0.10[^]	2.00±0.13[‡][***]
Mini-AQLQ	5.79±0.15	5.90±0.17[†]	5.01±0.21	5.84±0.17	6.11±0.21[‡][**,***]
Maximal VO_2	2.66±0.27	2.77±0.29	2.63±0.20	2.88±0.21	3.00±0.27[***]
Submaximal V_E/VO_2	23.21±0.73	23.64±0.80	24.89±1.08	23.78±0.74[^]	24.35±0.90
Maximal V_E/VO_2	28.46±0.88	28.65±1.39	28.84±1.02	27.44±0.78	28.48±1.17
Submaximal DI	0.42±0.03	0.42±0.02	0.45±0.02	0.48±0.03[^]	0.54±0.03[***]
Maximal DI	0.68±0.04	0.69±0.04	0.73±0.04	0.77±0.04	0.84±0.04

ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; VO_2: Oxygen uptake; V_E: Ventilation; DI: Dyspnea Index

[†]n=12 for paper measurements only; [‡]n=17 for paper measurements only; [#] significant differences at baseline between control and exercise group; *$p<0.05$ between groups from T1 to T2; ** $p< 0.05$ within exercise group from T2 to T3; ***$p<0.05$ within exercise group from T1 to T3; ^ statistical trend from T1 to T2; $p<0.10$.
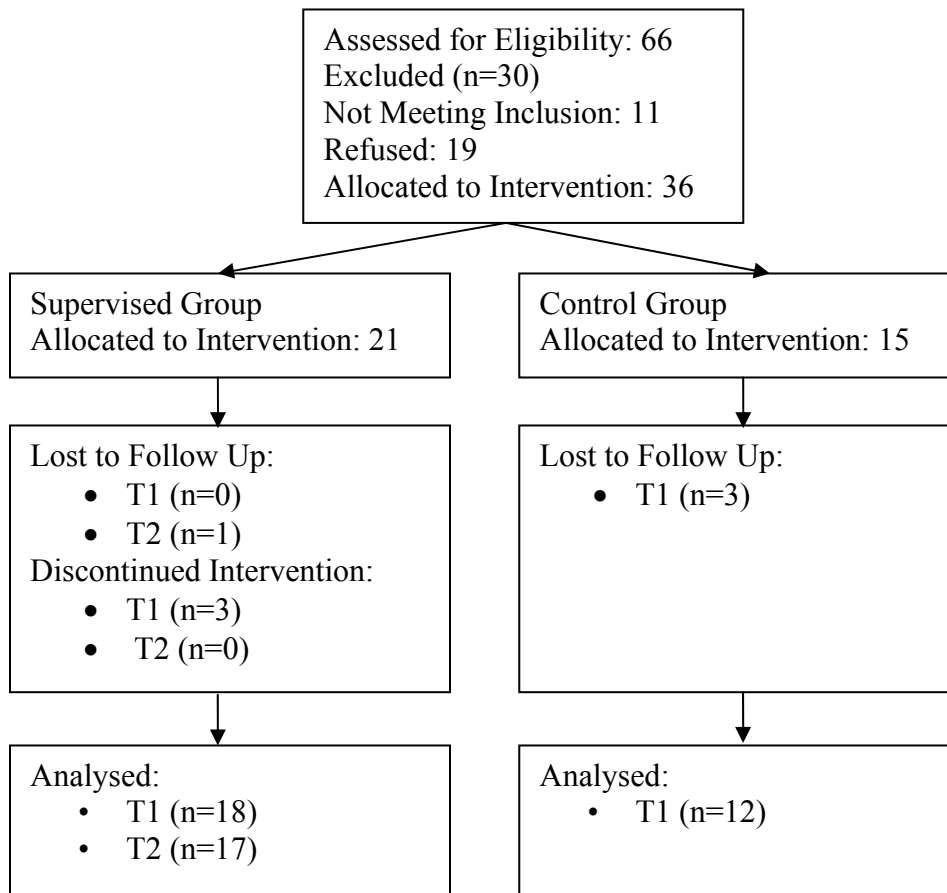
```
                    ┌─────────────────────────────────────┐
                    │ Assessed for Eligibility: 66        │
                    │ Excluded (n=30)                     │
                    │ Not Meeting Inclusion: 11           │
                    │ Refused: 19                         │
                    │ Allocated to Intervention: 36       │
                    └─────────────────────────────────────┘
```

```
┌──────────────────────────────┐        ┌──────────────────────────────┐
│ Supervised Group             │        │ Control Group                │
│ Allocated to Intervention: 21│        │ Allocated to Intervention: 15│
└──────────────────────────────┘        └──────────────────────────────┘
```

```
┌──────────────────────────────┐        ┌──────────────────────────────┐
│ Lost to Follow Up:           │        │ Lost to Follow Up:           │
│   • T1 (n=0)                 │        │   • T1 (n=3)                 │
│   • T2 (n=1)                 │        │                              │
│ Discontinued Intervention:   │        │                              │
│   • T1 (n=3)                 │        │                              │
│   • T2 (n=0)                 │        │                              │
└──────────────────────────────┘        └──────────────────────────────┘
```

```
┌──────────────────────────────┐        ┌──────────────────────────────┐
│ Analysed:                    │        │ Analysed:                    │
│   • T1 (n=18)                │        │   • T1 (n=12)                │
│   • T2 (n=17)                │        │                              │
└──────────────────────────────┘        └──────────────────────────────┘
```

Figure 1