The movement continuum in children with asthma attacks in Kuwait

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July 2017

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A thesis presented to the University of Glasgow in fulfilment of the thesis requirement for the degree of Doctor of Medicine

July 2017

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Author’s Declaration

I declare that this thesis is the result of my own work, except where otherwise acknowledged, and has not been submitted for a higher degree to any other university or institution.

Bandar Snafi Nassar Alshammari

Supervisor’s Declaration

I certify that the work reported in this thesis has been performed by Bandar Snafi Nassar Alshammari and that during the period of study he has fulfilled the conditions of the ordinances and regulations governing the Degree of Doctor of Medicine.

James Y. Paton

Disclosure Statement

I hereby declare that all of the research work for this thesis was undertaken by myself

No writing assistance was utilized in the production of this thesis.

This work was funded by Kuwait Government.

Abstract

Background

The major activity components that make up the 24 hours of daily life, the so-called “movement continuum” are sleep, comprising ~40% of time, sedentary behaviour (~40%), low intensity physical activity (LPA) (~15%), and moderate-to-vigorous physical activity (MVPA) (~5%). To address fully the impact of movement behaviour on children’s health, it is necessary to study the relationship between each of these components of the “movement continuum” and children’s health. Asthma is a chronic childhood disease that impacts children’s activity and alters the balance between movement continuum components. Few studies have attempted to investigate the association between asthma and movement continuum components.

The relationship between asthma in children and physical activity and sedentary behaviour is conflicting. Some studies suggested that asthmatic children are less physically active and more sedentary; others suggested that they are more active and less sedentary or that there are no differences between asthmatic and healthy children. The factors that led to this conflict are not clear. We conducted a systematic review that reviewed available published evidence regarding the association between objectively measured physical activity, sedentary behaviour and asthma in school aged children.

The effect of asthma attacks on the movement continuum components is unclear, especially in the Middle East area. We hypothesized that in the acute stage following an asthma attack; children are less physically active, more sedentary and have sleep disturbances compared to the recovery stage. During recovery from asthma attack, there is inter individual variability in changes of movement continuum components. We conducted an observational study to measure levels of asthma control and movement continuum components of Kuwaiti school aged children week 1 and week 4 following an asthma attack. The study also compared movement continuum components of asthmatics at week 4 following an asthma attack with the same measurements in healthy controls.

Methods

In our systematic review, a literature search of EMBASE, Medline, CINHAL, Cochrane library and PubMed was performed to identify articles published in English between 2000-2017 in which either physical activity or sedentary behaviour or both were assessed objectively in 6-12 years old school aged children with asthma in case-control, cross-sectional or longitudinal (cohort) studies.

In our prospective study we recruited 23 asthmatic children admitted to Kuwaiti hospitals following an asthma attack (mean age of 8.1 (SD 2.02) yrs). For the control group, 23 healthy children from Kuwait youth centres (mean age of 9.0 (1.72) yrs) were recruited. Measurements of asthmatic children at week 1 (acute stage) were compared to those at week 4 after discharge from hospital (recovery stage). Measurements of asthmatic children at the recovery stage were compared to those in healthy controls. Asthma symptoms were assessed by Childhood Asthma Control Test (CACT) questionnaire. Pulmonary function testing was carried out using a portable spirometer. Physical activity, sedentary behaviour and sleeping behaviour were investigated using ActivPAL™ accelerometers.

Results

In the systematic review, the literature search identified 71 publications. Of the studies identified, nine met the inclusion criteria (total subjects n= 2996 (asthmatics (n=839), and wheezers (n=37)). In eight studies (total subjects n=2644) there was no significant difference in physical activity between children with and without asthma. Only one study (n=352) reported that asthmatic children were less physically active. No study found that asthmatic children were more physically active. Sedentary behaviour was assessed objectively in 3 studies (n=609); one study suggested that asthmatic children were less sedentary; and two studies showed no differences in sedentary behaviour between children with and without asthma.

Our prospective study showed that CACT score improved significantly from week one to week four (week 1, 19.1 ± 4.39; week 4, 22.7 ± 3.77, P=0.000). The number of steps at week four was significantly higher than at week one

(week 4, 11876 ± 3924; week 1, 10087 ± 2720, *P*=0.02). Total sitting time at week 4 was significantly lower than at week 1 (week 4, 7.7 ± 1.10 h/day; week 1, 8.7 ± 1.13 hours/day, *P*=0.001).

During recovery from asthma attack changes in measures of activity continuum varied between individuals. Physical activity duration was increased in 14, but decreased in nine asthmatic children. Number of steps was increased in 16, decreased in six and remained the same in one asthmatic child. Total sitting time was decreased in 19, and increased in four asthmatic children. Sleeping time was increased in 13, decreased in eight and remained the same in two asthmatic children.

Physical activity parameters of asthmatic children at week four were significantly higher than those of healthy controls; duration of physical activity (asthmatics, 7.40 ± 1.12 hours/day; healthy, 6.63 ± 2.04 hours/day, *P*=0.038); total activity counts (asthmatics, 840 ± 271; healthy, 650 ± 157, *P*=0.006); and number of steps (asthmatics, 11876 ± 3924; healthy, 8602 ± 2128, *P*=0.001). Sedentary behaviour parameters of asthmatic children at week four were significantly better than those of healthy controls; total sitting time (asthmatics, 7.7 ± 1.10hours; healthy, 8.3 ± 1.56 hours, *P*=0.05); number of breaks in sitting (asthmatics, 247 ± 97; healthy, 199 ± 65, *P*=0.05); number of sedentary bouts (asthmatics, 254 ± 89; healthy, 209 ± 54, *P*=0.045); and fragmentation index (asthmatics, 33.5 ± 13.0; healthy, 26.2 ± 9.6, *P*=0.001).

In the summer in Kuwait, at the hottest time of the year, bed time shifted eight hours (0400 vs 2100) and wake up time shifted to late in the afternoon (1300-1400 vs 0500-0600).The summer sleep duration was ten hours, one hour longer than at other times of the year.

Conclusions

The balance of available evidence in the literature strongly suggests that asthmatic and healthy children were of similar physical activity.

This study showed that during recovery from asthma attack, asthma symptoms improved, physical activity increased and sedentary behaviour reduced. There were inter-individual variability changes in the activity

continuum during recovery. In Kuwait, asthmatic children admitted with an asthma attack were physically active, not sedentary and had no difference in sleep time compared to healthy controls. During the period of very high external environmental temperature in the summer in Kuwait, there was a significant association changes in children’s sleeping time and pattern.

Acknowledgements

I would like to thank my principal supervisor, Dr James Y. Paton, for his advice, support, patience and encouragement throughout the design and execution of this research including the completion of this thesis and for his guidance and advice in doing the systematic review.

I would like to thank my second supervisor, Dr Dalia Malkova, for her advice, support, patience and encouragement throughout the design and execution of this research including the completion of this thesis.

I would like to thank my previous second supervisor, Professor John J. Reilly, for advice, support, and encouragement throughout the design and execution of this research.

I would also like to thank Dr Zubaida Ibrahim .A. Alghaeed for her advice, support and patience on the analysis of ActivPAL data.

I would also like to thank pulmonology lab team for their advice, support and patience.

I would also like to thank Dr. David Young, for his helpful advice on the statistical analysis used in this thesis.

I would also like to thank Dr. Ali Sadiq, statistician of Kuwait ministry of health, for his helpful advice on the statistical analysis used in this thesis.

Special thanks to Mrs. Christine Kerr and Mrs. Karen Cooper for their continued support at various stages of my MD.

Many thanks for my Kuwaiti government for their support and encouragement.

Many thanks are given to my family for their support and encouragement.

This thesis is dedicated to my parents, my wife and my children.

Abbreviations

1A	Asthmatic patient after one week of discharge from hospital
2A	Asthmatic patient after four weeks of discharge from hospital
ACQ	Asthma Control Questionnaire
ACT	Asthma control test questionnaire
AEE	Activity energy expenditure
AM	Ante Meridiem (Latin for before midday) which is midnight to noon
ATAQ	Asthma Therapy Assessment Questionnaire
BMI	Body mass index
BMI Z score	Body mass index z-scores
BH	Bronchial hyper responsiveness
BR	Bronchial responsiveness
C	Comparable healthy children
CACT	Childhood asthma control test questionnaire
cm	centimeter
DEE	diet-induced energy expenditure
d	day
DLW	doubly labelled water method
ECP	Eosinophilic cationic protein
eNO	Exhaled nitric oxide
FEV1	Forced expiratory volume in 1 second
FI	Fragmentation index
FVC	Forced vital capacity
hrs	hour
kg	kilogram
LPA	light physical activity
LTE4	leukotriene E4

m	Meter
MET	Metabolic Equivalent of Task
MPA	Moderate physical activity
ms	Minutes
MSUP	Minimum sitting/upright period
MVPA	Moderate to vigorous physical activity
PA	Physical activity
PEFR	Peak expiratory flow rate
PFT	Pulmonary function test
PM	Post Meridiem (Latin for after midday) which is noon to midnight
PR	Pulmonary rehabilitation
KYC	Kuwait Youth Centers
REM	Rapid eye movement
RANTES	Regulated on activation, normal T-cell expressed and secreted
RMR	resting metabolic rate
Sec	second
SB	Sedentary behaviour
SBRN	Sedentary Behaviour Research Network
SD	Standard deviation
TEE	total energy expenditure
VPA	Vigorous physical activity
yrs	Years

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Chapter 1: Introduction

1 Introduction

1.1 Background

In the 1950s, Morris et al. (1) reported that individuals in physically active jobs such as bus conductors and postmen had less coronary artery disease than those whose jobs involved sitting for prolonged periods. This seminal study was one of the first to provide unequivocal evidence of the health benefits of physical activity, in this case on cardiovascular diseases in adults.

Physical activity has been defined as "any bodily movement produced by skeletal muscles that results in energy expenditure"(2). There is now substantial evidence that physical activity in children and young people, particularly moderate to vigorous physical activity (MVPA), can play a significant preventative role in a number of important and prevalent contemporary diseases, including obesity (3), improved cardio-metabolic profiles (4, 5) and increased bone mineral density (6), as well as mental health benefits with reduced rates of anxiety and depression (7) and improved academic achievement (8). Most importantly, studies tracking physical activity (PA) from childhood to adult suggest that physically active children are likely to be physically active adults with a consequent positive impact on adult's health (9, 10).

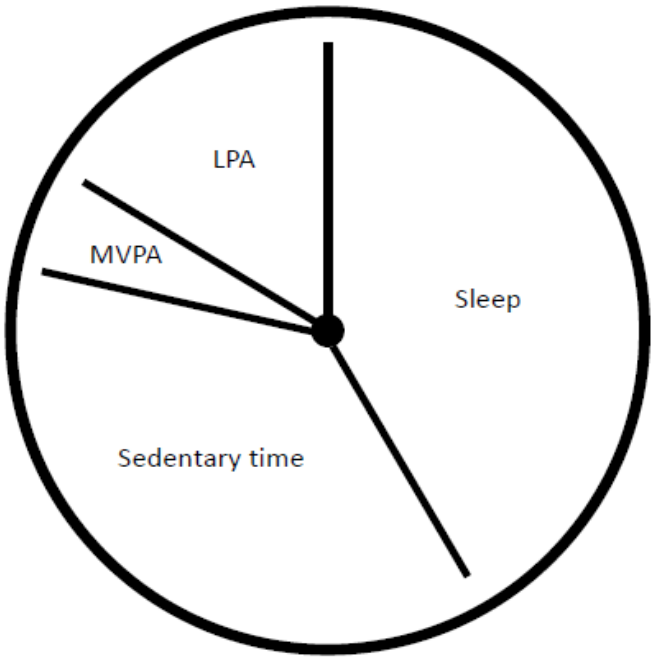
Despite the recognised health benefits of physical activity in adults and children and clear recommendations in evidence-based international guidelines about the recommended amounts of physical activity that should be undertaken daily, recent studies suggest that only a small percentage of the population actually meet guideline recommendations (11-15). Aspects of modern life such as the development of the motor car, television and modern computers have meant that most people in society have become increasingly sedentary and much less physically active (16-18).

Children may be at particular risk from this shift to a more sedentary life style, with physical inactivity and childhood obesity highlighted as amongst the greatest and most pervasive health challenges to children today (19). It is becoming clear that there is no easy solution to these health challenges and a range of strategies will be needed to address them.

To investigate the relationship between physical activity and health outcomes in children, most researchers have focused on the relationship between moderate-to-

vigorous physical activity (MVPA) and health outcomes (19). Despite the benefits of MVPA to health, brief reflection makes it clear that MVPA is likely to contribute only a small percentage of the 24 hrs daily activities of children (19, 20). Even among young children and young people who are active MVPA contributes less than 5% of a child's daily activities (19, 20).

The other major components that go to make up the 24 hours are sleep, comprising ~40% of time, sedentary behaviour (~40%) and low intensity physical activity (LPA) (~15%). These make up the other 95% of the day activity that is not taken up by MVPA (Figure 1-1) (19).



LPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity.

Figure 1-1: Estimated distribution of movement behaviours over the 24 h period, (picture modified from (19)).

It has gradually been realised that ignoring other components of the so-called "movement continuum" and focusing efforts only on MVPA limits our understanding of how the components of the movement continuum interact to affect children's health. For example, there is evidence showing that independent of MVPA, increased sedentary time is associated with unfavourable health outcomes such as increased BMI, increased risk of metabolic syndrome and poorer bone health (21-25). Similarly, undesirable

health outcomes such as obesity, type 2 diabetes, depression and poor academic performance are linked to decreased sleep duration (26-28). This is an issue of particular concern since a decrease in sleep duration has been observed over the past decades in children and young adults (29, 30). This might raise the question as to whether there is any relationship between sedentary time and sleep. This example illustrates the potential for interaction between the various components of the movement continuum (Figure 1-2). In order to address fully the impact of all these movement behaviours on children's health, it is necessary to study the relationship between all components of the "movement continuum" (i.e., sleep, sedentary time, light physical activity (LPA)) and children's health (19). Assuming, that one can be varied independently e.g. by increasing MVPA without affecting the others is likely to be far too simplistic (Figure 1-2) (31, 32).

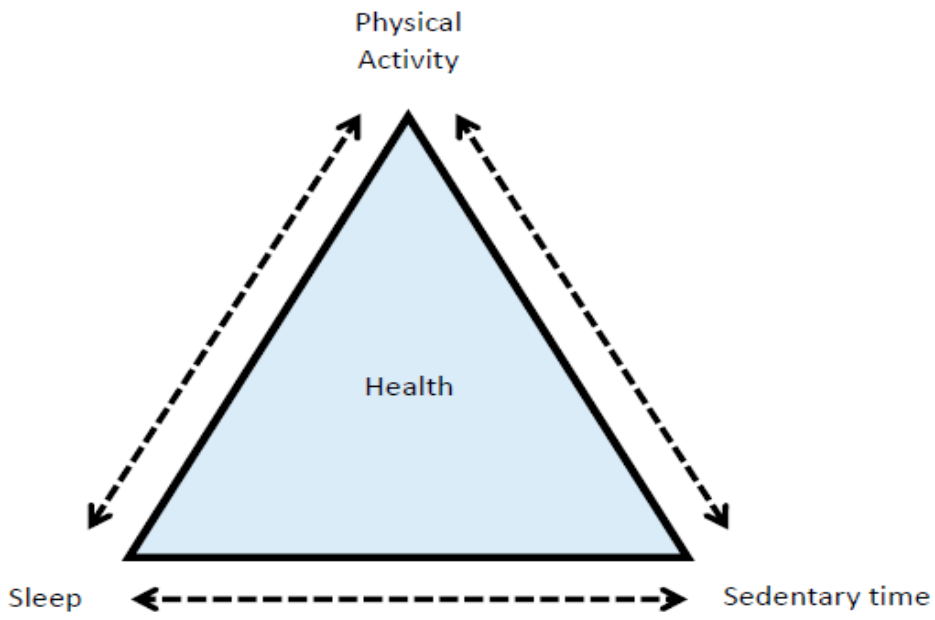


Figure 1-2: Interactions between movement and non-movement behaviours to collectively impact health. (picture modified from (19)).

While there is research interest in examining all aspects of the movement continuum in children, the focus to date has been on healthy children. A number of chronic childhood diseases impact on children's activity and are likely to alter the balance between the various components of the movement continuum. Asthma provides a particularly good opportunity to investigate these relationships. It is a very common childhood illness

(33) that has huge impact on the well-being and social lives of children and their families (34-36), on health services (37) and on economies of countries (38). Its prevalence is high all over the world (39). Exercise commonly provokes asthmatic symptoms in children (33). Sleep disturbance is common because of nocturnal symptoms of asthma (40). Acute asthma attacks are a common cause of severe illness leading to hospital admission (35). Consequent changes in a child's ability to exercise and sleep are likely to lead to significant adverse effects, on physical as well as educational and social components of life. Thus the relationship between asthma in children and its effect on all components of the movement continuum is likely to be important in developing a full understanding of the health impacts of asthma. To date there are very few studies that have attempted to investigate the association of asthma and components of the movement continuum other than studies of physical activity in children with asthma.

This introductory chapter briefly reviews published evidence examining the relationship between components of movement continuum (i.e. light physical activity (LPA), moderate and vigorous physical activity (MVPA), sedentary time and sleep) in healthy children. It then provides a brief overview of asthma in children before considering in detail the available evidence about asthma and the movement continuum in children.

Subsequent chapter describes the results of the studies for this thesis examining the relationship between components of the movement continuum (i.e., physical activity, sleep and sedentary time) and asthma in asthmatic children.

1.2 Physical activity (PA)

1.2.1 Introduction

In thinking about physical activity it is important to start by being clear about terms and definitions. This is because in lay parlance terms such as physical activity (PA), physical fitness and exercise are commonly used in a general way rather than precisely. Physical activity may be defined as movement of any part of body created by skeletal muscles leading to the enhancement in energy expenditure above resting metabolic rate (41). Physical fitness is a group of characteristics that people have or obtain; it has two components, health-related and specific-skill related fitness components (41). Health-related fitness components consist of five elements ((a) cardio-respiratory endurance i.e. the ability of cardiovascular and respiratory systems to supply energy to exercising

muscle while simultaneously removing waste metabolic products; (b) muscular endurance i.e. the capability of muscle groups to do external force for many repetitions or sequential exertions, (c) muscular strength: the magnitude of external force that can be exerted by muscle, (d) body composition: relative amounts of muscle, fat, bone , and other vital body components (e) flexibility: range of movement possible at joints. Skill related fitness components consist of six items; (a) agility: the ability to alter body position in a fast and accurate manner; (b) balance: the ability to maintain equilibrium in both static and dynamic situations; (c) co-ordination: the capability of performing motor function smoothly and precisely through co-ordinating senses like vision and hearing with other parts of the body; (d) speed: the ability to perform a movement in a short time interval; (e) power: the rate at which work can be done; (f) reaction time: the time interval between triggering an action and the start of that action. The five related fitness components of physical fitness are of general importance in the health of the public, while the six skill-related fitness components are important for athletic ability (41). Exercise in adults is usually planned, structured and often repetitive aimed at improving or maintaining one or more components of physical fitness (41). In children, exercise maybe planned and structured such as in a game or a run at school but it may also take a more spontaneous form as play(42, 43).

Physical activity is evaluated according to its duration, intensity, frequency and mode. Duration of physical activity measures the time spent in physical activity (44-46). Intensity of PA is reflected in energy expenditure required by the physical effort. According to CDC (the U.S. Centres for Disease Control and Prevention) and ACSM (the American College of Sports Medicine) guidelines (47), physical activities can be defined by level of intensity. Physical activity is often classified into levels of light (lower than 3.0 METs or 3.5 kcal/min), moderate (3.0 to 6.0 METs or 3.5 to 7 kcal/min), and vigorous (more than 6.0 METs or more than 7 kcal/min). Frequency of PA is the rate at which physical activity occurs or is repeated over a particular period of time while the mode of PA refers to the type of PA like running, jogging or walking (45, 46).

The law of thermodynamics states that the energy input into a system minus the energy output results in the energy stored in the system. In humans, any energy taken in that is in excess of that required for any outputs, will be stored, mostly as fat, in the body (48). Over time, any imbalances between input and output will results in either weight loss eventually leading to underweight/malnutrition or overweight/obesity (48). Energy

expended in PA is part of total energy expenditure (TEE). TEE consists of three components; resting metabolic expenditure - the resting metabolic rate (RMR), diet-induced energy expenditure (DEE), and physical activity or muscular activity energy expenditure (AEE) (45). The resting metabolic expenditure accounts for 60–70% of TEE (45) and represents the major part of energy expenditure. It is expended to maintain important bodily physiological functions such as body temperature, respiration, circulation etc at rest. A second component relates to diet-induced energy expenditure (DEE). This represents around 10% of daily energy expenditure and is energy spent in digestive processes such as digestion, absorption and storage of food (45). A third component relates to activity energy expenditure (AEE) in physical activity or muscular activity, usually constituting 20–30% of TEE (45). This component is affected by muscle mass, body weight, and the capacity for movement (45). Activity energy expenditure (AEE) has been further subdivided by Levine et al (49) into two components: (a) exercise energy expenditure (EEE), expended in organised sporting-like exercises in order to build and/or retain physical fitness; and (b) non-exercise activity thermogenesis (NEAT). NEAT is the energy expended for every activity other than sleeping, eating or sports-like exercise. It ranges from the energy expended walking to work through to energy expended in trivial activities such as fidgeting. It is the cumulative sum of a multitude of exothermic actions that make up an individual's daily energy expenditure and is an important reason for the variation in TEE among most people.

One part of the research in this thesis investigated PA of children with asthma particularly in terms of the duration of activity.

1.2.2 Factors influencing physical activity levels in children

Research has established a number of important factors that systematically influence physical activity in children.

1.2.2.1 Gender

One of the most important determinants of physical activity in children is gender. Multiple studies of different types, conducted in different countries have investigated gender differences in PA in different age groups including preschool children, school-aged children and adolescents (50-52).

The gender differences in PA among school-aged children have been investigated in different countries and by different methods. Subjective studies have made use of parent or child report or questionnaire while objective studies have mainly used accelerometry. For example, two subjective American studies investigated school aged children; the first one showed that according to parent-reported data, the PA of boys was more than that of girls; at baseline PA of boys was more than that of girls by ≥ 17.7% with a relatively small effect size Cohen's d =0.224 and by ≥ 39.6% with a medium effect size Cohen's d =0.683 at follow-up (one to nine years later) (53). The second study used self-reported data and showed that boys were more active than girls by ≥ 13.8% with a small effect size Cohen's d =0.295 (54). Spanish school aged children were investigated subjectively and reported that boys were more active than girls by ≥ 49.6% (55). Among British children aged ten years old monitored objectively by actigraph accelerometers (56), boys were more active than girls by ≥ 11.8% with medium effect size Cohen's d = 0.408. Australian children (57) (184 children five to six years old, 358 children 10 to 12 years) monitored by actigraph accelerometers and questionnaire over a 3-year period, showed that the level of objectively measured PA of boys were greater than that of girls. The moderate PA of boys was more than that of girls; in the younger age group (five to six years) the moderate PA of boys was more by ≥ 3.8% with a relatively small effect size Cohen's d =0.214 at baseline and by ≥ 4.9% with a relatively small effect size Cohen's d =0.204 at follow-up. In the older age group of 10-12 years old, the moderate PA of boys was more than that of girls by ≥ 13.8% with a medium effect size Cohen's d = 0.572 at baseline and by ≥ 24.2% with a medium effect size Cohen's d =0.772 at follow-up. The vigorous PA of boys was more than that of girls; in the younger age group (five to six years) the vigorous PA of boys was more by ≥ 26.3% with a medium effect size Cohen's d =0.774 at baseline and by ≥ 29.5% with a medium effect size Cohen's d =0.653 at follow-up. In the older age group of 10-12 years old, the vigorous PA of boys was more than that of girls by ≥ 30.1% with a medium effect size Cohen's d =0.756 at baseline and by ≥ 50% with a medium effect size Cohen's d =0.448 at follow-up. Thus these examples clearly illustrate that, from studies using different methods from different countries, in school aged children, boys are more active than girls.

Similarly, different types of studies using different methods in different countries have investigated the difference in PA between adolescent males and females. The accelerometer-determined minutes of MVPA of 1032 American children were followed

from age 9 to 15 years and showed that boys were more physically active than girls (58), during weekdays the minutes of MVPA of boys were more than that of girls by 17.5 minutes at age nine years, by 17.4 minutes at age 11years, by 19.3 minutes at age 12 years and by 19.5 minutes at age 15 years. During weekends the minutes of MVPA of boys were more than that of girls by 11 minutes at age nine years, by 14.5 minutes at age 11 years, by 19.5 minutes at age 12 years and by 17.7 minutes at age 15 years. Carver et al (59), used both actigraph accelerometers and questionnaire to study 276 Australian children aged 13–15 years old at two time points and showed that boys were more physically active than girls at the first time point by ≥ 22.2% with a medium effect size Cohen's d = 0.368 and at the second time point by ≥ 14.1% with a small effect size Cohen's d =0.219. Actigraph accelerometers were used by Crawford et al (60) to study the MVPA of 301 Australian children aged 10–12 years old at three time points (2001,2004 and 2006). They showed that MVPA of boys was more than that of girls by about 20 minutes per day at the first time point, by about 25 minutes per day at the second time point, and by about ten minutes per day at the third time point. In a UK cohort study (61), 5863 adolescents aged 11-12 years old were examined subjectively by a questionnaire and boys were found to participate more in vigorous activities than girls; at the beginning of the study the difference was small around 9% but by the end of the study (after five years) the difference was large > 80%. Two cross sectional American studies monitored PA of adolescents objectively by accelerometers and showed that boys were more physically active than girls (62, 63). In Canada, two subjective cross-sectional studies investigated the PA of adolescent and found that females were less physically active than males; in one of these studies the difference was about 15% (64) and in the other the difference was more than 17% at 12 years old and decreased as the child grew (65). A South Korean subjective study (66) investigated 1,097 youths by questionnaire and showed that PA of boys was significantly greater than that of girls; boys were more frequently active than girls by more than 70%, with boys spending more time (30-60 min) in PA compared to girls with a difference more than 50%. Boys also participated more in MVPA than girls with a difference more than 25%. From these examples again using different study designs and methods of monitoring adolescent PA in different countries, it can be concluded that adolescent girls are also less active than adolescent boys.

Among the studies that examined the association between PA and gender in preschool children, is the cross-sectional study conducted by Yu et al (67), in which 4936

Australian children aged four to five years old were studied. They showed that according to parent report, boys were participating more than girls in MVPA by more than 13%.

These examples are part of a large body of evidence in school aged and adolescent children that demonstrates that boys are more active than girls. This is consistent with the International Children's Accelerometry Database (ICAD) (68), which consists of data of 20 objective studies (ActiGraph accelerometers) conducted in ten countries and investigated 27,637 participants (2.8–18.4 years). The ICAD showed that boys were more active than girls at all ages.

There is some contradictory evidence to the general observation that boys are more active than girls. A Swedish study followed adolescents using pedometers for five years (69); at baseline, PA of boys was significantly higher than that of girls with a difference in the number of steps per day $\geq$ 15% and a medium effect size Cohen's d =0.719; at three years follow-up PA of girls had become significantly higher than that of boys with a difference in the number of steps per day $\geq$ 10% and medium effect size Cohen's d =0.462; and at five years follow-up there was no difference, with a small effect size Cohen's d =0.243. The PA of Canadian adolescents (70) were monitored by both accelerometers and self reported data over ten months; the self-reported data showed that males participate in PA more than females by $\geq$ 31.5% with a medium effect size Cohen's d =0.380 at baseline and by $\geq$ 13.2% with a relatively small effect size Cohen's d = 0.111 at the end of study, while accelerometer data showed that there was no gender difference in PA. An American longitudinal study (71), used self reported data and noted that at age 9-12 years old the level of PA of boys was higher than that of girls by $\geq$ 6%, but beyond the age of 12 level the PA of girls become higher than that of boys by $\geq$ 10%. American children (72), monitored objectively showed that there was no gender difference in participation in vigorous physical activity with a relatively small effect size Cohen's d =0.147. In preschool children in New Zealand (73), investigated by accelerometers there was no gender difference in PA. These studies either suggested that there was no gender difference or girls were more active than males. The reasons for the differences from the more general conclusion that boys are more active are not clear.

Why boys generally appear to be more active than girls is not known. One of the most important factors that might underlie this gender difference could be attributed to the

different roles the society assigns boys and girls in general, especially in relation to expectations around and opportunities for physical activity (55). At a young age girls are often socialized in different ways from boys, particularly with regards to risk-taking behaviours (59). In the case of boys, the participation in moderate and vigorous physical activity may be linked to social norms and traditional beliefs concerning physical activity and participation in community based physical activity organizations (72). Some cultures have attitudes and traditional beliefs about physical activity that may discourage girls to participate in dynamic and active physical activities (66). As a consequence boys may have more opportunities to and be more likely to engage in vigorous physical activities, whereas girls are more likely to participate in light or moderate physical activities. In addition, boys may participate more in physically active non-organized activities than girls (70).

1.2.2.2 Age

A second important determinant of physical activity levels in children is age. The activity patterns of young children are mostly related to play and are characterised by spontaneous, frequent, short bouts of movements that are irregular and rapidly alter between high and low intensity physical activity (42, 43, 48, 74).

A few studies reported a decline in PA in preschool age children as they get older. In New Zealand, a longitudinal study (73), investigated objectively preschool children (n=244) at ages three, four, and five years old, and showed that PA declined with age. The average accelerometry count decreased to >50% from age three to four years old among both boys and girls, with a relatively large effect size Cohen's d in both boys =0.919 and in girls d =0.940, but there was no additional decline occurring between four and five years old. However, there are few studies in this age group and more will be required to confirm if PA does indeed start to decline in the preschool age.

Among school aged children, the change in volume and intensity of PA with age were investigated by different methods and in different countries. In North-East England, Farooq et al (75), investigated physical activity objectively (by Actigraph accelerometer) in 545 children over eight years in a longitudinal cohort study with measurement at ages 7, 9, 12 and 15 years. The results showed that the total volume of physical activity and MVPA declined across the eight year period from age seven years. The total volume of physical activity declined; from age seven to nine years old by ≥8% in boys and ≥12% in girls; from age 9 to 12 years old by ≥ 20% in boys and ≥ 28% in

girls; and from age 12 to 15 years old by ≥ 13.6% in boys and ≥ 14.7% in girls. The MVPA declined; from age seven to nine years old by ≥7.3% in boys and ≥11% in girls; from age 9 to 12 years old by ≥ 13.8% in boys and ≥ 15.9% in girls; and from age 12 to 15 years old by ≥ 14.7% in boys and ≥ 13.5% in girls. In 10 years old British children (56), monitored by actigraph accelerometer for a year, the counts per minute decreased by ≥ 6.4% after 12 months. The MVPA level of 301 Australian children (aged 10–12 years old at baseline) was monitored by an actigraph over a five year period, and at the end of the monitoring period it declined to about ≥ 50% of its baseline value (60). An Australian longitudinal study (57), monitored PA of 542 children (184 children 5 to 6 years old, 358 children 10 to 12 years) by actigraph accelerometer and questionnaire showed that PA was decreased over a three year monitoring period. The decline in moderate PA was ≥ 37% in boys with a relatively large effect size Cohen's d = 2.339 and ≥ 38% in girls with a relatively large effect size Cohen's d = 2.127 in the younger age group (five to six years). In the older age group of 10-12 years old the decline in moderate PA was ≥ 35% in boys with a relatively large effect size Cohen's d = 1.499 and ≥ 42% in girls with a relatively large effect size Cohen's d =1.758. Thus the evidence clearly suggests that PA decreases as school aged children grow.

Many studies have investigated changes in PA with age among adolescents. Three longitudinal studies monitored PA objectively and showed that PA decreased with age. Nader et al (58), followed accelerometer-determined minutes of MVPA of 1032 American children from ages 9 to 15 years and showed that MVPA time decreased by 38 minutes per year in weekdays, and by 41 minutes per year during weekend. A Canadian study (70) showed that over a ten month school year the average activity counts per day declined by ≥ 30% with a relatively large effect size Cohen's d =0.986, the average moderate physical activity declined by ≥ 2% with a small effect size Cohen's d = 0.076 and the average vigorous physical activity declined by ≥ 40% with a relatively large effect size Cohen's d = 1.105. A Sweden study showed that from age 12.5 to 17.5 years old the drop in PA in boys was ≥ 25% with a large effect size Cohen's d =1.134 and for girls the drop in PA was ≥ 7% with a small effect size Cohen's d =0.310 (69). Two American longitudinal studies investigated PA by self-reported data; one showed that from 9 to 15 years old the decline in PA among boys was ≥ 20% and among girls was ≥ 15% (71), the other study showed that from 14 to 18 years old there was a decline by ≥ 65% in vigorous activity, ≥ 30% in moderate activity and ≥ 45% in MVPA (76). A Scottish longitudinal study (77), investigated

204 adolescent girls (mean age 11.83 ±0.39) using self-reported data and showed a decline in PA over the monitoring period (over 12 months); the PA was decreased to ≥ 9.12% with a medium effect size Cohen's d =0.435. Hence this evidence also suggested that PA of adolescents decreases over time as they get older.

Again, there is some contradictory evidence to the general observation that PA decreases with age. In a subjective longitudinal study, Alderman et al (53), showed that the PA of American children aged 4-15 years increased with age; PA increased from baseline to follow up by ≥ 48.5% among children aged 4 to 6 years old, by ≥ 46.3% among children aged 7 to 9 years old, by ≥ 40.6% among children aged 10 to 12 years old and by ≥ 25.7% among children aged 13 to 15 years old. Adkins et al (78), investigated 52 African-American girls aged 8-10 years old, and showed that changes in moderate to vigorous activity were not significantly correlated with the age. In a subjective cross sectional study, Henry et al (79), showed that there was no age difference in PA level among 58 adolescent females (age 11–16 years) of United Arab Emirates (UAE). Although Adkins et al (78), used computer science application (CSA) accelerometers to monitor PA, a reliable monitor, only girls were studied and the aim of the study was not to study relation of PA to age, rather was to study the association of PA to BMI, self-efficacy, parent's and family support to be active, the girl's perception of this support and neighbourhood safety and access to facilities, all design factors that might affect the credibility of the results. The other one can be challenged because it investigated PA by self-reported data that carries the risk of information bias.

In summary, most studies that have investigated the relation between age and PA in children found evidence that PA of children decreases with age. The age at which this decline starts to decrease significantly is an area of conflict; the International Children's Accelerometry Database (ICAD) (68), showed that both total volume of physical activity and MVPA start to decline after age of 5 years old; the UK national representative accelerometry measures showed that the decline of physical activity starts at around the age of school entry (80); the longitudinal study of Farooq et al (75) suggested that the total volume of physical activity and MVPA start to decline from age 7 years (75) and other longitudinal studies showed that PA increases progressively with age from preschool age until adolescent, when it starts to decline at around 9 to 15 years old onwards (53, 58, 71). Little is known about the reasons behind this decline, but it could be explained partly by a number of factors such as biological factors (e.g. changes in the dopamine system that acts on certain brain areas which are related to the

motivation for locomotion) (81) and social factors such as the academic study increases with age which necessitate sitting for long periods (71). This is an area where further research to define the factors leading to a decline in physical activity with age will be valuable. Only through better understanding will it be possible to determine decline in activity with age can be stopped or reversed.

It is widely accepted, that person who is physically active during childhood is expected to remain physically active in adulthood, a phenomenon known as "tracking"(82). If tracking of a physiological variable is present then an individual should maintain their relative position to the mean within a population over time (83). The review of Telama (9) of tracking studies in physical activity, showed that the stability (keeping in the same level or track) of physical activity throughout all life phases was low or moderate in men and in women it was lower. In early childhood stability was lower than in adolescence or in adulthood in both sexes. Also, it was even lower in transitional life phases when child grow from childhood to adolescence or from adolescence to adulthood (9).

Implications for the planned research in this study

So, to study PA of children, the researcher should consider these factors when recruiting subjects. Both females and males should be included in any research sample. Also, the age of both groups; the research and control groups should be of comparable age, otherwise the difference in level of PA observed may be related to declines associated with age rather than any other group differences.

1.2.3 The importance of physical activity for health

A recent systematic review (84) has reported on the relationships between objectively measured physical activity (total and all intensities) and health indicators (such as body composition, cardiometabolic biomarkers, physical fitness, behavioural conduct or pro-social behaviour, cognition and academic achievement, quality of life and well-being, harms, bone health, motor skill development, psychological distress and self-esteem) in school-aged children and youth aged 5-17 years. This review, which included a total of 162 studies investigated 204 171 participants from 31 countries, found positive association between PA and health indicators with evidence of favourable association between PA (total and all intensities) and adiposity, several cardiometabolic biomarkers (such as blood cholesterol level, blood pressure, triglycerides, insulin resistance, fasting

insulin and fasting glucose), physical fitness (including aerobic fitness, muscular size, strength and endurance), and bone health (bone mineral content and mineral density). This review supports the positive association between PA (total and all intensities) and the quality of life and well-being, the development of motor skill, and psychological distress. However, the evidence of the relationship between PA and other health indicators such as: fat free mass, behavioural conduct and social behaviour, cognition and academic achievement and self esteem was not strong. The authors suggested that PA of higher intensities (i.e., MVPA and VPA) had a stronger effect and more positive association with health indicators than PA of lower intensity (i.e., LPA and MPA). Furthermore, according to this review no studies reported injuries or other side effects associated with objectively measured PA of any intensity. The respiratory system is also influenced by PA, but in this thesis only the relation between asthma and PA will be discussed in detail in the next section.

1.2.4 Guidelines of physical activity for children and adolescents.

In order to provide guidance about the amount of PA that should be to be accomplished by a person to obtain health benefits from PA, guidelines for physical activity for children, adolescents and adults have been developed and are regularly updated by government and non-governmental health organizations. Such Guidelines for PA of children and adolescents have been developed by WHO (85) , UK (86), USA (87), Canada (88) and Australia (89) are summarised in (Table 1-1).

1.2.5 The suggested amounts of objectively monitored step-defined PA for children and adolescents.

The suggested amounts of objectively monitored step-defined PA for children and adolescents have been summarised by Tudor-Locke et al (90) (Table 1-2). For preschool children, whether boys or girls, 10000-14000 steps/day are recommended, which is equal to 60-100 minutes of MVPA. In addition, for children aged 6-11 years old, it is recommended that boys do 12000-16000 steps per day that is almost equal to 60 minutes of MVPA, while for girls 10000-13000 steps per day are recommended that is almost equal to 60 minutes of MVPA. Furthermore, for both boys and girls aged 12-19 years old, the recommendation is 10000-11700 steps per day equating which is almost equal to 60 minutes of MVPA.

Table 1-1 Guidelines of physical activity for children and adolescents

Country	Recommend physical activity for children < 5 years	Recommend physical activity for 5 – 17 or 18 years
WHO (85)		-Minimum 60 minutes of moderate-vigorous intensity PA daily. -PA greater than 60 minutes provide more health benefits. -Most PA should be aerobic, vigorous intensity activities incorporated, including those strengthening muscle and bone, minimum 3 times/week.
UK (86)	-PA encouraged from birth in safe environments. -At pre-school age do minimum 180 minutes (3 hours)/day. -Minimise sedentary time (being restrained or sitting) for long periods (other than sleeping time).	-Moderate to vigorous intensity PA for minimum 60 minutes for several hours/day. -Vigorous intensity activities, including those that strengthen muscle and bone should be incorporated minimum three days/week. -Minimise sedentary time (sitting) for long periods
USA (87)	Children should do 60 minutes or more of PA daily including: -Aerobic: ≥ 60 minutes/day should be moderate-or vigorous-intensity aerobic PA, and include vigorous-intensity PA minimum 3 days/week. -Muscle strengthening: as part of 60 minutes of daily PA, and should include muscle-strengthening PA on minimum 3 days/ week.	Adolescents should do 60 minutes or more of PA daily including: -Aerobic: ≥ 60 minutes/day should be moderate-or vigorous-intensity aerobic PA, and include vigorous-intensity PA minimum 3 days/week. -Muscle strengthening: as part of 60 minutes of daily PA, and should include muscle-strengthening PA on minimum 3 days/ week.

	-Bone strengthening: as part of ≥ 60 minutes of daily PA and include bone-strengthening PA on minimum 3 days/week.	-Bone strengthening: as part of ≥ 60 minutes of daily PA, and include bone-strengthening PA on minimum 3 days/week
Canada (88)		Should accumulate minimum 60 min of moderate-vigorous-intensity PA/day. This should include: -Vigorous-intensity activities minimum 3 days/week -Muscle and bone strengthening activities minimum 3 days/ week.
Australia (89)	-< 1 year PA in safe environments encouraged. -< 5 years do daily, minimum three hours of PA throughout the day.	For age 5-12 years -Should accumulate minimum of 60 min of moderate-vigorous-intensity PA/day which should consist of aerobic activities, including some vigorous intensity activity. -Strengthening muscle and bone activities minimum 3 day/week. -Additional health benefits achieved by engaging in more activities up to many hours/day.

Table 1-2: The suggested values of objectively monitored step-defined physical activity for children and adolescents

Gender	4-6 years	6-11 years	12-19 years
Boys	-Daily PA volume of 10000-14000 steps/day is associated with 60-100 minutes of MVPA	-Average 12000-16000 steps/day -MVPA of 60 minutes achieved within a volume of 13000 to 15000 steps/day	-Approximately 8000-9000 steps/day. -In 10-15 years old MVPA walking generates 3300-3500 steps in 30 minutes or 6600-7000 steps in 60 minutes. -MVPA of 60 minutes associated with 10000 to 11700 steps/day
Girls		- Average 10000 to 13000 steps/day - MVPA of 60 minutes achieved within a volume of 11000 to 12000 steps/day	- Approximately 8000-9000 steps/day. - MVPA walking generates 3300-3500 steps in 30 minutes or 6600-7000 steps in 60 minutes in 10-15 year olds - MVPA of 60 minutes associated with 10000 to 11700 steps/day

1.2.6 Compliance with the physical activity guidelines

While evidence suggests that PA in children is beneficial for many areas of health including metabolic syndrome (91-94), blood pressure (95-97), cardiovascular fitness (95, 98, 99), muscular strength and endurance (100-102), bone tissue (103-106), mental health(107, 108), and academic performance (109-111), an important caveat is that compliance with guidelines has been shown to be low in both adults and children and adolescents (112-115) (115-118).

1.3 Sedentary behaviour (SB)

1.3.1 Introduction

Lifestyles have changed significantly over the last few decades; tasks which needed PA to be performed in the past, can nowadays be effected with less effort or perhaps even while sitting at home (119). Previously preparing a meal, washing clothes or cleaning the house needed physical effort, while, nowadays it takes much less effort to do the same tasks (120, 121). Transportation, before, involved people walking or riding a horse to go somewhere, but nowadays all kinds of relatively effort free transportations are available (121). At work, many jobs that required PA can be done without it now (121). In earlier times, entertainment time was spent in play or taking part in sports; now, much time is spent watching TV or in front of computer screens. All these changes combined with increasing urbanisation have led to large increases in sitting time (Sedentary behaviour, SB) (123). There is a tendency that time spent in SB increases with age, including time spent in continuous sedentary behaviour lasting ≥ 30 min, at the expense of light-intensity PA. Overall, these changes add greatly to an increase in total sedentary behaviour (124).

There was an idea that SB and PA are interdependent i.e. when there is SB there is no PA and vice versa. The fact is that each one on its own is now considered an independent entity that has its own special determinants (125-127). SB is recognised where movement of the body is minimal and energy expenditure roughly equal that of resting metabolic rate (128). The Sedentary Behaviour Research Network (SBRN) (129) suggested that SB should be defined as " any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalent units (METs) while in a sitting or reclining posture". Many types of behaviours such as watching television (TV), working on computer, playing video games, sitting at work, and sitting in motorised

transportation are considered as SBs (130-132). Research studies and guidelines have mostly focused on screen based activities, such as time of watching TV, playing video games or working on a computer (131-133, 135, 136). This is despite the fact that time watching TV has been shown to be relatively poor proxy for total sedentary behaviour (137).

1.3.2 Parameters of sedentary behaviour

To define significant dimensions of SB that will affect health outcomes, it is necessary to monitor and quantify SB, assess its effect and investigate dose–response relationships. As noted, most studies investigating SB have used screen time (watching TV, playing video games and working on computer) as a surrogate marker for SB (131-133, 135, 136). To quantify and monitor SB more precisely, it is differentiated into volume of SB (or sitting time) and pattern (or fragmentation) of SB (138). The volume of SB (or sitting time) is assessed by measuring two parameters (138): a) total sitting time i.e. the total time in which person sits or lies per 24 hour other than sleeping time. b) percentage sitting time: this represents the total sitting time in hours other than sleeping time normalised to the total monitoring time in hours. Percentage sitting time has the advantage of showing the relative contribution of sedentary behaviour to the daily lifestyle of a person (139). It is now recognised that there are different patterns of sitting. Thus a person can sit uninterruptedly for a period of time or the same duration of sitting time may be broken up by brief periods of standing. The pattern (or fragmentation) of SB is assessed by: a) breaks in sitting (or up transitions) that is any interruptions in sitting time, defined as a transition from sit/lie to stand or to stepping (140-144). b) the distribution of sitting bouts according to their length by measuring the fragmentation index (141, 145, 146). Sitting bouts are described as sit/lie time interval in seconds terminated by postural change (141, 146). Fragmentation index is then the number of sedentary bouts normalised to the total sitting time in hours (141, 145, 146). The fragmentation index has the advantage of providing a single summary measure of how the breaks in sitting are accumulated. Fragmented sitting time with large number of short sitting bouts will result in a high fragmentation index (141, 145, 146).

1.3.3 Correlates of sedentary behaviour to gender

1.3.3.1 Gender

The association between SB and gender among children has been extensively studied. Examples include Corder et al (56), who monitored 844 British children aged nine to ten years old by actigraph accelerometers over 12 months, and showed that the sedentary time of girls was more than that of boys by 4.3% with a medium effect size Cohen's d = 0.504. Ridgers et al (147) who used questionnaires and accelerometers to investigate Australian adolescents aged 10–12 years old between two time points (T1: 2006, and T2: 2008) showed that girls were more sedentary than boys by > 5.1%. In New Zealand (73), 244 children were studied using parent reported data (about screen time and other sedentary activities like reading and music) at three, four, and five years old and showed that over the three years of the study, girls were more sedentary than boys by ≥10%. These examples are consistent with a systematic review conducted by Stierlin et al (148) that investigated the relationship between gender and sedentary behaviour. This review concluded that there is evidence for a consistent association between gender and objectively measured total SB with girls being more sedentary than boys.

There is some contradictory evidence to the general observation that girls are more sedentary than boys. Ball et al (57) measured subjectively the sedentary time (TV/Video viewing time) of 542 Australian children (184 children aged five to six years old, 358 children aged 10 to 12 years) over three years and showed that sedentary time of boys was more than that of girls; in the younger age group (five to six years) the sedentary time of boys was more by ≥ 4% with a relatively small effect size Cohen's d = 0.078 at baseline and by ≥ 3.5% with a relatively small effect size Cohen's d =0.075 at follow-up. In the older age group of 10-12 years old, the sedentary time of girls was more by ≥ 9.4% with a relatively small effect size Cohen's d =0.169 at baseline, but at follow-up the sedentary time of boys was more by ≥ 3.0% with a relatively small effect size Cohen's d =0.053. Lindquist et al (126) showed that among American children of different ethnic groups aged 6.5 to 13 years, there was no difference in SB (TV viewing hours) between boys and girls. Trost et al (72), showed that there was no gender difference in TV/Video games viewing hours per day among 198 African-American children with a mean age of 11.4 ± 0.6 years. According to self-reported data, Schmitz et al (127), found no gender difference in sedentary activity (TV/Video games viewing

hours) level among American adolescents. In a cohort study Van Jaarsveld et al (61), studied 5863 British adolescents aged 11-12 years old by a questionnaire and showed no gender differences in sedentary behaviour (TV/video viewing and video/computer game). The large cohort study of Griffiths et al (149) investigating SB in preschool children using parent-reported data of 13470 British children at three time points found that; at nine months, three and five years old, time spent using screen-entertainment for ≥ 2 hours in boys was significantly more than that of girls by ≥ 13.2%. In a five year longitudinal study, Brodersen et al (150) used self-reported data (about TV/video viewing and video/computer game) to study 5863 British adolescent students aged 11-12 years and showed that boys were more sedentary than girls throughout the study. Gordon-Larsen et al (125), also using self-reported data in 17 766 US middle and high schools adolescents aged 11–21 years showed that males participated more than females in the highest category of inactivity time (TV/video viewing and video/computer game); by ≥ 35.9% in the non-Hispanic whites, by ≥ 13.7% in the non-Hispanic blacks and Hispanics and by ≥ 19.4% in the Asians. These eight studies used subjective rather than objective (accelerometer based) measures. Further there is a focus on screen-based activities which as noted before do not necessarily provide a good proxy measure of total sedentary behaviour.

In summary, the weight of objective evidence suggests that girls are more sedentary than boys.

1.3.3.2 Age

Many studies reported an increase in the SB of children over time, starting from preschool age till adolescence and adult age. Pagani et al (151), followed up 1314 preschool Canadian children at age 5, 17, 29, 41, and 53 months and showed that TV viewing hours at 29 months increased from 8.82 hours per week to 14.85 hours per week by 53 months. Corder et al (56), used actigraph accelerometers to monitor 844 British children aged ten years old and showed that sedentary time increased over 12 months. Accelerometer data from 854 British children (152) showed that sedentary time was slightly increased over a year. Atkin et al (153), showed that sedentary time of 316 British children aged 11 years old increased over time, and between the ages of 11 and 14 years the daily sedentary time increased by around 30-40 minutes. Telford et al (154), used pedometers and accelerometers to show that sedentary time of Australian school aged children started to increase from age 11 to 12 years old; by ≥ 6% among

boys and by ≥7% among girls. Ortega et al (155), used actigraph accelerometers to follow 9 and 15 years old Estonian and Swedish children (Estonian children were followed for nine to ten years and Swedish children were followed for six years) and showed that from childhood to adolescence the sedentary time was increased to 20 min/day per year among boys and to 15 min/day per year among girls. The increment in sedentary time per year of Swedish children was greater than that of Estonian children by 8–11 min/day per year. Neumark-Sztainer et al (76), measured sedentary activity (TV and video times) of American adolescents girls by self-reported data, and showed that there was a positive association between TV viewing hours and age, and from 14 -16 years old there was an increase in TV and video times of ≥ 20% . This is consistent with a systematic review conducted by Stierlin et al that was published in 2015 which studied eleven studies (five objective and six subjective) and investigated the relationship between age and sedentary behaviour and suggested that there is evidence for a significant positive association between age and total sedentary time (148). However, the reason behind these changes in SB with age is not known. Also, the age at which SB starts to decrease significantly has not been clearly defined.

There is some contradictory evidence to the general observation that sedentary time increases with age but again the studies do not include objective measurements. Examples include: a longitudinal study conducted by Taylor et al (73) that used questionnaires to investigate total sedentary time of 244 New Zealand children at three time points three , four, and five years old, and which showed that total sedentary time level was almost the same between three and four years old, but declined by ≥10% between four and five years old; a cohort study conducted by Francis et al (156), used parental and self-reported data to track TV viewing and video game times of 434 American children at ages 5, 8, 11, and 13 years old showed that TV viewing and video game times were rather stable throughout the research; and Henry et al (79) who used activity diaries to measure number of hours spent watching television among 58 female adolescents from United Arab Emirates (UAE) aged 11–16 years and showed no age difference in number of hours spent watching television per day.

Hence according to most of the studies that have investigated the correlation of age with SB in children, there is evidence that SB of children increases with age.

Implications for the planned research in this study

At the time of recruiting subjects in order to study SB of children, it is essential for the researcher to take into account these factors. Both females and males should be included in the research sample, due to the gender difference in SB. Also, the age of both groups; the research and control groups should be of comparable age, if not, differences in observed level of SB might be related to expected differences that could be attributed to age differences.

1.3.4 Sedentary behaviour and health

A recent systematic review and meta-analysis conducted by Carson et al (157) reviewed studies that investigated the correlation between objectively and subjectively monitored sedentary behaviour and health markers such as body composition, physical fitness, metabolic syndrome, behavioural conduct and social behaviour, academic achievement and self-esteem among children aged 5-17 years. The review selected 235 studies; two studies were experimental studies (RCT and crossover trial), and 233 studies were observational studies; longitudinal (n = 49), case-control (n = 5), and cross-sectional (n = 179), of a total sample of 1657 064 from 71 different countries. This review suggested that long duration of TV and screen time was associated with undesirable outcomes in: body composition, cardiometabolic risk factors, behavioural conduct and social behaviour, low physical fitness and low self-esteem. However, long periods of reading and performing homework were related to higher academic achievement. Cliff et al (158) performed a systematic review and meta-analysis of 88 eligible observational studies, that investigated the relation between objectively monitored volume and pattern of sedentary behaviour and nine health indicators such as adiposity, cardiometabolic risk factors, physical fitness, bone and musculoskeletal, psychosocial, cognitive and academic achievement, and gross motor development in children and adolescents aged 2–18 years old. This review showed a positive association between sedentary behaviour and adverse health outcomes such as increased adiposity, greater cardiometabolic risk factors, lesser fitness, poorer bone and musculoskeletal health, adverse psychosocial outcomes, lower cognitive and academic achievement, and poorer gross motor development.

1.3.5 Sedentary behaviour guidelines

Sedentary behaviour guidelines for children have been recently developed by a number of bodies including the UK Department of Health (86), the American Academy of Paediatrics (136), the Canadian Society for Exercise Physiology (CSEP) with its partners (135), and the Australian Department of Health (89) (Table 1-3).

1.3.6 Compliance with sedentary behaviour guidelines

The current sedentary behaviour guidelines are only about the screen time, and do not make recommendations about the recommended hours of the total sedentary time or number of breaks in sedentary time. According to many reviews, the recommended screen (TV, computer, video games) limits are commonly exceeded by children and adolescents. Salmon et al (159) in his review which included papers studying SB in young children aged 2–18 years, illustrated that they were engaged in about two to four hours per day in screen based behaviours and being sedentary for around five to ten hours per day, well in excess of guideline suggestions.

1.4 Sleeping behaviour

1.4.1 Sleep definition

The final component of the movement continuum is sleep. Sleep can be defined as a mixture of physiologic and behavioural processes characterized by a reversible perceptual disconnection from and unawareness of the environment from which a person can awake spontaneously (160-162). It is usually associated with a lying position, behavioural calmness and eye closure (160-162). Sleep is a dynamic process controlled by neurons in the hypothalamus and brainstem (163-165). In children, total sleeping time per day decreases with age: from about 16-18 hours for full term newborn (161, 162, 166, 167); to 12-15 hours for 1 year old infant (161); 11 hours for 5 years old child; 9.25 hours for 12 years old child and 8 hours per day by 16 years old (161, 168, 169). However, the duration of sleeping depends on the method of measurement used. Colley et al (170), showed that sleeping time among children aged 6-11 years old was 9.7 hours per day according to parent reported data and 10.1 hours per day when measured objectively by using an accelerometer.

Table 1-3 Sedentary behaviour guidelines

Country	< 5 years	5 – 17 or 18 years
UK (86)	-Minimise sedentary time (being restrained or sitting) for long periods (other than sleeping time).	-Minimise sedentary time (sitting) for long periods
USA (136)	-Total media time including entertainment media should be limited to ≤ 1-2 hours/day for all children. -TV should be removed from children's bedroom. -Viewing TV should be discouraged for children below two years, and instead interactive activities that will promote proper brain development should be encouraged like talking, singing, playing, and reading.	
Canada (135)	Reduce sedentary time in awake time -Reduce prolonged sitting or being restrained for more than one hour at a time. -Screen time not recommended for those below two years. -Screen time restricted ≤ 1 hour/ day for those two to four years.	
Australia (89)	-Children < two years of age should not spend any time watching TV or electronic media. -Children < five years should not be sitting or being restrained or kept inactive for more than1 hour at a time.	-Time watching TV or electronic media minimized to ≤ 2 hours/day. -Break up long sitting periods.

The longest non-wear time (sit/lie) interval within a 24 hour period between two valid days that is measured by accelerometers was considered as the sleeping time of children (170). Furthermore, the ActivPAL™ accelerometer has the ability to demonstrate the sleep pattern by showing the average number of breaks in sitting (up transitions) per hour against time during 24 hours (146), that can be used to define wake up time and sleep onset time.

The sleeping–wakeful cycle is regulated by three mechanisms: a circadian rhythm, controlled by a pacemaker in the supra-chiasmatic nuclei of the anterior hypothalamus, influenced by the light-dark cycle, causing wakening during light (active phase of the cycle) and sleeping during darkness (rest phase of the cycle) (167, 171, 172); a homeostatic mechanism, known as process "S" or ('sleep pressure'), in which the need for sleep or sleep pressure develops throughout waking hours and is relieved by sleeping hours to restore body and mind alertness (162, 167, 171); and an ultradian rhythm that influences cycling between sleep stages through the duration of sleep, and which determines the timing and duration of sleep states (162, 167, 171). In addition, sleeping pattern can be affected by other internal (e.g. hormonal changes accompanying growth) or external factors (e.g. social life, and school stress) (161, 173, 174).

1.4.2 Sleeping pattern

One important external factor influencing the sleep patterns in children is attendance at school. In westernised countries (including Iceland (175), Australia (176), Italy (177, 178), Finland (179) Turkey (180) and Croatia (181)), in Middle Eastern countries (Kingdom of Saudi Arabia (182) and Israel (183)), and in Asian countries (such as Hong Kong (184, 185) and China (186)), it has been shown that during school holidays, there was a significant delay both in evening bed time ranging from 30 minutes to two hours and in morning rise time ranging from one to four hours with a longer total sleeping time of between 35 minutes to two hours. There were also differences between weekend and weekdays. In contrast, a cohort of New Zealand Caucasian children conducted by Nixon et al (187), showed that sleep duration was shorter by around 26.9 minutes on weekend nights and bed time was delayed by around 31 minutes at weekends but there was no significance difference in rise time. Also, among children of other countries such as; Nigerian children (188), Austrian children (189) and Chinese adolescents (190)) there were insignificant differences in sleep duration between weekend and school days, as well as insignificant differences in evening bed time between weekend and school days. The reasons for these varying effects are not understood.

Sleeping pattern and even sleeping time are also known to change with seasons with a prolongation of sleeping time in winter. For example, sleep duration in winter was 2% longer than that of spring among Danish school children (191). Icelandic children sleep longer in winter (192). In Strasbourg city (north-eastern France) (193), a shortening of sleep duration from January to May among children has been reported. Among New Zealand Caucasian children (187), sleep duration was shorter in summer than other seasons.

1.4.3 Sleep and health

Sleep problems in children and adolescents are directly related to their health, wellbeing and academic performance. Lack of sleep is associated with multiple health problems such as mood disturbances, cognitive function and performance problems (194). The sleep deprived child will be at increased risk of problems in vigilance and attention, emotional liability, and frustration distress (194), which will contribute to increased risk of lower school or academic performance (195, 196). Hale et al, (197) suggested that adequate sleep (time) has a protective effect against being overweight or obese. Chen et al (198), suggested that shorter sleep period in children can be associated with a 58% greater risk for being overweight or obese. Overweight/obesity reduces on average by 9% for each hour increase in sleep. Sleep deprivation can be caused by a pathological cause such as asthma or a non-pathological cause like the effects of watching an electronic screen. There is an evidence suggesting that screen media (TV, computer, video games), is associated with delayed bed time and shortened sleep (197). This may help explain some of the relationship between obesity and screen time which can cause delayed sleep onset and shorter sleep duration.

1.5 The movement continuum and children with chronic diseases

While there have been studies on the levels and adequacy of PA, SB and sleep in healthy children and adolescents as outlined above, there are surprisingly few such studies in children and adolescents with chronic diseases. In fact, numerous previous studies and national PA surveillance programs have actually excluded children and adolescents with chronic disease. A recent systematic review conducted by Saunders et al (199), reviewed 13 cross-sectional studies and one cohort study, a total 36 560 participants, and investigated the correlation between combinations of different levels of objectively monitored PA, subjectively or objectively monitored SB and sleep and health markers in children aged 5–17 years old. The health markers reviewed were: adiposity (ten cross-sectional studies),

cardio-metabolic risk factors (one longitudinal study and two cross-sectional studies), cardio- respiratory fitness (two cross-sectional studies), and musculoskeletal fitness (one cross-sectional studies). The review suggested that a combination of high levels of PA, long duration of sleep and low levels of SB was negatively associated with adiposity and cardio-metabolic risk factors. Also, it was suggested that combinations such as high levels of PA and long duration of sleep or high levels PA and low levels of SB were inversely associated with adiposity and cardio-metabolic risk factors. High levels of PA combined with low levels of SB were associated with beneficial effects on cardio-respiratory and musculoskeletal fitness. The review provided useful information concerning the relation between components of the movement continuum and health outcomes and included objective studies that examined large number of participants. Elmesmari et al (200) performed a systematic review and meta-analysis of 25 eligible studies with a total of 2062 children with chronic diseases and 1523 healthy participants, that investigated the relation between accelerometer monitored MVPA and sedentary time (ST) in children and adolescents with four chronic diseases; cardiovascular disease (seven studies), respiratory disease (seven studies), diabetes (seven studies), and malignancy (three studies)). Out of the 25 eligible studies, 16 studies compared levels of MVPA of patients to that of healthy children. Elmesmari found that there were no differences in MVPA between patients with cardiovascular diseases and type 1 diabetes and healthy children. However, MVPA of patients with respiratory disease (asthma and cystic fibrosis) was lower than that of healthy children. The review suggested valuable information concerning the relation between MVPA and ST and chronic diseases; it included objective studies that used one type of monitoring method (accelerometer) and examined large number of participants. Nevertheless, it can be argued that the studies were heterogeneous; conducted in different countries, examined different age groups, and although all these studies used accelerometers for monitoring MVPA and ST, they were of different types and models. These factors limit the generalizability of the results.

It is obvious that there are still few studies that have investigated the relation between the activity continuum and asthma in children and all of these studies have been conducted in developed countries. Further, there is no single study that investigated the association between the activity continuum and asthma in children in a Middle Eastern setting such as Kuwait. The present study sets out to examine the three main components of the movement continuum (physical activity, sedentary behaviour and sleep) in children with one of the

commonest chronic disease, asthma. In many ways, asthma in children provides a useful paradigm to investigate the effects of illness on the movement continuum. Poorly controlled, asthma is known to interfere with a child's ability to exercise and it affects sleep at night. In theory it, therefore, might disrupt all aspects of the movement continuum. Saunders et al (199) noted that the combination of high level of PA, long duration of sleep and low level of SB was negatively associated with adiposity. In the case of asthma the opposite can happen i.e. low level of PA, short duration of sleep and high level of SB occur. This might contribute to obesity which is a risk factor for asthma. Asthma attacks may occur (201, 202), which in the most severe form may result in hospital admission that again will lead disruption of all aspects of the movement continuum. The next section provides a brief overview of our current understanding of asthma in children and its impact.

1.6 Bronchial asthma

1.6.1 Definition

Asthma is a heterogeneous chronic inflammatory disorder of the airways (33) in which the airways are hyper-responsive (hyper-reactive) (33, 203). This arises as a response to various stimuli that activate a range of inflammatory cells and cellular elements in inflammatory pathways that are active in asthma, and which, in turn, induce airway hyper-responsiveness (hyper-reactivity) (33, 203). The end result is recurrent, reversible airflow obstruction within the lung, the diagnostic hallmark of asthma. This is manifest clinically as wheezing, breathlessness, chest tightness, and coughing, either persistently ('chronic asthma') or more intermittently and acutely ('asthma attack') (33, 203). Although there is no obvious agreement on definition of 'asthma attack', it can be described as acute worsening of asthma symptoms in combination with objective evidence of reduced expiratory airflow measured as Peak Expiratory Flow (PEF) or a reduced Forced Expiratory Volume in 1 sec (FEV_1) in association with reduced FEV_1/FVC ratio. Asthma attacks commonly result in urgent unplanned health care and necessitate emergency treatment with high dose bronchodilators and corticosteroids (33, 204-208).

1.6.2 Prevalence

The understanding of the global burden of asthma in children has increased over the last two decades. This has been clearly established because the data has been collected in a standardised manner as part of the International Study of Asthma and Allergies in

Childhood (ISAAC), which has involved 306 centres in 105 countries (39). The death rates for childhood asthma are very low, range from 0.0 to 0.7 per 100 000 (39) despite the fact that asthma is the most common chronic disease in children and is among the top 20 chronic conditions for global ranking of disability-adjusted life years in children (39). The ISAAC Phase One study involved over 700 000 adolescents and children from 156 centres in 56 countries and; it found marked worldwide variation in symptom prevalence of asthma, rhinitis and eczema that was not explained by the current understanding of these diseases. ISAAC Phase Three involved over 1 187 496 adolescents and children (237 centres in 98 countries). ISAAC Phase Three studies found that prevalence of asthma in children increased in the period from the mid-1990s to the mid-2000s, from 11.1% to 11.6% in six to seven years old age group, and from 13.2% to 13.7% in 13–14 years old age group (39). Asthma symptom prevalence was increasing in many locations especially in low- and middle-income countries where severity was also high. In the United Kingdom, the prevalence of asthma for the age group six to seven years old was 18.4% in ISAAC phase one and increased to 20.9% in the ISAAC phase three study; and for the age-group 13–14 year the prevalence in ISAAC phase one was 31.0% and decreased in ISAAC phase three to 24.7% (209). The prevalence of doctor diagnosed asthma in Scotland for the year 2003, among children below 16 years was 20% in boys and 12% in girls (210). In low and middle income countries including Middle Eastern countries, asthma is also highly prevalent. In Oman, the prevalence of asthma in 2009 was estimated to be 7.3% of adults (n=96,470) and 12.7% of children (n=58,344) (35, 211). In Kuwait the prevalence of asthma amongst 13-14 years old was 17.1% in the period between 1992 and 1998 (ISAAC phase one), and decreased to 7.6% in the period between 1999 and 2004 (ISAAC phase three) (209). The ISAAC studies, reported that Kuwait was ranked among the highest seven countries for the prevalence of night sleep disturbances due to wheeze for the age group 13–14 years old for the year 1997 (212). The situation for asthma attacks is less clear because there is a lack of data on the incidence of asthma attacks in the world (204). Although, through the last two decades, there has been a reduction in the rate of hospital admissions due to asthma attacks, this may not represent a real decline in asthma attack rate (204). In order to avoid hospitalisation and the associated costs, there is a drive to treat patients early and effectively (204). Asthma exacerbations display seasonal discrepancies with the highest incidence in autumn (213), which is positively linked to the seasonal changes in the rate of upper respiratory virus infections (214).

There is no single explanation for the increase in asthma prevalence that have been observed in many countries, but it might be explained by the interplay between many factors (215). These include improved diagnosis of asthma and clearer differentiation from other respiratory conditions (216, 217); changes in the environment due to living in more hygienic conditions with lower exposure to allergens such as microbes and parasites earlier in life but higher reactivity to environmental allergens at a later stage of development; greater exposure to indoor allergens (spending more indoor time with tighter housing); alterations in lung protective factors from changes in diet and type of food, or alterations in levels of micronutrient like vitamin D; diminished physical activity levels; high rate of delivery by caesarean section; and alteration in the interaction between immunity and environment from high rates of antibiotic use (218-222).

1.6.3 Symptoms of asthma

1.6.3.1 Chronic symptoms

Wheezing, coughing, breathlessness and nocturnal symptoms/awakenings point to a clinical diagnosis of asthma. Wheeze is a continuous (exceeds 250 ms) high-pitched (dominant frequency of 400 Hz or more) sound, sometimes with musical quality, produced by air turbulence in narrowed airways during expiration (33, 203, 223-225), commonly associated with asthma. It can be considered the most sensitive single symptom to diagnose asthma (226-228), but its absence does not rule out asthma (229). Furthermore, the diagnosis of asthma will be more likely if wheezing is associated with cough, dyspnoea, chest tightness, and if these symptoms deteriorate at night (nocturnal cough, nocturnal dyspnoea, nocturnal chest tightness) and result in awakening the patient, or if these symptoms are triggered by exercise, viral infection, inhalant allergens (e.g. animal dander, house-dust mites, mold, pollen), irritants (smoking or smoke, airborne chemicals), weather changes, stress, or strong emotional expressions (laughing or crying hard) and menses (33, 203, 228-230).

The mechanism behind these symptoms is not fully understood. Asthma is an inflammatory disease of the airways, characterised by reversible airflow obstruction and airway inflammation, bronchial hyper-responsiveness, and airway remodelling (231). Antigens or allergens entering the body, are recognised by the innate immune system (232) using germ-line-encoded receptors (233). These receptors recognize endotoxins or lipopolysaccharides of microorganisms which present in the environment in polluted air (234), in household dusts (235) and in organic dusts (236) along with many other antigens

or allergens. These receptors present in specialised cells such as dendritic cells lining respiratory airway, that engulf the allergen, process it and present it to naïve T cells in draining lymph nodes (237, 238). These cells proliferate and differentiate into helper T cells type 2 (Th2 cells) that act on B cells to produce certain IgE types. Class switching of B cells to produce specific IgE happens in response to two signals: one from interleukin-4 or interleukin-13 produced by Th2 cells (239); and the other signal results from binding of CD40 on B cells to its ligand on T cells (240). After B cell activation, specific IgE is synthesized and released in blood to bind to high-affinity IgE receptors (FcεRI) located on surface of mast cells or basophils, and to low-affinity IgE receptors (FcεRII or CD23) located on surface of lymphocytes, eosinophils, platelets, and macrophages (241). Once FcεRI receptor-bound IgE molecules of mast cells encounter triggering allergen again, bridging of these IgE molecules will lead to activation of these cells and release of inflammatory mediators (241), like histamine and leukotrienes which give rise to the early asthmatic (early-phase) reaction (242, 243). These molecules induce constriction of smooth muscles of airways that mostly resolves within an hour. A more prolonged late asthmatic (late-phase) reaction (243) may start four to six hours later. In this later phase, an inflammatory process in the airways takes place. This inflammatory process consists of cellular components including Th2 cells, lymphocytes, eosinophils, mast cells, macrophages, and neutrophils, and a number of mediators such as cytokines, interleukins, prostaglandins, and leukotrienes (244, 245). In this phase, the multiple inflammatory processes affect smooth muscle, epithelium and mucus secreting cells (Goblet cell) of airways and result in narrowing and plugging of the airways (244, 245). Hypertrophied airway smooth muscle leads to decreases in the diameter of airway lumen (244, 245). In addition, direct (viral and bacterial infection) or indirect injury to the respiratory epithelium cause its damage and may result in deposited cell debris inside airway lumen which also contributes to narrowing of the airway (244, 245). Finally, hyperplasia and hypertrophy of Goblet cells lead to an increase in the amount of mucus secretion which contributes to airway obstruction. This combination of airway inflammation, bronchial muscle constriction and plugging of airways with mucus produces the airways obstruction that is the hall mark of asthma.

1.6.3.2 Acute attack symptoms

Although there is no universal agreement on the definition of an ‘asthma attack’, it can be described as acute or sub-acute worsening of asthma symptoms that is triggered by various

stimuli, that induce bronchoconstriction and increased mucus production causing deterioration of asthma symptoms in combination with objective evidence of reduced expiratory airflow measured as Peak Expiratory Flow (PEF) or a reduced Forced Expiratory Volume in 1 sec (FEV_1) in association with reduced FEV_1/FVC ratio (33, 204-208).

In an asthma attack, there is airway constriction and obstruction as an outcome of inflammatory processes resulting in bronchoconstriction, oedema and mucus production (244, 245).

1.6.3.3 Risk factors for asthma

Different risk factors predispose to asthma. These factors can be divided into host and environmental factors. These risk factors of asthma are discussed further below.

Host factors include genetic factors, sex, obesity, type of delivery and psychological factors (33). Asthma has a genetic component, where several genes are responsible for development of asthma and asthma susceptibility is determined by interactions of these genes with other genes and/or environment (33, 203, 246-250). Some of these genes can be risk factors for immune reaction (33, 203, 251), life-threatening asthma (33, 252) or low level of lung function in asthmatics (33, 203, 252), and can determine drug response (33, 253-255). In addition, asthma is influenced by gender; before age of 14 years old it is commoner in boys than girls, while after 14 years and above the gender difference diminishes (33, 256, 257). Early life background is important with evidence that the type of delivery increases the risk of having asthma, and the risk increases when a child is delivered by caesarean section, being even higher with emergency caesarean section than with an elective one (258), especially if the child is of allergic parents (259). Psychological stress in the family can predispose child to asthma (260). More recently, obesity has been implicated in asthma (261). There is a positive association between high body weight at birth or during childhood and the risk of developing asthma (261, 262). Obesity is also linked to poor control of asthma and poor quality of life of asthmatic patients (261, 263) and reducing weight improves asthma symptoms and airway obstruction, reduces medication use and asthma attacks and improves pulmonary function indices (261, 264).

Environmental factors include allergens, infections, weather, smoking, food, and air pollution. Common aero-allergens include house dust mite, cockroaches, cat dander, dog dander and aspergillus mold (33, 203, 265-268). Infections have been involved in causing

asthma attacks (33, 203, 269-271). In particular, rhinovirus infection is very common and not only increases the severity and duration of lower airway infection, but greatly worsens lung function (33, 272). Weather has been implicated in the development of asthma (273) Exposure to tobacco smoke appears to be involved in the pathogenesis of asthma with the harmful effects of smoking evident from foetal life when a mother smokes during pregnancy (33, 203, 274). Also, being an infant of a smoking mother will increase the chances of being a wheezy child early in life and of being more prone to respiratory diseases (33, 275). Likewise, passive smoking renders infants and children more susceptible to lower respiratory tract infections that in turn can exacerbate asthma (33, 276, 277). Foods can be involved in predisposing to asthma, and the use of breast milk will lower the risk of wheezing illnesses in early childhood compared to formulas of cow's milk or soy protein (33, 278). More over susceptibility to asthma may be increased with consumption of meals rich in processed foods, foods low in antioxidants (such as fruits and vegetables), foods high in omega-6 polyunsaturated fatty acid (available in vegetable oil and margarine), and low in omega-3 polyunsaturated fatty acid (available in oily fish) (33, 279). There is an increasing recognition that air pollution predisposes to outbreaks of asthma, whether it is caused by high level of pollutants or allergens (33, 203, 280-282). Also, traffic air pollution can induce wheezing in the early years of childhood (33, 283).

1.6.3.4 Risk factors for childhood asthma attacks

Added to the previous risk factors of asthma, there are a number of additional risk factors for asthma exacerbations such as: poor compliance with asthma medications leading to poor asthma control (284-288); past history of asthma exacerbations, especially in the last year (288-290); viral infections especially rhinovirus, and other viruses such as respiratory syncytial virus, enteroviruses, corona virus and human metapneumovirus (288, 291, 292); and allergen sensitization and subsequent exposure (288, 293). Interaction between allergens and viruses can increase the severity of an asthma attack (33, 288, 294). Passive exposure to tobacco smoke has been implicated in increasing the rate of asthma attacks (288, 295). Similarly acute exposure to pollutants can trigger an asthma attack and increase its severity (33, 288, 296). Genetic susceptibility has also been implicated in predisposing to severe asthma exacerbations (288, 297, 298).

1.6.3.5 Morbidity from asthma

Asthma can place a huge burden on a child and his/her carer life and wellbeing. Globally asthma is considered one of the top 20 chronic conditions in terms of disability-adjusted life years (which is the sum of two components: years of life lost plus years lived with disability) among children (39). The social life of the patient and care givers is affected by school/work absenteeism, impaired school performance due to interrupted sleep, and limitations on their physical and social activities. Recent studies have confirmed the high level of morbidity. The AIRGNE study showed that asthmatic patients had experienced daytime asthma symptoms (in 68%), nocturnal symptoms (in 51%) in the previous four weeks, exercise-induced asthma in the previous 12 months (in 49 %) and school absences in children (in 51.7%) (299). The TENOR study (289), showed that 14% to 19% of adults, adolescents, and children with severe or difficult-to-treat asthma had one or more school or work absences in the 2 weeks prior to the study and in USA in 2008, 10.5 million school days and 14.2 million work days were lost due to asthma (37). The mental health of asthmatic patients and their carer's can be affected in terms of experiencing depression, anxiety and stress (300, 301).

1.6.3.6 Mortality from asthma

Asthma is a recognised cause of death. It is estimated that every year asthma causes around 346 000 deaths all over the world (33). However, deaths from asthma are generally rare at all ages and seem to be decreasing. Globally, the death rates of asthma among children range from 0.0 to 0.7 per 100 000 (39). There was a drop in the age-standardised mortality from asthma from 9.0 to 5.2/100 000 per year between 1990 and 2010(39). However, the population that has asthma also has higher all-cause mortality. A Canadian (Ontario) study conducted in the period 1999-2008 investigated the mortality rates and causes of death of subjects from 0-99 years old and showed that asthma-specific mortality rates per 100,000 asthma population decreased from 13.6 in 1999 to 6.2 in 2008, while all-cause mortality among asthmatic patients was higher than in the general population (302). Similarly, in the period from 2000 to 2006 in Denmark (303), 49 cases of uncontrolled asthma were identified out of 625 sudden unexpected death cases of individuals aged 1–35 years. Out of the 49 uncontrolled asthma cases 13 (27%) died because of acute asthma attack, and the remaining 36 cases died of comorbid conditions.

1.6.3.7 Burden of asthma on health services and economy

The burden of chronic asthma on health services differs from that of the acute asthma attacks. In Scotland, in the year between 2003-2004 there were 60,553 GP consultations for allergic diseases, with a rate of 39 per 1000 patients. Around half of those consultations were for asthma, a rate of 20 per 1000 patient (210). In addition, allergic patients admitted to hospital (24,189 admissions) constituted 1.5% of the total admissions, of which asthma accounted for 83%, in Scotland in the same period (210). Globally, acute asthma attacks contribute to a large proportion of the workload among accident and emergency visits and hospitalisation (37, 288, 299, 300). In 2007, in USA, there were 1.75 million asthma-related emergency department visits and 456,000 asthma hospitalizations (37). In seven European countries (UK, France, Germany, Italy, Netherlands, Spain, Sweden) in 1999, a survey of 753 asthmatic children was conducted and showed that 36% of children required an unplanned urgent care visit in the previous year and 18% of children required one or more emergency department (ED) visits due to asthma in the last 12 months (288). The AIRGNE study (Asthma Insights and Reality in the Gulf and the Near East) was conducted between January 2007 and March 2008 in five Arabian countries including Kuwait, Oman, United Arab Emirates, Jordan and Lebanon and showed that asthmatic patients had used health services frequently in the previous year with emergency room (ER) visits in 52% and hospitalisations in 23% (299). Likewise the duration of hospital stay due to an asthma attack has increased. A US nationwide inpatient sample for the period between 2001 and 2010 showed that the hospital length of stay of asthma had increased from 3.7 days in 2001 to 3.9 days in 2010, and increased from 3.9 days to 8.3 days when patients required mechanical ventilation (38). Further, asthma attack can make things worse by increasing the rate of admission due to asthma; a review of data of 53156 Australian children that were admitted because of asthma in the period 1997–2009 showed that 9459 (28%) of those children had two or more admissions over this period, 10263 children were readmitted within one year and around 2401 (5%) of admissions were repeated admission within 28 days (304).

Asthma presents a large financial burdens not just on patients and their families but also on the economies. The cost of asthma treatment is great; large amount of money were expended during 2008 in high income countries such as Canada (USD 654 million), Germany (USD 2740–4430 million), Singapore (USD 49.36 million), Switzerland (USD 1413 million) and United States (USD 2300–8256 million) in asthma management planning, patient education, and treatment whether in outpatient, emergency or in-patient hospital care

(39). In USA between the periods 2001 and 2010, asthma hospitalization cost increased from USD 5,611 in 2001 to USD 7,230 in 2010, and when mechanical ventilation was required the costs increased up to USD 21,556 (38). In the UK 12.5 million GP consultations per year for allergic diseases cost the NHS around 211 to 311 million pounds; the cost of hospital admissions exceeds 68 million pounds per year (36). NHS Scotland spends more than £130 million per year in the care of allergic diseases, which is nearly £1.5 million per year for the GP consultations for allergic disorders, £10.2 million per year for hospital admissions and around £120 million for the community prescribed treatments for allergic diseases with most of the expense being in primary care and related to asthma (210). In Oman the annual expenditure of treatment of asthma after excluding the cost of medications, was 70,238,311 USD for children, and when the cost of medications included, the annual expenditure of asthma treatment was increased to 159,900,761 USD (35, 211). Asthma also affects the economy through the loss of work days of the carer and decline in his or her job performance due to the stress caused by a child's sickness (305-311).

1.6.3.8 Asthma and exercise

Exercise-induced asthma (EIA) is an airway obstruction following vigorous exercise that causes breathlessness, cough, wheeze and an obstructive picture on lung function with a decline in the forced expiratory volume in 1 second (FEV_1) and other spirometric parameters (312, 313). It is a key feature of childhood asthma with most (~70%) children and adolescents with asthma developing bronchoconstriction following physical exercise (312, 314). Characteristically, bronchoconstriction induced by exercise occurs 2 to 4 minutes following exercise, peaking from 5 to 10 minutes later (312). The degree of obstruction increases as the duration and intensity of exercise increases (315-317). Following termination of exercise, in about 30-60 minutes, air way constriction usually resolves spontaneously and symptoms will fade away without need for drugs (317). For approximately half of sufferers, their airways will be resistant to bronchoconstriction induced by further exercise for a period of approximately two hours following exercise, a phenomenon known as the refractory period (316). A small proportion of patients experience a late asthmatic response, called the 'late phase response' in which a decline in lung functions occurs around 2 to 8 hours following exercise (318, 319).

1.6.3.9 Asthma and activity continuum

1.6.3.9.1 Introduction

The description of asthma in the previous section shows that it is a disease that influences the components of activity continuum, particularly in relation to disruption of sleep because of asthma symptoms and to effects on activity. Asthmatic children can be affected by restrictions of their physical activity resulting in avoidance of exercise to prevent aggravating asthma symptoms. Lack of exercise might be expected to make them more sedentary. They frequently experience nocturnal symptoms that disturb their sleep resulting in being tired the following day, which then has knock-on effects on their attendance and performance at school. In this section, the evidence available about the relationship between asthma and all components of the movement continuum is considered.

1.6.3.9.2 Physical activity and asthma

The relationship between PA and asthma in children is surprisingly unclear with studies investigating difference in PA level between asthmatic and non-asthmatic children showing conflicting results.

Table 1-4 Studies suggesting that physical activity of asthmatic children is more than that of healthy children

	Study	Country	Participants	Method	Outcome
1-	Weston et al (320) (cross-sectional study)	New Zealand	408 (11-13 yrs old) asthmatic and non-asthmatic	Questionnaire	Asthmatic more active than non-asthmatics
2-	Ownby et al (321) (longitudinal study)	USA	636 (8-9 yrs old) asthmatic and non-asthmatic children	Questionnaire	Asthmatic more active than non-asthmatics (6,438 against 5,432 METs /year)
3-	Kim et al (322) (cross-sectional study)	Korea	72943 (13–18 yrs old) asthmatic and non-asthmatic	Questionnaire	Asthmatics 1.14 times more likely to perform MPA for ≥ 5 days/week than those without current asthma.

A number of studies showed that asthmatic children were more physically active than healthy children (Table 1-4). In 1989 Weston et al (320) used questionnaires to evaluate behaviours and attitudes related to physical activity and asthma in 408 New Zealand schoolchildren aged 11-13 years. The study suggested that asthmatic children were more

physically active than non-asthmatic children (Table 1-4). A longitudinal study conducted by Ownby et al (321), also used a questionnaire to look at the relationship between physical activity, obesity and asthma in 773 US schoolchildren aged eight to ten years. Again, the study suggested that asthmatic children were more active (Table 1-4). Finally, in a cross sectional internet based survey, Kim et al (322) investigated the PA of sample of 72 943 Korean students aged 13–18 years and showed that those with current asthma were more likely to participate in moderate PA than non asthmatics (Table 1-4). However, these studies may be challenged because they were subjective studies relying on questionnaire data which was self-reported with a risk of reporting bias.

Many more studies have suggested that asthmatic children were less active than normal children. As examples, nine studies of different types and different sample sizes that examined asthmatic children of different ages, in different countries, and used different monitoring methods are listed in (Table 1-5). Firrincieli et al (323) investigated the physical activity of 144 US pre-school children aged three to five years old with history of wheezing by actiwatch accelerometers and showed that children with history of wheezing had low levels of physical activity(Table 1-5). Brasholt et al (324) conducted a nested within cohort study in Denmark and used accelerometers to study the association between asthma and physical activity in 253 Danish asthmatic children aged five years old (Table 1-5). The study suggested that physical activity was inversely related to bronchial hyper responsiveness. A cohort study carried out by Bringolf-Isler et al (325) in Switzerland that used Actigraph accelerometers and questionnaires to study 352 asthmatic and non-asthmatic children aged seven to ten years old and showed that asthmatic children were less physically active (Table 1-5). In USA, Lang et al (326), conducted a telephone survey interviewing parents of 137 asthmatic children and 106 non asthmatic controls aged 6-12 years old, and suggested that asthmatic were less active (Table 1-5). Kitsantas et al (327) used questionnaires to study the physical activity and fitness of 172 American adolescent girls (asthmatics constituted 22% of the sample) aged from 14-18 years old (Table 1-5). This study suggested that asthmatic girls were less physically fit and less active than non-asthmatic girls. In the UK Glazebrook et al (328), used questionnaires to compare physical activity of 56 asthmatics to 61 non asthmatics aged 7-14 years and showed that asthmatics were less physically active than healthy children (Table 1-5). In a cross-sectional survey, Chiang et al (329), compared 120 asthmatic children of mild to moderate asthma to 309 non-asthmatic Chinese children aged 9-11 years old and suggested that asthma impedes participation in vigorous physical activity but not moderate to vigorous physical activity

(Table 1-5). Nystad et al (330), used questionnaires to study 2188 Norwegian school children aged 6-16 years old and found that asthmatics were less physically active than healthy children (Table 1-5). In a cross sectional study, Cheng et al (331), used questionnaires to compare 120 stable asthmatic Chinese children aged 6-12 years old to 109 healthy controls and suggested that asthmatic children were less active and participated less in sport activities (Table 1-5). Thus, two objective cohort studies and one objective and sex subjective cross-sectional studies all suggested that asthmatic children were of less PA than normal children, (Table 1-5).

Table 1-5 Studies suggesting that physical activity of asthmatic children is less than that of healthy children

	Study	**Country**	**Participants**	**Method**	**Outcome**
1-	Firrincieli (323) (cross-sectional study)	USA	144 (3-5 yrs old) asthmatic and non-asthmatic children	Actiwatch accelerometer	Mean activity units (AU) of wheezing children (607 AU /min) lower than non wheezing children (695 AU/min)
2-	Brasholt et al (324) (nested study within cohort study)	Denmark	253 (5 yrs old) asthmatic and non-asthmatic children	Actical accelerometer	PA inversely associated with bronchial responsiveness
3-	Bringolf-Isler et al (325) (cohort study)	Switzerland	352 (7-10 yrs old) asthmatic and non-asthmatic children	-GT3X actigraph accelerometer -Questionnaire	Asthmatics less physically active
4-	Lang (326) (cross-sectional study)	USA	243 (6-12 yrs old) asthmatics and non-asthmatics	Telephone interviewing parents	Asthmatics mean amount of daily PA lower than non-asthmatics (116 vs146 minutes)
5-	Kitsantas (327) (cross-sectional study)	USA	172 (14-18 yrs old) adolescent girls	Questionnaire	Asthmatic girls less physically fit
6-	Glazebrook (328) (cross-sectional study)	UK	117 (7-14 yrs old) asthmatics and non-asthmatics	Questionnaire	Asthmatics reported less PA than non asthmatics (median total PA 4 per day vs 6 per day)
7-	Chiang et al (329) (cross-sectional study)	China	120 (9-11 yrs old) asthmatic and non-asthmatic children	Questionnaire	Asthma impedes participation in VPA but not MVPA. Asthmatics (77.5%) vs non asthmatics (81.1%) achieved recommendations of the United Kingdom Expert Consensus Group (MVPA ≥420 mins/week)

8-	Nystad et al (330) (cross-sectional study)	Norway	2188 (6-16 yrs old) asthmatic and non-asthmatic children	Questionnaire.	Positive association between bronchial hyper-responsiveness and decreased hours of exercise per week
9-	Cheng et al (331) (cross-sectional study)	China	232 (7-14 yrs old) asthmatic and non-asthmatic children	Questionnaire	Asthmatics (8.94)%) vs non asthmatics (26.61%) achieved ≥60 minutes of exercise per day

There is also a body of literature suggesting no difference between the physical activity of asthmatic and non-asthmatic children (Table 1-6). These studies were of different types, different sample sizes, examined asthmatic children of different severities and different ages, were conducted in different countries, and used different monitoring methods (Table 1-6). In 1997, Nystad et al (332) published his cross-sectional study, in which 4585 Norwegian school children aged 7-16 years old were surveyed by questionnaires to compare physical activity level of asthmatic to non asthmatic children. This study suggested that physical activity of both groups were similar (Table 1-6). Jones et al (333), studied 13,222 American high school students aged 9-12 years old, surveyed by questionnaires, and suggested that both asthmatic and non asthmatics were similar in vigorous or moderate physical activity or strengthening exercises (Table 1-6). Furthermore, in a cross sectional study in the Netherlands, Van Gent et al (334), used accelerometers, diaries and questionnaires to examine the effects of asthma on physical activity of 81 diagnosed asthmatics, 130 undiagnosed asthmatics and 202 healthy controls aged seven to ten years old. The study suggested that both asthmatic and non asthmatic children were of similar physical activity (Table 1-6). A cohort study of Eijkemans et al (335) used both accelerometers and self-reported data to compare physical activity of 81 Dutch wheezier children to 221 non wheezier children aged four to five years old and suggested that both wheezy children and non-wheezy children had similar physical activity levels (Table 1-6). In 2009 four studies were published; two in USA, one in Denmark, and one in Norway. Rundle et al (336) used actiwatch accelerometers to study 433 American children aged four years old and found that there was no association between asthma symptoms and PA(Table 1-6). A case controlled interventional study was conducted by Walders-Abramson (337), to compare the PA of a group of 59 asthmatic American children aged 10-16 years old to a group of 59 non asthmatic children using pedometers. The physical activity of the two groups was compared at baseline and after walking programme and found that both asthmatic and non asthmatic children were of similar physical activity both at baseline and after walking programme (Table 1-6). In Denmark, Vahlkvist et al (338) conducted a case–

controlled study and used RT3 accelerometers to compare physical activity of newly diagnosed untreated asthmatic children to that of healthy controls aged 6–14 years old. The study suggested that there was no difference in physical activity between asthmatic and non-asthmatic children (Table 1-6). Accelerometers were used by Berntsen et al (339), to compare differences in physical activity between 95 asthmatic and 79 non-asthmatic Norwegian children aged 13-14 years old and showed that both asthmatics and non-asthmatics were similar in time spent in moderate to very vigorous intensity PA (Table 1-6). In the following year, Vahlkvist et al (340), conducted another case–controlled study in Denmark and used the same RT3 accelerometers used in his previous study, to compare physical activity between 55 newly diagnosed untreated asthmatic children and 154 healthy controls aged 6–14 years old. The study showed that at baseline there were no differences between asthmatics and their controls in daily activity except in 38 asthmatic children (most of them were of uncontrolled asthma) who spent less time in vigorous activity than controls (Table 1-6). At the end of the study, there were no differences in daily physical activity between the two groups; neither time at rest, light-vigorous, moderate-vigorous or vigorous activity (Table 1-6). This was followed by two studies one in USA and another in Korea. Tsai et al (341) did a secondary analysis of a cross-sectional study where accelerometers were used to investigate the PA of 27 asthmatic and 27 non-asthmatic American children aged 9-11 years old and showed that both asthmatic and non-asthmatic children were of similar physical activity (Table 1-6). Kim et al (322) conducted a questionnaire survey to study 72 943 Korean children aged 13–18 years old and showed that there was no significant difference in vigorous or moderate PA between asthmatic and non-asthmatic children (Table 1-6). In 2013, Vangeepuram et al study (342) was published. This study was a cross-sectional study used pedometers and self-reported data to investigate PA of 1182 American girls aged six to eight years old (191 were asthmatic girls) and showed that there were no significance differences in PA between asthmatic and non-asthmatic children (Table 1-6). Within the same year, a case controlled study of Lawson et al (343) showed that there was no difference in PA between asthmatic and non-asthmatic Canadian children investigated by questionnaires (Table 1-6). Similarly, in the following year four studies from different countries suggested the same finding. Driessen et al (344) used actiGraph accelerometers to follow up the physical activity of 347 Dutch children from second year of life and showed that there was no difference in PA between asthmatic and non-asthmatic children and there might be no role for PA in the development of respiratory symptoms in pre-school children (Table 1-6). Fedele et al (345), suggested that

there was no difference in accelerometer measured PA of 175 obese non-asthmatic and 73 obese asthmatic American children aged 7-12 years (Table 1-6). Similarly, Sousa et al (346) compared PA measured by accelerometers of 79 asthmatic to 42 non-asthmatic Brazilian children aged 7-12 years old and showed that there was no difference in PA between them (Table 1-6). Likewise, Santos-Silva et al (347) reached the same finding by using physical activity questionnaires to compare PA of 155 controlled asthmatic to 158 healthy control Portuguese children aged 5-18 years old (Table 1-6). Therefore, 17 studies; twelve objective studies and five subjective studies, all showed that there were no difference in PA between asthmatic and non-asthmatic children (Table 1-6).

Table 1-6 Studies suggesting that there is no difference in physical activity between asthmatic and healthy children

	Study	Country	Participants	Method	Outcome
1-	Nystad et al (332) (cross-sectional study)	Norway	4585 (7–16 yrs old) asthmatic and non-asthmatic children	Questionnaire	No significant difference in exercise frequency
2-	Jones (333) (cross-sectional study)	USA	13,222 (9-12yrs old) asthmatic and non-asthmatic children	Questionnaire	No significant differences in participation in VPA or MPA or strengthening exercises
3-	Van Gent (334) (cross-sectional study)	Netherland	413 (7–10 yrs old) asthmatics and non-asthmatics	-PAM accelerometer -Activity diary - Questionnaire	No difference in PA between study groups
4-	Eijkemans (335) (cohort study)	Netherland	305 (4-5 yrs old) asthmatic and non-asthmatic children	-Actigraph accelerometer -Questionnaire	Similar activity levels for wheezing and non wheezing children
5-	Rundle et al (336) (cohort study)	USA	433 (4 yrs old) asthmatic and non-asthmatic children	Actiwatch accelerometer	No significant difference in mean physical activity counts per minute
6-	Walders-Abramson et al (337) (case-controlled study)	USA	118 (10-16 yrs old) asthmatic and non-asthmatic children	Pedometer	No significant difference in median steps between asthmatics (baseline steps: 6348, follow-up steps: 7644) and non asthmatics (baseline steps: 6825, follow-up steps: 9364)
7-	Vahlkvist (338) (case-controlled study)	Denmark	214 (6–14 yrs old) asthmatic and non-asthmatic children	RT3 accelerometer	No significant differences in overall daily PA , time spent in high or vigorous activity
8-	Berntsen	Norway	174 (13–14 yrs old)	Armband	No significant difference in

	(339) (case–controlled study)		asthmatic and non-asthmatic children	activity monitor	aerobic fitness, total energy expenditure and time of MVPA during week and weekend
9-	Vahlkvist et al (340) (cohort study)	Denmark	209 (6–14 yrs old) asthmatic and non-asthmatic children	RT3 accelerometer	-At baseline no differences between asthmatics and non-asthmatics in daily PA except in 38 children (uncontrolled asthma) spent less time in vigorous activity than controls. -At study end (asthma symptoms controlled) no difference in daily physical activity (neither time at rest, light-vigorous, moderate-vigorous or vigorous activity)
10-	Tsai et al (341) (secondary analysis of cross-sectional study)	USA	54 (9-11 yrs old) asthmatic and non-asthmatic children	Actiwatch accelerometer	No difference in PA (light, moderate, vigorous and MVPA)
11-	Kim et al (322) (cross-sectional study)	Korea	72 943 (13–18 yrs old) asthmatic and non-asthmatic adolescents	Questionnaire	No significant differences in participation in VPA or MPA, strengthening exercise or physical education classes
12-	Vangeepuram et al (342) (cross-sectional study)	USA	Total 1182 girls (6–8yrs old) asthmatic and non-asthmatic children	-Pedometer -Questionnaire	No significance difference in step counts)
13-	Lawson et al (343) (case-controlled study)	Canada	295 (6-18 yrs old) asthmatic and non-asthmatic children	Questionnaire	No significant difference in activity level between asthmatics (79.3 %) and non asthmatics (77.4 %)
14-	Driessen et al (344) (sub cohort study)	Netherland	347 (25 months old) asthmatics and non-asthmatics	ActiGraph accelerometer	No difference in total activity
15-	Fedele et al (345) (cross-sectional study)	USA	248 (7-12 yrs old) obese asthmatics and obese non-asthmatics	Sensewear armband accelerometer	No significant difference in PA (total activity)
16-	Sousa et al (346) (cross-sectional study)	Brazil	121 (7-12 yrs old) asthmatic and non-asthmatic children	Power Walker-610 accelerometer	No difference in PA (total number of steps, and number of steps in moderate physical activity)
17-	Santos-Silva et al (347) (cross-sectional study)	Portugal	313 (5–18yrs old) asthmatic and non-asthmatic children	Physical Activity Questionnaire (PAQ)	No differences in physical activity score between allergic and healthy children (2,40 ±0,7 vs 2,48 ±0,62)

These studies were very heterogeneous using different sample sizes, different monitoring methods and conducted in different places which limit the generalisability of their findings. Thus there is a clear disagreement in the area of the relationship between asthma and

physical activity in children in the literature. Even those studies which reached similar results were heterogeneous, of different types, using different sample sizes, examining asthmatic children of different severities and different ages, and were conducted in different countries, and used different monitoring methods. Perhaps not surprisingly, the results of two systematic reviews conducted to review studies examined the relationship between physical activity and asthma in children were different. Eijkemans et al (348) did a systematic review and meta-analysis which suggested that the severity of asthma was negatively associated with the PA level. A total of 39 studies in this review investigated the PA of asthmatic and non asthmatic participants of a very wide age range, from preschool age till adult age. There were five subjective longitudinal studies that used questionnaires to monitor PA and thirty four cross-sectional studies; 27 of which were subjective studies and used questionnaires to monitor PA and seven were objective studies; six of which used accelerometer and one used pedometers to monitor PA. However, Cassim et al (349), did a systematic review and meta-analysis that reviewed objective studies (accelerometer or pedometer devices) that compared the PA of asthmatic and non-asthmatic children and adolescents aged until 18 years old. They showed that there was no difference in PA between asthmatic and non-asthmatic children. In this review, twelve studies were selected: one longitudinal, ten cross-sectional and one case-control. Four studies examined preschool aged children; one cohort and two cross-sectional studies showed that asthmatics were not less physically active than non-asthmatics and only one cross-sectional study showed that children with history of wheezing were significantly less active than non-wheezing children. Only one cross-sectional adolescent study showed that asthmatics and non-asthmatics were similar in MVPA. Seven studies examined school-aged children; one case-control and six cross-sectional studies all showed that there were no differences in PA between asthmatics and non-asthmatics. The results of these two systematic reviews were different and this might be due several reasons such as: the difference in the age range of the studies included as physical activity levels change with age (53, 68, 75, 80). Most of studies included in Eijkeman's review were subjective (used questionnaire to monitor PA, a method that is limited by recall bias) while studies included in the Cassim review were objective (used accelerometer or pedometer devices to monitor PA). This difference in PA monitoring methods might have led to different results. Asthma was diagnosed differently in the studies included in these reviews, in some of these studies asthma was diagnosed according to self-reported data and in other studies it was diagnosed by a doctor or according to pulmonary function test (PFT), that means the severity of asthma and degrees of

bronchoconstriction of participants were different and that might led to variations in the degree of restriction of their PA and variations in the results. There is a need for a systematic review of studies that investigated PA of asthmatic children of similar age ranges, similar degree of asthma severity using objective monitoring methods to monitor PA. In an attempt to provide greater clarity about differences in PA among primary school children with asthma and healthy children, the researcher of this thesis undertook such a systematic review. The methodological details and the results are presented in Chapter2.

1.6.3.9.3 Sedentary behaviour and asthma

There are a small number of studies that have investigated the association of asthma and sedentary behaviour in children. Most of these studies as noted in section 1.3.1 have focused on screen based activities, such as time of watching TV, playing video games or working on a computer as a representative for total sedentary behaviour.

Multiple studies reported a positive relation between SB and asthma. Examples include: Tsai et al (350) with self-reported data of 2290 Taiwanese children aged 11–12 years old that showed that watching TV ≥ 3 hrs/day was linked to high incidence of respiratory symptoms; a survey of 700 Greece children aged 11-12 years old conducted by Priftis et al (351), suggested that asthma symptoms were positively associated with watching TV or playing videogames time among boys, but not among girls; Corbo et al (352) used parent reported data of 20,016 Italian children aged 6–7 years, to report that asthma was more associated with watching TV for ≥ 5 hours per day; a longitudinal study conducted by Sherriff et al (353), that followed up a 3065 British children, showed that the prevalence of asthma at 11.5 years of age is positively associated with the length of TV watching time per day. Also, those children who were free of wheezing at 3.5 years old and were watching TV for more than 2 hours/day were more likely to have developed asthma compared to those who were watching TV for less time; Tsai et al (354) used self-reported data from 1329 Taiwanese children aged 11–12 years old and suggested a significant correlation between respiratory symptoms and both TV viewing time per day and self reported sedentary time per weekend day in Taiwanese girls. As part of the International Study of Asthma and Allergies in Childhood (ISAAC) phase three, Mitchell et al (355), studied 76,164 children (21,653 with objective data and 54,511 with parent reported data) aged 6–7 years old from 29 centres and 17 countries and 201,370 adolescents (48,202 with objective data, 150,286 with parent reported data and 2882 data collection method could not be ascertained) aged

13–14 years from 73 centres and 35 countries and showed that watching TV for ≥ 5 hours/day was linked to an increased risk of asthma symptoms. Almost all of these studies have mostly focused on screen based activities as a representative of total sedentary behaviour. An exception was the study of Mitchell that used both objective and subjective data to monitor sedentary behaviour. Thus overall, the results of these studies might be challenged due to the fact that TV watching time has been shown to be not a good proxy representative for total sedentary behaviour (137). It is worth noting that these studies are looking at the relation between sedentary behaviour and the development of asthma rather than any relation between established asthma and sedentary behaviour activity.

Other studies showed no relation between SB and asthma, while a third group reported that children with asthma were less sedentary than non-asthmatics. According to secondary analysis of a cross-sectional study where accelerometer was used, Tsai et al (341) reported that there was no difference in sedentary behaviour of 27 asthmatic and 27 non asthmatic American children aged 9-11 years. In a cross-sectional study conducted by Vangeepuram et al (342) that used both pedometer and self-reported data to investigate sedentary behaviour of 1182 American girls (191 were asthmatic) aged 6-8 years old, there was no significant difference in SB between asthmatic girls and non-asthmatic girls. Finally, Bringolf-Isler et al (325) investigated the sedentary behaviour of 352 Switzerland children (42 asthmatic) using self-reported data and Actigraph accelerometer measurements and suggested that asthmatic children were less sedentary than non asthmatic children. Although these studies used objective methods of activity monitoring, they were heterogeneous in type and place of study, in sample size, in age and severity of asthma of asthmatic children and in monitoring methods used, which limits the generalisability of the results of these studies.

Similar to what was noted above about the disagreement in the relationship between asthma and PA in children, it is evident that there is a conflict about the relationship between asthma and SB in children in the literature. Even those studies that reached similar results were heterogeneous; different types of studies, examined asthmatic children of different severities and different ages, conducted in different countries, and used different monitoring methods. Again, these factors limit the generalizability of the results of these studies. Hence, once again, there is a need for systematic review to review studies that investigated SB of asthmatic children of a similar age range, similar degree of asthma severity and used objective monitoring methods to monitor PA. In an attempt to provide greater clarity about

differences in SB among primary school children with asthma and healthy children, the researcher undertook just such a systematic review. The methodological details and the results are presented in Chapter 2. Furthermore, from the data reviewed it appears that there are no studies that have investigated factors other than the total amount of SB in children with asthma, which indicates a need for research to investigate the relationship of both volume and pattern of SB to the severity of asthma in children. Again, the present study set out to examine the association of both volume (total sitting time and percentage sitting time) and pattern (number of breaks, number of sedentary bouts and fragmentation index) of SB to the degree of severity of asthma in children.

1.6.3.9.4 Sleep and asthma

The relationship between asthma and sleep is complex and contradictory, some studies showing that asthma disturbs sleep of children while others do not.

Among studies which showed that asthma disrupts sleep include: Kales et al (356), who monitored sleep of 10 asthmatics children aged 7-15 years old for 25 nights by polysomnography and showed that sleep of asthmatic children was interrupted by recurrent awakenings and diminished sleep time; Sadeh et al study (357) who monitored sleep of 40 Israeli asthmatic children aged 8.2 to 15.4 years old by actigraph accelerometer and sleep questionnaire and showed that asthmatic children had low percent of quiet sleep, extra morning tiredness, extra morning wakeup difficulty, were less alert and preferred later bedtime; Desager et al (358) who investigated 1234 Belgians children aged 6–14 years by ISAAC questionnaire and a separate sleep questionnaire and suggested that wheezing was significantly associated with restless sleep, nocturnal awakenings, daytime sleepiness and tiredness; Verhulst et al (359) who analyzed 652 ISAAC questionnaires of Sri Lankan children aged 6–12 years and suggested that wheezing children reported restless sleep, nocturnal awakenings, daytime tiredness more than non-wheezing children. In contrast, the cohort study of Tirosh et al (360) investigated 752 Israeli children aged 4 months to 4 years by questionnaire and showed that there was no difference between asthmatics and healthy comparison in sleep characteristics such as number of nights per week in which sleep was interrupted, awakenings number, day and night sleep latency, settling, awakening time, sleep duration, night sleep and settling age onset. In a longitudinal study Stores et al(361), examined sleep of 20 British asthmatic children (mean age of 10.8 yrs) by home polysomnography and parental questionnaires when asthma was not controlled and when controlled, and illustrated that independent of asthma control the sleep time of asthmatics

was similar to that of healthy children, but the sleep disruption resolved when asthma symptoms were controlled. In a cohort study, Camhi et al (362) investigated 452 American children aged 3-14 years old by questionnaire and showed no significant association between asthma and sleep troubles, but wheezing was significantly associated with difficulty in falling asleep, staying asleep, early awakening and inability to get back to sleep. Finally, Ronchetti et al (363) conducted questionnaire based cross-sectional surveys in Rome at two time points, in 1992 (examined 1,262 students aged 6–14 years) and 1998 (examined 1,210 students aged 6–14 years), and showed insignificant associations between sleep troubles and asthma.

Similar to what is noted above about the disagreement in the relationship between asthma and PA and SB in children, in the literature there is thus a contradiction in the area of the relationship between asthma and sleep in children, with some studies suggested that asthma disturbs sleep of children while others do not. Even those studies which reached similar results were heterogeneous: different types of studies, different ages and different severities of asthmatic children, different monitoring methods and performed in different countries. These factors restrict the generalizability of the results of these studies. Therefore, to reach evidence in this area, there is again a need for systematic review to review studies that investigated sleep of asthmatic children of a similar age range, with similar degrees of asthma severity and preferably using objective monitoring methods to monitor PA.

1.7 Methodological background for studying components of the movement continuum in children with asthma

1.7.1 Introduction

This section describes the methods that have been used in studying and assessing control of asthma symptom, physical activity, sedentary and sleep behaviours.

1.7.2 Asthma symptom control assessment

Asthma control is the term used to characterise how well the symptoms of asthma are reduced or removed by treatment (364). Asthma control is of importance to the patient. Asthma control refers to control of the clinical manifestations of disease. The goal of asthma treatment is to gain full control of asthma, a control that should be maintained for a prolonged time with treatment causing the least possible side effects and at the lowest possible cost (364). It is increasingly recognised that no single measurement can capture all

dimensions of asthma control and different dimensions of asthma control are measured by using several methods. Amongst the most commonly used are: 1) clinical interview of the patient 2) subjective assessments of symptoms using questionnaires and 3) objective methods such as measurements of pulmonary function (PFT).

1.7.2.1 Subjective methods of assessing asthma

In measuring asthma control, subjective assessments assess common asthma symptoms, such as limitation of physical activity, nocturnal disturbance, and amount of rescue medication used to relieve asthma symptoms to decide whether asthma is controlled or not. Traditionally, a doctor would question the parent and child about relevant symptoms and the use of relieve medication. The doctor would internally evaluate the answers to reach a qualitative assessment of asthma control. Nowadays, standardised, validated and responsive questionnaires have been developed for assessing asthma control in children. These are now widely available and are particularly useful in research studies. Examples include: the Asthma Control Test (ACT) (365), Asthma Quiz for Kidz (366), The Asthma Therapy Assessment Questionnaire (ATAQ) (367), Childhood Asthma Control Test (CACT)(368), and Paediatric Asthma Control Questionnaire (PACQ) (369). Such questionnaires ask the parent or child to answer questions about how the child's asthma has been controlled in a time period, usually the last week or the last month depending on the questionnaire and allow a semi-quantitative assessment of asthma control. However, they may be subject to recall bias owing to the fact that answering these questionnaires may be affected by mood and memory of the patients or care-givers who answer them. Different questionnaires are used in different parts of the world. Translations of such questionnaires into different language are often quite limited in their availability. Commonly used examples are discussed in detail below.

Asthma Control Test (ACT)

The Asthma Control Test (ACT) was developed by Nathan et al (365) and assesses asthma control over the last four weeks by five criteria: amount of time that asthma interfered with life at work, school or home; frequency of shortness of breath; frequency of night-time waking due to asthma symptoms; frequency of use of rescue medications; and patient self-assessment of degree of asthma control. Each item is scored from 1 to 5 points where 1 is uncontrolled and 5 well controlled. The total scoring for ACT then can range from 5 (indicating poor control) to 25 (indicating good control) providing a numerical score

indicating the degree of asthma control. A score of 19 or less indicates poorly controlled asthma. This instrument has been validated for subjects aged 12 years or over.

Asthma Quiz for Kidz

The Asthma Quiz for Kidz is a validated questionnaire developed by Ducharme et al (366). It was developed for completion by children between 9 and 17 years of age, or by their parents for children younger than 9 years. Depending on the question, it asks the respondent to reflect on recent asthma symptoms and then to answer 6 questions dichotomously as follows: were there asthma symptoms such as cough, wheezing and difficulty in breathing for 4 days (or more) out of last seven days? (Y/N); was their waking at night caused by asthma symptoms for one or more times in last 7 days? (Y/N); was their use of blue puffer or pump for 4 or more times in last 7 days? (Y/N), did the subject undertake less exercise or sport due to asthma symptoms in last 7 days? (Y/N); did the subject miss school or regular activities because of coughing, wheezing or difficulty breathing in last 30 days? (Y/N); were there any unplanned clinic or hospital visit because of coughing, wheezing or having a hard time breathing in last 30 days? (Y/N). Each item of the Asthma Quiz for Kidz is scored 1, and the total score can range from 0 to 6 points, where 0 is controlled and 2 or more out of 6 is uncontrolled asthma, and should prompt the need to consult a paediatrician.

Asthma therapy assessment questionnaire (ATAQ) for children and adolescents (370)

The Asthma Therapy Assessment Questionnaire (ATAQ) for children and adolescents is used to help in discovering those asthmatics at risk for undesirable outcomes of asthma. ATAQ is a brief questionnaire completed by parent or guardian that can help in identifying probable care problems such as poor control of asthma symptom, behaviour and attitude barriers, self-efficacy barriers, and communication gaps. Asthma control is assessed by seven questions related to symptoms and consequences of asthma within the last four weeks (wheeze or difficult breathing during exercise, wheeze when not exercising during day, nocturnal awakenings with wheeze or difficult breathing, school absence due to asthma, loss of daily activities due to asthma, use of quick reliever and parent assessment of child’s asthma control) with each item scored from 0 to 1 point and the response for the seven questions summed. The total score ranges from 0 to 7 where 0 is uncontrolled and 7 well controlled asthma. Behaviour and attitude barriers to effective asthma management are evaluated by two questions; dissatisfaction with any part of current asthma treatment and

use of controller medications. Self-efficacy barriers are assessed by three items; belief that child is taking medications as directed, a belief that medications are useful to control asthma and that the parent has access to enough information to help child control his/her asthma. Communication gaps with treatment providers are evaluated by five items; patient and provider joint decision-making, provider knowledge of child's preferences for taking asthma medicines, provider reviews of medications with child and parent, whether patient received written instructions on what to do when having an asthma attack, and whether patient received written instructions on how to take medicines on days when not having an asthma attack.

Childhood asthma control test (CACT)

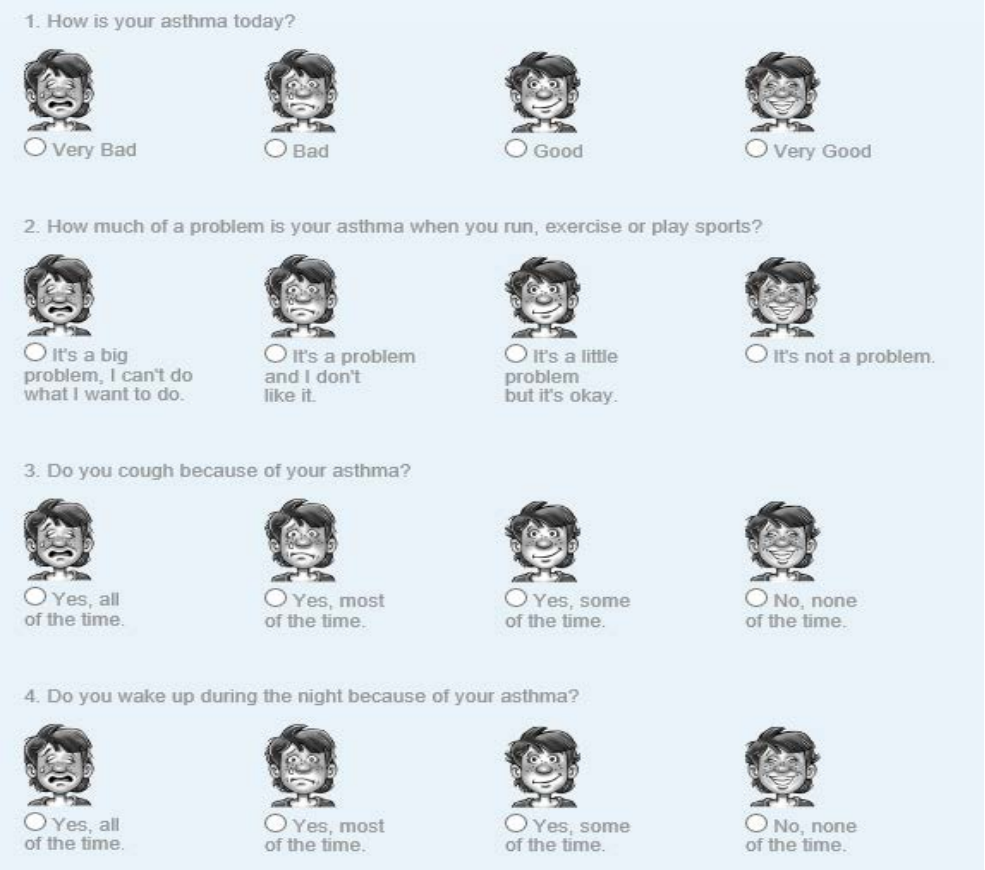


Figure 1-3: Childhood asthma control test questionnaire; child section (371)

The Childhood Asthma Control Test Questionnaire (CACT) was developed by GlaxoSmithKline (371) and validated by Liu et al (372). It was developed for children

between 4 years and 11 years. The CACT consists of 7 questions in two parts; one completed by the child with asthma and one by his/her parent/guardian. The child part consists of 4 questions (Figure 1-3), while the parent/guardian part consists of 3 questions (Figure 1-4). The child section assesses asthma control based on four items: daytime asthma symptoms, restriction of activity due to asthma, frequency of cough owing to asthma and waking at night because of asthma. Each item of the child's part is scored by the child from 0 to 3, where 0 means symptoms very bad and 3 means symptoms very good or no symptoms. The sum of responses in this part ranges from 0 indicating uncontrolled asthma to 12 indicating well controlled asthma.

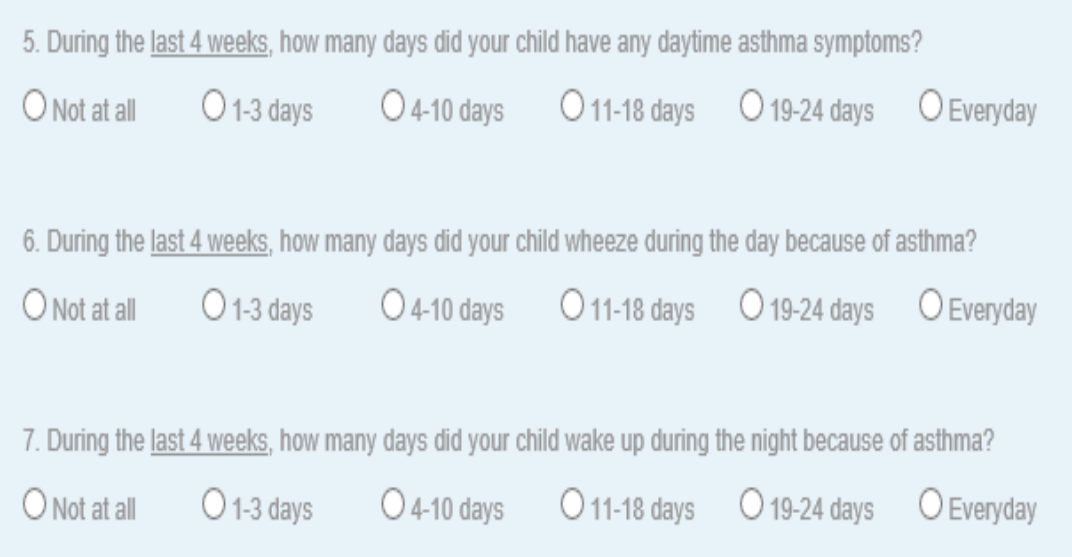


Figure 1-4: Childhood Asthma Control test Questionnaire questions to be answered by parent/guardian of child (371)

The parent/guardian section of CACT (Figure 1-4) is related to asthma control over the previous 4 weeks and asks about any asthma symptoms, wheeze due to asthma and waking due to asthma. Each item of this part is scored from 0 to 5, where 0 means symptoms are very bad, while 5 means symptoms are very good or there are no symptoms. The sum of responses in this part ranges from 0 indicating uncontrolled asthma to 15 indicating well controlled asthma. The total score of the two parts of CACT are added together with results ranging from 0 indicating uncontrolled asthma to 27 indicating well controlled asthma.

Paediatric Asthma Control Questionnaire (PACQ)

The PACQ was developed to assess asthma control by Juniper et al (369). It requires recall of asthma symptoms in the last week to answer the questions. The first five questions are about asthma symptoms (waking at night, day time symptoms, restriction to activity, breathlessness, and wheeze), the sixth question is about the number of puffs of short-acting β2-agonist used every day. The seventh question relates to airway calibre measured as FEV_1 and recorded as percentage of predicted normal value. Items of the ACQ are equally weighted and scored between 0 and 7. A composite ACQ score is the mean of the seven items and lies between 0 indicating well controlled and 6 indicating extremely poorly controlled asthma. The PACQ therefore differs from other scales listed here because it is a composite score of subjective and one objective measure of asthma control.

1.7.2.2 Objective methods of assessing asthma

Pulmonary Function test (Spirometry)

Spirometry (meaning literally the *measuring of breath*) is the most common of the physiological tests used to measure pulmonary function (PFTs). Spirometry specifically measures the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled (373). Around 50% of 6 years old and 85% of 10 years old children can perform the required forced expiratory manoeuvre which can be repeated within the same testing session (374, 375). In order to get valid and reliable results, both the equipment and the testing techniques used in spirometry must be carefully standardised. The American Thoracic Society and European Respiratory Society have published guideline documents describing in detail how spirometry should be performed and interpreted (373, 375, 377). To make sure that these standards are applied and to avoid accuracy falls from poor quality measurements, particularly in children, it is desirable to perform spirometry in specialised units based in hospitals using appropriately trained staff (378, 379). Calibrating spirometers before use, ensuring good maintenance of equipment, and ensuring spirometry testing is performed by well-trained and experienced person are all important in maintaining quality control (375). In addition, the patient plays a major role in this test. It is essential to instruct and encourage the patient during testing to give a maximal forced expiratory effort while performing the test (375). Commonly made measurements from spirometry include the forced vital capacity (FVC), the forced expiratory volume in 1 second (FEV_1) and the FEV_1/FVC ratio. FVC is total quantity of air forcefully exhaled following a maximum inspiration (380, 381), FEV_1 is amount of air exhaled in the first second of a forced

expiration starting immediately after a maximum inspiration (380, 381). In children, measurements of FEV_1 and FEV_1/FVC must be related to normative reference data. Reductions in FEV_1 and FEV_1/FVC below the lower limits of normal values (the normal FEV_1/FVC ratio is greater than 0.9 in children (33)) indicate the presence of airway obstruction. PFT results in children are influenced by age, height, sex, and race, so are best expressed as a standard deviation or Z score which provides a standardised measure of lung function in relation to a reference population (382). The FEV_1 is a good marker of airway obstruction owing to its reproducibility and its linear relationship with worsening of airway obstruction (383). It also related to the future risk of asthma attacks in children (384).

Airway obstruction can also be assessed by peak expiratory flow (PEF). Although, PEF meters are very cheap and easy to use, they are not as accurate as FEV_1 in indicating severity of airway obstruction (383).

1.7.3 Physical Activity assessment

Measuring PA is not easy especially in children. Further in assessing physical activity it is necessary to think carefully about what is being measured. Physical activity has a number of dimensions, such as frequency, duration, intensity and mode of activity, all of which may be important to measure. Frequency can be defined as the number of PA episodes within certain time interval; duration can represent the length of a single bout of PA or it may be aggregated into how much activity occurs in a given time period. Intensity refers to the physiological effort correlated with performing PA while mode of PA refers to the types of PA e.g. running, jogging or walking (45, 46). Many valid and reliable methods have been developed for assessing physical activity in children for use in research studies (385). These methods broadly fall into three groups: (a) criterion (reference) methods; (b) objective methods and (c) subjective methods. The last two methods have been commonly used in epidemiological research and clinical studies for evaluating physical activity (46).

In the following sections, the methods of assessing PA in children are summarised.

1.7.3.1 Methods of monitoring physical activity

1.7.3.1.1 Criterion methods of monitoring physical activity

Criterion methods for physical activity assessment in children and adolescents include direct and indirect calorimetry, doubly labelled water (DLW), and direct observation. These have often been used to validate simpler methods (386).

Direct calorimetry measures the heat production of an individual performing an activity when placed in an insulated chamber (calorimeter) where the heat produced is transferred to surrounding water. This is a very accurate method for measuring energy expenditure (387). Although this method can accurately measure EE and thus assess PA, it is impractical due to the complexity of the equipment and its high cost so it is not often used in studies in children.

Indirect calorimetry is used to measure EE at rest and during stable exercise from the consumption of O_2 and the production of CO_2 while breathing into a ventilated hood (or in a respiration chamber) over a period of up to 30 min. Fractions of O_2 and CO_2 gases are estimated in total expired gas volume measured by gas sensors, and converted into values for O_2 consumption and CO_2 production in ml/min, and finally into EE at rest or during exercise expressed as kcal (or kJ)/day(388-392). This method is a time-consuming process performed on an individual basis making it impractical for assessing PA of studies of large numbers of subjects, but it can be used to validate simpler forms of PA assessment in children (386).

Doubly labelled water (DLW) is considered the gold standard method for evaluating energy expenditure (EE). In this method, a standardised amount of two stable non-radioactive-labelled isotopes (^2H and ^{18}O) is consumed by the child as water enriched with heavier isotopes of hydrogen and oxygen ($^2H_2{}^{18}O$). Most of the hydrogen and oxygen isotopes are lost through excretion and evaporation, but some of the oxygen isotope in the doubly labelled water equilibrates with carbon dioxide and is expired in air. Deuterium (2H) is cleared from body only as water (^2H_2O), while ^{18}O is removed either as water ($H_2{}^{18}O$) or carbon dioxide ($C^{18}O_2$), over a period of between 5 and 14 days. The rate of elimination of these isotopes is measured and the difference in elimination rates provides a measure of CO_2 production and hence of energy expenditure (393). This method is safe, easily applied and is not affected by and does not affect PA patterns. It has been validated in adults but not in children. Its accuracy in adults ranges from 3 to 10% (394, 395) with a relatively low within-subject variability (396). However, it is costly and there are difficulties obtaining the ^{18}O isotope.

In direct observation (Behavioural) methods, the PA of children is either observed directly while playing, exercising or walking in a confined area such as home or school for a certain time interval or all activity is recorded on videotape for later analysis. Data gained from this method is either recorded manually on a coding form or fed into a computer that

summarizes it as a score (385, 397-399). This procedure has the advantage of observing and documenting the type and intensity of activity as well as the environment in which activity is carried out. It is useful for studying small children who have limited recall ability and cannot remember their activity exactly. However, it is costly, requires well-trained observers and cannot be applied in large population studies. The method can only be used in relatively confined spaces. For older subjects there is the possibility that if they know they are being observed their activity may be influenced. Studies have shown this method is reliable (repeatable) (400-402) and valid (400, 401).

1.7.3.1.2 Subjective methods of monitoring physical activity

Subjective methods are the most commonly used method of monitoring PA (46, 385, 403) using approaches such as self-report, interviews, proxy-report (informed by another person usually parent for children under 10 years old), diaries and questionnaires (46, 385, 399, 403-405). Subjective methods are generally low cost and do not require a well- trained researcher to apply them. These points are amongst the main reasons behind their extensive use in large populations and in epidemiological studies. They have limitations, such as recall bias and they may be affected by the opinions and perceptions of the reporter (46, 385, 403). These methods have often been shown to be of low reliability and validity (406).

1.7.3.1.3 Objective Methods of monitoring physical activity

Objective measures of physical activity make use of devices such as pedometers and accelerometers that can measure movement counts and acceleration, respectively.

1.7.3.1.3.1 Pedometers

Pedometers represent the simplest valid (407) and reliable (408) type of motion sensors that can be attached to subjects for monitoring the acceleration and deceleration of movement in a vertical direction. They can be used to assess number of steps taken over a long duration of time (409). In the majority of pedometer types, steps are recorded in response to a foot hitting the ground (representing the vertical force or vertical acceleration of hips during the movement) (410-412).

This moves a vertical lever arm that is supported by a spring inside the pedometer making a mechanical contact that records a step (410-412). By calibrating the pedometer for an individual’s stride length, one can calculate how much distance has been covered (412). Since pedometers record the total number of steps taken they can provide a measure of total

ambulatory activity, and hence they can be used in studies measuring total volume of walking activity (46, 409). The devices are now cheap and reusable (408, 409, 413, 414). However, a pedometer does not evaluate intensity, pattern, duration, or frequency of activity bouts, and studies have shown errors at low and high speeds with underestimates at both slow and fast walking speeds (409, 414, 415).

1.7.3.1.3.2 Accelerometers

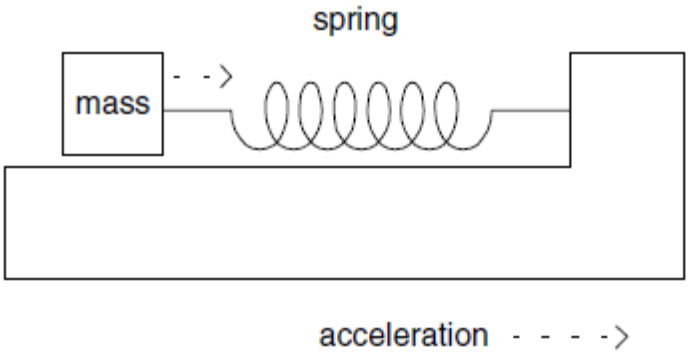


Figure 1-5: A piezoelectric accelerometer works like a simple mass spring system reproduced from (416)

Accelerometers are motion sensors in which movement is recorded by piezo-electric transducers and converted by microprocessors into movement counts (409). The most modern versions include an inclinometer that enables the device to recognise whether a person is either sitting/lying (horizontal) or standing (vertical). Current accelerometers are small devices that are usually attached to the hip, the wrist or ankle. They do not interfere with or interrupt PA and are reusable (409, 417). The pattern and intensity of activity and total accumulated activity can be monitored (417). Because of their validity, low cost, small size, ability to monitor sit-stand-sit movement cycle and the fact that they can record data continuously for long durations of days without loss of quality and reliability (418-420) they have become the method of choice for the objective monitoring of movement in field conditions. Because of their small size, PA in children is now commonly investigated using accelerometers (417), especially in assessing habitual physical activity in preschool children. Nevertheless, accelerometers have some disadvantages. They do not reliably detect upper body torso movements in some types of physical activity like swimming and cycling (418). Many are also not water proof so cannot be used during water based activities.

Accelerometers used in studying PA are either piezoelectric, piezo-resistive, or differential capacitor devices. Essentially, all share the same mechanism of function which is that of a spring mass system (seismic mass) within the accelerometer (Figure 1-5). A small mass responds to acceleration by stretching or compressing the spring, and then the displacement of spring is recorded to estimate acceleration (416, 420). Piezo-resistive accelerometers are composed of polysilicon springs (arranged in a Wheatstone bridge configuration) located on the surface of micro-machined poly-silicon structure. The electrical resistance of the spring changes according to the applied acceleration force and the voltage produced is proportional to the amplitude of acceleration (416, 420). Piezo-electric accelerometers are composed of a piezo-electric element with a seismic mass (spring mass system). When acceleration is applied, the seismic mass causes the piezoelectric element to move. Charge builds up on one side of sensor resulting in an output voltage signal that is proportional to the acceleration force applied (420). Differential capacitor accelerometers are composed of a differential capacitor, with central plates connected to the moving mass and fixed external plates. The principle of function of this type depends on the fact that the capacitor will be unbalanced when acceleration is applied. This causes an output wave that is proportional to the amplitude of acceleration applied (416, 420).

Accelerometer output depends on its position in the body, its orientation in relation to the body, and the posture and the activity of the subject to whom the accelerometer is attached (416). The choice of accelerometer location on the body is important in monitoring body movement and it should be attached to the body part whose movement is being assessed (416). Accelerometers are typically of two types: (a) uniaxial accelerometers where acceleration is recorded in one direction (usually vertical), (b) triaxial accelerometer where acceleration is recorded in three orthogonal axes to give a three dimensional picture of acceleration (416). At rest, accelerometer output is influenced by its orientation in relation to the force of gravity, while, the signal of a moving body is a combination of the body's orientation in relation both to gravity and the movement (416). The majority of human movements range in frequency between 0.3 and 3.5 Hz (416, 421). A filter with a cut off frequency between 0.1 and 0.5 Hz is used to sort the two components of static orientation and body movement (416, 422-424).

An important concern of monitoring PA of children by accelerometers is the reactivity of the monitored child to the accelerometer used (425-427). Child awareness of being monitored by accelerometer may influence the habitual PA especially on the first day of

monitoring, where the child becomes more active and then his/her activity level decreases afterwards (427). Therefore the reactivity to the accelerometer may influence the validity of the results of PA assessment, so that it is recommended for the researcher to familiarize the child to be monitored on the accelerometer for a day and to select the start days randomly (427).

Various types of accelerometers are available, and are used either for research or in monitoring individual health care. An acceptable accelerometer should have certain characteristics such as: (a) its output should be reproducible (b) its output should be valid in that it should measure what it is assumed to measure and (c) it should be feasible to use the device in terms of the cost of the device and its software cost, the expertise needed to use it, and the degree to which the device is accepted by the person being studied(428). Examples of available devices that have been commonly used in research studies include the RT3 tri-axial research tracker kit, ActiGraph GT1M, Actigraph models (GT3X and GT3X+), Cyma StepWatch3, IDEEA (Intelligent Device for Energy Expenditure and PA), and the ActivPAL™. The RT3 tri-axial research tracker kit is a valid (429, 430) three-dimensional accelerometer that provides tri-axial vector data in activity units, metabolic activity units or kilocalories and is attached to waist. Its reproducibility has not been evaluated for assessing PA. ActiGraph GT1M (also known Computer Science and Applications (CSA) and Manufacturing Technology Inc. (MTI) monitor) is a small, and light-weight uniaxial piezoelectric accelerometer that is usually attached to the hip. It has good reproducibility, validity and feasibility in assessing PA in children and adolescents (428). This device is capable of measuring activity and steps counts, calories and activity levels in both adults and children (428, 431-433). Actigraph models (GT3X and GT3X+) contain an inclinometer that makes it capable of detecting postures. Furthermore, it has been used in studying sleep pattern in assessing cycles of sleep/wake, sleep latency and sleep efficiency (general circadian rhythms) (434-436). Cyma StepWatch3 (known as Step Activity Monitor (SAM)), is a validated, small ankle mounted step counter controlled by a microprocessor that is able of recording steps or leg swings, in short adjustable time intervals, over durations of more than a month (420, 437-439). IDEEA (Intelligent Device for Energy Expenditure and PA) uses several sensors attached to various body parts, and is capable of monitoring PA, evaluating functional capacity, analysing gait and assessing energy expenditure. Although, it has the ability to distinguish between many types of activity and gait parameters and also provide data on onset, period and frequency and intensity of each activity, it is difficult to use for long term PA monitoring due to the multiple number of

sensors that is required to be attached (420). The ActivPAL™ (PAL Technologies Ltd, Glasgow) is a uni-axial piezoresistive accelerometer with a sampling rate equivalent to 10 Hz that is attached to the mid thigh (440, 441). The device contains an inclinometer that can be used to classify postural position (sitting/lying, standing, and walking) based on measures of postural position recorded on data from the thigh sensor. The device has the ability to record continuously for about eight successive days, which allows the monitoring of PA through measuring total activity counts and number of steps over several days (441). Its small size and light weight (weighs 15 grams and 53 x 35 x 7 mm in dimensions), features that make it very suitable for measuring PA and usual postural changes in children (442). ActivPAL™ had been validated for measuring walking (443, 444), posture and motion of daily physical activities in healthy adults (440, 445), recording postural changes in pre-school children(446), recording length of time of sitting/lying, standing, and walking, and recording sit-to-stand and stand-to-sit transition counts. It can also count steps in children (447).

1.7.4 Sedentary behaviour assessment

To explore the effect of sedentary behaviour (SB) on health, it is necessary to monitor and quantify SB accurately to be able to measure SB between and within individuals over time (404, 405, 448) using methods that are valid and reliable (405, 448). Current measures for quantifying SB include; 1) monitoring the volume of SB by measuring the total sitting time per day and the percentage of total time spent sitting per day; 2) describing the pattern (or fragmentation) of sitting time by describing the distribution of sitting bouts according to their length and measuring breaks in sitting (or up transitions) (138).

In the following sections, the methods of assessing SB in children are summarised.

1.7.4.1 Methods of monitoring sedentary behaviour

1.7.4.1.1 Criterion methods of monitoring sedentary behaviour

As noted above in Direct Observation (Behavioural) methods children are either observed directly while playing, exercising, walking or sitting in a confined area for a certain time interval or recorded on videotape for later analysis. This method can be considered as the gold standard method for assessing SB (399, 405). The advantages and disadvantages of this method were mentioned above in section 1.7.3.1.1.

1.7.4.1.2 Subjective methods of monitoring sedentary behaviour

Subjective methods are the most commonly used method of monitoring SB (404, 405) using approaches such as self-report, interviews, proxy-report (informed by another person usually parent for children under 10 years old), diaries and questionnaires (399, 404, 405). Although TV watching time does not encompass all SB time (137), most SB questionnaires have assessed TV watching time in adults and children (133, 404, 405). The advantages and disadvantages of this method were mentioned above in section 1.7.3.1.2.

1.7.4.1.3 Objective Methods of monitoring sedentary behaviour

Objective measures of sedentary behaviour make use of devices such as accelerometers that can measure the volume and pattern of SB.

1.7.4.1.3.1 Accelerometers

The mechanism of action, types, advantages and disadvantages of accelerometers were described above in section 1.7.3.1.3.2. The modern versions often include an inclinometer that enables the device to recognise whether a person is either sitting/lying or standing which make it useful for monitoring sedentary behaviour objectively.

Various accelerometers have been used in monitoring SB. The actigraph (described above in section 1.7.3.1.3.2) has been the most commonly used accelerometer for measuring SB objectively in different age groups (449, 450). The GT3X and GT3X+ models of actigraph contain an inclinometer which enables the device to recognise whether a subject is either sitting/lying or standing (405, 451) and thus enables the device to monitor sedentary behaviour. The Actical is a hip-mounted, small sized, light weighted, water resistant, omni-directional (able to measure movement in all directions: x, y, and z axis) accelerometer that has been used to monitor SB of adults and children (170, 452, 453). The disadvantage of this device is that it lacks the appropriate cut off point used to differentiate sedentary time from standing time, thus standing time might be misclassified as sedentary time (452). The ActivPAL™ (described above in section 1.7.3.1.3.2) contains an inclinometer that enables the device to classify postural position (sitting/lying, standing, and walking) based on measures of postural position recorded on data from the thigh sensor, which makes it suitable for monitoring SB through measuring the number and duration of sit/lie periods and number of breaks in sitting over a period of up to eight successive days (441). ActivPAL™ had been validated for monitoring posture and motion of daily physical activities in healthy adult (440, 445), recording postural changes in pre-school children (446), recording length

of time of sitting/lying, standing, and walking, recording sit-to-stand and stand-to-sit transition counts and it can also count steps in children (447).

1.7.5 Sleeping behaviour assessment

To study the effect of sleep behaviour on health, it is necessary to quantify sleep behaviour. Current measures for quantifying sleep behaviour include; 1) monitoring the volume of sleep by measuring sleep time and 2) assessing the pattern of sleep. There are many valid and reliable methods that have been used for assessing sleep behaviour. Again, these methods broadly fall into three groups: (a) criterion methods; (b) subjective methods; and (c) objective methods.

In the following sections, the methods of assessing sleep behaviour in children are summarised.

1.7.5.1 Methods of monitoring sleep behaviour

1.7.5.1.1 Criterion methods of monitoring sleep behaviour

Polysomnography (160, 162, 166, 167, 454) is the gold standard procedure allowing continuous monitoring of sleep stages by using electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG) and measurement of a number of physiologic parameters throughout sleeping. Cardio-respiratory parameters such as air flow, oxygen saturation, respiratory movements, heart rate, electrocardiogram, and limb movements are monitored during sleep. Polysomonography is a complicated procedure that needs well-trained personnel, and is time-consuming and costly.

1.7.5.1.2 Subjective methods of monitoring sleep behaviour

Sleep habits questionnaires and structured sleep diaries (358, 359, 362, 454) are used to allow subjective reporting of sleep. Although they have the advantages of low cost and ease of use, they are limited by the low degree of accuracy to recall information and the variability inherent subjective reporting.

1.7.5.1.3 Objective methods of monitoring sleep behaviour

Objective measures of sleeping behaviour make use of devices such as accelerometers that can measure the volume and pattern of sleeping behaviour.

1.7.5.1.3.1 Accelerometers

The mechanism of action, types, advantages and disadvantages of accelerometers were described above in section 1.7.3.1.3.2. The newer versions of accelerometers that contain an inclinometer allow the devices to identify sitting/lying or standing periods making them useful for monitoring sleeping behaviour objectively. After recording at night, the output of these devices is downloaded and by the aid of software algorithms, the activity of person can be assigned to sleeping and wakefulness.

Various types of accelerometers have been used in monitoring sleeping behaviour. Actigraph (described above in section 1.7.3.1.3.2) is an established objective method used for measuring sleeping behaviour (455, 456). The Actical accelerometer has been used to monitor sleeping behaviour (170) with the advantages and disadvantages was described above in section 1.7.3.1.3.2. The ActivPAL™ contains an inclinometer that enables the device to classify postural position (sitting/lying, standing, and walking) and the ability to record continuously for long periods which make it suitable for monitoring sleeping behaviour through measuring the sleep time and sleep pattern. To measure the sleep time, all these accelerometers consider the longest sit/lie interval within 24 hours between two valid days as the sleeping time (170, 357). Furthermore, the ActivPAL™ has the ability to demonstrate the sleep pattern by observing the mean number of breaks in sitting (up transitions) per hour against time during 24 hours (146).

As noted before various types of accelerometers are available, and used in monitoring individual PA, SB and sleep behaviour. An acceptable accelerometer should have certain measurement characteristics such as reproducibility, validity and feasibility; it should be reusable, be capable of monitoring PA, SB and sleep behaviour continuously for several days, and be small in size and weight. As the ActivPAL™ (PAL Technologies Ltd, Glasgow) fulfilled these criteria; the researcher used this device in the present study to monitor the activity continuum of both asthmatic and healthy children.

1.8 Kuwait in context

Kuwait lies in the North West area of the Arabian Gulf (Figure 1-6) , surrounded by the Gulf of Arabia in the east, Saudi Arabia in southwest, and the Republic of Iraq to the north and east (457). Kuwait comprises over 17818 square kilometres total land area(457). The characteristic climate of Kuwait is extremely harsh with very hot summers and short cold

winters (457). In mid 2012 the population of Kuwait was 3,806,643; 1,195,806 (31.4%) were Kuwaitis and 2,610,837 (68.6%) were Non-Kuwaitis (458). In 2012 the Kuwaiti males were 49.07% and females 50.92 % of the Kuwaiti population, while in non-Kuwaitis population males constitute 64.97% and females 35.02%(458). Kuwait is a wealthy country with a reserve of around 98 billion barrels of oil, which constitutes about 10% of world reserves (457). Education and health services are freely provided for Kuwaiti citizens. The health services are easily accessed with around 100% coverage of the population (457). In the period 2008-2012, there was a 9.5% increase in the percentage of live births, and the ratio of male-female among live births was about 104:100 in 2012 (458). The infant mortality rate declined from 9.1 /1000 live births in 2008 to 7.7/1000 live births in 2012(458). For the period 2008 – 2012 the death rate of males (61.8%) was higher than that of females (38.2%), in 2012 the total number of deaths was 5950 and the major causes of death were circulatory conditions and heart diseases, external causes (notably transport

Figure 1-6: Kuwait Map reprinted from (459).

accidents) and neoplasms (458). There are 6 health areas/regions in Kuwait: Capital, Hawali, Ahmadi, Jahra, Farwania and Al Sabah all controlled by the Ministry of Health (457, 458). Each health area consists of multiple primary health centres and specialized clinics (representing primary health care) and one general hospital as a minimum (representing secondary health care); added to that there are many specialized hospitals which are present in Sabah health area. Secondary care in Kuwait is delivered by 6 admitting hospitals (Figure 1-7): Amiri hospital, Mubarak hospital, Sabah hospital, Jahra hospital, Farwaneya hospital and Adan hospital. There is also the Defence hospital which belongs to Ministry of Defence, the Handicapped hospital which belongs to Ministry of social affairs, and Ahmadi hospital which belongs to the Kuwait Oil Company(457, 458).

In addition, there was an expansion in the health services for the same period. There was an increase in the number of physicians from 2.1/1000 population in 2008 to 2.7/1000 population in 2012(458). The number of hospital beds were increased from 1.8/1000 population in 2008 (561 patients for each bed) to 2.1 /1000 population in 2012 (478 patients for each bed) (458). This expansion was associated with an increase in the number of patients in all sectors of health services; primary health care visits increased from 9.0 million visits in 2008 to 11.8 million visits in 2012; there was an increase in number of emergency department visits from 2839176 in 2008 to 3579560 in 2012; an increase in outpatient visits from 1950247 in 2008 to 2495121 in 2012; and an increase in the number of discharges from hospitals from 53.7/1000 population in 2008 to 56.8 /1000 population in 2012(458). All this led to an increase in the health care cost per person from 172 K.D (Kuwaiti Dinar= 2.28 British Pound the rate of 2016) in 2008 to 258 K.D in 2012(458). In 2012 the number of outpatient visits due to chest diseases (including asthma cases) was 40344, number of patients with chest diseases discharged from hospitals was 7733 and for asthma was 2977(458). The average length of stay in hospital for asthma was 5.3 days for the same year(458). The death rate due to respiratory system diseases (including asthma cases) in 2012 was 11.0 / 100,000 population (458).

Figure 1-7 Secondary care hospitals distribution in Kuwait reprinted from (460) with some modifications. Amiri hospital (A) Mubarak hospital (M), Sabah hospital (S), Jahra hospital (J), Farwaneya hospital (F) and Adan hospital (AD).

1.9 Aim of the study

1.9.1 Hypotheses

1. Children with asthma within a week following an asthma attack have poorer asthma control, are less physically active, more sedentary, and have more sleep disturbance compared to one month following an attack as the child recovers from the attack.
2. Changes in measures of physical activity, sedentary behaviour and sleeping are individual.
3. There are differences in the components of the movement continuum between children with asthma at one month of recovery following asthma attack and healthy children.

1.9.2 Aims

The aims of the present MD thesis were four fold:

1. To conduct a systematic review of studies investigating the relationship between asthma and activity continuum measured by objective methods in school-aged children with asthma compared to healthy children. We choose to focus on younger children to avoid some of the social factors that influence activity in adolescents. The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (461) and included studies investigating levels of physical activity and sedentary behaviour measured objectively using accelerometry in asthmatic school aged children (6-12 years old) compared to healthy control subjects published in English between 2000-2016.
2. To conduct an observational longitudinal study investigating continuum of physical activity in children with asthma admitted to hospitals in Kuwait with an asthma attack, at two time points; one week after discharge from the hospital and one month after discharge from the hospital. The aim was to investigate the pattern of recovery over time from an asthma attack and to assess whether changes in asthma symptoms, lung function, physical activity, sedentary behaviour and sleeping behaviour occurred at similar rates and to investigate how long on average it takes a child to recover following an acute attack.
3. To investigate whether changes in asthma symptoms, in measures of physical activity, sedentary behaviour and sleeping behaviour during recovery from asthma attack are individual and to investigate possible predictors of change.

4. To compare components of movement continuum in children with asthma at week 4, at the recovery time from asthma attack and healthy children. Comparing the difference in movement continuum between asthmatic and non-asthmatic children would add to the debate about physical activity differences between children with asthma and healthy controls.

Chapter 2:
Asthma and physical activity and sedentary behaviour, a systematic review

2 Asthma and physical activity and sedentary behaviour, a systematic review

2.1 Introduction

Asthma is a chronic inflammatory disease of the airways (33) that has considerable impact on the health, well-being and social life of patients (34, 35), on their parents and caregivers (301), on health services (37, 311) and on economies of countries (35, 39). Its prevalence is high all over the world (39). The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three involved over 1 187 496 adolescents and children (237 centres in 98 countries) and found that prevalence of asthma in children increased in the period from the mid-1990s to the mid-2000s, from 11.1% to 11.6% in 6–7 years old age group, and from 13.2% to 13.7% in 13–14 years old age group (39). Asthma attacks are a common feature of the illness that frequently lead to hospital admission (38). Asthma in children is associated with exercise-induced symptoms (33), that may interfere with the physical activity of asthmatic children and may decrease their physical activity level rendering them more sedentary than their peers.

The relationship between asthma in children and physical activity and sedentary behaviour is important in its management. However, the evidence in this area is conflicting. Some studies suggest that children with asthma are less physically active (323, 326), and more sedentary (354) than children without asthma; others have suggested that children with asthma are more active and less sedentary (321) or that there is no differences between children with asthma and children without asthma in their physical activity and sedentary behaviour (462). Furthermore, even the systematic reviews and meta-analysis conducted to review studies examining the relationship between physical activity and asthma in children showed different results. For example, Eijkemans et al review (348) concluded that the severity of asthma was negatively associated with the level physical activity while Cassim et al (349), concluded that there was no difference in PA between asthmatics and non-asthmatics children. Reasons behind this conflict are not clear. This heterogeneity may be attributed to the fact that many of these studies even those studies which reached similar conclusions were very heterogeneous, using different study designs, different sample sizes, examining children with asthma of different severities and different ages, conducted in different countries, and used different monitoring methods. This heterogeneity limits the comparability of the results of these studies, which in turn limits ability to reach conclusion

about the impact of asthma on activity. In order to reach evidence in this area, there is a need for systematic review to review studies that investigated PA of asthmatic children of a similar age range, with similar degree of asthma severity and using objective monitoring methods to monitor physical activity and sedentary behaviour. Based on these criteria, we have undertaken a systematic review to bring together the available evidence about physical activity and sedentary behaviour in children with asthma.

The objectives of the review were to review the relevant literature to answer the following question: in school aged children between 6 and 12 years of age with asthma compared to healthy children with no history of asthma, are levels of physical activity and/or sedentary behaviour measured objectively in studies using case-control, cross-sectional or longitudinal (cohort) study designs different between the groups.

In this chapter we describe the findings of this systematic review.

2.2 Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table 2-4) (461).

2.2.1 Eligibility criteria

To be eligible for inclusion in the review, papers had to meet all of the following criteria as per PICOS principles: **P**opulation (children aged from 6-12 years old); **I**ntervention or exposure: children with diagnosed asthma; **C**omparison (where applicable): healthy children matched for relevant criteria (in particular age, gender); **O**utcome (accelerometer measured physical activity and/or sedentary behaviour of at least 3 days and 6 hours/day). All **S**tudy designs were considered eligible (cross-sectional, longitudinal, case-control studies and intervention studies if pre-intervention data could be extracted). We looked for original research studies, published in English, in peer-reviewed journals between 2000 and 2017.

Rationale for Inclusion Criteria

The study focused on children between 6 and 12 years old because children between 6 and 12 are likely to be in primary school and will generally be pre-pubertal. Older adolescent children with asthma may have other social and environmental influences that may affect their activity levels independent of any effects related to asthma. In children younger than six years the diagnosis of asthma can be less certain because of an overlap with children

with viral-associated wheezing that only causes intermittent symptoms that may have resolved completely by the time they enter primary school. Questionnaire based studies about activity or studies based on parental recall of a child's activity have a number of biases associated with them that make the conclusions from such studies difficult to compare. Accordingly, this review concentrated on studies that used objective methods (accelerometers or pedometers) to measure activity and sedentary behaviour because these methods would now be considered as the gold standard methods for objective measurements of activity and sedentary behaviour. In the main, these methods have only come into widespread use fairly recently and hence we only searched for studies published since the year 2000. No limitations were placed on publication sample size or country of origin.

Studies that included participants with co-morbid acute or chronic medical diseases or conditions that may have impacted their physical activity were excluded. Since the aim of the review was to examine habitual levels of physical activity and sedentary behaviour, studies that measured these variables for less than 6 hours per day or over two days or less were excluded. Studies that focused only on specific periods of the day (e.g. school activity only, or outdoor activity only, or weekend or weekday activity only, or after-school only) were also excluded.

2.2.2 Information sources

A systematic literature search was performed to identify all papers describing objectively measured activity levels and sedentary behaviour in children with asthma compared with children without asthma. Databases were searched between the years 2000 up to March 2017 to increase the generalisability, since levels of physical activity and/or sedentary behaviour might be different now than in the past, and because accelerometry became more widely used in research from the early 2000's. The databases were searched separately. The literature search was conducted using the five most relevant electronic databases: MEDLINE OVID; PubMed (NLM); Cochrane library; EMBASE; and CINAHL. Articles were also identified by hand searching the reference lists of published reviews and related cited articles. The results were combined and any duplicates were removed. Details of the specific search strategies used are listed in (appendix A).

Certain search keywords were used in the literature search conducted in the five most relevant electronic databases. Medline (Ovid) electronic database was searched and the search keywords used were: exp Child/, exp Adolescent/, (child* or adolesc* or teen* or

youth or girl* or boy*).tw, (young adj1 (person or people)).tw, exp Exercise/, exp Motor Activity/, exp Sports/, exercis*.tw, physical* activ*.tw, (active adj2 (living or lifestyle)).tw, sedentary behavi?r.tw, exp Sedentary Lifestyle/, ((sedentary or sitting or screen or TV or television or computer or PC or video games) adj2 time).tw, exp Accelerometry/, exp Actigraphy/, acceleromet*.tw, actigraph.tw, activity monitor*.tw, (objective adj1 (measure* or monitor* or assess*)).tw, exp Asthma/, asthma.tw, exp Respiratory Tract Diseases/, exp Respiratory Hypersensitivity/, (respiratory adj2 allerg*).tw, wheez*.tw, Pulmonary/ or exp lung diseases, obstructive/ or exp lung diseases, "chronic lung disease".tw and "chronic respiratory disease".tw.

The search keywords used in the search of EMBASE (ovid) electronic database were: exp Child/, exp Adolescent/, (child* or adolesc* or teen* or youth or girl* or boy*).tw, (young adj1 (person or people)).tw, exp Exercise/, exp Motor Activity/, exp Sports/, exercis*.tw, physical* activ*.tw, (active adj2 (living or lifestyle)).tw, sedentary behavi?r.tw, exp Sedentary Lifestyle/, ((sedentary or sitting or screen or TV or television or computer or PC or video games) adj2 time).tw, exp Accelerometry/, exp Actigraphy/, acceleromet*.tw, actigraph.tw, activity monitor*.tw, (objective adj1 (measure* or monitor* or assess*)).tw, exp Asthma/, asthma.tw, exp Respiratory Tract Diseases/, exp Respiratory Hypersensitivity/, (respiratory adj2 allerg*).tw, wheez*.tw, Pulmonary/ or exp lung diseases, obstructive/ or exp lung diseases, "chronic lung disease".tw and "chronic respiratory disease".tw.

The search keywords used in the search of Pubmed electronic database were: Child, Adolescent, (((((child*[tw]) OR adolesc*[tw]) OR teen*[tw]) OR youth [tw]) OR girl* [tw]) OR boy* [tw], ("young person" [tw]) OR "young people" [tw], Exercise, exercis*[tw], physical* activ* [tw], "Motor Activity", Sports[tw], ("active living" [tw]) OR "active lifestyle" [tw], sedentary behav* [tw], "Sedentary Lifestyle", (((((("sedentary time" [tw]) OR "sitting time" [tw]) OR "screen time" [tw]) OR "television time" [tw]) OR "computer time" [tw]) OR " video games time" [tw], Accelerometry, Actigraphy, acceleromet*[tw], actigraph* [tw], activity monitor* [tw], (("objective measure*"[tw]) OR "objective monitor* "[tw]) OR "objective assess*"[tw], Asthma, asthma [tw], Respiratory Tract Diseases, Respiratory Hypersensitivity, respiratory allerg* [tw], wheez*[tw], ((Pulmonary diseases) OR lung diseases) OR obstructive lung diseases, "chronic lung disease"[tw] and "chronic respiratory disease"[tw].

The search keywords used in the search of Cochrane Central Register of Controlled Trials electronic database were: MeSH descriptor: [Child] explode all trees, MeSH descriptor: [Adolescent] explode all trees, child* or adolesc* or teen* or boy* or girl* or youth:ti,ab,kw (Word variations have been searched), young near/1 (person or people):ti,ab,kw (Word variations have been searched), MeSH descriptor: [Motor Activity] this term only, MeSH descriptor: [Exercise] explode all trees, MeSH descriptor: [Sports] explode all trees, MeSH descriptor: [Sedentary Lifestyle] explode all trees, physical* activ*:ti,ab,kw (Word variations have been searched), exercis* or sport*:ti,ab,kw (Word variations have been searched), active near/2 (living or lifestyle):ti,ab,kw (Word variations have been searched), sedentary behavi?r:ti,ab,kw (Word variations have been searched), (screen or sedentary or sitting or TV or television or computer or PC or video games) near/2 time:ti,ab,kw (Word variations have been searched), MeSH descriptor: [Accelerometry] explode all trees, acceleromet*:ti,ab,kw (Word variations have been searched), actigraph*:ti,ab,kw (Word variations have been searched), activity near/1 monitor*.:ti,ab,kw (Word variations have been searched), MeSH descriptor: [Respiratory Tract Diseases] explode all trees, respirator*near/1 disease*:ti,ab,kw (Word variations have been searched), asthma*:ti,ab,kw (Word variations have been searched) and respiratory near/1 allerg*:ti,ab,kw (Word variations have been searched).

The search keywords used in the search of CINAHL electronic database were: S8 "young" (Searched as Keyword), "boy*" (Searched as Keyword), "girl*" (Searched as Keyword), "youth" (Searched as Keyword), "adolesc*"(Searched as Keyword), "child*" (Searched as Keyword), (MH "Adolescence+"), (MH "Child+"), ""computer time"" (Searched as Keyword), ""television time"" (Searched as Keyword), ""screen time""(Searched as Keyword), ""sitting time""(Searched as Keyword), ""screen"" (Searched as Keyword), ""computer""(Searched as Keyword), ""sedentary time"" (Searched as Keyword), (MH "Video Games+"), (MH "Television"), (MH "Sitting"), "sedentary" (Searched as Keyword), (MH "Life Style, Sedentary"), "sedentary behavi?r" (Searched as Keyword), ""SEDENTARY behavior in children""(Searched as Keyword), "(active lifestyle)" (Searched as Keyword), (MH "Activities of Daily Living+"), "sport*" (Searched as Keyword), "exercis*" (Searched as Keyword), "physical* activ*" (Searched as Keyword), (MH "Sports+"), (MH "Motor Activity+"), (MH "Exercise+"), (MH "Physical Activity"), ""objective assess*"" (Searched as Keyword), ""objective monitor*""(Searched as Keyword), "objective measure*" (Searched as Keyword), ""activity monitor* ""(Searched as Keyword), ""actigraph"" (Searched as Keyword), (MH"Actigraphy"),

"acceleromet*"(Searched as Keyword), (MH"Accelerometry"), (MH "Accelerometers"), ""objective assess*"" (Searched as Keyword), ""objective monitor*""(Searched as Keyword), "objective measure*" (Searched as Keyword), ""activity monitor* ""(Searched as Keyword), ""actigraph"" (Searched as Keyword), (MH "Actigraphy"), "acceleromet*"(Searched as Keyword), (MH "Accelerometry"), (MH "Accelerometers").

2.2.3 Study Selection

Titles, abstracts, and full-text articles were screened. Reference lists of eligible studies were examined for potentially eligible studies, and studies, which cited other potentially eligible studies, were identified and tested for eligibility. Reasons for exclusion are summarised in the study flow diagram (Figure 2-1).

2.3 Identification of eligible studies

The PRISMA flow diagram with numbers of included and excluded articles at each step of the review process is provided in (Figure 2-1). A total of 267 publications were identified by the search; 71 publications derived from Medline, 110 studies from EMBASE, 43 publications from PubMed, 5 studies from Cochrane Data bases and 38 studies from CINAHL (Figure 2-1). After screening for eligibility by reviewing the titles and abstracts 177 articles were excluded because children were not 6-12 years old, or the article was not published in English or was not published between 2000-2017. A further 74 articles were also excluded because they did not meet eligibility criteria. These included experimental studies without asthma as clinical outcome, studies without control group, and studies of exercise induced asthma. Out of the remaining 16 full-text articles of potentially relevant studies, 10 studies were excluded because they were duplicate publications of the same studies. Hand searching of bibliographies led to three further studies being added. This resulted in a final total of 9 studies that met the inclusion criteria and were included in this systematic review (Figure 2-1).

The characteristics of these nine studies are summarised in (Table 2-1). In total, these studies included school aged children (n= 2996): children with asthma (n=839), with wheezing (n=37) and controls (n= 2120). Eight studies (325, 334, 338, 340, 341, 345, 346, 463) examined both genders of children while one study examined only female children (342).

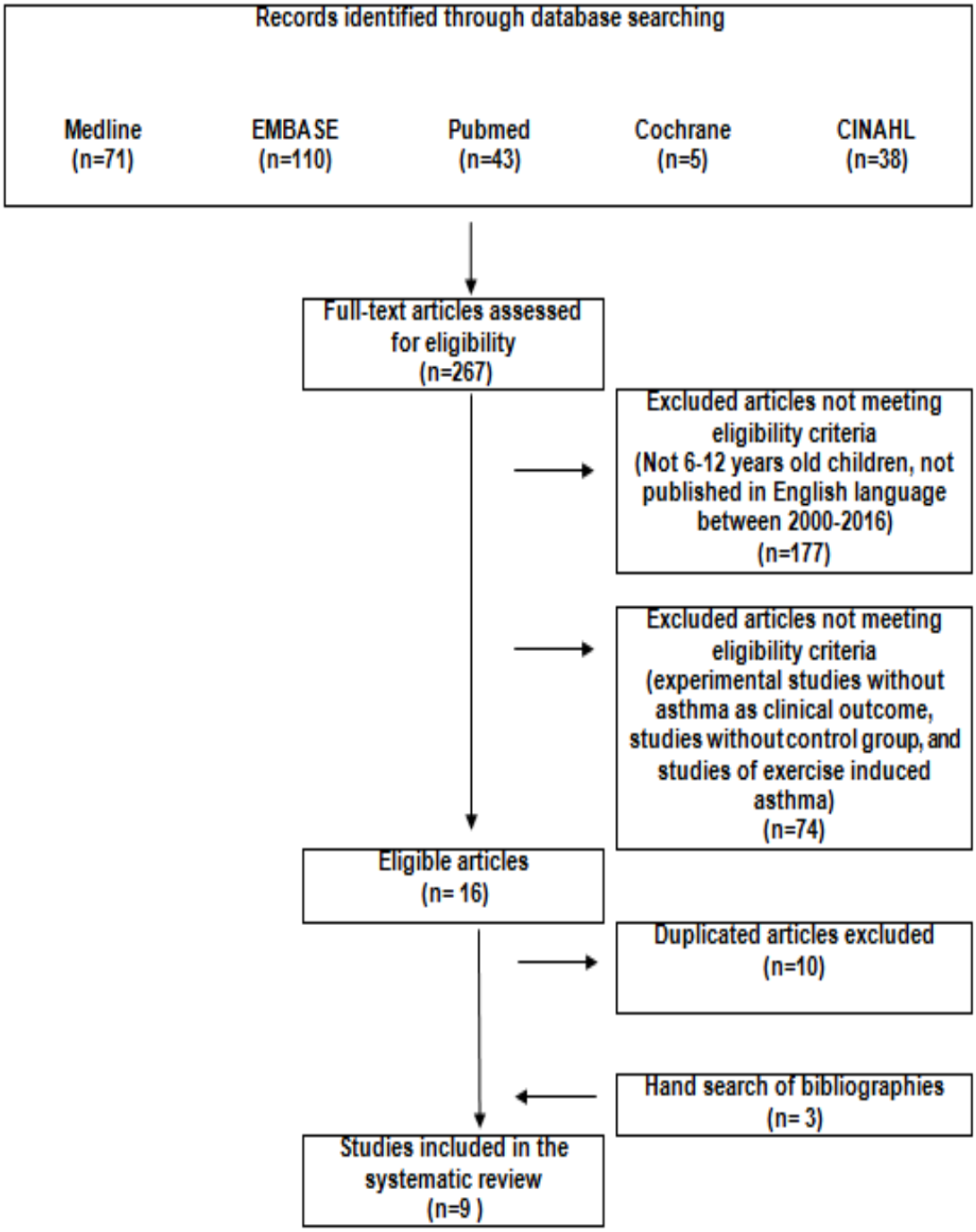


Figure 2-1: The PRISMA flow diagram with numbers of included and excluded articles at each step of the review process.

Table 2-1: Descriptive characteristics of studies investigated physical activity and sedentary behaviour in asthmatic and non-asthmatic school aged children using objective measures

Study	Country	Participants	Asthma severity	Asthma treatment	Age	Method	Monitoring Days	Outcome	Gender Difference in PA
Fedele et al (345) (cross-sectional study)	USA 2014	248 children (data of this study was from secondary analysis of the study of the Extension Family Lifestyle Intervention Project (E-FLIP for Kids)) -175 healthy obese children -73 asthmatic obese children (Obesity: BMI ≥ 85th percentile for age and gender)	Controlled asthma (self reported history of health professionals diagnosis of asthma)	Not reported	7-12 yrs	Sensewear armband accelerometer (PA measured as time spent in PA ≥ 3 METS which is indicative of moderate to vigorous PA)	7 days	No significant difference in PA (total activity) between children with asthma and healthy children	Not reported
Bringolf-Isler et al (325) (cohort study)	Switzerland 2013	352 children (from the Swiss sample of the large European GABRIEL study designed to study farming and rural environments and their impact on childhood asthma and atopic diseases). -42 children with asthma -37 children with wheezing	Controlled asthma (asthma defined as wheeze in the past 12 months, or asthma inhaler use ever, or a physician's diagnosis of asthma at least once, or history of wheezing bronchitis more than once in the past)	Not reported	7-10 yrs	Questionnaire and Accelerometer (model GT3x, Actigraph, Pensacola, Fla) Cut-offs for sedentary, light, moderate, and vigorous physical activity were 0-50, 51-1499,1500-2600,and >2600 counts x 30s, respectively	7 days	Children with asthma less physically active (light activity) than healthy children	Not reported

Vangeepuram et al (342) (cross-sectional study)	USA 2013 3 sites: New York City, San Francisco, Southwest Ohio and Northern Kentucky	-Total 1182 girls -Asthmatic girls were 191	Different levels of asthma severity (based on positive Brief Pediatric Asthma Screen (BPAS) score and parental report of physician diagnosed asthma)	Asthma controller medications (inhaled corticosteroid with or without long acting beta agonists and/or leukotriene receptor	6–8 yrs	-Pedometer (Yamax SW-200 Digi-walker) -Questionnaire (parents asked about activities hours/ week and months/year)	≥ 4days	No significance difference in PA (step counts) between children with asthma and healthy children	Only girls assessed
Sousa et al (346) (cross-sectional study)	Brazil 2014	121 children (Asthmatic children were recruited from paediatric outpatient clinic of a public health hospital in Sa˜o Paulo. Healthy children were among the children of employees of the same hospital) -79 children with asthma -42 healthy children	32 mild, 24 moderate and 23 severe asthma (based on self reported asthma diagnosis and treatment and spirometry)	Asthma controller medications	7-12 yrs	Accelerometer (Power Walker-610, Yamax, Japan) physically active, a child's make 15 000 and 12 000 steps per day for the boys and girls, respectively and below these values were classified as sedentary	6 days (4 week days and 2 weekend)	No difference in PA (total number of steps, and number of steps in moderate physical activity) between asthmatic and healthy children	Not reported
Tsai et al (341) (secondary analysis of a cross-sectional study)	USA 2012	54 children (27 children with asthma & 27 healthy children) -data of this study was derived from secondary analysis of a cross-sectional study on youth sleep patterns conducted in Washington, USA	Stable asthma (self reported health professionals diagnosis of asthma)	Not reported	9-11 yrs	Actiwatch 64, Mini-Mitter Philips Respironics) Cut-offs for sedentary, light, moderate, and vigorous PA were 0-49, 50-699, 700-2,499 and > 2,500 counts per minute respectively	7 days	No difference in PA (light, moderate, vigorous and MVPA) between asthmatic and healthy children	Not reported

Vahlkvist et al (338) (case–controlled study)	Denmark 2009	214 children -57 suspected asthmatic children recruited from general practice -157 healthy controls recruited from local schools	Newly diagnosed, untreated asthma, most of cases were mild (based on spirometry)	Most asthma cases were mild and little need for rescue β2 blocker	6–14 yrs *	RT3 accelerometer (Stayhealthy, Monrovia, CA, USA)	20.1 days (2–27) for asthmatics & 21.6 days (7–28) for controls	No signficant differences in overall daily PA, time spent in high or vigorous activity	Not reported
Vahlkvist et al (340) (cohort study)	Denmark 2010	- 55 suspected, untreated asthmatics recruited from general practice -154 healthy controls recruited from local schools	- At baseline asthma was mild uncontrolled & untreated -After treatment asthma was controlled (based on spirometry)	37 asthmatics received budesonide 400 mcg daily dose & 16 asthmatics received 467 mcg fluticasone propionate daily dose, after baseline period	6–14 yrs *	RT3 accelerometer	Not reported	-At baseline: no differences between asthmatic and healthy children in daily PA except in 38 asthmatic children (most uncontrolled asthma) spent less time in vigorous PA than healthy controls. -At study end: no difference in daily PA (time at rest, light-vigorous, MVPA or vigorous PA) between the two groups.	Not reported

Van Gent (334) (cross-sectional study)	Netherland 2007	1614 children recruited from 41 primary schools in 4 cities in Netherland -81 diagnosed asthma -130 undiagnosed asthma - 202 children were selected randomly out of the remaining healthy controls	Diagnosed asthma and undiagnosed asthma (based on self reported asthma diagnosis and spirometry)	Not reported	7–10 yrs	- PAM accelerometer (activity equivalent to 3-6 METs defined as moderate intensity activity and activity >6 METs as vigorous intensity activity). - Activity Diary - Questionnaire (habitual activity estimation scale (HAES)).	5 days	No difference in PA between study groups	Not reported
Yiallouros et al (463) (cross-sectional study)	Cyprus 2015	Out of 1,463 primary school students a random sample of 794 children aged 8–9 years old selected. - 104 asthmatics (67 boys; 44 inactive asthma, 23 active asthma and 37girls; 24 inactive asthma, 13 active asthma). - 99 controls (59 boys and 40 girls)	Diagnosed asthma based on self reported data. -Active asthma (have one episode of wheezing in the last 12 months) - Inactive asthma (no wheezing episodes in the last 12 months)	Not reported	8–9 yrs	Biaxial accelerometers (Actigraph, Pensacola, FL)	7 days	No difference in PA and sedentary activity levels between the three groups; active and inactive asthma and non-asthmatic children.	Girls with active asthma have lower MVPA than their peers

***Note:** These two studies investigated children aged 6-14 years old which is different from the inclusion criteria (6-12 years old) of this review and were included, because by reviewing the results of these two studies it was found that the mean age (95% CI); was 9.60 (9.1–10.1) for asthmatics, 9.7 (9.4–10.0) for non-asthmatics in the first study (338) and 9.6 (±0.5) for asthmatics, 9.7 (±0.5) for non asthmatics in the second study (340).

2.3.1.1 Diagnosis of asthma and/or wheezing

In 5 studies (325, 341, 342, 345, 463), asthma was defined based on self reported doctor's diagnosis or asthma symptoms. In the study by Fedele et al (345) to determine child asthma, the parents were asked ''Has a doctor or health care professional ever said your child has asthma?''. Similarly, Bringolf-Isler et al (325) defined asthma as the presence of wheeze in the previous 12 months, or the use of asthma treatment, or a doctor diagnosis of asthma at least once, or a past history of recurrent wheezing bronchitis. Tsai et al (341), diagnosed asthma by asking parents of asthmatic children to provide names of diagnosing health professionals and asthma treatment. In the study of Vangeepuram et al (342), asthma was diagnosed by both self report of a health professionals diagnosis of asthma by the question "Has a doctor or nurse ever said that (CHILD'S NAME) has asthma?" and a positive score on the Brief Pediatric Asthma Screen (BPAS). This consists of four questions about asthma symptoms including wheeze, persistent cough, night cough and response to air temperature changes (positive BPAS score: a positive response to at least one of four asthma symptom questions or BPAS 1+). In the study of Yiallouros et al (463), asthma was determined by asking parents the question "Has your child ever had a diagnosis of asthma confirmed by a doctor?" and the asthmatic children were further subdivided into two groups; (a) active asthmatic group when wheezing reported in the last 12 months, and (b) inactive asthmatic group, if no wheezing reported in the last 12 months.

The other 4 studies (334, 338, 340, 346) combined self-report of an asthma diagnosis with spirometry in defining asthma. In Sousa et al study (346), the physician had diagnosed asthma, evaluated treatment intensity and asthma control in line with the Global Initiative for Asthma (GINA). In addition, spirometry was done pre- and post- inhalation of salbutamol (bronchodilator: BD) and the presence of reversibility in FEV_1 was checked to diagnose asthma. Vahlkvist et al (338) in his study in 2009 used spirometry to define asthma by assessing the variability in FEV_1 in response to inhalation of bronchodilator or methacholine and exercise challenge. Similarly, Vahlkvist et al (340) in 2010 study, determined asthma by spirometry and examined the variability in FEV_1 in response to inhalation of bronchodilator or methacholine challenge. In addition, van Gent et al (334) in his study, diagnosed asthma by self-report of doctor's asthma diagnosis or asthma symptoms (questionnaire contained the ISAAC core questions on asthma symptoms), airway reversibility to bronchodilator, and bronchial hyperresponsiveness to hypertonic saline.

2.3.1.2 Physical activity measuring devices

A number of different accelerometers were used to measure PA in the eligible studies. These included a sensewear armband accelerometer (Fedele et al (345)). a Power Walker-610, Yamax, Japan (Sousa et al (346)), an Actiwatch 64 (Tsai et al (341)), RT3 accelerometer (Vahlkvist et al (338, 340)), GT3X Actigraph (Bringolf-Isler et al (325) and Yiallouros et al (463)) and accelerometer type AM 100; Pam B.V., The Netherlands (Van Gent (334)) and pedometer Yamax (Vangeepuram et al (342)).

2.3.1.3 Physical activity and sedentary behaviour findings

In total, eight studies investigated 2644 subjects, of which 797 were children with asthma (334, 338, 340-342, 345, 346, 463), and noted no significant difference in objectively measured physical activity between asthmatic and healthy children (Table 2-2). One study of 352 subjects, of which 42 had asthma (325), reported that children with asthma were less physically active than non-asthmatic children (Table 2-2). Also, despite Yiallouros et al (463) study generally showed no difference in PA levels between the three groups; active and inactive asthma and non-asthmatic children, this study found that the MVPA of girls with active asthma was significantly lower than that of healthy girls. No study suggested that asthmatic were more physically active than children without asthma.

Sedentary time was assessed objectively in 3 studies only (325, 341, 463), the results of which were diverse. In one study, 42 asthmatic children were less likely to be sedentary (325) (Table 2-2). Two studies (total number of asthmatics= 131 subjects) suggested no difference in sedentary activity between asthmatic and non asthmatic children (341, 463) (Table 2-2).

Table 2-2: Observed/reported physical activity and sedentary behaviour levels from the studies investigated physical activity and sedentary behaviour in asthmatic and non-asthmatic school aged children using objective measures

Study	Total PA	Light PA	Moderate PA	Vigorous PA	MVPA	Sedentary Behaviour	PA Outcome
Fedele et al (345)	Similar	Not reported	Not reported	Not reported	Not reported	Not reported	No difference in PA
Bringolf-Isler et al (325)	Less in asthmatics	Not reported	Not reported	Not reported	Not reported	Less in asthmatics	PA & SB Less in asthmatics
Vangeepuram et al (342)	Similar	Not reported	Not reported	Not reported	Not reported	high in asthmatics*	No difference in PA and SB
Sousa et al (346)	Similar	Not reported	Not reported	Not reported	Similar	Not reported	No difference in PA
Tsai et al (341)	Not reported	Similar	Similar	Similar	Similar	Similar	No difference in PA & SB
Vahlkvist et al (338)	Similar	Not reported	Not reported	Similar	Not reported	Not reported	No difference in PA
Vahlkvist et al (340)	Not reported	Similar	Similar	Similar	Similar	Not reported	No difference in PA
Van Gent (334)	Similar	Not reported	Similar	Similar	Not reported	Not reported	No difference in PA
Yiallouros et al (463)	Similar	Similar	Not reported	Not reported	Similar in boys, but less in girls with active asthma	Similar	No difference in PA and SB

***Note:** in this study SB were measured subjectively by questionnaire

2.4 Discussion

The present systematic review provides a critical review of the published evidence regarding physical activity, measured objectively in children with asthma between 6 and 12 years compared with healthy controls. Only 9 studies met the inclusion criteria and could be included in the review. Although the number of studies was small, the total number of subjects with physical activity objectively measured was substantial (n= 2996) including children with asthma (n=839), with wheezing (n=37) and controls (n= 2120).

Eight of nine studies (2644 subjects) suggested no significant difference in physical activity between children with and without asthma, while, only one study (352 subjects) suggested that asthmatic children were less physically active than controls (Table 2-1 and Table 2-2).

Only one study (Bringolf-Isler et al (325)), found that the PA of asthmatic children was decreased compared to healthy controls. Asthma symptoms are triggered by PA (33), and accordingly it might be expected that children decrease their activity in order to avoid asthma symptoms. Also, asthma in children is commonly associated with exercise-induced asthma symptoms (464), that might limit the children's ability to exercise and be physically active. It is probably that such factors that resulted in a lower PA in children with asthma compared to healthy comparisons.

However, eight studies of 2644 total subjects (1847 healthy controls and 797 asthmatic children) found no difference in physical activity between asthmatic and non-asthmatic school aged children, a result that is at first sight surprising. As noted earlier, asthma in children is commonly associated with exercise-induced symptoms that may restrict the PA of asthmatic children and lead to differences in physical activity levels. It is noteworthy that the studies included contained little information on current asthma control or severity. Thus effective use of asthma controller treatment regimes may have caused stabilization of asthma symptoms to the degree that there were no limitations to their physical activity. Alternatively, many of the subjects included in the studies may have had relatively mild asthma which resulted in no restriction to PA. Alternatively, the lack of a difference might reflect the fact that contemporary healthy children are thought to be much less active. However, there is no available objective data about the PA history in earlier years of both asthmatic and healthy children because the development of accelerometry as a tool to investigate physical activity is relatively recent.

This systematic review also provides an outline of the published evidence regarding the association between sedentary behaviour and asthma. In an extensive search, we only found 3 studies that described the association between asthma in children and objectively measured sedentary behaviour. Although the number of these studies was small, the total number of assessed subjects was large (n= 609) and sedentary behaviour was measured objectively by motion sensors. Again, the results of these studies were inconsistent and heterogeneous. The Bringolf-Isler et al (325) study (asthmatics number= 42 subjects), surprisingly, showed that the asthmatic children were less likely to be active and less likely to be sedentary, which was not expected. Asthma symptoms are triggered by PA (33), which cause asthmatic children to decrease their activity and to be more sedentary in order to avoid asthma symptoms. Also, children with asthma are frequently suffering from exercise-induced asthma symptoms (464), which might renders them more sedentary than healthy children to avoid these symptoms. This finding is questionable, as there was no data on previous habitual activity levels of both asthmatic and healthy children, it is not known whether healthy children were unusually more sedentary and contributed to this finding. On the other hand, Tsai et al (341) and Yiallouros et al (463) studies (total number of asthmatics number= 131 subjects), suggested no difference in sedentary activity between asthmatic and non asthmatic children. Due to this diversity in sedentary behaviour outcomes of these three studies, it is difficult to draw a conclusion about the relationship between asthma in children and sedentary behaviour.

In general, there were several limitations in these studies (Appendix B). First, the widely quoted cohort study of Bringolf-Isler et al (325) was published as a research letter and not a full paper. It is a post hoc investigation of physical activity and sedentary behaviour in children with asthma and healthy children in farming and non-farming settings. The question of the study was not clearly focused with respect to the factor under our investigation. Data for this study was collected originally for another purpose (the large European GABRIEL study to study farming and rural environments and their effect on childhood asthma and atopic diseases). As a consequence the sample itself may be not relevant nor the sample size sufficient to detect group differences in physical activity and sedentary behaviour levels. Also, other aspects of the study were poorly addressed e.g. it is unknown how many people were asked to take part in each arm of the study. The likelihood that some participants might be particularly active or inactive at the time of enrolment is unidentified. Number of dropout is not specified. Additionally, outcome was poorly addressed and measured each time using different measurement tool. Furthermore, it was

not reported whether the main potential confounders were identified and taken into account in the study design and analysis.

Similarly, the eight studies which showed that there was no difference in physical activity between asthmatic and non-asthmatic school aged children, had several limitations (Appendix B). These studies were heterogeneous in a number of ways. The design of these studies were different: they were either case–controlled studies (338), cross-sectional studies (334, 341, 342, 345, 346, 463), or cohort studies (340). Also, the data of some studies was collected originally for another purpose: Vangeepuram et al (342) study used data from three Breast Cancer and the Environment Research Program sites; Tsai et al's (341) study was a secondary analysis of a cross-sectional study of youth sleep patterns in the northwest coastal region of Washington State in USA; data in the study of Fedele et al (345) was from secondary analysis of the Extension Family Lifestyle Intervention Project (E-FLIP for Kids) study and Yiallouros et al (463) study was part of a larger community-based study, conducted in primary schools to examine both (a) the change in asthma prevalence in children and allergies in urban and rural areas of Cyprus (Phase 1) and (b) investigate the relation of environmental and lifestyle risk factors with paediatric asthma prevalence (Phase 2); in this case the sample itself may be not relevant and or the sample size may not be sufficient to detect group differences in physical activity and sedentary behaviour levels. In addition, some studies were community based (334, 341, 342, 345, 463), some hospital and community based (338, 340), while others were only hospital based studies (346) where the sample might not be representative of the larger population. Some studies (338, 340, 341, 345) did not indicate how many of the people were asked to take part in each of the groups being studied and whether or not comparison is made between participants and non-participants to establish their similarities or differences. A number of these studies investigated children of different age ranges; 6–8 years old (342), 6-14 years old (338, 340), 7–10 years old (334), 7-12 years old (345, 346) , 8-9 years old (463) and 9-11 years old (341). This might lead to different results, due to the fact that physical activity and sedentary behaviour levels changes with age (57, 73). As noted, some of these studies investigated only one gender (342), that might affect the credibility of the results, as there is recognizable evidence showing that girls are less active than boys (53, 67, 126). Further, the ethnic composition of these studies varies widely because they were conducted in a number of different countries and drew from different ethnic groups including USA (341, 342, 345), Brazil (346), Denmark (338, 340) Cyprus (463) and the Netherlands (334), which again might lead to differences in physical activity and sedentary behaviour levels (465,

466). The definition of asthma used and the disease severity varied among these studies. Some studies (325, 341, 342, 345, 463) defined asthma according to parent or self-reported doctor's diagnosis of asthma or presence of asthma symptoms or asthma treatment, while, other studies (334, 338, 340, 346) combined both parent or self-reported asthma diagnosis with spirometry in defining asthma. The differences in defining asthma might lead to differences in degrees of bronchoconstriction of the participants which might lead to differences in the results. Similarly, these studies investigated asthmatic children of different severities and levels of asthma control such as stable asthma (341, 345), asthma on controller medications (342, 346), mild asthma (338), uncontrolled and untreated asthma (340) active and inactive asthma (463) and undiagnosed asthma (334). The differences in disease severities and control might also lead to differences in degrees of bronchoconstriction that occurred with exercise and which might lead to different results. Further, most of the studies (334, 338, 340-342, 345, 346) did not report whether or not some eligible subjects might be particularly physically active or inactive at the time when physical activity was assessed. In addition, these studies used different devices to monitor PA. The devices used included the sensewear armband accelerometer (345), Pedometer (342), accelerometer (Power Walker-610, Yamax, Japan) (346), actiwatch 64 (Mini-Mitter Philips Respironics) (341), RT3 accelerometer (Stayhealthy, Monrovia, CA, USA) (338, 340), PAM accelerometer (type AM 100; Pam B.V., The Netherlands) (334) and actigraph (Actigraph, FL) (463) which might results in different physical activity and sedentary behaviour levels. In some of these studies (342, 345, 346, 463), no evidence from other sources was presented to prove the validity and reliability of the PA monitoring methods, which might make the credibility of the results of these studies questionable. One study had used a pedometer for physical activity measurements (342). This device has limitations compared to other objective measures such as accelerometers because a pedometer does not evaluate intensity, pattern, duration, or frequency of activity bouts, and studies have shown errors at low and high speeds with underestimates at both slow and fast walking speeds (409, 414, 415). The percentage of drop out from both arms of the study before the study was completed was not recorded in some of these studies (334, 341, 342, 345, 346). In a number of studies it was not reported that the important potential confounders were identified and taken into account in the study design and analysis (334, 338, 340, 346). According to these factors the three types of bias; selection, information and confounding bias cannot be ruled out in these eight studies. The many differences between the studies generally precluded any attempts to combine data and perform a meta-analysis.

Two systematic reviews and meta-analysis were conducted to review studies examining the relationship between physical activity and asthma in children showed different results. A systematic review and meta-analysis to review the evidence of the relationship between physical activity and asthma in children, adolescents and adults was performed by Eijkemans et al (348), and published in 2012. A total of 39 studies were selected; five subjective longitudinal studies that used questionnaire to monitor PA and thirty-four cross-sectional studies; 27 were subjective studies used questionnaire to monitor PA and seven were objective studies; six used accelerometers and one used pedometer to monitor PA. The studies included were of a very wide age range; the longitudinal studies were four adult studies and one study from adolescence till middle adult age. The 34 cross-sectional studies included 25 studies of children, one of children adolescence age and above and eight adult studies. In most of these studies, asthma was diagnosed according to self-reported data, and only in few studies was it diagnosed by a doctor or according to pulmonary function test (PFT). Despite that the systematic review suggested that the severity of asthma was negatively associated with the level of PA. It can be argued that it included heterogeneous studies, PA monitoring methods were different, few studies used objective methods with most of the studies using questionnaire likely to be limited by recall bias. The studies were of a very wide age range from preschool age till adult age which made them incomparable because of the change of physical activity with age (53, 68, 75, 80). Asthma was diagnosed in different ways resulting in the severity of asthma and degrees of bronchoconstriction of participants being different and leading to variations in the results. These factors might limit the generalizability of the finding. Cassim et al (349), published his systematic review and meta-analysis that reviewed studies that objectively (used accelerometer or pedometer devices) investigated PA of children and adolescents aged until 18 years old to compare PA between asthmatics and non-asthmatics. In the review twelve studies were selected: one longitudinal, ten cross-sectional and one case-control. Four studies examined preschool aged children; one cohort and two cross-sectional studies showed that asthmatics were not less active than non-asthmatics and only one cross-sectional study showed that children with history of wheezing were significantly less active than non-wheezing children. Only one cross-sectional adolescent study showed that asthmatics and non-asthmatics were similar in MVPA. Seven studies examined school aged children; one case-control and six cross-sectional studies and all showed that there were no difference in PA between asthmatics and non-asthmatics. Accordingly, the review concluded that the evidence showed that there were no difference in PA between asthmatics and non-asthmatics. There was some limitations to Cassim et al review such as: studies included were of a wide age range, from

preschool until adolescence which means that there was a difference in the level of PA between participants of these studies, and asthma were diagnosed differently in these studies. However, the studies selected were objective studies which mean that the data collected in these studies were more likely to be valid and reliable. Similar to Cassim et al (349), this systematic review suggest that there is no difference in physical activity between asthmatic and healthy school aged children.

2.5 Conclusion

In conclusion, the results of this systematic review of objectively measured physical activity in school aged children with asthma suggest that the physical activity of asthmatic children was similar to that of healthy comparisons. On the basis of the data included in the present review and the finding of a lack of difference between children with asthma and those without, there is no evidence of a relationship between asthma and physical activity. This implies that it is recommended that asthmatic children after their asthma symptoms controlled to be allowed to return back to normal life style and participate in exercise programmes.

At present, the relationship between asthma in children and sedentary behaviour is not clear. More studies should address these issues.

Table 2-3: PRISMA 2009 Checklist

Section/topic	No.	Checklist item	Reported on page
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Synthesis of results	14		76-77
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Chapter 3: Movement continuum changes following asthma attack

3 Movement continuum changes following asthma attack

3.1 Introduction

Most research studies investigating the relationship between activity and health outcomes in children focus only on the relationship with moderate-to-vigorous physical activity (MVPA) (19, 467, 468). In children, however, MVPA constitutes only ~5% of the daily activities, while about 95% of the 24hrs activity comprising sleep (~40%), sedentary behaviour (~40%) and low intensity physical activity (LPA) (~15%) (19). There is an evidence that independent of MVPA, increased sedentary time is associated with negative health outcomes (24), while diminished sleep time is linked with obesity, type 2 diabetes, depression and poor academic performance (26, 27, 469). Conversely, spending more time in LPA compared to sedentary time during waking hours is associated with beneficial health outcomes (31, 32). These findings emphasise that it is not sufficient to study only MVPA and suggest that the other components of the movement continuum such as sedentary, sleeping behaviour and LPA are potentially important to children's health (19).

At present, most of this research investigating all parameters of the movement continuum and its relationship with health indicators in children is limited in amount (199). Some chronic childhood diseases affect children's activity and might alter the balance between various components of the movement continuum. Asthma offers a particularly good opportunity to examine these relationships in the context of an important childhood illness. Asthma is a very common childhood illness (33) throughout the world (39), affecting the well being and social life of patients (34-36), and causing a huge load on health services (37) and on economies of countries (38). Asthmatic symptoms are commonly induced by exercise and activity in children and affect their ability to take part in exercise (33). Sleep disturbance is common because of nocturnal symptoms (357). Asthma attacks are a common cause of significant illness leading to hospital admission (35). It is highly likely that limitations in a child's activity and disturbance in their sleep might cause significant unfavourable health effects. Despite the potential importance, the relationship between asthma in children and the components of the movement continuum has not yet attracted much research. An examination of the relationship between the various components of movement continuum in children with asthma attack is the subject of this chapter.

Asthma attack can be described as acute worsening of asthma symptoms in combination with objective evidence of reduced expiratory airflow measured as Peak Expiratory Flow

(PEF) or a reduced Forced Expiratory Volume in 1 sec (FEV_1) in association with reduced FEV_1/FVC ratio. Asthma attacks commonly result in urgent unplanned health care and necessitate emergency treatment with high dose bronchodilators and corticosteroids (33, 204-208). It can be expected that during acute period of asthma attack particularly in children who are hospitalised because of attacks, that asthma symptoms will be present, children would be less physically active, more sedentary and have some sleep disturbances. So far, there is a lack of studies in the literature that investigated different components of the "movement continuum" in the acute stage of asthma attack in children. Therefore, this study for the first time aimed to investigate the movement continuum (physical activity, sedentary behaviour and sleeping behaviour) in children after one week following discharge from the hospital due to asthma attack.

There are few studies in the literature that investigated how long it took children to recover from an asthma attack. In one study, Covar et al (205), showed that symptoms and PEF (peaked expiratory flow) score of asthma exacerbation return to baseline level within a maximum period of 10 days. In the light of this previous study, we hypothesised that all indices of asthmatic children; asthma symptoms, PFT, total activity, sedentary behaviour and sleep will be back to normal within 4 weeks duration following asthma attack. Therefore, this study aimed to investigate levels of asthma control (in terms of asthma symptoms, lung function) and aspects of the movement continuum (physical activity, sedentary behaviour and sleeping behaviour) not only at one week after acute asthmatic attack but also at one month of recovery.

The evidence on difference in total PA measured by objective and subjective methods between asthmatic and healthy children is not consistent, some studies showing PA of asthmatic children is higher (320, 321) or lower (323, 326-328) than that of normal children while others suggest that there is no difference (334, 335, 339, 462). Similarly, the relationship between sedentary behaviour and asthma in children is surprisingly unclear with studies investigating difference in sedentary behaviour level between asthmatic and non-asthmatic children showing contradictory results (325, 355, 463), although here there are many fewer studies. Further, the relationship between sleep and asthma in children is also unclear with studies investigating difference in sleep between asthmatic and non-asthmatic children showing contradictory results(357, 363). Most important, currently there is a lack of studies in the literature investigating the inter-relationship between the different components of the "movement continuum" in children with asthma compared to healthy children. Since four weeks following asthma attack, the components of the movement

continuum are expected to be re-established (205) and to represent habitual PA, collecting data at this time point of recovery can be used for comparison of activity continuum of asthmatic children with healthy children and further contribute to the debate in differences in PA,SB and sleep between asthmatic and healthy children.

3.2 Participants and methods

3.2.1 Participants

Inclusion criteria for asthmatic children

This study recruited Kuwaiti asthmatic children aged 6 to 12 years old admitted to Kuwait hospitals because of an asthma attack. When a child was admitted with an acute asthma attack, the local clinical senior or treating doctor in the Kuwaiti hospitals contacted the researcher to inform him of the admission and to discuss whether the child met the inclusion criteria for the study. If the child met the inclusion criteria, the researcher met the family to discuss participation. Parents/guardians and asthmatic children were given preliminary information and a letter of invitation to take part in the study. This letter explained the purpose of the study and the data to be collected such as their gender, age, weight, height, asthma control using a questionnaire, lung function, physical activity, sedentary behaviour and data on sleeping behaviour. Those who agreed to take part in study were asked to complete a written consent form for the parent while the child was asked to complete an assent form. The inclusion criteria for asthmatic children were being asthmatic, aged 6 -12 years old and child able to give assent and parent/guardian able to give informed consent. Children with acute asthma attacks younger than 6 years were not included because it was considered that they generally would be unable to perform spirometry reliably. In Kuwait, children older than 12 years come under the care of the adult medical department rather than the paediatric department.

Inclusion criteria for healthy children

Comparable healthy children were recruited on the basis of comparable age range to asthmatic children (6 -12 years old) and not being asthmatic nor having a history of asthma. Comparable healthy children were recruited from Kuwait Youth Centres (KYC). The initial plan was to recruit healthy children from schools to provide a comparison with the children with asthma. Unfortunately, there was a delay in obtaining approval from the Joint Committee for the Protection of Human Subjects in Research of the Health Sciences Centre (HSC) & Kuwait Institute for Medical Specialization (KIMS). This arose because the time

the researcher applied to get ethical approval from the Ministry of Education coincided with the time of the final examinations in schools and summer holiday. As a consequence, the ministry of education postponed the process of ethical approval to the following academic year, which usually starts at the end of September, 4 months later. Instead, to make better use of time, the researcher changed the plan and decided to look for healthy controls from Kuwait Youth Centres (KYC), which are under the control of the Kuwait Public Authority for Youth and Sport. KYC are places where social and sport activities are provided for the children aged 6-12 years old. The researcher applied to get ethical approval from the Kuwait Public Authority for Youth and Sport and the Authority granted approval. Healthy controls were recruited from KYC. Children eligible for recruitment and their parent/guardians were given information sheet about the study and the reasons for asking for their participation in the study and details of the data to be collected. Those who agreed to take part in study were asked to complete a written consent form for the parent while the child was asked to complete an assent form. Only eligible children with completed assent and consent forms were allowed to participate in the study. The inclusion criteria for the healthy controls were being healthy children with no history of respiratory, cardiovascular or neurological diseases, aged between 6 and 12 years old, child able to give assent and parent/guardian able to give informed consent.

Exclusion criteria for children with asthma

Since the aim of the study was to investigate the spectrum of activity after asthma attack, we excluded children with any other disease of the lungs (e.g. cystic fibrosis, pneumonia), any chest wall or respiratory muscles diseases (e.g. kyphoscoliosis or muscular dystrophy), any cardiac disease (e.g. congenital heart diseases) and any developmental delay that might affect their ability to perform spirometry. As noted above children had to be 6 or above and below 12 years. Children out with this age range were excluded. Children who did not give assent or whose parents refused to give informed consent were also excluded.

Exclusion criteria for healthy children

Subjects were excluded if they were aged below 6 and above 12 years old, had asthma or a history of asthma in the past and did not provide assent and consent. They were also excluded if they had any of the chronic illnesses listed above under.

Sample size

The main outcome of interest in the present study was a difference in activity between children with asthma and healthy children. Using data from Firrincieli et al (323) on the mean difference and standard deviation (SD) of the differences in total volume of physical activity (measured using an Actiwatch as counts per minute) between children with wheeze and children without wheeze the power calculation is as follows; the mean difference between groups in Firrincieli study was 120 counts per minute, (SD 140 counts per minute). Using these values, for 90 % power with P = 0.05, gave an estimate of 17 paired comparisons (using Minitab 16.0). Note that our study consists of both paired and unpaired t test comparisons for the physical activity, and the power calculation for a paired t test has much higher power than unpaired t tests. Paired comparisons here refer to the comparison within the asthmatic patients, between two time points. While the unpaired comparison refers to the comparison between asthmatic patients and healthy controls. If the differences in total volume of physical activity between these two groups/comparisons are similar to those observed by Firrincelli when comparing wheeze versus non wheeze groups, then this study would only need around 17 paired comparisons (i.e. 34 measures for the asthma study, 34 measures for the comparison with matched healthy controls).

Also note that:

a. This power calculation is an estimate with some uncertainty about it.

b. Since the power calculation may be an approximation, and since it was expected that not all patients or controls would complete the study exactly as planned, the researcher aimed to enter more than 17 pairs for each of study. On the basis of this power calculation, the researcher aimed to recruit about 20 children measured twice to answer the within child comparison for the asthma patients, and 40 children for the comparison with healthy controls (20 asthmatic patients and 20 matched controls).

Ethical approval

In order to get approval to recruit asthmatic patients from Kuwait hospitals, the study proposal was submitted to the Joint Committee for the Protection of Human Subjects in Research of the Health Sciences Centre (HSC) & Kuwait Institute for Medical Specialization (KIMS). Study proposal was submitted to the HSC & KIMS committee and reviewed and their approval was granted on 12 April 2012, (Appendix C).

For the healthy controls, the study proposal and the HSC & KIMS committee approval were submitted to Kuwait Public Authority for Youth and Sport in order to get approval to recruit healthy controls from KYC that is controlled by this authority. Study proposal was reviewed and their approval was granted on 21 June 2012 see (Appendix C).

3.2.2 Study design and population

The study was an observational study of Kuwaiti asthmatic children aged 6 to 12 years old admitted to Kuwait hospitals because of an asthma attack between 14th April 2012 and 31st January 2013. The Kuwaiti children with acute asthma attacks were compared to a group of healthy children who were members of the Kuwait Youth Centres (KYC). Each asthmatic patient was studied twice (Figure 3-1), seven days after discharge from hospital, and at four weeks after discharge from hospital. During each investigation the following were measured in the hospital at both time points in the children with asthma attacks: age (yrs); weight (kg); height (cm); childhood asthma control test questionnaire; pulmonary function test (PFT). An activPAL was placed and a period of 7 days monitoring started. Once completed the data from the accelerometer was downloaded and analysed to compute measures of physical activity (PA), sedentary behaviour (SB), and sleeping behaviour from the accelerometry data. The healthy controls had all the same measurements made in the hospital but on one occasion only (Figure 3-1).

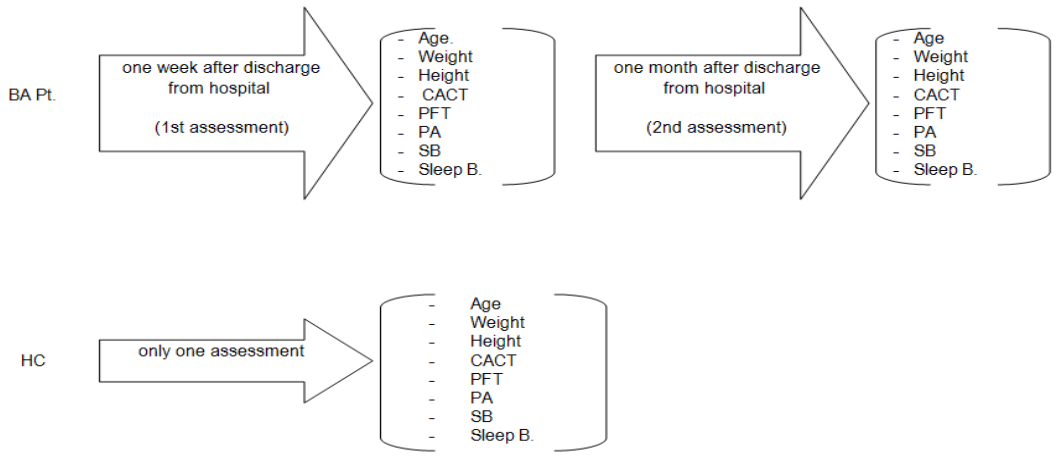

Figure 3-1 Study design; CACT (childhood asthma control test questionnaire), PFT (pulmonary function test), PA (physical activity),SB (sedentary behaviour) and sleeping behaviour (Sleep B) of asthmatic children (BA Pt) were investigated twice; one week and one month after discharge from hospital, and once for healthy controls (HC).

3.2.3 Methods of data collection

3.2.3.1 Age and gender

The date of birth and sex were recorded for each child. The decimal age of each child was calculated from their date of birth to the date of the start of data recording.

3.2.3.2 Anthropometric measurements

Weight

A) Upright scale, type Detecto Weigh Beam Eye-Level

B) Position while measuring weight

Figure 3-2 Measuring weight using upright scale, type Detecto Eye-Level Weigh Beam, reprinted from (470)

Weight was measured to the nearest 0.1 kg using an upright beam balance scale (Detecto Eye-level Weigh Beam scale) (Figure 3-2 (A)). This scale was manufactured by Cardinal Scale Manufacturing Company (based in Webb City, Missouri, USA) (470). The weight was measured using the same device in all subjects. Subjects were weighed at the same time of day with their shoes off and not wearing any heavy clothing while their weight was measured (471). They stood on the platform facing the wall with their arms at their sides not holding the bar or other parts of scale (Figure 3-2 (B)). On each occasion, the large weight and small weight indicators were returned to zero. With the subject on the scale, the balance bar was brought to balance in the centre by moving first the larger weight and then the

smaller weight until the pointer was in balance. The weight was recorded to the nearest 0.1kg.

Height

Figure 3-3: Measuring height using upright scale, type Detecto Eye-Level Weigh Beam, reprinted from (470).

Height was measured to the nearest 0.1 cm. The same type of measuring device (Detecto Eye-Level Weigh Beam (Figure 3-2 (A)) was used for all subjects. Subject's height was measured at the same time of day. They were measured with their shoes off standing on the platform with their arms at their sides not holding the bar or other parts of scale, facing the wall (Figure 3-3). The height bar was adjusted to rest on the subject's head, digit at movable ruler part taken, and recorded to the nearest 0.1cm.

WHO reference data for BMI

Body mass index (BMI) was calculated by dividing subjects body weight in kilograms by the square of their height in metres (kg/m2) (472). In children, to take account of sex differences and changes with age overweight and obesity relative to the mean are expressed as BMI standard deviation scores (BMI Z score) (472). This requires an appropriate reference standard (472). The researcher used the WHO reference data for children and adolescents aged between 2 and 19 years old (473). WHO Anthro software (version 3.2.2,

January 2011 accessible at: http://www.who.int/childgrowth/software/en/) was used to calculate height, weight and BMI Z scores. Depending on their BMI Z scores, a child was classified as:

- underweight if BMI Z score was < -2SD (473).
- overweight if their BMI Z score was >+1SD (corresponding to BMI 25 kg/m^2 at age 19 years) (473).
- obese if BMI Z score >+2SD (corresponding to BMI 30 kg/m^2 at age 19 years) (473).

3.2.3.3 Asthma severity and asthma control assessment

Childhood Asthma Control Test (CACT) use

The Childhood Asthma Control Test Questionnaire (CACT) was developed by GlaxoSmithKline (371) and validated by Liu et al (372), and provides a subjective assessment of symptoms (section 1.7.2.1). It is available only in English and is intended for use with English speakers. There is currently no Arabic version of this questionnaire. The researcher used the CACT by interviewing the participants and their parents and asking the questions in Arabic, explaining the possible answers and recording the verbal grading given by each child and parent and saving the response to calaculate an overall score. The reason behind not translating the CACT questionnaire to Arabic was that the process of translating such a questionnaire would be both costly and time consuming.

The CACT consists of seven questions, four questions completed by the asthmatic child and three questions completed by his parent/guardian. The four child questions are about daytime asthma symptoms, restriction of activity due to asthma, frequency of cough and waking at night because of asthma. Each question of the child's part is scored from 0 (very bad symptoms) to three (no symptoms), and the sum of responses of these questions ranges from 0 indicating uncontrolled asthma to 12 indicating well controlled asthma. The items of the child's part were explained to the child, and then the child was asked to choose the picture. The three parent/guardian questions are related to asthma control over the previous four weeks and asks about any asthma symptoms, wheeze due to asthma and waking at night due to asthma. Each question of this part is scored from 0 (very bad symptoms) to five (no symptoms), and the sum of responses in this part ranges from 0 indicating uncontrolled asthma to 15 indicating well controlled asthma. The total score of the seven questions of CACT are added together with results ranging from 0 indicating uncontrolled asthma to 27 indicating well controlled asthma.

The Pulmonary Function test (Spirometry)

Spirometry is a measure of pulmonary function. The researcher measured the forced vital capacity (FVC) in litres, the forced expiratory volume in 1 second (FEV_1) in litres and the ratio of FEV_1/FVC ratio as measures of airway obstruction.

Measuring device

Figure 3-4: Koko spirometer, reprinted from (474) .

The spirometric measures were measured using a hand-held electronic portable spirometer, the KoKo Spirometer (Figure 3-4), manufactured by nSpire Health Incorporation. The associated software (KoKo Merlin Client version of the KoKo PFT system) was installed on a laptop computer. The system consists of pneumotach (respiratory air flow measuring device), USB cable (connecting spirometer to computer to run KoKo PFT) and KoKo single use mouth filter attached to the pneumotach, designed to filter viruses and bacteria and obstruct expectorated materials from passing inside pneumotach. The filter is important in reducing contamination and the need for cleaning and disinfection. In order to get valid spirometric results, equipment and techniques used in spirometry should conform to the American Thoracic Society and the European standards (373, 375, 377). Both flow-volume and volume-time curves should be displayed during measurement and should be able to be printed to provide a hard copy result. The flow–volume curve is useful to evaluate the extent of patient effort during the initial part of spirometry procedure, while the volume–time curve is useful to evaluate the last part of the spirometry procedure (373, 375). Further, prior to performing pulmonary function test, KoKo spirometer should be calibrated using volume calibration syringe. According to the manufacturer recommendation, it is preferable to leave power to the KoKo Spirometer on at all times, or at least to power it on and warm it up for 15 minutes before calibration or testing. This is done by connecting the spirometer to the computer by USB cable. It is recommended that the KoKo spirometer be stored and

transported between 40–70°C temperatures. Also, the KoKo Spirometer can work in a wide range of environmental conditions: in temperatures between 20-35°C, relative humidity 0-100%, barometric pressure of 550-780 mmHg. All these factors were included within the standard operating procedure developed for the study.

Standard operating procedure for the measurement of spirometry using the KoKO spirometer

KoKo Spirometer was powered on and warmed up for 15 minutes before calibration or testing; by connecting spirometer to laptop by USB cable. Temperature, pressure and humidity of the hospital environment in which the test was performed were taken from the biochemistry laboratory and fed into KoKo Spirometer program. The temperature in Kuwait hospitals during most of the measurement times was around 25°C with a range of 21-25°C. Barometric pressure was constantly around 761-762 mmHg. KoKo Spirometer was calibrated prior to testing using a 3 Liter syringe by placing the free opening of KoKo filter to that of calibrating syringe, choosing the calibration icon from the main menu of the KoKo Spirometer program and then calibrating the pneumotach (373, 375). After calibration, patient data was entered into KoKo Spirometer program to create a new test. Reference values for this study came from Wang (Peds) (NHANES III) (475-477). There are no reference values for children's lung function available for the Middle Eastern area. Finally, before the start of measurement, a new KoKo filter was placed securely on pneumotach handle. The pneumotach was then held by the patient. The computer attached to KoKo Spirometer was around by 1.5m away from the subject as recommended in the manufacturer's recommendations. Before the actual test, the patient was instructed as follows (373, 375): to sit on an armchair without wheels and with a straight back; to clip his/her nose by using a nose clip; to hold pneumotach, put opening of filter in the mouth, close the lips tightly around filter opening, breathe normally without effort (tidal volume), then to take as big a breath in as he/she can and when his/her lungs are full to blow out as fast and as far as he/she can. Then when all air is expired, patient is asked to take a further big breath in. After instructing the patient, FVC test is selected using test type icon, and the FVC manoeuvre is started using the start test icon in the software. Finally, the patient is asked to begin the test. The manoeuvre is repeated 3 times or more, especially if volume–time and flow–volume curves show improper performance or artefacts (Appendix D) (373, 375). However, if the child becomes exhausted the test is discontinued(373, 375). The pulmonary function test is considered of good quality when it shows no artefacts in the volume–time and flow–volume curves (Appendix D) affecting measurements. Artefacts

may arise from coughing in early seconds of exhalation, a closed glottis, early cessation of test, less than maximal effort, air leaks when mouth or lips are not closed enough or filter opening is obstructed by tongue (373, 375). After performing test, the best results (good test performance curves (i.e. ‘‘usable curves’’) of FVC and FEV1 of at least three forced expiratory curves were saved, so that they could be reviewed. Volume-time and flow-volume curves of FVC and FEV1 were viewed. The best (the largest) reading of FVC and FEV_1, were taken not necessarily from the same curve but, could be taken from the 3 different curves(373, 375). Spirometry testing was performed twice for children with asthma. The first measurement was one week following discharge from hospital, while the second measurement was one month after discharge. Healthy controls were tested once.

3.2.3.4 Accelerometry for physical Activity, sedentary and sleeping behaviours assessment

As noted before in section 1.7.3.1.3.2 various types of accelerometers are available, and used in monitoring individual PA and SB. An acceptable accelerometer should have certain characteristics such as reproducibility, validity, feasibility, reusable, small size and light weight. The ActivPAL™ (PAL Technologies Ltd, Glasgow) was used in the present study and fulfilled these criteria (440, 441). The ActivPAL™ is a uni-axial piezoresistive accelerometer with a sampling rate equivalent to 10 Hz, usually attached to the mid-thigh. It contains an inclinometer that can classify postural positions and it is capable of recording PA continuously for long period. It has been validated for recording postural changes, sitting/lying time, standing, walking, sit-to-stand and stand-to-sit transition counts and can also count steps in children (442, 446, 447).

Standard set up for measurement of physical activity and posture

Prerequisite for activPAL monitor working

ActivPAL^{TM} professional software, was downloaded from PAL Technologies Ltd web site, and installed on the computer used in conjunction with ActivPAL device. Operating system of computer in which ActivPAL^{TM} professional software is installed was Windows 7.

Charging activPAL monitor

To charge the ActivPal^{TM}, a docking station was connected to computer by USB cable, and then ActivPAL device placed into one of five sockets of docking station. An orange light

indicates the device is charging. After the hours required for full charge this light disappears signifying end of charging process and indicating the device is now fully charged.

Programming ActivPAL monitor

ActivPAL device was placed in the programming socket of docking station while connected to computer. Then from file menu of ActivPAL™ professional software, reprogramming was selected to clear the ActivPAL device memory and prepare it for measurements. The software gives option to choose starting date and time of recording. Once recording date and time are entered, the ActivPAL device starts recording, and flashes green light throughout recording process.

Placement ActivPAL monitor

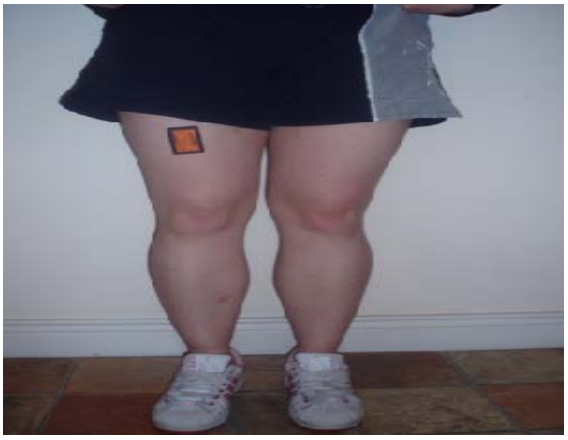

Figure 3-5: Placement of activPAL monitor directly on skin of the child's thigh anteriorly midway between hip and knee, reprinted from (143)

After programming activPAL monitor so that it was ready for recording, it was placed directly on skin of the child's thigh anteriorly midway between hip and knee (Figure 3-5). The device was fixed in this position by PALstickies™ a hydro-gel adhesive patch, and secured in position by a covering with Tegaderm™.

Recording

In this study, the participants and the parent/guardian were instructed to attach the activPAL™ for 7 consecutive days. The families were advised to leave the device on throughout the night. However, as the device is not waterproof, parents were advised to remove the monitor during the times of any showering, bathing or swimming during the

monitoring period and reattach the device once the water based activity was completed. Parents were provided with a daily activity recording sheet and asked to note any time the device was removed as well as the time the device was reattached.

Data Processing

After completion of the monitoring and removal and return of the device, the activPAL^{TM} data were downloaded onto a computer using the activPAL^{TM} Professional Research Edition software (Version 5.8.2.3). Data were then analysed and sorted into sit/lie, stand or walk intervals. In addition, the data were also reprocessed by another software programme, HSC PAL analysis software v 2.14, developed by Dall and Granat at Glasgow Caledonian University, which is capable of defining time in seconds at which postural transitions occurred (446) (Figure 3-6). The indices generated from the activPAL^{TM} Professional Research Edition software (Version 5.8.2.3) were the total activity count, number of steps and the number of breaks in sitting (Figure 3-7). Indices generated by HSC PAL analysis software v 2.14, were the total sitting time, the percentage sitting time, the number of sitting bouts, the fragmentation index, the sleeping time and the sleeping pattern (Figure 3-7).

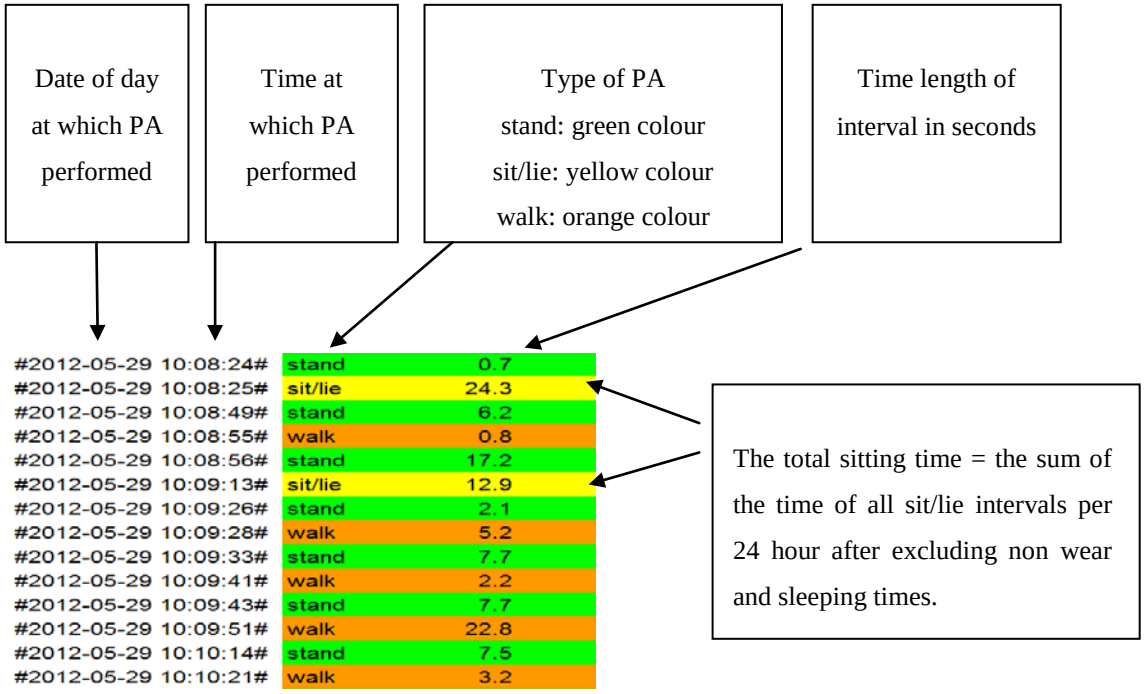

Figure 3-6: Example of file produced by HSC PAL analysis software v 2.14 file.

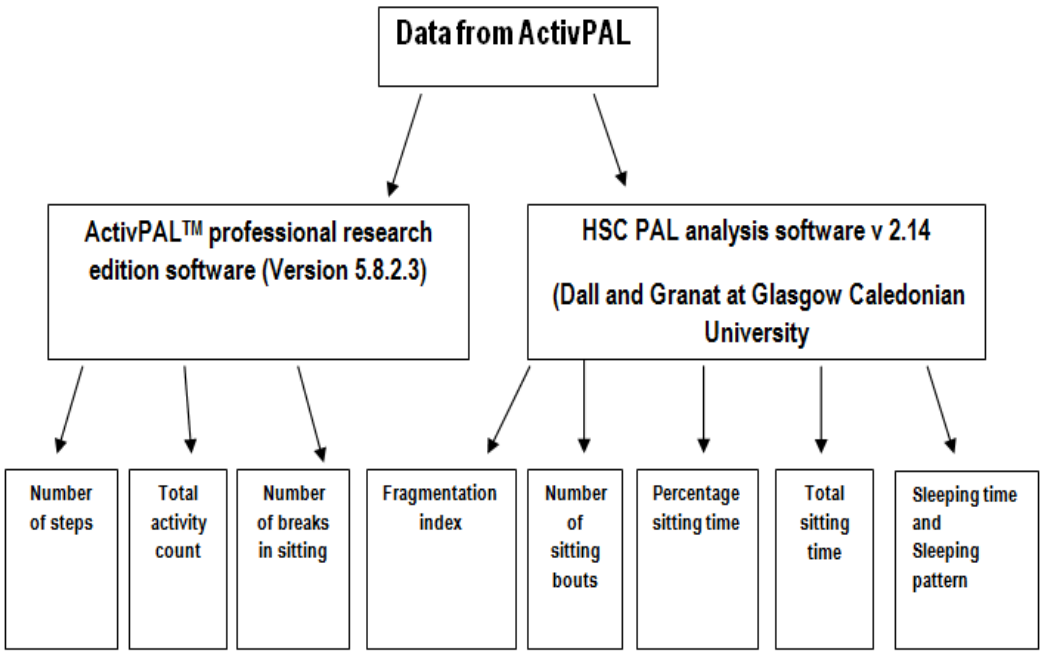

Figure 3-7: The products of software programmes used in the analysis of ActivPAL data

Non-wear time (Missing data)

Non-wear time was recognised from the times on the daily activity recording sheets given to the parent/guardian where the parent/guardian documented any time the device was removed as well as the time the device was reattached. Further, periods lasting 60 minutes or more which appeared as unchanging extended ‘‘sit/lie’’ periods in the activPAL™ file (as the accelerometer when removed is placed in a horizontal plane and records no movement), were considered as a non-wear time as defined in previous studies (143). Once the non-wear time was identified it was excluded from the raw activPAL™ files before analysis. “Non-wear time” occurring during expected periods of sleep at night (defined as the longest sit/lie interval within 24 hours between two valid days (170, 357)) were identified and was not excluded.

Parameters measured: monitoring days and monitoring hours

Previous studies investigated the proper time for monitoring activity and sedentary behaviour using accelerometers and it was found that the number of days required for reliable monitoring of usual physical activity and sedentary behaviour was four to nine days (478, 479). More detailed studies have shown that placing a monitor for three weekdays for at least six hours while awake was enough to get reliable results (446). In the present study, each child was asked to wear the activPAL™ monitor continuously, 24hrs a day, for

between five and seven days. In practice, in this study, the device wear time was always much greater than the minimum previously established for reliable data.

Total monitoring time is the average of total monitoring time in hours per 24 hours, after excluding sleeping time and non-wear time. Schools in Kuwait start at 0730 and to attend on time, children wake up early in the morning mostly at 0600-0630, and that was obvious from the file created by HSC PAL analysis software v 2.14. According to this, 0630 was chosen for this study as the usual start of monitoring time of the day and 0629 of the next day was the end time of this day. The total monitoring time per day was calculated by taking the average of total monitoring times.

3.2.3.5 Physical activity

The physical activity of subjects in this study was assessed by; the PA duration in hours per day the total activity count per day and the number of steps per day.

Physical activity duration in hours per day

The duration of PA in hours per day was obtained by subtracting the sum of time of SB (total sitting time) in hours and sleeping time in hours from the total 24 hours of the day (PA hrs/24hrs = (SB hrs/24hrs + sleeping time hrs/24hrs) – 24hrs).

Total activity counts per day

The total activity count from the activPAL is a measure of the total volume of physical activity per day. The higher this value the more active is the child. The activity count was derived from data that was downloaded using activPAL^{TM} professional research edition software (Version 5.8.2.3). The total activity count was calculated by taking the average of total activity counts produced by participants each 15 second epoch per 24 hours after excluding non wear and sleeping time and then averaged for all of the monitoring days.

Number of steps per day

Number of steps per day was derived from data that was downloaded using activPAL^{TM} professional research edition software (Version 5.8.2.3). Number of steps per day was calculated by taking the total number of steps taken by the subject each day, then taking the average number of steps for the whole monitoring time.

3.2.3.6 Sedentary behaviour

To quantify and monitor SB, it was differentiated into: 1) volume of sitting time 2) pattern (or fragmentation) of sitting time. The volume of sitting time is represented by both the total sitting time/day and the percentage sitting time/per day. The pattern (or fragmentation) of sitting time is represented by distribution of sitting bouts according to their length (as reflected in fragmentation index (FI) and breaks in sitting (up transitions) (138).

Volume of sedentary behaviour: total sitting time, percentage sitting time

Total sitting time

Awake time was defined by the first up transition in the morning. The end of awake time was identified from the last up transition in the evening, indicating the beginning of sleeping time. The total time recorded as ‘‘sit/lie’’ during awake hours was then calculated. Total ‘‘sit/lie’’ time was derived from data that was downloaded using HSC PAL analysis software v 2.14 file (Figure 3-6). After excluding non-wear and sleeping times, all ‘‘sit/lie’’ times of participant per 24 hour were summed and then taking the average ‘‘sit/lie’’ times for the whole monitoring time.

Percentage sitting time

Percentage sitting time is calculated in order to know the relative contribution of sedentary behaviour to the daily lifestyle of child. The percentage sitting time is the total sitting time in hours normalised to the total monitoring time in hours (percentage sitting time = total sitting time (hrs)/ monitoring time (hrs)) (139).

Pattern (fragmentation) sedentary behaviour: breaks in sitting (up transitions), number of sitting bouts and fragmentation index

Breaks in sitting (Up transitions)

Breaks in sitting were identified as ‘Up transitions,’ that is the transitions or postural shifts from ‘‘sit/lie’’ posture to ‘‘stand’’ posture (143) during awake time. To avoid double counting, only ‘up’ transitions from sit/lie to stand were counted and not stand to sit/lie transitions. The number of up transitions per hour was calculated by the original activPAL^{TM} Professional Research Edition software (Version 5.8.2.3) and summarized as breaks per hour (Figure 3-7). The up transitions for each day were summed and then the up

transitions for each child for all recording days averaged to give the average number of up transitions for each child for all recording days (Figure 3-8).

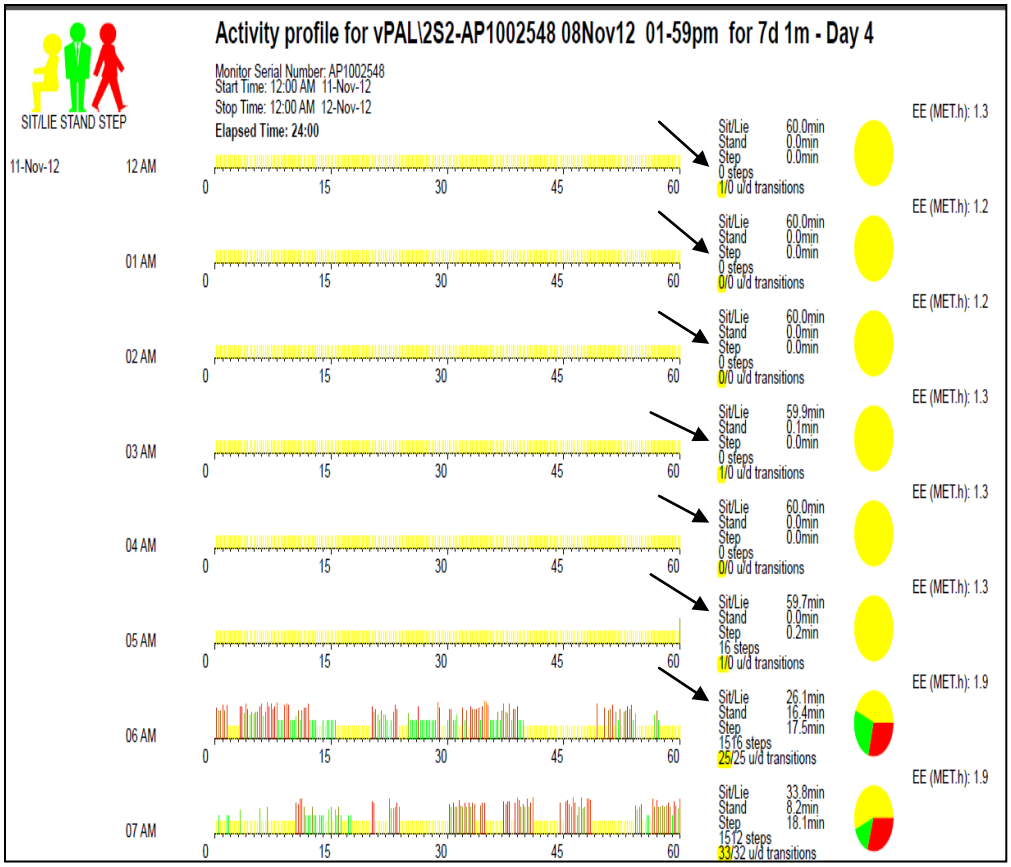

Figure 3-8 Breaks in sitting (Up transitions) appears in the activity profile as red spikes

Number of sitting bouts

Sitting bouts are described as sit/lie time interval (measured in seconds) terminated by postural change (141, 146), and were expressed as a number using file produced by HSC PAL analysis software v 2.14 (146, 446, 480). Distribution and length of sitting bouts can be illustrated by the fragmentation index (141, 145, 146). The number of sitting bouts for each day was averaged to give the average number of sitting bouts per day for each child.

Fragmentation index

Fragmentation index is the number of sedentary bouts normalised to the total sitting time in hours (FI= number of sedentary bouts/total sitting time in hours) (141, 145, 146). This measure has advantage that the length of sitting bouts can be illustrated by fragmentation

index. This allows an assessment of whether sitting time is composed of a large number of short bouts or small number of long bouts (145). Fragmenting sitting time with large number of short sitting bouts will result in a higher fragmentation index (141, 145, 146).

Sleeping behaviour: sleeping time and sleep pattern

The sleeping behaviour of subjects in this study was assessed by both the sleeping time per day and the sleeping pattern.

Sleeping time

The longest non-wear time interval within a 24 hour interval between two valid days was regarded by Colley et al (170) as the sleeping time of children. Separately, Alghaeed et al (146), showed that the average number of breaks in sitting (up transitions) per hour over the 24 hours, could be used to define wake up time and sleep onset time. Accordingly, the longest sit/lie interval within 24 hours between two valid days, was matched with the interval when the average number of breaks over the 24 hours was lowest and was used to define the start and end of sleep at night. In Kuwait, the school starts at 0730. To attend on time, children usually go to bed at around 2100 - 2200 and wake around 0600-0630, so the onset of sleep (longest non-wear time interval within a 24 hour interval between two valid days) usually starts around 2100-2200 and ends around 0600-0630. The longest sit/lie interval within 24 hours between two valid days for each day was measured, and then the sleep time for the monitoring days were averaged to give the average duration of sleep per day for each child.

Sleep pattern

Any disruptions of sleep such as changes in bed time, wakeup at night were spotted by observing the curve of the average number of breaks in sitting (up transitions) per hour over the 24 hours and any spike in this curve in the period of sleep at night indicates sleep disturbance. The sleep disruptions of a suffering subject can be observed in the curve of number of breaks in sitting of the day in which he suffered from sleep disturbances separately, but these disruptions disappear when observing the curve of the average number of breaks in sitting for the whole recording period (5-7 days) and the curve will appear smooth without spikes as if there are no sleep disturbances. This is because sleep disruptions of each day occur in a different time which means that they will cancel each other when the average number of breaks in sitting for the whole recording days is calculated.

Unfortunately, at the present time there is no valid metric method for describing these sleep disruptions for the whole recording days.

3.2.4 Data analysis

Statistical analysis was done using IBM SPSS Statistic (Version 22). Data were checked for normality using IBM SPSS Statistic (Version 22). Normally distributed data were presented as mean and standard deviation, while non-normally distributed data were presented as median and interquartile range. Paired methods for comparisons were used to compare data at baseline and one month in subjects with asthma after discharge from the hospital, either paired 't' test for normally distributed differences, or Wilcoxon test if not. Un paired or two sample methods for comparisons were used to compare data of the asthmatic patients at one month after discharge from the hospital with the healthy control group data, either as independent sample 't' test for the normally distributed differences, or Mann-Whitney U test if not. For all statistical tests a p value of < 0.05 was considered statistically significant.

The inter individual variability of changes in the movement continuum between the two time points, after one week and after one month of discharge from hospital, was evaluated by the percent change. The percent change in the value of the variable between two time points is the result of subtraction of the old value (value of variable after one week) from the new value (value of variable after one month), then divide by the old value (the percent change = value of variable after one month - value of variable after one week/ value of variable after one week × 100).

3.3 Results

3.3.1 Participants and flow diagram

The total number of children recruited in this study was 80 participants; 51 asthmatic patients aged from 6 to 12 years old admitted to Kuwait hospitals due to asthma attack, and 29 healthy children aged from 6 to 12 years old, members of Kuwait Youth Centres (KYC) (Figure 3-9). Out of the 51 asthmatic patients screened for this study seven male children with acute asthma attack aged from 7 to 12 years old did not meet the inclusion criteria (Figure 3-9): three children were cases of developmental disability; one child was myopathic; one child had Down's syndrome; one child had congenital heart disease and one had ADHD (Attention Deficit Hyperactivity Disorder). Of the 44 remaining children, 16

were not able to complete the first part of the study in full (Figure 3-9) and were excluded from the study: these included 11 males and 5 females, aged 6 to 11 years old, who were

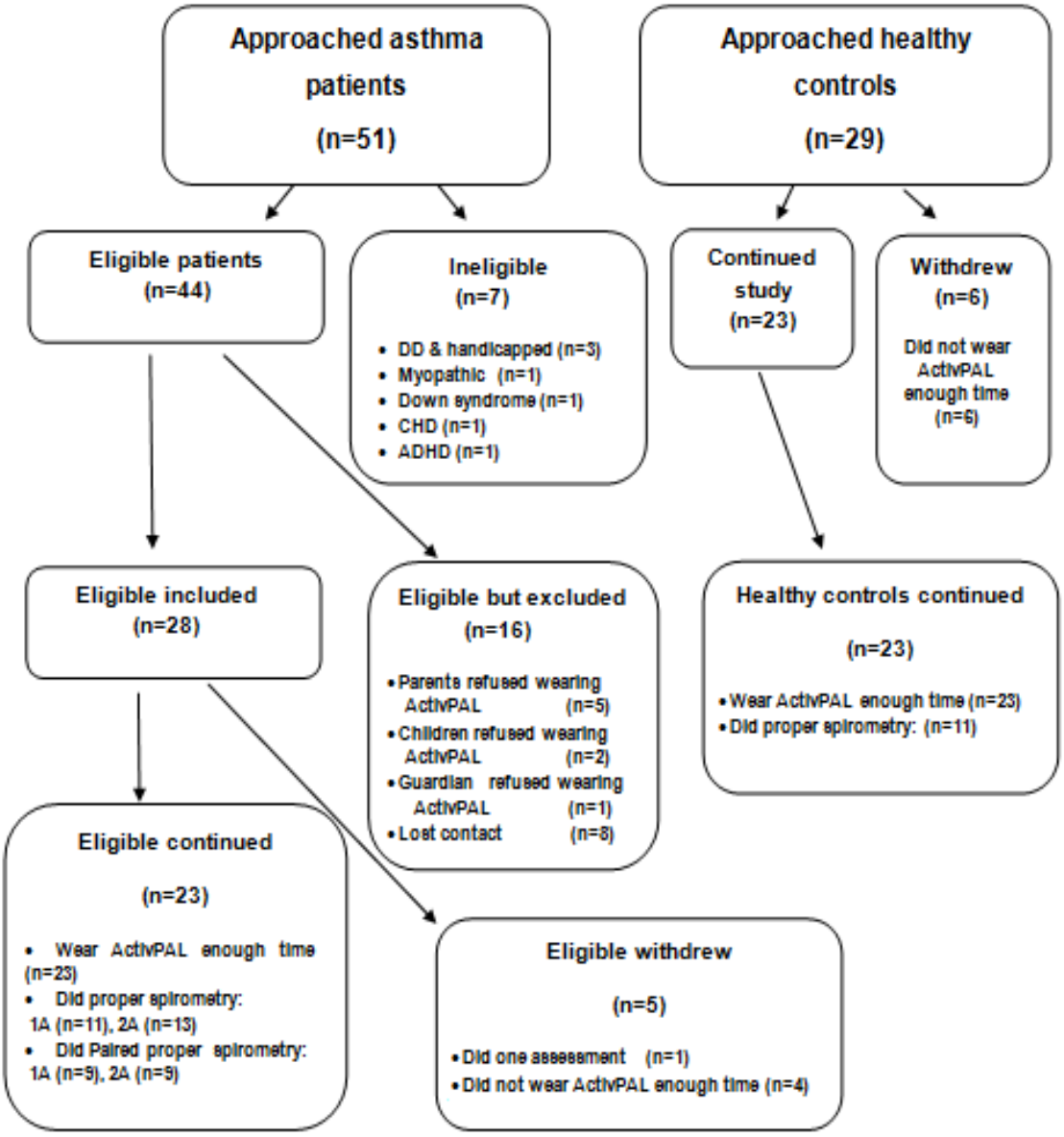

Figure 3-9 Participants and flow diagram; 1A: asthmatics one week after discharge from hospital, 2A: asthmatics four weeks after discharge from hospital, DD: developmental disability, CHD: congenital heart disease, ADHD: Attention Deficit Hyperactivity Disorder.

known to have asthma and who had been admitted to hospital with an asthma exacerbation and had no history of other diseases other than asthma. Reasons behind their exclusion were as follows: in five, their parents rejected wearing ActivPAL, two children refused to wear ActivPAL, one orphan patient agreed to do spirometry and wear ActivPAL, but his guardian

refused to participate in the study. In a further, eight patients the researcher lost contact with them. Twenty eight eligible patients completed the first assessment. Of these 28, only 23 continued the second study assessment. Five withdrew from the study before completing the second assessment: one child did only one assessment and contact had been lost by the second assessment, four patients did not wear ActivPAL for a sufficiently long time (Figure 3-9). Twenty nine comparable healthy children gave informed consent and were screened, only 23 continued the study; six did not wear ActivPAL sufficiently long enough and withdrew (Figure 3-9). Furthermore, only 11 asthmatic children one week after discharge from hospital (1A), 13 asthmatic children four weeks after discharge from hospital (2A) and 11 healthy control (C), completed spirometry according to American Thoracic Society and European standards (373, 375, 377) (Figure 3-9).

All children with asthma had been diagnosed before admission and had a past history of previous admissions due to asthma attacks. The duration of inpatient stays ranged from 4-9 days (mean = 5 days) with one child being admitted to paediatric intensive care unit. Almost all of them received systemic steroids (methyleprednisolone dose 0.5-1 mg/kg intravenous (Kuwait guidelines)) according to the severity of their asthma. All of them received inhaled steroids during their hospital stay. After discharge from hospital, they were prescribed asthma treatment according to severity of their pre-existing disease. At follow-up it was noted that some of the patients were taking their treatment regularly, while others admitted they were not and had stopped taking some of their treatment, especially the inhaled steroids.

3.3.2 Participants characteristics

Both males and females were included in this study; each arm of the study consisted of 17 males and six females (Table 3-1). There was no significant difference between mean age of asthmatic and healthy children (Table 3-1). Mean height of healthy children was significantly higher than that of asthmatic children one week (P= 0.02) and four weeks (P= 0.02) after discharge from hospital (Table 3-1). There was no significant difference in height Z score between healthy children and asthmatic children four weeks after discharge from hospital (Table 3-1). Mean weight of the healthy children was significantly higher than that of asthmatic children four weeks after discharge from hospital (P= 0.01) (Table 3-1). Similarly, mean weight Z score of healthy children was significantly higher than that of asthmatic children four weeks after discharge from hospital, (P= 0.01) (Table 3-1). Mean BMI of the healthy children was significantly higher than that of asthmatic children four

weeks after discharge from hospital (P= 0.01) (Table 3-1). As expected, the mean BMI Z score of the healthy children was significantly higher than that of asthmatic children four weeks after discharge from hospital (P= 0.02) group (Table 3-1).

Table 3-1: Participants characteristics; 1A: asthmatic children one week after discharge from hospital, 2A: asthmatic children four weeks after discharge from hospital, C: healthy children, values are mean ± SD (n=23)

Variable	1A	2A	C
Age (years)	8.1 ± 2.02	8.1 ± 2.02	9.0 ± 1.72
Gender	Males:17 Females:6	Males:17 Females:6	Males:17 Females:6
Height (cm)	125.5 ± 12.70	125.6 ± 12.49	133.5 ± 11.26
Height Z score	- 0.3 ± 1.11	- 0.4 ± 1.06	0.2 ± 1.84
Weight (kg)	27.8 ± 12.53	28.2 ± 12.77	34.2 ± 8.23
Weight Z score	- 0.1 ± 1.49	- 0.1 ± 1.49	0.9 ± 1.36
BMI (kg/m^2)	17.0 ± 4.48	17.0 ± 4.53	19.0 ± 3.27
BMI Z score	0.1 ± 1.52	0.1 ± 1.53	1.1 ± 1.24

There were two underweight (BMI Z score < -2 Z score) asthmatic children one week after discharge from hospital, and two underweight asthmatic children four weeks after discharge from hospital. Participants of normal weight included 16 asthmatic children one week after discharge from hospital, 16 asthmatic children four weeks after discharge from hospital and 10 healthy children. Overweight participants (BMI Z score > +1 Z score) were 2 asthmatic children one week after discharge from hospital, 2 asthmatic children four weeks after discharge from hospital and 10 healthy children. There were similar number of obese children (BMI Z score > + 2 Z score) amongst the asthmatic and the healthy children (n = 3).

3.3.3 Respiratory system assessment

The severity of asthma symptoms was evaluated by the Childhood Asthma Control Test questionnaire (CACT), are presented in Table 3-2.

Table 3-2: Childhood asthma control test questionnaire (CACT); the child section score, the parents/guardian section score and the total score of childhood asthma control test questionnaire, the higher the score the better asthma symptoms , values are mean ± SD (n=23)

	Variable	After 1 week	After 4 weeks	P value
Child section of childhood asthma control test questionnaire (CACT) score	-Daytime asthma symptoms	1.8 ± 0.39	2.1 ± 0.42	0.03
	-Activity restriction	1.8 ± 0.58	2.2 ± 0.74	0.012
	-Asthma induced cough	1.8 ± 0.42	2.3 ± 0.56	0.001
	-Asthma induced night awake	2.2 ± 0.80	2.7 ± 0.54	0.001
Parents/guardian section of childhood asthma control test questionnaire (CACT) score	-Number of days child has daytime asthma symptoms	3.3 ± 1.15	4.0 ± 1.04	0.018
	-Number of days child has asthma induced wheeze	4.3 ± 0.98	4.6 ± 0.84	0.22
	-Number of days child awake at night due to asthma	3.8 ± 1.62	4.7 ± 0.63	0.01
Total childhood asthma control test questionnaire (CACT) score		19.1 ± 4.4	22.7 ± 3.8	0.000

Mean CACT score of child section of asthmatic children one week after discharge from hospital was significantly lower than that of asthmatic children four weeks after discharge from hospital in daytime asthma symptoms (P= 0.03), restriction of activity due to asthma (P= 0.012), frequency of cough caused by asthma (P= 0.001) and awake at night because of asthma (P= 0.001) (Table 3-2). The Mean CACT score of parents/guardian section of asthmatic children one week after discharge from hospital was significantly lower than the score of asthmatic children four weeks after discharge from hospital in number of days asthmatic child suffered daytime asthma symptoms (P= 0.018) and number of days

asthmatic child wake up at night due to asthma (P= 0.01) (Table 3-2). The total CACT score is the sum of scores of both child section and parents/guardian section. Mean total CACT score of asthmatic children one week after discharge from hospital was significantly lower than the score of asthmatic children four weeks after discharge from hospital (P= 0.0001), (Table 3-2).

The severity of the obstructive lung changes were evaluated by pulmonary function test (PFT) and are presented in (Table 3-3). Overall, those who completed satisfactory spirometry were only 11 asthmatic children at week one after discharge from hospital patients, 13 asthmatic children at four weeks after discharge from hospital and 11 healthy controls with only nine children with asthma completing spirometry at both time points. The statistical analysis was done for results of those asthmatic children who completed spirometry on two time points. There was no significant difference in forced vital capacity (FVC) Z score of asthmatic children measured at week one and week four following asthma attack (Table 3-3). Similarly, there was no significant difference in forced vital capacity (FVC) Z score between asthmatic children measured at week four and that of healthy controls (Table 3-3). There was no significant difference in forced expiratory volume in one second (FEV1) Z score of asthmatic children measured at week one and week four following asthma attack (Table 3-3). The forced expiratory volume in one second (FEV1) Z score of asthmatic children measured at week four was significantly higher (P=0.012) than that of healthy controls (Table 3-3). There was no significant difference in the ratio FEV1/FVC Z score of asthmatic children measured at week one and week four following asthma attack (Table 3-3). Similarly, there was no significant difference in the ratio FEV1/FVC Z score between asthmatic children measured at week four and that of healthy controls (Table 3-3).

Table 3-3: Pulmonary function test indices; Forced vital capacity (FVC) Z score, Forced expiratory volume in one second (FEV1) Z score, and FEV1/FVC Z score measured at week one and at week four in asthmatic children following asthma attack and in healthy controls, values are mean ± SD ((Asthmatic children after week one; n=9), (Asthmatic children after four weeks; n=9), (Healthy controls; n=11))

	Asthmatic children at week 1 and week 4			**Asthmatic children at week 4 and healthy controls**		
Variable	Asthmatic Week 1	Asthmatic Week 4	P* value	Asthmatic Week 4	Healthy	P• value
FVC Z score	-1.1 ± 1.82	-0.9 ± 1.77	0.5	-0.9 ± 1.77	-0.04 ± 0.77	0.15
FEV1 Z score	-1.3 ± 1.86	-1.4 ±1.66	0.9	-1.4 ±1.66	0.1 ±0.67	0.012
FEV1/FVC Z score	- 0.5 ± 1.31	- 0.8 ± 1.51	0.27	- 0.8 ± 1.51	0.2 ± 1.10	0.1

Note: P*value: compare values at week one and week four in asthmatic children.
P• value: compare values of asthmatic children at week four and healthy controls.

3.3.4 Activity continuum

3.3.4.1 Physical activity

The number of days the ActivPAL was worn for monitoring activity continuum is presented in (Table 3-4). The number of days the ActivPAL was worn ranged from three to seven days, with a mean number in excess of five days for all groups ranging from 5.4 to 5.7 days (Table 3-4). There was no significant difference in number of days the ActivPAL was worn for monitoring activity continuum of asthmatic children at week one and at week four (Table 3-4). Similarly, there was no significant difference between number of days the ActivPAL worn for monitoring activity continuum of asthmatic children at week four and healthy controls (Table 3-4).

The mean number of hours for monitoring activity continuum was presented in (Table 3-4). The mean number of hours for monitoring ranged from 13.0 to 14.1 hrs/day (Table 3-4). The mean number of hours for monitoring activity continuum of asthmatic children at week one was significantly higher than that of week four (P=0.000) (Table 3-4). However, there was no significant difference between the mean number of hours for monitoring activity continuum of asthmatic children at week four and healthy controls.

Physical activity measurements included physical activity duration in hours per day presented in (Table 3-5), total activity count per day presented in (Table 3-5) and number of steps per day presented in (Table 3-5). There was no significant difference in physical activity duration in hours per day of asthmatic children measured at week one and week four following asthma attack (Table 3-5). The physical activity duration in hours per day of asthmatic children measured at week four was significantly higher (P=0.038) than that of healthy controls. There was no significant difference in the mean total activity count of asthmatic children measured at week one and week four following asthma attack (Table 3-5). Again, the mean total activity count of asthmatic children measured at week four was significantly higher (P=0.006) than that of healthy controls (Table 3-5). The mean number of steps of asthmatic children measured at week four was significantly higher (P = 0.022) than that of week one (Table 3-5). The mean number of steps of asthmatic children measured at week four was significantly higher (P = 0.001) than that of healthy controls (Table 3-5).

Table 3-4 Monitoring time of activity continuum; number of days ActivPAL worn for monitoring activity continuum and total monitoring time in hours per day for asthmatic children at week one and at week four and healthy controls, values are mean ± SD (n=23, for both groups)

	Asthmatic children at week 1 and week 4			**Asthmatic children at week 4 and healthy controls**		
Variable	Asthmatic Week 1	Asthmatic Week 4	P* value	Asthmatic Week 4	Healthy	P• value
Number of days ActivPAL worn	5.7 ± 1.06	5.5 ± 0.99	0.4	5.5 ± 0.99	5.4 ± 0.90	0.7
Total monitoring time in (hrs/day)	14.1 ± 1.16	13.0 ± 1.33	0.000	13.0 ± 1.33	13.2 ± 1.25	0.6

Note: P*value: compare values at week one and week four in asthmatic children.
P• value: compare values of asthmatic children at week four and healthy controls.

Table 3-5 Physical activity parameters; physical activity duration in hours per day, total activity count per day and number of steps per day measured at week one and at week four in asthmatic children following asthma attack and in healthy controls, values are mean ± SD (n=23, for both groups)

	Asthmatic children at week 1 and week 4			**Asthmatic children at week 4 and healthy controls**		
Variable	Asthmatic Week 1	Asthmatic Week 4	P* value	Asthmatic Week 4	Healthy	P• value
Physical activity duration (hrs day)	6.72 ± 1.32	7.40 ± 1.12	0.067	7.40 ± 1.12	6.63 ± 2.04	**0.038**
Total activity counts /day	750 ± 229	840 ± 271	0.072	840 ± 271	650 ± 157	**0.006**
Number of steps / day	10087 ± 2720	11876 ± 3924	**0.022**	11876 ± 3924	8602 ± 2128	**0.001**

Note: P*value: compare values at week one and week four in asthmatic children.
P• value: compare values of asthmatic children at week four and healthy controls.

3.3.4.2 Sedentary behaviour

Sedentary behaviour measurements included: 1) volume of sitting time: the total sitting time/day presented in (Table 3-6) the percentage sitting time/per day presented in (Table 3-6), 2) pattern (or fragmentation) of sitting time: number of breaks in sitting (up transitions) presented in (Table 3-6), number of sedentary bouts presented in (Table 3-6) and fragmentation index presented in (Table 3-6).

The mean total sitting time of asthmatic children measured at week four was significantly lower (P = 0.001) than that of week one (Table 3-6). The mean total sitting time of asthmatic children measured at week four was significantly lower (P = 0.05) than that of healthy controls (Table 3-6). There was no significant difference in percentage sitting time per day of asthmatic children measured at week one and week four following asthma attack (Table 3-6). There was no significant difference in percentage sitting time per day between asthmatic children measured at week four following asthma attack and healthy controls (Table 3-6).

There was no significant difference in the mean number of breaks in sitting per day of asthmatic children measured at week one and week four following the asthma attack (Table 3-6). The mean number of breaks in sitting per day of asthmatic children measured at week four was significantly higher (P=0.055) than that of healthy controls (Table 3-6). There was no significant difference in the mean number of sedentary bouts per day of asthmatic children measured at week one and week four following asthma attack (Table 3-6). The mean number of sedentary bouts per day of asthmatic children measured at week four was significantly higher (P = 0.045) than that of healthy controls (Table 3-6).There was no significant difference in the fragmentation index of asthmatic children measured at week one and week four following asthma attack (Table 3-6). The fragmentation index of asthmatic children measured at week four was significantly higher (P =0.001) than that of healthy controls (Table 3-6).

Table 3-6 Sedentary behaviour parameters; total sitting time, percentage sitting time, breaks in sitting (Up transitions) per day, number of sedentary bouts per day and fragmentation index measured in asthmatic children at week one and at week four following asthma attack and in healthy controls. Values are mean ± SD (n=23, for both groups)

	Asthmatic children at week 1 and week 4			**Asthmatic children at week 4 and healthy controls**		
Variable	Asthmatic Week 1	Asthmatic Week 4	P* value	Asthmatic Week 4	Healthy	P• value
Total sitting time (hrs/ day)	8.7 ± 1.13	7.7 ± 1.10	**0.001**	7.7 ± 1.10	8.3 ± 1.56	**0.05**
Percentage sitting time	62.1 ± 8.15	60.0 ± 8.74	0.28	60.0 ± 8.74	63.7 ± 10.68	0.21
Number of breaks in sitting / day	257 ± 114	247 ± 97	0.51	247 ± 97	199 ± 65	0.055
Number of sedentary bouts/ day	266 ± 105	254 ± 89	0.46	254 ± 89	209 ± 54	**0.045**
Fragmentation index	31.1 ± 13.06	33.5 ± 13.00	0.20	33.5 ± 13.00	26.2 ± 9.57	**0.001**

Note: P*value: compare values at week one and week four in asthmatic children.
P• value: compare values of asthmatic children at week four and healthy controls.

3.3.4.3 Sleeping behaviour

There was no significant difference in the sleeping time of asthmatic children measured at week one and week four following asthma attack (Table 3-7). There was no significant difference in the sleeping time between asthmatic children measured at week four following asthma attack and healthy controls (Table 3-7). At the groups level no sleep disruptions were found in the acute and recovery stage of asthma attack. However, on individual basis sleep disruptions such as wakeup at night were spotted by observing the curve of the number of breaks in sitting (up transitions) per hour over the 24 hours for those asthmatic children suffering from sleep disturbances, while in the plots of mean number of breaks in sitting per hour against time during 24 hours of all asthmatic children these disruptions were not evident.

Table 3-7 Sleeping time in hours per day measured at week one and at week four in asthmatic children following asthma attack and in healthy controls, values are mean ± SD (n=23)

Asthmatic children at week 1 and week 4		
Asthmatic Week 1	Asthmatic Week 4	P value
8.6 ± 1.03	8.9 ± 1.33	0.6
Asthmatic children at week 4 and healthy controls		
Asthmatic Week 4	Healthy	P value
8.9 ± 1.33	9.0 ± 1.26	0.2

3.3.5 The Inter individual variability

The individual changes in movement continuum of asthmatic children between week one and week four following asthma attack were presented as a percent of change. The inter individual variability of changes in the movement continuum following asthma attack are presented for physical activity duration in hours per day (Figure 3-10), number of steps per day (Figure 3-11), total sitting time per day (Figure 3-12) and sleeping time (Figure 3-13).

There was individual variability of changes in the physical activity duration of asthmatic children following asthma attack (Figure 3-10). The percent change of physical activity duration of 14 asthmatic children was increased following asthma attack (Figure 3-10). However, the percent change of physical activity duration of nine asthmatic children was decreased following asthma attack (Figure 3-10). There was individual variability of changes in the number of steps per day of asthmatic children following asthma attack (Figure 3-11). The percent change of number of steps per day of 16 asthmatic children was increased following asthma attack (Figure 3-11). However, the percent change of number of steps per day decreased in six asthmatic children and remained the same in one asthmatic child following asthma attack (Figure 3-11). There was individual variability of changes in total sitting time per day of asthmatic children following asthma attack. The percent change of total sitting time per day of 19 asthmatic children was decreased following asthma attack (Figure 3-12). The percent change of total sitting time per day increased in four asthmatic children following asthma attack (Figure 3-12). There was individual variability of changes in sleeping time per day of asthmatic children following asthma attack (Figure 3-13). The percent change of sleeping time per day of 13 asthmatic children was increased following asthma attack (Figure 3-13). However, the percent change of sleeping time per day decreased in eight asthmatic children and remained the same in two asthmatic children following asthma attack (Figure 3-13).

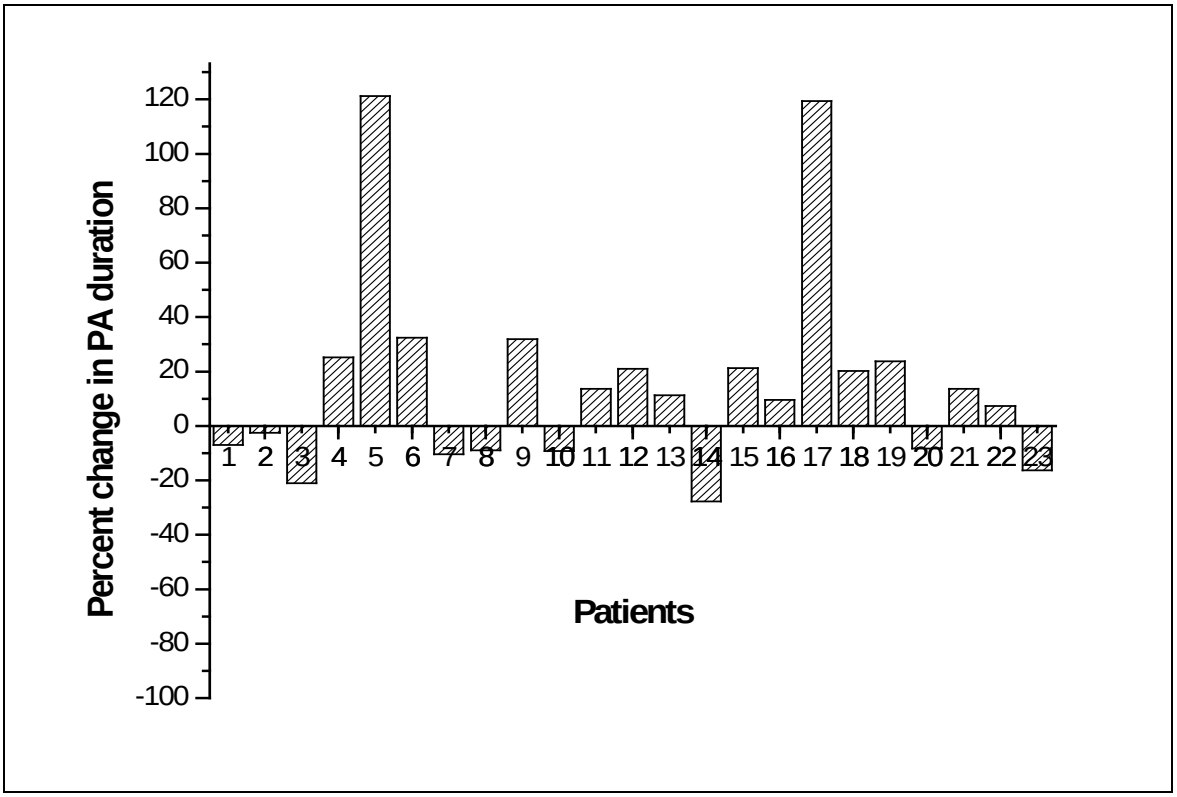

Figure 3-10: Individual changes in the percent change of physical activity duration of asthmatic children between week four and week one following asthma attack.

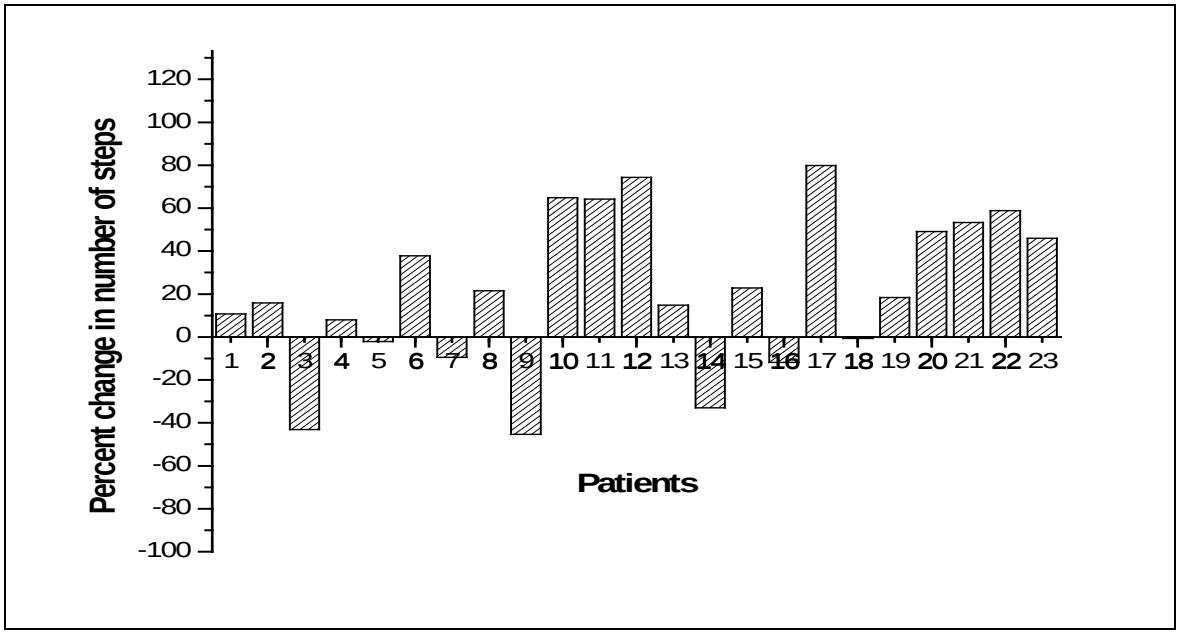

Figure 3-11: Individual changes in the percent change of number of steps per day of asthmatic children between week four and week one following asthma attack.

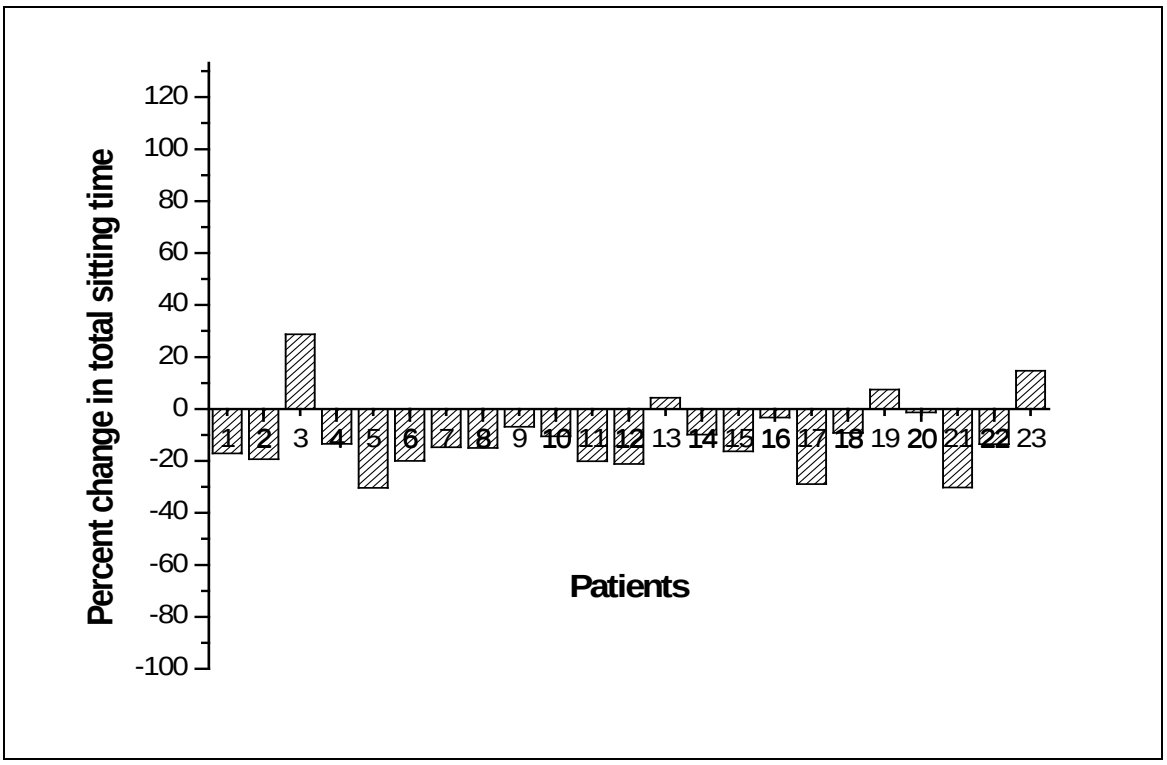

Figure 3-12: Individual changes in the percent change of total sitting time per day of asthmatic children between week four and week one following asthma attack.

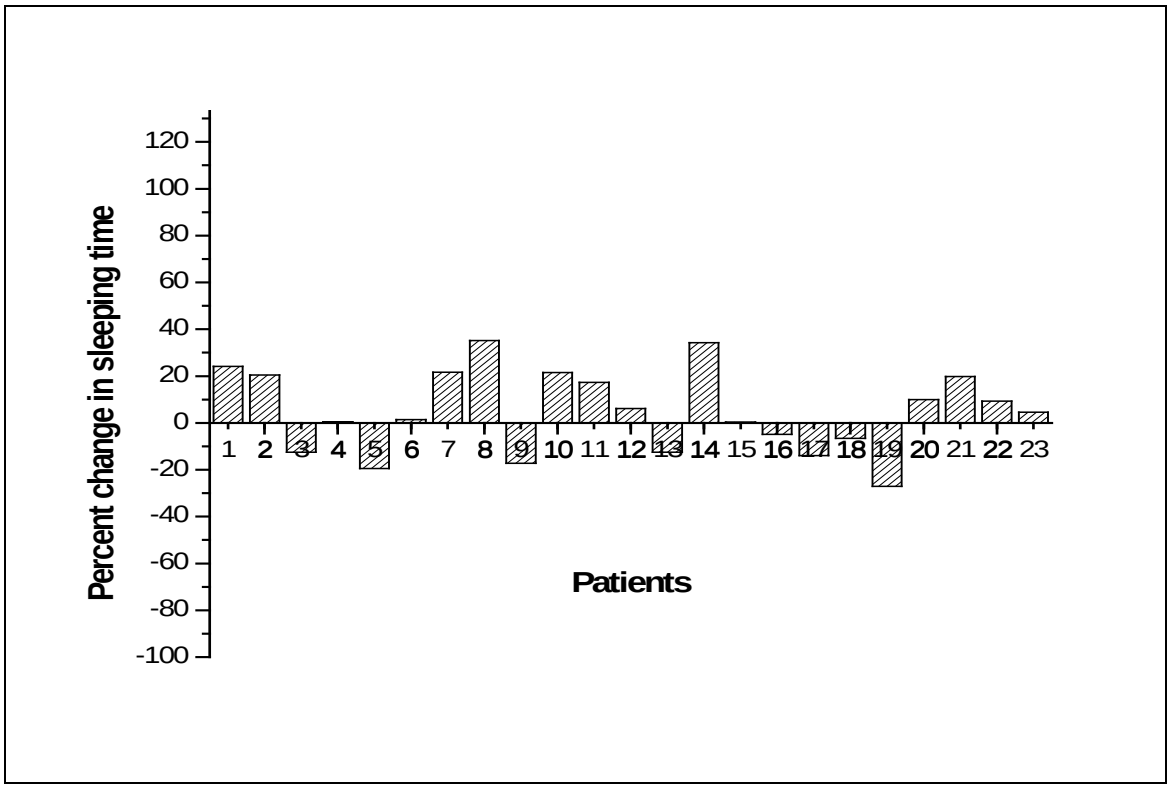

Figure 3-13: Individual changes in the percent change of sleeping time per day of asthmatic children between week four and week one following asthma attack.

Reasons behind the inter individual variability

To check if there is any role for the value of the component of the movement continuum at the first time point (one week after of discharge from hospital) in the inter individual variability, the ranks of the data of the two time points were compared by Spearman's rank correlation (Table 3-8). There was a significant positive correlation between the value of number of steps and total sitting time after one week and their values after four weeks of discharge from hospital (Table 3-8). However, there was no rank correlation between the values of physical activity duration and sleep time after one week and their values after four weeks of discharge from hospital.

In order to investigate the reasons behind this inter individual variability, correlations between the percent change of physical activity duration, number of steps, total sitting time, sleeping time and age, BMI Z score and childhood asthma control test (CACT) score were done.

The Spearman's rho correlation coefficient (r) test was used to assess the mutual relationship between these non parametric variables. There was no significant correlation between age and BMI Z score and the percent change of the physical activity duration, number of steps, total sitting time and sleep time (Appendix E). There was a significant negative correlation between CACT and the percent change of the number of steps (r: -.438) (Appendix E).

Table 3-8 Spearman's rank correlation of physical activity duration one week (PA,W) and four weeks (PA,M) after discharge , number of steps one week (Steps,W) and four weeks (Steps,M) after discharge , total sitting time one week (SB,W) and four weeks (SB,M) after discharge and sleeping time one week (Sleep,W) and four weeks (Sleep,M) after discharge from hospital.

	PA,W	**Steps, W**	**SB, W**	**Sleep, W**	**PA, M**	**Steps, M**	**SB,M**	**Sleep, M**
PA,W	1.000	.490*	-.675**	-.433*	.012	.314	-.162	.050
Steps, W	.490*	1.000	-.500*	.002	.170	.431*	-.202	-.124
SB, W	-.675**	-.500*	1.000	-.267	.119	-.131	.425*	-.257
Sleep, W	-.433*	.002	-.267	1.000	.010	-.209	-.408	.203
PA, M	.012	.170	.119	.010	1.000	.336	-.054	-.682**
Steps, M	.314	.431*	-.131	-.209	.336	1.000	-.311	-.054
SB, M	-.162	-.202	.425*	-.408	-.054	-.311	1.000	-.618**
Sleep, M	.050	-.124	-.257	.203	-.682**	-.054	-.618**	1.000

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

3.4 Discussion

The present study was conducted in Kuwait between14th April 2012 and 31st January 2013 on asthmatic children admitted to the hospital due to asthma attack and investigated them at week one and at week four after discharge from the hospital. This study tests the hypothesis that children at one month following an asthma attack recover from the asthma symptoms and become more physically active, less sedentary and have less sleep disturbances than during acute stage of asthma (one week after discharge from the hospital). In addition this study contributed to the debate about differences in physical activity between asthmatic children and comparable controls. This was achieved by comparing activity continuum of asthmatic children measured at week four after discharge from the hospital and comparable healthy children recruited from Kuwait youth centres.

All children with asthma had been diagnosed as asthmatic before admission to the hospital. They were admitted to hospital due to asthma attacks. The combination of a previous asthma diagnosis and admission due to asthma attack places their diagnosis of asthma on a secure basis. Data on asthma control showed that as expected, asthma control improved in the month following discharge from hospital. The total score of childhood asthma control test questionnaire (CACT) of asthmatic children was significantly increased one month after discharge from the hospital, which suggests that asthma symptoms, physical activity, asthma induced cough and night sleep disturbances of asthmatic patients improved in the period between one week and one month after discharge from hospital. The number of participants who were able to perform spirometry according to American Thoracic Society and European standards (373, 375-377) was small, yet, there was no significant difference in pulmonary function test (PFT) results between asthmatic patients in the two time points, which suggests that PFT scores of asthmatics had returned to baseline before the first assessment and it did not change during the month after discharge from the hospital. In summary, the results of the assessment of the severity of asthma suggests that there was an improvement in asthma control over one month after discharge from the hospital, but no significant improvement in lung function in the same period with evidence of a mild degree of obstructive lung function that was statistically not significant. This is consistent with Covar et al (205) who showed that symptoms and peaked expiratory flow (PEF) score following an asthma attack returned to baseline level within a maximum period of 10 days. In the light of this previous study, we had expected that our study was performed on a timescale when changes in the measured outcomes might be seen.

Measures of physical activity such as number of steps improved after one month after discharge from hospital. In addition, comparison of the parameters of volume and pattern of sedentary behaviour such as percentage sitting time, number of breaks in sitting, number of sedentary bouts and fragmentation index showed that the asthmatic patients were not sedentary. Further, this study showed that asthmatic children one month after discharge from hospital met the recommended number of daily step count; 12027 in boys and 10303 in girls (90). These findings support the notion that ten days is sufficient for recovery from asthma attack (205) and imply that one month recovery following attack is probably long enough to allow children to return back to normal life style and participate in exercise programmes. In summary, the results of physical activity and the volume and fragmentation of sedentary behaviour of the present study shows that Kuwaiti asthmatic children were active and not sedentary at both the acute and the recovery stage of asthma attack.

In this study, somewhat surprisingly, it was found that measures of physical activity such as duration of PA, total activity count, and number of steps of asthmatic children one month after discharge from hospital were significantly higher than those of healthy controls. It should be noted that although in this study there was no statistical significant difference between mean age of children with asthma and healthy controls, the asthmatic children were slightly younger (mean age of 8.1 ± 2.02 years) than the healthy children (mean age of 9.0 ± 1.72 years). Therefore, data obtained on comparison of asthmatic children and controls should be considered with caution. Our finding of higher physical activity in asthmatic children is consistent with Weston et al (320), Ownby et al (321) and Kim et al (322) studies that used self and parent reported data to show that asthmatic children were of more physical activity than healthy children. In contrast, our findings were not consistent with our own systematic review and Cassim et al (349) systematic review and meta-analysis that showed that objectively monitored physical activity of asthmatic children were not different than that of healthy children. The outcomes of the present study were not expected. Asthma in children is expected to be associated with exercise-induced symptoms (33) which might be expected to restrict the physical activity of asthmatic children and lead to lower levels of physical activity. There has been a discussion as to whether exercise-related respiratory symptoms in asthmatic children actually reflect that asthmatic children have higher levels of activity than normal children, contributing to them being diagnosed as having asthma (320, 321). However, there was no available data about the previous history of physical activity for either the asthmatic children or the healthy controls in the present. Consequently, we have no data to address the question as to whether know whether the children with asthma

were actually more active before the asthma attack than healthy controls. Moreover, this finding may suggest that asthma by itself does not affect physical activity in children with asthma. In summary, these findings in this Kuwaiti population of children, shows that the level of physical activity of children with asthma improved one month following an acute asthma attack. Also, at the recovery stage, the asthmatic children were more active than healthy children. Healthy children in Kuwait in this sample were not meeting current activity guidelines.

The findings of the sedentary behaviour were in line with findings of the physical activity. The total sitting time of asthmatic children at the recovery stage (one month after discharge from the hospital) was significantly lower than that of healthy controls. On the other hand, there was no difference in the percentage sitting time between asthmatic children at the recovery stage and healthy children. This suggests that there was no difference in the volume of sedentary behaviour between asthmatic children at the recovery stage and healthy children. In this study for the first time, data on the fragmentation of sedentary behaviour of asthmatic children was achieved. It was found that parameters of the fragmentation of sitting behaviour (number of breaks in sitting, number of sedentary bouts and fragmentation index) of the asthmatic children at the recovery stage were significantly higher than those of the healthy controls. This means that the sitting time of asthmatic patients at the recovery stage were fragmented into a large number of shorter sitting bouts when compared to that of the healthy children. These results should be handled with caution since there was one year age difference between asthmatic and healthy children, and the volume of sedentary behaviour increases with age (56, 152, 153).

Our findings of the sedentary behaviour were consistent with Tsai et al (341) and Yiallouros et al (463) studies that showed that there were no differences in the objectively measured volume of sedentary behaviour between school aged children with and without asthma. However, our data contradict with the findings of the study of Bringolf-Isler et al (325) who suggested that objectively measured volume of sedentary behaviour of asthmatic school aged children, was lower than that of healthy school aged children. Our data were not expected, asthmatic patients were expected to be if anything more sedentary, as asthma symptoms are triggered by physical activity (33) and asthmatic children are frequently suffering from exercise-induced asthma symptoms (464), which cause asthmatic children to decrease their activity and to be more sedentary in order to avoid asthma symptoms. In summary, the results of the volume and fragmentation of sedentary behaviour of the present study shows that Kuwaiti asthmatic children at the recovery stage

were not sedentary compared to healthy children. To date we know of no studies that have looked at the relationship between asthma and the fragmentation of sedentary behaviour, in the same manner as was done in this study.

This was the first study to investigate changes in sleep time and pattern in asthmatic children after asthma attack. On the groups level there was no significant difference in sleep duration between asthmatic children at acute and recovery stages and no sleep disruptions were found in the acute and recovery stages of asthma attack. However, on individual basis asthmatic children suffered from sleep disruptions. This was clear by observing the plots of mean number of breaks in sitting per hour against time during 24 hours for each asthmatic child alone. Conversely, in the plots of mean number of breaks in sitting per hour against time during 24 hours of all asthmatic children these disruptions disappeared. At present, there is a lack of valid metric method to describe these sleep disruptions for the whole group. This area of the quality of sleep, therefore, needs to be considered at an individual level.

These sleep findings were not expected, especially in the asthmatic patients one week after discharge from hospital. Asthma is associated with nocturnal symptoms (33). Our finding might be explained in the light of the finding of Stores et al (361) study, who investigated sleep of asthmatic children by polysomnography and showed that sleep duration was not affected by the state of asthma, while sleep disturbances were related to the degree of control of asthma symptoms; when asthma symptoms were uncontrolled sleep disturbances were present, while when asthma symptoms controlled, there were no sleep disturbances. Further, Sadeh et al (357) used Actigraph accelerometer to study sleep of asthmatic children and showed that the sleep duration of asthmatic children was not affected but they had sleep of poor quality. Our findings are inconsistent with the finding of Kales et al (356) study who monitored the sleep of asthmatic children by polysomnography and showed that their sleep was interrupted by recurrent awakes and diminished sleep time.

This study also aimed to compare sleeping behaviour of asthmatic children at recovery stage (week four) and healthy controls. We admit that for this comparison this study lacked power and therefore, our finding that there was no significant difference in the sleep time between asthmatic children at the recovery stage and healthy controls should be confirmed by further studies recruiting bigger number of participants and applying more advanced sleep monitoring methods such as Polysomnography (162). Nevertheless, our findings are consistent with the finding of Stores et al (361) study, who showed that when asthma

symptoms controlled, there is no difference in sleep duration and pattern between asthmatic children and healthy children. This, broadly, might indicate that after one month, nocturnal asthma symptoms had been controlled more effectively and quickly to the degree that there were no night sleep disturbances.

According to the best of our knowledge this is the first study investigated the inter individual variability of changes in the movement continuum following asthma attack. Although the grouped data of the activity continuum of the asthmatic patients between two time points showed some significant statistical differences in some parameters, the individual data of those asthmatic patients showed inter individual variations in changes between these two time points. The physical activity duration, number of steps, sedentary behaviour (SB) and sleeping time of asthmatic children, either increased or decreased or remained the same after one month. Thus, some patients were behaving in a different manner than their group behaviour. This was obvious from the percent change in the value of the parameters between the two time points. There was inter individual variability of change in the percent change of each element of the activity continuum between the two time points. This was obvious from the graphs of the percent change of the parameters of activity continuum.

In attempt to explore the reasons behind this inter individual variability of change in activity continuum, Spearman's rank correlation was done to compare the ranks of the data of the two time points, which enabled a check of whether the score of the parameter at the first time point affect its value at the second time point. A significant positive correlation was found between the score of number of steps and total sitting time at first and second time points. This, means that patient with high score of number of steps at the first time point, will get high score of number of steps at the second time point. The same thing will happen for total sitting time. This was not the case for physical activity duration and sleeping time which might be due to the small sample size of this study. Therefore, imprecisely, the inter individual variability of change in movement continuum among asthmatic children can be attributed to the score of activity continuum parameter at the first time point. Furthermore, correlations between percent change in parameters of activity continuum and age, BMI Z score were tested and showed that they play no role in this individual variability of change. On the other hand a significant negative correlation was found between changes in childhood asthma control test (CACT) score and number of steps, which is difficult to explain. This is to let the door open for research to explore this area.

Finally, this study confirms that in order to monitor activity it is important to measure all parts of the activity continuum; a complete picture for the 24 hours activities of the individual will help in investigating the determinants or the health outcomes of the different components of the activity continuum. Continuous monitoring make it possible to observe unexpected observations. The appropriate way to accomplish this is by using objective methods of low cost, valid, reliable and easy to use such as accelerometry.

The present study has several strengths. First of all for the first time this study provides information on the movement continuum in asthma attack in school aged children during acute stage and recovery stage, which is an understudied area of research. The main strength in the present study was that it is the only study to examine the movement continuum and asthma longitudinally and objectively after asthma attack in school aged children; patients were measured twice at two time points; acute stage and recovery time and compared to healthy children. It is also one of the only very few studies of children with asthma in an Arabian country in the Middle East area. The fact that the children had a history of asthma and been hospitalised with an asthma attack means there is a high degree of certainty about the diagnosis of asthma with expectations that there would be disruptions and changes in the movement continuum. It is the first study to measure both the volume and patterning of sedentary behaviour in asthmatic children, and compared them to healthy children. The size of the sample was powered for the comparison of activity continuum parameters between asthmatic children in the acute and recovery stages following asthma attack that means the results of these finding are credible and generalizable. The size of the sample was powered for the comparison of total activity count and number of steps between asthmatic and healthy children that means also the results of these finding are credible and generalizable. In addition, the mean number of days ActivPAL worn in this study was ranging between 5.7 and 5.4 days, which was consistent with required days for proper monitoring (446, 478, 479). Also, mean number of monitoring hours of this study was ranging between 13.0 and 14.1 hours, which was consistent with the required hours for appropriate monitoring hours (446). This means that the duration of monitoring was sufficient to provide an adequate assessment of habitual physical activity. As a consequence all measures generated by ActivPAL device were probably fairly reliable measures of usual physical activity, sedentary and sleep behaviours. Finally, the present study is the only study to provide information on the inter individual variability for change in activity continuum of the asthmatic patients during recovery from asthma.

As all studies, this study has some limitations. There was a small age difference between study groups; asthmatic children were younger by one year than healthy children. Although there was no significant statistical difference in age between study groups, there is evidence that younger children are more active and less sedentary, so the results of the components of the activity continuum might be affected by this age difference. In addition, it was intended to recruit more than 20 participants for measuring pulmonary function test (PFT), but unfortunately, only a relatively small number performed adequate PFTs. This is despite the fact the researcher instructed participants in the proper technique of spirometry technique according to American Thoracic Society and European standards (373, 375-377) and demonstrated the technique himself for the participants. It is important to stress the point that the recommendations and guideline of sedentary behaviour were all about the duration of screen time (86, 89, 135, 136), there was no recommendation about the proper objectively measured total sitting time, to which we can compare our results. Although this study showed useful results on the activity continuum of asthmatic and healthy children, this data might be affected by reactivity bias. As noted in section 1.7.3.1.3.2, child awareness of being monitored by accelerometer may increase his/her PA especially in the first day of monitoring, and to minimise this reactivity it is recommended to familiarize the child on the accelerometer for a day and to select the start days randomly (427), unfortunately, this was not done in this study. Although the present study showed that there was no difference in sleep duration between asthmatic and healthy controls, a post-hoc power calculation for the comparison of sleep duration between asthmatic and healthy children, using G-power software showed that the study was underpowered. Using Minitab 17 statistical software, for the mean difference of standard deviation of sleep time of asthmatic and healthy controls of 0.07, to pick up a difference in sleep time of one hour at a power of 80% 60 participants will be needed, and to find a difference in sleep time of half an hour at a power of 80% 118 participants will be needed. One limitation that affected the sample size was the number of available activPAL devices; at the beginning of the research the available devices were ten and in the middle of the research period one was lost during the monitoring of one of the participants. Each device was in use for around eight days at any one time. Therefore, it was difficult recruit more participants, due to the limited number of devices. A further important limitation is that the ActivPAL accelerometer used to evaluate movement continuum in our study has at present no cut-offs for intensities of PA, so that it was not possible to differentiate between different intensities of physical activity. In addition, ActivPAL accelerometer is not ideal for monitoring sleep disturbances. Further, nothing is known about the past history of the components of movement continuum of all participants. Hence,

it is difficult to judge whether the results obtained in this study are related to the time of study or to their previous history of the components movement continuum. Finally, there was no enough data about treatment of asthmatic children in this study and their compliance with the treatment. This might be of value in interpreting the inter individual variability in changes of movement continuum among asthmatic children.

This work highlights the need for further research in the components of the movement continuum in children with asthma. In the immediate future, a study of asthmatic children with different degrees of asthma severities and with more detailed information on other possible relevant confounding factors such as age, gender, asthma treatment, diet intake and social life (especially smoking parents) would be of interest. In addition, it is important in this future study to take care of the children's past history of the movement continuum, to differentiate between the disease effect on movement continuum and the previous history of movement continuum. The inter individual variability of changes of components of movement continuum of asthmatic patients during recovery and the reasons behind it should be investigated in greater detail.

More generally, this study has highlighted the need for Arabian Middle East countries such as Kuwait, Kingdom of Saudi Arabia, Bahrain, Qatar, United Arab Emirates (UAE) and Oman, which share similar socioeconomic level and environmental influences, to work together on topics relevant to child health. For example, there is a need for reference values specific for children of Arab descent for many medical measures such as; weight, weight Z score, height, height Z score, BMI, BMI Z score, and pulmonary function test values (FVC, FVC Z score, FEV1, FEV1 Z score, FEV1/FVC), as the case in the present study there were no regionally based reference values for these measurements and the only alternative were an international references which might be not representative for the population of this area. Also, in this Arabian area, there should be research to develop a subjective method for monitoring control of asthma symptoms, including validated questionnaires in the Arabic language suitable for use across the Middle East. Research on a larger scale should be conducted to study the movement continuum of different gender and different ages and its relationship to many health outcomes. The present study showed that Kuwaiti healthy children were of high BMI Z score, low physical activity indices and high sedentary behaviour indices. This problem, its risk factors and its management needs further study.

In conclusion this study showed that in a group of asthmatic Kuwaiti children, asthma symptoms, physical activity and sedentary behaviour recovered from week one to week four

following asthma attack. Further, these asthmatic children at the recovery stage were physically active, not sedentary and had no difference in sleep time when compared to a comparable group of healthy Kuwaiti children**.** During the recovery from asthma attack there was inter individual variability in changes in physical activity, sedentary behaviour and sleeping that could not be predicted from age or BMI. At present, there is no explanation for these individual variabilities. Monitoring of sleep behaviour requires a device that has the ability both to measure sleep time and to record sleep disruptions properly.

Chapter 4: Seasonal changes in sleep

4 Seasonal changes in sleep

4.1 Introduction

This study has highlighted that there is an increasing awareness of the importance of monitoring all components of the "movement continuum" (i.e., sleep, sedentary time, light physical activity (LPA)), in studying the effects of daily movement activities on children's health. In this chapter, we present a new finding in sleep behaviour of Kuwaiti children that was found while analysing the data recorded by the ActivPAL accelerometer.

Sleep can be described as a reversible perceptual detachment from and unawareness of the environment from which a person can recover spontaneously (160-162). In sleep, the sleeping person frequently lies down, is calm and closes his/her eyes (160-162). Sleep mechanism is controlled by both hypothalamus and brainstem (163-165).

The sleeping–wakeful cycle is controlled by three mechanisms: a circadian rhythm, that is regulated by a pacemaker in the supra-chiasmatic nuclei of the anterior hypothalamus, influenced by the light-dark cycle, causing awake during light and sleep during darkness (167, 171, 172); a process "S" (or 'sleep pressure') is a homeostatic mechanism, that causes the development of desire for sleep throughout awake hours and is relieved by sleep (162, 167, 171); and an ultradian rhythm that influences cycling between sleep stages throughout sleep, and determines timing and duration of sleep states (162, 167, 171). In addition, sleep pattern can be influenced by internal factors (e.g. hormonal changes accompanying growth) or external factors (e.g. social life, and school stress) (161, 173, 174).

An important external factor affecting the sleep patterns in children is attendance at school (Table 4-1). In westernised countries (including Iceland (175), Australia (176), Italy (177, 178), Finland (179) Turkey (180) and Croatia (181)), in Middle Eastern countries (Kingdom of Saudi Arabia (182) and Israel (183)), and in Asian countries (such as Hong Kong (184, 185) and China (186)), it has been shown that during school holidays, there was a significant delay both in evening bed time ranging from 30 minutes to 2 hours and in morning rise time ranging from 1 to 4 hours with a longer total sleeping time of between 35 minutes to 2 hours (Table 4-1). However, in other countries a different effect has been observed. In a cohort of New Zealand Caucasian children, Nixon et al (187), showed that sleep duration was shorter by around 26.9 minutes on weekend nights and bed time was delayed by around 31 minutes at weekends but there was no significance difference in rise

Table 4-1 Bedtime, wake-up time and sleep duration of children in weekends and weekdays in different countries

Country	Weekend during school time			Weekday during school time		
	Bedtime	Wake-up time	Sleep duration	Bedtime	Wake-up time	Sleep duration
Iceland (175)	Delayed	Delayed from early adolescence	longer by 15 ± 47 min from 9 yrs old onward			
Australia (176)	Delayed (09:22)	Delayed (00:24)	Longer (8:51)	22:47	(07:04)	Shorter (7:55)
Italy (177)	Delayed (01.15)	Delayed (10.55)	Longer (545 (min))	23.05	7.10	460 (min)
Italy(178)	Delayed (23:20)	Delayed (9:29)	Longer (10 h 08 m)	22.14	7:10	8 h 59 m
Finland (179)	after 22.00	Between 07.00-10.00	-9.4-13yr>9hrs -13.1-17.1yrs >9hrs	Before 22.00	Before 07.00	-9.4-13yr >9hrs -13.1-17.1yr 7-9hrs
Turkey (180)	Delayed 23:46	Delayed 09:11	Longer 9.40 hrs	23:16	06:41	7.42 hrs
Croatia (181)	Delayed 00:36	Delayed 10:13	Longer 9:17 (h:min)	22:50-23:28	06:39-08:38 (h:min)	7:31- 8:52 (h:min)
Kingdom of Saudi Arabia (182)	Delayed 23.1 ± 7.1	Delayed 9.3 ± 1.6	Longer 9.96 ± 1.4	21.3 ± 1.8	5.9 ± 0.5	8.4 ± 1.1
Israel (183)	Delayed 01:45	Delayed 11:30	Longer 9:53 ± 1:49	22:58	06:45	7:23 ± 1:07
Hong Kong (184)	Delayed 22:55	Delayed 8:59	Longer 10:04- 0:55	22:21	07:31	9:10-0:56
Hong Kong (185)	Delayed 00:23-00:32	Delayed 9:55- 10:31	Longer 550- 585 (min)	23:20-23:28	06:56-06:57	442-433
China (186)	Similar Majority 22:00-22:30	Delayed Majority 08:00-09:00	Longer Majority <8.5hrs	Majority 22:00-22:30	Majority 06:00-06:30	Majority <8hrs
New Zealand (187)	Delayed 20:42	07:17	Shorter by 26.9 (min)	20:11	07:08	Longer by 26.9 (min)
Nigeria (188)	Almost similar 22.08	Delayed 07.37	Longer 10.09 ± 1.32	21.53	07.02	9.33 ± 2.29
Australia (189)	Delayed 21.45	Delayed 07:58	Almost similar 10.22	20:20	06:34	10.23
China (190)	Almost similar 10:17	Delayed 08:13	Longer 09.36-1.56	10:08	05:50	07.50-1.05

time (Table 4-1). In other countries, there were insignificant differences in sleep duration between weekend and school days, as well as insignificant differences in evening bed time between weekend and school days (Nigerian children (188), Austrian children (189) and Chinese adolescents (190)) (Table 4-1).

Sleeping pattern and even sleeping time are also known to change with seasons usually with a prolongation of sleeping time in winter (Table 4-2). For example, sleep duration in winter was 2% longer than that of spring among Danish school children (191) (Table 4-2). Among New Zealand Caucasian children (187), sleep duration was shorter in summer than other seasons (Table 4-2). In Strasbourg city (north-eastern France) (193), a shortening of sleep duration from January to May among children has been reported (Table 4-2).

Table 4-2: The seasonality of sleep in different countries

Country	The seasonality of sleep
Denmark (191)	winter sleep duration is 2% longer than that of spring
New Zealand (187)	summer sleep duration shorter than in other seasons
Strasbourg city (north-eastern France) (193)	shortening of sleep duration from January to May

With global warming environmental temperatures particularly during summer are rising at times to very high levels. The effect of environmental temperature on children's sleeping patterns has not been investigated. Following the observation of a shift in the timing of children's sleep during the analysis of the data, this section describes a systematic evaluation of the duration and timing of the beginning and ending of sleep in school aged children studied in Kuwait over the period of the highest summer temperatures in summer and compared them to times of year when the environmental temperatures were lower. In addition, sleep time and pattern during school days and weekends at different times of the year were compared.

4.2 Methods

Chapter three describes the children studied. Briefly, we studied 2 groups of 6-12 years old school children. The first group (n = 23) were Kuwaiti children with asthma, who had been admitted to hospital between 14th April 2012 and 31st January 2013 with an asthma attack. The second group were a comparative group (n = 23) of otherwise healthy Kuwaiti children.

The timing of the study is particularly relevant in this section. The study was conducted between 14th April 2012 and 31st January 2013. During school time (period from October to June), 58 participants were studied: 43 asthmatic children and 15 healthy children. During school holidays (in the period from July to September, coinciding with the hottest time of the year) 11 participants were studied: 3 asthmatic children and 8 healthy children. The sleeping behaviour of each child with asthma was studied twice; first, one week after discharge from hospital; the second time four weeks after hospital discharge. In contrast, the healthy children were only examined once.

Data on sleeping behaviour were collected using ActivPAL™ monitors (PAL Technologies Ltd, Glasgow, UK). The ActivPAL™ is a uni-axial piezoresistive accelerometer with a sampling rate equivalent to 10 Hz that is attached to the mid thigh as described previously in section 3.2.3.4.

Recording

The participants and the parent/guardian were instructed to attach the activPAL™ for 7 consecutive days, to leave the device worn throughout the night and to remove the monitor during the times of any showering or swimming during the monitoring period and reattach the device once the water based activity was completed. Parents were provided with a daily activity recording sheet and asked to note any time the device was removed as well as the time the device was reattached.

Data processing

After completion of the monitoring and removal and return of the device, the activPAL^{TM} data were downloaded onto a computer using the activPAL^{TM} Professional Research Edition software (Version 5.8.2.3). Data were then analysed and sorted into sit/lie, stand or walk intervals. In addition, the data were also processed by another software programme, HSC PAL analysis software v 2.14, developed by Dall and Granat at Glasgow Caledonian University, which is capable of defining time in seconds at which postural transitions occurred (446), to generate the sleeping time and the sleeping pattern.

Sleeping time

The longest non-wear time interval within 24 hour interval between two valid days was regarded by Colley et al (170) as the sleeping time of children. This is identical to the longest sit/lie interval within 24 hours between two valid days recorded by ActivPAL

accelerometer. Separately, Alghaeed et al (146), showed that the average number of breaks in sitting (up transitions) per hour over 24 hours, could be used to define wake up time and sleep onset time. Accordingly, the longest sit/lie interval within 24 hours between two valid days was matched with the interval when the average number of breaks over the 24 hours was lowest and was used to define the start and end of sleep at night.

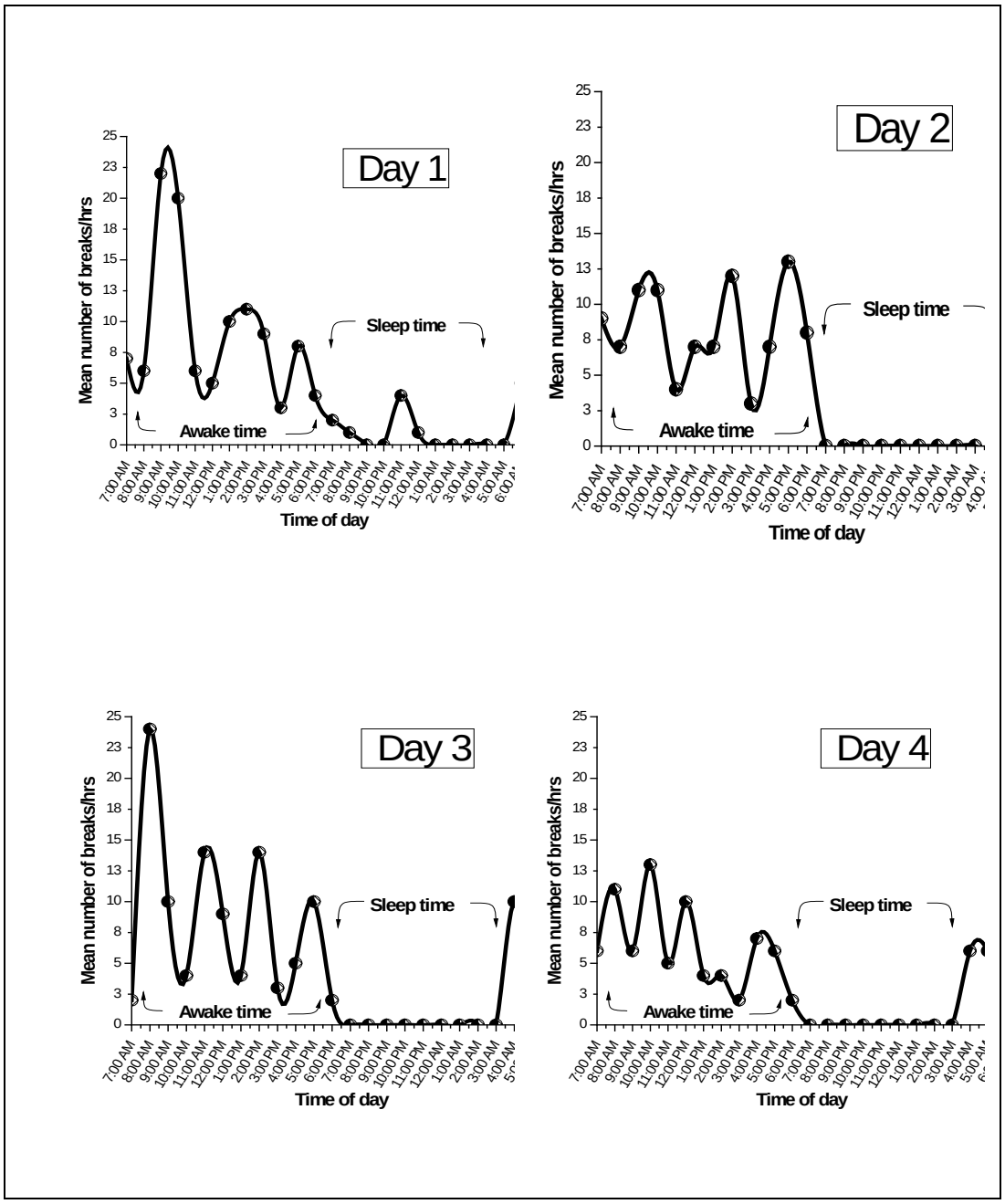

Figure 4-1: Sleeping and awake time of one participant tracked for 4 days. The interval of decreased level of average number of breaks in sitting (the flat area between two valid days) in the graph of average number of breaks over the 24 hrs is considered as sleeping time. After matching the longest sit/lie interval between two valid days with this flat area, the time of this long sit/lie interval is considered the duration of the sleep time.

As an example, records of the mean number of breaks in sitting per hour against time for 24 hours of one participant are demonstrated in (Figure 4-1). In this participant, the mean

number of breaks in sitting per hour increased in the early morning at around 0300 - 0500 indicating the transition to awake (Figure 4-1). The number of breaks in sitting reduced gradually at around 1800 - 2100 indicating the start of the transition to sleep (Figure 4-1). Breaks in activity stayed at its lowest or zero level for a number of hours until around 0300 - 0500 when number of breaks in sitting started to rise indicating the end of sleeping time and the beginning of a new awake time (Figure 4-1).

In Kuwait, the school starts at 0730. To attend on time, children usually go to bed at around 2100 - 2200 and awake around 0600-0630, so the onset of sleep (longest non-wear time interval within a 24 hour interval between two valid days) most probably starts at 2100-2200 and end at 0600-0630. The longest sit/lie interval within 24 hours between two valid days for each day was measured, and then the sleep time for the monitoring days were averaged to give the average duration of sleep per day for each child.

In order to investigate seasonal changes in sleeping time, the summer was considered to start from the school holiday in July until the end of school holiday in late September, even though summer officially extends over a longer period starting in May and ending in September. This was to rule out the influence of parents in setting bedtime of children during the school term (481, 482). We also evaluated the timing and duration of sleeping during school days and weekends to see how the sleep differed and to investigate how it compared with timings during summer holiday (481, 482).

Since the monitoring time of both asthmatic children and healthy children (Table 3-4) were consistent with the required time for proper monitoring (446, 478, 479), and there was no significant difference in their sleeping time (Table 3-7), the data from the 69 participants were used. This was for the purpose of investigating seasonal changes in the timing of sleep onset.

4.3 Results

Eleven participants were studied during the school holiday (summer time: the period from July to late September; 3 asthmatics 8 controls) and were monitored for an average of 5.5 days and 13.5 hours per day. Fifty eight participants were studied during school time (a period from October to June) for an average of 5.6 days and 13.0 hours per day.

The plot of mean number of breaks in sitting per hour against time during 24 hours, showed striking differences in sleeping pattern during school holidays (summer time: July–late

September) compared with that of school time (other times of the year; a period from October to June) (Figure 4-2).

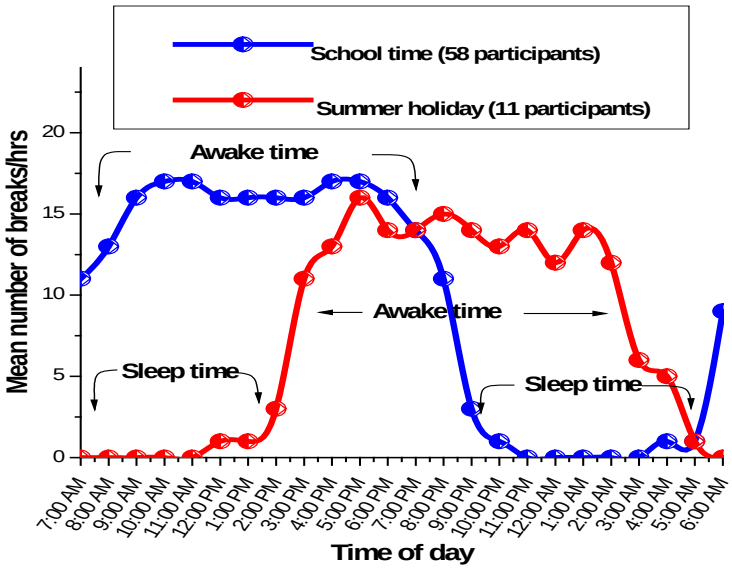

Figure 4-2: The pattern of postural change during school holiday (summer time: July–late September) and school time (other times of the year; a period from October to June); at school time participants were active from 0500-0600 till 2000 (awake time), then the activity (number of breaks in sitting per hour) start to decrease at 2100 until 0500 (sleep time). During summer (July–late September) participants were active from 1300-1400 till 0300-0400 (awake time), then the activity start to decrease at 0400-0500 till 1300-1400 (sleep time).

During the period of school time, participants were active from around 0500 - 0600 till 2000, being the expected awake times for participants during these 9 months of the year (Figure 4-2). Then, typically the number of breaks in sitting per hour started to decrease at 2100 until around 0500 marking the sleep time for participants in these 9 months of the year (Figure 4-2). In addition, the duration of the sleep time (the longest sit/lie interval within 24 hours between two valid days) was around 9 hours. In contrast, during the period of school holiday (summer time: July–late September), participants were active from afternoon at around 1300-1400 till 0300-0400, indicating the awake time for participants in these 3 months of the year (Figure 4-2). Then the number of breaks in sitting per hour decrease at 0400 till 1300 indicating the period of sleep (Figure 4-2). The duration of the sleeping time in the summer time was around 10 hours that was significantly ($P = 0.026$) more than other times of the year.

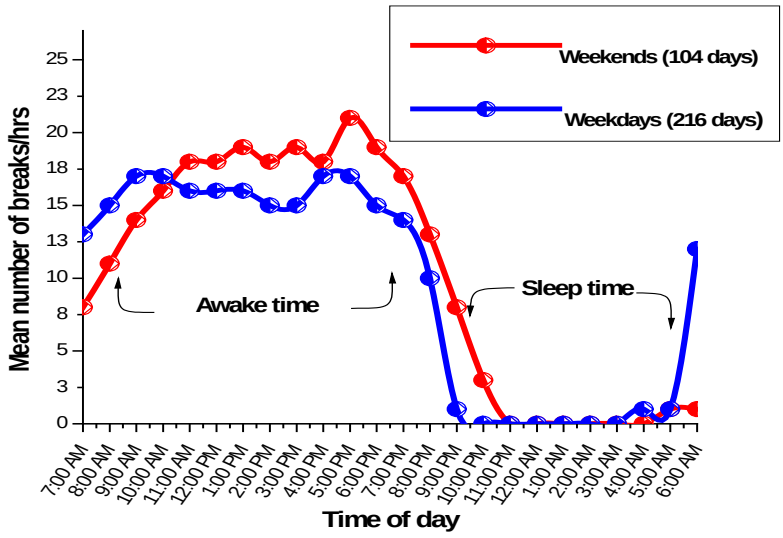

Figure 4-3: Average pattern of postural change during school time, in weekdays and weekends; at weekdays in school time participants were active from 0500 - 0600 till 2100 (awake time), then the activity (number of breaks in sitting per hour) start to decrease at 2100 until 0500 (sleep time). During weekend days participants were active from 0600 till 2300 (awake time), then the activity started to decrease at 2300 till 0600 (sleep time).

In the school time, there were 216 school days monitored and 104 weekend days monitored. During the weekdays in school time, participants (n = 58) were awake and active from around 0500-0600 until 2100 and then asleep until around 0500, compared to 0600 until 2300 at the weekend days (Figure 4-3). The duration of the sleep time (the longest sit/lie interval between two valid days) in schooldays was 9.0 hrs compared to 8.2hrs at week end (Table 4-3). The sleeping time of schooldays was significantly higher (P= 0.007) than that of week end.

Table 4-3: Sleeping time in hours per day measured at school days (n=216 day) and weekends (n=104 day), values are mean ± SD

school days	Weekend days	P value
9.0 ± 2.3	8.2 ± 1.9	0.007

4.4 Discussion

This study shows striking differences in the sleeping times of school age children during the Kuwaiti summer compared with other times of year. During the summer holidays (July–late September), there appeared to be a much larger shift in the timing of sleep and awake times with children going to bed late in the early hours of the morning and waking up late in the afternoon. In addition, children in summer slept for one hour more than at other times of the

year. In contrast, in school time, the period from October to June, children generally woke early and went to bed early. During school time, in weekdays the children woke up and went to bed earlier than in weekends (Figure 4-3). In addition, sleep duration on weekdays was longer than during weekends.

Ramadan is a holy month for Muslims, in which they fast during the daytime, pray in the night and take Sahoor (the last meal before fasting) late at night. Although the children are not obliged to do the worship of Ramadan i.e. not fasting in daytime and not praying at night in this month, they might stay awake for the late hours of the night with their parents and go to bed late, which will make them wake up late. In the year in which research was conducted, Ramadan was in the summer from 20 July 2012 to 18 August 2012. The number of children studied in Ramadan was six and those studied after Ramadan was five.

This delay in bed time and bed rise time during the summer holidays is therefore completely different from the pattern between week days and weekends during the school term. It does not seem likely that these very large changes in bed times are solely attributable to changes in parental supervision. We speculate that the shift in sleeping behaviours might be attributable to two factors; for the six children studied during Ramadan their sleep might be affected by the effect of Ramadan and the large difference in temperature between the summer and other seasons (Figure 4-4); for the five children studied after Ramadan their sleep might be affected by the large difference in temperature between the summer and other seasons (Figure 4-4). In Kuwait in the summer time during the months July to September, the maximum outside day time temperatures are regularly in excess of 50Cº. This is despite that almost every house in Kuwait is air conditioned with the temperature inside houses ranging between 18 to 22 Cº. Owing to this high outside temperature in the Kuwaiti summer time, children cannot play outside during daytime and even their parents discourage them to do so and choose to shift their activity to a later time when the outside temperature decreases. This change in the schedule of activities was associated with a shift in the bedtime and rise time. We hypothesise that this 8 hours shift in sleeping time with later waking in summer might be response to the high environmental temperature encountered during the summer. Our data show that children woke around midday with their activity increasing in the late afternoon and evening when the environmental temperature was decreasing.

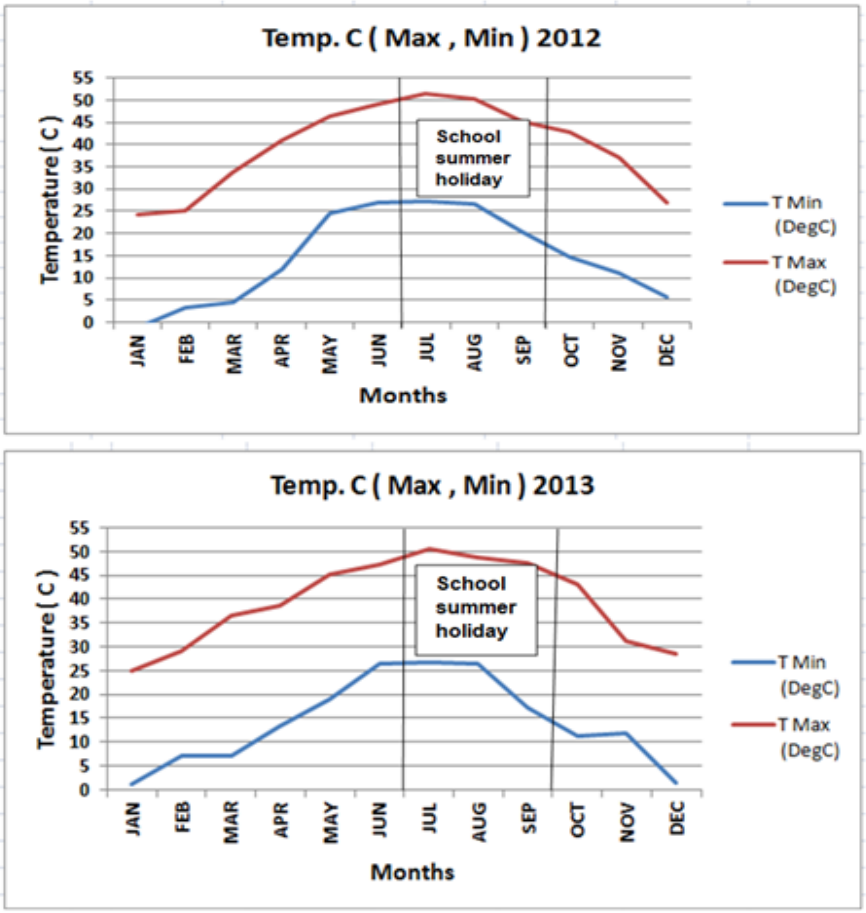

Figure 4-4: Kuwait temperature for the period 2012 and 2013. Note: T Min: minimum temperature, T Max: maximum temperature, Deg C: degree Celsius (483).

It is of interest to compare our data with other data on sleeping patterns in different seasons. There is limited data from studies of Middle Eastern countries. This is focused on the differences between weekdays and weekends. BaHammam et al (182) used self reported data of elementary school children in Saudi Arabia, and showed that during school time, bed time and rise time were delayed by about two hours and three hours respectively during the weekend compared to week days, and total sleeping time was increased by more than 1.5 hour at weekends compared to week days. Self reported; data of Israel adolescents aged 14 ± 0.8 years old (183), suggested that during weekends, the bed time was delayed by more than 2.5 hours, the wake-up time was delayed by more than four hours, and the sleep duration was longer by more than two hours. In the Far East, there was a significant delay in both bed time and wake time and a significant increment in sleep duration during weekend and long holidays compared to school days among Chinese children (184, 185) and Chinese adolescents (186). Likewise, in Nigeria (484), the sleep duration was increased at weekends compared to school days. In New Zealand (187), actiGraph accelerometer data of seven

years children showed that bedtime was delayed at weekends (mean 2042) compared with weekdays (mean 2011), $P < 0.001$, but there was no significant difference in the rise time between weekends and weekdays. Sleep duration was 26.9 minutes less on weekend nights than on school nights. The difference in sleep duration between weekends and weekdays of Icelandic children (175), increased with age being always longer in weekends and the bedtime and rise time was delayed in weekends compared to weekdays, and this difference increased with age. On the other hand, Hoedlmoser et al (189), suggested that although bed time and awake time were delayed during weekends compared to school days, there was no significant difference in sleep duration between weekend and school days among Austrian children. This study showed that for school aged children in Kuwait the bed time and rise time were delayed in weekends that are consistent with most of the studies noted above (175, 182-186, 189), and sleep duration during weekends was shorter than during the school weekdays that is in agreement with Nixon et al study (187) and in contrast with the other above studies.

Few studies have investigated the seasonal variations in sleep among children. Hijorth et al (191) used an ActiGraph™ accelerometer (GT3X) and questionnaire to examine the seasonal and weekly changes in lifestyle indicators such as physical activity, sedentary behaviour, cardio-respiratory fitness and sleep duration in 834 healthy Austrian children aged 8–11 years old. The study was conducted from August 2011 to June 2012, with baseline measurements performed in autumn (late August to November 2011, minimum and maximum temperature: 7.2; 13.0 °C and sunshine: 301 hours), the second measurements were in winter (November 2011 to February 2012, minimum and maximum temperature: −0.6;4.2 °C and sunshine: 229 hours), and the third measurements were in spring (March to beginning of June 2012, minimum and maximum temperature: 4.5;11.7 °C and sunshine: 575 hours). The study suggested that the sleep duration in winter was 2% longer than that of spring. Nixon et al (187), investigated sleep in seven year old Caucasian children in New Zealand by using actiGraph accelerometer. The study showed that sleep duration was influenced by season, with sleep duration 40.5 minutes longer in winter, 31.1 minutes longer in autumn, and 14.8 minutes longer in spring than that in summer. Thorleifsdottir et al (175), followed up Icelandic children for more than ten years by questionnaire survey and found that both nocturnal and total sleep duration were slightly shorter in spring than in winter among six to ten years old children on weekends. Finally, Mantz et al (193), investigated six years old children in Strasbourg city (north-eastern France), and found a shortening of sleep duration from January to May. In contrast this study showed that in

Kuwait during summer time when the environmental temperature exceeds 50Cº, there appeared to be a large shift in the bed and awake times with children sleep late and awake late. In addition, children in summer slept for 1 hour more than at other times of the year.

The important clinical implication for this finding is that the seasonal variations can be considered as a potential confounder that might influence the validity of the results of an experiment that investigates the activity continuum. In conducting research aiming to investigate the activity continuum, the researcher should take into account in the study design and analysis that the seasonal variation in sleep might affect the other parameters of the activity continuum. It is more logical to study the activity continuum across the four seasons, so that the influence of seasonal variation on the parameters of activity continuum will be clear. Furthermore, more research is needed to study the seasonal changes in sleeping time and pattern and its effects on the health of children.

In conclusion, in keeping with most studies in children, the present study suggested that there was a delay in bed time by two hours and in rise time by one hour during school weekends in Kuwait. However, in contrast to almost all of the studies above there was a decrease in sleep duration during weekends in school time. The small number of studies in children which studied seasonal variations in sleeping time and pattern were mainly conducted in temperate or cold countries. The majority of these studies found evidence of seasonal variations in sleeping time and pattern and suggested that in winter sleeping time was longer and the onset of sleep delayed compared to summer. The present study from Kuwait is unique because of the very high summer temperatures encountered. In this study, the difference in bed time and rise time between weekdays and weekends during school time was far less than that observed between summer holiday and other times of the year. Thus the summer pattern cannot be explained by the removal of school-related sleep restriction alone. Some other factor must be in play. Although children in Kuwait would usually be sleeping in an air-conditioned environment, we speculate that the change must in some way be related to the high external environmental temperatures.

A change in sleeping pattern in relation to external temperature has not been described before in children and appears to be a new phenomenon. This was an unexpected finding in a small number of children and further research will be required to establish whether it is a more general feature of children's sleep. If confirmed, it has to be studied thoroughly and its effects on the health of children have to be explored. The apparently shifting pattern of sleep

would also need to be considered by future studies of physical activity, sedentary behaviour, and sleep in children in Kuwait.

Chapter 5: General discussion

5 General Discussion

The existing literature about the relationship between asthma attack and physical activity, sedentary behaviour and sleep behaviour (activity continuum) in children had been reviewed in the introduction and showed that the evidence on differences in the relationship between asthma and the parameters of activity continuum in children is debatable; some studies showing that PA of asthmatic children is higher (320, 321) or lower (323, 326-328) than that of normal children while others suggesting that there is no difference (334, 335, 339, 462). Likewise, despite the small number of studies that investigated the relationship between sedentary behaviour and asthma in children, they suggested contradictory results (325, 355, 463). In addition, studies investigating the difference in sleep between asthmatic and healthy children showed contradictory results(357, 363). These contradictory results may be related to methodology problems in these studies, improper participants, uncertain diagnosis of asthma, insufficient sample size, poorly matched participants …etc. Therefore, a systematic review based on the conflict in this field was included in this thesis. The systematic review aimed to review the available published evidence about the relationship between objectively measured physical activity, sedentary behaviour and asthma in 6-12 years old school aged children.

A literature search was conducted to identify articles published in English between 2000-2017, in which the associations between asthma and these parameters were assessed objectively. Out of 71 publications searched in the literature, nine studies met the inclusion criteria, and were selected. In these selected studies, the total number of participants investigated was n = 2996 (asthmatics (n=839), and wheezers (n=37)). Eight studies of total number of participants n=2644, showed that there was no significant difference in physical activity between asthmatic and healthy children. However, one study of total number of participants n=352, suggested that asthmatic children were less physically active compared to healthy children. This review found no study that showed that asthmatic children were more physically active compared to healthy children. Among the studies selected, only three studies assessed sedentary behaviour objectively, of total number of participants n=609. These studies showed diverse results; one study suggested that children with asthma were less sedentary; and two studies showed no differences in sedentary behaviour between children with and without asthma. According to the systematic review presented in this thesis, we concluded that the available evidence strongly suggests that there was no difference between the physical activity of asthmatic and healthy children. In addition, it is

not possible to identify whether the relative inactivity of contemporary children confounds any relative decrease in activity in children with asthma.

An important finding obtained from the literature review conducted in the introduction, was that there were no studies that investigated the relationship between asthma attack during the acute stage and the activity continuum in children. Therefore, this study conducted in this thesis was the very first study to test the hypothesis that at one month following asthma attack (the recovery stage) patients achieve an improvement in asthma symptoms, an increase in physical, reduced sedentary behaviour and sleep disturbances. Furthermore, this study contributed to the debate regarding differences in physical activity, sedentary behaviour and sleep behaviour between asthmatic and healthy children. This study was conducted in Kuwait where asthma prevalence is high, and recruited asthmatic children admitted to the hospital due to asthma attack. The study showed that respiratory symptoms improved at the recovery stage. In addition, the physical activity increased at recovery time. There was no difference in sedentary behaviour and sleep behaviour between the acute and recovery times. This was in concordance with previous studies (205), that showed asthma symptoms and peaked expiratory flow (PEF) score following an asthma attack returned to baseline level within a maximum period of 10 days. This implies that four weeks period is sufficient for recovery from asthma attack and allows children to return to normal life style.

For the first time the inter individual variability of changes in the components of movement continuum following asthma attack were investigated. The individual data of some asthmatic patients showed inter individual variations in changes between the acute and recovery stage. The physical activity parameters of most of asthmatic children were increased after one month, while for the others either decreased or remained the same. Likewise, the sedentary behaviour (SB) in most asthmatic patients was decreased after one month while in others it was either increased or remained the same. Similarly, sleeping time of asthmatic patients was either decreased, increased or remained the same after one month. This inter individual variability of changes in the components of movement continuum following asthma attack has no definite explanation at present, and indicates the need for further research to explore this area. Therefore, individual approach to asthmatic children during recovery from asthma attack could be recommended.

This study contributed to the debate about differences in physical activity between asthmatic and healthy children. It showed that measures of physical activity such as duration of physical activity, total activity count, and number of steps of asthmatic children at the

recovery stage were significantly higher than those of healthy children. The physical activity results is consistent with previous studies (320-322) that suggested that asthmatic children were more physically active compared to healthy children. These results contradict our systematic review that showed that there was no difference in objectively measured physical activity between asthmatic and healthy children. In addition, at the recovery stage, sedentary parameters of asthmatic children such as the total sitting time, number of breaks in sitting, number of sedentary bouts and the fragmentation index were significantly higher than those of healthy children. This shows that asthmatic children were less sedentary compared to healthy children, which is consistent to Bringolf-Isler et al (325) study. There were no differences in sleeping time and pattern between asthmatic and healthy children. This finding is consistent with Stores et al (361), who showed that there was no difference in the sleep time of asthmatic children in the acute and recovery stage of the disease, but sleep disturbances disappear when asthma symptoms controlled in the recovery stage. Despite this study showed good results in sleep behaviour, it should be noted that the sleep data was under powered for the comparison between asthmatic and healthy children.

While analyzing the data, seasonal changes in the time and pattern of sleep of the participants had been observed. Therefore, a decision was made to analyze the data in this aspect. This analysis showed that possibly related to the large difference in temperature between the summer and other seasons in Kuwait, the awake times and bedtimes of children were different between these seasons. During the October to June apart from the summer, children in the study woke up early in the morning and went early to the bed. While, during the summer (July – September), there was a huge shift in bed time and wake up time, the children woke up late in the afternoon and went to bed late in the early morning. This 8 hours shift in sleeping time and the delay in awake time in summer might be an escape mechanism to avoid the high degrees of temperature which sometimes raised beyond 50C^{o} in daytime in summer in Kuwait, so that children were sleeping during daytime hours when temperature was high and woke up and started their activity late afternoon when temperature decreased. In addition, children in summer were sleeping 1 hour more than other times of the year.

The present study has several strengths. This the first and only study that investigated the movement continuum and asthma symptoms immediately following an acute attack objectively and provided information on the changes of movement continuum during the recovery from asthma attack in school aged children. Also, this is the first study that examined children with asthma in an Arabian country in the Middle East area. The

diagnosis of asthma was based on solid basis. It is the first study to assess the pattern of sedentary behaviour in asthmatic children. It is the only study that provided information about the inter individual variability in changes of activity continuum of the asthmatic patients during recovery from asthma. Participants were monitored for enough time so that the results were reliable (446, 478, 479). This study showed a new phenomenon, a change in the sleep pattern associated with the high temperature in the summer in Kuwait.

This study has some limitations. These include the small age difference between asthmatic and healthy children that might have some effects on the results of the components of the activity continuum; there are no recommendations or guidelines about the proper objectively measured sedentary behaviour duration that we can compare our data to it; the study was underpowered for the comparison of sleep duration between asthmatic and healthy children; the activPAL device has no cut-offs for intensities of PA, unable to differentiate between sit and lie period and not ideal for monitoring sleep disturbances; and nothing is known about the past history of components of the movement continuum of all participants.

This work highlights the need for further research into the components of the movement continuum in children with chronic diseases such as asthma. A better knowledge and understanding of the association between different severities of chronic diseases and movement continuum would provide useful information that can help in the management of diseased children and speed their recovery so that they can return back to normal health and activity. In the future, it would be useful when studying children with chronic diseases to examine patients in different severities of the disease and to consider other possible relevant confounding factors such as age, gender, treatment, diet intake, social life and season. In addition, it is important in future studies to take care of children's past history in movement continuum. Also, the inter individual variability of changes in the components of the movement continuum during recovery of the disease should be investigated. The phenomenon of changes in sleeping behaviour and its potential effects on children's health both in Kuwait and other countries with very high summer temperature merits more extensive study.

Chapter 6: Conclusion

6 Conclusion

Several conclusions can be drawn from this work. The systematic review identified that there was no difference in objectively measured physical activity between asthmatic and healthy children. However, this finding of the systematic review was not consistent with our finding from this study of higher physical activity in asthmatic children. This study showed that almost all parameters of the activity continuum had recovered from week one to week 4 following asthma attacks. During the recovery from asthma attack there was inter individual variability of changes in the movement continuum. There are no predictors for the inter individual variability of changes in the movement continuum during recovery and there is no explanation for the individual variabilities. This study showed that in Kuwait, asthmatic children admitted with an asthma attack were physically active, not sedentary and had no difference in sleep time when compared to a comparable group of healthy Kuwaiti children**.** Also, this study showed a new phenomenon, a huge shift in bed and rise time of children associated with the high temperature in the summer in Kuwait. Finally, it was clear that sleep behaviour should be monitored by device that is capable of assessing both sleep time and sleep disturbances efficiently.

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Appendix A

Search Strategies used to search the literature

A. Medline (ovid): 2000 - 2016 week 01, searched 01 January 2016

1. exp Child/

2.exp Adolescent/

3.(child* or adolesc* or teen* or youth or girl* or boy*).tw.

4.(young adj1 (person or people)).tw.

5. 1 or 2 or 3 or 4----→ (n=2909927) records

6. exp Exercise/

7. exp Motor Activity/

8. exp Sports/

9. exercis*.tw.

10. physical* activ*.tw.

11. (active adj2 (living or lifestyle)).tw.

12. sedentary behavi?r.tw.

13. exp Sedentary Lifestyle/

14. ((sedentary or sitting or screen or TV or television or computer or PC or video games) adj2 time).tw.

15. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14---→ (n=459385) records

16. exp Accelerometry/

17. exp Actigraphy/

18. acceleromet*.tw.

19. actigraph.tw.

20. activity monitor*.tw.

21. (objective adj1 (measure* or monitor* or assess*)).tw.

22. 16 or 17 or 18 or 19 or 20 or 21---→ (n=30085) records

23. exp Asthma/

24. asthma.tw.

25. exp Respiratory Tract Diseases/

26. exp Respiratory Hypersensitivity/

27. (respiratory adj2 allerg*).tw.

28. wheez*.tw.

29. Pulmonary/ or exp lung diseases, obstructive/ or exp lung diseases

30. "chronic lung disease".tw.

31. "chronic respiratory disease".tw.

32. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31--→ (n=1170650) records

33. 5 and 15 and 22 and 32 ----→ (n=70) records out of (n=4570047) records for our search on #33

34. limit 33 to (yr="2000 -Current" and "child (6-12 years)" and English)-→(n= 28) records out of (n=4097948) records for our search on #33

35. (n=28) records screened --→ (n=22) excluded (not meeting eligibility criteria) and (n=6) Studies included

B. EMBASE (ovid): 2000 - 2016 week 01, searched 05 January 2016

1. exp Child/

2.exp Adolescent/

3.(child* or adolesc* or teen* or youth or girl* or boy*).tw.

4.(young adj1 (person or people)).tw.

5. 1 or 2 or 3 or 4 ----→ (n=2016016) records

6. exp Exercise/

7. exp Motor Activity/

8. exp Sports/

9. exercis*.tw.

10. physical* activ*.tw.

11. (active adj2 (living or lifestyle)).tw.

12. sedentary behavi?r.tw.

13. exp Sedentary Lifestyle/

14. ((sedentary or sitting or screen or TV or television or computer or PC or video games) adj2 time).tw.

15. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 --- →(n=707132) records

16. exp Accelerometry/

17. exp Actigraphy/

18. acceleromet*.tw.

19. actigraph.tw.

20. activity monitor*.tw.

21. (objective adj1 (measure* or monitor* or assess*)).tw.

22. 16 or 17 or 18 or 19 or 20 or 21 ----→(n=38276) records

23. exp Asthma/

24. asthma.tw.

25. exp Respiratory Tract Diseases/

26. exp Respiratory Hypersensitivity/

27. (respiratory adj2 allerg*).tw.

28. wheez*.tw.

29. Pulmonary/ or exp lung diseases, obstructive/ or exp lung diseases

30. "chronic lung disease".tw.

31. "chronic respiratory disease".tw.

32. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 ---→(n=1336524) records

33. 5 and 15 and 22 and 32 ----→ (n=110) records out of (n=4097948) records for our search on #33

34. limit 33 to (yr="2000 -Current" and "child (6-12 years)" and English)-→ (n=24) records

35. (n=24) records screened --→ (n=21) excluded (not meeting eligibility criteria) and (n=3) Studies included

C. Pubmed: 2000 - 2016 week 02, searched 10 January 2016

1# Child

2# Adolescent

3# (((((child*[tw]) OR adolesc*[tw]) OR teen*[tw]) OR youth [tw]) OR girl* [tw]) OR boy* [tw]

4# ("young person" [tw]) OR "young people" [tw]

5# #1 or #2 or #3 or #4-→(n=3030645) records

6# Exercise

7# exercis*[tw]

8# physical* activ* [tw]

9# "Motor Activity"

10# Sports[tw]

11# ("active living" [tw]) OR "active lifestyle" [tw]

12# sedentary behav* [tw]

13# "Sedentary Lifestyle"

14# (((((("sedentary time" [tw]) OR "sitting time" [tw]) OR "screen time" [tw]) OR "television time" [tw]) OR "computer time" [tw]) OR " video games time" [tw]

15# #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14→(n=374520) records

16# Accelerometry

17# Actigraphy

18# acceleromet*[tw]

19# actigraph* [tw]

20# activity monitor* [tw]

21# (("objective measure*"[tw]) OR "objective monitor* "[tw]) OR "objective assess*"[tw]

22# #16 or #17 or #18 or #19 or #20 or #21→ (n=17005) records

23# Asthma

24# asthma [tw]

25# Respiratory Tract Diseases

26# Respiratory Hypersensitivity

27# respiratory allerg* [tw]

28# wheez*[tw]

29# ((Pulmonary diseases) OR lung diseases) OR obstructive lung diseases

30# "chronic lung disease"[tw]

31# "chronic respiratory disease"[tw]

32# 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31→ (n=1238289) records

33# 5 and 15 and 22 and 32 ----→ records identified (n=43) out of (n=4660459) records for our search on #33

34# limit 33 to (yr="2000 -Current" and "child (6-12 years)" and English)-→ (n=16) records

35. (n=16) records screened --→ (n=10) excluded (not meeting eligibility criteria) and (n=6) Studies included

D. Cochrane Central Register of Controlled Trials: Issue 12 of 12, December 2015, searched 15 January 2016

#1 MeSH descriptor: [Child] explode all trees

#2 MeSH descriptor: [Adolescent] explode all trees

#3 child* or adolesc* or teen* or boy* or girl* or youth:ti,ab,kw (Word variations have been searched)

#4 young near/1 (person or people):ti,ab,kw (Word variations have been searched)

#5 #1 or #2 or #3 or #4

#6 MeSH descriptor: [Motor Activity] this term only

#7 MeSH descriptor: [Exercise] explode all trees

#8 MeSH descriptor: [Sports] explode all trees

#9 MeSH descriptor: [Sedentary Lifestyle] explode all trees

#10 physical* activ*:ti,ab,kw (Word variations have been searched)

#11 exercis* or sport*:ti,ab,kw (Word variations have been searched)

#12 active near/2 (living or lifestyle):ti,ab,kw (Word variations have been searched)

#13 sedentary behavi?r:ti,ab,kw (Word variations have been searched)

#14 (screen or sedentary or sitting or TV or television or computer or PC or video games) near/2 time:ti,ab,kw (Word variations have been searched)

#15 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

#16 MeSH descriptor: [Accelerometry] explode all trees

#17 acceleromet*:ti,ab,kw (Word variations have been searched)

#18 actigraph*:ti,ab,kw (Word variations have been searched)

#19 activity near/1 monitor*.:ti,ab,kw (Word variations have been searched)

#20 #16 or #17 or #18 or #19

#21 MeSH descriptor: [Respiratory Tract Diseases] explode all trees

#22 respirator* near/1 disease*:ti,ab,kw (Word variations have been searched)

#23 asthma*:ti,ab,kw (Word variations have been searched)

#24 respiratory near/1 allerg*:ti,ab,kw (Word variations have been searched)

#25 #21 or #22 or #23 or #24

#26 #5 and #15 and #20 and #25

#27 (n=5) records screened --→ (n=5) excluded (not meeting eligibility criteria) and (n=0) Studies included

There are 5 results from 912712 records for your search on #26 - #5 and #15 and #20 and #25 in Trials in the strategy currently being edited--→ 5 Trials excluded (not meeting eligibility criteria) ---→ Trials included (n=0)

E. CINAHL: 2000 – 1st March 2015

59. (n=22) records screened --→ (n=21) excluded (not meeting eligibility criteria) and (n=1) Studies included

S58 Limiters - Published Date: 20000101-20160231; English Language; Age Groups: Child: 6-12 years---→22 studies ---→21 studies excluded and 1 study included.

S57 S9 AND S33 AND S43 AND S56 ---→ identified (n=38) out of 940950 records for our search on S57

S56 S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55--→ 87670 records

S55 "chronic respiratory disease"(Searched as Keyword)

S54 (MH "Lung Diseases, Obstructive+") OR (MH "Pulmonary Disease, Chronic Obstructive+")

S53 (MH "Lung Diseases+")

S52 (MH "Respiratory Hypersensitivity+")

S51 ""respiratory obstruction""(Searched as Keyword)

S50 ""respiratory allerg*""(Searched as Keyword)

S49 ""respiratory disease*"" (Searched as Keyword)

S48""chronic lung disease""(Searched as Keyword)

S47 (MH "Respiratory Tract Diseases")

S46 "wheez*"

S45 "asthma*" (Searched as Keyword)

S44 (MH "Asthma+")

S43 S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42---→ 24146

S42 ""objective assess*"" (Searched as Keyword)

S41 ""objective monitor*""(Searched as Keyword)

S40 "objective measure*" (Searched as Keyword)

S39 ""activity monitor* ""(Searched as Keyword)

S38 ""actigraph"" (Searched as Keyword)

S37 (MH "Actigraphy")

S36 "acceleromet*"(Searched as Keyword)

S35 (MH "Accelerometry")

S34 (MH "Accelerometers")

S33 S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32--→ 260467

S32 ""computer time"" (Searched as Keyword)

S31 ""television time"" (Searched as Keyword)

S30 ""screen time""(Searched as Keyword)

S29 ""sitting time""(Searched as Keyword)

S28""screen"" (Searched as Keyword)

S27""computer""(Searched as Keyword)

S26 ""sedentary time"" (Searched as Keyword)

S25 (MH "Video Games+")

S24 (MH "Television")

S23 (MH "Sitting")

S22 "sedentary" (Searched as Keyword)

S21 (MH "Life Style, Sedentary")

S20 "sedentary behavi?r" (Searched as Keyword)

S19 ""SEDENTARY behavior in children""(Searched as Keyword)

S18 "(active lifestyle)" (Searched as Keyword)

S17 (MH "Activities of Daily Living+")

S16 "sport*" (Searched as Keyword)

S15 "exercis*" (Searched as Keyword)

S14 "physical* activ*" (Searched as Keywo rd)

S13(MH "Sports+")

S12 (MH "Motor Activity+")

S11(MH "Exercise+")

S10 (MH "Physical Activity")

S9 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8--→568667

S8 "young" (Searched as Keyword)

S7 "boy*" (Searched as Keyword)

S6 "girl*" (Searched as Keyword)

S5 "youth" (Searched as Keyword)

S4 "adolesc*"(Searched as Keyword)

S3 "child*" (Searched as Keyword)

S2 (MH "Adolescence+")

S1 (MH "Child+")

Appendix B

Checklist of the studies of the systematic review

Study number: 1

Study identification Fedele DA, Janicke DM, Lim CS, Abu-Hasan M. An examination of comorbid asthma and obesity: assessing differences in physical activity, sleep duration, health-related quality of life and parental distress. J Asthma. 2014;51(3):275-81.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
A cross-sectional study		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Adequately addressed
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Not reported
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not addressed
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	No reported
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not applicable
ASSESSMENT		
1.7	The outcomes are clearly defined	Well covered
1.8	The assessment of outcome is made blind to exposure status.	Not addressed
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not addressed
1.10	The method of assessment of exposure is reliable.	Well covered
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Not addressed
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Well covered
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	No
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	-Cases: (n=73) asthmatics & obese -Controls: (n=175) non asthmatic obese.
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital	Community based study investigated obese American boys and girls aged 7-12 yrs

	based	
3.3	What environmental or prognostic factor is being investigated in this study?	Anthropometric measurements , dietary intake, PA, sleep, health-related quality of life, parent distress
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	Comparisons made between non asthmatic obese and asthmatics & obese in different levels of , dietary intake, PA, sleep, health-related quality of life, parent distress
3.5	For how long are patients followed up in the study?	It is a cross sectional study
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	-BMI using a Harpendeon stadiometer for height and a calibrated and certified digital scale for weight -dietary intake using the Block Kids 2004 questionnaire -PA using Sensewear armband accelerometer -sleep duration using Sensewear armband accelerometer -health-related quality of life using Pediatric Quality of Life Inventory (PedsQL)
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study- e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	Non significant (p=0.084) difference in levels of PA between obese asthmatics and obese non asthmatics
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	Not reported
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	-Study helped to answer our key question -Study conclusion: no significant difference in PA between obese asthmatics and non asthmatics obese

Study number: 2

Study identification Bringolf-Isler B, Graf E, Waser M, Genuneit J, von Mutius E, Loss G, et al. Association of physical activity, asthma, and allergies: a cohort of farming and nonfarming children: J Allergy Clin Immunol. 2013 Sep;132(3):743-746.e4. doi: 10.1016/j.jaci.2013.03.042. Epub 2013 May 16.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cohort study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Poorly addressed
SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Poorly addressed
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Not reported
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Not reported
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not reported
ASSESSMENT		
1.7	The outcomes are clearly defined	Poorly addressed

1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Adequately addressed
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Adequately addressed
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Not reported
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	Yes
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Unacceptable (–) reject
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Cannot say
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	No
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	Cases: 79 (22.4%) Controls: 273 (77.6%)
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Community based study investigated farming and non farming Swiss boys and girls aged 7-10 yrs
3.3	What environmental or prognostic factor is being investigated in this study?	-PA -Sedentary behaviour
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	Comparisons made between farming and non-farming different levels of PA and sedentary behaviour.
3.5	For how long are patients followed up in the study?	2007-2009
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	Accelerometer measured PA and sedentary behaviour.
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	Odds ratio of asthmatics counts/min: - Unadjusted: 0.95 (0.64-1.40) - Covariate adjusted: 0.87 (0.53-1.41) - Restricted to autumn/winter (n=250) 0.68 (0.36-1.31)
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	Not reported
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	-To a lesser extent yes -Shows that asthmatic had less PA (light activity) than non asthmatics

Study number: 3

Study identification Vangeepuram N, McGovern KJ, Teitelbaum S, Galvez MP, Pinney SM, Biro FM, et al. Asthma and physical activity in multiracial girls from three US sites. Journal of Asthma. 2013;51(2):193-9.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cross sectional study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		

1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Adequately addressed
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Not reported
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not reported
ASSESSMENT		
1.7	The outcomes are clearly defined	Adequately addressed
1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Not addressed
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Not reported
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Adequately addressed
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	No
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	991 non asthmatic girls 191 asthmatic girls
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g. age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Community based, multiethnic (33.5% White, 4.8% Asian, 30.6% non Hispanic Black and 30.7% Hispanic) American girls aged 6–8 years
3.3	What environmental or prognostic factor is being investigated in this study?	PA and sedentary behaviour
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	comparisons made between different levels of PA and sedentary behaviour
3.5	For how long are patients followed up in the study?	It is a cross sectional study
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	PA and sedentary behaviour measured by pedometer (Yamax SW-200 Digi-walker) and questionnaire (parents asked about activities hours/ week and months/year)
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	- No significance difference in PA and SB -Adjustments made for confounding factors (age, self-reported race/ethnicity, body mass index and level of caregiver education)
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	Not reported
3.9	Does this study help to answer your key question?	-To a lesser extent yes,

	Summarise the main conclusions of the study and indicate how it relates to the key questions?	showed the two groups were of similar PA and SB

Study number: 4

Study identification Sousa AW, Cabral AL, Martins MA, Carvalho CR. Daily physical activity in asthmatic children with distinct severities. J Asthma. 2014;51(5):493-7.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cross sectional study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Adequately addressed
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Not reported
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not reported
ASSESSMENT		
1.7	The outcomes are clearly defined	Well covered
1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Well covered
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Not reported
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Not reported
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	No
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Unacceptable (–) reject
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	asthmatic (n= 79) non asthmatics (n= 42)
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Hospital based, Brazilian boys and girls, aged 7–12 years
3.3	What environmental or prognostic factor is being investigated in this study?	PA
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	Comparisons made between different levels of asthma and PA
3.5	For how long are patients followed up in the study?	Not reported
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	PA measured by accelerometer (Power Walker-610, Yamax, Japan); physically active

		children make 15 000 and 12 000 steps per day for the boys and girls, respectively and below these values were classified as sedentary
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	No significant difference in PA(total number of steps, and number of steps in moderate physical activity) between asthmatics and non asthmatics
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	Not reported
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	- Yes -Showedt no difference in PA between asthmatic and non asthmatics

Study number: 5

Study identification Tsai SY, Ward T, Lentz MJ, Kieckhefer GM. Daytime physical activity levels in school-age children with and without asthma. Nurs Res. 2012;61(4):252-9.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cross sectional study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Adequately addressed
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Not reported
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Not reported
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not reported
ASSESSMENT		
1.7	The outcomes are clearly defined	Adequately addressed
1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Well covered
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Adequately addressed
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Well covered
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	No
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association	Yes

	between exposure and outcome?	
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	(n=27) asthmatic (n=27) non asthmatics
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Community based, multi- ethnic American boys and girls (American Indian/Alaska Native, Asian, Native Hawaiian or other Pacific Islander, Black or African American and White), aged 9–11 years
3.3	What environmental or prognostic factor is being investigated in this study?	PA and sedentary behaviour
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	Comparisons made between asthmatic and non asthmatics and different levels of PA and sedentary behaviour
3.5	For how long are patients followed up in the study?	2004 - 2006
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	PA and SB measured by Actiwatch 64, (Mini-Mitter Philips Respironics)
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	No significant difference in PA & SB between asthmatic and non asthmatics
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	Not reported
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	- Yes -Showed no significant difference in PA & SB between asthmatic and non asthmatics

Study number: 6

Study identification Vahlkvist S, Pedersen S. Fitness, daily activity and body composition in children with newly diagnosed, untreated asthma. Allergy. 2009;64(11):1649-55. Epub 2009/06/06.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well case control study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The cases and controls are taken from comparable populations	Well covered
1.3	The same exclusion criteria are used for both cases and controls.	Adequately addressed
1.4	What percentage of each group (cases and controls) participated in the study?	Cases: (n=57) asthmatics Controls:(n=157) non asthmatics
1.5	Comparison is made between participants and non-participants to establish their similarities or differences.	Not reported
1.6	Cases are clearly defined and differentiated from controls.	Well covered
1.7	It is clearly established that controls are non-cases	Well covered
ASSESSMENT		
1.8	Measures will have been taken to prevent knowledge of primary exposure influencing case ascertainment	Not reported
1.9	Exposure status is measured in a standard, valid and reliable way.	Well covered
CONFOUNDING		
1.10	The main potential confounders are identified and taken into account in the design and analysis	Not reported
STATISTICAL ANALYSIS		

1.14	Confidence intervals been provided?	Yes
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number cases and controls separately	Cases: (n=57) asthmatics Controls:(n=157) non asthmatics
3.2	What are the main characteristics of the study population? Include all characteristics used to identify both cases and controls -e.g.age, sex, social class, disease status	Hospital and community based study of asthmatics and non asthmatics Danish boys and girls, aged 6–14 years
3.3	What environmental or prognostic factor is being investigated in this study?	PA, cardiovascular fitness and body composition
3.4	What comparisons made in this study? Normally only one factor will be compared, but in some cases the extent of exposure may be stratified. Note all comparisons here.	PA, cardiovascular fitness and body composition compared between newly diagnosed untreated asthmatics and non asthmatics
3.5	For how long are patients followed up in the study?	1 year
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	PA measured by RT3 accelerometer
3.7	What size of effect is identified in the study? Effect size should be expressed as an odds ratio. If any other measures are included, note them as well. Include P value and any confidence intervals that are provided.	No significant difference in PA between asthmatic and non asthmatics
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	A grant from Danish Paediatric Asthma Centre.
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	- Yes -Shows that no significant difference in PA between newly diagnosed untreated asthmatic and non asthmatics

Study number: 7

Study identification Vahlkvist S, Inman MD, Pedersen S. Effect of asthma treatment on fitness, daily activity and body composition in children with asthma. Allergy. 2010;65(11):1464-71		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cohort study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Well covered
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Not reported
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	(n=2) asthmatics (n=3) non asthmatics
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not applicable
ASSESSMENT		

1.7	The outcomes are clearly defined	Well covered
1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Well covered
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Not reported
1.12	Exposure level or prognostic factor is assessed more than once	Well covered
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Not reported
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	Yes
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	Cases: (n=55) asthmatics Controls:(n=154) non asthmatics
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Hospital and community based study of Danish asthmatics and non asthmatics boys and girls, aged 6–14 years
3.3	What environmental or prognostic factor is being investigated in this study?	PA, cardiovascular fitness and body composition and a variety of asthma outcomes
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/prognostic, or different levels of the factor?	PA, cardiovascular fitness and body composition and a variety of asthma outcomes between newly diagnosed untreated asthmatics (at two time points: baseline and after one year of treatment) and non asthmatics
3.5	For how long are patients followed up in the study?	1 year
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	PA measured by RT3 accelerometer
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	No significant difference in PA between asthmatic (at two time points: baseline and after one year of treatment) and non-asthmatics
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	A grant from Danish Paediatric Asthma Centre and by an unconditional grant from Glaxo-SmithKline.
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	- Yes -Shows that no significant difference in PA between newly diagnosed untreated asthmatic (at two time points: baseline and after one year of treatment) and non asthmatics

Study number: 8

Study identification Van Gent R, van der Ent CK, van Essen-Zandvliet LE, Rovers MM, Kimpen JL, de Meer G, et al. No differences in physical activity in (un)diagnosed asthma and healthy controls. Pediatr Pulmonol. 2007;42(11):1018-23. Epub 2007/09/29.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cross sectional study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The three groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Well covered
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Not reported
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not reported
ASSESSMENT		
1.7	The outcomes are clearly defined	Well covered
1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Well covered
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Well covered
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Not reported
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	Yes
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	(n= 81) diagnosed asthma (n=130) undiagnosed asthma (n=202) healthy controls
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Community based study of Dutch diagnosed asthmatics, undiagnosed asthmatics and healthy controls, boys and girls aged 7–10 years
3.3	What environmental or prognostic factor is being investigated in this study?	Daily PA
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	Different levels of daily PA compared between diagnosed asthmatics, undiagnosed asthmatics and healthy controls
3.5	For how long are patients followed up in the study?	Not reported
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	Daily PA measured by PAM accelerometer

3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	No significant difference in Daily PA between diagnosed asthmatics, undiagnosed asthmatics and healthy controls.
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	Not reported
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	-Yes , showed no difference in PA between diagnosed and undiagnosed asthmatics and healthy controls.

Study number: 9

Study identification Yiallouros PK, Economou M, Kolokotroni O, Savva SC, Gavatha M, Ioannou P, et al. Gender differences in objectively assessed physical activity in asthmatic and non-asthmatic children. Pediatr Pulmonol. 2015;50(4):317-26.		
Guideline topic:		Key Question No:
SECTION 1: INTERNAL VALIDITY		
In a well conducted cross sectional study:		Does this study do it?
1.1	The study addresses an appropriate and clearly focused question.	Well covered
SELECTION OF SUBJECTS		
1.2	The three groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Well covered
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Not reported
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	Well covered
1.6	Comparison is made between full participants and those lost to follow up, by exposure status	Not reported
ASSESSMENT		
1.7	The outcomes are clearly defined	Well covered
1.8	The assessment of outcome is made blind to exposure status.	Not reported
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	Not reported
1.10	The method of assessment of exposure is reliable.	Well covered
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	Not reported
1.12	Exposure level or prognostic factor is assessed more than once	Not reported
CONFOUNDING		
1.13	The main potential confounders are identified and taken into account in the design and analysis	Well covered
STATISTICAL ANALYSIS		
1.14	Have confidence intervals been provided?	Yes
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes
SECTION 3: DESCRIPTION OF THE STUDY		
3.1	How many patients are included in this study? List the number in each group separately	- 104 asthmatics (67 boys; 44 inactive asthma, 23 active

		asthma and 37girls; 24 inactive asthma, 13 active asthma) - 99 controls (59 boys and 40 girls)
3.2	What are the main characteristics of the study population? Include all relevant characteristics-e.g.age, sex, ethnic origin, comorbidity, disease status, community/hospital based	Community based study of Cyprus asthmatics (active and inactive) and healthy controls, boys and girls aged 8–9 years
3.3	What environmental or prognostic factor is being investigated in this study?	PA and sedentary activity levels
3.4	What comparisons made in this study? Are comparisons made between presence or absence of an environmental/ prognostic, or different levels of the factor?	Different levels of PA and sedentary activity levels compared between asthmatics (active and inactive) and healthy controls, boys and girls aged 8–9 years
3.5	For how long are patients followed up in the study?	PA and sedentary activity measured for 8 days
3.6	What outcome measure(s) are used in the study? List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.	Biaxial accelerometers (Actigraph, Pensacola, FL)
3.7	What size of effect is identified in the study? List all measures of effects in the units used in the study-e.g. absolute or relative risk. Include P value and any confidence intervals that are provided. Note: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc	No significant difference in Daily PA between diagnosed asthmatics, undiagnosed asthmatics and healthy controls.
3.8	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.	European Regional Development Fund, Republic of Cyprus Through the Cyprus Research Promotion Foundation; Number: Project HEALTH/0506/17.
3.9	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key questions?	-Yes -Shows that no difference in PA and sedentary activity levels between the three groups; active and inactive asthma and non-asthmatic children. - Girls with active asthma have lower MVPA than their peers

Appendix C

Ethical approval

Ethical approval from the Joint Committee for the Protection of Human Subjects in Research of the Health Sciences Centre (HSC) & Kuwait Institute for Medical Specialization (KIMS)

JOINT COMMITTEE FOR THE PROTECTION OF
HUMAN SUBJECTS IN RESEARCH OF THE
HEALTH SCIENCES CENTRE (HSC)
& KUWAIT INSTITUTE FOR MEDICAL SPECIALIZATION (KIMS)

Ref.: VDR/JC/532
Date: April 12, 2012

To: Dr. Bandar S. Al-Shammari
MD Student – Child Health Department
Faculty of Medicine
University of Glasgow

From: Dr. Ibrahim A. Hadi
Secretary General
KIMS

Dr. Ibrahim A. Hadi
Secretary General
Kuwait Institute For Medical Specializations(KIMS)

Sub: Project title: What is the Time Course of Recovery from an Asthma Exacerbation and the Relation between the Recovery from an Asthma Exacerbation and the Physical Activity Levels of Asthmatic Children?

The above mentioned project has been reviewed by the Joint Committee for the Protection of Human Subjects in Research and the following decision has been given:

Decision: Ethical approval granted

Best regards.

N.R

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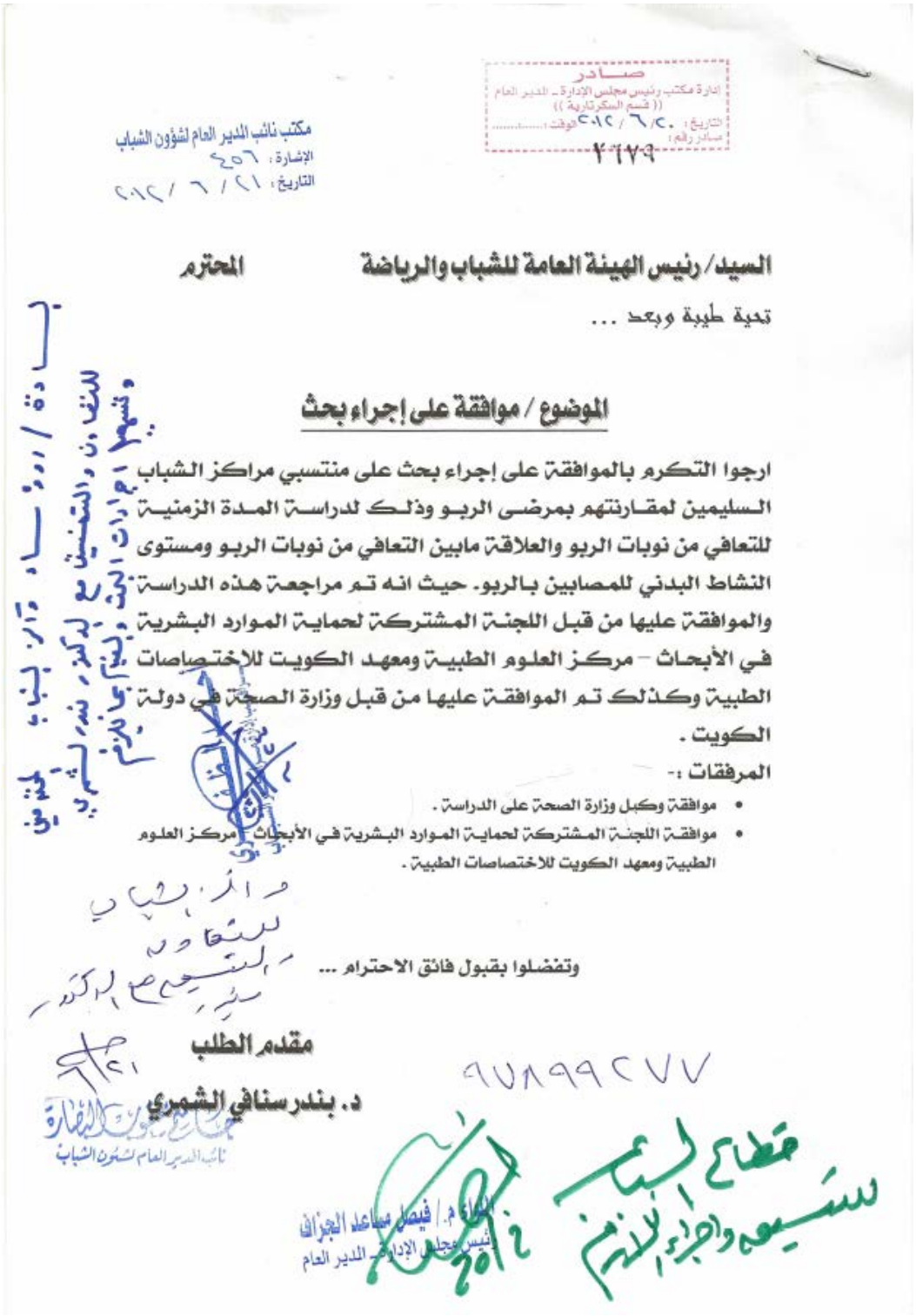
Tel. (965) 25319481 – Fax. 25318455 – P.O.Box: 24923 Safat, Code No. 13110, Kuwait

Kuwait Public Authority for Youth and Sport study approval



صـــادر
إدارة مكتب رئيس مجلس الإدارة - المدير العام
((قسم السكرتارية))
التاريخ : ٢٠ / ٦ / ٢٠١٢ الوقت : .....
صادر رقم :
٢٦٢٩

مكتب نائب المدير العام لشؤون الشباب
الإشارة : ٤٥٦
التاريخ : ٢١ / ٦ / ٢٠١٢

السيد/ رئيس الهيئة العامة للشباب والرياضة المحترم

تحية طيبة وبعد ...

الموضوع / موافقة على إجراء بحث

ارجوا التكرم بالموافقة على إجراء بحث على منتسبي مراكز الشباب السليمين لمقارنتهم بمرضى الربو وذلك لدراسة المدة الزمنية للتعافي من نوبات الربو والعلاقة مابين التعافي من نوبات الربو ومستوى النشاط البدني للمصابين بالربو. حيث انه تم مراجعة هذه الدراسة والموافقة عليها من قبل اللجنة المشتركة لحماية الموارد البشرية في الأبحاث – مركز العلوم الطبية ومعهد الكويت للاختصاصات الطبية وكذلك تم الموافقة عليها من قبل وزارة الصحة في دولة الكويت .

المرفقات :-

- موافقة وكيل وزارة الصحة على الدراسة .
- موافقة اللجنة المشتركة لحماية الموارد البشرية في الأبحاث – مركز العلوم الطبية ومعهد الكويت للاختصاصات الطبية .

وتفضلوا بقبول فائق الاحترام ...

مقدم الطلب

د. بندر سنافي الشمري

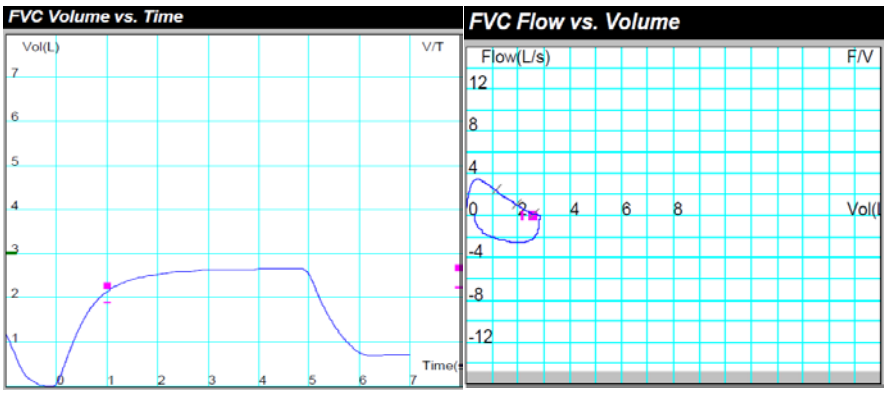
نائب المدير العام لشؤون الشباب

اللواء م. / فيصل مساعد الجراح
رئيس مجلس الإدارة - المدير العام

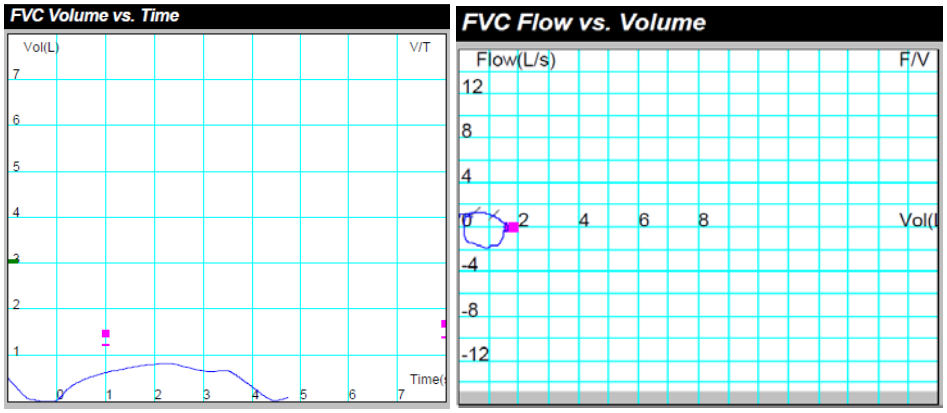
Appendix D

FVC Flow-Volume and FVC Volume-Time curves curve

Good performance or good quality test of FVC Flow-Volume curve shows a steep rise which begins from the volume axis (x-axis) to a peak (Peak Expiratory Flow (PEF)), after reaching the PEF, air is expired and the curve descends to bottom (FVC), followed by forced inspiration that has roughly a similar curve to that of the forced expiration, but the PIF (Peak Inspiratory Flow) is not as clear as PEF & FVC Volume-Time curve shows a steep rise to a plateau



Bad performance or bad quality test FVC Flow-Volume lacks either a steep rise or a PEF or both & FVC Volume-Time curves lacks either a steep rise or a plateau or both.



Appendix E

The correlations of the individual variability in change in activity continuum

The correlations between the percent change of the activity continuum, age, BMI Z score, Childhood asthma control test (CACT) score and pulmonary function test (PFT) of asthmatic patients

The Spearman's rho correlation between the percent change of the activity continuum and age of asthmatic patients

		AGE	Percent change of PA time	Percent change of number of Steps	Percent change of total sitting time	Percent change of Sleep time
AGE	Correlation Coefficient	1.000	.088	-.166	-.191	.111
	Sig. (2-tailed)		.691	.448	.382	.614
	N	23	23	23	23	23
*. Correlation is significant at the 0.05 level (2-tailed).						
**. Correlation is significant at the 0.01 level (2-tailed).						

The Pearson correlation between the percent change of the activity continuum and BMI Z score of asthmatic patients

		BMI Z score	Percent change of PA time	Percent change of number of Steps	Percent change of total sitting time	Percent change of Sleep time
BMI Z score	Pearson Correlation	1	.131	.130	-.061	.069
	Sig. (2-tailed)		.553	.554	.781	.755
	N	23	23	23	23	23
*. Correlation is significant at the 0.05 level (2-tailed).						
**. Correlation is significant at the 0.01 level (2-tailed).						

The Spearman's rho correlation between the percent change of the activity continuum and CACT score of asthmatic patients

		CACT	Percent change of PA time	Percent change of number of Steps	Percent change of total sitting time	Percent change of Sleep time
CACT	Correlation Coefficient	1.000	.268	-.438*	.140	-.378
	Sig. (2-tailed)	.	.216	.037	.523	.076
	N	23	23	23	23	23
*. Correlation is significant at the 0.05 level (2-tailed).						
**. Correlation is significant at the 0.01 level (2-tailed).						