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# **Physical activity and aerobic fitness in childhood; -associated with asthma?**

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*Oskar and Johannes,  
Let's play*



## SUMMARY

The prevalence of childhood asthma in the Western world has increased the last decades, whereas knowledge of asthma prevalence in districts where “Westernized lifestyle” is not adopted is inadequate. Even though there is a general lack of studies including objective physical activity measurements and direct measurements of maximal oxygen consumption, the overriding public perception of today’s children and adolescents is that they are less physical active and with lower levels of aerobic fitness than the youth of previous generations. Recently, reduced physical activity level and low aerobic fitness have been proposed to increase the risk of asthma. However, there is no consensus whether a sedentary lifestyle or decreased physical activity increase asthma risk. Evaluating a childhood population from a rural district, where “Westernized lifestyle” is not adopted, is to make comparison with children representing a traditional rural lifestyle.

The *aims* of the present thesis were: (1) to determine the prevalence of asthma symptoms in children living in a rural district in North-Tanzania, (2) to compare aerobic fitness and habitual physical activity between North-Tanzanian and Norwegian children, (3) examine if level of aerobic fitness and physical activity is related to asthma and, (4) to evaluate objective methods for assessing physical activity.

The present thesis is based upon studying *four different populations*: 326 rural living Tanzanian school children (9-10 yrs old); 174 urban living Norwegian adolescents (13-14 yrs old) with or without asthma (cases and controls) from the Environment and Childhood Asthma birth cohort study from Oslo (ECA); and 20 Norwegian adults who participated in a validation study. In addition 379 urban living children from the Norwegian part of the European Youth Heart Study (EYHS) were used for comparison of aerobic fitness and habitual physical activity with the Tanzanian children.

The Tanzanian children completed a standardised video questionnaire

(International Study of Asthma and Allergies in Childhood (ISAAC)) showing the symptoms and signs of asthma. Aerobic fitness was estimated from a standardised indirect maximal cycle ergometer test and habitual physical activity using a standardised questionnaire in the Norwegian EYHS children as well as the Tanzanian children.

In the Norwegian ECA adolescents, asthma was defined by at least two of the following criteria fulfilled: (1) dyspnoea, chest tightness and/or wheezing; (2) a doctor's diagnosis of asthma; (3) use of asthma medication. Aerobic fitness in this cohort was measured during maximal running on a treadmill with oxygen consumption measurements. Physical activity was recorded by wearing an activity monitor (SenseWear™ Pro<sub>2</sub> Armband) for four consecutive days.

In the validation of physical activity monitors, 20 adults wore four activity monitors (Armband, ActiGraph, ActiReg® and ikcal) and a portable oxygen analyzer for 120 minutes performing free living activities of a range of intensities. The cut of points defining moderate, vigorous and very vigorous intensity were 3, 6 and 9 times resting metabolic rate.

Our *main findings* were as follows: Any asthma symptoms last year were reported by 24% of the rural living Tanzanian children (paper 1). The prevalence of wheeze ever was significantly higher in the urban living Norwegian ECA children (mean and 95% confidence intervals; 31 (27-34)%) at 10 years, than the rural living Tanzanian children (17 (10-23)%) ( $p=0.007$ ). The prevalence of current wheeze was not significantly different. The rural living Tanzanian and the urban living Norwegian EYHS children had similar relative aerobic fitness (47.3 (45.5-49.0) vs. 45.9 (44.9-46.9) ml · kg<sup>-1</sup> · min<sup>-1</sup> in boys and 40.3 (37.2-43.4) vs. 40.5 (39.5-41.5) ml · kg<sup>-1</sup> · min<sup>-1</sup> in girls) (paper 2). Neither aerobic fitness nor physical activity was associated with asthma or asthma symptoms in Norwegian ECA adolescents or Tanzanian children (paper 1 and 4). All included physical activity monitors underestimated total energy expenditure (by 5 to 21%). ActiReg® ( $p=0.004$ ) and ActiGraph ( $p=0.007$ ) underestimated energy expenditure in moderate to very vigorous intensity physical activity (MVPA). The physical activity monitors Armband and ActiGraph

overestimated time in MVPA by 2.9 and 2.5% and iKcal and ActiReg<sup>®</sup> underestimated time in MVPA by 11.6 and 98.7%, respectively.

In conclusion; 1) twenty four per cent of 9-10 year old children from a rural district in North-Tanzania reported asthma symptoms, 2) Tanzanian and Norwegian children had similar relative aerobic fitness, 3) aerobic fitness or physical activity was not associated with asthma or asthma symptoms in children and 4) recorded time in moderate to very vigorous intensity physical activity and energy expenditure varies substantially among physical activity monitors.

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## **LIST OF PAPERS**

### **Paper 1**

Berntsen S, Lødrup Carlsen KC, Hageberg R, Aandstad A, Mowinckel P, Anderssen SA, Carlsen KH. Prevalence of asthma symptoms in children from a rural district in North-Tanzania, and its relation to aerobic fitness and body fat. Accepted the 15<sup>th</sup> of December 2008, for publication in Allergy and published online in March 2009, pending the print journal

### **Paper 2**

Aandstad A, Berntsen S, Hageberg R, Klasson-Heggebø L, Anderssen SA. A comparison of estimated maximal oxygen uptake in nine and ten year old schoolchildren in Tanzania and Norway. British Journal of Sports Medicine 2006 ;40: 287-292.

### **Paper 3**

Berntsen S, Hageberg R, Aandstad A, Mowinckel P, Anderssen SA, Carlsen KH, Andersen LB. Validity of physical activity monitors in adults participating in free living activities. Accepted the 1<sup>st</sup> of July 2008, for publication in British Journal of Sports Medicine and published online the 15<sup>th</sup> of July 2008, pending the print journal.

### **Paper 4**

Berntsen S, Lødrup Carlsen KC, Anderssen SA, Mowinckel P, Hageberg R, Kørner Bueso A, Carlsen KH. Norwegian adolescents with asthma are physical active and fit. Allergy 2009 ;64:421-426.

**ABBREVIATIONS**

ECA:	Environment and Childhood Asthma study
EYHS:	European Youth Heart Study
ISAAC:	International Study of Asthma and Allergies
kcal:	Kilocalorie (the quantity of heat necessary to raise the temperature of 1 kg of water 1°C)
MET:	Metabolic Equivalents
MVPA:	Moderate to very vigorous intensity physical activity
$\dot{V}O_2\text{max}$ :	The highest rate at which an individual can consume oxygen during exercise ( $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ )
$\dot{V}O_2\text{peak}$ :	Highest recorded oxygen consumption during an exercise test ( $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ )

## 1 INTRODUCTION

Regular physical activity during childhood and adolescence is associated with several health benefits, including more favorable cardiovascular health, mental health, musculoskeletal health, and prevention of unhealthy weight gain (1). Physical activity is reported to have positive effects on self-esteem in children and adolescents (2) and in unhappy children with asthma, quality of life and morbidity are reported to improve with low intensity asthma-education-exercise programmes, even without changes in lung function or exercise tolerance (3). Aerobic fitness is also reported to be positively associated with psychological functioning in asthmatic children (4). However, evidence for additional beneficial effects of physical activity or exercise training in children and adolescents with asthma is sparse. In a Cochrane review, physical training improved aerobic fitness without changing baseline lung function, exacerbations or symptoms in children and adolescents with asthma (5). However, recent published data indicates regular physical training to improve quality of life and asthma symptom score in addition to aerobic fitness (6;7).

As many as 90% of children and adolescents with asthma not receiving anti-inflammatory treatment, has been reported to have symptoms of asthma and reduction in lung function after physical exercise (8;9). On the other hand, participation in regular physical activity and training play an important role in the rehabilitation of asthmatic children (10;11) because aerobic conditioning lessens the prospect of an asthma attack by reducing the ventilatory requirement for any activity (12).

Even though there is a general lack in most countries of studies including objective physical activity measurements, the overriding public perception of today's children and adolescents is that they are less physically active than the youth of previous generations. A decrease in aerobic fitness the last decades in most "Western societies" is also reported (13). In recent years, reduced physical activity level and low aerobic fitness are suggested to increase the risk of asthma (14;15). On the other hand, asthma and

asthma symptoms are reported to be more common in elite athletes compared with age-matched control persons (16-18). Observations suggest that high intensity exercise performed on a regular basis might contribute to the development of asthma in athletes previously unaffected by the disease (19). In healthy subjects, exercising intensely for long periods of time breathing large volumes of cold and/or dry air, air containing irritant gases, particular matter, or allergens could result in the same airway response as documented in asthmatic subjects (20).

Increasing prevalence of both overweight, obesity (21) as well as asthma (22;23) in children and adolescents is reported, and a number of longitudinal studies have reported increasing risk of developing new asthma or asthma symptoms in obese children and adolescents (24-27). The causality however, is not known (28). It was recently suggested that the lack of physical activity more than the obesity itself increased the risk of asthma disease (29). Genes, environmental factors including diet, physical activity and gene-environment interactions have been suggested to be involved in the pathogenesis of obesity and asthma (29;30).

The increasing attention, focusing on the role of urbanisation, modern fast food and sedentary lifestyle including decreased physical activity levels in the development of asthma, may suggest moving away from the rural traditional way of life resulting in loss of preventive factors for asthma. Even in Sub-Saharan African countries, the prevalence of exercise-induced bronchoconstriction (31-33) and asthma symptoms (34;35) have been shown to be higher in urban vs. rural areas and hospital admissions for asthma appear to have increased in parallel with rapid urbanisation (36). However, this urban-rural gradient may also be influenced by social, financial, cultural and socio-economical barriers as well as the organization of national health care systems in rural districts in developing countries (37). In addition problems of inaccurate translation and vocabulary differences from written questionnaires may not reflect the occurrence of asthma since children may have different understanding of the concept of wheezing, a word which is important for but not synonymous with asthma.

In most languages, an exact equivalent of “wheeze” is lacking (38). This raises two possibilities in which either there are differences in the prevalence of asthma between rural and urban districts or Western countries, or there is an underreporting of asthma in children living in a rural country district where “Westernized lifestyle” is not adopted. However, no difference was in the prevalence of video-reported symptoms between rural and urban areas, whereas the written questionnaire indicated more severe forms of asthma in the latter (39).

One way to attempt to answer whether an active lifestyle exerts a protective effect in the prevention of asthma, is to look at populations living a traditional way of life. A comparison of aerobic fitness or habitual physical activity levels in children living in a rural country district where “Westernized lifestyle” is not adopted vs. children from Western countries and its relation to asthma may increase our understanding of “lifestyle” asthma. Another possibility is to compare children with and without asthma.

## 2 REVIEW OF THE LITERATURE

### 2.1 Definitions

#### 2.1.1 Asthma and asthma symptoms

Wheeze has been described as continuous high pitched adventitious lung sounds, which are superimposed and usually louder than normal breath sounds (40). The high-pitched musical sounds are produced when the calibre of the airways is narrowed, as in asthma, and appear to involve an interaction between the airway wall and the gas moving through the airway (41). In English speaking countries wheeze is now commonly understood. Agreement between self-reported wheeze from written- and video questionnaires tends to be higher for the English-speaking children (38), with lower asthma symptom reports using video compared to written questionnaire data (42).

There is no clear definition of the asthma phenotype; however, asthma has been described as “*a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment*” (43).

A clinical diagnosis of asthma is suggested by symptoms such as episodic breathlessness, wheezing, cough and chest tightness; however, in some subjects with asthma, wheezing may be absent or only detected when the person exhales forcibly, even in the presence of significant airflow limitation (44). Episodic symptoms after an allergen exposure, seasonal variability of symptoms, presence of allergies and a positive family history of asthma are also helpful diagnostic guides. Ideally, diagnosis of asthma should be based on clinical evidence, which includes a detailed clinical history, respiratory assessment (including measurement of reversible



airflow-limitation and/or bronchial hyperresponsiveness) and consideration of differential diagnosis (44). In the Environmental Childhood Asthma study (45) asthma at 10 years was defined by at least two of the following three criteria fulfilled:

1. Dyspnoea, chest tightness and/or wheezing 0-3 years and/or after three years
2. A doctors diagnosis of asthma
3. Used asthma medication ( $\beta$ -2 agonists, sodium chromoglycate, corticosteroids, leukotriene antagonists and/or aminophylline) 0-3 years and/or after three years.

There are differences in diagnostic practices among countries including self-reported asthma symptoms and physician-diagnosed asthma (46). Lack of uniform guidelines for the diagnosis of asthma makes it difficult to compare prevalence of diagnosed asthma among countries. Even though asthma diagnosis should be based on clinical evidence, standardised written- or video questionnaires describing or showing the symptoms and signs of asthma have been used in epidemiological studies to try to overcome language cultural related differences (47).

The differences between perceived asthma symptoms (30%) in a population and the doctor's diagnosis of asthma (16%) (45) highlights the risk of underestimating asthma by diagnosis alone. Asthma has also been under-diagnosed in adolescents when asthma definition was based on asthma symptoms and one or more obstructive airway abnormalities (48).

### **2.1.2 Physical activity and aerobic fitness**

Physical activity can be defined as any bodily movement produced by the contraction of skeletal muscles that substantially increases energy expenditure (49;50) and is characterised by its intensity, duration, frequency and mode of activity (51). Ideally, all these aspects should be recorded during physical activity measurements. Physical activity level varies with methods of assessment (52). Even though different activity

monitors record different aspects of physical activity such as acceleration, position changes, heart rate etc., objectively recorded physical activity is preferred because children may recall only ~50% of physical activity in the previous week when using e.g. questionnaires (53). Furthermore, in obese subjects, self reported physical activity has been over-reported compared to objective measurements (54), particularly after attending management programmes for weight reduction (55).

In contrast to physical activity, which is related to the movements performed, physical fitness has been defined as a set of attributes that people have or achieve that relates to ability to perform physical activity (49). Physical fitness is comprised of skill-related, health-related, and physiological components (50). Health related components of physical fitness are cardio-respiratory endurance, muscular strength and -endurance, flexibility and body composition (49). Cardio-respiratory or aerobic fitness is related to the ability to perform large muscle, dynamic, moderate to vigorous intensity exercise for prolonged periods. Maximal oxygen consumption ( $\dot{V}O_2\text{max}$ ), the highest rate at which an individual can consume oxygen during exercise, limits the capacity to perform aerobic exercise and is recognised as the best single measure of aerobic fitness (50). As the term  $\dot{V}O_2\text{max}$  conventionally implies the existence of a  $\dot{V}O_2$  plateau, it has gradually become more common in paediatric exercise science to define the highest oxygen consumption observed during an exercise test to exhaustion as  $\dot{V}O_2\text{peak}$  (56). Only a minority of children and adolescents exhibit a classical  $\dot{V}O_2$  plateau; however, data have demonstrated that those who plateau do not have higher  $\dot{V}O_2$ , heart rate and RER or post exercise blood lactate values than those not eliciting a  $\dot{V}O_2$  plateau (56).

## **2.2 Prevalence of asthma**

The percentage of children and adolescents<sup>1</sup> reported to ever have had asthma has increased the last decades (57); with a 20.2% lifetime prevalence of asthma in 10 year old children in Oslo, Norway, reported in 2005 (45). Large variations in the prevalence of asthma symptoms have also been observed between centres worldwide in 13-14 year old adolescents, with the highest prevalence in Western countries (8-31%) and lowest in African (9-20%), some east European (3-20%) and Asian countries (5-13%) (58). In addition, the prevalence of exercise-induced bronchoconstriction (31) and asthma symptoms (34) are reported to be higher in urban vs. rural areas in some African countries. It has been suggested that the current increase in asthma is occurring in children who would be regarded as at low risk of developing asthma suggesting that much of the increase in asthma prevalence is occurring in children without a significant genetic predisposition (59).

Thirty years ago, Carswell et al. (60) reported a prevalence of recurrent episodes of asthma symptoms and breathlessness in 7.8% of 242 school children living in rural villages in South-West Tanzania. The medical history was obtained by Swahili-speaking natives with medical experience. A recent study (61) conducted in 294 urban (Dar es Salaam) and 511 rural (in the foothills of Mount Kilimanjaro) living Tanzanian children showed a prevalence of self-reported asthma symptoms, using a written questionnaire, in 1.9-5.2% in children and adolescents. Different methodology makes it difficult to draw any conclusion about asthma trends from these studies. Lack of general asthma knowledge as well as different understanding the word “wheeze” may affect detection of asthma based on written questions alone (38). Like for most European languages, an exact equivalent of “wheeze” in the Swahili language is absent (38) and a translated written questionnaire may not have the same precision as the

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<sup>1</sup> In the present thesis, children is defined as persons 6 to 12 years of age and adolescents as persons 13 to 18 years of age

original validated questionnaire (62). For this reason, prevalence of current wheeze in 13-14 year old adolescents in sub-Saharan countries based on video questionnaire data, are reported to be lower (4-12%) than for written questionnaire data (10-21%) (63-65). In addition, two studies (31;33) including a free running test screening for exercise-induced bronchoconstriction conducted in urban and rural South-Africa and Kenya found the prevalence of exercise-induced bronchoconstriction ranging from 9-23% with large regional variations.

### ***2.3 Physical activity and aerobic fitness levels***

In recent years it has been claimed that children and adolescents have reduced their level of physical activity and fitness (66). Physical activity in a clearly defined contexts such as active transport or commuting to school, school physical education, and organised sports is declining in many countries (66) and the percentage of inactive adolescents seems to rise (67). Two recently published prospective studies, using objective recording of physical activity among Danish (68) and Swedish (69) school children, did not support that children are becoming less physically active. It has to be underlined that both studies were carried out within the last 10 years. Trends towards decreased physical activity and increased inactivity from 1993 to 2003 among American adolescents was reported in a large questionnaire based study, although generally small but statistically significant changes was reported (70). In contrast, Australian data indicates increased participation in self-reported physical activity from 1985 to 2004 (71). Participation in physical education, sports activities, active transport or commuting to school did not change in the same period (72).

It is challenging to conclusively describe physical activity trends because of the absence of suitable baseline data and method discrepancies (66). Suspicions that children are getting less physically active also build on indirect evidence that children are getting fatter (73). Few empirical studies including objective physical activity data have been conducted to test the assumption that children and adolescents are less physical active (66).

Five large population-based cross sectional studies in Western children and adolescents are conducted within the last five years, where physical activity was measured objectively (74-78). The percentage of *children* who participated in more than 60 minutes of moderate to very vigorous intensity physical activity (MVPA) every day<sup>2</sup> ranged from 0.4-98% in girls and 5-97% in boys, respectively (74-78). Adolescents are on average, significantly less physically active than children, and boys are more active than girls (74;76;77). The percentages of *adolescents* who met the physical activity guidelines ranged from 5-62% in girls vs. 10-82% in boys, respectively (74;77;78). In Africa, some small sample size studies including objectively measured physical activity report higher physical activity level in boys compared to girls (79), and a decline in physical activity level with age (80). However, different methods and cut-off points defining MVPA makes comparison of physical activity data challenging.

Among *children* from Western countries, mean  $\dot{V}O_2$  peak values of 36-50 ml · kg<sup>-1</sup> · min<sup>-1</sup> and 41-58 ml · kg<sup>-1</sup> · min<sup>-1</sup> in girls and boys respectively are reported, respectively (81-85). In *adolescents* somewhat higher levels are reported in both girls (40-49 ml · kg<sup>-1</sup> · min<sup>-1</sup>) and boys (52-61 ml · kg<sup>-1</sup> · min<sup>-1</sup>), respectively (82;86). In three small sample size studies conducted in Sub-Sahara, mean  $\dot{V}O_2$  peak values in children and adolescents in the range of 47-55 ml · kg<sup>-1</sup> · min<sup>-1</sup> are reported (87-89), whereas several studies report estimated aerobic fitness values from shuttle run or fitness tests (90-92).

In a large study (13) including more than 25 million children and adolescents from 27 countries, aerobic fitness estimated from a shuttle run test declined 0.46% per year from 1970 to 2003. The mean decline in aerobic fitness ranged from 0.74% in North America to 0.31% in Europe. However, the rate of decline in high income countries was marginally

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<sup>2</sup> Children and adolescents should participate daily in 60 minutes or more of moderate to vigorous physical activity (1).

higher than the decline in middle and low income countries. This is in line with Scandinavian data in children (93) and young adults (94). However, recently published data suggest reductions in aerobic fitness only in girls (95) or in the most unfit children (96). Secular trend studies including direct measurement of  $\dot{V}O_2$ peak are scarce.

#### **2.4 Risk factors for asthma development**

Factors that influence the risk of asthma can be divided into those that initiate or cause the development of asthma and those that trigger asthma symptoms, some do both (97). The mechanisms whereby these factors influence the development and expression of asthma are complex and interactive and involve genes, environment as well as gene-environment interactions (29;98). Asthma has a heritable component (99) with higher risk of asthma in children with parents with a history of asthma (100;101). In addition, developmental aspects, such as maturation of the immune response (102), infectious exposures during the first years of life (103-106) and maternal smoking during pregnancy (107) are important factors that modify the risk of asthma.

Ethnic factors associated with asthma are likely to reflect underlying genetic variances with an overlay of socioeconomic and environmental factors (108). Higher risk for asthma are reported in American children living in an urban setting, independent of socioeconomic status (109). The higher prevalence of asthma in developed countries and in urbanized populations is thought to be multi-factorial including sensitisation to allergens, lifestyle and environment (110) with increasing attention to “Western lifestyle”, including unhealthy diet and sedentary lifestyle with decreased physical activity (111). However, asthma symptoms have also been associated with underweight in children (112) and adolescents (113).

Lower levels of aerobic fitness (peak power output) has been associated with higher risk of developing asthma in a Danish prospective study (15). In addition, Flaherman and Rutherford reported increasing risk of asthma or

asthma symptoms in obese children and adolescents in a meta-analysis published recently (28). Despite numerous genetic and environmental associations relating asthma to obesity, it is unlikely that this relationship is due to any one single factor (114). The level of physical activity may be an independent risk factor for the development of obesity and asthma. However, as an environmental factor it may also interact with the genes in its association with asthma. Overweight and obese children and adolescents may display a more negative attitude towards physical activity (115). Low physical activity levels may be an independent risk factor for asthma (29). However, it may also interact with obesity in its association with asthma. In addition, children and adolescents with asthma who experience exercise limitations because of uncontrolled disease may have lower physical activity levels and aerobic fitness (116;117). Inactivity may then increase the risk for weight gain and development of overweight and obesity (118).

Published data do not support the hypothesis that asthma cause obesity (119). Mechanisms other than bronchoconstriction are also reported to be responsible for dyspnoea in obese subjects (120). In a systematic review, weight reduction in obese subjects with asthma is reported to improve lung function, asthma symptoms, morbidity and health status (121). Trends in overweight and obesity can not explain the increase in asthma but may be explained by obesity being a marker of recent lifestyle changes associated with both asthma and overweight or obesity (122), such as poor diet and physical inactivity. A diet high in fruit, vegetables and fish has been found protective for development of childhood asthma in some studies (123-125) and some evidence suggests an inverse association between omega-3 polyunsaturated fatty acids intake and asthma symptoms (126). A beneficial association between intake of antioxidant vitamins and -minerals and development of asthma has also been reported (127). The benefit of diet with respect to asthma may come from combined nutritional value in particular foods or the combined interaction of foods or combined effects of food in a healthy diet (128). However, this will not be further elaborated in the present thesis.

## **2.5 *Aerobic fitness, physical activity and asthma***

Comparisons of habitual physical activity levels of children and adolescents with and without asthma have given inconsistent results with higher (129;130), lower (117;131;132) or similar physical activity levels (133;134) reported in children and adolescents with asthma. In a large cross sectional study, physical activity was associated with increased risk of current asthma in Norwegian children and adolescents exercising more than seven hours a week (133), whereas self-reported physical activity was not associated with a history of asthma. However, the prevalence of asthma symptoms was reported to be lower among inactive subjects from the same study population (135). This could suggest that those who are engaged in sports or exercise report asthma symptoms differently from inactive subjects. On the other hand, in the same cross sectional study, the prevalence of bronchial hyperresponsiveness increased with decreasing hours of exercise per week in children and adolescents with asthma only (136).

There is no consensus whether a sedentary lifestyle or low level of physical activity increase asthma risk. A high level of self-reported physical activity was associated with higher prevalence of diagnosed asthma in 636 US children (129), whereas participating in physical activity (self-reported) more than 3 times a week was associated with reduced occurrences of asthma symptoms in children in a large cross sectional study from Taiwan (137). Only three studies reported objectively measured physical activity levels (132;134;138). Lower physical activity levels were reported in a small study in US children aged 3-5 years with a history of asthma symptoms (132), whereas no differences in physical activity levels were found in a large study in Dutch children with undiagnosed asthma, diagnosed asthma and controls (134). Dutch children 4-5 years of age with current asthma symptoms were also reported to have similar activity levels compared to children with no symptoms ever (138). However, asthma has been reported to interfere with children's ability to participate in vigorous physical activity (139). In a German study, 254 teachers in 46 schools



estimated that only 60% of the children and adolescents with asthma took part in physical education lessons on the same basis as their healthy peers (140). This has been confirmed in an Australian study where asthma negatively affected participation in sporting activities (141).

Watching television more than 3 hours per day was associated with more frequent asthma symptoms in 2290 Taiwanese children (137). An association between current asthma and sedentary behaviour has also been reported in other American (142;143), Italian (144) and Greek (145) studies. On the other hand, in a large study 15 years ago including more than 7000 US children, number of hours of television watching was not associated with current asthma (146).

There is also contradictory evidence regarding the aerobic fitness levels of children and adolescents with asthma. Reduced (116;147) or similar (148;149) aerobic fitness levels are reported in asthmatic subjects. Aerobic fitness is reported to be limited in adolescents with severe asthma (116). This is in contrast to other reports (150) who found no association between asthma severity and aerobic fitness.

In a prospective population-based study in asymptomatic Danish children, an inverse relationship between aerobic fitness (peak power output) and physician diagnosed asthma was reported over the following 11 years (15). In studies involving adult twins, leisure time physical activity (14) and conditioning exercise (151) were reported to be protective for developing asthma. On the other hand, a protective effect of a sedentary lifestyle on the risk of asthma in Danish monozygotic twins has also been reported (152). However, in the Danish study, the physical activity variable distinguished only subjects doing less than two hours per week of light leisure time exercise activities from those doing more. The physical activity variable was in fact a measure of inactivity, and the authors suspected their findings to be false-positive because of the direction of the effect (152).

Using well designed methodologies when studying aerobic fitness and physical activity levels is important (153). Different exercise ergometers, test modes and protocols influence the measured aerobic fitness level (154-156). In addition, few studies have included direct measurement of oxygen consumption. At present, only scarce information is available regarding objective measurement of physical activity in asthmatic adolescents (153). Different descriptions or definitions of asthma, sample size and selection may also explain the divergence among studies (117;129-134).

### **3 NEED OF NEW INFORMATION**

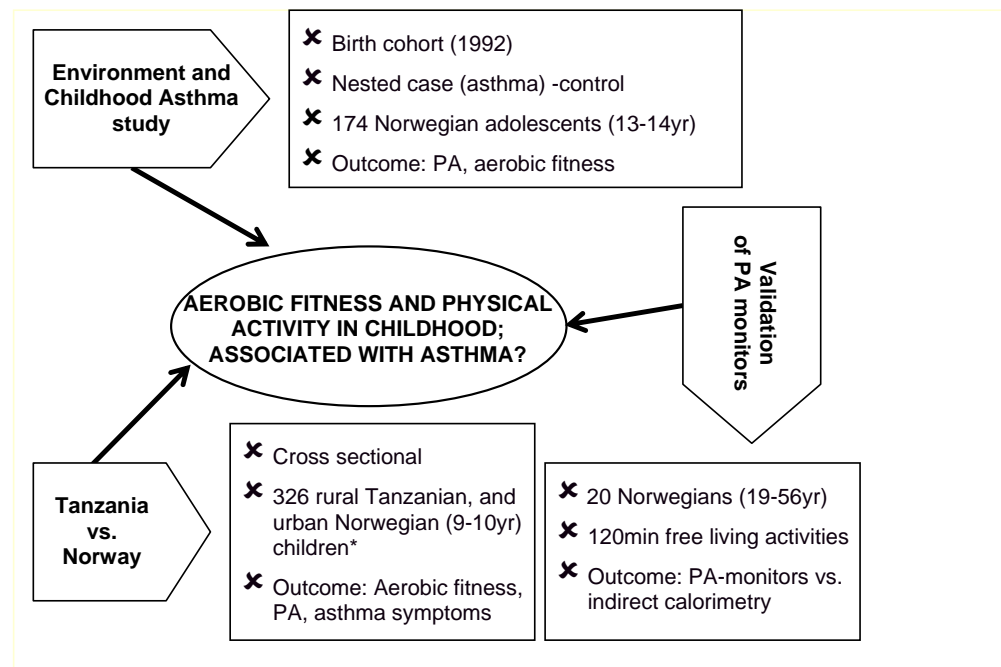
The cause of the increase in asthma is thought to be multi-factorial with an increasing attention to the role of the Western lifestyle including a sedentary lifestyle as well as decreased physical activity. Lack of suitable baseline data in the Western world makes it challenging to conclusively describe physical activity and aerobic fitness trends, and whether low levels of physical activity or aerobic fitness increase the risk of asthma disease. Evaluating a childhood population from a rural district in East-Africa, where “Westernized lifestyle” is not adopted, is to make comparison with children representing a traditional rural lifestyle. There is a lack of knowledge of prevalence of asthma, using methods other than written questionnaires, in children living in rural country districts where “Westernized lifestyle” is not adopted. Previous studies comparing aerobic fitness between these and Western children have also had shortcomings in terms of differences in methodology and small sample sizes. In addition, the consistency of the relationship between physical activity or inactivity and asthma is not clear and possible causality is largely unknown. The present thesis aims to test this association in two populations with large cultural and lifestyle differences. Comparison of physical activity monitors in a free living condition including direct measurements of oxygen consumption is also scarcely reported in the literature.

#### **4 AIMS OF THE STUDY**

1. To determine the prevalence of asthma symptoms in children living in a rural district in North-Tanzania.
2. To assess whether children living in a rural district in North-Tanzania have higher aerobic fitness level than Norwegian children.
3. Is aerobic fitness and physical activity associated with asthma in children?
4. To evaluate objective methods for assessing physical activity.

## 5 SUBJECTS AND METHODS

The present thesis is based on four different study populations (fig. 1). Three hundred and twenty six rural living Tanzanian school children (2003), 379 urban living Norwegian school children from the European Youth Heart Study (EYHS) (2000), 174 Norwegian adolescents with or without asthma from the Environment and Childhood Asthma birth cohort study (ECA) in Oslo (2005/-06) and 20 Norwegian adults who participated in the validation study of physical activity monitors (2007), are included.



**Fig. 1.** Overview design, outcomes and subjects included in the present thesis.

\*379 children (9-10yr) from the Norwegian part of the EYHS were used as a basis for comparison of aerobic fitness and habitual physical activity, whereas 1019 children (9-10yr) from ECA were used as comparison of prevalence of asthma symptoms with the rural Tanzanian children.

Abbreviations: PA, physical activity.

## **5.1 Study design**

### **5.1.1 The Tanzania study**

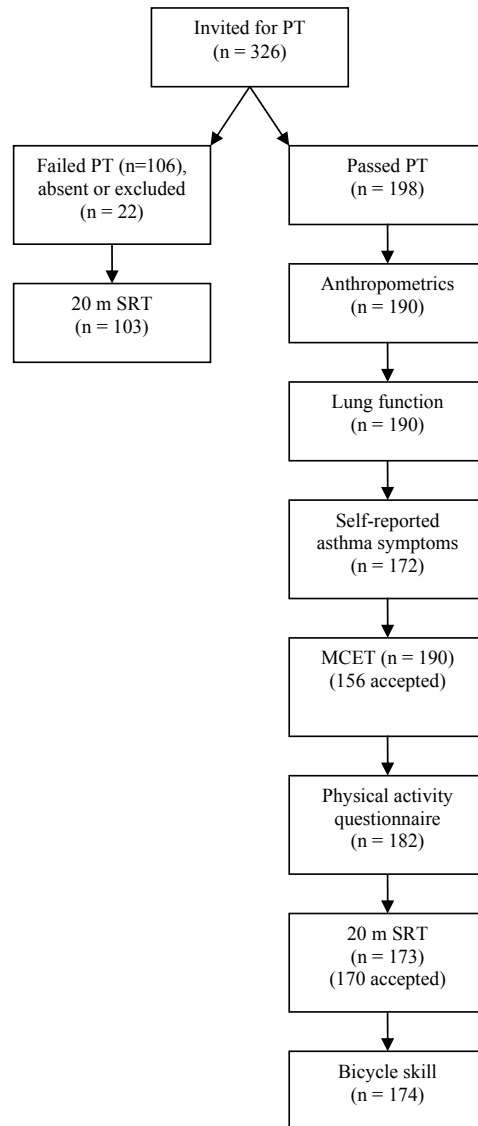
The Tanzania study is a cross sectional study. The data were collected during a period of six weeks in May and June 2003 at their respective schools. The Tanzanian children were tested at an altitude of 1800 meters above sea level.

### **5.1.2 European Youth Heart Study**

Details of the study design has been given previously (157). In short, this cross sectional study was conducted as a part of the EYHS, an international multi-centre study in 9-10 and 15 year old children (158). Only data from 9-10 year olds are reported in the present thesis. Aerobic fitness was assessed using a maximal bicycle protocol, habitual physical activity using an objective activity monitor (data not reported in the present thesis) and a questionnaire. The Norwegian EYHS children were tested at their respective schools at sea level (~20-200 metre above sea level) in year 2000.

### **5.1.3 The Environment and Childhood Asthma study**

The Environment and Childhood Asthma study is an ongoing birth cohort study of children born in Oslo. A primary cohort of 3754 children at birth was established during 15 months from January 1<sup>st</sup>, 1992 (159). Several follow-up studies have been conducted. Paper 4, included in the present thesis, is based on a 13-year follow up study conducted between October 2005 and June 2006 in the adolescents with current asthma and without asthma at 10 years of age. The study consisted of one day of clinical investigation and four days home activity monitoring.



**Figure 2.** Flowchart of test order for the Tanzanian children.

PT, preliminary cycle ergometer test; 20 m SRT, 20 meter shuttle run test;

MCET; maximal cycle ergometer test.

#### 5.1.4 The Validation study of activity monitors

The present validation study consists of one day of clinical investigation including measurement of resting metabolic rate (RMR) and one day activity and energy expenditure monitoring at home or at the participants work

indoors and/or outdoors. The four activity monitors and the portable oxygen analyzer were attached to the participant for 120 minutes during daytime. During this period the participants performed various lifestyle and sporting activities such as conditioning- and strength exercises, ball games, home repair, occupational- and home activities. The data were collected in 2007.

## **5.2 Subjects**

### **5.2.1 Rural Tanzanian children**

Five primary schools were randomly selected from three areas in Mbulu district, Manyara region in North Tanzania. All school children aged 9-10 years old (born in 1993) were identified at each of the five schools and asked to participate in the study giving a sample of 326 boys and girls. The precise date of birth was not usually known, and age was interpolated from the year of birth. All 326 Tanzanian children carried out a 10 minute pre test on the cycle ergometer to evaluate the child's ability to cycle on a stationary cycle ergometer with a steady pedal rate of 70 – 80 rpm. During the preliminary test, 106 (35%) of the subjects were not able to maintain a steady pace (fig. 2), mostly because of frequently slipping off the pedal when cycling. Only children able to cycle satisfactorily were included in the final analysis of aerobic fitness in the present thesis. The physical characteristics of the Tanzanian children are reported in table 1.

### **5.2.2 Norwegian children from the European Youth Heart Study**

In the Norwegian part of EYHS, a total of 578 pupils (4<sup>th</sup> grade) from nine randomly selected primary schools in Oslo were invited (158). Four-hundred and ten children participated in the study and 379 had an accepted maximal bicycle test. The physical characteristics of the Norwegian EYHS children are reported in table 1.

### **5.2.3 Norwegian adolescents with and without asthma**

From the 10-year follow up of the ECA-study (45), all 147 children with current asthma and 163 controls without lower respiratory disease, born at the same day or closest to adolescents with current asthma, were invited to participate in the present study of which 174 (56%) agreed to participate. In total, 95 (66 boys) of the adolescents had asthma and 79 (41 boys) did not. 35 of the participants with current asthma at 10 years did not report symptoms or use of asthma medication in the last months at 13 years. Four out of the controls had current asthma by definition at 13 years (definition of asthma is given in the “Methods”). Participants were categorised as case (asthma) if having current asthma at 10 or 13 years of age by definition.

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 with asthma used their regular medications. The physical characteristics of the Norwegian ECA adolescents are reported in table 1.

### **5.2.4 Adults participating in the validation study of activity monitors**

Fourteen men and six women (19-56 years of age) volunteered to participate in the study which aimed to evaluate monitors for recording physical activity. Participants were mainly recruited from the Norwegian School of Sport Sciences and the Norwegian Military Academy in Oslo. Their physical characteristics are shown in table 1. All participating subjects were of Caucasian origin without any overt disease or use of medications which could have influenced results such as energy expenditure. All participants were non-smokers.



**Table 1.** The physical characteristics of the rural living Tanzanian school children, the urban living Norwegian EYHS school children, ECA adolescents (with asthma and controls), and the adults participating in the validation study of physical activity monitors. Data are given as mean and SD in parentheses unless otherwise stated\*.

	Rural		Urban		Norwegian		Norwegian adolescents		Adults	
	Tanzanian (n=190)	Norwegian (n=379)	Norwegian adolescents without asthma (n=79)	Norwegian adolescents with asthma (n=95)	with asthma	without asthma	with asthma	without asthma	with asthma	without asthma
Age (yrs)*	- (9-10) <sup>#</sup>	9.7 (9-10)	13.6 (13-14)	13.6 (13-14)	13.6 (13-14)	13.6 (13-14)	13.6 (13-14)	13.6 (13-14)	33.3 (19-56)	33.3 (19-56)
Body Mass (kg)	27 (3.4)	33 (5.9)	53 (10.8)	53 (10.8)	51 (9.7)	51 (9.7)	51 (9.7)	51 (9.7)	76 (13.9)	76 (13.9)
Stature (cm)	134 (5.5)	139 (6.3)	164 (9.0)	164 (9.0)	162 (7.2)	162 (7.2)	162 (7.2)	162 (7.2)	177 (8.4)	177 (8.4)
Gender (% girls)	46.8	48.0	48.1	48.1	30.5	30.5	30.5	30.5	30.0	30.0
Underweight (%)	37.4	7.9	13.9	13.9	13.7	13.7	13.7	13.7	0.0	0.0
Overweight (%)	0.5	12.1	6.3	6.3	14.7	14.7	14.7	14.7	35.0	35.0
Obese (%)	0.0	1.2	3.8	3.8	1.1	1.1	1.1	1.1	5.0	5.0

\* Mean (Min-Max)

<sup>#</sup> The precise date of birth was not usually known. Age was interpolated from the year of birth, giving all Tanzanian children an age of 9 to 10 yrs.

<sup>§</sup> For definition of underweight, overweight and obesity, see "Methods".

### 5.3 *Methods*

#### 5.3.1 **Self reported asthma symptoms**

In the Tanzanian children all participants accomplished a *video questionnaire* (International version AVQ 3.0) used in the ISAAC, showing the symptoms and signs of asthma (38): wheezing at rest, exercise-induced wheezing, waking at night with wheezing, nocturnal coughing and severe attack of asthma. Each sequence was followed by three questions: has your breathing ever been like the subject's in the video, if "yes in the last 12 months?" (classified as current) and if "yes" again "in the last month" (appendix B). The questions were translated into Swahili (appendix A)). The subjects were guided and interviewed by a Swahili and Iraqw (the local language) speaking research assistant. The term "wheezing" was not mentioned at any stage in the video questionnaire. The video questionnaire was conducted prior to the *written questionnaire* (appendix C), consisting of five questions corresponding to the five sequences depicted in the video questionnaire. Assistance was provided by the Swahili and Iraqw speaking research assistant when requested by the child. Data from the video questionnaire are given when referring to asthma symptoms or wheeze in the Tanzanian children.

Any asthma symptoms were defined as wheeze at rest, after exercise, waking with wheeze or severe attack of asthma from the video questionnaire. Waking with cough as the only symptom was not included in the definition of asthma symptoms.

In the Norwegian ECA adolescents, asthma symptoms were recorded using a *parental structured interview* including central ISAAC questions related to asthma symptoms (validated in Norwegian language (22)) of the child (appendix E). The symptom questions correspond to sequences depicted in the AVQ 3.0 video questionnaire. In the present thesis, self-reported dyspnoea, chest tightness and/or wheezing are defined as wheeze. Detailed questions of medication use, airway symptoms and experienced symptom

provoking factors including exercise limitations, lifestyle and diseases (45) were also carried out (appendix E and H).

In the ECA study, *asthma* at 10 and 13 years was defined by at least two of the following three criteria fulfilled (45):

1. Dyspnoea, chest tightness and/or wheezing 0-3 years and/or after three years
2. A doctors diagnosis of asthma
3. Used asthma medication ( $\beta$ -2 agonists, sodium chromoglycate, corticosteroids, leukotriene antagonists and/or aminophylline) 0-3 years and/or after three years.

At 10 years, *current asthma* was defined as asthma (by definition above) plus at least one of the following (45):

1. Dyspnoea, chest tightness and/or wheezing in the last 12 months
2. Use of asthma medication ( $\beta$ -2 agonists, sodium chromoglycate, corticosteroids, leukotriene antagonists and/or aminophylline) in the last 12 months
3. Positive exercise-induced asthma test

At 13 years, *current asthma* was defined as asthma (by definition above) plus at least one of the following:

1. Dyspnoea, chest tightness and/or wheezing in the last 12 months
2. Use of asthma medication ( $\beta$ -2 agonists, sodium chromoglycate, corticosteroids, leukotriene antagonists and/or aminophylline) in the last 12 months.

### **5.3.2 Anthropometric measurements**

*Body mass* was measured with the subject wearing light clothing and without shoes (Seca 709, Germany; paper 3 and 4 and Soehnle, Type 7516, Germany; paper 1 and 2) to the nearest 0.1 kg. *Stature* was measured to the nearest 0.5 cm by using a stadiometer (paper 3 and 4) or a tape measure attached to the wall (paper 1 and 2). BMI was calculated as body mass (kg)

divided by stature (m) squared. Cut off points for underweight, overweight and obesity were according to international standard (160-162).

In the Norwegian ECA adolescents, *pubertal stage* was assessed by means of Tanner criteria (163). Using brief observation and asking about date/year of menarche (in girls) and about pubertal changes (development), pubertal stage was identified using a modified 3-point scale (no development, development has begun and development is already completed on each of several characteristics) according to Petersen et al. (164).

*Skinfold thickness* was measured with a Harpenden fat calliper in the Norwegian ECA adolescents and the Tanzanian children (paper 1, 2 and 4) at the biceps (not measured in the Tanzanian children), triceps, subscapular and suprailiac region. Two measurements were taken at each position, and if the difference between the two measurements was more than 2 mm, a third measurement was taken. The mean value of the two closest measurements was used for analysis.

*Waist circumference* was measured to midway between the costal arch and the iliac crest with a metal anthropometric tape to the nearest 0.5 cm at the end of a gentle expiration (paper 4). Skinfolds or waist circumference data are not reported in the thesis.

### 5.3.3 Aerobic fitness

Aerobic fitness was assessed using the same maximal bicycle protocol in the Tanzanian children and the Norwegian EYHS children, respectively. In the Norwegian ECA adolescents, aerobic fitness was determined during maximal treadmill running.

Maximal power output ( $W_{\max}$ ) was measured from the *maximal cycle ergometer test* (165) conducted on an electronically-braked cycle ergometer (Monark 839 Ergomedic, Sweden). A relative  $\dot{V}O_2$  peak was calculated from the equation:  $\dot{V}O_2 \text{ peak (ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}) = (12.44 \cdot W_{\max} + 250)/\text{body mass}$  (157). Initial and incremental power output were 20 W for children

weighing < 30 kg and 25 W for children weighing  $\geq$  30 kg. Every third minute the power output increased, until exhaustion. Heart rate (HR) was registered throughout the test (Polar Pacer, Finland). The criteria for having reached maximal effort were a HR  $\geq$  185 bpm and a subjective assessment that the child had reached his or her maximal effort. The cycle ergometer was calibrated electronically twice a day and mechanically once a day or every time after being moved. Eighteen randomly chosen Tanzanian subjects were retested after three weeks to calculate reproducibility of the maximal cycle ergometer test. The coefficient of variation between the first test and the re-test was 8% and a 3% higher aerobic fitness was demonstrated in the re-test ( $p < 0.001$ ) (reported in paper 2). The maximal cycle ergometer test has been validated in 21 Scandinavian 9 year old children. The correlation between maximal power output and  $\dot{V}O_2$  peak was  $r = 0.93$  and the standard error of estimation for predicted  $\dot{V}O_2$  peak was 4.8% (157). Ultimately, results from 156 Tanzanian maximal cycle ergometer tests were accepted according to the criteria for having reached maximal effort (fig. 2).

As part of the methodology consideration *bicycle skill* was examined in the Tanzanian children by observing the subjects riding a regular children's bicycle for about 100 meters. Children able to cycle freely, without touching the feet to the ground, were characterized as accustomed to bicycling. Children who failed this test were characterized as unaccustomed to bicycling. Bicycle skill was not examined in the Norwegian sample; however, most Norwegian children are accustomed to bicycling. We also carried out a *20 meter shuttle run test* on a flat area of a schoolyard or on a football field in 276 of the Tanzanian children (paper 2). The running protocol and calculation of aerobic fitness are reported in detail previously (166). In short, the children was required to run back and fourth on the 20 m course and to touch the 20 m line at the same time that a sound signal was emitted from a pre recorded CD. The frequency of the sound signals increased in such a way that running speed increased by  $0.5 \text{ km} \cdot \text{h}^{-1}$  each minute from a starting speed of  $8.5 \text{ km} \cdot \text{h}^{-1}$ . Correlation coefficients of  $\geq$

0.7 between  $\dot{V}O_2$  peak predicted from the 20 meter shuttle run test and direct measurements are reported for children and adolescents (166;167).

In the Norwegian ECA adolescents, aerobic fitness determined as  $\dot{V}O_2$  peak during *treadmill running* (Woodway ELG 2, Woodway GmbH, Weil am Rhein, Germany), started at five kilometres per hour ( $\text{km}\cdot\text{h}^{-1}$ ) and an inclination of 5.3%. The speed increased with  $2\text{ km}\cdot\text{h}^{-1}$  after five minutes running, thereafter  $1\text{ km}\cdot\text{h}^{-1}$  each minute until a maximal speed of  $11\text{ km}\cdot\text{h}^{-1}$  was reached. With no increments in speed, the inclination of the treadmill was raised 1% each minute until exhaustion. Heart rate was recorded continuously (Polar Vantage, Polar Electro KY, Kempele, Finland). Minute ventilation ( $\dot{V}_E$ ), respiratory exchange ratio (RER),  $\dot{V}O_2$  and carbon dioxide production ( $\dot{V}CO_2$ ) were measured after four minutes running using the Oxycon Champion (Erich Jaeger® GmbH & Co KG, Hoechberg, Germany). Calibration was conducted before each test period. The main criterion for having reached maximal effort was a subjective assessment by the test leader that the participants had reached his or her maximal effort. The second criterion was a RER above 1.00, HR above  $200\text{ beats}\cdot\text{min}^{-1}$  or reporting perceived exertion (RPE) above 17 using the Borg-RPE-Scale (168).

#### 5.3.4 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 in the Norwegian ECA adolescents (paper 4) and MasterScope in the Tanzanian children (paper 1), Erich Jaeger® GmbH & Co KG, Würzburg, Germany) according to criteria of European Respiratory Society (169). Total lung capacity (TLC), residual volume (RV) and specific airway resistance ( $sRaw$ ) were measured with a body plethysmograph in the Norwegian ECA adolescents (reported in paper 4) (Masterlab BodyPro, Erich Jaeger® GmbH & Co KG, Würzburg, Germany) according to criteria of European

Respiratory Society (170). The predicted values of Zapletal et al. (171) were used for comparisons in the Norwegian ECA adolescents whereas lung function values (per cent of predicted) from reference equations derived from the Tanzanian children are presented in paper 1. The following prediction equations were derived from the Tanzanian children (height in cm; boy = 1 and girl = 0):

$$FEV_1: -0.23 + 0.03 \cdot \text{Height} - 0.12 \cdot \text{Gender}$$

$$FEF_{50}: -1.70 + 0.04 \cdot \text{Height}$$

$$FVC: -2.43 + 0.03 \cdot \text{Height} - 0.13 \cdot \text{Gender}$$

The highest FEV<sub>1</sub>, FVC and FEF<sub>50</sub> are included in the analysis. All individual flow-volume curves were reviewed for technical acceptability. Response to inhaled salbutamol was measured using 0.4 mg salbutamol (Airomir™ Autohaler™, 3M Pharmaceuticals, St. Paul, MN). A ≥ 12% increase in FEV<sub>1</sub> 15 minutes after inhalation, compared to baseline ( $\Delta FEV_1 = (FEV_1 \text{ post} - FEV_1 \text{ pre}) / FEV_1 \text{ pre}$ ) was defined as a reversible airflow-limitation. Lung function data is not reported in the thesis.

### 5.3.5 Diet

The Norwegian ECA adolescents received four pre-coded food diaries (172), one for each day. They had to record their food intake and were instructed (verbally and watching a video) how to fill in the diary. The recordings of the diet were performed the same days as the activity recording. Daily intake of energy was computed using the food database and software system (KBS, version 4.9.) developed at the Department of Nutrition, University of Oslo. In paper 4 total energy intake is presented only, while these data is not reported in the thesis.

### 5.3.6 Physical activity and energy expenditure

In the Tanzanian children habitual physical activity was recorded using a *questionnaire* consisting of questions pertaining to means of transportation to school, physical activity during school breaks, participation in after-school sports activities and hours of television viewing and time at

computer each day (appendix G). The questions were selected from a validated questionnaire used in the European Youth Heart Study (157) and translated into Kiswahili (appendix F). The subjects filled in the questionnaire guided by a Kiswahili and Iraqw speaking research assistant. The Norwegian ECA adolescents and the EYHS children answered the same physical activity questions (appendix H).

Habitual physical activity was recorded *objectively* with SenseWear™ Pro<sub>2</sub> Armband (BodyMedia Inc., Pittsburgh, PA, USA) in the Norwegian ECA adolescents. The Armband was worn on the right arm over the triceps brachii muscle at the midpoint between the acromion and olecranon processes. The adolescents and their parents used an additional form to indicate when the monitor was not in use, such as during water activities. Energy expenditure was computed at 1-minute intervals. The cut off point defining MVPA were 3 Metabolic Equivalents (METs). 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). The adolescents received the monitor during their visit at the lab. The recording of physical activity started on a Wednesday or on a Sunday (random order) and included three week days and one weekend day. The adolescents also wore the activity monitor during the lab visit when sub maximal and maximal running was performed on the treadmill. Oxygen consumption was measured with Oxycon Champion (Erich Jaeger® GmbH & Co KG, Hoechberg, Germany) for comparison of energy expenditure.

The adults participating in the validation study of the *activity monitors* wore four activity monitors: 1. Armband, 2. ActiGraph (7164, LLC, Fort Walton Beach, FL, USA), 3. ActiReg® (PreMed AS, Oslo, Norway) and 4. iKcal (Teltronic AG, Biberist, Switzerland), and a portable oxygen analyzer (MetaMax II, Cortex Biophysic, Leipzig, Germany) for 120 minutes doing a variety of activities of different intensities. A measurement of RMR in the morning, on another day, according to international guidelines (173) and using the same oxygen analyzer was performed for calculating cut off points for



MVPA (paper 3). The data from the MetaMax II was analyzed with Metasoft v1.1 (Cortex Biophysic, Leipzig, Germany). Absolute  $\dot{V}O_2$  data were transformed into  $\text{kcal} \cdot \text{min}^{-1}$  multiplying  $\dot{V}O_2$  in  $\text{l} \cdot \text{min}^{-1}$  with the factor 4.82 (174).

The *Armband* has been validated against doubly labelled water and includes a two-axis accelerometer, a heat flux sensor, a galvanic skin response sensor, a skin temperature sensor and a near-body ambient temperature sensor (175). The monitor was worn on the right arm over the triceps brachii muscle at the midpoint between the acromion and olecranon processes. The data from the monitor was downloaded with software developed by the manufacturer (Innerview Professional Research Software Version 5.1).

*ActiGraph 7164* measures acceleration in the vertical plane and has been validated in several studies; however, these validation studies are population specific (176). The monitor was attached using an elastic belt at the participants' hip. The amount of energy expenditure and the cut off points defining MVPA were calculated by the formula of Freedson et al. (177) as recommended by the manufacturer.

*ActiReg*<sup>®</sup> measures body position and body motion and has been validated against doubly labelled water (178). The monitor has two pairs of body position sensors and two pairs of body motion sensors connected by cables to a battery-operated storage unit fixed to a waist belt. One of the position- and motion sensors was attached by medical tape to the chest and the other one to the front of the right thigh. The position codes and the amount of position changes were downloaded with software developed by the manufacturer (ActiCalc 32, Institute for Nutrition Research, University of Oslo, Norway).

*ikcal* measures heart rate and acceleration in the vertical and horizontal planes and has to our knowledge been validated in studies using whole-body indirect calorimetry and indirect calorimetry; however, the studies have not been published. The monitor was attached to the chest using an elastic belt around

the sternum according to instructions of the manufacturer. Data from the monitor was downloaded with software developed by the manufacturer.

A more detailed description of the procedures and the activity monitors are reported in paper 3.

#### **5.4 Ethical considerations**

In the Tanzanian population research clearance was obtained from the University of Dar es Salaam. Approval was also given by the local ministry of education and the local authorities in Mbulu district, and headmasters from the five primary schools visited. All children were given verbal information about the test procedures, and they could withdraw from the study at any time and for any reason.

The Norwegian part of the European Youth Heart Study, the validation study of physical activity monitors and the Environment and Childhood Asthma study were approved by the Data Inspectorate of Norway and the Regional Medical Research Ethics Committee. Written informed consent to take part was obtained from the participants and their parents if younger than 18 years old.

#### **5.5 Statistical analysis**

Sample size considerations in the Tanzanian children were based on calculations of sample size in the EYHS establishing that at each study location 200 children per gender group would give an acceptable level of power (80%) for most projected analyses (157). Three hundred and twenty six Tanzanian children were included. In the 13-year follow-up of ECA, a sample size calculation were based on a SD of daily hours of MVPA of 1.0 hour and a significance level of 0.05 to obtain 80% power, 64 subjects were required in each group to detect a mean difference of 0.5 hour. Sample size calculation was in the validation study of physical activity monitors, based on a SD of MVPA of 25 minutes and a significance level of 0.05 with 80%

power. We needed 17 subjects to detect a mean difference of 25 minutes between the activity monitors.

Demographic data are given as mean values and standard deviation (SD) unless otherwise stated and results as mean with 95% confidence intervals (CI). Prevalence of asthma symptoms is presented as mean percentage with 95% CI. Agreement between video- and written questionnaire was estimated using Cohen's kappa. Differences in prevalence in asthma symptoms between boys and girls, Tanzanian children and Norwegian ECA children at (10 years) were tested using the Chi-square test. The Chi-square test was also used when testing differences in physical activity patterns (data from questionnaire) among the Tanzanian children and the Norwegian EYHS children as well as the Norwegian ECA adolescents with and without asthma.

Differences in aerobic fitness between Tanzanian and Norwegian EYHS children were tested using independent sample t-test.

Associations between aerobic fitness and asthma symptoms in the Tanzanian children were tested by analysis of covariance adjusting for gender and bicycle skill (since experience and skill in bicycling influenced the result of the maximal cycle ergometer test). The dependent variable aerobic fitness, as well as gender and bicycle skill, were also analysed for associations with asthma symptoms using logistic regression analysis.

Associations between physical activity level, aerobic fitness and asthma in the Norwegian ECA adolescents were assessed by analysis of covariance adjusting for age, pubertal stage (entered puberty or not) and gender.

Physical activity data were further adjusted for mean hours each day the Armband was worn (reported in paper 4). The underlying assumptions of the analyses of covariance were assessed using Jackknife Residuals and Cook's d.

Bland-Altman plots were constructed to show the relationship of the mean differences (activity monitor minus indirect calorimetry) for accumulated energy expenditure and time in MVPA (reported in paper 3). The mean

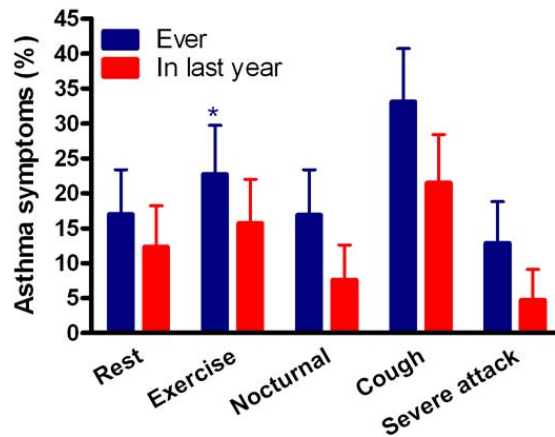
differences and limits of agreements were calculated (179). A two-way mixed, single measure, intra class correlation coefficient (ICC(3,1)) was performed for evaluating the extent of agreement between physical activity monitor and indirect calorimetry for accumulated energy expenditure and time in MVPA. A two-way analysis of variance was performed to determine differences in accumulated energy expenditure and time in MVPA obtained with the activity monitors and indirect calorimetry. Tukey post hoc testing was performed to locate significant differences. To test if the activity monitors underestimated or overestimated the energy expenditure in each intensity level, we calculated the absolute value of the difference at each time point (120 measurements, one per minute). For each individual, the cut off points defining moderate, vigorous and very vigorous intensity were 3, 6 and 9 times RMR. We calculated the mean of the absolute differences for each individual at the three levels of intensity. The mean for the 20 individuals serves as an estimate of the error with which each activity monitor misses the energy expenditure measured with indirect calorimetry at each intensity level. To test if the activity monitors underestimated or overestimated energy expenditure measured with indirect calorimetry, we applied a standard one-sample t-test for the absolute values for each activity monitor. In addition, for each individual and the three levels of intensity, we calculated the percentage the activity monitors underestimated or overestimated energy expenditure measured with indirect calorimetry. For the mean of these percentages, we applied the central limit theorem and performed a normal test to establish whether there is a tendency to underestimate or overestimate the energy expenditure in each intensity level.

Statistical significance level was set to 5%. Statistical analyses were performed in Statistical Package for Social Sciences Version 15.0 (SPSS, Chicago, IL, USA), Number Cruncher Statistical System (NCSS Inc. Version 2007, Kaysville, Utah, USA) and SAS<sup>®</sup> (SAS Institute Inc., Version 9.1.3, North Carolina, USA).

## 6 RESULTS

### 6.1 Prevalence of asthma symptoms

Any asthma symptoms last year were reported by 24% of the Tanzanian children, whereas symptoms at rest ever or in the last year were reported by 17% and 12%, respectively (fig. 3). Significantly more boys (27%) than girls (14%) reported exercise-induced symptoms ever ( $p=0.04$ ). Cough symptoms in the last year was reported by 22%, whereas 15% of the children reported nocturnal cough only. Severe attacks of asthma in the last 12 months were reported in five percent of the participants (fig. 3).



**Fig. 3.** Self-reported asthma symptoms in Tanzanian 9-10 year old children using a video questionnaire (mean percentage with 95% confidence intervals (CI)).

\* Significantly more boys than girls reported exercise-induced symptoms ever ( $p=0.04$ )

The prevalence of current wheeze at rest was 11 (7-16) % when using the written questionnaire (unpublished data). There was agreement between responses to the video and written questionnaire in 67-94% of subjects for each question (unpublished data). “Waking with cough” showed 67% agreement while, “Severe attacks” showed 94% agreement. Each question demonstrated significant agreement ( $P<0.001$ ) beyond chance (table 2).

The main source of disagreement occurred where there were positive responses to the written questionnaire, but negative responses to seeing

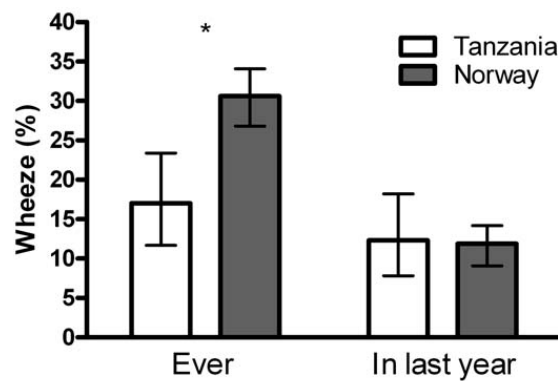
symptom illustrated on the video as for “Waking with cough” (unpublished data).

**Table 2.** Agreement between Written and Video Questionnaire *n* (%) in self-reported asthma symptoms in the rural Tanzanian children

Written Question.	Yes	Yes	No	No	Kappa
Video Question.	Yes	No	Yes	No	
Rest	7 (4.1)	11 (6.4)	14 (8.2)	139 (81.3)	0.28*
Exercise	14 (8.1)	30 (7.4)	13 (7.6)	115 (66.9)	0.25*
Nocturnal	2 (1.2)	2 (1.2)	11 (6.4)	157 (91.2)	0.21*
Cough	24 (13.9)	44 (25.6)	13 (7.6)	91 (52.9)	0.25*
Severe attacks	3 (1.8)	4 (2.4)	5 (2.9)	158 (92.9)	0.37*

\*  $P < 0.001$  indicating significant agreement beyond chance

In the Norwegian ECA children (at 10 years of age) self-reported wheeze ever and current were 31% and 12%, respectively (fig. 4). The prevalence of wheeze ever was significantly higher in the urban living Norwegian ECA children than the rural living Tanzanian children ( $p=0.007$ ). The prevalence of current wheeze was not significantly different (fig. 4).



**Fig. 4.** Self-reported wheeze in Tanzanian and Norwegian (ECA) 9-10 year old children (mean percentage with 95% CI). Symptoms were reported using a video questionnaire in Tanzania and a structured parental interview in Norway.

\* Significantly higher ( $p=0.002$ ) prevalence of asthma symptoms in Norwegian children.

## 6.2 Aerobic fitness and physical activity in Norwegian vs. Tanzanian children

The rural living Tanzanian and the urban living Norwegian EYHS children had similar relative aerobic fitness (47.3 (45.5-49.0) vs. 45.9 (44.9-46.9) ml · kg<sup>-1</sup> · min<sup>-1</sup> in boys and 40.3 (37.2-43.4) vs. 40.5 (39.5-41.5) ml · kg<sup>-1</sup> · min<sup>-1</sup> in girls) when bicycle skill was taken into account (fig. 5). If bicycle skill was *not* taken into consideration, the rural living Tanzanian girls attained 8% lower aerobic fitness compared to the urban living Norwegian EYHS girls, while there was no significant difference between Tanzanian and Norwegian boys of same age (fig. 5). Experience and skill in bicycling influenced the result of the maximal cycle ergometer test. Tanzanian boys and girls who were accustomed to bicycling (AB) achieved a 12% higher aerobic fitness compared to boys and girls unaccustomed to bicycling. Yet, in the 20 meter shuttle run test there was no difference in aerobic fitness between the Tanzanian accustomed and unaccustomed children (reported in paper 2). Tanzanian boys and girls attained 21.6% and 36.0%, respectively, higher aerobic fitness in the 20 meter shuttle run test (reported in paper 2) compared to the maximal cycle ergometer test ( $p < 0.001$ ).

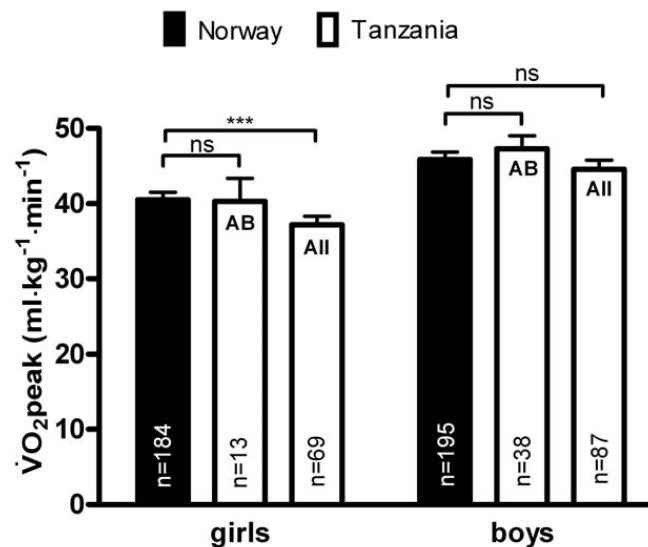


Fig. 5. Aerobic fitness ( $\dot{V}O_2$  peak) in Norwegian EYHS and Tanzanian 9-10 year old children (180). AB = only subjects accustomed to conventional bicycling are included. All

= all children, both accustomed and unaccustomed to conventional bicycling are included.

Values are reported as means (95% CI).

Significance: \*\*\* =  $p < 0.001$ ; ns = not significant.

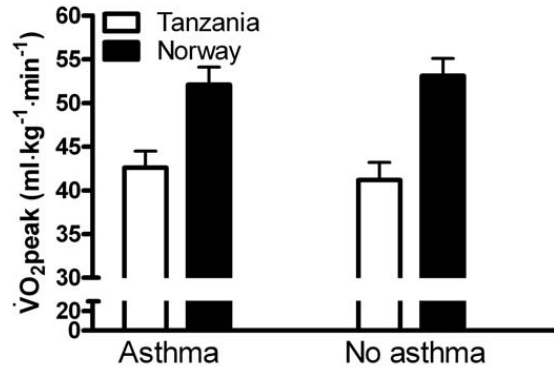
The majority of the Tanzanian and Norwegian EYHS children walked for transportation to school, but the Tanzanian children had to travel for a significantly longer time (reported in paper 2). Approximately 40% of the rural living Tanzanian children walked to school for at least 30 minutes, vs. 5% of the urban living Norwegian EYHS children.

There was no significant difference in aerobic fitness measured from the maximal cycle ergometer test or the 20 meter shuttle run test between Tanzanian children who walked short versus long distances to school (reported in paper 2). Tanzanian boys were less active in playing outdoor games after school compared to Norwegian EYHS boys, while no significant difference was found between Norwegian EYHS girls and Tanzanian girls (reported in paper 2).

### ***6.3 Aerobic fitness and physical activity in relation to asthma***

Asthma was not significantly associated with aerobic fitness in any of the two populations (rural living Tanzanian children and urban living Norwegian ECA adolescents), either in univariate analyses or after adjusting for the included covariates and confounders (fig. 6).





**Fig. 6.** Adjusted\* aerobic fitness ( $\dot{V}O_2$ peak) in Tanzanian 9-10 year old children who reported asthma symptoms or not, and Norwegian 13-14 year old ECA adolescents with and without asthma (mean and 95% CI). Aerobic fitness was assessed using a maximal bicycle procedure in the Tanzanian children whereas in the Norwegian ECA adolescents aerobic fitness was determined during maximal treadmill running.

\* Adjusted for age, gender and pubertal stage in Norwegian ECA adolescents. In the Tanzanian children, aerobic fitness was adjusted for gender and bicycle skill.

Furthermore, the Norwegian ECA adolescents with and without asthma had similar total energy expenditure and hours of MVPA during week and weekend days also after adjustment for age, pubertal stage (entered as puberty or not), gender, and mean hours each day the Armband was worn (table 3). However, 37% of the Norwegian ECA adolescents with current asthma reported that asthma caused limitations in physical activities vs. 5% in the asthma ever group ( $p=0.005$ ) (unpublished data). Adolescents with current asthma reporting exercise limitations also participated in significantly less very vigorous intensity physical activity (0.14 (0.08-0.25) vs. 0.31 (0.20-0.47) hours per day) than current asthmatics not reporting exercise limitations ( $p=0.034$ ) (unpublished data). Adjusting for regular use of inhaled corticosteroids and use of  $\beta_2$ -agonists when participating in physical activity, did not influenced the results. Self reported exercise limitation was not associated with reduced time in moderate and vigorous physical activity.

**Table 3.** Adjusted\* hours in moderate to very vigorous intensity physical activity and total energy expenditure at week- and weekend days in Norwegian 13-14 year old adolescents with and without asthma (controls).

	<b>Asthma (n=95)</b>	<b>Controls (n=79)</b>	<b>P-value**</b>
	Mean (95% CI)	Mean (95% CI)	
MVPA, <i>Week</i>	4.4 (4.0-4.8)	4.6 (4.2-5.0)	0.41
(hours·day <sup>-1</sup> ) <i>Weekend</i>	3.8 (3.4-4.3)	3.5 (3.0-4.0)	0.32
TEE, <i>Week</i>	2446 (2336-2556)	2386 (2269-2503)	0.41
(kcal·day <sup>-1</sup> ) <i>Weekend</i>	1992 (1862-2121)	1860 (1719-2001)	0.13

# Abbreviations: MVPA, hours in Moderate to very Vigorous intensity Physical Activity; TEE, Total Energy Expenditure.

\* Adjusted for age, pubertal stage (entered as puberty or not), gender, and mean hours each day the Armband was worn. Data are given as adjusted means with 95%CI in parentheses.

\*\* P-values for any differences between groups.

All participants fulfilled the international physical activity guidelines during week days and 95% of the adolescents with asthma fulfilled the physical activity recommendation vs. 87% of the controls (not significant) during weekends (reported in paper 4). Norwegian ECA adolescents with and without asthma had significantly lower total energy expenditure during weekend compared to week days ( $p<0.001$ ). However, only controls had significantly fewer minutes in MVPA during weekends ( $p=0.001$ ) (table 3). The Norwegian ECA adolescents with and without asthma participated in exercise or sport activities on average four times a week. Almost 70% of the participants reported the exercise or sport activities as strenuous. The adolescents with and without asthma participated in similar kind of activities. Sixty to seventy per cent of the adolescents participated in endurance training or ball game activities at least weekly (reported in paper 4). Sixty four per cent of the adolescents had at least three hours of physical education per week at school, and 78% participated in physical education classes weekly (reported in paper 4). Twenty seven per cent of the Norwegian ECA adolescents watched television for at least two hours during week days, while 38% of the adolescents spent at least two hours in front of the computer each day (reported in paper 4), with no significant difference related to asthma.

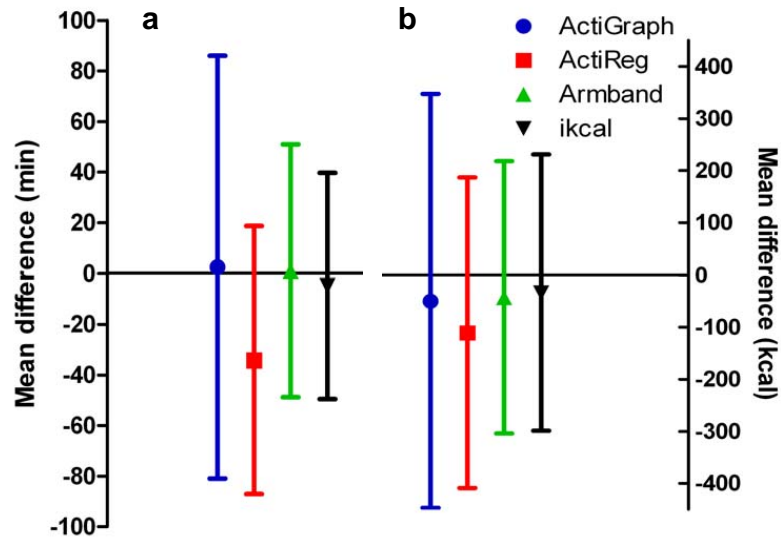
## **6.4 Objective methods for measuring physical activity**

### **6.4.1 Armband vs. indirect calorimetry during treadmill running**

The ICC was 0.88 ( $p < 0.0001$ ) and limit of agreement (mean differences  $\pm$  1.96 SD of the differences)  $-6.0 \pm 25.8$  kcal respectively when comparing energy expenditure by indirect calorimetry vs. Armband (data not published). The Norwegian 13-14 year old ECA adolescents were *walking and running on the treadmill* during measurements. The Armband significantly underestimated the total energy expenditure during the treadmill test ( $p < 0.0001$ ). The underestimation increased when inclination was raised compared to speed. The underestimation of energy expenditure increased systematically by 3% for each increased unit of oxygen consumption ( $\text{kcal} \cdot \text{min}^{-1}$ ) ( $p < 0.004$ ) (data not published).

### **6.4.2 Activity monitors vs. indirect calorimetry in free living conditions**

A *variety of activities and intensities* were performed by the adults participating in the validation of activity monitors (reported in paper 3). The mean differences between activity monitors and indirect calorimetry in MVPA activity ranged from  $-34.2$ - $2.5$  min (fig. 7a). The Armband and ActiGraph overestimated time in MVPA with 2.9 and 2.5%, whereas iKcal and ActiReg<sup>®</sup> underestimated time in MVPA with 11.6 and 98.7% respectively. The ICCs were 0.54 (0.13-0.79) ( $p = 0.007$ ) and 0.54 (0.15-0.79) ( $p = 0.006$ ) for Armband and iKcal, respectively (table 4). However, the ICC between Armband and iKcal was 0.84 (0.63-0.93). There was no statistical agreement ( $p > 0.05$ ) for time in MVPA between indirect calorimetry and ActiGraph or ActiReg<sup>®</sup>.



**Fig. 7.** Mean differences in (a) minutes in moderate to very vigorous intensity physical activity and (b) accumulated energy expenditure during 120 minutes activity (activity monitor minus indirect calorimetry) for ActiGraph, ActiReg, Armband and ikcal vs. indirect calorimetry (mean  $\pm$  95%CI).

All monitors underestimated total energy expenditure during 120 minutes of activity (fig. 7b). The underestimation ranged from 5-21%, respectively.

**Table 4.** Intra class correlation coefficient between physical activity monitor and indirect calorimetry for time in moderate to very vigorous intensity physical activity and accumulated energy expenditure (95%CI).

	MVPA	TEE
ActiGraph	nsa	0.55 (0.16-0.79)
ActiReg	nsa	0.47 (0.02-0.75)
Armband	0.54 (0.13-0.79)	0.73 (0.44-0.88)
ikcal	0.54 (0.15-0.79)	0.71 (0.41-0.87)

# Abbreviations: MVPA, hours in Moderate to very Vigorous intensity Physical Activity; TEE, Total Energy Expenditure; nsa, no statistical agreement.

ActiReg<sup>®</sup> significantly underestimated the accumulated energy expenditure ( $p < 0.02$ ) compared to the other monitors. The ICC ranged from 0.47

(ActiReg) to 0.73 (Armband) (table 4). ActiReg<sup>®</sup> ( $p=0.004$ ) and ActiGraph ( $p=0.007$ ) also underestimated energy expenditure in MVPA (reported in paper 3).

## 7 GENERAL DISCUSSION

### 7.1 *Main findings in relation to previous studies*

The *prevalence of wheeze* last year (12%) in the Tanzanian children was similar to or higher than the 0-21% previously reported by written questionnaire based studies conducted in the sub-Saharan African countries (34;35;60;61;63-65;181), and was similar to the 9-33% reported in 13-14 year olds from many “Westernized societies” (58) including the Norwegian ECA children (12%). However, when comparing reports of current wheeze from video questionnaire data, the prevalence of symptoms in the present thesis is similar to the 11-12% recently reported in other sub-Saharan countries (64;65), but higher than the 4% reported in Kenya a decade ago (63).

To our knowledge, the prevalence of asthma or asthma symptoms in Tanzania have been reported in two previously published studies (60;61). Thirty years ago, Carswell et al. (60) reported a prevalence of recurrent episodes of asthma symptoms and breathlessness in 7.8% of 242 school children living in rural villages in South-West Tanzania. The medical history was obtained by Swahili-speaking natives with medical experience. A recent study (61) conducted in 294 urban (Dar es Salaam) and 511 rural (in the foothills of Mount Kilimanjaro) living Tanzanian children showed a prevalence of self-reported current wheeze, using a written questionnaire, in 1.9-5.2% in children and adolescents. Different methodology to diagnose or define asthma, environment and living conditions may explain the wide range of prevalence of asthma symptoms among countries and districts (58). In general, agreement between written- and video questionnaires tends to be higher in English-speaking children (38). The Tanzanian children participating in the present thesis had a non-English speaking background and most of them preferred to speak the local language Iraqw, and not Swahili or English which are the official languages in Tanzania. An explanation for the poor agreement between the written and the video questionnaire is the fact that written and video questions do not represent

exactly the same situation. Children who respond negatively to the written questionnaire but positively to the video may be uncertain about the meaning of the written term but recognised the symptoms when it was shown to them audiovisual (38). In the present study, the best agreement between written- and video questionnaire was for the “severe attacks” question. Lower agreement has been reported for this question in a population of mixed ethnic background (182); however, “nocturnal wheeze” and “nocturnal cough”, with “fair” agreement in the present study, corresponds to the findings of Gibson et al. (182). The main source of disagreement for “waking with cough” in the present study was due to positive responses to the written questionnaire, but negative responses to seeing symptom illustrated on the video.

The Tanzanian children in the present thesis lived in a rural setting in the highlands of Northern Tanzania, whereas other studies conducted in sub-Saharan countries have included urban populations or populations from areas more similar to “Westernized societies” (34;35). The prevalence of diagnosed asthma may be underestimated in rural districts in developing countries due to social, financial, cultural and socio-economical barriers as well as the organisation of national health care systems (37). However, no difference has been found in the prevalence of video-reported symptoms between rural and urban areas, whereas the written questionnaire indicated more severe forms of asthma in the urban living children possibly due to lack of appropriate treatment (39). The relatively high occurrence of asthma symptoms in Tanzania in the present study could be due to lack of asthma control because of little or no disease specific treatment. None of the children reported use of asthma medications. It has been reported that 60-90% of conditions in need of medical attention in this area do not get it at the present time (183).

The high prevalence of asthma symptoms in the Tanzanian children could also be due to factors other than asthma. Non-atopic wheeze related to viral infections (184), other respiratory symptoms due to tuberculosis or malaria (185) or exposure to the combustion products of indoor fires (186) have

been reported to be common in rural parts of East-Africa. Cough or difficult breathing has also been reported to be frequent in this population of Tanzanian children, and 22% of all paediatric admissions to public hospitals in North Tanzania are due to pneumonia (184). The families of our Tanzanian children had a standard way of living and cooking took place outdoors. The diet was relatively monotonous and consisted largely of maize gruel or stiff porridge, partly supplemented with animal milks and vegetables, but included seldom meat. The prevalence of underweight in the Tanzanian study population was 37%, and similar to previously reported in the same area (187). As reported in paper 1, the higher occurrence of any asthma symptoms in the Tanzanian children with lower skinfolds might be related to nutritional and growth restriction affecting normal lung growth. However, the effect of underweight, overweight and body composition are not further elaborated in the present thesis.

The *aerobic fitness level* of the Tanzanian children is similar to a previous published study from Tanzania (87), although 5-10% lower than reported from studies in Kenya (89) and South Africa (88). The values in Norwegian and Tanzanian were similar to the mean aerobic fitness values of 36-50 ml · kg<sup>-1</sup> · min<sup>-1</sup> and 41-58 ml · kg<sup>-1</sup> · min<sup>-1</sup> in girls and boys, respectively, reported in Western countries (81-85). Difference in aerobic fitness between these studies, as well as aerobic fitness values reported in the Norwegian ECA adolescents, could be due to use of different test ergometers. During treadmill running children and adolescents, on average, achieve 8-10% higher  $\dot{V}O_2$  peak values compared to bicycling on a cycle ergometer (154;188-190). The aerobic fitness values in the Tanzanian children achieved during the maximal cycle ergometer test were most likely underestimated because of lower work economy with higher oxygen consumption for a given power output. Pedalling with lower mechanical efficiency has been reported in other ethnic groups unaccustomed to conventional bicycling (191). The Tanzanian children were tested at 1800 metre above sea level. A 3-5% increase in aerobic fitness has been suggested if measured at sea level (192). However, inconsistencies in the



literature makes it difficult to quantify how much higher the aerobic fitness would have been if the Tanzanian children had been tested at sea level (192-194).

In comparison with the Tanzanian children from Mbulu district, which may have retained a relatively traditionally rural lifestyle, many other Sub-Saharan areas have experienced accelerated urbanization into a “Western lifestyle”. The level of aerobic fitness of a population is, in addition to heredity, dependent on nutritional status, physical activity level and morbidity rate (191). In the present study, the underweight children had similar aerobic fitness compared to children of normal weight (reported in paper 1). Malnutrition and inadequate energy intake in children from Sub-Saharan countries are not associated with lower aerobic fitness levels in some studies (88;91), although reduction in performance in strength exercises are reported (91). Adaptation to nutritional and environmental stress explaining high aerobic fitness levels in undernourished children has been suggested (88). It is suggested that adjusting aerobic fitness for body size rather than body mass has less bias when comparing children of different body size (195;196). However, absolute  $\dot{V}O_2$  peak, not adjusting for body mass, would have changed aerobic fitness into favour of the children of normal weight (paper 1).

Both the majority of Tanzanian and the Norwegian EYHS 9-10 year old children travelled to school by foot, but the Tanzanian children had to walk longer distances than the Norwegian EYHS children. Almost 40% of the Tanzanian children walked for more than half an hour to get to school, compared to 5% among the Norwegian children. The intensity of the movement was not evaluated, but from our experiences, the Tanzanian children walked rather than ran. Relatively large amounts of daily physical activity are reported in many Sub-Saharan populations (80;89); however, the intensity of the physical activity is of rather low character (89). Improvement in aerobic fitness during childhood is probably only achieved when the training intensity is high (197). The Tanzanian boys were less

active in playing outdoor games after school compared to Norwegian boys, while no difference was found between Norwegian and Tanzanian girls. Tanzanian girls from the same area are reported to spend much time helping their mothers in household chores, milking and fetching water and firewood while boys become increasingly involved in herding activities that involve high levels of physical activity (187). Lower levels of habitual physical activity could explain some of the larger gender difference in aerobic fitness in the Tanzanian (15%) compared to Norwegian girls (9%).

Similar *aerobic fitness* in children and adolescents with and without asthma is in agreement with others (148;149). However, the aerobic fitness of the Norwegian ECA adolescents in the present thesis are approximately  $10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  higher than reported by Santuz et al. (148) in Italian children and adolescents recruited from a out-patient clinic. The aerobic fitness level in the Norwegian ECA adolescents is similar to that reported in healthy adolescents from Western countries ( $40\text{-}49 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  for girls vs.  $52\text{-}61 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  for boys, respectively) (82;86). Reduced aerobic fitness levels in asthmatic subjects are reported in some studies (116;147), such as in adolescents with severe asthma (116), whereas others found no correlation between asthma severity and aerobic fitness (150). Different exercise ergometers or test modes and protocols influence the measured aerobic fitness level (154-156) and few of the published studies have included direct measurement of oxygen consumption as was done in the present thesis.

In a prospective population-based study in asymptomatic Danish children, an inverse relationship between aerobic fitness (peak power output) and subsequent development of physician diagnosed asthma was reported (15). Physical inactivity has been suggested as an explanation for the lower aerobic fitness in some adolescents with asthma (198). A previous report indicates that the majority of severely asthmatic children with low levels of aerobic fitness can achieve a normal fitness after participation in a physical rehabilitation program (199). However, Garfinkel et al. reported adults with asthma perceiving their disease as a limiting factor to improved aerobic

fitness (200). The association between asthma and low aerobic fitness or physical activity levels reported in some studies (116;117;147) can be due to poor asthma control (201). Subjects with asthma may limit the intensity of their physical activity because of dyspnoea (202). However, engagement in significant levels of physical activity can lead to improved detection of asthma; particularly exercise-induced asthma. Consequently, physical activity levels in children and adolescents with asthma may appear artificially high because already active children and adolescents are more likely to be diagnosed as having asthma (203). 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. The Norwegian ECA adolescents with asthma were fit and had high physical activity levels. Use of asthma medications and good asthma control can make the conditions favourable for a physical active lifestyle and influence physical activity levels in children with asthma, and therefore their level of aerobic fitness (204). Approximately half of the adolescents with asthma used inhaled corticosteroids regularly. Inhaled glucocorticosteroids are currently the most effective anti-inflammatory medications for treatment of asthma (205).

Whether inactivity negatively influences airway inflammation in children is largely unknown. In general, the resting immune status of a fit child seems to be similar to that of a less fit child (206). However, low grade inflammation has been shown in unfit but not fit overweight and obese children (207). No change in airway inflammation was found in children with asthma after 12 weeks aerobic training of moderate intensity (50 minutes, twice a week) (208), whereas, physical training reduced airway inflammation in mice (209-211) and adult athletes (212). On the other hand elite sled dogs had significantly higher nucleated macrophages and eosinophil counts after a 1,100 mile endurance race compared with sedentary dogs not participating in the race (213). Endobronchial biopsies from competitive cross country skiers without asthma showed markedly higher number of lymphoid aggregates (214), T-lymphocyte, macrophage and eosinophil counts compared to non-asthmatic controls (215), whereas,

exhaled nitric oxide (eNO) was not changed after 12 weeks aerobic training in children with mild asthma (216).

A balance between the pro- and the anti-inflammatory effects of exercise in asthma has been suggested to be null in respect to markers of airway inflammation, such as eNO (208). If regular physical activity reduces the degree of airway inflammation in children with asthma, thereby improving symptoms and reduces the amount of medication required, has to be confirmed in future studies. However, it should be remembered that physically active children and adolescents as well as athletes, during training are more exposed to pollutants and allergens in ambient air due to hyperventilation and inhalation of larger amounts of air (217).

Bronchial hyperresponsiveness has been inversely related to physical activity in adults (218) and children (136). In contrast, male 19-21 years old competitive cross country skiers vs. inactive controls demonstrated increased bronchial hyperresponsiveness in the winter season (219). In healthy adults, an increase in bronchial hyperresponsiveness was reported after prolonged physical activity of moderate intensity in ozone levels often found in ambient air (220). Participating in physical activity outdoor when pollution levels are high, children may have higher relative exposures than adults (221). In communities with high ozone concentrations, the relative risk of developing asthma in children participating in three or more types of sports was 3.3, compared with children playing no sports. Sports had no effect in areas of low ozone (222). Recently, it was observed that children doing outdoor recreational activities have a significant increase in eNO, related to ambient ozone levels (223).

Asthma and asthma symptoms are reported to be more common in elite athletes compared with age-matched control persons (16-18). Observations suggest that high level exercise performed on a regular basis might contribute to the development of asthma in athletes previously unaffected by the disease (19). In healthy subjects, exercising intensive for long periods of time breathing large volumes of cold and/or dry air, air

containing irritant gases, particular matter, or allergens could result in the same airway response as documented in asthmatic subjects (20). The relationship between physical activity and asthma may be modelled in the form of a “J” curve. This model suggest that while the risk for asthma may decrease below that of a sedentary individual when one engages in regular physical activity of moderate to vigorous intensive character, risk may rise above average during large amounts of high-intensity activity performed under extreme conditions. A combination of endurance training and an environmental hazard such as cold air, seasonal allergens, pollutants or respiratory virus infections may increase the risk for asthma in athletes as well as the highly active child (217). In addition, large amounts of very vigorous intensity physical activity has been associated with increased risk for upper respiratory tract infections (224).

The percentage of Norwegian ECA adolescents who were *physically active* (MVPA) more than 60 minutes every day were higher than previously reported in Western countries (74;77). The similar physical activity levels in Norwegian ECA adolescents with asthma compared to controls are supported by others (133;134), although few other studies have included objective physical activity measures. In contrast, higher (129;131) or lower physical activity levels has also been reported (117). Different descriptions or definitions of asthma, sample size and selection may explain the divergence among studies. Inconsistence between studies may also be related to different methodologies. The importance of using well designed methodologies when measuring physical activity has been highlighted (153).

In the present study time in MVPA assessed with the *activity monitors* was somewhat less precise compared to assessment of total energy expenditure. For Armband and ikcal, 53 and 54% of the variation were explained by differences among the participants and 47 and 46 % by differences between the two different physical activity monitors. Eighty four per cent of the variation between the two monitors for assessment of time in MVPA was explained by differences among the participants. The lack of statistical

agreement between indirect calorimetry and ActiReg<sup>®</sup> as well as ActiGraph was supported by the underestimation of energy expenditure in MVPA. An explanation for the low agreement could be limitations of uniaxial accelerometers and motion sensors, since accelerometers are insensitive to certain types of activities such as bicycling and strength training (176).

Information on reported time in MVPA among different models is lacking; however, Strath et al. compared five ActiGraph accelerometer cut off points for predicting time spent in different intensity categories (225). Different accelerometer cut off points gave substantially different estimates of time in MVPA. Errors of energy expenditure prediction and cut off points defining MVPA could lead to misclassification of duration and frequency of physical activity. Leenders et al. found no difference in time spent in light, moderate and vigorous intensity physical activity during a seven days assessment using ActiGraph, a pedometer and a triaxial accelerometer (226).

Despite an average percentage underestimation of estimated accumulated energy expenditure from 5 to 21%, the activity monitors ActiGraph, Armband and ikcal provided relatively similar results. ActiReg<sup>®</sup> significantly underestimated estimated energy expenditure compared to indirect calorimetry as well as compared to the other three activity monitors. The ICC of 0.73 and 0.71 for Armband and ikcal vs. 0.55 and 0.47 for ActiGraph and ActiReg<sup>®</sup> illustrates that for Armband and ikcal, a larger part of the variance was explained by differences among individuals.

To our knowledge, no studies have reported on comparisons of energy expenditure assessed with Armband or ikcal with indirect calorimetry in free living activities. However, St-Onge et al. (175) reported mean estimated energy expenditure to be significantly lower for Armband than measured with doubly labelled water and their ICC, 0.81, was somewhat higher compared to the present study. Comparisons of energy expenditure assessed with Armband and indirect calorimetry in children have produced diverging results. Arvidsson et al. (227) reported underestimation of energy

expenditure in most activities in 20 healthy Swedish children, in contrast to Dorminy et al. (228), who reported overestimation of energy expenditure during all activities in African American children. King et al. (229) compared estimated energy expenditure using ActiGraph and Armband with indirect calorimetry during treadmill walking and running. ActiGraph gave the best estimate of total energy expenditure at walking and jogging speeds whereas Armband was best for estimation of total energy expenditure. ActiReg<sup>®</sup> was recently validated against doubly labelled water and indirect calorimetry in a sample of adults (178), in which some underestimation of energy expenditure was present, but to a smaller degree than in the present study. ActiGraph has been validated against indirect calorimetry in several studies; however, a majority of the studies were conducted in the laboratory, including participants performing activities like treadmill walking and running (176). In the literature, correlation coefficients between physical activity monitors estimating energy expenditure and indirect calorimetry, seem to be lower during normal life style activities compared to walking and running on a treadmill at submaximal intensities (176). The ICC of 0.55 between ActiGraph and indirect calorimetry in the present study in a free living condition, is in line with results reported by others (230-233).

## ***7.2 Methodological strengths, limitations and considerations***

The main strength of the present thesis is the opportunity to test the same hypothesis in different populations with dissimilar culture and way of living.

Another strength are the well characterised Norwegian ECA adolescents with and without asthma recruited in a nested case-control study, as part of an observational prospective cohort of healthy newborn children followed for 13 years. This design gives the ability to use a reference population that are well characterised and described by combining clinical diagnosis, symptoms and use of asthma medications, not only relying on self-reported asthma symptoms. Since none of the Tanzanian children reported use of asthma medications or had a doctor's diagnosis of asthma, a strict definition

of asthma could not be obtained. Instead the standardised video questionnaire was used to provide the participating children with a visual representation of wheezing or depictions of asthma symptoms on the assumption that they might not understand the concept of wheezing. However, the possibilities of bias with differential diagnosis of asthma can not be ruled out. For practical reasons, measures of bronchial hyperresponsiveness were not measured in the Tanzanian children. However, lung function and reversibility to a  $\beta_2$ -agonist was measured. None of the children had FEV<sub>1</sub>/FVC ratios below 80%, an index of obstructive airways in adults, and three per cent of the children had reversible airflow limitation defined as  $\geq 12\%$  increase in FEV<sub>1</sub> 15 minutes after inhalation of a  $\beta_2$ -agonist (salbutamol) (reported in paper 1). Therefore we could not test the association between asthma symptoms and abnormal FEV<sub>1</sub>/FVC ratio or reversible airflow limitation. On the other hand, due to great overlap of measurements between healthy children and those with previous asthma symptoms, the diagnostic accuracy of baseline lung function tests are reported to be poor (234).

The use of standardised and objective methods when measuring aerobic fitness is also strength of the present thesis. In addition, objective measures of physical activity and direct measurements of  $\dot{V}O_2$  peak in the Norwegian ECA adolescents were included. Physical activity monitors give reliable measures of physical activity and having advantages compared to self reports with recall biases (235), although only one measurement period in the present study. The main reason for not including objective measures of physical activity in the Tanzanian children was because we did not had access to monitors at that time. Instead we included the same physical activity questionnaire as used among the Norwegian school children and adolescents. Aerobic fitness was also measured in the 9-10 year old Tanzanian and Norwegian EYHS children by using the same standardized bicycle protocol in both samples. Both treadmill and bicycle ergometer are suitable for use in children and adolescents (236). However, studies of populations not accustomed to bicycling may consider using other test



methods than a maximal cycle ergometer test, since this test likely underestimates aerobic fitness in subjects unaccustomed to bicycling.

The included Tanzanian children were representative of 9-10 year old school children living in Mbulu district. The cause for the present age group was the comparison with already collected data on 379 Norwegian school children of same age (paper 2). The Norwegian EYHS children were representative of school children living in Oslo. Participation in an ongoing cohort may influence lifestyle due to knowledge regarding asthma management and the adolescents may not be representative of the entirely general Western youth population. However, the included Norwegian adolescents may represent an urban Nordic lifestyle. There were no significant differences at 10-year follow up with respect to socioeconomic factors, BMI, lung function, bronchial hyper responsiveness, use of inhaled corticosteroids or  $\beta$ -2 agonist, prevalence of wheeze and exercise induced bronchoconstriction between the adolescents in the present study and those who did not participate. The intention with the present validation study was to include men and women of different ages with a wide variety of BMI. The reason for including subjects 19-56 years of age is because it covers the adult population which the currently published physical activity recommendations include (237). We can not generalise our findings to children or other populations; however, we hope to address some of the challenges associated with comparisons of physical activity recordings of different activity monitors in free living activities, where information is lacking in the literature.

Data collection in the field, as in rural Tanzania, in a different culture without electricity, with problems of imprecise translations and vocabulary differences may offer challenges. Illiteracy was also common among the parents and the precise date of children's birth was not usually known. This is in contrast to a well-equipped laboratory setting used in Norway. Different altitudes in the highlands of Tanzania and sea level in Oslo, Norway, has to be kept in mind since low barometric pressure, because of

higher altitude or breathing hypoxic air, decrease  $\dot{V}O_2$  peak in most individuals (238). An increase in  $\dot{V}O_2$  peak has been suggested if subjects born and living at moderate altitude, were tested at sea level (192), but inconsistencies in the literature (193;194) makes it difficult to quantify how much higher the estimated  $\dot{V}O_2$  peak if the Tanzanian children were tested at sea level. However, whether the Tanzanian children should have been tested at sea level or the Norwegian EYHS children at moderate altitude, both away from the environment where they grew up and live, will only be speculative thoughts.

A difference in aerobic fitness (reported in paper 1) was assessed by analysis of covariance adjusting for gender (and bicycle skill for aerobic fitness since experience and skill in bicycling influenced the result of the maximal cycle ergometer test). Aerobic fitness in Tanzanian children and Norwegian EYHS children were compared using an independent sample t-test (paper 2). In the finale analysis children not accustomed to regular bicycling were excluded. Adjusting for bicycle skill, when comparing aerobic fitness in Tanzanian and Norwegian EYHS children does not make sense, since the majority of Norwegian compared to the Tanzanian children is accustomed to conventional bicycling.

Sample size considerations in Tanzania were based on calculations of sample size in the European Youth Heart Study establishing that at each study location 200 boys and 200 girls would give an acceptable level of power for most projected analyses (157). We included 326 Tanzanian children, but unfortunately only 198 children were able to cycle satisfactorily during the preliminary test and were invited to participate in the maximal cycle ergometer test. In addition, results from only 156 Tanzanian maximal cycle ergometer tests were accepted and we can not rule out type II errors in paper 1 and 2. However, 100 children in each group has been reported as sufficient in order to demonstrate 5% difference in mean  $\dot{V}O_2$  peak between to populations (239). In the Norwegian ECA adolescents, sample size calculations were based on the variable daily hours

in MVPA and a sample of 64 subjects in each group were required. Ninety-five children with asthma and 79 controls were included in the present study. However, we can not rule out type II errors for the variable aerobic fitness.

A limitation in the validation of physical activity monitors was the lack of data on reliability between and within activity monitors. Ideally a second measurement period should have been carried out; however, reproducing the same type, duration and intensity of activities in our subjects participating in free living activities is almost impossible.

### **7.3 *Future perspectives***

Based upon the results of the present thesis the following research topics should be addressed in the future:

The prevalence of asthma symptoms in other rural Tanzanian or East African areas should be confirmed in a new study including measurements of bronchial hyperresponsiveness. Ideally, a follow-up study in the same children including objective measurements of physical activity, direct measurements of  $\dot{V}O_2$  peak as well as bronchial hyperresponsiveness should have been carried out. However, since tracking the Tanzanian children is not feasible, carrying out a follow-up study in this population is impossible or extremely difficult.

Prospective studies to estimate the risk of asthma development in children and adolescents including objective measurements of physical activity and direct measurement of  $\dot{V}O_2$  peak with valid definitions of asthma are needed.

In the present thesis systemic inflammatory changes after prolonged or lack of physical activity and its association to airway inflammation on asthma

development has not been debated. Whether or not airway inflammation is affected by physical training during childhood is largely unknown.

Additional comprehensive studies comparing physical activity monitors with indirect calorimetry under free living conditions in children and adolescents are needed to evaluate the validity of previous and next generations physical activity monitors.

## **8 CONCLUSIONS**

1. Twenty four per cent of 9-10 year old children from a rural district in North-Tanzania reported asthma symptoms, which suggests that asthma may be as prevalent in rural living Tanzanian children compared to Nordic urban living children.
2. Tanzanian and Norwegian children had similar relative aerobic fitness estimated from a cycle ergometer test; however, the comparison is hampered by differences in altitude and poor cycle ergometer skills in the Tanzanian children, both of which are likely to cause underestimation of aerobic fitness.
3. Aerobic fitness or physical activity was not associated with asthma or asthma symptoms in any of the populations.
4. Recorded time in moderate to vigorous intensity physical activity and energy expenditure varies substantially among physical activity monitors, necessitating detailed report of type of monitors used in studies.

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## **ERRATA**

### **Paper 1**

Since submission to the doctoral committee, paper 1 has been published online (pending the print journal) in its original form only with minor changes (after proof correction) in the title, objectives as well as tables, to *Allergy*.

### **Paper 4**

Since submission to the doctoral committee, paper 4 has been published in its original form to *Allergy* (March 2009).

**The following changes have been made from the thesis was originally submitted to the doctoral committee:**

#### *Review of the literature*

Page 8 # 3: ...respiratory assessment (including measurement of reversible airflow-limitation and/or **bronchial hyperresponsiveness**) and consideration of differential diagnosis...

#### *Aims of the study*

Page 19: 2. To assess whether living in a rural district in North-Tanzania have higher **aerobic fitness level** than Norwegian children...

#### *Results*

Page 41 # 1: Furthermore, the Norwegian ECA **adolescents** with and without asthma...

#### *References*

Page 61: (16) "Ref Type: Journal (Full)" has been deleted  
(17) "Ref Type: Journal (Full)" has been deleted  
(219) "Ref Type: Journal (Full)" has been deleted

**PAPERS 1-4**



**Paper 1**

Berntsen S, Lødrup Carlsen KC, Hageberg R, Aandstad A, Mowinckel P, Anderssen SA, Carlsen KH. Prevalence of asthma symptoms in children from a rural district in North-Tanzania, and its relation to aerobic fitness and body fat. Accepted the 15<sup>th</sup> of December 2008, for publication in *Allergy* and published online in March 2009, pending the print journal.

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## Original article

# Asthma symptoms in rural living Tanzanian children; prevalence and the relation to aerobic fitness and body fat

**Objective:** To determine the prevalence of asthma symptoms in children from a rural district in North-Tanzania, and their relationship to aerobic fitness and body fat.

**Methods:** In Manyara region in Tanzania, children (aged 9–10 years) were randomly selected to participate in the present cross-sectional study. Hundred and seventy two participants completed a video questionnaire showing the symptoms and signs of asthma. Lung function was measured by maximum forced expiratory flow-volume curves. Aerobic fitness was estimated from a standardized indirect maximal cycle ergometer test and sum of three skinfolds reflected body fat.

**Results:** Twenty four per cent reported asthma symptoms last year. Severe wheezing attacks last year were reported in 5% of the participants. Thirty seven per cent of the participants were underweight. Underweight children had significantly lower ( $P < 0.02$ ) lung function (per cent of predicted). Lower body fat was associated with higher occurrence of asthma symptoms (odds ratio and 95% CI; 0.45 (0.22–0.95;  $P = 0.04$ ). Aerobic fitness was not associated with asthma symptoms.

**Conclusions:** More than every fifth 9–10 year old child from a rural district in North-Tanzania reported asthma symptoms. Lower body fat was associated with higher occurrence of asthma symptoms, but aerobic fitness was not associated with asthma symptoms.

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Key words: Africa; lifestyle; lung function; underweight; wheezing.

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The percentage of children and adolescents reported to ever have had asthma or asthma symptoms has increased over the last decades (1); however, large variations in the prevalence of asthma symptoms have been observed between centres worldwide, with the highest prevalence in Western countries and the lowest in African, Asian and some east European countries (1).

The prevalence of exercise-induced bronchoconstriction (2) and asthma symptoms (3) have been shown to be higher in urban than in rural areas in some African countries. In South Africa, hospital admissions for asthma appear to have increased in parallel with rapid urbanization (4). No single factor that accounts for this urban-rural difference is identified (5). The cause of the increase in asthma is thought to be multi-factorial including allergen sensitization, lifestyle and environment changes (6) with increasing attention to 'Western

lifestyle', including an unhealthy diet and a sedentary lifestyle with decreased physical activity (7).

Paediatric aerobic fitness has decreased in the last decades in most 'Western societies' (8), whereas obesity and overweight among children and adolescents have increased dramatically in economically developed countries and in urbanized populations (9). Exercising more than once per week has been found to be inversely related to new onset of wheeze in adolescents (10). In addition, participation in vigorous physical activity may influence aerobic fitness (11) and lower levels of work capacity has been associated with higher risk of developing asthma (12). Furthermore, a number of longitudinal studies have reported increasing risk of developing asthma or asthma symptoms in obese children and adolescents (13); however, asthma symptoms have also been associated with underweight in children (14) and adolescents (15).

The associations between asthma, physical activity or fitness and body fat is not well known in children living in rural country districts where 'Westernized lifestyle' has not been adopted. The objective of the present study was to determine the prevalence of asthma symptoms in children from a rural district in North-Tanzania and their relationship to aerobic fitness and body fat.

## Material and methods

### Study design and subjects

Five primary schools were randomly selected from three areas in Mbulu district, Manyara region in northern Tanzania at an altitude about 1850 m above sea level. A detailed description of the study area and mode of living was published elsewhere (16). All schoolchildren ( $n = 326$ ) aged 9 and 10 years (born in 1993) were identified at each of the five schools and invited to participate in the study. All 326 children carried out a 10 min cycle ergometer test to evaluate the child's ability to cycle on a stationary cycle ergometer. During the preliminary test, 106 (35%) of the participants were not able to maintain a steady pace, mostly because of frequently slipping off the pedal when cycling. Only the 190 children able to cycle satisfactorily with an aerobic fitness test were included in the present study (17). Hundred and seventy two children had complete asthma symptoms data and 156 children got an accepted aerobic fitness test.

The precise date of birth was not usually known and age was interpolated from the year of birth. Eight tribes were represented in the sample, with a representative 87% of the subjects belonging to the Iraqw tribe. Data were collected during a period of 6 weeks in May and June 2003 (17).

### Procedures

**Video questionnaire.** To overcome the potential problems of inaccurate translation and vocabulary differences from written questionnaires, a video questionnaire (International version AVQ 3.0) developed within the International Study of Asthma and Allergies in Childhood (ISAAC) (18) was carried out in the participating children. The video questionnaire shows the symptoms and signs of asthma: Wheezing at rest, exercise-induced wheezing, waking at night with wheezing, nocturnal coughing and severe wheezing attacks. Each sequence was followed by three questions: 'Has your breathing ever been like the subject's in the video', if 'Yes', 'in the last 12 months?' (classified as current) and if 'Yes' again 'In the last month'. The questions were translated into Swahili. The children were guided and interviewed by a Swahili and Iraqw (the local language) speaking research assistant. The term 'wheezing' was not mentioned at any stage in the video questionnaire.

**Anthropometrics.** Body mass was measured to the nearest 0.1 kg, using an electronic scale (Soehnle, Type 7516, Germany). Height was measured to the nearest 5 mm, using a tape measure attached to the wall. BMI was calculated as body weight (kg) divided by height (m) squared. Underweight was defined according to cut off points for children derived by Cole et al. (19). Skinfold thickness was measured with a Harpenden fat caliper at the triceps, subscapular and suprailiac.

**Lung function and reversible airflow limitation.** 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 (MasterScope, Erich Jaeger® GmbH & Co KG, Würzburg, Germany) according to the general acceptability and reproducibility criteria of European Respiratory Society (20). All individual flow-volume curves were reviewed for technical acceptability.  $FEV_1$ ,  $FEF_{50}$  and FVC are presented as absolute values and per cent of predicted using the following prediction equations (height in cm; boy = 1 and girl = 0):

$$FEV_1: -0.23 + 0.03 \cdot \text{Height} - 0.12 \cdot \text{Gender}$$

$$FEF_{50}: -1.70 + 0.04 \cdot \text{Height}$$

$$FVC: -2.43 + 0.03 \cdot \text{Height} - 0.13 \cdot \text{Gender}$$

The prediction equations were derived from the same Tanzanian population as recommended by European Respiratory Society and American Thoracic Society (21). The highest  $FEV_1$ , FVC and  $FEF_{50}$  are included in the analysis. Reversible airflow limitation was measured using 0.4 mg salbutamol (Airomir™ Autohaler™; 3M Pharmaceuticals, St. Paul, MN, USA). A  $\geq 12\%$  increase in  $FEV_1$  15 min after inhalation, compared to baseline [ $\Delta FEV_1 = (FEV_1 \text{ post} - FEV_1 \text{ pre})/FEV_1 \text{ pre}$ ] was defined as a reversible airflow-limitation (21).

**Aerobic fitness.** Maximal power output was measured from a standardized indirect maximal cycle ergometer test conducted on an electronically braked cycle ergometer (Monark 839 Ergonomic, Sweden) and aerobic fitness was estimated. Bicycle skill was examined in the participating children by observing the subjects riding a regular children's bicycle for about 100 m. Details regarding the maximal cycle ergometer test and bicycle skills are described in Aandstad et al. (17).

### Ethics

Research clearance was obtained from the University of Dar es Salaam. Approval was also given by the local ministry of education, the local authorities in Mbulu district and headmasters from the five primary schools visited. All children were given verbal information about the test procedures and they could withdraw from the study at any time without any reason.

### Statistical analysis

Demographic data are given as mean values and standard deviation (SD) unless otherwise stated and results as mean with 95% confidence intervals (CI).

Chi-square and independent *t*-tests were used to analyse differences between boys and girls, while Mann-Whitney was used, if data were skewed. Asthma symptoms were defined as wheeze at rest, after exercise, waking with wheeze or severe attack of asthma. Waking with cough as the only symptom was not included in the definition of asthma symptoms.

Difference in the outcome variables was assessed by analysis of covariance adjusting for gender [and bicycle skill for aerobic fitness as experience and skill in bicycling influenced the result of the maximal cycle ergometer test (17)]. The underlying assumptions of the analysis of covariance were assessed using Jackknife Residuals and Cook's *d*. The independent variables, skinfolds and aerobic fitness, as well as the included confounders, were also analysed for associations with asthma symptoms using logistic regression analysis. Further stratifying by gender was not feasible due to small groups. Statistical significance level was set at 5%. Statistical analyses were performed with Statistical Package for Social Sciences Version 15.0 (SPSS, Chicago, IL, USA).



## Asthma symptoms in Tanzanian children

Table 1. Descriptive data of the participating Tanzanian children (Mean and Standard Deviation unless otherwise stated)

	Boys (n = 101)	Girls (n = 89)	Gender differences (P-value)
Height (cm)	134 (5.5)	134 (5.5)	0.96
Body mass (kg)	26.5 (3.15)	26.8 (3.65)	0.68
BMI (kg/m <sup>2</sup> )	14.8 (1.05)	14.8 (1.31)	0.70
Underweight; n (%)	40 (40)	31 (35)	0.75
Σ 3 skinfolds (mm)	13.4 (2.89)	15.8 (3.48)	<b>&lt;0.001</b>
VO <sub>2</sub> peak (ml/kg/min)	44.6 (5.78)	37.2 (4.55)	<b>&lt;0.001</b>
FEV <sub>1</sub> (l)	1.73 (0.230)	1.62 (0.275)	<b>0.004</b>
FVC (l)	1.76 (0.254)	1.63 (0.285)	<b>0.001</b>
FEF <sub>50</sub> (l/s)	2.91 (0.620)	3.05 (0.621)	0.14

Body Mass Index, BMI; Sum of three skinfolds, Σ 3skinfolds; Peak estimated oxygen consumption, VO<sub>2</sub>peak; Forced Expiratory Volume after one second, FEV<sub>1</sub>; Forced Vital Capacity, FVC; Forced Expiratory Flow at 50% of FVC, FEF<sub>50</sub>. Statistically significant values are given in bold.

### Results

The descriptive data of the participating 9 to 10-year-old Tanzanian schoolchildren are presented in Table 1. Aerobic fitness was higher ( $P < 0.001$ ) in boys, whereas body fat was significantly higher ( $P < 0.001$ ) among girls. Thirty seven per cent of the participants were underweight. FEF<sub>50</sub> was similar in boys and girls, whereas the boys had higher FEV<sub>1</sub> and FVC (Table 1;  $P = 0.004$  and  $0.001$ ). None of the participants reported use of asthma medications like inhaled corticosteroids or β<sub>2</sub>agonists or reported a doctor's diagnosis of asthma.

Asthma symptoms last year by video questionnaire were reported by 24%, whereas wheeze at rest or current wheeze was reported by 17% and 12% respectively. Significantly more boys (27%) than girls (14%) reported exercise-induced wheeze ever ( $P = 0.04$ ). Severe wheez-

Table 3. Lung function (% of predicted), aerobic fitness (VO<sub>2</sub> peak) and indices of body fat content in the Tanzanian children. Data are presented by those reporting asthma symptoms last year and children without asthma symptoms (Mean and 95% confidence intervals)

	Any asthma symptoms (n = 41)	No asthma symptoms (n = 131)	P-value*
FEV <sub>1</sub> (% of predicted)	99.1 (95.5–102.7)	99.7 (97.6–101.7)	0.78
FVC (% of predicted)	99.7 (95.9–103.5)	99.5 (97.3–101.6)	0.91
FEF <sub>50</sub> (% of predicted)	98.0 (91.8–104.3)	100.3 (96.7–103.8)	0.54
VO <sub>2</sub> peak(ml/kg/min)‡	42.6 (40.7–44.5)	41.2 (40.3–42.2)	0.20
Σ 3skinfolds (mm)†	13.7 (12.7–14.7)	14.9 (14.3–15.4)	<b>0.04</b>

Sum of three skinfolds, Σ 3skinfolds; Peak estimated oxygen consumption, VO<sub>2</sub>peak; Forced Expiratory Volume after one second, FEV<sub>1</sub>; Forced Vital Capacity, FVC; Forced Expiratory Flow at 50% of FVC, FEF<sub>50</sub>.

\*Difference between groups.

†Adjusted for gender.

‡Adjusted for gender and bicycle skill.

Statistically significant values are given in bold.

ing attacks in the last 12 months were reported in 5% of the participants (Table 2). There was a tendency for higher occurrence of severe wheezing attacks last year in underweight children ( $P = 0.08$ ).

No children had a FEV<sub>1</sub>/FVC below 0.80 and one boy and four girls had a reversible airflow-limitation, with a ≥ 12% increase in FEV<sub>1</sub> 15 min after inhalation of salbutamol, compared to baseline. Lung function was similar in children with and without asthma symptoms (Table 3); however, underweight children had significantly lower FEV<sub>1</sub>, FVC and FEF<sub>50</sub> (per cent of predicted) compared with children of normal weight (Table 4). The underweight children had significantly lower body fat ( $P < 0.001$ ) than children of normal weight (Table 4).

Aerobic fitness was not associated with current asthma symptoms ( $P = 0.19$ ) when adjusting for gender and bicycle skill (Table 3). In the logistic regression analysis,

Table 2. Asthma symptoms in Tanzanian children using video questionnaire [per cent with 95% confidence intervals (CI)]

	Total (n = 172)		Boys (n = 94)		Girls (n = 78)		Gender differences (P-value)
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Wheeze at rest							
Ever	29	17.0 (11.7–23.4)	15	16.0 (9.2–25.0)	14	18.2 (10.3–28.6)	0.83
In last year	21	12.3 (7.8–18.2)	11	11.7 (6.0–20.0)	10	13.0 (6.4–22.6)	0.82
Wheeze after exercise							
Ever	39	22.7 (16.6–29.7)	27	28.7 (19.9–39.0)	12	15.4 (8.2–25.3)	<b>0.04</b>
In last year	27	15.7 (10.6–22.0)	18	19.1 (11.8–28.6)	9	11.5 (5.4–20.8)	0.21
Waking with wheeze							
Ever	29	16.9 (11.7–23.4)	14	14.9 (8.4–23.7)	15	19.2 (11.2–29.7)	0.54
In last year	13	7.6 (4.1–12.6)	9	9.6 (4.5–17.4)	4	5.1 (1.4–12.6)	0.39
Waking with cough							
Ever	57	33.1 (26.2–40.7)	30	31.9 (22.7–42.3)	27	34.6 (24.2–46.2)	0.75
In last year	37	21.5 (15.6–28.4)	21	22.3 (14.4–32.1)	16	20.5 (12.2–31.2)	0.85
Severe wheezing attacks							
Ever	22	12.9 (8.2–18.8)	12	12.8 (6.8–21.2)	10	13.0 (6.4–22.6)	0.99
In last year	8	4.7 (2.1–9.1)	5	5.3 (1.7–12.0)	3	3.9 (0.8–11.1)	0.73

Statistically significant values are given in bold.

Table 4. Lung function (% of predicted), aerobic fitness ( $\dot{V}O_2$  peak) and indices of body fat content (skinfolds) in underweight and normal weight children (Mean and 95% confidence intervals)

	Underweight ( <i>n</i> = 71)	Normal weight ( <i>n</i> = 119)	<i>P</i> -value*
FEV <sub>1</sub> (% of predicted)	95 (92–97)	103 (101–105)	<b>&lt;0.001</b>
FVC (% of predicted)	95 (92–97)	103 (101–105)	<b>&lt;0.001</b>
FEF <sub>50</sub> (% of predicted)	95 (90–100)	103 (100–106)	<b>0.01</b>
$\dot{V}O_2$ peak (ml/kg/min)‡	42.4 (41.0–43.7)	41.1 (40.1–42.1)	0.14
Σ 3skinfolds (mm)†	13.2 (12.5–13.9)	15.5 (14.9–16.0)	<b>&lt;0.001</b>

Sum of three skinfolds, Σ 3skinfolds; Peak estimated oxygen consumption,  $\dot{V}O_2$  peak; Forced Expiratory Volume after one second, FEV<sub>1</sub>; Forced Vital Capacity, FVC; Forced Expiratory Flow at 50% of FVC, FEF<sub>50</sub>.

\*Difference between groups.

†Adjusted for gender.

‡Adjusted for gender and bicycle skill.

Statistically significant values are given in bold.

adjusting for gender and bicycle skill, the odds ratio (OR) for asthma symptoms in children with lower aerobic fitness was 1.07 (95% CI; 0.97–1.17) and not significant ( $P = 0.19$ ).

Body fat was significantly ( $P = 0.04$ ) lower in children with current asthma symptoms than in those without symptoms (Table 3). A logistic model showed an OR of 0.45 (0.22–0.95;  $P = 0.04$ ) for asthma symptoms if increasing sum of three skinfolds by 5 mm.

## Discussion

In the present study, we aimed to determine the prevalence of asthma symptoms in children from a rural district in North-Tanzania and their relationship to aerobic fitness and body fat. Twenty four per cent reported asthma symptoms last year. Lower body fat was associated with higher occurrence of asthma symptoms, but aerobic fitness was not associated with asthma symptoms.

The prevalence of asthma symptoms in children from a rural district in North-Tanzania where 'Westernized' lifestyle is not adopted was higher than previously reported by written questionnaire based studies conducted in the sub-Saharan African countries (3, 5, 22–24) and was comparable to those reported from many 'Westernized societies' (1). Thirty years ago, Carswell et al. (24) found a prevalence of recurrent episodes of wheeze and breathlessness in 7.8% of children in South-West Tanzania. A recent study (23) conducted in an urban (Dar es Salaam) and rural region in Tanzania (in the foothills of Mount Kilimanjaro) showed wheeze prevalence in 1.9–5.2%. Both studies were based on self-reported symptoms of wheeze or asthma from written questionnaires. Two studies (2, 25), including a free running test screening for exercise-induced bronchoconstriction conducted in urban and rural South-Africa and Kenya, demonstrated a prevalence of exercise-induced bronchoconstriction ranging from 8.9 to 22.9% with large regional differences.

Different methodology to diagnose or define asthma, environment and living conditions may explain the divergent prevalence of asthma symptoms among countries and districts. Our participants lived in a rural setting in the highlands of northern Tanzania, whereas other studies have included urban populations or populations from areas more similar to 'Westernized societies' (3, 5). Prevalence of diagnosed asthma may be underestimated in rural districts in developing countries due to social, financial, cultural and socio-economic barriers as well as the organization of national health care systems (26). The relatively high occurrence of asthma symptoms in the present study could also be due to lack of asthma control because of little or no disease-specific treatment. None of the children reported use of asthma medications.

The divergence among centres could also be due to the children's different understanding of the concept of wheezing, a word which is important, but not synonymous with asthma. As in most European languages, an exact equivalent of 'wheeze' in the Swahili language is absent (18) and a translated written questionnaire may not have the same precision as the original validated questionnaire (27). In general, agreement between written- and video questionnaire tends to be higher for English-speaking children (18). The children participating in the present study had a non-English speaking background and most of them preferred to speak the local language Iraqw and not Swahili which is the official language in Tanzania.

The high report of asthma symptoms in the present study could also be due to factors other than asthma. Non-atopic wheeze related to viral infections (28), other respiratory symptoms due to tuberculosis or malaria (29) or exposure to the combustion products of indoor fires (30) have been reported to be common in rural part of East-Africa. Cough or difficult breathing has been reported to be frequent in this population of Tanzanian children and 22% of all paediatric admissions to public hospitals in North-Tanzania are due to pneumonia (28).

The inverse association between body fat and asthma symptoms has, to our knowledge, not been reported previously; however, Kwon et al. (14) found a U-shaped curve with the extremes of BMI percentile in urban US boys) with parent/guardian reporting current asthma symptoms. Boys who were underweight had almost threefold OR of reporting asthma symptoms vs. boys of normal weight. This is consistent with the results from a study (15) conducted in 17-year-old Israeli males where underweight (BMI below 5th percentile) was associated with 80% increase in odds for bronchial and lung conditions like asthma compared with males of normal weight.

The higher occurrence of asthma symptoms in children with lower body fat might be related to nutritional and growth restriction affecting normal lung growth. Rural children who are underweight may be malnourished

because of either inadequate diets or frequent infections (31). In the present study, underweight children had reduced lung function compared to children of normal weight; however, lower body fat was not associated with reduced lung function. Lower correlations between skinfold measurements and body mass have been found for African-American children compared with Caucasians (32) and could explain this divergence.

We could not detect any association between aerobic fitness and current asthma symptoms. The explanation could be the homogeneous characteristics of the participants. None of the children was actually unfit. In contrast, Rasmussen et al. (12) found lower levels of work capacity to be associated with higher risk of developing asthma in a prospective study.

#### Strength and limitations

Due to the cross sectional design of the present study, we cannot conclude that there is any causal relationship between body fat and asthma symptoms.

There are difficulties and problems associated with questionnaire responses across languages and cultures. Recent studies suggest that lack of general asthma knowledge as well as understanding the word 'wheeze' may affect detection of asthma based on written questions alone (18). We used the standardized video questionnaire to provide the participating children with a visual representation of wheezing or depictions of asthma symptoms on the assumption that they might not understand the concept of wheezing; however, we cannot exclude the possibilities of bias with differential diagnosis of asthma. The other strengths of the present study are the standardized and objective methods when measuring

index of body fat, lung function and aerobic fitness. On the other hand, because of the great overlap of measurements between healthy children and those with previous asthma symptoms, the diagnostic accuracy of baseline lung function tests is generally poor (33). None of the children had FEV<sub>1</sub>/FVC ratios below 80%, indices of obstructive airways and 3% of the children had reversible airflow limitation. Therefore, we could not test the association between asthma symptoms and abnormal FEV<sub>1</sub>/FVC ratio or reversible airflow limitation. In addition, the precise date of birth was not usually known and age was interpolated from the year of birth. All participating children were considered to be of the same age, and we were therefore unable to adjust for age.

In conclusion, more than every fifth 9–10 year old child from a rural district in North-Tanzania reported asthma symptoms. The higher occurrence of asthma symptoms in children with lower body fat indicates the importance of improving nutritional status to prevent development of respiratory disease; however, whether low body fat increases the risk of developing asthma has to be confirmed using a longitudinal study design. Aerobic fitness was not associated with asthma symptoms.

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**Paper 2**

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## ORIGINAL ARTICLE

## A comparison of estimated maximal oxygen uptake in 9 and 10 year old schoolchildren in Tanzania and Norway

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**Objective:** To compare estimated maximal oxygen uptake ( $\dot{V}O_{2max}$ ) in Tanzanian and Norwegian children, by using the same bicycle protocol in both samples.**Methods:** Maximal oxygen uptake was estimated from an indirect maximal watt cycle ergometer test in 156 rural boys and girls in Tanzania. Similarly aged urban Norwegian boys and girls ( $n=379$ ) who underwent the same test were used for comparison. The Tanzanian children also participated in a 20 metre shuttle run test and a test of bicycle skill. The Tanzanian children were tested at altitude (~1800 metres), while the Norwegian children were tested at sea level.**Results:** In the cycle ergometer test, estimated relative  $\dot{V}O_{2max}$  was similar in Tanzanian and Norwegian boys, while Tanzanian girls had 8% lower estimated  $\dot{V}O_{2max}$  compared with Norwegian girls ( $p<0.001$ ). Only one third of the Tanzanian children were able to ride a conventional bicycle. Excluding subjects not able to ride a bicycle, there was no difference in estimated  $\dot{V}O_{2max}$  between Norwegian and Tanzanian children. The Tanzanian boys and girls reached significantly higher estimated  $\dot{V}O_{2max}$  in the shuttle run test compared with the cycle ergometer test ( $p<0.001$ ).**Conclusions:** Tanzanian and Norwegian children attained similar relative  $\dot{V}O_{2max}$  in the cycle ergometer test. However, the comparison was hampered by differences in altitude and the poor cycle ergometer skills in the Tanzanian children, both of which probably underestimated their  $\dot{V}O_{2max}$ .

Over the past few decades, East African runners have dominated international middle and long distance running. Kenyans and Ethiopians have been the most successful, but neighbouring countries have also produced good runners. There are many hypotheses for the East African runners' superiority.<sup>1</sup> According to Hamilton and Weston,<sup>2</sup> a combination of genetics, training, environment, lifestyle, and social factors are involved.

Several research groups have examined the difference in physiological determinants of long distance performance in highly trained white and African runners.<sup>3–6</sup> Saltin and colleagues<sup>7</sup> showed that major physical characteristics, such as maximal oxygen uptake ( $\dot{V}O_{2max}$ ) and muscle morphology, were similar in elite Kenyan and Scandinavian runners. They also reported that urban Kenyan teenage boys ( $n=6$ ) had similar relative  $\dot{V}O_{2max}$  to untrained teenage Danish boys,<sup>9</sup> while rural Kenyan boys ( $n=4$ ) reached 30% higher relative  $\dot{V}O_{2max}$ . Saltin *et al*<sup>7</sup> concluded that the physically active childhood, later combined with high intensity training, leads to the high  $\dot{V}O_{2max}$  observed in Kenyan runners, and that a high aerobic capacity, together with good running economy, makes Kenyan runners so successful.

If it is true that East African children are more physically active than children in the western world, this might result in a higher  $\dot{V}O_{2max}$  among East Africans. Three decades ago, Davies<sup>10</sup> measured  $\dot{V}O_{2max}$  directly in urban and rural Tanzanian schoolchildren aged 7–17 years old. This sample was only representative of the healthy population of children, as subjects with signs of malnutrition or anaemia were excluded. Davies reported no difference in absolute  $\dot{V}O_{2max}$  (l/min) between rural and urban Tanzanian children, and also noted that these values were similar to studies of European children. Recently, Larsen *et al*<sup>11</sup> measured  $\dot{V}O_{2max}$  directly from treadmill running in 30 adolescent Kenyan town and village boys. The town boys attained relative  $\dot{V}O_{2max}$  values similar to untrained Danish adolescent boys,<sup>9</sup> while Kenyan village boys reached about 10% higher values. However, the

Danish sample was measured from a maximal bicycle test, which will produce about 7–13% lower  $\dot{V}O_{2max}$  than found in treadmill running.<sup>12,13</sup>

Previous studies comparing aerobic fitness between East African and western children or adolescents have had shortcomings in terms of method differences, small sample sizes, and old reference material. The aim of the present study was to compare aerobic fitness in Tanzanian and Norwegian children by using the same test procedures in both samples and larger sample sizes than in previous studies. The study investigated whether East African nations have an advantage over western nations even in early childhood, through a higher  $\dot{V}O_{2max}$  in the childhood population.

## MATERIALS AND METHODS

## Ethics

Research clearance was obtained from the University of Dar es Salaam. Approval was also given by the local ministry of education and the local authorities in Mbulu district, and headmasters from the five primary schools visited. Consent for participation of the Tanzanian children was provided by the principals of the school acting in loco parentis for the children. All children were given verbal information about the test procedures, and they could withdraw from the study at any time and for any reason.

## Subjects

Five primary schools were randomly selected from three wards in Mbulu district, Manyara region, in northern Tanzania. All schoolchildren ( $n=326$ ) aged 9 and 10 years old (born in 1993) were identified at each of the five schools and invited to participate in the study. Eight tribes were represented in the sample, with a representative 87% of the

**Abbreviations:** CV, coefficient of variation; HR, heart rate; MWCE, maximal watt cycle ergometer; SRT, shuttle run test

subjects belonging to the Iraqw tribe. The data were collected during a period of 6 weeks in May and June 2003.

The 379 subjects from the Norwegian part of the European Youth Heart Study (EYHS) were used as a basis for comparison with the Tanzanian sample. The Norwegian sample was examined in 2000, and consisted of randomly selected 9 and 10 year old children from nine primary schools in Oslo.<sup>14</sup>

### Testing methods

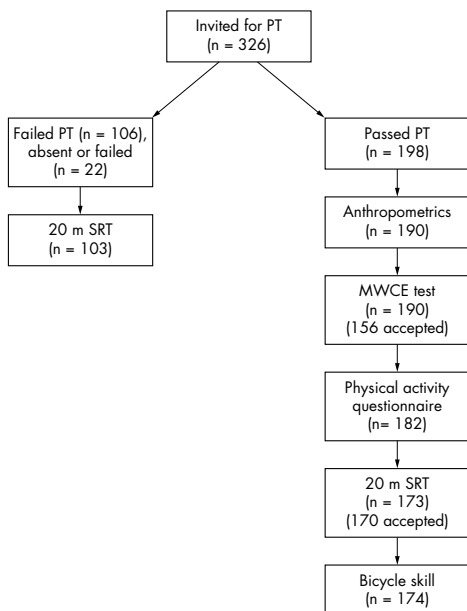
The test procedures were standardised to ensure similarity with respect to data gathering in Norway and Tanzania. A flowchart of the test order for the Tanzanian subjects is given in fig 1. The Norwegian subjects underwent anthropometric measurements, the maximal watt cycle ergometer (MWCE) test, and completion of the physical activity questionnaire.

### Preliminary cycle ergometer test

All Tanzanian subjects carried out a 10 minute preliminary cycle ergometer test to evaluate the child's ability to cycle on a stationary cycle ergometer with a steady pedal rate of 70–80 rpm. During the preliminary test, 106 (35%) of the subjects were not able to maintain a steady pace, mostly because the foot frequently slipped off the pedal when cycling. Only children able to cycle satisfactorily were invited to participate in the MWCE test. Ultimately, results from 156 Tanzanian MWCE tests were accepted.

### Anthropometrics

Body weight was measured to the nearest 0.1 kg, using an electronic scale (Soehnle, Type 7516, Germany). Height was measured to the nearest 5 mm, using a tape measure attached to the wall (table 1).



**Figure 1** Flowchart of test order for the Tanzanian subjects. PT, preliminary cycle ergometer test; 20 metre SRT, 20 metre shuttle run test; MWCE test, maximal watt cycle ergometer test.

### Maximal watt cycle ergometer test

Maximal power output ( $W_{max}$ ) was measured from the MWCE test<sup>15</sup> conducted on an electronically braked cycle ergometer (Monark 839 Ergomedic, Sweden). A relative  $\dot{V}O_{2max}$  was calculated from the equation:  $\dot{V}O_{2max}$  ( $ml \cdot kg^{-1} \cdot min^{-1}$ ) =  $(12.44 W_{max} + 250) / \text{body mass}$ .<sup>16</sup>

Initial and incremental workload were 20 W for children weighing <30 kg and 25 W for children weighing  $\geq 30$  kg. Every third minute, the load increased, until exhaustion was reached. Heart rate (HR) was registered throughout the test (Polar Pacer, Finland). The criteria for having reached maximal effort were a HR  $\geq 185$  beats/min and a subjective assessment that the child had reached his or her maximal effort. The cycle ergometer was calibrated electronically twice a day and mechanically once a day or every time after being moved. All bicycle tests in Tanzania were conducted indoor with mean air temperature 22.1°C (confidence intervals (CI) 21.8 to 22.5), relative humidity 60.0% (CI 58.8 to 61.2) and barometric pressure 82.7 kPa (CI 82.6 to 82.8). The Tanzanian children were tested at an altitude between 1750 and 1800 metres above sea level, while the Norwegian children were tested at sea level. Eighteen randomly chosen Tanzanian subjects were retested after 3 weeks to calculate the reproducibility of the MWCE test. The coefficient of variation between the first test and the re-test was 8%, and a 3% higher estimated  $\dot{V}O_{2max}$  was demonstrated in the re-test ( $p < 0.001$ ). The MWCE test has been validated in 21 Scandinavian 9 year old children. The correlation between maximal power output and  $\dot{V}O_{2max}$  was  $r = 0.93$  and the standard error of estimation for predicted  $\dot{V}O_{2max}$  was 4.8%.<sup>16</sup>

### Physical activity

Habitual physical activity was registered using a questionnaire consisting of eight questions pertaining to means of transportation to school, physical activity during school breaks, and participation in after school sports activities. The questions were selected from a validated questionnaire<sup>14</sup> used in the EYHS and translated into Kiswahili. The subjects filled in the questionnaire guided by a Kiswahili and Kiraqwa speaking research assistant.

### 20 metre shuttle run test

A 20 metre shuttle run test (SRT) was carried out on 276 of the Tanzanian children who participated in the study. The running protocol and calculation of estimated maximal oxygen uptake were according to Léger *et al.*<sup>17</sup> The running took place on a flat area of the schoolyard or on a football field. Correlation coefficients of  $\geq 0.7$  between  $\dot{V}O_{2max}$  predicted from the 20 metre SRT and direct measurements have been reported for children and adolescents.<sup>17, 18</sup>

### Bicycle skill

Bicycle skill was examined in the Tanzanian sample by observing the subjects riding a regular children's bicycle for about 100 metres. Children able to cycle freely without touching their feet to the ground were characterised as accustomed to bicycling. Children who failed this test were characterised as unaccustomed. Bicycle skill was not examined in the Norwegian sample.

### Statistics

SPSS software (version 11.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Differences in height, weight,  $HR_{max}$ ,  $W_{max}$ , and estimated  $\dot{V}O_{2max}$  between groups were tested using the independent samples  $t$  test. The  $\chi^2$  test and the Mann-Whitney  $U$  test were used when comparing differences in physical activity patterns, while one way analysis of variance with Tukey post hoc test was used to analyse  $\dot{V}O_{2max}$  in relation to physical activity. The one



**Table 1** Anthropometrical characteristics of Tanzanian and Norwegian 9 and 10 year old schoolchildren

Country	Sex	n	Weight (kg)	Height (m)	BMI(kg/m <sup>2</sup> )
Tanzania	Boys	87	26.7 (26.0 to 27.3)*	1.34 (1.33 to 1.35)*	14.8 (14.6 to 15.0)*
	Girls	69	27.2 (26.3 to 28.0)*	1.35 (1.33 to 1.36)*	15.0 (14.6 to 15.3)*
	Total	156	26.9 (26.3 to 27.4)*	1.34 (1.33 to 1.35)*	14.9 (14.7 to 15.1)*
Norway	Boys	195	33.5 (32.8 to 34.3)	1.40 (1.39 to 1.41)	17.0 (16.7 to 17.3)
	Girls	184	33.1 (32.2 to 34.0)	1.39 (1.38 to 1.39)	17.2 (16.8 to 17.5)
	Total	379	33.3 (32.7 to 33.9)	1.39 (1.39 to 1.40)	17.1 (16.9 to 17.3)

Values are reported as means (95% CI). \*p<0.001 from the corresponding Norwegian value.

sample *t* test, calculation of coefficient of variation (CV) and Pearson's product moment correlation coefficient was used to calculate reproducibility of the MWCE test. All data are reported as mean values with 95% confidence intervals (95% CI). The level of significance was set at p<0.05.

## RESULTS

### Estimated maximal oxygen uptake

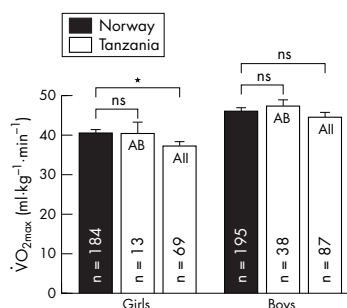
When bicycle skill was not taken into consideration, Tanzanian girls attained 8% lower relative  $\dot{V}O_{2max}$  in the MWCE test compared with Norwegian girls, while there was no significant difference between Tanzanian and Norwegian boys (table 2). However, experience and skill in bicycling influenced the result of the MWCE test. Tanzanian boys and girls who were accustomed to bicycling achieved a 12% higher estimated  $\dot{V}O_{2max}$  in the MWCE test compared with boys and girls unaccustomed to bicycling (table 3), whereas there was no difference in estimated  $\dot{V}O_{2max}$  between the Tanzanian accustomed and unaccustomed children in the 20 metre SRT (table 3). Thus, the Tanzanian  $\dot{V}O_{2max}$  values in the MWCE test (table 2) are probably an underestimate.

Of 174 Tanzanian subjects, 54 (31%) were considered to be accustomed to conventional bicycling, while the rest were characterised as unaccustomed. When comparing the Tanzanian children accustomed to bicycling with the Norwegian children, no significant difference in relative  $\dot{V}O_{2max}$  estimated from the MWCE test was revealed for either sex (fig 2).

Tanzanian boys and girls attained 21.6% and 36.0%, respectively, higher estimated  $\dot{V}O_{2max}$  in the 20 metre SRT (table 4) compared with the MWCE test (table 3; AB subjects) (p<0.001).

### Physical activity

The majority of both Tanzanian and Norwegian children walked to school, but the Tanzanian children had to travel a significantly longer distance (table 5). There was no significant difference in  $\dot{V}O_{2max}$  measured from the MWCE test or the 20 metre SRT between Tanzanian children who walked short *versus* long distances to school. Tanzanian boys were less active in playing outdoor games after school compared with Norwegian boys, while no significant



**Figure 2** Estimated maximal oxygen uptake ( $\dot{V}O_{2max}$ ) in Norwegian and Tanzanian 9 and 10 year old schoolchildren. AB, only subjects accustomed to conventional bicycling are included. All, all children, both accustomed and unaccustomed to conventional bicycling are included. Values are reported as means (95% CI). Significance: \*p<0.001; ns = not significant.

difference was found between Norwegian and Tanzanian girls.

## DISCUSSION

The study demonstrates that estimated relative  $\dot{V}O_{2max}$  from the MWCE test does not differ between Norwegian and Tanzanian 9–10 year old schoolchildren when only children accustomed to conventional bicycling are included in the analysis. The study also revealed that the Tanzanian children attained significantly higher estimated  $\dot{V}O_{2max}$  in the 20 metre SRT compared with the MWCE test.

### Estimated $\dot{V}O_{2max}$ from the maximal watt cycle ergometer test

In the MWCE test, a 12% higher  $\dot{V}O_{2max}$  was reported for Tanzanian boys and girls accustomed to bicycling compared with their unaccustomed counterparts. In the 20 metre SRT there was no significant difference in  $\dot{V}O_{2max}$  between accustomed and unaccustomed Tanzanian children. The most likely explanation for this discrepancy is that the

**Table 2** Maximal heart rate ( $HR_{max}$ ), maximal watt ( $W_{max}$ ), and estimated relative maximal oxygen uptake ( $\dot{V}O_{2max}$ ) from the maximal watt cycle ergometer test in Tanzanian and Norwegian 9 and 10 year old schoolchildren

Country	Sex	n	$HR_{max}$ (beats/min)	$W_{max}$ (W)	$\dot{V}O_{2max}$ (ml.kg <sup>-1</sup> .min <sup>-1</sup> )
Tanzania	Boys	87	195.6 (194.0 to 197.2)	75.3 (71.8 to 78.9)*	44.6 (43.3 to 45.8)
	Girls	69	196.1 (194.3 to 197.8)	60.7 (57.6 to 63.9)*	37.2 (36.1 to 38.3)*
Norway	Boys	195	193.5 (192.1 to 194.8)	102.1 (99.4 to 104.9)	45.9 (44.9 to 46.9)
	Girls	184	193.8 (192.4 to 195.2)	85.5 (83.2 to 87.8)	40.5 (39.5 to 41.5)

Values are reported as means (95% CI). \*p<0.001 from the corresponding Norwegian value. All other differences were not significant.

**Table 3** Estimated maximal oxygen uptake ( $\dot{V}O_{2max}$ ) from the maximal watt cycle ergometer test (MWCE test) and the 20 metre shuttle run test (20 metre SRT) in Tanzanian schoolchildren, who were accustomed (AB) or unaccustomed (UB) to conventional bicycling.

Country	Sex	MWCE test $\dot{V}O_{2max}$ ( $ml \cdot kg^{-1} \cdot min^{-1}$ )		20 metre SRT $\dot{V}O_{2max}$ ( $ml \cdot kg^{-1} \cdot min^{-1}$ )	
		AB	UB	AB	UB
Tanzania	Boys	47.3 (45.5 to 49.0)* (n=38)	42.1 (40.6 to 43.7) (n=43)	58.6 (57.3 to 60.0) (n=31)	57.3 (56.6 to 58.0) (n=51)
	Girls	40.3 (37.2 to 43.4)** (n=13)	36.1 (35.0 to 37.2) (n=49)	54.7 (52.9 to 56.5) (n=14)	55.2 (54.4 to 55.9) (n=62)

Values are reported as means (95% CI) (n). \* $p < 0.001$ ; \*\* $p < 0.01$  from the corresponding UB value. All other differences were not significant.

MWCE test underestimated  $\dot{V}O_{2max}$  in children unable to cycle on a conventional bicycle, due to their poorer cycle ergometer skill. Estimation of  $\dot{V}O_{2max}$  from indirect performance tests is exposed to bias if work efficiency of the tested subjects differs from the work efficiency of the subjects used to produce the test equation.<sup>19</sup> The equation we used to estimate  $\dot{V}O_{2max}$  from the MWCE test is based on measurements taken from Scandinavian children, who were probably accustomed to conventional bicycling.<sup>16</sup> Hence,  $\dot{V}O_{2max}$  is probably underestimated among the unaccustomed Tanzanian children. Thus, including only accustomed Tanzanian children gives the most valid comparison of  $\dot{V}O_{2max}$  between the Tanzanian and Norwegian children. Even though one third of the Tanzanian children managed to cycle on a conventional bicycle, most were, in our visual judgement, less accustomed to bicycling than Norwegian children of the same age. This might indicate that even  $\dot{V}O_{2max}$  values in the accustomed Tanzanian children were underestimated compared with the Norwegian subjects. However, Davies<sup>10</sup> examined the  $\dot{V}O_2$ /watt relationship in Tanzanian and western children working on a cycle ergometer. No differences were found, despite the fact that many of the Tanzanians had never pedalled any type of cycle, except for the familiarisation prior to the study.

Larsen *et al*<sup>11</sup> measured  $\dot{V}O_{2max}$  in Kenyan boys at an altitude of ~2000 metres, and suggested a 3–5% increase in  $\dot{V}O_{2max}$  if measured at sea level, referring to Favier *et al*.<sup>20</sup> Other studies have demonstrated greater increases in  $\dot{V}O_{2max}$  when subjects native to moderate or high altitude were tested at sea level.<sup>21,22</sup> Altitude should be kept in mind when analysing the  $\dot{V}O_{2max}$  values in the Tanzanian children, but inconsistencies in the literature make it difficult to quantify how much higher the estimated  $\dot{V}O_{2max}$  would have been if the Tanzanian children had been tested at sea level.

It is suggested that allometric scaling of  $\dot{V}O_{2max}$  has less bias than  $\dot{V}O_{2max}$  expressed relative to body weight, when comparing individuals of different size.<sup>23,24</sup> There was a great difference in body size between the Norwegian and Tanzanian children, thus analysis with allometric scaling was carried out. Expressing  $\dot{V}O_{2max}$  as  $ml/kg^{0.75}/min$  favoured the Norwegian children compared with the Tanzanian. For example, Norwegian girls reached 14% higher  $\dot{V}O_{2max}$  compared with Tanzanian girls using allometric scaling (96.4 and 84.6  $ml/kg^{0.75}/min$ , respectively), while the conventional ratio method only revealed a 9% higher  $\dot{V}O_{2max}$  in Norwegian girls compared with Tanzanian girls. However, as

$\dot{V}O_{2max}$  is most typically expressed per kilogram of body mass, the results have been presented in the conventional way.

#### Estimated $\dot{V}O_{2max}$ from the 20 metre shuttle run test

The 20 metre SRT was carried out for three reasons. Firstly, we wanted to detect if relative  $\dot{V}O_{2max}$ , estimated from the 20 metre SRT, differed between the children who passed the preliminary cycle ergometer test and those who failed. For the boys, a 2.4% higher  $\dot{V}O_{2max}$  was found among the successful group ( $p < 0.05$ ). There was no significant difference in  $\dot{V}O_{2max}$  between girls who passed and girls who failed the preliminary test. Secondly, the 20 metre SRT, combined with the cycling skill test, should give us an idea of whether the MWCE test underestimates Tanzanian children who were unaccustomed to conventional bicycling. As previously discussed, this seemed to be the case. Finally, the 20 metre SRT is one of the most widely used tests to assess aerobic fitness in children and adolescents.<sup>25</sup> The results can be compared with a large number of studies worldwide, but the different existing protocols and equations often complicate direct comparison. Tanzanian boys and girls performed well in the 20 metre SRT, compared with what is previously reported in other international studies of children.<sup>17,26–28</sup> On average, the Tanzanian boys ( $n = 121$ ) and girls ( $n = 152$ ) continued running until level 8 (57.5  $ml \cdot kg^{-1} \cdot min^{-1}$ ) and level 7 (54.8  $ml \cdot kg^{-1} \cdot min^{-1}$ ), respectively. Leger *et al*<sup>17</sup> have presented normal values for the 20 metre SRT in a large number of Canadian children. Canadian boys aged 9 years old were able to run to level 5 (51.5  $ml \cdot kg^{-1} \cdot min^{-1}$ ), while Canadian girls of the same age continued until level 4 (49.2  $ml \cdot kg^{-1} \cdot min^{-1}$ ). Similar or slightly lower results have been demonstrated in 9 year old children from Portugal<sup>28</sup> and Switzerland,<sup>27</sup> while no such data have yet been gathered in Norway. Comparing the Tanzanian 20 metre SRT results with the aforementioned studies on western children, the Tanzanians achieved an 11–17% higher estimated  $\dot{V}O_{2max}$ .

While the Tanzanian 20 metre SRT results were significantly better compared with western values, Tanzanian and Norwegian children reached similar estimated  $\dot{V}O_{2max}$  in the MWCE test. This discrepancy might be explained by a better running efficiency in the East African population compared with the western children, as reported in studies on adult East African runners.<sup>7,29,30</sup> Another explanation is that the Tanzanian children actually have a higher relative  $\dot{V}O_{2max}$  compared with Norwegian and other western children, but

**Table 4** 20 metre shuttle run results in Tanzanian 9 and 10 year old schoolchildren: number of levels completed, final speed, and estimated maximal oxygen uptake ( $\dot{V}O_{2max}$ )

Sex	n	Levels (no.)	Final speed (km/h)	$\dot{V}O_{2max}$ ( $ml \cdot kg^{-1} \cdot min^{-1}$ )
Boys	121	8.4 (8.2 to 8.6)	12.2 (12.1 to 12.3)	57.5 (56.9 to 58.0)
Girls	152	7.3 (7.1 to 7.5)	11.6 (11.5 to 11.7)	54.8 (54.3 to 55.3)
Total	273	7.8 (7.6 to 7.9)	11.9 (11.8 to 12.0)	56.0 (55.6 to 56.4)

**Table 5** Physical activity patterns in Norwegian and Tanzanian 9 and 10 year old schoolchildren

	Norway				Tanzania			
	Boys		Girls		Boys		Girls	
	n	%	n	%	n	%	n	%
Means of transportation to school								
Foot	194	94	183	94	87	90	75	88
Other	11	6	12	6	10	10	10	12
Total	205	100	195	100	97	100	85	100
Travelling time to school, boys* and girls*								
<5 min	56	27	60	31	6	6	9	10
5–15 min	114	55	92	47	21	22	16	19
15–30 min	28	14	34	17	33	35	28	32
30–60 min	6	3	7	4	23	24	23	27
>1 hour	1	1	2	1	12	13	10	12
Total	205	100	195	100	95	100	86	100
Participation in outdoor games after school, boys*								
Hardly ever or never	38	18	70	36	47	48	34	40
1–2 days/week	67	33	63	32	16	17	18	21
Most days	61	30	49	25	16	17	7	8
Every day	39	19	13	7	18	18	27	31
Total	205	100	195	100	97	100	86	100

\*p<0.001 between the Norwegian and Tanzanian values. All other differences were not significant.

that the general low efficiency in the cycle test underestimated the MWCE test results, as previously hypothesised.

The study demonstrated a 21.6% and 36.0% higher estimated  $\dot{V}O_{2max}$  in the 20 metre SRT compared with the MWCE test in Tanzanian boys and girls, respectively. This difference is partly explained by the fact that children and adults yield about 7–13% higher  $\dot{V}O_{2max}$  in running compared with cycling.<sup>12, 13</sup> Another explanation for the difference is the possible underestimation in the MWCE test. It should also be mentioned that different equations exist for predicting  $\dot{V}O_{2max}$  from the MWCE test<sup>15, 31</sup> and the 20 metre SRT.<sup>32</sup> Using other equations could produce different estimated values for  $\dot{V}O_{2max}$ , but we used the equations we felt were the most reliable and applicable in regard to our samples.

Irrespective of discussions regarding  $\dot{V}O_{2max}$ , the shuttle run results clearly demonstrated that the Tanzanian children were good runners.

### Physical activity

It has been claimed that one of the reasons why East African runners perform so well in international running is because of high levels of physical activity during childhood.<sup>7</sup> The present study showed that the majority of both Tanzanian and the Norwegian children travelled to school by foot, but the Tanzanian children had to walk longer distances than the Norwegian children. Urban Norwegian children typically walk short distances from home to school. Almost 40% of the Tanzanian children walked for more than 30 minutes to get to school, compared with 5% of Norwegian children. The intensity of the movement was not evaluated, but from our experience, the Tanzanian children walked rather than ran. Improvement in  $\dot{V}O_{2max}$  during childhood is probably only achieved when the training intensity is high.<sup>33</sup> This might contribute to why we did not find any differences in  $\dot{V}O_{2max}$  between Tanzanian children covering long or short distances by foot for transportation to school.

### CONCLUSIONS

No difference in estimated  $\dot{V}O_{2max}$  was found between Norwegian and Tanzanian 9–10 year old children, as long as subjects unaccustomed to bicycling were excluded from the analysis. However, the study has some limits. The Tanzanians were tested at moderate altitude while the

Norwegians were tested at sea level. In addition, an indirect test such as the MWCE test has sources of error when estimating  $\dot{V}O_{2max}$  compared with direct measurements. Finally, we would recommend that future studies of populations not accustomed to bicycling should consider using test methods other than the MWCE test, as this test probably underestimates  $\dot{V}O_{2max}$  in subjects unaccustomed to bicycling.

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### What is already known on this topic

- The success of East African runners is not fully understood.
- Few studies have examined differences in  $\dot{V}O_{2max}$  between western and African children.
- However, it has been shown that rural East African boys attain 10–30% higher relative  $\dot{V}O_{2max}$  compared with Scandinavian boys.
- Previous studies have had small sample sizes and different test methods.

### What this study adds

- This study showed that Tanzanian and Norwegian children attained similar relative  $\dot{V}O_{2max}$  estimated from the maximal watt cycle ergometer test.
- However, the Tanzanian children reached a significantly higher estimated  $\dot{V}O_{2max}$  in the 20 metre shuttle run test, and it is likely that the Tanzanian cycle ergometer results are underestimated.

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**Paper 3**

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## Validity of physical activity monitors in adults participating in free living activities

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Title for running head: Validity of physical activity monitors

*Keywords: accelerometer, energy expenditure, indirect calorimetry, measurement, motion sensor.*

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We hereby confirm that the work has been seen and approved by all co-authors. Regional ethics committee (east Norway) approved the protocol and the study. The study was conducted in accordance with the Declaration of Helsinki.

### COMPETING INTEREST

None of the authors have any competing or conflicts of interests with regard to this manuscript.

## ABSTRACT

**Background:** For a given subject, time in moderate to very vigorous intensity physical activity (MVPA) varies substantially among physical activity monitors.

**Objective:** The primary objective of the present study was to determine whether time in MVPA recorded with SenseWear™ Pro<sub>2</sub> Armband (Armband), ActiGraph, iKcal and ActiReg<sup>®</sup> is different compared to indirect calorimetry. The secondary objective was to determine whether these activity monitors estimate energy expenditure different compared to indirect calorimetry.

**Material and methods:** Fourteen men and six women wore the activity monitors and a portable oxygen analyzer for 120 minutes doing a variety of activities of different intensities. Resting metabolic rate (RMR) was measured with indirect calorimetry. The cut off points defining moderate, vigorous and very vigorous intensity were 3, 6 and 9 times RMR.

**Results:** Armband and ActiGraph overestimated time in MVPA by 2.9 and 2.5% and iKcal and ActiReg<sup>®</sup> underestimated time in MVPA by 11.6 and 98.7%, respectively. ActiReg<sup>®</sup> ( $p=0.004$ ) and ActiGraph ( $p=0.007$ ) underestimated energy expenditure in MVPA and all monitors underestimated total energy expenditure (by 5 to 21%).

**Conclusions:** Recorded time in MVPA and energy expenditure varies substantially among physical activity monitors. Thus, when comparing physical activity level among studies, it is essential to know the type of physical activity monitor being used.



## INTRODUCTION

In the currently published physical activity recommendations for adults it is stated that to promote and maintain health, all healthy adults aged 18-65 yr need moderate intensity aerobic (endurance) physical activity for a minimum of 30 min on five days each week or vigorous intensity aerobic physical activity for a minimum of 20 min on three days each week.[1]

Physical activity is characterised by its intensity, duration, frequency and mode of activity.[2] Ideally, all these aspects should be recorded during physical activity measurements. Direct measurement of energy expenditure by heat production, or indirect by oxygen consumption ( $\dot{V}O_2$ ), is limited to small populations or short time periods because of the cost of assessment to both the investigator and the participant.[3] Assessment of oxygen consumption has the advantage that it is possible to compare minute by minute data, which is not possible when devices are compared with heat production. A portable oxygen analyser - as used in the present study - costs approximately \$ 40 000 and a bomb calorimeter or respiratory chamber costs millions. Still, such measurements are useful as criteria for evaluating other methods of physical activity recordings. In a daily free living setting, doubly labelled water is recognised as a reference method for the assessment of total energy expenditure; however, doubly labelled water only gives an integrated assessment of total energy expenditure during the measurement period.[4] This method does not assess day-to-day or hour-by-hour energy expenditure, or information of duration, frequency and intensity of moderate to very vigorous physical activity,[5] as oxygen consumption measurements do. MetaMax II (Cortex Biophysic, Leipzig, Germany), a portable oxygen analyzer validated against the Douglas-bag technique,[6,7] is suitable for measurements of  $\dot{V}O_2$  in subjects participating in free living activities.

The validity of newly introduced monitors needs to be carefully examined.[8] A number of studies have simultaneously evaluated the validity of two or more different makes and models of activity monitors in adults [9-13]. Notably, the majority of these studies have addressed the question of whether multiaxial accelerometers as Tritrac-R3D (RT3 Triaxial Research Tracker (StayHealthy, Inc., Monrovia, CA, USA)) provide more valid assessments of physical activity and/or energy expenditure than do single axis accelerometers as ActiGraph (7164, LLC, Fort Walton Beach, FL, USA) or included loco motor movement activities in a laboratory setting.[14] Since different activity monitors record different aspects of physical activity such as acceleration, position changes, heart rate etc., comparisons of physical activity data may be complicated. It is important to investigate the validity of activity monitors when comparing physical activity data among studies using different monitors. To date, a comparison of the activity monitors ActiGraph 7164, ActiReg<sup>®</sup>, iKcal and SenseWear<sup>™</sup> Pro<sub>2</sub> Armband (Armband) in a free living condition including direct measurements of oxygen consumption is unavailable. It is therefore difficult to make informed decisions regarding which monitor might be optimal when conducting epidemiological studies. The present study focuses only on reporting time in MVPA and estimated energy expenditure across monitors, not to develop calibration equations and determining activity cut off points for specific intensities or types of physical activity.

The primary objective of the present study was to determine whether time in MVPA recorded with ActiGraph, ActiReg<sup>®</sup>, iKcal and SenseWear<sup>™</sup> Pro<sub>2</sub> Armband is different compared to indirect calorimetry. The secondary objective was to determine whether these activity monitors estimate energy expenditure different compared to indirect calorimetry.

## **MATERIAL AND METHODS**

### **Participants**

Fourteen men and six women (19-56 years of age) volunteered to participate in the present study.

All participating subjects were of Caucasian origin without any overt disease or use of medications which could have influenced results such as energy expenditure. All participants were non-smokers.

The Regional Medical Ethics committee and the Data Inspectorate approved the study. The study subjects signed an informed consent form after being given oral and written information about the study objectives and methods.

### **Procedures**

Prior to measurements, participants had their stature and body mass measured (in light clothing, without shoes) using a stadiometer and a physician's scale, respectively. Measurements were performed at the participant's work or home indoors and/or outdoors. The four activity monitors were attached to the body of the participant according to the instructions of the manufacturer. The best resolution data was collected with each monitor. All devices were synchronized with a digital clock prior to measurement. One of the monitors, ikcal, was calibrated according to the manufacturer's instructions after being attached to the body. After finishing this calibration procedure, the portable oxygen analyzer and the breathing mask were attached to the participant and the measurement started. The measurement period lasted for 120 minutes during daytime. During this period the participants performed various lifestyle and sporting activities such as conditioning- and strength exercises, ball games, home repair, occupational- and home activities. We did not limit type and intensity of activities except being in contact with water. The test leader was on-site, but not supervising the activities. Type and estimated length of activities were registered after completion of the measurement period by interviewing the participant. In addition to the main measurements, we also performed a measurement of RMR in the morning, on another day, according to international guidelines and using the same oxygen analyzer.[15]

### **Indirect calorimetry**

MetaMax II was used for measurements of  $\dot{V}O_2$ . Expired gases were collected via a breathing mask. A gas calibration of the  $O_2$  and  $CO_2$  analyzers, volume calibration of the volume transducer and calibration of the pressure analyzer were performed before all tests according to manufacturer. Data was analyzed with Metasoft v1.1 (Cortex Biophysic, Leipzig, Germany).

### **Activity monitors**

#### *ActiGraph 7164 accelerometer*

ActiGraph 7164 measures acceleration in the vertical plane and has been validated in several studies; however, these validation studies are population specific.[16] ActiGraph was calibrated against a standardized vertical movement. The monitor was attached using an elastic belt at the participants' hip, near spina iliaca anterior superior. The amount of energy expenditure and the cut off points defining moderate, vigorous and very vigorous intensity were calculated by the formula of Freedson et al. as recommended by the manufacturer.[17]

*ActiReg<sup>®</sup>*

ActiReg<sup>®</sup> (PreMed AS, Oslo, Norway) measures body position and body motion and has been validated against doubly labelled water.[18] The monitor has two pairs of body position sensors and two pairs of body motion sensors connected by cables to a battery-operated storage unit fixed to a waist belt. One of the position- and motion sensors was attached by medical tape to the chest and the other one to the front of the right thigh. The position codes and the amount of position changes were downloaded with software developed by the manufacturer (ActiCalc 32, PreMed AS, Oslo, Norway).

*ikcal*

ikcal (Teltronic AG, Biberist, Switzerland) measures heart rate and acceleration in the vertical and horizontal planes and has to our knowledge been validated in studies using whole-body indirect calorimetry and indirect calorimetry; however, the studies have not been published. The monitor was attached to the chest using an elastic belt around the sternum according to instructions of the manufacturer. Data from the monitor was downloaded with software developed by the manufacturer.

*SenseWear<sup>™</sup> Pro<sub>2</sub> Armband*

SenseWear<sup>™</sup> Pro<sub>2</sub> Armband (BodyMedia Inc., Pittsburgh, PA, USA) has been validated against doubly labelled water and includes a two-axis accelerometer, a heat flux sensor, a galvanic skin response sensor, a skin temperature sensor and a near-body ambient temperature sensor.[19] The monitor was worn on the right arm over the triceps brachii muscle at the midpoint between the acromion and olecranon processes. The data from the monitor was downloaded with software developed by the manufacturer (Innerview Professional Research Software Version 5.1, BodyMedia Inc., Pittsburgh, PA, USA).

**Data processing**

Data from the direct measurements of  $\dot{V}O_2$  and the four activity sensors were imported into Microsoft Excel<sup>®</sup> and synchronized for further analysis. All data were computed at one minute intervals. Absolute  $\dot{V}O_2$  data were transformed into  $\text{kcal} \cdot \text{min}^{-1}$  multiplying  $\dot{V}O_2$  in  $\text{l} \cdot \text{min}^{-1}$  with the factor 4.82.[20]

**Statistical analysis**

Sample size calculation was based on a standard deviation (SD) of time in MVPA of 25 minutes and a significance level of 0.05 with 80% power. We needed 17 subjects to detect a mean difference of 25 minutes between the activity monitors.

Bland-Altman plots were constructed to show the relationship of the mean differences (activity monitor minus indirect calorimetry) for accumulated energy expenditure and time in MVPA. The mean differences and limits of agreements were calculated according to Bland and Altman.[21] A two-way mixed, single measure, intra class correlation (ICC(3,1)) was performed for evaluating the extent of agreement between the physical activity monitors and indirect calorimetry for accumulated energy expenditure and time in MVPA. A two-way analysis of variance was performed to determine differences in accumulated energy expenditure and time in MVPA obtained with the activity monitors and indirect calorimetry. Tukey post hoc testing was performed to locate significant differences.

To test if the activity monitors underestimated or overestimated the energy expenditure in each intensity level, we calculated the absolute value of the difference at each time point (120 measurements, one per minute). For each individual, the cut off points defining moderate, vigorous and very vigorous intensity were 3, 6 and 9 times RMR. We calculated the mean of the absolute differences for each individual at the three levels of

intensity. The mean for the 20 individuals serves as an estimate of the error with which each activity monitor misses the energy expenditure measured with indirect calorimetry at each intensity level. To test if the activity monitors underestimated or overestimated energy expenditure measured with indirect calorimetry, we applied a standard one-sample t-test for the absolute values for each activity monitor. In addition, for each individual and the three levels of intensity, we calculated the percentage the activity monitors underestimated or overestimated energy expenditure measured with indirect calorimetry. For the mean of these percentages, we applied the central limit theorem and performed a normal test to establish whether there is a tendency to underestimate or overestimate the energy expenditure in each intensity level.

Level of significance was set to 0.05. Analyses were conducted in SAS<sup>®</sup> (SAS Institute Inc., Version 9.1.3, North Carolina, USA) and SPSS<sup>®</sup> (Statistical Package for Social Sciences, Version 15 for Windows. SPSS Inc. Chicago, USA, 2006).

## RESULTS

The physical characteristics of the participants are shown in table 1.

**Table 1.** Physical characteristics of the 20 participating subjects (Mean, standard deviation (SD) and minimum (Min) and maximum (Max))

	Males (n=14)			Females (n=6)		
	Mean	SD	Min-Max	Mean	SD	Min-Max
Age (yrs)	31	9.6	19-56	39	7.6	27-46
Weight (kg)	78	9.6	66-102	71	21.3	51-110
Height (cm)	181	5.7	173-191	170	8.9	159-184
BMI (kg·m <sup>-2</sup> )	24	2.3	21-28	24	6.1	20-36
RMR (kcal·min <sup>-1</sup> )	1.3	0.26	0.8-1.8	1.1	0.12	1.0-1.3

Abbreviations: Body Mass Index, BMI; Resting Metabolic Rate, RMR

A variety of activities and intensities were performed by the participants. Eleven participants carried out conditioning exercises like brisk walking, running or bicycling whereas sedentary activities, home activities, home repair or occupation activities were performed by all 20 participants. Strength training or ball games were carried out by five participants.

### Time in moderate to very vigorous intensity physical activity

The coefficient of variation for time in MVPA during 120 minutes activity were 43% for indirect calorimetry and 74, 95, 53 and 52% for ActiGraph, ActiReg<sup>®</sup>, Armband and ikcal, respectively. The mean differences and limits of agreements from the Bland-Altman plots for time in MVPA were 2.5 ±83.5, -34.2±52.9, 1.1 ±49.9 and -4.9 ±44.6 min (mean differences ± 1.96 SD of the differences) for ActiGraph, ActiReg<sup>®</sup>, Armband and ikcal, respectively (fig 1). The Armband and ActiGraph overestimated time in MVPA with 2.9 and 2.5%, whereas ikcal and ActiReg<sup>®</sup> underestimated with 11.6 and 98.7% respectively. The ICC were 0.54 (95% CI: 0.13-0.79) and 0.54 (0.15-0.79) for Armband and ikcal ( $p=0.007$  and  $0.006$ ); however, the ICC between Armband and ikcal was 0.84 (0.63-0.93). There was no statistical agreement ( $p>0.05$ ) for time in MVPA between indirect calorimetry and ActiGraph or ActiReg<sup>®</sup>.

### Energy expenditure during moderate, vigorous and very vigorous intensity physical activity

Energy expenditure calculated from the Freedson equation for the ActiGraph-data significantly underestimated energy expenditure in moderate, vigorous and very vigorous intensity physical activity (all  $p<0.001$ ) whereas the ActiReg<sup>®</sup> significantly underestimated energy expenditure in vigorous and very vigorous intensity physical activity (both  $p<0.001$ ) (fig 2). Energy expenditure during moderate, vigorous and very vigorous intensity physical activity were underestimated in 67, 80 and 90% of the time points for ActiGraph vs. 68 and 91% for ActiReg<sup>®</sup>. The ikcal significantly overestimated energy expenditure in moderate intensity physical activity ( $p=0.03$ ) and underestimated vigorous ( $p=0.02$ ) and very vigorous intensity physical activity ( $p<0.001$ ) (fig 2). Energy expenditure during moderate intensity physical activity was overestimated in 57% of the time points whereas 56 and 87% of the points were underestimating energy expenditure in vigorous and very vigorous intensity physical activity. The Armband significantly overestimated energy expenditure in moderate intensity physical activity ( $p=0.02$ ) and underestimated very vigorous intensity physical activity ( $p<0.001$ ) (fig 2). Energy expenditure during very vigorous intensity physical activity was underestimated in 92% of the time points. When examining underestimation of energy expenditure in MVPA, only ActiGraph ( $p=0.004$ ) and ActiReg<sup>®</sup> ( $p=0.007$ ) were significantly different from indirect calorimetry. Energy expenditure during MVPA was underestimated in 73 and 74% of the time points.

**Total energy expenditure**

The coefficient of variation for accumulated energy expenditure during 120 minutes of activity were 35% for indirect calorimetry and 47, 29, 34 and 32% for ActiGraph, ActiReg<sup>®</sup>, Armband and ikcal, respectively. Comparing accumulated energy expenditure during 120 minutes of activity, the mean differences and limits of agreements from the Bland-Altman plots were  $-50.0 \pm 396.7$ ,  $-111.1 \pm 298.2$ ,  $-43.4 \pm 261.0$  and  $-33.9 \pm 265.2$  kcal for ActiGraph, ActiReg<sup>®</sup>, Armband and ikcal, respectively (fig 3). ActiGraph, ActiReg<sup>®</sup>, Armband and ikcal underestimated total energy expenditure by 15, 21, 9 and 5% respectively. ActiReg<sup>®</sup> significantly underestimated the accumulated energy expenditure ( $p < 0.02$ ) compared to the other monitors. The ICC were 0.73 (0.44-0.88) and 0.71 (0.41-0.87) for Armband and ikcal (both  $p < 0.001$ ), vs. 0.55 (0.16-0.79) and 0.47 (0.02-0.75) for ActiGraph and ActiReg<sup>®</sup> ( $p = 0.005$  and 0.004).

Figure 4 shows an individual plot of minute-by-minute energy expenditure for a male participant performing 40 minutes brisk walking outdoors, 40 minutes bicycling on a regular bicycle and then walking around for another 40 minutes. The male individual in figure 5 is performing brisk walking the first 25 minutes, then 15 minutes running, 30 minutes playing table tennis, and 50 minutes carrying books and papers. The figures illustrate the large variations of energy expenditure for a given subject.

## DISCUSSION

The Armband and ActiGraph overestimated time in MVPA, and ikcal and ActiReg<sup>®</sup> underestimated time in MVPA, respectively. ActiReg<sup>®</sup> and ActiGraph underestimated energy expenditure in MVPA and all activity monitors underestimated total energy expenditure.

### Time in moderate to very vigorous intensity physical activity

Time in MVPA assessed with the activity monitors was somewhat less precise compared to assessment of total energy expenditure. On the basis of ICC, we noted that for Armband and ikcal, 53 and 54% of the variation were explained by differences among individuals and 47 and 46 % by differences by the two different physical activity monitors. Eighty four per cent of the variation between the two monitors for assessment of time in MVPA was explained by differences among individuals. The deficiency of statistical agreement between indirect calorimetry and ActiReg<sup>®</sup> and ActiGraph was supported by the absolute differences analysis at each time point, comparing underestimation of energy expenditure in MVPA. An explanation for the low agreement could be limitations of uniaxial accelerometers and motion sensors, since accelerometers are insensitive to certain types of activities such as bicycling and strength training.[16]

Information on reported time in MVPA among diverse makes and models is lacking; however, Strath et al. compared five ActiGraph accelerometer cut off points for predicting time spent in different intensity categories.[22] Different accelerometer cut off points gave substantially different estimates of time in MVPA. Errors of energy expenditure prediction and cut off points defining MVPA activity could lead to misclassification of duration and frequency of physical activity. Leenders et al. found no difference in time spent in light, moderate and vigorous intensity physical activity during a seven days assessment using ActiGraph, a pedometer and a triaxial accelerometer.[13]

### Total energy expenditure

Despite an average percentage underestimation of estimated accumulated energy expenditure from 5 to 21%, the activity monitors ActiGraph, Armband and ikcal provided relatively similar results. ActiReg<sup>®</sup> significantly underestimated estimated energy expenditure compared to indirect calorimetry as well as compared to the other three activity monitors. The ICC of 0.73 and 0.71 for Armband and ikcal vs. 0.55 and 0.47 for ActiGraph and ActiReg<sup>®</sup> illustrates that for Armband and ikcal, a larger part of the variance was explained by differences among individuals.

To our knowledge, no studies have reported on comparisons of energy expenditure assessed with Armband or ikcal with indirect calorimetry in free living conditions; however, St-Onge et al. reported mean estimated energy expenditure to be significantly lower for Armband than measured with doubly labelled water.[19] The ICC, 0.81, was somewhat higher compared to the present study. King et al. compared estimated energy expenditure using ActiGraph and Armband with indirect calorimetry, during treadmill walking and running.[11] ActiGraph was the best estimate of total energy expenditure at walking and jogging speeds whereas Armband was the best estimate of total energy expenditure. ActiReg<sup>®</sup> was recently validated against doubly labelled water and indirect calorimetry in a sample of adults. Some underestimation of energy expenditure was present, but to a smaller degree compared to the present study.[18] ActiGraph has been validated against indirect calorimetry in several studies; however, a majority of the studies were conducted in the laboratory, including participants performing activities like treadmill walking and running.[16] In the literature, correlation coefficients between physical activity monitors estimating energy expenditure and indirect calorimetry, seem to be lower during life style activities compared to walking and running at submaximal intensities.[16] The ICC of 0.55 in the present study

between ActiGraph and indirect calorimetry in a free living condition, is in line with results reported by others [9,10,23,24].

### **Strengths and limitations**

The present study has strengths and limitations. A wide range of activities of different intensities were performed among the participants, and energy expenditure during activities as well as at rest (RMR) was measured with the same portable oxygen analyzer. It may not be feasible to wear a breathing mask for longer periods and was together with the power supply or capacity of the batteries the main reasons for 120 minutes of measurement.

MetaMax is found to overestimate oxygen consumption with three to five per cent compared to the Douglas Bag technique, [6,7] and calculation of energy expenditure from oxygen consumption data should ideally adjust for which substrates that are undergoing oxidation.[25] In addition, the energy demand during very vigorous intensity physical activity may be covered through anaerobic energy-yielding metabolic processes not measurable with oxygen consumption. These factors may influence the evaluation of activity monitor compared to indirect calorimetry, but not the comparison among activity monitors.

Our participants were limited to a relatively small sample of 19-56 year old men and women mainly recruited from the Norwegian School of Sport Sciences and the Norwegian Military Academy in Oslo, Norway. The intention was to include men and women of different ages with a wide variety of BMI covering the adult population which the currently published physical activity recommendations include.[1] We can not generalize findings to other ethnic and age groups, which should be included in further studies.

In the present study we did not assess reliability of the activity monitors. To our knowledge, reproducing the same type, duration and intensity of activities in our subjects participating in free living activities is quite demanding.

There are limitations to the use of accelerometers, as well as other activity monitors such as those included in the present study, in predicting energy expenditure and time in MVPA in free living individuals. No single regression equation appears to accurately predict energy expenditure based on acceleration scores for all activities because of the unique relationships between movement and energy expenditure for different activities [10,26]. The use of a portable oxygen analyzer as in the present study covering a wide range of activities that people perform in their daily lives, may provide the most useful way to capture the appropriate balance between locomotor activities and free-living activities.

Direct observational methods are especially useful in studies that aim to go beyond pure assessment of physical activity to include the study of physical and social environmental influences.[27] The main reason for not observing mode of activity in the present study is because indirect calorimetry was used as a "gold standard" for energy expenditure. Indirect calorimetry gives a more valid and reliable information of energy expenditure compared to direct observation.[28] In addition, direct observation is impractical on a population basis.[3]

Different sampling intervals (Epoch) among the monitors may have influenced our results; however, Armband and ActiReg<sup>®</sup> have 60 seconds as default epoch, while ikcal has 10 seconds epoch respectively. The empirical evidence for whether different epochs influence recorded time in MVPA is limited.[29] One exception to this might be physical activity above vigorous intensity.

Measurement of RMR was performed in the morning on another day and may have influenced our results. The reason for measurement of RMR another day was that assessment periods in most participants took place in the afternoon. International guidelines recommend fasting for at least 6 hours before measurement of RMR, and repeated measures of RMR vary three to five percent over 24 hours and up to 10% over weeks or months.[15]



### **Conclusion**

When comparing time in MVPA and total energy expenditure among studies and when doing follow ups, it is essential to consider type of physical activity monitor, since for a given subject time in MVPA and total energy expenditure varies substantially among physical activity monitors. Based on the present study, we can not single out one physical activity monitor as being superior to the others; however, some evidence indicates that ActiReg<sup>®</sup> is less valid in estimating energy expenditure as well as very vigorous intensity physical activity. Additional comprehensive studies comparing physical activity monitors with indirect calorimetry under free living conditions in children, adolescents and adults are needed to evaluate the validity of previous and next generation's physical activity monitors.

### **What is already known on this topic**

- Objective methods to assess physical activity using various types of activity monitors have been recommended as an alternative to self-report because they are not subject to many of the sources of error associated with self-report measures.

### **What this study adds**

- When comparing time in moderate to very vigorous intensity physical activity and total energy expenditure among studies and when doing follow ups, it is essential to consider type of physical activity monitor, since for a given subject time in moderate to very vigorous intensity physical activity and total energy expenditure varies substantially among physical activity monitors used.

### FIGURE LEGENDS

Figure 1. Bland-Altman plots depicting mean differences for minutes in moderate to very vigorous intensity physical activity during 120 minutes of activity (activity monitor minus indirect calorimetry) for ActiGraph (a), ActiReg<sup>®</sup> (b), Armband (c) and iKcal (d). The solid line represents the mean, and the dashed line represents the 95% confidence intervals of the observations.

Figure 2. Mean difference in energy expenditure ( $\text{kcal} \cdot \text{min}^{-1}$ ) in moderate, vigorous and very vigorous intensity physical activity during 120 minutes of activity between ActiGraph, ActiReg<sup>®</sup>, Armband, iKcal and indirect calorimetry. A negative value indicates underestimation whereas positive values indicate overestimation. \* $p < 0.05$  and # $p < 0.001$ .

Figure 3. Bland-Altman plots depicting mean differences for accumulated energy expenditure during 120 minutes of activity (activity monitor minus indirect calorimetry) for ActiGraph (a), ActiReg<sup>®</sup> (b), Armband (c) and iKcal (d). The solid line represents the mean, and the dashed line represents the 95% confidence intervals of the observations.

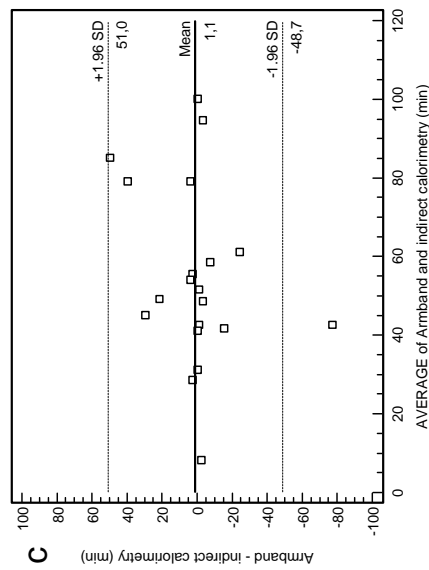
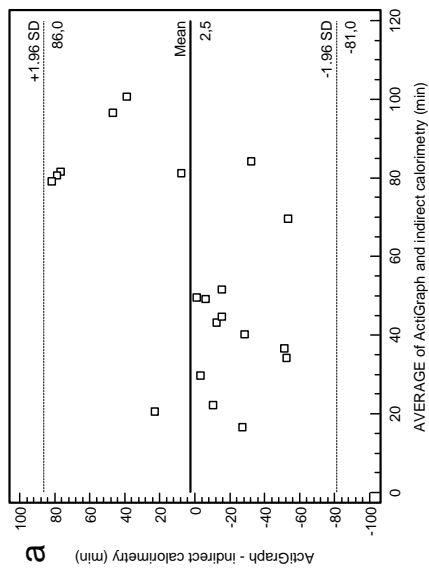
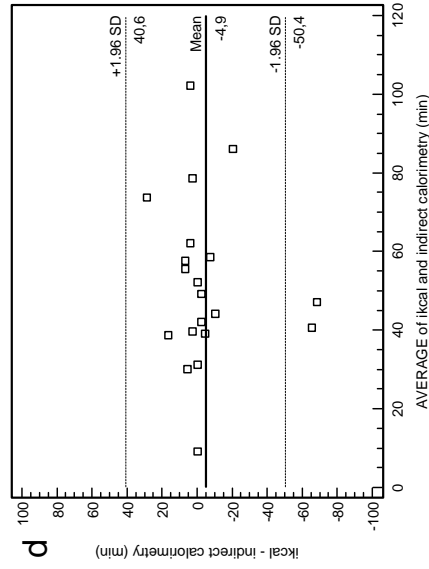
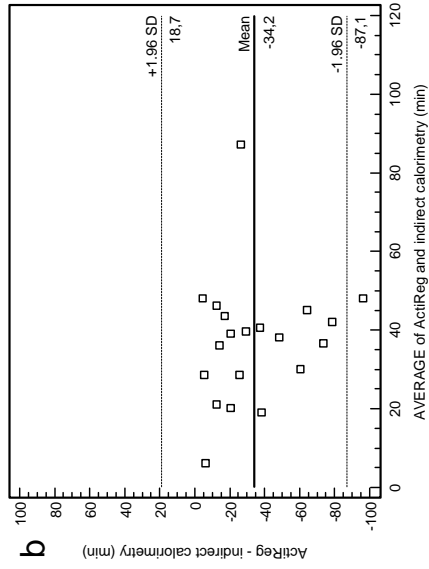
Figure 4. Individual plot of minute-by-minute energy expenditure (32 yr old male) during 120 minutes of activity. The participant walked for 40 minutes, followed by 40 minutes of bicycling (regular bicycle) and then walking around for 40 minutes.

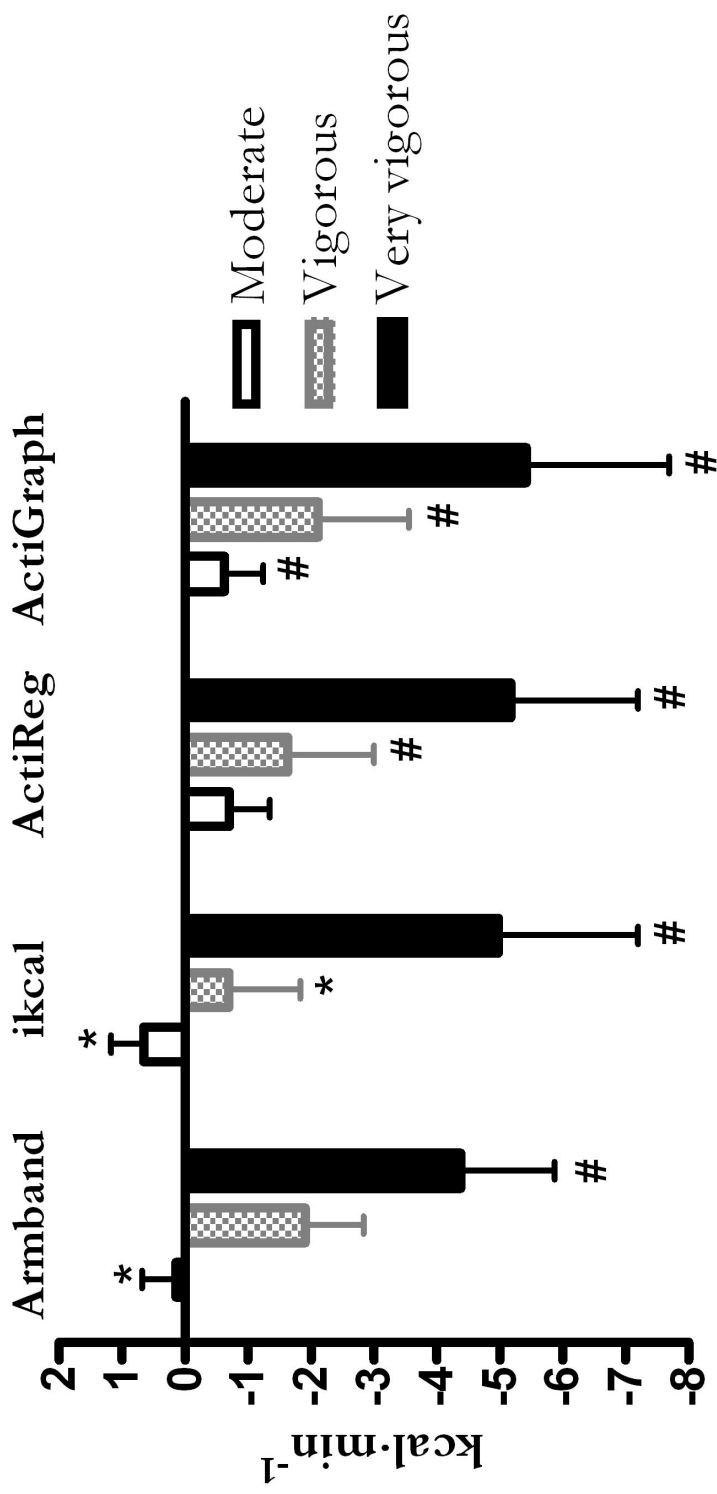
Figure 5. Individual plot of minute-by-minute energy expenditure (34 yr old male) during 120 minutes of activity. The participant perform brisk walking the first 25 minutes, then 15 minutes of running, 30 minutes playing table tennis, and 50 minutes carrying books and papers.

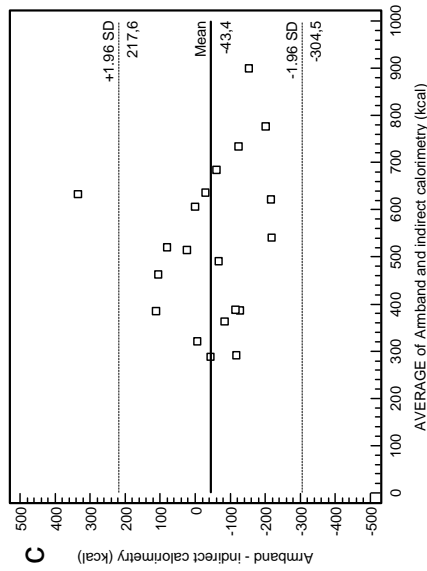
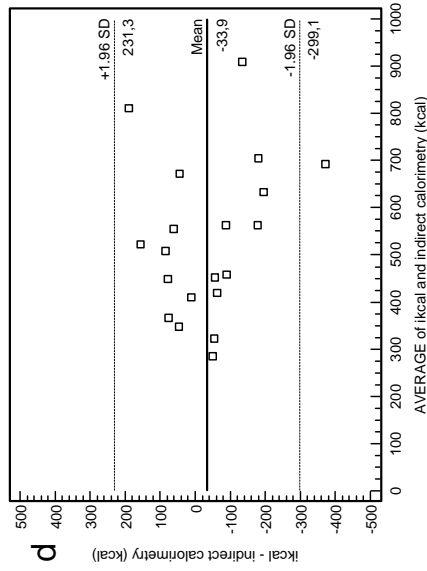
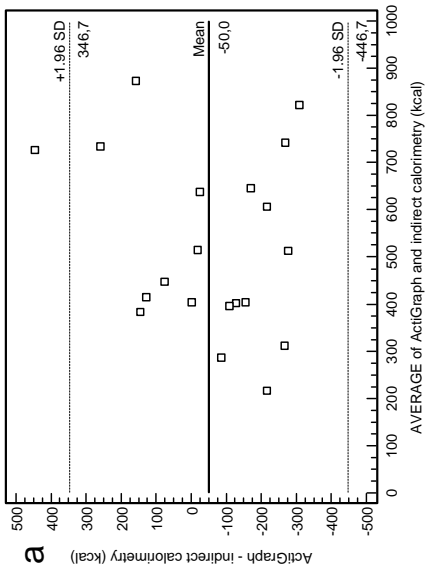
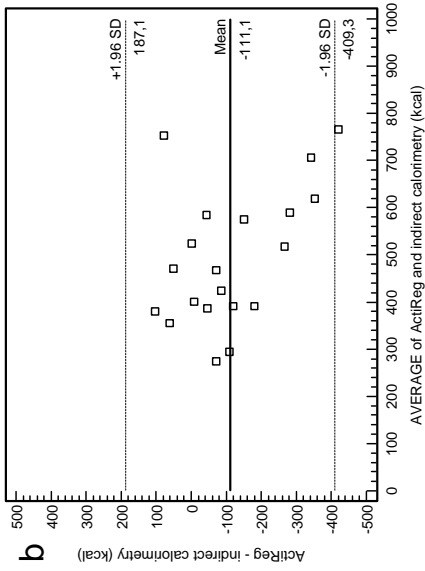
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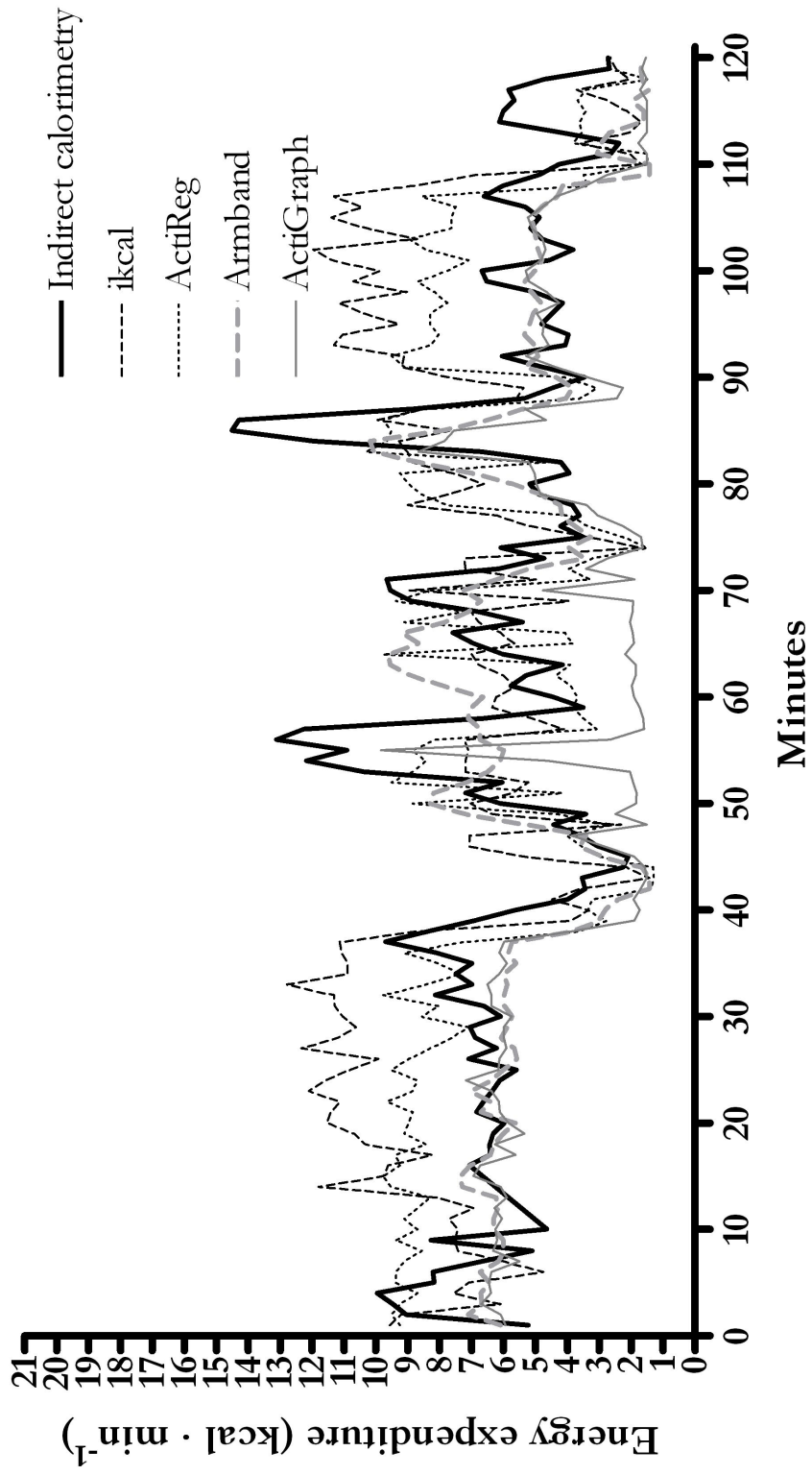
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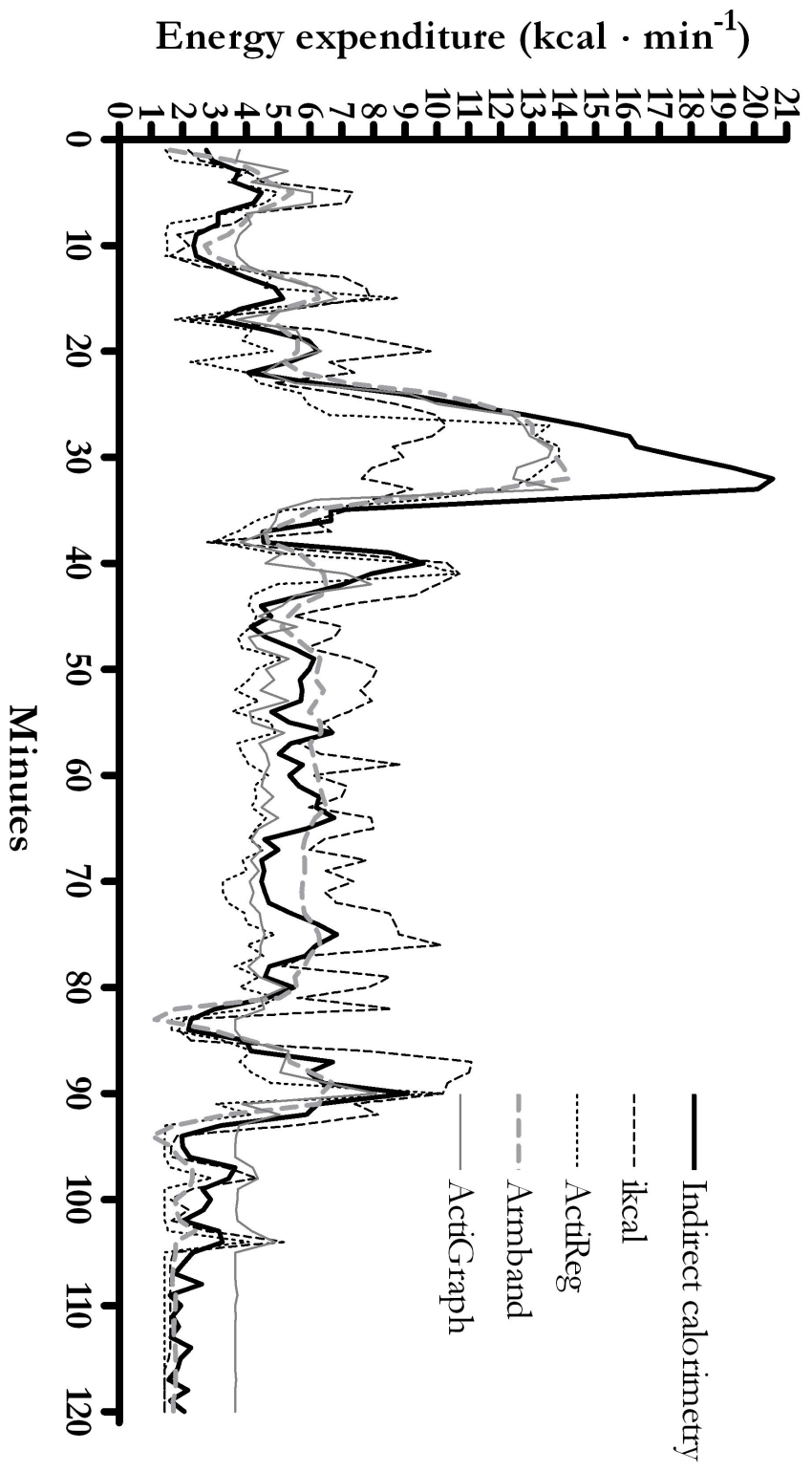














**Paper 4**

Berntsen S, Lødrup Carlsen KC, Anderssen SA, Mowinckel P, Hageberg R, Kørner Bueso A, Carlsen KH. Norwegian adolescents with asthma are physical active and fit. Allergy 2009; 64:421-426.

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## Original article

# Norwegian adolescents with asthma are physical active and fit\*

**Background:** Evidence regarding habitual physical activity levels and aerobic fitness of asthmatic compared to nonasthmatic children and adolescents is contradictory, and it is unclear if low physical activity levels can contribute to asthma development. The present study therefore aimed to determine whether adolescents with asthma have reduced physical activity levels and aerobic fitness, or increased energy intake and body fat compared to controls.

**Methods:** From the environment and childhood asthma study in Oslo, 174 (13- to 14-year old) adolescents, 95 (66 boys) with and 79 (41 boys) without asthma performed maximal running on a treadmill with oxygen consumption measurement (aerobic fitness) and had the sum of four skinfolds and waist circumference recorded (body fat), followed by wearing an activity monitor and registering diet for four consecutive days. Asthma was defined by at least two of the following three criteria fulfilled: (1) dyspnoea, chest tightness and/or wheezing; (2) a doctor's diagnosis of asthma; (3) use of asthma medication. Participants with asthma used their regular medications.

**Results:** Neither aerobic fitness, total energy expenditure nor hours in moderate to very vigorous intensity physical activity during week and weekend differed between adolescents with and without asthma. Energy intake and body fat was similar in both groups.

**Conclusions:** Total energy expenditure, aerobic fitness and hours in moderate to very vigorous intensity physical activity were not reduced and energy intake and body fat measured with skinfolds not increased among Norwegian adolescents with asthma.

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Key words: aerobic fitness; energy intake; lifestyle; overweight; physical activity.

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\*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 Ga<sup>2</sup>len network.

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The percentage of children and adolescents reported to have had asthma at some time in their lives has increased in the last decades (1), with a 20.2% lifetime prevalence of asthma in Oslo, Norway reported in 2005 (2). The cause of the increase in asthma is thought to be multi-factorial including allergen sensitization, lifestyle changes and environment (3) with increasing attention to 'Western lifestyle', urbanization, unhealthy diet and sedentary lifestyle with decreased physical activity (4). Exercising more than once per week has been found inversely related to new onset of wheeze in adolescents; however, this association disappeared when active smoking was taken into account (5). In addition, participation in moderate and vigorous physical activity may influence aerobic fitness (6), and lower levels of work capacity has been associated with higher risk of developing asthma (7). A number of longitudinal studies have also reported increasing risk of developing asthma or asthma symptoms in obese children and adolescents (8); however, the causality is not known.

Comparisons of habitual physical activity levels of children and adolescents with and without asthma have given inconsistent results with higher (9, 10), lower (11–13) or similar physical activity levels (14, 15) reported in asthmatic subjects. Only two studies reported objectively measured physical activity levels, in which, Firrincieli et al. (13) found lower physical activity levels among children aged 3–5 years with a history of wheezing whereas van Gent et al. (15) found no differences in physical activity levels in children 7–10 years with undiagnosed asthma, diagnosed asthma and controls. At present, only scarce information is available regarding objective measurement of physical activity in asthmatic adolescents 13–18 years of age. The present study therefore aimed to determine whether adolescents with asthma have reduced objectively measured physical activity levels, secondarily to examine differences in aerobic fitness, total energy intake and body fat in adolescents with and without asthma.

## Material and methods

### Study design

The present nested case-control study is part of the birth cohort 'Environment and Childhood Asthma' study in Oslo, described elsewhere (16). This 13-year follow-up study conducted between October 2005 and June 2006 consisted of 1 day of clinical investigation and 4 days home monitoring including adolescents with current asthma and without asthma at 10 years.

The study was approved by the Data Inspectorate of Norway and the Medical Research Ethics Committee. Written informed consent to take part was obtained from the participating children and their parents.

### Subjects

From the 10-year follow up (2), all 147 children with current asthma and 163 controls without lower respiratory disease, born at the same day as adolescents with current asthma, were invited to participate in the present study of which 174 (56%) agreed to participate. Ninety-five (66 boys) of the adolescents had asthma and 79 (41 boys) did not. *Asthma* was defined by at least two of the following three criteria fulfilled (2):

1. Dyspnoea, chest tightness and/or wheezing 0–3 years and/or after 3 years.
2. A doctors diagnosis of asthma.
3. Used asthma medication ( $\beta$ -2 agonists, sodium chromoglycate, corticosteroids, leukotriene antagonists and/or aminophylline) 0–3 years and/or after 3 years.

There were no significant differences at 10-year follow-up with respect to socioeconomic factors (income and education), body mass index (BMI), lung function, bronchial hyper responsiveness, use of inhaled corticosteroids or  $\beta$ -2 agonist, prevalence of wheeze and exercise induced bronchoconstriction between the adolescents in the present study and those invited, but who did not want to participate.

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 with asthma used their regular medications.

### Methods

The present study included a parental structured interview including central international study of asthma and allergies in Childhood questions related to airways symptoms (validated in Norwegian language (17)) of the child, in addition to detailed questions of medication use, lifestyle and diseases (2). Information regarding type and frequency of physical activity as well as transportation to school, hours of television viewing and time at computer each day was collected using a physical activity questionnaire.

**Anthropometrics.** Body mass was measured with the subject wearing light clothing and without shoes (Seca 709, Seca, Hamburg, Germany) to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm by using a stadiometer. BMI was calculated as body mass (kg) divided by height (m) squared. Overweight and obesity were calculated according to Cole et al. (18). The waist circumference was measured to midway between the costal arch and the iliac crest with a metal anthropometric tape to the nearest 0.5 cm at the end of a gentle expiration. Pubertal stage was assessed by means of Tanner

criteria (19). Skinfold thicknesses were measured with a Harpenden fat caliper at the biceps, triceps, subscapular and suprailiac region.

**Lung function.** Forced expiratory volume in 1 s ( $FEV_1$ ), 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), residual volume (RV) and specific airway resistance (sRaw) were measured with a body plethysmograph (Masterlab BodyPro, Erich Jaeger® GmbH & Co KG) according to criteria of European Respiratory Society (20, 21). The predicted values of Zapletal et al. (22) were used for comparisons. All individual flow-volume curves were reviewed for technical acceptability. Response to inhaled salbutamol was measured using 0.4 mg salbutamol (Airomir™ Autohaler™; 3M Pharmaceuticals, Maplewood, MN, USA). A  $\geq 12\%$  increase in  $FEV_1$  15 min after inhalation, compared to baseline ( $\Delta FEV_1 = (FEV_1 \text{ post} FEV_1 \text{ pre}) / FEV_1 \text{ pre}$ ) was defined as a reversible airflow-limitation.

**Physical activity.** Habitual physical activity was measured with SenseWear™ Pro2 Armband (BodyMedia Inc., Pittsburgh, PA, USA). The participants received the monitor during their visit at the laboratory. The recording of physical activity started on a Wednesday or on a Sunday (random order) and included 3 week days and 1 weekend day. The monitor was worn on the right arm over the triceps brachii muscle at the midpoint between the acromion and olecranon processes. The participants and their parents used an additional form to indicate when the monitor was not in use, such as during water activities. Energy expenditure was computed at 1-min intervals. The cut off points defining moderate to very vigorous intensity were three metabolic equivalents (METs). 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).

**Aerobic fitness.** Aerobic fitness was determined as highest oxygen consumption ( $\dot{V}O_{2\text{peak}}$ ) during treadmill running (Woodway ELG 2, Woodway GmbH, Weil am Rhein, Germany), starting at 5 km/h and an inclination of 5.3%. The speed increased with 2 km/h after 5 min running, thereafter 1 km/h each minute until a maximal speed of 11 km/h was reached. With no increments in speed, the inclination of the treadmill was raised 1% each minute until exhaustion. Heart rate (HR) was recorded continuously (Polar Vantage, Polar Electro KY, Kempele, Finland). Minute ventilation ( $\dot{V}_E$ ), respiratory exchange ratio (RER), oxygen consumption ( $\dot{V}O_2$ ) and carbon dioxide production ( $\dot{V}CO_2$ ) were measured after 4 min running using the Oxycon Champion (Erich Jaeger® GmbH & Co. KG, Hoechberg, Germany). Calibration was conducted before each test period. The main criterion for having reached maximal effort was a subjective assessment by the test leader that the participants had reached his or her maximal effort. The second criterion was a RER above 1.00, HR above 200 beats/min or reporting perceived exertion (RPE) above 17 using the Borg-RPE-Scale (23). A  $\dot{V}O_2$  plateau was defined as a change in  $\dot{V}O_2$  during the final 2 min of running  $\leq 2$  ml/kg/min (24); however, absence of a  $\dot{V}O_2$  plateau was not used as exclusion criteria for not reaching maximal effort.

**Diet.** The participants received four precoded food diaries (25), one for each day. They had to record their food intake and were instructed (verbally and watching a video) how to fill in the diary. The recordings of the diet were performed the same days as the activity recording. Daily intake of energy was computed using the food database and software system (KBS, version 4.9; Department of Nutrition, University of Oslo, Oslo, Norway) developed at the

Department of Nutrition, University of Oslo. In the present study, total energy intake is presented only.

#### Statistical analysis

Sample size calculations were based on a standard deviation (SD) of daily hours of moderate to very vigorous intensity physical activity of 1.0 h and a significance level of 0.05 to obtain 80% power, 64 subjects were required in each group to detect a mean difference of 0.5 h.

Demographic data are given as mean values and SD 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. Differences in outcome variables between groups were assessed by analysis of covariance adjusting for age, pubertal stage (entered puberty or not) and gender (core set variables). Physical activity data were also adjusted for mean hours each day the Armband was worn. The underlying assumptions of the analysis of covariance were assessed using Jackknife Residuals and Cook's *d*. Further stratifying by gender was not feasible due to small groups. Statistical significance level was set to 5%. Statistical analyses were performed with Statistical Package for Social Sciences Version 15.0 (SPSS, Chicago, IL, USA).

#### Results

Adolescents with asthma and controls did not differ significantly with respect to body mass, height, reversible airflow limitation, TLC (% of predicted), RV/TLC or sRaw (Table 1); however, adolescents with asthma had significantly lower FEV<sub>1</sub>, FEV<sub>50</sub> (% of predicted) and FEV<sub>1</sub>/FVC compared to controls. Among the adolescents with asthma, 47% used inhaled corticosteroids regularly, 60% used β<sub>2</sub>-agonists regularly and 47% used β<sub>2</sub>-agonists when participating in physical activity. Exercise was reported as the most important symptom provoking factor in 36% of the adolescents with asthma, and 36% of those with asthma reported activity limitations due to their asthma. One of the

adolescents with asthma only reported active daily smoking vs. none of the controls. The mean use of the activity monitor during week days was 21.2 (95% CI; 20.8–21.5) vs 16.4 (15.6–17.2) h/day during weekend days, and not different between the two groups, with recordings for 4 days in 95% of the subjects. During maximal running on the treadmill 51% (controls) and 58% (with asthma) of the adolescents reached a  $\dot{V}O_2$  plateau. Highest recorded heart rate was 196 (194–198) beats/min and RER<sub>peak</sub> was 1.08 (1.06–1.09), and not significantly different between adolescents with and without asthma (*P* > 0.2).

#### Physical activity, sedentary time and aerobic fitness

Neither total energy expenditure nor hours in moderate to very vigorous intensity physical activity during week and weekend days were different between adolescents with asthma and controls when adjusted for the core set variables (Table 2). Although, both groups had significantly lower total energy expenditure during weekend days (*P* < 0.001), only controls (*P* = 0.001) had significantly smaller quantity of minutes in moderate to very vigorous intensity physical activity during weekends. All participants fulfilled the international physical activity guidelines during week days and 95% of the adolescents with asthma fulfilled the physical activity recommendation vs 87% of the controls (not significant) during weekends. The adolescents participated in exercise or sport activities on average four times a week. Almost 70% of the participants reported the exercise or sport activities as strenuous. The adolescents with and without asthma participated in similar kind of activities. Sixty to seventy per cent of the adolescents participated in

Table 1. Descriptive data of the participating subjects presented by asthma and controls

	Asthma ( <i>n</i> = 95)	Controls ( <i>n</i> = 79)	<i>P</i> -value**
Age (years); mean (min–max)*	13.6 (12.8–14.3)	13.6 (12.6–14.3)	0.96
Weight (kg)	53.2 (10.8)	50.5 (9.7)	0.09
Height (cm)	164 (9.0)	162 (7.2)	0.16
FEV <sub>1</sub> (% of predicted)	100 (12.6)	104 (12.5)	<b>0.04</b>
FEF <sub>50</sub> (% of predicted)	86 (20.8)	98 (21.8)	<b>&lt;0.001</b>
FEV <sub>1</sub> /FVC	85 (6.7)	87 (6.0)	<b>0.008</b>
FEV <sub>1</sub> reversibility (% increase)	4 (5.0)	3 (4.5)	0.21
TLC (% of predicted)	104 (13.1)	104 (11.7)	0.85
RV/TLC (%)	27 (7.0)	26 (5.6)	0.37
sRaw (kPa s)	0.84 (0.27)	0.81 (0.27)	0.46

FEV<sub>1</sub>, forced expiratory volume after 1 s; FVC, forced vital capacity; FEF<sub>50</sub>, forced expiratory flow at 50% of FVC; TLC, total lung capacity; RV, residual volume; sRaw, specific resistance of airways; min, minimum; max, maximum.

\*Data are given as mean and SD in parentheses unless otherwise stated.

\*\**P*-values for any differences between groups.

Table 2. Adjusted\* hours in moderate to very vigorous intensity physical activity, total energy expenditure and total energy intake at week and weekend days, and highest recorded oxygen uptake presented by asthma and controls

	Asthma ( <i>n</i> = 95)	Controls ( <i>n</i> = 79)	<i>P</i> -value**
MVPA (h/day)			
Week	4.4 (4.0–4.8)	4.6 (4.2–5.0)	0.41
Weekend	3.8 (3.4–4.3)	3.5 (3.0–4.0)	0.32
Total energy expenditure (kcal/day)			
Week	2446 (2336–2556)	2386 (2269–2503)	0.41
Weekend	1932 (1862–2121)	1860 (1719–2001)	0.13
Total energy intake (kcal/day)			
Week	1909 (1782–2036)	1911 (1776–2047)	0.98
Weekend	2043 (1841–2246)	2145 (1931–2359)	0.44
$\dot{V}O_2$ (ml/kg/min)	52.1 (50.1–54.1)	53.1 (51.1–55.1)	0.40

Data are given as adjusted means with 95% CI in parentheses.

MVPA, hours in moderate to very vigorous intensity physical activity;  $\dot{V}O_2$ , highest recorded oxygen uptake during treadmill test; week, during weekdays, Monday to Friday; weekend, during weekend days, Saturday and Sunday.

\*Adjusted for age, pubertal stage (entered as puberty or not), gender and mean hours each day the armband was worn (physical activity data only).

\*\**P*-values for any differences between groups.

endurance training or ball game activities at least weekly. Sixty-four per cent of the adolescents had at least 3 h of physical education per week at school, and 78% participated in PE every time.

Neither hours playing computer nor television watching differed between groups. Twenty-seven per cent of the adolescents watched television for at least 2 h during week days, while 38% of the adolescents spent at least 2 h in front of the computer each day.

Adjusted  $\dot{V}O_{2peak}$  did not differ between adolescents with asthma and controls (Table 2).  $\dot{V}O_{2peak}$  was approximately 8% lower ( $P < 0.001$ ) for girls compared to boys (pooled data).

#### Energy intake and body fat

Adjusted energy intake was not significantly different during week and weekend days between adolescents with asthma and controls (Table 2). None of the groups had significantly higher energy intake during weekend *vs* week days.

Adjusted sum of skinfolds was not significantly different between groups [38.6 (35.5–41.7) mm in adolescents with asthma *vs* 37.0 (33.7–40.2) mm in controls]; however, adjusted waist circumference was significantly higher ( $P = 0.04$ ) in adolescents with asthma [73.4 (71.6–75.3) *vs* 71.0 (69.0–73.0)], and 16% of the adolescents with asthma were classified as overweight, according to cut-off points developed by Cole et al. (18), compared to 10% of the controls ( $P = 0.053$ ). Prevalence of obesity were not significant different between adolescents with asthma and controls.

#### Discussion

Norwegian adolescents with asthma had not reduced aerobic fitness, total energy expenditure and hours in moderate to very vigorous intensity physical activity compared to adolescents without asthma. The adolescents with asthma participated in similar sport activities as controls. Total energy intake and sum of skinfolds were similar, whereas waist circumference was higher among adolescents with asthma. Prevalence of overweight tended to be higher among adolescents with asthma.

The corresponding physical activity levels in adolescents with asthma compared to controls in the present study are supported by others (14, 15), although few studies have included objective physical activity measures. In contrast Ownby et al. (9) found higher levels of physical activity among children with asthma and, Kitsantas and Zimmerman (12) and Lang et al. (11) reported that children and adolescents were less active than controls. Inconsistency between studies may be related to different methodologies and inclusion criteria. For a given subject the measured time in moderate to

vigorous intensity physical activity varies substantially among physical activity monitors used (26). The relative high physical activity level in adolescents with asthma in the present study could be due to the use of asthma medications and good asthma control. Approximately half of the adolescents with asthma used inhaled corticosteroids regularly. Including encouragement of participation in regular physical activity plays an important role in the management of individuals with asthma (27).

Similar aerobic fitness in adolescents with and without asthma is in agreement with others (28); however, the aerobic fitness of the participants in the present study are approximately 10 ml/kg/min higher compared to Santuz et al. (28). Varray et al. (29) found aerobic fitness to be limited in adolescents with severe asthma. This is in contrast to Pianosi and Davis (30) who found no correlation between asthma severity and aerobic fitness. These findings may highlight the importance of not considering children and adolescents with asthma as a homogeneous group. Lower aerobic fitness in adolescents with asthma appears to be related to the degree of inactivity and can be potentially normalized (31). Participation in physical activity with vigorous intensity may influence aerobic fitness in the same manner as in those without asthma (6).

Corresponding daily energy intake in adolescents with asthma compared to controls are supported by others (32), although few studies have included estimates of daily energy intake.

The tendency of a higher prevalence of overweight in adolescents with asthma using the BMI cut-off points developed by Cole et al. (18) is supported by others (8). The higher waist circumference but not sum of skinfolds in the present study is; however, contradictory. Maffeis et al. (33) showed waist circumference to be a better predictor of overweight in children than skinfold measurements. Small groups may explain the inconsistent results regarding estimates of body fat.

It is reported that overweight children with asthma experience greater limitation of physical activity (30). In the present study, 36% of those with asthma reported activity limitations due to their asthma. Due to small groups, stratifying by overweight was not possible; however, motivation and introducing active play may increase participation in physical activity in leisure time and result in weight reduction, improve lung function, asthma symptoms, morbidity and health status (34).

The main strengths of the present study are the objective measurements of physical activity and direct and maximal testing of aerobic fitness. Physical activity monitors give reliable measures of physical activity and having advantages compared to self reports with recall biases (35). The adolescents were also recruited from the same population based birth cohort. The inclusion criteria are the same except for asthma which is required to be a case.



Sample size calculations were based on the variable daily hours in moderate to very vigorous intensity physical activity and a sample of 64 subjects in each group were required; however, we can not rule out type II errors for other variables. In addition participation in an ongoing cohort may influence lifestyle due to knowledge regarding asthma management and, the adolescents may not be representative of the general European youth population. It cannot be ruled out whether other groups of children or adolescents with asthma have lower physical activity levels and aerobic fitness or higher amount of body fat. Still, there were no significant differences at 10-year follow up with respect to socioeconomic factors, BMI, lung function, bronchial hyperresponsiveness, use of inhaled corticosteroids or  $\beta$ -2 agonist, prevalence of wheeze and exercise induced bronchoconstriction between the adolescents in the present study and those did not participated.

In conclusion, aerobic fitness, total energy expenditure and hours in moderate to very vigorous intensity physical activity were not reduced in Norwegian adolescents with asthma. The adolescents with asthma participated in the same kind of sport activities as controls. Total energy intake and sum of skinfolds were not increased either, whereas waist circumference was higher among adolescents with asthma. There was a tendency that the prevalence of overweight was higher among adolescents with asthma.

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## **APPENDICES**

- A. Video questionnaire in Swahili
- B. Video questionnaire in English
- C. Central questions related to asthma symptoms (in Swahili)
- D. Central questions related to asthma symptoms (in English)
- E. Parts of the interview form (in Norwegian)
- F. Physical activity questionnaire (in Swahili)
- G. Parts of the physical activity questionnaire (in English)
- H. Parts of the physical activity questionnaire (in Norwegian)
- I. Approval letters from the Regional Medical Research Ethics Committee (in Norway)
- J. Research Clearance, University of Dar es Salaam, Tanzania



## **Appendix A: Video questionnaire in Swahili**



1. Uliwahi kupumua namna hii:  
wakati wowote katika maisha yako? Ndiyo Hapana  
kama ni ndiyo; mwaka uliopita? Ndiyo Hapana  
kama ni ndiyo; mara moja au zaidi kwa mwezi? Ndiyo Hapana
  
2. Pumzi yako ilikuwa kama wa kijana ambaye kwenye video  
kufuatayo na mazoei:  
wakati wowote katika maisha yako? Ndiyo Hapana  
kama ni ndiyo; mwaka uliopita? Ndiyo Hapana  
kama ni ndiyo; mara moja au zaidi kwa mwezi? Ndiyo Hapana
  
3. Uliwahi kuamshwa usiku namna hii:  
wakati wowote katika maisha yako? Ndiyo Hapana  
kama ndiyo; mwaka uliopita? Ndiyo Hapana  
kama ndiyo; mara moja au zaidi kwa mwezi? Ndiyo Hapana
  
4. Uliwahi kuamshwa usiku namna hii:  
wakati wowote katika maisha yako? Ndiyo Hapana  
kama ndiyo; mwaka uliopita? Ndiyo Hapana  
kama ndiyo; mara moja au zaidi kwa mwezi? Ndiyo Hapana
  
5. Pumzi yako ilikuwa kama hii:  
wakati wowote katika maisha yako? Ndiyo Hapana  
kama ndiyo; mwaka uliopita? Ndiyo Hapana  
kama ndiyo; mara moja au zaidi kwa mwezi? Ndiyo Hapana





## **Appendix B: Video questionnaire in English**



- 1 Has your breathing ever been like this:
- at any time in your life? Yes No
  - if YES,; in the last year? Yes No
  - if YES,; one or more times a months? Yes No
- 2 Has your breathing been like the boy in the video following exercise:
- at any time in your life? Yes No
  - if YES,; in the last year? Yes No
  - if YES,; one or more times a months? Yes No
- 3 Have you been woken like this at night:
- at any time in your life? Yes No
  - if YES,; in the last year? Yes No
  - if YES,; one or more times a months? Yes No
- 4 Have you been woken at night like this:
- at any time in your life? Yes No
  - if YES,; in the last year? Yes No
  - if YES,; one or more times a months? Yes No
- 5 Has your breathing been like this:
- at any time in your life? Yes No
  - if YES,; in the last year? Yes No
  - if YES,; one or more times a months? Yes No



**Appendix C: Central questions related to asthma symptoms  
(in Swahili)**



1. Uliwahi kupumua kwa shida au kutoa sauti hifuani wakati wowote kwa muda uliopita?

Ndiyo Hapana

Kama umejibu “hapana” tafadhali ruka mpaka swali la sita (6).

2. Uli pumua kwa shida au ulipumua kwa kutoa sauti kifuani kwa miezi 12 iliyopita?

Ndiyo Hapana

Kama umejibu “hapana” tafadhali ruka mpaka swali la sita (6).

3. Mara ngapi ulishikwa na tatizo la kupumua kwa shida kwa miezi 12 iliyopita?

Hakuna 1 mpaka 3 4 mpaka 12 zaidi ya 12

4. Katika miezi 12 iliopita, ni mara ngapi, kwa wastani ulisumbuliwa na tatizo la kupumua kwa shida wakati wa kulala?

Sijapata shida lolote  
Chini ya usiku moja kwa wiki  
Usiku moja au zaidi kwa wiki

5. Kwa miezi 12 iliyopita shida ya kupumua limezidi kiasi cha kukuzuia katika maongezi kufikia neno moja au mawili katika ya pumzi mbili?

Ndiyo Hapana

6. Uliwahi kuwa na pumu?

Ndiyo Hapana

7. Kwa miezi 12 iliyopita, kifua chako kilikuwa kinatoa sauti wakati au baada ya mazoezi?

Ndiyo Hapana

8. Kwa miezi 12 iliyopita ulikuwa unakohoa usiku, zaidi ya makahazi ya kawaida ya mafua au mafua na homa?

Ndiyo Hapana





**Appendix D: Central questions related to asthma symptoms  
(in English)**



1. Have you *ever* had wheezing or whistling in the chest at any time in the past?

Yes No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

2. Have you had wheezing or whistling in the chest *in the last 12 months*?

Yes No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

3. How many attacks of wheezing have you had *in the last 12 months*?

None

1 to 3

4 to 12

More than 12

4. *In the last 12 months*, how often, on average, has your sleep been disturbed due to wheezing?

Never woken with wheezing

Less than one night per week

One or more nights per week

5. *In the last 12 months*, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?

Yes No

6. Have you *ever* had asthma?

Yes No

7. *In the last 12 months*, has your chest sounded wheezy during or after exercise?

Yes No

8. *In the last 12 months*, have you had a dry cough at night, apart from a cough associated with a cold or chest infection?

Yes No



**Appendix E: Parts of the interview form (in Norwegian)**



## Respirasjon

Kode 

Etter forrige undersøkelse

85. Har barnet hatt tung pust, tetthet eller piping/vesing i brystet?

1. Ja.  
 2. Nei

Hvis ja, spm. 85

87. Hvor mange perioder med tung pust, tetthet eller piping/vesing i brystet har barnet hatt siden siste us?

1. Ingen    2. 1-3  
 3. 4-12    4. mer enn 12

Hvis ja, spm. 85

89. Hvor mange dager med tung pust, tetthet eller piping/vesing i brystet har barnet hatt siste 14 dagene?

1. Ingen    2. 1-3  
 3. 4-12    4. mer enn 12

Hvis ja, spm. 85

91. Hvis ja, hvilken/hvilke årstider er verst?

- Vår                    a   
Sommer                b   
Høst                    c   
Vinter                    d

86. Har barnet hatt tørr hoste om natten uten å være forkjølet eller ha andre luftveisinfeksjoner?

1. Ikke etter siste us.  
 2. Siste 3 år  
 3. Siste 12 mndr  
 4. Siste 14 dager

Hvis ja, spm. 85

88. Hvor mange perioder med tung pust, tetthet eller piping/vesing i brystet har barnet hatt siste 12 måneder?

1. Ingen    2. 1-3  
 3. 4-12    4. mer enn 12

Hvis ja, spm. 85

90. Er/var det årstids- variasjon i barnets symptomer?

1. Ja  
 2. Nei

Hvis ja, spm. 85

92. Hva er/var det som utløser/forverrer symptomene?

- |              |                            |               |                            |
|--------------|----------------------------|---------------|----------------------------|
| Infeksjoner  | a <input type="checkbox"/> | Pollen        | f <input type="checkbox"/> |
| Anstrengelse | b <input type="checkbox"/> | Pelsdyr       | g <input type="checkbox"/> |
| Kald luft    | c <input type="checkbox"/> | Mat/drikke    | h <input type="checkbox"/> |
| Tåke/rå luft | d <input type="checkbox"/> | Sterke lukter | i <input type="checkbox"/> |
| Sigarettøyk  | e <input type="checkbox"/> | Annet,        | j <input type="checkbox"/> |
|              |                            | Hva:          |                            |

93. Har barnet, etter siste undersøkelse fått diagnosen astma?

- a  1. Ja  
 2. Nei

Hvis ja, hvilken alder?

- b  år

Hvis ja, har barnet etter din mening fortsatt astma?

- c  1. Ja  
 2. Nei

Hvis nei, alder ved symptomslutt:

- d  år

94. Har barnet noen gang brukt medisin for luftveiene?

1. Ja  
 2. Nei

Draft



Hvis ja spm. 94

Har barnet brukt: (som hjemme behandling)

Kode

Etter siste undersøkelse (siste 3 år)

1. Ikke etter siste undersøkelse 2. Siste 3 år 3. Siste 12 mndr. 4. Siste 14 dager

95

		DOSE:
$\beta$ -2 agonist på forstøver	a <input type="text"/>	-----
$\beta$ -2 agonist som spray	b <input type="text"/>	-----
$\beta$ -2 agonist som spray m/kammer	c <input type="text"/>	-----
$\beta$ -2 agonist som pulver	d <input type="text"/>	-----
$\beta$ -2 agonist som mikstur/tabletter	e <input type="text"/>	-----
Langtidsvirkende $\beta$ -2 agonist, Formoterol(oxis, foradi) Salmeterol(serevent)	f <input type="text"/>	-----
Lomudal som spray	g <input type="text"/>	-----
Lomudal som pulver	h <input type="text"/>	-----
Lomudal på forstøver	i <input type="text"/>	-----
Inhalasjonssteroider som spray	j <input type="text"/>	-----
Inhalasjonssteroider som spray m/kammer	k <input type="text"/>	-----
Inhalasjonssteroider som pulver	l <input type="text"/>	-----
Inhalasjonssteroider på forstøver	m <input type="text"/>	-----
Leukotrienantagonist (singulair)	n <input type="text"/>	-----
Ipratropiumbromid (Atrovent)	o <input type="text"/>	-----
Adrenalin på forstøver	p <input type="text"/>	-----
Kombinasjon Inhalasjonsteroider og langtidsvirkende $\beta$ 2 agonist (symbicort el. seretide)	q <input type="text"/>	-----
Hyposen-sibilisering (allergi-vaksinasjon)	r <input type="text"/>	-----
Systemiske steroider	s <input type="text"/>	-----





Kode

96. Hvis barnet har brukt  $\beta$ -2 agonist siste 12 mnd/14 dager, hvor stort har forbruket i gjennomsnitt vært pr. brukeruke?

Siste 12 mnd		Siste 14 dager	
a <input type="text"/>	1. Daglig 2. 4-6 dager/uke 3. 1-3 dager/uke	d <input type="text"/>	
Antall puff/dag	b <input type="text"/> <input type="text"/>	e <input type="text"/> <input type="text"/>	
Hvor mange uker	c <input type="text"/> <input type="text"/>	f <input type="text"/> <input type="text"/>	

103. Hvis barnet bruker inhalasjonssteroider, bruker barnet det kun ved forverrelser?

a  1. Ja  
2. Nei

Hvis ja, hvor mange perioder brukte barnet inhalasjonssteroider siste år? b

97. Har barnet brukt  $\beta$ 2 agonist (hurtigvirkende astmamedisin) i forbindelse med fysisk aktivitet de siste 12 måneder?

1. Ja  
 2. Nei

98. Hvis barnet har brukt inhalasjonssteroider, hva var alder ved behandlingsstart?

a  år

Bruker barnet fortsatt inhalasjonssteroider?

b  1. Ja  
 2. Nei

Hvis nei, alder ved seponering:

c  år

104. Hvordan vil du karakterisere barnets helse i forhold til astma/astmalignende symptomer?

Siste 3 år	Siste 12 mnd	Siste 14 dager
a <input type="text"/>	b <input type="text"/>	c <input type="text"/>

1. Ikke syk i det hele tatt
2. Svært lite syk
3. Endel syk, men ikke særlig plagsomt
4. Mye syk, men tolerabelt for familien
5. Svært mye syk, går utover familien

99. Hvis barnet har brukt inhalasjonssteroider siste 12 mnd/14 dager, hvilken type og hvor stor dose?

Siste 12 mnd		Siste 14 dager	
a <input type="text"/>	1. Flutide 2. Pulmicort/Becotide 3. Annen	c <input type="text"/>	
hvilken:			
b <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Dose (ug/dag)	d <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	

100. Hvis barnet bruker inhalasjonssteroider, bruker barnet det hele året?  1. Ja  
 2. Nei

101. Hvis ja, hvor mange måneder, siste år?

102. Hvis nei, hvilken/hvilke deler av året bruker barnet inhalasjonssteroider?

- a  Sommer c  Vinter  
b  Høst d  Vår



Kode

<p>105. Hvor mye har barnet vært borte fra skolen pga astma?</p> <p><u>Siste 12 mnd</u>      1. Intet fravær      <u>Siste 14 dager</u></p> <p>a <input type="text"/>      2. &lt; 5 dager      b <input type="text"/></p> <p>3. 5-10 dager</p> <p>4. &gt; 10 dager</p>	<p>109. Føler barnet (spør det) at astmaen hemmer dets fysiske aktivitet?</p> <p>a <input type="text"/> 1.Ja 2.Nei</p> <p>Føler du at astmaen vanligvis hemmer barnets fysiske aktivitet nå?</p> <p>b <input type="text"/> 1.Ja 2.Nei</p>
<p>106. Hvor mange ganger har barnet vært hos doktor pga astma de siste 12 måneder?</p> <p>Rutinekontroll <input type="text"/><input type="text"/> a      Pga akutte forverrelser <input type="text"/><input type="text"/> b</p>	<p>110. Har barnet vært innlagt på sykehus pga astma/ obstruktivt pustebesvær?</p> <p>a <input type="text"/> 1.Ja 2.Nei</p> <p>Hvis ja, antall innleggelse: b <input type="text"/><input type="text"/></p> <p>Alder første innleggelse c <input type="text"/><input type="text"/>      Alder siste innleggelse d <input type="text"/><input type="text"/></p> <p>Ved hvilket/hvilke sykehus:</p>
<p>107. Hva slags behandling fikk barnet ved innleggelsene? (<u>Antall innleggelse med aktuell behandling</u>).</p> <p>a <input type="text"/><input type="text"/>      b <input type="text"/><input type="text"/>      c <input type="text"/><input type="text"/></p> <p>i.v. behandling      Inhalasjonsbehandling      Systemiske steroider</p>	<p>111. Har barnet vært på behandlingsreiser pga astma?</p> <p><input type="text"/> 1.Ja 2.Nei</p>
<p>108. Har barnet vært innlagt på Voksentoppen og/eller Geilomo?</p> <p>a <input type="text"/> 1.Ja 2.Nei</p> <p>Hvis ja, antall ganger:      Voksentoppen      Geilomo</p> <p>b <input type="text"/><input type="text"/>      c <input type="text"/><input type="text"/></p>	<p>112. Har barnet kommet i puberteten?</p> <p><input type="text"/> 1.Ja 2.Nei 3.Vet ikke 4. Ferdig</p>
	<p>Hvis ja,</p> <p>113. Hva var alder ved Menarche (1. menstruasjon)? <input type="text"/><input type="text"/> år</p>
<p>114. Dato for siste menstrasjon ( første dag): a <input type="text"/><input type="text"/> . <input type="text"/><input type="text"/> . <input type="text"/><input type="text"/></p> <p>dd      mm      åå</p> <p>Ikke aktuelt: b <input type="text"/></p>	



Kode

115. Matinntak siste 4 timer:

	Ja	Nei
Skinke/kjøttpålegg	a <input type="checkbox"/>	<input type="checkbox"/>
Spinat	b <input type="checkbox"/>	<input type="checkbox"/>
Grønn salat	c <input type="checkbox"/>	<input type="checkbox"/>

Medisiner siste dose av:

	<u>Dato</u>	<u>Klokka</u>	<u>Ikke aktuelt:</u>
116. $\beta$ -2 agonist, (kortids)	a <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> dd mm åå	b <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>	c <input type="checkbox"/>
117. $\beta$ -2 agonist, (langtids)	a <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> dd mm åå	b <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>	c <input type="checkbox"/>
118. Inhalasjonssteroid	a <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> dd mm åå	b <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>	c <input type="checkbox"/>
119. Leukotrienantagonist (singulair <sup>®</sup> )	a <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> dd mm åå	b <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>	c <input type="checkbox"/>
120. Kombinasjonspreparat	a <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> dd mm åå	b <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>	c <input type="checkbox"/>





**Appendix F: Physical activity questionnaire (in Swahili)**



## *Mazoezi ya viungo*

Tafadhali jibu maswali haya. Zungushia duara kwenye namba ya jibu sahihi.

1. Wewe ni mvulana au msichana?

Mvulana  1

Msichana  2

2. Unatumia usafiri gani kwenda shule?

Kwa gari au pikipiki  1

Kwa basi au treni  2

Kwa baiskeli  3

Kwa mguu  4

3. Unatumia muda gani hadi kufika shule?

Chini ya dakika 5  1

Dakika 5 mpaka 15  2

Dakika 15 mpaka 30  3

Dakika 30 mpaka saa 1  4

Zaidi ya saa 1  5

4. Huwa unafanya nini shuleni wakati wa mapumziko ya asubuhi?

Unakaa chini (unaongea, unasoma)  1

Unasimama, unatembea  2

Unakimbia na kucheza michezo  3

5. Huwa unafanya nini shuleni wakati wa mapumziko ya mchana (zaidi ya kula chakula)?

Unakaa chini (kuongea, kusoma) 1

Unasimama, unatembea 2

Unakimbia na kucheza michezo 3

Unakwenda nyumbani kula chakula 4

6. Ni mara ngapi unashiriki kwenye mazoezi ya viungo kwenye vilabu vya michezo, vya shughuli za vijana, vya skauti ya kiume na kike, n.k.?

Mara chache sana au sishiriki kabisa 1

Mara moja au mbili kwa wiki 2

Mara nyingi 3

Kila siku 4

7. Ni mara ngapi unacheza michezo nje baada ya shule?

Mara chache sana au sichezi kabisa 1

Mara moja au mbili kwa wiki 2

Mara nyingi 3

Kila siku 4

8. Unaishi wapi?

Katikati ya jiji 1

Pembeni ya jiji 2

Mjini 3

Kijijini 4



**Appendix G: Parts of the Physical activity questionnaire (in English)**



2. *How do you usually travel to school?*

by car or motorcycle

by bus or train

by bicycle

by foot

3. *How do you usually travel home from school?*

by car or motorcycle

by bus or train

by bicycle

by foot

4. *How long does it usually take you to travel to school from your home?*

less than 5 minutes

5 to 15 minutes

15 to 30 minutes

30 minutes to 1 hour

more than 1 hour

5. *What do you normally do at morning break?*

sit down (talking, reading)

stand, walk around

run around playing games

6. *What do you normally do at lunch break (apart from eating lunch)?*

sit down (talking, reading)

stand, walk around

run around playing games

go home for lunch

7. *How often do you take part in exercise at clubs such as sport clubs, youth clubs, scouts/guides etc.?*

Hardly ever or never

Once or twice a week

Most days

Every day

8. *How often do you play games outside after school?*

Hardly ever or never

Once or twice a week

Most days

Every day



**Appendix H: Parts of the Physical activity questionnaire (in Norwegian)**



**Hvordan kommer du deg vanligvis til skolen? (Sett bare ett kryss)**

- Med bil eller motorsykkel
- Med buss, trikk, t-bane eller tog
- Med sykkel
- Går

**Hvordan kommer du deg vanligvis hjem fra skolen? (Sett bare ett kryss)**

- Går
- Med bil eller motorsykkel
- Med buss, trikk, t-bane eller tog
- Med sykkel

**Hvor lang tid bruker du vanligvis til skolen?**

*(Sett bare ett kryss)*

- Mindre enn 5 minutter
- 6 til 15 minutter
- 16 til 30 minutter
- 31 minutter til 1 time
- Mer enn 1 time

**Utenom skoletid: Hvor mange ganger i uka driver du idrett/mosjon slik at du blir andpusten eller svett?**

ganger per uke

**Omtrent hvor mange timer per uke bruker du på dette? (Sett bare ett kryss)**

- 0 timer
- 1-2 timer
- 3-4 timer
- 5-7 timer
- 8-10 timer
- 11 timer eller mer

**Hvor slitsom er denne idretts-/mosjonsaktiviteten? (Sett bare ett kryss)**

- Driver ikke idrett/mosjon
- Litt anstrengende
- Ganske anstrengende
- Meget anstrengende
- Svært anstrengende

**Hvor ofte har du drevet med følgende treningsaktiviteter i løpet av de siste 12 måneder i snitt? (Sett ett kryss for hver aktivitetsgruppe)**

	Aldri	Under	1	Flere
		1 gang	gang	ganger
		pr uke	pr uke	pr uke
Utholdenhetsidrett (feks løp, sykling, langrenn, svømming).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lag-/ballidretter (feks squash, håndball, fotball, ishockey).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Styrkeidrett (feks bryting, vekttrening).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Kampsport (feks judo, karate, taekwondo)...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tekniske idretter (feks ridning, alpint, telemark, friidrett, snowboard, golf, rullebrett/skøyter).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Risikoidrett (feks elvepadling, fjellklatring, paragliding).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Annet.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



**Hvilke av disse passer best for deg? (Sett bare ett kryss)**

- Jeg røyker eller snuser ikke, og kommer heller ikke til å begynne.
- Jeg røyker eller snuser ikke, men kommer kanskje til å begynne
- Jeg røyker eller snuser hver dag, men har akkurat startet
- Jeg røyker eller snuser hver dag, og har gjort det i over 6 måneder

**Hvor mange kroppsøvings-/gymtimer har du på timeplanen hver uke?**

*(Sett bare ett kryss)*

- Mindre enn en time per uke
- En til to timer per uke
- Tre til fire timer per uke
- Fem eller flere timer per uke

**Hvor ofte deltar du i kroppsøvings-/gymtimene på skolen?**

*(Sett bare ett kryss)*

- Nesten aldri eller aldri
- En til to timer i måneden
- Ukentlig
- Nesten hver gang
- Hver gang

**Når står du vanligvis opp en skoledag? (Sett bare ett kryss)**

- Før 6.30
- Mellom 6.30 og 7.00
- Mellom 7.00 og 7.30
- Etter 7.30

**Når legger du deg vanligvis en skoledag?**

*(Sett bare ett kryss)*

- Før 20.00
- Mellom 20.00 og 21.00
- Mellom 21.00 og 22.00
- Etter 22.00

**Hvor mange timer ser du vanligvis på TV før du går på skolen?**

*(Sett bare ett kryss)*

- Ingen
- Mindre enn 1 time
- Mellom 1 til 2 timer
- Mer enn 2 timer

**Hvor mange timer ser du vanligvis på TV etter skolen? (Sett bare ett kryss)**

- Ingen
- Mindre enn 1 time
- Mellom 1 til 2 timer
- Mellom 2 til 3 timer
- Mer enn 3 timer

**Hvor mange timer bruker du vanligvis på foran PC (spill eller internett) eller med TV spill (playstation, X-box eller lignende) på en ukedag (mandag til fredag)? (Sett bare ett kryss)**

- Ingen
- Mindre enn 1 time
- Mellom 1 til 2 timer
- Mellom 2 til 3 timer
- Mer enn 3 timer

**Appendix I: Approval letters from the Regional Medical  
Research Ethics Committee (in Norway)**





# UNIVERSITETET I OSLO

DET MEDISINSKE FAKULTET

Professor Kai-Håkon Carlsen  
UiO

Regional komité for medisinsk forskningsetikk  
Sør- Norge (REK Sør)  
Postboks 1130 Blindern  
NO-0318 Oslo

**Dato:** 15.12.04  
**Deres ref.:**  
**Vår ref.:** S-04331

Telefon: 228 44 666  
Telefaks: 228 44 661  
E-post: [rek-2@medisin.uio.no](mailto:rek-2@medisin.uio.no)  
Nettadresse: [www.etikkom.no](http://www.etikkom.no)

## **ASTMALIV- Astma, Trening, Mat og LIVsstil (en oppfølgingsstudie av Miljø og Barneastma)**

Komiteen behandlet prosjektet i sitt møte 13.12.04.

Komiteen har ingen merknader til prosjektsøknaden.

Komiteen har følgende merknad til pasientinformasjon og samtykkeerklæring:

1. Siden samtykkeskjemaene er utformet som de er, kan det være en fordel at begrepet frivillig kommer inn også på disse, f.eks. på denne måten: "Jeg har lest informasjonen og vet at det er frivillig å delta, og at jeg kan trekke meg når jeg vil uten å oppgi grunn." Komiteen ber om at samtykkeerklæringene får denne tilføyelsen.

### Vedtak:

"Komiteen tilrår at prosjektet gjennomføres."

Vi ønsker lykke til med prosjektet!

Med vennlig hilsen

Sigurd Nitter-Hauge  
Professor dr.med.  
Leder

Tone Haug  
Rådgiver  
Sekretær





**UNIVERSITETET I OSLO**  
**DET MEDISINSKE FAKULTET**

Doktorgradsstipendiat Sveinung Berntsen  
Norges idrettshøgskole  
Pb. 4014 Ullevål Stadion  
0806 Oslo

**Regional komité for medisinsk forskningsetikk**  
**Sør- Norge (REK Sør)**  
Postboks 1130 Blindern  
NO-0318 Oslo

Telefon: 228 44 666

Telefaks: 228 44 661

E-post: [rek-2@medisin.uio.no](mailto:rek-2@medisin.uio.no)

Nettadresse: [www.etikkom.no](http://www.etikkom.no)

**Dato:** 31.1.07

**Deres ref.:**

**Vår ref.:** S-07015a

**S-07015a Validering av Armband, MTI, ACTIREG og IKCAL mot Metamax II [2.2007.62]**

Vi viser til søknad mottatt 24.1.07 med følgende vedlegg: Prosjektbeskrivelse; Informasjonsskriv med samtykkeerklæring.

Komiteen behandlet søknaden i sitt møte onsdag 24.1.07.

Komiteen har følgende merknader til prosjektsøknaden:

1. For et doktorgradsprosjekt er det vanlig at hovedveileder oppføres som prosjektleder.
2. Komiteen ber om å få tilsendt den invitasjonen som skal sendes ut til aktuelle deltakere ved Norges idrettshøgskole og Krigsskolen ved Linderud. Komiteen foreslår alternativt til slik invitasjon at det innsendte informasjonsskriv bearbejdes og sendes ut som en forespørsel om deltaking.

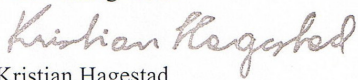
Komiteen har følgende merknader til pasientinformasjon:

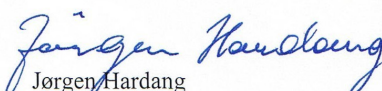
1. Dersom informasjonsskrivet skal sendes ut som første forespørsel, må det:
  - Ha heading med logo(er), evt. bør det på annen måte fremgå tidlig hvor informasjonsskrivet kommer fra.
  - Innledes med: "Forespørsel om deltaking i forskningsprosjekt" (og evt. prosjektets tittel) som hovedoverskrift.
2. Selv om det ikke benyttes slik, bør
  - "Behandles anonymt" erstattes med "--- aidentifisert", da kodenøkkel beholdes. Evt. gis en kort forklaring av hva "aidentifisering" betyr.
  - Samtykkeerklæringen skal kun inneholde samtykket. Deltakerne skal ved sin underskrift ikke behøve å stadfeste annet enn å ha mottatt informasjon om prosjektet, og at de ønsker å delta. Deltakerne skal ha kopi av både informasjonsskriv og samtykkeerklæring.

Vedtak:

Komiteen ber om svar på merknad samt revidert informasjonsskriv og samtykkeerklæring. Forutsatt tilfredsstillende tilbakemelding, tilrås prosjektet. Komiteens leder tar stilling til dette ved mottatt svar.

Med vennlig hilsen

  
Kristian Hagestad  
Fylkeslege cand.med., spes. i samf.med  
Leder

  
Jørgen Hardang  
Sekretær





**Appendix J: Research Clearance, University of Dar es  
Salaam, Tanzania**





**UNIVERSITY OF DAR ES SALAAM**  
OFFICE OF THE VICE-CHANCELLOR  
P.O. BOX 35091 • DAR ES SALAAM • TANZANIA

Ref. No: AB3/12(B)  
Date: 24<sup>th</sup> March, 2003  
To: The Regional Education Officer,  
**Arusha.**

**UNIVERSITY STAFF AND STUDENTS RESEARCH CLEARANCE**

The purpose of this letter is to introduce to you **Mr. Sveinung Bermtsen** who is a bonafide student of the University of Dar es Salaam and who is at the moment conducting research. Our staff members and students undertake research activities every year especially during the long vacation.

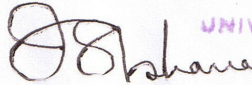
In accordance with a government circular letter Ref.No.MPEC/R/10/1 dated 4<sup>th</sup> July, 1980 the Vice-Chancellor was empowered to issue research clearances to the staff and students of the University of Dar es Salaam on behalf of the government and the Tanzania Commission for Science and Technology, a successor organization to UTAFITI.

I therefore request you to grant the above-mentioned member of our University community any help that may facilitate him to achieve research objectives. What is required is your permission for him to see and talk to the leaders and members of your institutions in connection with his research.

The title of the research in question is "**The aerobic capacity and lung functions of pupils age nine and ten in Tanzania.**"

The period for which this permission has been granted is from **31<sup>st</sup> March** to **11th July 2003** and will cover the following areas/offices: **Regional Education Office.**

Should some of these areas/offices be restricted, you are requested to kindly advise him as to which alternative areas/offices could be visited. In case you may require further information, please contact the Directorate of Research and Publications, Tel. 2410500-8 Ext. 2087 or 2410743.

*for*  
  
**Prof. M.L. Luhanga**  
**VICE-CHANCELLOR**

VICE CHANCELLOR  
UNIVERSITY OF DAR ES SALAAM  
P. O. BOX 35091  
DAR ES SALAAM

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Website address: [www.udsm.ac.tz](http://www.udsm.ac.tz)





**UNIVERSITY OF DAR ES SALAAM**  
OFFICE OF THE VICE-CHANCELLOR  
P.O. BOX 35091 • DAR ES SALAAM • TANZANIA

Ref. No: AB3/12(B)  
Date: 24<sup>th</sup> March, 2003  
To: The Regional Administrative Secretary,  
**Arusha Region.**

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*for*  
**Prof. M.L. Luhanga**  
**VICE-CHANCELLOR**

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