Berntsen, S., Carlsen, K. C. L., Anderssen, S. A., Mowinckel, P., Carlsen, K.-H. (2013). Factors associated with aerobic fitness in adolescents with asthma. *Respiratory Medicine, 107*, 1164-1171.

Factors associated with aerobic fitness in adolescents with asthma

Sveinung Berntsen [1], Karin C. Lødrup Carlsen [1,3], Sigmund A. Anderssen [2],

Petter Mowinckel [1], Kai-Håkon Carlsen [1,2,3].

[1]Department of Paediatrics, Oslo University Hospital; Oslo; Norway

[2] Department of Sports Medicine, Norwegian School of Sport Sciences; Oslo; Norway

[3] Faculty of Medicine, University of Oslo; Oslo; Norway

The study is performed within the ORAACLE (the Oslo Research Group of Asthma and Allergy in Childhood; the Lung and Environment) which is part of the GA²LEN network. GA²LEN is a project of the EU 6th framework programme for research contract n° FOOD-CT-2004-506378.

Present address for corresponding author and reprint request:

Sveinung Berntsen,

Department of Public Health, Sport and Nutrition,
Faculty of Health and Sport Sciences
University of Agder
Postal address: Post Box 422, NO-4604 Kristiansand, Norway
Tel: +47 38 14 10 45
E-mail: sveinung.berntsen@uia.no

Title for running head: Aerobic fitness in adolescents with asthma

Word counts: Manuscript (not including abstract, references, tables and acknowledgements): 2951

Abstract: 250

There is no competing or conflicts of interests.

Abstract

Background: In adolescents with asthma, information on factors associated with cardiorespiratory fitness levels is limited. The present study aimed to determine if objectively measured physical activity as well as potential relevant factors such as lung function, asthma exacerbations, use of inhaled corticosteroids or skin fold thickness are associated with direct measurements of peak oxygen uptake ($\dot{V}O_2peak$) in adolescents with asthma.

Methods: From a nested case-control study at 13-years in the Environment and Childhood Asthma birth cohort study in Oslo, Norway, 86 13-years old adolescents with and 76 without asthma performed maximal running on a treadmill with $\dot{V}O_2peak$ measured. The sum of four skin fold thicknesses was recorded, followed by wearing an activity monitor for four consecutive days. Lung function was measured by maximum forced expiratory flow-volume curves and body plethysmography. Asthma exacerbations and use of medication were registered by parental structured interview. Data were analyzed using multiple regression analysis.

Results: Vigorous physical activity (coefficients with 95% confidence intervals; 1.73 (0.32, 3.14)) and skin fold thickness -0.35 (-0.41, -0.28)) were significantly associated with $\dot{V}O_2peak$ in adolescents with asthma. Neither use of inhaled corticosteroids, lung function nor number of asthma exacerbations was associated with $\dot{V}O_2peak$ when taking physical activity and skin fold thickness into account. In the adolescents without asthma only skin fold thicknesses was negatively associated with $\dot{V}O_2peak$ -3.5 (-4.1, -2.8).

Conclusions: $\dot{V}O_2peak$ appears to be determined by vigorous physical activity level in Norwegian adolescents with asthma and not by asthma-related factors such as use of inhaled corticosteroids, lung function nor number of asthma exacerbations.

Keywords: Body fat, Exacerbations, Lung function, Physical activity, Robust regression

Introduction

Physical activity (1-3) and improved cardiorespiratory fitness (4) are reported to have positive effects on self-esteem and psychological functioning in children with asthma, and quality of life and morbidity improved with low intensity asthma-education-physical training programmes (1). In a recently updated Cochrane review, physical training was reported to improve cardiorespiratory fitness, health-related quality of life as well as asthma symptoms without changing baseline lung function in children and adolescents with asthma (5). Participation in regular physical activity and training also plays an important role in the rehabilitation of asthmatic children because aerobic conditioning lessens the risk of an asthma attack by reducing the ventilatory requirement for exercise (6). Importantly, improvements in asthma control have been associated with significant improvements in moderate-vigorous physical activity level in children with newly diagnosed asthma (7).

Cardiorespiratory fitness in adolescents with asthma is reported to be reduced (8-10) in adolescents with severe asthma disease (9). On the other hand, others found no association between asthma severity and cardiorespiratory fitness, but rather to self-perceivement of physical capability (11). The reduced cardiorespiratory fitness among subjects with asthma has been explained by physical inactivity (12), with the possibility of obtaining normal cardiorespiratory fitness for the majority of subjects with asthma after participation in a physical rehabilitation program or through obtaining improved asthma control (7;13). The association between asthma and low cardiorespiratory fitness or physical activity levels reported in some studies (8;9;14) can also be due to poor asthma control including insufficient medical treatment, asthma exacerbations and reduced lung function (15). Subjects with asthma may limit the intensity of their physical activity because of fear of exercise-induced dyspnoea (16).

In adolescents with asthma, little is known with respect to factors that may limit cardiorespiratory fitness levels. In addition, it is unclear to what extent cardiorespiratory fitness is influenced by physical activity or exercise training, asthma-related factors such as anti-inflammatory asthma medication, lung function or number of exacerbations in children and adolescents with asthma.

The present study aimed to determine if objectively measured levels of physical activity as well as potential relevant factors such as lung function, asthma exacerbations, use of inhaled corticosteroids or skin fold thickness, as a measure of body fat, are associated with direct measurements of peak oxygen uptake ($\dot{V}O_2peak$) in adolescents with asthma.

Subjects and methods

Study design

The present nested case-control study is a part of the birth cohort “Environment and Childhood Asthma” study in Oslo, described elsewhere (17). In short, this prospective population based birth cohort study conducted clinical investigations at birth (including lung function measured in 802 neonates), at two years children with recurrent bronchial obstruction and their healthy counterparts born closest in time were investigated in a nested case-control study, at ten years of age, all children attending the lung function measurements at birth and/or the 2-year clinical investigation; all together 1019 children were investigated. Inclusion to the 13-year follow-up was limited to a nested case-control group of children. Invitations were sent to all those defined with current asthma (n= 147) vs. 163 children matched by birth date but otherwise randomly chosen with no asthma or other lower respiratory tract disease at 10 years (for definitions see below) (18). This 13-year follow up study conducted between October 2005 and June 2006 consisted of one day of clinical investigation and four days of home monitoring including adolescents with and without asthma.

The study was approved by the Regional Committees (South-Norway; S-04331) for Medical and Health Research Ethics and the Data Inspectorate of Norway. Written informed consent was obtained from the participating children and their parents.

Subjects

Of the 310 children (47 % with asthma) invited for the present study 174 children (56%) attended, of whom 86 (49%) had asthma (59 boys) and 76 (41 boys) were control subjects. *Asthma* was defined by at least two of the following three criteria fulfilled (19):

1. Dyspnoea, chest tightness and/or wheezing without having a common cold

2. A doctors diagnosis of asthma

3. Use of asthma medication.

Exclusion criteria were any other overt disease which might influence the results, respiratory tract infection during the last 3 weeks before attending the visit, and use of medication which could interfere with the tests. Participants used their regular medications. Final analyses included all 162 adolescents with both accepted aerobic fitness test as well as physical activity data (at least one weekday and one weekend day).

Methods

The present study included a parental structured interview including central International Study of Asthma and Allergies in Childhood questions related to airways symptoms **(asthma exacerbations were based on the question asking for "number of attacks of wheezing last 12 months")**, in addition to detailed questions of medication use, lifestyle and diseases (19).

Anthropometric measurements

Body height and length with body mass calculated, were measured with the subject wearing light clothing and without shoes (Seca 709, Germany). Height was measured using a stadiometer. Overweight and obesity were calculated according to Cole et al (20). Pubertal stage was assessed by means of Tanner criteria (21). Skin fold thickness was measured with a Harpenden skinfold caliper (Holtain, Dyfed, UK) at the biceps, triceps, subscapular and supra-iliac region and given as the sum of the four measurements.

Lung function

Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and forced expiratory flow at 50% of FVC (FEF_{50}) were measured by maximum forced expiratory flow-volume curves (Masterlab, Erich Jaeger® GmbH & Co KG, Würzburg, Germany) and total lung capacity (TLC) and residual volume (RV) were measured with a body plethysmograph (Masterlab BodyPro, Erich Jaeger® GmbH & Co KG, Würzburg, Germany) according to criteria of European Respiratory Society (22;23). Reference values by Zapletal et al. (24) were used for calculation of predicted values.

Physical activity

Habitual physical activity was recorded 24 hours a day with SenseWear™ Pro_2 Armband (BodyMedia Inc., Pittsburgh, PA, USA) for four consecutive days as described previously (18). SenseWear™ Pro_2 Armband (Armband), contains a two-axis accelerometer, a heat flux sensor, a galvanic skin response sensor, a skin temperature sensor and a near-body ambient temperature sensor, and collects minute-by-minute, storing data, for up to 14 days. The cut off points defining moderate and vigorous intensity physical activity were above 3 and 6 metabolic equivalents (METs; 1 MET correspond to an oxygen consumption of 3.5 ml · kg^{-1} · min^{-1}), respectively (25). The data from the monitor was downloaded and analysed with software developed by the manufacturer (Innerview Professional Research Software Version 5.1, BodyMedia Inc., Pittsburgh, PA, USA).

Cardiopulmonary exercise testing

Highest recorded oxygen uptake ($\dot{V}O_2$ peak) expressed in ml · kg^{-1} · min^{-1} during treadmill running (Woodway ELG 2, Woodway Gmbh, Weil am Rhein, Germany) until exhaustion was measured (18). Heart rate (HR) was recorded every minute (Polar Vantage, Polar Electro KY, Kempele, Finland). Minute ventilation ($\dot{V}E$), respiratory exchange ratio (RER) and oxygen uptake ($\dot{V}O_2$) were measured and recorded every minute after four minutes of running using an oxygen analyzer with mixing chamber (Oxycon Champion, Erich Jaeger® GmbH & Co

KG, Hoechberg, Germany). Calibration was conducted before each test. The main criterion for having reached maximal effort was a subjective assessment by the test leader that the participant had reached his or her maximal effort. The second criterion was a RER above 1.00, HR above 190 beats · min^{-1} or reporting perceived exertion (RPE) above 17 using the Borg-RPE-Scale (26).

Statistical analyses

Demographic data are given as mean values with standard deviation unless otherwise stated and results as mean with 95% confidence intervals (CI). Chi-square tests and independent t-test were used to analyse differences between groups. Physical activity data were adjusted for mean hours each day the Armband was worn. Robust multiple regression (27), Huber's method (C=1.345) was applied to assess whether moderate and vigorous physical activity, skin fold thickness, use of inhaled corticosteroids, number of asthma exacerbations and lung function were related to $\dot{V}O_2$ peak. First stratified analyses (asthma vs. non-asthma) were carried out checking whether use of inhaled corticosteroids or number of asthma exacerbations (adolescents without asthma did not use inhaled corticosteroids nor reported asthma exacerbations) were associated with $\dot{V}O_2$ peak. Thereafter analyses including all participants were performed. All multivariate models included adjustments for age, gender and puberty, when relevant. The dependent variables were removed in a step-down fashion as suggested by Hosmer and Lemeshow (28). Statistical significance level was set to 5%. Statistical analyses were performed with Statistical Package for Social Sciences Version 15.0 (SPSS, Chicago, IL, USA) and Number Cruncher Statistical System 2007 Version 07.1.12 (NCSS, LLC. Kaysville, Utah, USA.

Results

Adolescents with and without asthma were similar with respect to moderate- and vigorous physical activity, skin fold thickness, height, FEV_1 (%predicted), TLC (%predicted) and RV/TLC. However, adolescents with asthma had significantly lower FEV_1/FVC, FEF_{50} (%predicted) and higher body mass compared to adolescents without asthma (P<0.05) (table 1). Among the included boys 69% had asthma vs. 54 % of the girls, although not significantly different. Asthma-related factors such as use of medications, number of asthma exacerbations last year as well as activity limitations due to their asthma are reported in table 1. One of adolescents with asthma reported active daily smoking vs. none of the children without asthma. The activity monitor was used for more hours during week- than during weekend days (mean and 95% confidence intervals; 21.2 (20.8-21.5) vs. 16.4 (15.6-17.2) hours · day^{-1}), similar in the two groups, with recordings for four days in 95% of the subjects.

Adolescents with and without asthma did nor differ significantly with respect to $\dot{V}E$ peak, RERpeak, RPE peak, HRpeak and $\dot{V}O_2$peak (table 2).

$\dot{V}O_2$peak was higher in adolescents with asthma using inhaled corticosteroids last year, although not significantly (54.9 (50.2, 54.5) vs. 54.9 (52.0, 57.8) ml · kg^{-1}· min^{-1} ;P=0.14). Adolescents with asthma reporting four or more periods with asthma exacerbations had lower $\dot{V}O_2$peak compared to adolescents without symptoms, although not significantly ((51.1 (46.7, 55.7) vs. 55.2 (52.5, 58.0) ml · kg^{-1}· min^{-1}; P=0.13)). In stratified analysis including only adolescents with asthma, use of inhaled corticosteroids and number of asthma exacerbations in the last year were not associated with $\dot{V}O_2$peak in adolescents with asthma. Moderate physical activity (R^2 = 0.03; P=0.05) and vigorous physical activity (R^2 = 0.14; P<0.001), skin fold thickness (R^2 = 0.44; P<0.001), TLC (R^2 = 0.03; P=0.04), were all associated with

$\dot{V}O_2$peak in robust *bi-variate regression analysis* including all children (table 3). However, moderate physical activity was *negatively* associated with $\dot{V}O_2$peak . Total physical activity (moderate *and* vigorous) was weakly associated (0.79 (0.11, 1.46); *P*=0.02) with $\dot{V}O_2$peak explaining 4% of the variability. Although FEF_{50} and FEV_1 were not associated with $\dot{V}O_2$peak overall, a significant interaction between asthma and FEF_{50} demonstrated that FEF_{50} was negatively associated with $\dot{V}O_2$peak in adolescents with asthma only (table 3). FEF_{50} was also positively associated with $\dot{V}$Epeak (*P*=0.02) in a gender adjusted multivariate analysis explaining 14% of the variability.

In *robust multiple regression analysis*, physical activity (moderate and vigorous), skin fold thickness and gender explained 59% of the variability in $\dot{V}O_2$peak . Moderate physical activity was a confounder, influencing vigorous physical activity, although not associated with $\dot{V}O_2$peak . Vigorous physical activity was associated with $\dot{V}O_2$peak in adolescents with asthma only (interaction between asthma and vigorous physical activity) (table 3). A 60 minutes daily increase in vigorous physical activity was associated with 1.73 (0.32, 3.14) ml · $kg^{-1} \cdot min^{-1}$ increase in $\dot{V}O_2$peak in adolescents with asthma when adjusted for skin fold thickness, moderate physical activity and gender. Skin fold thickness was negatively associated (*P*<0.001) with $\dot{V}O_2$peak in both groups (table 3).

Discussion

In the present study, vigorous physical activity level was positively and skin fold thickness negatively associated with $\dot{V}O_2$peak in adolescents with asthma. In the adolescents without asthma, skin fold thickness but *not* vigorous physical activity was negatively associated with $\dot{V}O_2$peak . $\dot{V}O_2$peak was not associated with use of inhaled corticosteroids, lung function nor the number of asthma exacerbations in the last months among adolescents with asthma.

A positive association between physical activity and $\dot{V}O_2$ peak in asthmatics has been reported previously (10;12;29;30), whereas Pianosi et al. (11) could not find any association. However we are not aware of studies including objective measurements of physical activity and direct measurements of $\dot{V}O_2$peak . Vahlkvist et al. (10) used an activity monitor in their study; however, cardiorespiratory fitness was estimated from maximal power output during an maximal bicycle ergometer test.

In a systematic review (31), activity or training of high intensity was highlighted as important for improvement in cardiorespiratory fitness in children. The present study confirms the importance of *vigorous physical activity* for improvements in $\dot{V}O_2$peak in adolescents with asthma as well. However, 60 minutes daily increase in vigorous physical activity was associated with less than 2 ml · kg^{-1}· min^{-1} increase in $\dot{V}O_2$peak in children with asthma when adjusted for skin fold thickness, moderate physical activity and gender.

Physical inactivity due to exercise induced bronchoconstriction is suggested as one explanation for the lower aerobic fitness in adolescents with asthma (12). Previous reports also indicate that both children with severe and also uncontrolled asthma with low levels of cardiorespiratory fitness can achieve a normal fitness after participation in a physical rehabilitation program under optimal control of their asthma (10;13). The association between asthma and low cardiorespiratory fitness or physical activity levels reported in some studies (8;9;14) can also be due to poor asthma control, or due to children not wanting to participate in physical activity due to anticipation of EIB (7;15). Brasholt et al. (32) reported recently physical activity level to be independent of asthma diagnosis in pre-schoolers; however, physical activity level was reduced with increasing bronchial responsiveness, illustrating the importance of optimal asthma control. Subjects with asthma may limit the intensity of their physical activity because of anticipated exercise-induced dyspnoea (16). However, engagement in significant levels of physical activity has been reported to lead to improved detection of asthma; particularly exercise-induced asthma (33). The association can also be bidirectional, with low fitness leading to more asthma symptoms, which would then, in turn, lead to decreased effort and even lower fitness level. Adolescents with asthma in the present study were fit and had high physical activity levels. Use of anti-inflammatory asthma medications and optimal asthma control may induce favourable conditions for a physically active lifestyle and influence physical activity levels and further their level of cardiorespiratory fitness (10;34). However, in the final model asthma-related factors such as use of inhaled corticosteroids, lung function and number of exacerbations were not associated with $\dot{V}O_2peak$. If asthma is well controlled, the level of physical activity thus may be more important than the disease per se in determining $\dot{V}O_2peak$.

As reported by others (29;30), we found no association between *lung function* and $\dot{V}O_2peak$ when taking physical activity and skin fold thickness into account. In contrast Wong et al. (8) reported a negative association between FEV_1 and $\dot{V}O_2peak$. Inconsistencies between studies may be related to different study populations and methods of aerobic fitness measurements. The majority of adolescents with asthma in the present study had lung function values (FEV_1 and TLC) comparable to adolescents without asthma, and only FEV_1/FVC and FEF_{50} was reduced. The high FEV_1-values could be a result of anti-inflammatory asthma medications and optimal asthma control. Furthermore, no adolescents with asthma included in the present study suffered from severe asthma according to previously published definitions (35). However, the positive association between FEF_{50} and $\dot{V}E$peak in adolescents with asthma may indicate expiratory flow limitations during high intensity exercise forcing them to utilize a larger fraction of the ventilatory capacity (36). Exercise-induced flow limitations are reported even in well-controlled subjects with asthma (37). However, baseline lung function may not reflect lung function during high intensity exercise in subjects with asthma illustrating the complexity of multiple factors operating during exercise (36). Unfortunately, we did not record tidal flow-volume loops during exercise in the participating adolescents, and thus cannot assess this.

Skin fold thickness, body fat or body composition have also previously been described as important negatively factors associated with $\dot{V}O_2$peak or aerobic fitness in children and adolescents with (11;38) and without asthma (39;40). A high fat mass combined with low muscle mass is reported to explain almost 50% of the variability in $\dot{V}O_2$peak (39;40), confirming the findings of the present study with 44% of the variability in $\dot{V}O_2$peak explained by skin fold thickness.

The main *strengths* of the present study are the objective measurements of physical activity and direct and maximal testing of cardiorespiratory fitness. Physical activity monitors give reliable measures of physical activity and having advantages compared to self-report with recall biases. The strength of the association depends highly on the quality of both the fitness and the physical activity assessment. Unfortunately, only a little more than 50% of the invited subjects attended the study. However, the distribution of children with and without asthma was generally similar to that of the entire invited group, and the associations we described are therefore likely to reflect what may have been found with a higher attendance rate. Furthermore, we performed only one time-point of objectively measured physical activity level that may not be representative of children's physical activity level over the previous last years. **Unfortunately we do not have quality of life data nor were using the asthma control questionnaire in the present study. However, based on the definition of Lang et al. (35) none of our adolescents had severe asthma. It cannot be ruled out whether asthma-related factors such as use of inhaled corticosteroids, lung function or number of exacerbations influence aerobic fitness in groups of children or adolescents with more severe asthma or for which control is not achieved.**

In *conclusion*, $\dot{V}O_2$peak appears to be determined by vigorous physical activity level in Norwegian adolescents with asthma and not by asthma-related factors such as use of inhaled corticosteroids, lung function nor number of exacerbations.

Acknowledgements

The ECA-study was sponsored initially by the Norwegian Research Council, and the 10-year follow up has been sponsored by The University of Oslo, The Norwegian Foundation for Health and Rehabilitation, The Norwegian Association for Asthma and Allergy, the Kloster foundation, Voksentoppen BKL, the Norwegian Research Council, Astra-Zeneca, Pharmacia and the Hakon group. The present study was supported by grants from the Eastern Norway Regional Health Authority. The authors would like to thank Rune Hageberg, Anne Kørner Bueso and Solveig Knutsen for assisting in the study.

AUTHOR`S CONTRIBUTION: SB; designed study, collected data, analyzed data, wrote paper. KCLC; designed study, wrote paper**.** SAA; designed study, wrote paper. PM; designed study, analyzed data, wrote paper**.** KHC; designed study, wrote paper**.**

References

(1) Flapper BC, Duiverman EJ, Gerritsen J, Postema K, van der Schans CP. Happiness to be gained in paediatric asthma care. Eur Respir J 2008 Dec;32(6):1555-62.

(2) Carlsen KH. Rehabilitation in asthma. In: Donner CF, Ambrosino N, Goldstein R, editors. Pulmonary rehabilitation. 1 ed. London: Hodder Arnold; 2005. p. 249-58.

(3) Pedersen BK, Saltin B. Evidence for prescribing exercise as therapy in chronic disease. Scand J Med Sci Sports 2006 Feb;16 Suppl 1:3-63.

(4) Strunk RC, Mrazek DA, Fukuhara JT, Masterson J, Ludwick SK, LaBrecque JF. Cardiovascular fitness in children with asthma correlates with psychologic functioning of the child. Pediatrics 1989 Sep;84(3):460-4.

(5) Chandratilleke MG, Carson KV, Picot J, Brinn MP, Esterman AJ, Smith BJ. Physical training for asthma. Cochrane Database Syst Rev 2012;5:CD001116.

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

(7) Vahlkvist S, Inman MD, Pedersen S. Effect of asthma treatment on fitness, daily activity and body composition in children with asthma. Allergy 2010 Nov;65(11):1464-71.

(8) Wong TW, Yu TS, Wang XR, Robinson P. Predicted maximal oxygen uptake in normal Hong Kong Chinese schoolchildren and those with respiratory diseases. Pediatr Pulmonol 2001 Feb;31(2):126-32.

(9) Varray A, Mercier J, Savy-Pacaux AM, Prefaut C. Cardiac role in exercise limitation in asthmatic subjects with special reference to disease severity. Eur Respir J 1993 Jul;6(7):1011-7.

(10) Vahlkvist S, Pedersen S. Fitness, daily activity and body composition in children with newly diagnosed, untreated asthma. Allergy 2009 Nov;64(11):1649-55.

(11) Pianosi PT, Davis HS. Determinants of physical fitness in children with asthma. Pediatrics 2004 Mar;113(3 Pt 1):e225-e229.

(12) Fink G, Kaye C, Blau H, Spitzer SA. Assessment of exercise capacity in asthmatic children with various degrees of activity. Pediatr Pulmonol 1993;15:41-3.

(13) Ludwick SK, Jones JW, Jones TK, Fukuhara JT, Strunk RC. Normalization of cardiopulmonary endurance in severely asthmatic children after bicycle ergometry therapy. J Pediatr 1986 Sep;109(3):446-51.

(14) Lang DM, Butz AM, Duggan AK, Serwint JR. Physical activity in urban school-aged children with asthma. Pediatrics 2004 Apr;113(4):e341-e346.

(15) Croft D, Lloyd B. Asthma spoils sport for too many children. Practitioner 1989 Jul 8;233(1472):969-71.

(16) Malkia E, Impivaara O. Intensity of physical activity and respiratory function in subjects with and without bronchial asthma. Scand J Med Sci Sports 1998 Feb;8(1):27-32.

(17) Lodrup Carlsen KC. The environment and childhood asthma (ECA) study in Oslo: ECA-1 and ECA-2. Pediatr Allergy Immunol 2002;13 Suppl 15:29-31.

(18) Berntsen S, Carlsen KC, Anderssen SA, Mowinckel P, Hageberg R, Bueso AK, et al. Norwegian adolescents with asthma are physical active and fit. Allergy 2009 Mar;64(3):421-6.

(19) Carlsen KCL, Haland G, Devulapalli CS, Munthe-Kaas M, Pettersen M, Granum B, et al. Asthma in every fifth child in Oslo, Norway: a 10-year follow up of a birth cohort study. Allergy 2006;61(4):454-60.

(20) Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000 May 6;320(7244):1240-3.

(21) Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child 1976 Mar;51(3):170-9.

(22) Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J 2005 Aug;26(2):319-38.

(23) Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J 2005 Sep;26(3):511-22.

(24) Zapletal A, Paul T, Samanek M. Lung function in children and adolescents methods, reference values. Basel: Karger; 1987.

(25) Ridley K, Ainsworth BE, Olds TS. Development of a Compendium of Energy Expenditures for Youth. Int J Behav Nutr Phys Act 2008 Sep 10;5(1):45.

(26) Borg G. Perceived exertion as an indicator of somatic stress. Scand J Rehabil Med 1970;2(2):92-8.

(27) Hamilton LC. Regression with graphics: a second course in applied statistics. Belmont, Calif.: Duxbury Press; 1992.

(28) Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed ed. New York: Wiley; 2000.

(29) Santuz P, Baraldi E, Filippone M, Zacchello F. Exercise performance in children with asthma: is it different from that of healthy controls? Eur Respir J 1997 Jun;10(6):1254-60.

(30) Garfinkel SK, Kesten S, Chapman KR, Rebuck AS. Physiologic and nonphysiologic determinants of aerobic fitness in mild to moderate asthma. Am Rev Respir Dis 1992 Apr;145(4 Pt 1):741-5.

(31) Baquet G, Van Praagh E, Berthoin S. Endurance training and aerobic fitness in young people. Sports Med 2003;33(15):1127-43.

(32) Brasholt M, Baty F, Bisgaard H. Physical activity in young children is reduced with increasing bronchial responsiveness. J Allergy Clin Immunol 2010 May;125(5):1007-12.

(33) Williams B, Powell A, Hoskins G, Neville R. Exploring and explaining low participation in physical activity among children and young people with asthma: a review. BMC Fam Pract 2008;9:40.

(34) 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 Mar;54(3):202-6.

(35) Lang A, Carlsen KH, Haaland G, Devulapalli CS, Munthe-Kaas M, Mowinckel P, et al. Severe asthma in childhood: assessed in 10 year olds in a birth cohort study. Allergy 2008 Aug;63(8):1054-60.

(36) Haverkamp HC, Dempsey JA, Miller JD, Romer LM, Pegelow DF, Rodman JR, et al. Gas exchange during exercise in habitually active asthmatic subjects. J Appl Physiol 2005 Nov;99(5):1938-50.

(37) Kosmas EN, Milic-Emili J, Polychronaki A, Dimitroulis I, Retsou S, Gaga M, et al. Exercise-induced flow limitation, dynamic hyperinflation and exercise capacity in patients with bronchial asthma. Eur Respir J 2004 Sep;24(3):378-84.

(38) Strunk RC, Rubin D, Kelly L, Sherman B, Fukuhara J. Determination of fitness in children with asthma. Use of standardized tests for functional endurance, body fat composition, flexibility, and abdominal strength. Am J Dis Child 1988 Sep;142(9):940-4.

(39) Dencker M, Thorsson O, Karlsson MK, Linden C, Wollmer P, Andersen LB. Daily physical activity related to aerobic fitness and body fat in an urban sample of children. Scand J Med Sci Sports 2008 Dec;18(6):728-35.

(40) Vinet A, Mandigout S, Nottin S, Nguyen L, Lecoq AM, Courteix D, et al. Influence of body composition, hemoglobin concentration, and cardiac size and function of gender differences in maximal oxygen uptake in prepubertal children. Chest 2003 Oct;124(4):1494-9.

Tables

Table 1. Descriptive data of the participating adolescents presented by asthmatics and non-asthmatics. Data are given as mean and standard deviation (SD) in parentheses unless otherwise stated*.

	Asthmatics (n=86) Mean (SD)	**Non-asthmatics** (n=76) Mean (SD)	***P*-value****
Age (yrs); *Mean (Min-Max)**	13.6 (12.8-14.3)	13.6 (12.6-14.3)	0.64
Body mass (kg)	53.7 (10.6)	50.7 (9.7)	**0.05**
Height (cm)	164 (9)	162 (7)	0.12
Skin fold thickness (mm)	37.4 (13.1)	36.5 (12.9)	0.61
FEV_1 (% of predicted)	101 (11)	104 (13)	0.14
FEV_1/FVC	85 (6)	87 (6)	**0.03**
FEF_{50} (% of predicted)	89 (20)	98 (22)	**0.005**
TLC (% of predicted)	105 (13)	104 (12)	0.65
RV/TLC (%)	27 (7)	26 (6)	0.72
Use of ICS last 12mo; n (%)	41 (48)	NA	-
Use of β_2-agonists prior to activity; n (%)	40 (47)	NA	-
Asthma exacerbations last 12mo; n (%)	51 (66)	NA	-
Activity limitations due to asthma; n (%)	27 (31)	NA	-
Moderate PA (hours $\cdot$ day^{-1})	3.7 (1.4)	3.5 (1.4)	0.37
Vigorous PA (hours $\cdot$ day^{-1})	1.5 (1.0)	1.6 (1.1)	0.77

#Abbreviations: Min, Minimum; Max, Maximum; FEV_1, Forced Expiratory Volume in one second; FVC, Forced Vital Capacity; FEF_{50}, Forced Expiratory Flow at 50% of FVC; ICS, Inhaled CorticoSteroids; NA, Non-Applicable; PA, Physical Activity; RV, Residual Volume; TLC, Total Lung Capacity; $\dot{V}O_2peak$, highest recorded oxygen uptake during treadmill test.

** *P*-values for any differences between groups. Statistically significant values are given in bold.

Table 2. Data from the exercise test of the participating adolescents presented by asthma and controls. Data are given as mean and standard deviation (SD) in parentheses unless otherwise stated*.

	Asthma (n=86) Mean (SD)	**Controls** (n=76) Mean (SD)	***P*-value****
$\dot{V}E$ peak (l · min^{-1})	98 (18.1)	94 (16.6)	0.12
RER peak	1.08 (0.066)	1.07 (0.056)	0.50
RPE peak	18 (1.3)	18 (1.1)	0.33
HR peak (beats · min^{-1})	196 (7.5)	196 (8.1)	0.57
$\dot{V}O_2$ peak (ml · kg^{-1} · min^{-1})	53.5 (7.7)	53.4 (9.2)	0.95

[#]Abbreviations: $\dot{V}E$ peak, highest recorded ventilation; RERpeak, highest recorded respiratory exchange ratio; RPE peak, highest reporting perceived exertion; HRpeak, highest recorded heart rate; $\dot{V}O_2$peak , highest recorded oxygen uptake during treadmill test.

[**] *P*-values for any differences between groups.

Table 3. Regression summaries for bivariate- and multivariate analysis with the dependent variable $\dot{V}O_2$ peak. The intermediate multivariate analysis included an interaction with asthma if significant. In the final multivariate analysis $\dot{V}O_2$peak was also adjusted for gender. The coefficients are given with 95% confidence intervals.

	Bivariate analysis		**Intermediate multivariate analysis**		**Final multivariate analysis**	
	Coefficients	*P*-value	Coefficients	*P*-value	Coefficients	*P*-value
Skin fold thickness (mm)	-0.41 (-0.48, -0.33)	<0.001	-	-	-0.35 (-0.41, -0.28)	<0.001
FEV_1 (% of predicted)	-0.04 (-0.15, 0.07)	0.46	-	-	-	-
FEF_{50} (% of predicted)	-0.06 (-0.11, 0.01)	0.06	-0.13 (-0.21, -0.05)*	0.003	-	-
TLC (% of predicted)	0.11 (0.01, 0.21)	0.04	-	-	-	-
Moderate PA (hours · day^{-1})	-0.93 (-1.86, -0.01)	0.05	-	-	-0.44 (-1.11, 0.24)[#]	0.20
Vigorous PA (hours · day^{-1})	3.04 (1.80, 4.27)	<0.001	-	-	0.05 (-1.28, 1.38)	0.94
Vigorous PA*Asthma	-	-	-	-	1.73 (0.32, 3.14))[¤]	0.05

Abbreviations: FEV_1, Forced Expiratory Volume in one second; FEF_{50}, Forced Expiratory Flow at 50% of Forced Vital Capacity; PA, Physical Activity; TLC, Total Lung Capacity; $\dot{V}O_2$peak , highest recorded oxygen uptake during treadmill test.

[*] FEF_{50} was associated with $\dot{V}O_2$peak in the adolescents with asthma only (intermediate multivariate analysis).

[#] Moderate PA was a confounder, influencing Vigorous PA, although not associated with $\dot{V}O_2$peak .

[¤] Vigorous PA was significantly associated with $\dot{V}O_2$peak in adolescents with asthma only (interaction).