Iowa Research Online
The University of Iowa's Institutional Repository

University of Iowa
Iowa Research Online

Theses and Dissertations

2010

Physical activity, cardiorespiratory fitness, adiposity, and cardiovascular health in children and adolescents

Soyang Kwon
University of Iowa

Copyright 2010 Soyang Kwon

This dissertation is available at Iowa Research Online: http://ir.uiowa.edu/etd/535

Recommended Citation
Kwon, Soyang. "Physical activity, cardiorespiratory fitness, adiposity, and cardiovascular health in children and adolescents." PhD (Doctor of Philosophy) thesis, University of Iowa, 2010.
http://ir.uiowa.edu/etd/535.

Follow this and additional works at: http://ir.uiowa.edu/etd

Part of the Clinical Epidemiology Commons

PHYSICAL ACTIVITY, CARDIORESPIRATORY FITNESS, ADIPOSITY, AND CARDIOVASCULAR HEALTH IN CHILDREN AND ADOLESCENTS

by

Soyang Kwon

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Epidemiology
in the Graduate College of
The University of Iowa

May 2010

Thesis Supervisor: Professor Kathleen F. Janz

ABSTRACT

The goal of this dissertation research was to better understand relationships among physical activity (PA), cardiorespiratory fitness, adiposity, and cardiovascular (CV) health in children and adolescents. The aim of the first paper was to examine whether fitness and adiposity are independently associated with CV risk factors during puberty. Study participants were 126 prepubertal Caucasian children participating in a longitudinal four-year follow-up study. Fitness level was determined by VO_2 max (L/min) obtained from maximal graded exercise testing and adiposity level was determined by the sum of skinfolds. Gender-specific individual growth curve models, including both VO_2 max and the sum of skinfolds simultaneously, were fit to predict CV risk factor variables. Models also included covariates such as age, height, weight, and pubertal stage by the Tanner criteria. In both boys and girls, total cholesterol, triglyceride, LDL-C, and systolic blood pressure percentile were positively associated with the sum of skinfolds ($P < 0.05$), but not with VO_2 max ($P > 0.05$). In conclusion, fitness was not associated with CV risk factors, after adjusting for adiposity, among healthy adolescents. This study suggests that adiposity may play a role in the mechanism underlying the effect of fitness on CV health during puberty. The aim of the second paper was to examine whether early adiposity level is inversely associated with subsequent PA behaviors in childhood. Study participants were 326 children participating in the Iowa Bone Development Study. PA and fat mass were measured using accelerometers and dual energy X-ray absorptiometry (DXA) at approximately 5, 8, and 11 years of age. Gender-specific generalized linear models were fit to examine the association between percent body fat (BF%) at age 8 and intensity-weighted moderate- to vigorous-intensity PA (IW-MVPA) at age 11. After adjusting for IW-MVPA at age 8, an interval between the age 5 and 8 examinations, residualized change scores of BF% and IW-MVPA from age 5 to 8 and mother's education level, BF% at age 8 was inversely associated with IW-MVPA at age 11 among boys ($P < 0.05$). After adjusting for IW-MVPA at age 8, physical maturity,

and family income, BF% at age 8 was inversely associated with IW-MVPA at age 11 among girls ($P < 0.05$). Categorical analysis also showed that the odd of being in the lowest quartile relative to the highest quartile of IW-MVPA at three-year follow-up for boys and girls with high BF% was approximately four times higher than the odd for those with low BF% ($P < 0.05$). This study suggests that adiposity levels may be a determinant of PA behavior. Specific intervention strategies for overweight children may be needed to promote PA. The aim of the third paper was to examine whether accelerometer-measured daily light-intensity PA is inversely associated with DXA-derived body fat mass during childhood. The study sample was 577 children participating in the longitudinal Iowa Bone Development Study. Fat mass and PA were measured at about 5, 8, and 11 years of age. Two PA indicators were used, applying two accelerometer count cut-points: the daily sum of accelerometer counts during light-intensity PA (IW-LPA) and the daily sums of accelerometer counts during high-light-intensity PA (IW-HLPA). Measurement time point- and gender-specific multivariable linear regression models were fit to predict fat mass based on IW-LPA and IW-HLPA, including covariates, such as age, birth weight, fat-free mass, height, IW-MVPA and maturity (only for girls). Among boys, both IW-LPA and IW-HLPA were inversely associated with fat mass at age 11 ($P < 0.05$), but not at ages 5 and 8. Among girls, both LPA variables were inversely associated with fat mass at ages 8 and 11 ($P < 0.10$ for LPA at age 11, $P < 0.05$ for others), but not at age 5. In conclusion, this study suggests that light-intensity PA may have a preventive effect against adiposity among older children.

Abstract Approved:_____
Thesis Supervisor

_____
Title and Department

_____
Date

PHYSICAL ACTIVITY, CARDIORESPIRATORY FITNESS, ADIPOSITY, AND CARDIOVASCULAR HEALTH IN CHILDREN AND ADOLESCENTS

by

Soyang Kwon

A thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Epidemiology
in the Graduate College of
The University of Iowa

May 2010

Thesis Supervisor: Professor Kathleen F. Janz

Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

Soyang Kwon

has been approved by the Examining Committee
for the thesis requirement for the Doctor of Philosophy
degree in Epidemiology at the May 2010 graduation.

Thesis Committee: _____
Kathleen F. Janz, Thesis Supervisor

_____
Trudy L. Burns

_____
Linda G. Snetselaar

_____
Larry T. Mahoney

_____
Gideon K. D. Zamba

TABLE OF CONTENTS

LIST OF TABLES iv

LIST OF FIGURES vi

LIST OF ABBREBIATIONS vii

CHAPTER

1. INTRODUCTION 1

1.1 Research Hypotheses and Aims 1
1.2 Brief Introduction of Research Methods 2
1.3 Childhood Obesity and Its Health Consequences 4
1.4 Determinants of Adiposity 5
1.5 Measurement of Adiposity 5
1.6 Physical Activity Levels in Children and Adolescents 8
1.7 Determinants of Physical Activity 9
1.8 Measurement of Physical Activity 10
1.9 Measurement of Cardiorespiratory Fitness 14
1.10 Growth and Development during Puberty 15
1.11 Relationship between Physical Activity and Cardiorespiratory Fitness 16
1.12 Relationship between Physical Activity and Adiposity 17
1.13 Relationship between Cardiorespiratory Fitness and Cardiovascular Risk 22
1.14 Significance of Research 24

2. ASSOCIATIONS OF CARDIORESPIRATORY FITNESS AND ADIPOSITY WITH CARDIOVASCULAR RISK FACTORS DURING PUBERTY: THE MUSCATINE HEART STUDY 26

2.1 Introduction 26
2.2 Methods 28
2.3 Results 31
2.4 Discussion 33
2.5 Summary of Findings 36

3. THE EFFECT OF ADIPOSITY ON PHYSICAL ACTIVITY DURING CHILDHOOD: THE IOWA BONE DEVELOPMENT STUDY 41

3.1 Introduction 41
3.2 Methods 42
3.3 Results 46
3.4 Discussion 48
3.5 Summary of Findings 51

4. AN ASSOCIATION BETWEEN LIGHT-INTENSITY PHYSICAL ACTIVITY AND ADIPOSITY DURING CHILDHOOD: THE IOWA BONE DEVELOPMENT STUDY 57

4.1 Introduction 57
4.2 Methods 58
4.3 Results 62
4.4 Discussion 63
4.5 Summary of Findings 66

5. CONCLUSIONS 74

5.1 Overall Findings of Research 74
5.2 Additional Findings and Discussion 75
5.3 Research Findings and Hypotheses 73
5.4 Public Health Implications 77
5.5 Future Research Directions 78

APPENDIX

A. ACCELEROMETER DATA 85

B. LIGHT-INTENSITY PHYSICAL ACTIVITY STUDY REVIEW 86

C. CARDIORESPIRATORY FITNESS AND CARDIOVASCULAR RISK FACORS 97

D. ADIPOSITY AND SUBSEQUENT PHYSICAL ACTIVITY 101

E. LIGHT-INTENSITY PHYSICAL ACTIVITY AND ADIPOSITY 102

REFERENCES 104

LIST OF TABLES

Table

1.1 Prevalence of adherence to physical activity recommendations.....9

2.1 Prticipant characteristics according to study year and gender 37

2.2 Descriptive analysis of cardiovascular risk factors according to study year and gender.....38

2.3 Age-adjusted least-squares means of VO_2 max and the sum of skinfolds according to gender and pubertal stage.....39

2.4 Associations of the sum of skinfolds and VO_2 max with cardiovascular risk factors in boys and girls 40

3.1 Description (means and 95% confidence intervals) of participants.....52

3.2 Comparisons of the means of IW-MVPA at age 11 between potential covariate categories 53

3.3 Associations between MVPA at age 11 and the exposure variable and potential covariates 54

3.4 Generalized linear models of IW-MVPA at age 11 predicted by BF% at age 8 55

3.5 Odds of being in the lowest tertile relative to the highest tertile of IW-MVPA at age 11 for boys and girls with high vs. low percent body fat at age 8.....56

4.1 Descriptive characteristics of study participants by gender and examination time point 64

4.2 Pearson correlation coefficients between physical activity variables by gender and examination time point.....65

4.3 Age-, height-, and fat-free mass-adjusted partial Pearson correlation coefficients between IW-LPA and IW-HLPA and fat mass by gender and examination time point 66

4.4 Regression parameter estimates of IW-LPA and IW-HLPA in multivariable linear regression models to predict fat mass based on IW-LPA and IW-HLPA 67

5.1 Maximum likelihood parameter estimates of adiposity indicators at age 8 in generalized linear models to predict physical activity indicators at age 11 based on adiposity at age 8 82

5.2 Parameter estimates of time spent in light-intensity physical activity in multivariable linear regression models to predict fat mass based on time spent in light-intensity physical activity.....83

5.3 Multivariable linear regression models to predict fat mass based on energy intake and IW-HLPA 84

B1. Calibration studies suggesting accelerometer count cut-points for categorization of physical activity intensity 86

B2. Descriptive studies of accelerometer-measured daily inactivity and light-intensity physical activity 87

B3. Association studies of accelerometer-measured daily inactivity and light-intensity physical activity with health outcomes 92

C1. Mixed models to predict systolic blood pressure 98

C2. Mixed models to predict diastolic blood pressure 98

C3. Mixed models to predict total cholesterol 98

C4. Mixed models to predict triglyceride pressure 99

C5. Mixed models to predict high-density lipoprotein cholesterol 99

C6. Mixed models to predict low-density lipoprotein cholesterol 100

E1. Multivariable linear regression models to predict IW-LPA among boys 102

E2. Multivariable linear regression models to predict IW-LPA among girls 102

E3. Multivariable linear regression models to predict IW-HLPA among boys 103

E4. Multivariable linear regression models to predict IW-HLPA among girls 103

LIST OF FIGURES

Figure

1.1 Hypothetical model of relationships among physical activity, cardiorespiratory fitness, adiposity, and cardiovascular health.....1

1.2 Prevalence of obesity in U.S. children, National Health and Nutrition Examination Survey (NHANES).....4

1.3 Linear regression analysis to compare percent body fat by DXA with percent body fat by the four-compartment model 6

1.4 Predicted levels of fat mass index (FMI) and fat-free mass index (FFMI) at 6 years and 17 years of age according to body mass index (BMI)-for-age z score in the Pediatric Rosetta Study 8

1.5 Actigraph uniaxial accelerometer (model number 7164, pensacola, FL).....11

1.6 Regresion line and 95% confidence interval for metabolic equivalent (MET) score versus accelerometer counts 12

1.7 Categorization of physical activity intensity using accelerometer counts 13

3.1 Conceptual model of the reverse causal hypothesis between early adiposity and subsequent physical activity 42

4.1 Scatter plots of fat mass over age in boys and girls 72

4.2 Daily time allocation for physical activity intensities according to gender and measurement time point 73

5.1 Hypothetical model of relationships among physical activity, cardiorespiratory fitness, adiposity, and cardiovascular health.....78

A1. Example of accelerometer data of one day for a five-year-old child.....85

C1. Distribution of Tanner stage according to study year among boys.....97

C2. Distribution of Tanner stage according to study year among girls 97

D1. Scattor plots of transformed iw-mvpa at age 11 and percent body fat at age 8 among boys (n=142) 101

D2. Scattor plots of transformed iw-mvpa at age 11 and percent body fat at age 8 among girls (n=184).....101

LIST OF ABBREVIATIONS

- BF%: percent body fat
- BMI: body mass index
- BP: blood pressure
- $ct \cdot min^{-1}$: accelerometer movement counts per minute
- CV: cardiovascular
- CVD: cardiovascular disease
- CVR-score: cardiovascular risk score
- DBP: diastolic blood pressure
- DXA: dual energy X-ray absorptiometry
- FMI: fat mass index
- HDL-C: high-density lipoprotein cholesterol
- HLPA: high-light-intensity physical activity
- IW-HLPA: intensity-weighted high-light-intensity physical activity
- IW-LPA: intensity-weighted light-intensity physical activity
- IW-MVPA: intensity-weighted moderate- to vigorous-intensity physical activity
- LDL-C: low-density lipoprotein cholesterol
- LPA: light-intensity physical activity
- MVPA: moderate- to vigorous-intensity physical activity
- PA: physical activity
- SBP: systolic blood pressure
- TC: total cholesterol
- TG: triglyceride
- Time LPA: time spent in light-intensity physical activity
- Time MVPA: time spent in moderate- to vigorous-intensity physical activity
- VO_2 max: maximal oxygen uptake

CHAPTER 1

INTRODUCTION

1.1 Research Hypotheses and Aims

The goal of this dissertation was to better understand relationships among physical activity (PA), cardiorespiratory fitness, adiposity, and cardiovascular (CV) health in children and adolescents. There has been an increase in the prevalence of a cluster of CV risk factors and type 2 diabetes mellitus among children and adolescents, along with an increase of obesity among these age groups. A low PA level has been widely assumed to be one contributor to obesity. Based on a literature review, a hypothetical model was proposed to postulate causal relationships among PA, cardiorespiratory fitness, adiposity, and CV health (Figure 1.1). The following three hypotheses were derived from the hypothetical model:

Hypothesis 1: Cardiorespiratory fitness has a beneficial impact on cardiovascular health, after accounting for adiposity, in children and adolescents (pathway A in Figure 1.1).

Hypothesis 2: A high level of adiposity negatively influences physical activity participation in children (pathway B in Figure 1.1).

Hypothesis 3: Daily light-intensity physical activity has a preventive effect against adiposity in children (pathway C in Figure 1.1).

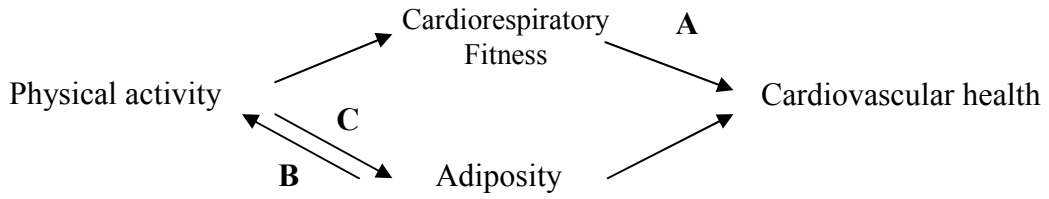


Figure 1.1 Hypothetical model of relationships among physical activity, cardiorespiratory fitness, adiposity, and cardiovascular health

This dissertation includes three research papers designed to achieve the following three aims which were specified to test the aforementioned hypotheses:

Aim 1: To determine whether cardiorespiratory fitness is associated with cardiovascular risk factors during puberty after accounting for adiposity, using data from a sub-study of the Muscatine Heart Study.

Aim 2: To determine whether early adiposity level is inversely associated with subsequent physical activity behaviors during childhood, using the longitudinal Iowa Bone Development Study data.

Aim 3: To determine whether daily light-intensity physical activity is inversely associated with adiposity during childhood, using the longitudinal Iowa Bone Development Study data.

1.2 Brief Introduction of Research Methods

The first paper (chapter 2) was designed to achieve Aim 1. Existing datasets from a four-year follow-up sub-study of the Muscatine Heart Study were used to achieve the study aim. The Muscatine Heart Study is one of the first studies to examine CV risk in children. A four-year follow-up sub-study within the Muscatine Heart Study was conducted from 1991 to 1995 in order to characterize the growth of the heart related to changes in blood pressure, body size, physical fitness, and PA through puberty. In the sub-study, 126 prepubertal Caucasian children were enrolled in the study at baseline. Maximal oxygen consumption (VO_2 max) was measured once a study year. Skinfold thickness and blood pressure were measured quarterly. A blood sample was drawn at study years 1, 2, and 5. Total cholesterol, triglyceride, and high-density lipoprotein cholesterol (HDL-C) plasma levels were analyzed; low-density lipoprotein cholesterol (LDL-C) level was calculated. In statistical analysis, gender-specific individual growth curve models were estimated to predict CV risk factors using mixed model approaches. The intercept and centered age were fit as random effects. VO_2 max (L/min), the sum of skinfolds, centered age, height, weight, and pubertal stage were fit as fixed effects.

For the second and third papers, the Iowa Bone Development Study data were used. The Iowa Bone Development Study is an ongoing prospective cohort study of bone health during childhood. The study participants are a sub-set of Midwestern children recruited during 1998 to 2001 from a cohort of 890 families participating in the Iowa Fluoride Study. Serial examinations have been conducted at child's ages approximately 5, 8, 11, 13, 15, and 17. Data collected at child's ages 5, 8, and 11 were used for these two papers. The second paper (chapter 3) was designed to achieve Aim 2. In the Iowa Bone Development Study data, 326 children who completed accelerometer and dual energy X-ray absorptiometry (DXA) measurements at all of three examinations (child's ages 5, 8, and 11) were included for data analysis. Gender-specific generalized linear models were fit to examine a temporal association between percent body fat (BF%) at age 8 and intensity-weighted moderate- to vigorous-intensity PA (IW-MVPA) at age 11. Measurement data at child's age 5 were used to account for the preceding change of BF% and IW-MVPA from the age 5 to 8 examinations. In addition, potential covariates such as age, an interval between the age 5 and 8 examinations, physical maturity, IW-MVPA at age 8, parents' physical activity levels, parents' education levels, and family income were considered.

The third paper (chapter 4) was designed to achieve Aim 3. Five hundred seventy-seven Iowa Bone Development Study participants who completed accelerometer and DXA measurements at least one of three examinations (child's ages 5, 8, and 11) were included for data analysis. Gender- and examination time point-specific multivariable linear models were fit to examine the cross-sectional associaition between intensity-weighted light-intensity PA (IW-LPA) and fat mass. Birth weight, IW-MVPA, physical maturity, energy intake, height, and fat-free mass were considered as potential covariates.

1.3 Childhood Obesity and Its Health Consequences

In the last three decades, the prevalence of obesity (body mass index (BMI) ≥ 95th percentile) among U.S. children and adolescents has dramatically increased (Figure 1.2).[1,2] In the U.S. population, it is estimated that 18.5 million, or 24%, of all children 2 to 19 years of age will be considered obese by the year 2020.[3] The increase represents an important public health problem, because obesity in childhood tends to persist into adulthood,[4] and obesity in adults increases the risk of many chronic diseases and health conditions, including hypertension, dyslipidemia, type 2 diabetes mellitus, coronary heart disease, and stroke.[5] Therefore, the population attributable risk of obesity for chronic disease is expected to continue to increase. Furthermore, conditions such as type 2 diabetes mellitus, hypertension, and hypercholesterolemia, which were previously seen primarily in adults, have become more common among children and adolescents, along with an increase of childhood obesity.[4,6,7] Childhood obesity also influences quality of life, impacting psychological and social functioning,[8,9] presumably through perceived negative self- and peer-attitudes about body shape. For example, Schwimmer *et al.*[10] reported that children and adolescents with severe obesity have a lower health-related quality of life than their counterparts with cancer.

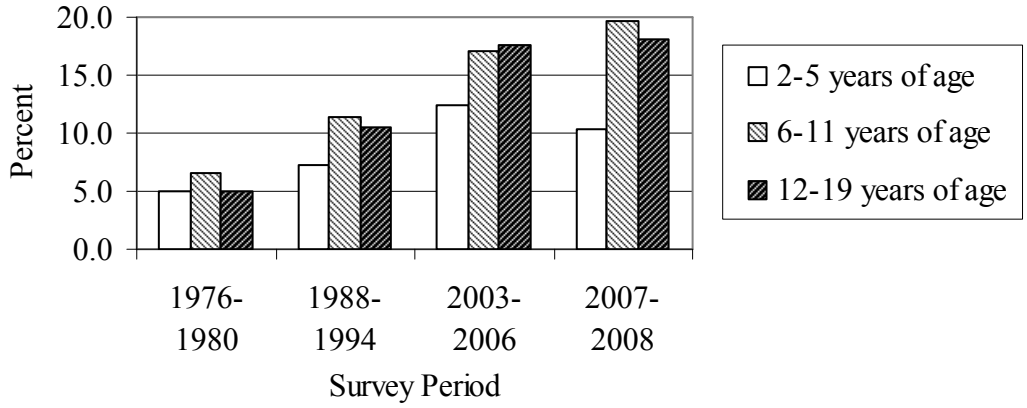


Figure 1.2 Prevalence of obesity in U.S. children, National Health and Nutrition Examination Survey (NHANES)

1.4 Determinants of Adiposity

Adiposity status is largely determined by genetics and an environment that encourages an adverse balance between energy intake and energy expenditure.[11] A relationship between energy expenditure and adiposity is further discussed in chapter 1.12. Differences in genetic susceptibility explains variation in the predisposition to obesity.[12] Many twin, adoption and family studies have indicated a significant contribution of genetic factors to obesity pathogenesis.[13] In addition, the prenatal period is important for the development of obesity and environmental conditions experienced in utero may have a life-long effect on later body composition and the propensity to become obese.[14] Birth weight is frequently used as an indicator of the conditions experienced prenatally.[15] A systemic review of the effect of birth weight on adiposity and fat distribution later in childhood and early adulthood suggested a positive association between increased birth weight and overweight in childhood.[15] More recently, Rogers *et al*.[16] reported that birth weight was positively associated with both lean body mass and total body fat measured by DXA among 3,006 boys and 3,080 girls 9 to 10 years of age (a 2 to 3% increase in total body fat per 1-standard deviation increase in birth weight, $P < 0.05$). In summary, genetic predisposition to body composition, birth weight, energy intake, and energy expenditure should be considered to predict adiposity.

1.5 Measurement of Adiposity

Dual energy X-ray absorptiometry (DXA) is one of the most accurate measures of adiposity in children. DXA was developed to measure bone mineral density with minimal x-ray exposure. But, DXA scans have been adopted to assess adiposity, because they allow one to obtain accurate assessment of fat mass. A DXA scan procedure is painless and non-invasive, and its radiation exposure is minimal. DXA machines are increasingly available throughout hospitals and clinics, and scans are easily performed on children of all ages. DXA has been proven to be an excellent measure of fat mass against

the gold standard, four-compartment model in children and adolescents ($R^2 = 0.85$, Figure 1.3).[17,18]

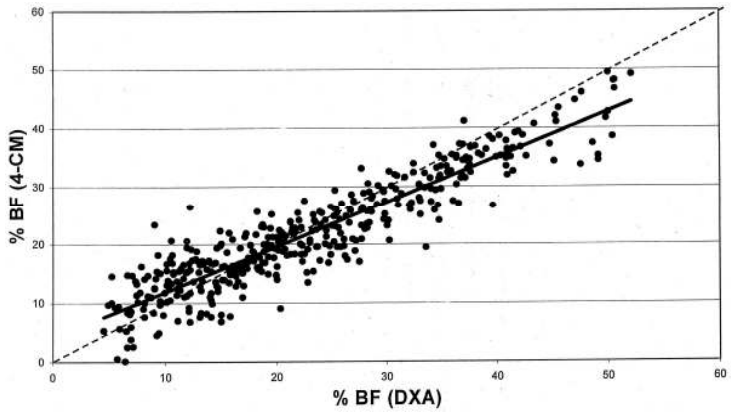


Figure 1.3 Linear regression analysis to compare percent body fat (%BF) by DXA with percent body fat (%BF) by the four-compartment (4-CM) model

Source: Sopher AB, Thornton JC, Wang J, Pierson RN,Jr, Heymsfield SB, Horlick M. Measurement of percentage of body fat in 411 children and adolescents: a comparison of dual-energy X-ray absorptiometry with a four-compartment model. *Pediatric*s. 2004;113(5):1285-1290.

The **skinfold thickness** is another measure of adiposity. The measurement can use from 3 to 9 different standard anatomical sites around the body. The right side is usually measured for consistency. The tester pinches the skin at the appropriate site to raise a double layer of skin and the underlying adipose tissue, but not the muscle. The skinfold caliper is then applied 1 cm below and at a right angle to the pinch, and a reading in millimeters (mm) is taken a few seconds later. The mean of two measurements should be taken. If the two measurements differ greatly, a third should then be taken, and the median value should be used. Fat mass can be estimated using prediction equations from skinfolds. However, because the standard error of estimation (SEE) of fat mass estimated based on skinfolds is considerable (3 to 5%),[19] the sum of skinfolds may be a

better measure than fat mass estimated based on skinfolds for ranking adiposity level within a population.

Body mass index (BMI) is defined as body weight divided by height squared (kg/m^2). Fat mass index (FMI) is defined as fat mass divided by height squared (kg/m^2). Fat-free mass index (FFMI) is defined as fat-free mass divided by height squared (kg/m^2). Standardized for height^2, FMI and FFMI indicate the contribution of fat mass and fat-free mass, respectively, to BMI (Figure 1.4). BMI is widely used as a surrogate measure of adiposity, particularly in large-scale epidemiologic studies, because of its ease of use. However, it is a measure of excess weight relative to height, rather than excess adiposity.[20] In contrast to the association in adults, the association between BMI and adiposity is variable and relatively weak among children ($r < 0.6$),[21-24] although BMI can be a good measure to categorize adiposity levels if an appropriate cut-point is applied.[23] The weak association among children and adolescents may be attributable to the asynchronous changes that occur in the levels of fat mass and fat-free mass during growth.[23] Freedman *et al.*[23] showed that the same absolute BMI value can result from various combinations of FMI and FFMI. BMI performs well as an adiposity indicator among relatively heavy children (e.g., BMI $\geq$ 85th percentile), but not among thinner children. The magnitude of the association between BMI and adiposity has also been reported to differ by gender and age. The associations of adiposity with BMI have been shown to be weaker among boys ($r \approx 0.5$) than among girls ($r \approx 0.8$).[21,25,26] The association between body density (as an inverse indicator of adiposity level) and BMI was weaker as well among 14- to 16-year-old boys ($r = -0.59$) than among 7- to 10-year-old boys ($r = -0.80$).[27] In addition, BMI tends to explain less of the variance in CV risk factors than do other adiposity indicators, such as FMI or BF% (fat mass divided by body weight).[28]

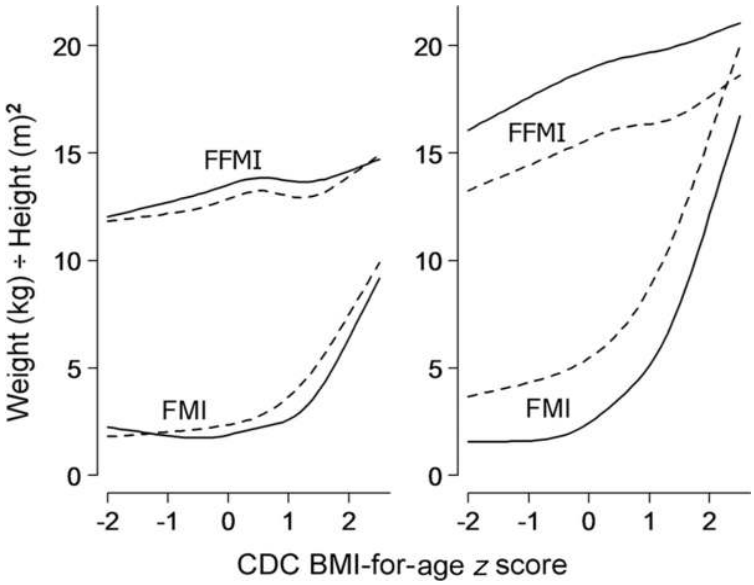


Figure 1.4 Predicted levels of fat mass index (FMI) and fat-free mass index (FFMI) at 6 years (left) and 17 years (right) of age according to body mass index (BMI)-for-age z score in the Pediatric Rosetta Study

Source: Freedman DS, Sherry B. The validity of BMI as an indicator of body fatness and risk among children. *Pediatrics*. 2009;124 Suppl 1:S23-34.

Note: The solid lines represent boys, and the dashed lines represent girls.

1.6 Physical Activity Levels in Children and Adolescents

Physical inactivity is widely assumed to be one contributor to obesity. Furthermore, physical inactivity has been reported to increase CV disease (CVD) risk.[29] PA guidelines have been suggested for disease prevention and health-related physical fitness and health promotion. Most recently, the Department of Health and Human Services (HHS) released the 2008 Physical Activity Guidelines for Americans.[30] The new recommendations indicate that children should engage in 60 or more minutes per day of moderate- to vigorous-intensity PA (MVPA), including 1) vigorous-intensity PA (VPA) at least 3 days per week, 2) muscle-strengthening PA at least 3 days per week, and 3) bone-strengthening PA at least 3 days per week.

Accelerometer-measured PA data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 showed that among children 6 to11 years of

age, 49% of boys and 35% of girls achieved the recommended amount of MVPA (Table 1.1).[31] The prevalence of the adherence to PA recommendations dramatically dropped among adolescents. For 12 to 15 year olds, only 12% of boys and 3% of girls adhered to the recommendation. The magnitude of the gender difference also increased during adolescence.

Table 1.1 Prevalence of adherence to physical activity recommendations: NHANES 2003-2004

Age range	Boys (n=611)	Girls (n=570)
6-11 years	48.9%	34.7%
12-15 years	11.9%	3.4%

Source: Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exer*c. 2008;40(1):181-188.

Note: Adherence to physical activity recommendations was defined as 60 or more minutes of at least moderate-intensity activity on 5 of 7 days per week.

1.7 Determinants of Physical Activity

Potential determinants of PA can be categorized into the following five categories:[32] 1) demographic and biological variables (e.g., age and parental overweight), 2) psychological, cognitive, and emotional variables (e.g., self-esteem, attitude, and perceived benefits), 3) behavioral attributes and skills (e.g., previous PA participation), 4) social and cultural variables (e.g., parental encouragement), and 5) physical environment variables (e.g., access to facilities). In the 1996 Surgeon General's Report on PA,[33] the most consistent modifiable correlates, as opposed to demographic and biological factors, were identified as self-efficacy, physical or sports competence, perceived benefits, perceived barriers, intention, enjoyment, physical education attitudes, parental encouragement, direct help from parents, peer and sibling support, access to play spaces

and equipment, and time spent outdoors. In another review of 54 studies of correlates of PA of adolescents,[32] 9 of the 12 variables identified in the Surgeon General's Report were confirmed as consistently associated with PA of children or adolescents: perceived physical competence, intention, barriers, parent support, direct help from parents, support from significant others, program/facility access, opportunities to be active, and time spent outdoors. A more recent review[34] suggested that gender (boy), socio-economic status, parents' PA participation, and peers' PA participation are positively, and age is negatively, associated with PA levels. In this research, family income, parent's education levels, parents' PA participation, gender, age, previous PA participation, and adiposity status were considered to predict PA level.

1.8 Measurement of Physical Activity

An accurate and reliable measurement of PA has been a challenge. Traditionally, studies have used self-report PA questionnaires to assess PA levels. However, self-reported PA data are subject to measurement error due to recall bias and social desirability effects.[35] Self-reported PA data have shown a lack of accuracy, particularly in children.[36-38] In the NHANES 2003-2004, MVPA levels estimated by an objective measure (accelerometer) were significantly lower than those by a subjective measure (self-report PA questionnaire) among children and adolescents.[31] If one assumes that accelerometry data are closer to the truth, these results demonstrate that children tend to overestimate their PA.[31] It appears that using an objective measure such as accelerometers, rather than a subjective measure such as self-report PA questionnaires, is critical to minimize measurement error.

Accelerometers have become popular as an objective PA measure not only because of their accuracy and reliability, but also because of their practical benefits, such as their small size, light weight, minimum discomfort for subjects, large memory storage, and easy application (Figure 1.5). While less than 10 original research articles using accelerometers in children were published each year before 1996, approximately 90 were

published in each year during 2003 and 2004.[39] In 2009, more than 100 original research articles were published (simple subject search in the PubMed with search terms, “2009”, “accelerometer”, and “children”). Accelerometers provide real-time (time-stamped) data so that frequency, intensity, and duration of free-living PA can be estimated by integrating movement signals over a given time interval, which is known as an epoch. For example, the Actigraph (Pensacola, FL) is a uniaxial accelerometer designed to detect vertical accelerations ranging from 0.05 to 2.00 Gs with a frequency response of 0.25 to 2.50 Hertz. These parameters allow for the measurement of normal human movement with the rejection of the high frequency vibrations from other sources. The accelerations are filtered and digitized with the magnitude summed over a specific interval of time. The summed value of the movement count is stored in memory. The stored data can be downloaded to a personal computer (PC). An example of accelerometer data is presented in Appendix A.

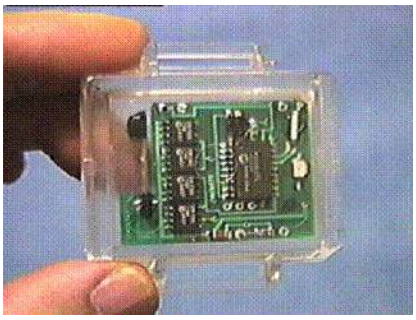


Figure 1.5 Actigraph uniaxial accelerometer (model number 7164, Pensacola, FL)

1.8.1 Accelerometry Data Reduction

1.8.1.1 Accelerometer Count Cut-point for Physical Activity Intensity Categorization

Energy expenditure during PA is often expressed as metabolic equivalent (MET). One MET is considered as the resting metabolic rate obtained during quiet sitting. PA

intensity categories can be defined using METs as follows: light intensity is defined as 1.1 to 2.9 METs, moderate intensity as 3.0 to 5.9 METs, and vigorous intensity as 6.0 METs or greater. According to a study by Treuth *et al.*,[40] in 14-year-old girls, walking at 2.5 mph and 3.5 mph correspond to 3.2 METs and 4.3 METs, respectively. Running at 5.0 mph corresponds to 7.8 METs.

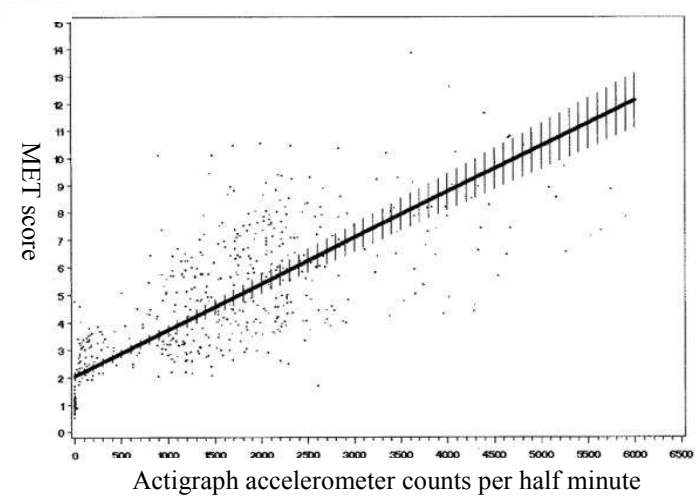
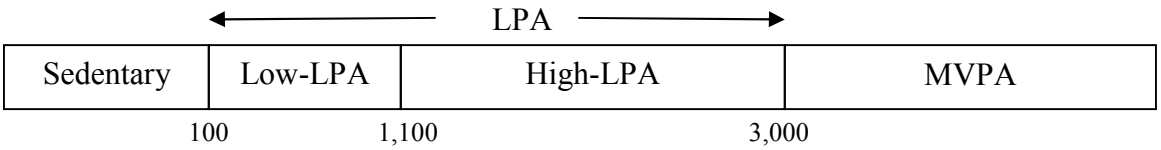


Figure 1.6 Regression line and 95% confidence interval for metabolic equivalent (MET) score versus accelerometer counts

Source: Treuth MS, Schmitz K, Catellier DJ, et al. Defining accelerometer thresholds for activity intensities in adolescent girls. *Med Sci Sports Exer*c. 2004;36(7):1259-1266.

Several studies have shown a linear, positive relationship between accelerometer movement counts per minute ($ct \cdot min^{-1}$) and activity intensity, as defined by energy expenditure (MET score) measured using the gold standard, indirect calorimetry (Figure 1.6).[41-43] Accelerometer movement counts can be used to categorize PA intensity and quantify the duration of activity. The 3,000 $ct \cdot min^{-1}$ point is commonly used as a lower threshold to define MVPA in children.[40,44] However, accelerometer count cut-points suggested to define inactivity or light-intensity PA (LPA) vary across different studies,

the kind of accelerometer device used, and subjects' ages.[40,44-49] Table A1 provides a summary of studies suggesting the cut-points to define inactivity or LPA. To define inactivity, for example, Treuth *et al.*[40] suggested less than 100 Actigraph ct·min^{-1} among adolescents 13 to 14 years of age, while Reilly *et al.*[46] suggested less than 1,100 Actigraph ct·min^{-1} among children 3 to 4 years of age. In the current research, I applied two different accelerometer count ranges to define LPA: (1) 110 to 2,999 ct·min^{-1} and (2) 1,100 and 2,999 ct·min^{-1}. The latter LPA range was labeled high-LPA (Figure 1.7).



<Actigraph accelerometer movement counts per minute>

Figure 1.7 Categorization of physical activity intensity using accelerometer counts

Note: LPA = light-intensity physical activity, MVPA = moderate- to vigorous- intensity physical activity.

1.8.1.2 The Number of Minutes per Day and Days of Measurement

Studies have used a monitor-wearing time of 8 to 10 waking hours per day and 3 to 4 days (including at least one weekend day) as inclusion criteria of accelerometry data. Mattocks' examination found that the use of various monitor-wearing hours per day (7, 8, 9, and 10 hours) showed little difference in reliability among 7,159 children 11 years of age.[50] The study also revealed that 3 days of monitor-wearing was needed for an intraclass correlation coefficient (ICC) of 0.7 in estimating total activity counts per day, where ICC was defined as the ratio of between individual variance to the sum of the between- and within-individual variance.

1.9 Measurement of Cardiorespiratory Fitness

Cardiorespiratory fitness refers to the ability of the circulatory and respiratory systems to supply oxygen to skeletal muscles during PA. VO_2 max is the maximum amount of oxygen that one can use in one minute. It is considered as the standard indicator of cardiorespiratory fitness. VO_2 max can be estimated using a gas analyzer during maximal or submaximal graded exercise testing. A gas analyzer provides real-time oxygen uptake by analyzing expired air from a subject. Usually, VO_2 at the moment of max heart rate, max VO_2 plateau (or over peak), respiratory exchange ratio of 1.15 (or greater) or voluntary exhaustion is considered as VO_2 max. Although in adults a tapering or plateau of VO_2 max is utilized as an indicator of a true maximal value, it is not common for children to demonstrate a tapering or plateau during exercise testing.[51] When children achieve a certain heart rate or respiratory exchange ratio criteria, a maximal value can be assumed.

VO_2 max is often expressed as an absolute rate in liters of oxygen per minute (L/min) or as a relative rate in milliliters of oxygen per kilogram of body weight per minute (body weight-adjusted VO_2 max, mL/kg/min). Body weight-adjusted VO_2 max is to estimate cardiorespiratory fitness level accounting for body size. In adults, VO_2 max is typically expressed relative to body weight. Among some children, however, heaviness may simply mean rapid growth. Furthermore, a lean child will have a greater body weight-adjusted VO_2 max than an obese child who has an identical oxygen delivery capacity, because body fat is largely metabolically inert.[51] Armstrong and Welsman[52] argued that normalization of VO_2 max by body weight may "overcorrect" for differences in body size between individuals and test duration for indirect cardiorespiratory fitness tests involving weight-bearing activity, and it may underestimate VO_2 max in heavier children. Therefore, some investigators have expressed VO_2 max relative to fat-free mass (mL/kg fat-free mass/min) or allometrically-derived body weight exponents such as $weight^{0.67}$ or $weight^{0.75}$.[51] Statistical methods can be introduced to handle this issue. For

example, an absolute rate of VO_2 max (mL/min) can be used, adjusted for body size such as height and body weight in statistical modeling. In this research, an absolute rate of VO_2 max (L/min) was used as an indicator of cardiorespiratory fitness level in examining the effects of cardiorespiratory fitness and adiposity simultaneously on CV risk factors, because all of these three variables of interest (cardiorespiratory fitness, adiposity, and a particular CV risk factor) are interrelated with body size.

1.10 Growth and Development during Puberty

Endocrine changes during puberty bring secondary sexual development, cognitive change, increases in growth velocity, and dramatic change in body composition.[53] There is significant sexual dimorphism in puberty, not only in the timing of the pubertal event, but also in body composition. Girls are, on average, advanced in maturity status compared to boys.[54] For boys, puberty takes about 3 years to complete, but may range from 2 to 5 years, and the typical sequence of pubertal events is adrenarche, beginning of the growth spurt, genital development, beginning of pubic hair, and peak height velocity.[55] Completion of puberty in girls averages 4 years but may range from 1.5 to 8 years. In the average girls, the growth spurt starts about one year before breast development and this is followed by an average of 1.1 years until peak height velocity, and then followed in an average of one year by menarche.[55] Boys gain greater amounts of fat-free mass and skeletal mass during puberty, whereas females acquire significantly more fat mass. Fat distribution also changes, with boys being a more android body shape and girls being a more gynecoid shape. To estimate adiposity level during puberty, therefore, maturity status should be taken into account. Genital and pubic hair development for boys and breast and pubic hair development for girls are often used as a sexual maturity indicator. Peak height velocity is a measure of the maximum rate of growth in stature during a growth spurt. Year (distance) from peak height velocity is used as a non-invasive measure of physical maturity. Mirwald and colleagues[56] have developed the equations to calculate year from peak height velocity including three

somatic dimensions (height, sitting height, and leg length), age, and their interaction.

Such change during puberty influences cardiorespiratory fitness level estimated by graded exercise tests. Particularly, when cardiorespiratory fitness level is expressed in body weight-related value, one should be cautious in that the estimate may not represent a true cardiorespiratory fitness level due to body composition change during puberty. Mota *et al*.[57] showed that within a given chronological age group, sexual maturity status accounts for a small, but significant (adjusted $R^2 = 0.07$), portion of the variance in cardiorespiratory fitness level; however, there was no (positive or negative) consistent trend in change of fitness level with advance in pubertal stage. There is some evidence supporting that maturity status influences PA. It has been hypothesized that sex-related differences in PA behavior during adolescence are largely explained by maturity status. Several studies[54,58] reported that, although boys were more physically active than girls at each age among adolescents, the sex difference in PA level was eliminated when biological maturity status was controlled for. Sexual maturity has also been shown to influence the patterns of CV risk factor development.[59-61] For example, as sexual maturation progresses during puberty, total cholesterol decreases, with the decrease being greater in boys than in girls.[59] Sex hormone profiles most probably account for the maturity effect.[60] In summary, maturity status should be considered in establishing relationships between PA, cardiorespiratory fitness, adiposity, and CV risk factors in adolescents.

1.11 Relationship between Physical Activity and Cardiorespiratory Fitness

Cardiorespiratory fitness is determined by a modifiable factor, such as PA, and several non-modifiable factors, such as age, gender, ethnicity, and genetics. Therefore, cardiorespiratory fitness levels can vary among those with the same PA level due to heterogeneity of other determinants. Particularly in children, a cross-sectional relationship between PA and cardiorespiratory fitness has been demonstrated to be weak

(r = 0.16 to 0.17).[52,62] Nonetheless, because cardiorespiratory fitness can be measured more objectively by cardiorespiratory fitness tests than PA by self-report, and because PA is the principal modifiable determinant of cardiorespiratory fitness, cardiorespiratory fitness has often been used as a proxy of PA level in research studies.

1.12 Relationship between Physical Activity and Adiposity

1.12.1 Physical Activity and Energy Expenditure

Energy expenditure during PA is a major component of total energy expenditure. Amount of energy expenditure during PA is positively linearly associated to total volume of PA. PA energy expenditure per minute is positively linearly associated to intensity of PA. Therefore, PA is assumed to influence obesity via the effect of PA on energy expenditure. In this energy expenditure perspective, it is critical to consider not only PA duration, but also its intensity in investigating a relationship between PA and adiposity. Although many studies have considered only PA duration, (e.g., daily minutes spent in MVPA (Time MVPA)), intensity-weighted PA may be a better indicator of PA level.

1.12.2 The Effect of Light-Intensity Physical Activity in Adiposity

MVPA involves high energy expenditure and research studies[63,64] have shown that MVPA has a preventive effect on obesity. Although the beneficial effect of regular MVPA on preventing obesity is well acknowledged by the public, the majority of Americans do not meet MVPA recommendations.[31] Given low participation in MVPA, LPA may play a role in obesity prevention, because LPA involves more energy expenditure than being sedentary, although less energy expenditure than MVPA. Levine and colleagues have argued that exercise activity thermogenesis is negligible for the majority of Americans,[65] while non-exercise activity thermogenesis (NEAT), such as fidgeting and slow walking, is a predominant constituent of activity thermogenesis and total energy expenditure.[66] Montgomery *et al*.[67] reported that time spent being sedentary

and time spent in LPA (Time LPA), but not Time MVPA, were associated with daily PA energy expenditure among 104 children (median of 5.4 year of age). This result may imply that the proportion of time distributed between sedentary behaviors and LPA determines daily PA energy expenditure, given a minor contribution of MVPA to daily PA energy expenditure: this study sample spent much less time in MVPA (4% of waking hours) than in LPA (20% of waking hours). Considering such a contribution of LPA to daily PA energy expenditure, LPA should be considered in PA research to better understand comprehensive PA effects on adiposity.[68-73]

Because LPA tends to be performed frequently in daily life, it is a challenge to accurately quantify LPA using PA questionnaires.[74] The development of accelerometry as an objective measure of PA provides new possibilities for objectively assessing the full range of intensity of PA, from sedentary to vigorous, in free-living subjects over a number of days,[73] and for studying the health effects of all intensity levels of PA. Table A2 summarizes descriptive studies of accelerometer-measured LPA in children and adolescents. Butte's[75] and Treuth's[76] studies suggest that Time LPA may decrease with age during childhood and adolescence. Time LPA difference by gender varied across the studies, probably because of applications of different accelerometer cut-points for defining LPA. Table A3 provides a summary of studies on associations between LPA and health outcomes.

In research examining the effect of LPA on adiposity, two cross-sectional studies[75,76] demonstrated an inverse association between Time LPA and adiposity. Treuth *et al*.[76] examined a cross-sectional relationship between several adiposity indicators (BMI, fat mass, and BF%) and accelerometer-measured Time LPA in 229 elementary, middle, and high school boys and girls in rural Maryland. Participants were asked to wear Actiwatch accelerometers during the entire day for 6 complete days (4 school days and 2 weekend days). Accelerometer data were considered to be complete if 70% or more of the day (1,000 minutes) was recorded for at least 4 of the 6 days, with 2 of the days on

the weekend. Fat mass was measured using a bioelectrical impedance analysis (BIA). They found that Time LPA was inversely associated with adiposity in all three school levels among girls (Spearman correlation coefficients between fat mass and Time LPA = -0.41 for elementary students, -0.51 for middle school students, and -0.42 for high school students, $P < 0.05$), but not among boys (Spearman correlation coefficients between fat mass and Time LPA = -0.12 for elementary students, -0.08 for middle school students, and -0.17 for high school students, $P > 0.05$). In this sample, time spent in moderate-intensity PA (MPA) and VPA were not associated with adiposity.

Butte *et al.*[75] examined a cross-sectional relationship between adiposity and accelerometer-measured Time LPA among 473 overweight and 424 non-overweight children (mean of 10.9 years of age) participating in the VIVA LA FAMILIA Study in Houston, TX. Participants were asked to wear Actiwatch accelerometers for 24 hours for 3 consecutive days. To be valid and useable data, a 24-hour day was required to have 1,000 minutes or more out of the 1,440 minutes per day. Fat mass was measured using DXA. Overweight boys spent about 50 minutes less per day in LPA than non-overweight boys. Overweight girls spent about 30 minutes less per day in LPA than non-overweight girls. Time LPA was inversely associated with BF%, adjusted for gender and age (gender- and age-adjusted partial correlation coefficients = -0.30, $P < 0.001$). Furthermore, the correlation was stronger than a correlation between time spent in MPA and BF% (gender- and age-adjusted partial correlation coefficients = -0.07, $P < 0.05$).

However, four other cross-sectional studies[77-80] have shown no association between Time LPA and BMI level. At this time, too little research exists on LPA effects on health to draw any conclusions. More research is required to examine health effects of objectively measured LPA. If daily LPA is proved to have a preventive effect against excess body fat accumulation, promoting LPA would be a realistic and practical strategy for inactive children to gradually increase PA and to prevent excess fat accumulation.

1.12.3 The Role of Adiposity in Determining Physical Activity

Although PA has been shown to contribute to obesity, it is also possible that obesity may be a determinant of PA behavior. The reverse causation[81,82] hypothesis (adiposity status influences PA behaviors) is raised on the assumption that children who are gaining excessive body fat may reduce PA over time. Godin *et al.*[83] suggested a theoretical model of the reverse causation hypothesis based on Ajzen's Theory of Planned Behavior (TPB).[84] The theory assumes that behavioral intention is the most important determinant of behavior. Behavioral intention is influenced by a person's attitude toward performing certain behaviors, and by beliefs about whether individuals who are important to the person approve or disapprove of the behaviors. According to this model, adiposity may impact PA behaviors by influencing cognition, such as intention (motivation) and perceived behavioral control (ease or difficulty in engaging in the behavior, e.g., social barriers). Must and Tybor[81] suggested that, given the fact that PA in children often occurs as part of organized sport, overweight children may be less likely to want to participate, either due to fears of being teased or because they are "less athletic." In a review of exercise interventions in obese youth, Henderson *et al.*[85] concluded that overweight youth have a lower compliance rate with PA programs than non-overweight youth. This study conclusion supports the reverse causation hypothesis.

There are several adult population-based, prospective cohort studies[86-90] which explicitly addressed the reverse causation hypothesis. Of them, Petersen's study is the most significant in that it included a large sample and used data measured at three-time points over 15 years. Petersen *et al.*[86] examined the effect of BMI on subsequent PA behaviors in a representative sample of the Copenhagen adult population (3,653 women and 2,626 men) participating in the Copenhagen City Heart Study. Survey data were collected three times: the first survey, the second survey after 5 years, and the third survey after 10 years. Leisure-time PA was divided into three levels: low (< 2 hours per

week of PA, such as walking, cycling, or light gardening), medium (2-4 hours per week), and high (> 4 hours per week). This study examined if high BMI at the second survey is associated with a low level of leisure-time PA at the third survey. Data from the first survey were used to take into account the preceding changes in BMI and leisure-time PA levels from the first to the second survey. Potential confounding factors, such as gender, age, smoking status, education level, alcohol consumption, familiar predisposition to obesity, and occupational PA, were considered. Using logistic regression models, they showed that high BMI at the second survey significantly increased the odd of low PA at the third survey (odds ratio (OR) and 95% confidence interval (CI) of low PA at the third survey in a fully adjusted model = 1.87 (1.35, 2.59) for the first highest quintile of BMI at the second survey, and 1.12 (0.79, 1.59) for the second highest quintile, reference group: middle quintile of BMI).

In addition, Bak *et al.*[87] reported that being obese was inversely associated with leisure-time PA level at two-year follow-up among 1,143 obese and 1,278 non-obese men in Copenhagen and adjacent regions (OR of being inactive at the follow-up for those with obesity at baseline = 3.07, 95% CI = 0.96, 9.88, reference group = those with 15 to 21 kg/m^2 of BMI). Similarly, Mortensen *et al.*[88] found that a high BMI had an effect on becoming sedentary among 4,998 middle-aged men and women participating in the University of North Carolina Alumni Heart Study: OR and 95% CI of being inactive at age 46 per 1 kg/m^2 of BMI at age 44 =1.10 (1.07, 1.14); and those of becoming inactive at age 54 per 1 kg/m^2 of BMI at age 46 =1.12 (1.08, 1.17). Weiss *et al.*[89] showed that high BMI at baseline was associated with becoming inactive during a five-year follow-up among 527 Canadian adults in low-income communities (OR and 95% CI of becoming inactive at follow-up for overweight and obese participants at baseline = 1.57 (1.03, 2.40), reference group = normal-weight participants at baseline). Ekelund *et al.*[90] also demonstrated that BMI, fat mass, and waist circumference at baseline were significant predictors of heart rate monitor-measured time spent being sedentary at a 5.6 year follow-

up among 393 middle-aged whites (regression parameter coefficient of BMI at baseline to predict the amount of time spent being sedentary (% of daytime hour) at follow-up = 1.10, 95% CI = 0.58, 1.63). In summary, these five prospective cohort studies in adults have consistently demonstrated that obesity is inversely associated with subsequent PA level.

No study to date has explicitly addressed the reverse causation hypothesis for children. Sallis *et al.*[91] investigated numerous potential correlates of PA in children and reported no effect of skinfold-measured adiposity at baseline on one-day accelerometer-measured PA level at a two-year follow-up in a social-cognitive model for investigating determinants of PA behavior. Their null finding may be partially due to measurement error of adiposity estimated by skinfold thickness. In addition, only one-day PA may not represent child's typical PA level. The role of adiposity in determining PA among children should be investigated more.

1.13 Relationship between Cardiorespiratory Fitness and Cardiovascular Risk

Hypertension, hypercholesterolemia, type 2 diabetes mellitus, and a cluster of CV risk factors (called *the metabolic syndrome*) have increased in the adolescent population.[92-95] Because the clustering of CV risk factors in childhood has been demonstrated to predict not only development of pediatric type 2 diabetes mellitus,[96] but also metabolic syndrome, type 2 diabetes mellitus, and CVD later in adulthood,[97,98] it is important to identify determinants of CV risk factors in adolescents for interventions to reduce childhood type 2 diabetes mellitus and the risk of chronic diseases later in life.

The detrimental effects of obesity on CV health in children and adolescents are well documented.[4,6,7,99] Cardiorespiratory fitness has also been suggested to influence CV health in children and adolescents.[100-108] Considering the adiposity effect in an association between cardiorespiratory fitness and CV health would help understand the pathway by which cardiorespiratory fitness influences CV health. Some investigators have examined

the effects of cardiorespiratory fitness on CV risk in adolescents, controlling for adiposity and the results are inconsistent. The cross-sectional studies of Eisenmann and colleagues[109-112] and the European Youth Heart Study[113,114] have showed that cardiorespiratory fitness was associated with the metabolic syndrome or a CV risk score, adjusting for adiposity. Kwon *et al.*[115] have also demonstrated that a cardiorespiratory fitness effect on CV risk factors was significant after controlling for weight status, particularly among boys, in a representative sample of U.S. adolescents (NHANES 1999-2002). However, other cross-sectional studies[116-120] have reported that significant associations between cardiorespiratory fitness and CV risk factors were not retained after adjustment for adiposity.

A longitudinal study design has an advantage over a cross-sectional design to examine a causal relationship because it establishes a temporal relationship between the exposure and outcome. Only a few longitudinal studies have been conducted to examine the independent effects of adiposity and cardiorespiratory fitness on CV health. Of them, McMurray's study is one of the most significant longitudinal studies. McMurray *et al.*[121] examined a temporal relationship between cardiorespiratory fitness in childhood and the metabolic syndrome in adolescence among 389 participants, using data from the Cardiovascular Health in Children and Youth Study (CHIC).[122] Measurements at baseline (7 to 10 years of age) and at seven-year follow-up (14 to 17 years of age) were taken. Cariorespiratory fitness level was determined by predicted VO_2 max obtained during a multi-stage submaximal cycle ergometry test. Predicted VO_2 max was categorized into tertiles. BMI level as an adiposity indicator was dichotomized into two groups (BMI $\geq$ 95th percentile vs. < 95th percentile). In a logistic model, the outcome variable was the presence or absence of the metabolic syndrome at follow-up, and the exposure variables were VO_2 max category and BMI category. Gender, elevated blood pressure, and elevated total cholesterol at baseline were included as covariates. The study found that adolescents with the metabolic syndrome were six times more likely to be in the lowest

tertile of VO_2 max at 7 to 10 years of age (reference group: the highest tertile) than those without the metabolic syndrome. In addition, a nested case-control study[123] showed that young adults with the metabolic syndrome at 32 and 36 years of age had a lower cardiorespiratory fitness level at age 13 than counterparts without the metabolic syndrome, after controlling for skinfold-measured adiposity, among 364 men and women from the Amsterdam Growth and Health Longitudinal Study. However, Eisenmann *et al.*[124] found that high-fit adolescents had no better CVD risk profiles in their young adulthood than low-fit adolescents within an identical adiposity category among 48 participants, using data from the Aerobics Center Longitudinal Study. In summary, longitudinal studies have also shown conflicting results on an association between cardiorespiratory fitness and CV risk in youth, after accounting for adiposity. More longitudinal studies are required to clarify whether the effect of cardiorespiratory fitness on CV health is independent of the adiposity effect in children and adolescents.

1.14 Significance of Research

Obesity is one of the most significant public health issues worldwide. Childhood obesity particularly raises a public-health concern because of the increased social burden in that obesity leads to a wide range of co-morbidities later in life. This research focused on understanding the roles of adiposity and cardiorespiratory fitness in determining CV health risk and a bi-directional relationship between PA and adiposity. Although the link between cardiorespiratory fitness and PA and health has been established in adults, much less scientific documentation for such a relationship exists in youth. A better understanding of the relationship during childhood may provide evidence to implement more aggressive PA interventions for preventing obesity and reducing CV risk among children and adolescents, and further reducing CVD risk later in life and the social burden of the disease. Testing the reverse causation hypothesis may provide the evidence for PA promotion interventions from an early age, before excess body fat is accumulated. It would also suggest the necessity of specific intervention strategies for overweight

children to promote PA. In the contemporary epidemic of childhood obesity and low MVPA participation, daily LPA may play a role in childhood obesity prevention. If daily LPA is proved to have a preventive effect against adiposity, promoting LPA would be an alternative strategy for preventing obesity in children. It may be a realistic and practical strategy for inactive children to gradually increase PA, by moving from sedentary state to LPA and to MVPA. This research is expected to provide evidence to support interventions and suggest specific intervention strategies for promoting PA, preventing obesity, and improving CV health among children and adolescents.

CHAPTER 2

ASSOCIATIONS OF CARDIORESPIRATORY FITNESS AND ADIPOSITY WITH CARDIOVASCULAR RISK FACTORS DURING PUBERTY: THE MUSCATINE HEART STUDY

2.1 Introduction

Puberty is a stage of life during which there are tremendous biological changes, including sexual maturation, growth spurts, and significant changes in body composition. For example, BF% increases in both boys and girls during childhood, but boys develop muscle mass and girls increase and redistribute body fat during puberty;[19] therefore, the magnitude of the gender differences in fat mass and fat-free mass increases. In particular, girls are more likely to decrease cardiorespiratory fitness (hereafter 'fitness')[125] and become overweight during puberty.[126]

Although both adiposity and fitness are independently associated with cardiovascular (CV) disease, CV disease mortality, and all-cause mortality risk in adults,[127-129] the strength of associations between adiposity and fitness and CV risk may differ during puberty. Chronological age, gender, and sexual maturity status may be modifiers and/or confounders in the associations between adiposity and fitness and CV risk factors among adolescents.

Although age and sexual maturity status are positively correlated, individuals experience puberty at various chronological ages. Ondrak *et al.*[118] reported that, among three age groups (8 to 10, 11 to 13, and 14 to16 years of age), the variance in the CV risk score (a composite CV risk factor index including high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglyceride (TG), systolic blood pressure (SBP), diastolic blood pressure (DBP), and fasting insulin) attributed to adiposity was greatest in the youngest group and declined in older age groups, whereas the variance in the CV risk score attributed to fitness was greater in the 11 to 13 and 14 to16 year-old groups than in the 8 to10 year-old group. Boreham *et al.*[116] found that the adiposity effect on CV risk

factors was greater in boys at 12 years of age than at 15 years of age, while the fitness effect was not observed in participants of any age group. Mota *et al*.[57] showed that sexual maturity status accounted for approximately 55% of variation for boys and 40% for girls in a multivariable regression model including sexual maturity status, percent body fat, height, and age to predict fitness level estimated by the 20-m shuttle run test; however, there was no (positive or negative) consistent trend in change of fitness level with advance in pubertal stage. Sexual maturity status has also been shown to influence the patterns of CV risk factor development.[59-61] For example, as sexual maturation progresses during puberty, TC decreases, with the decrease being greater in boys than in girls.[59] Sex hormone profiles most probably account for the maturity effect.[60] However, the direction of the influence of maturity depending on CV risk factors is not constant with maturity and may differ by gender.

Difference in the magnitude of the associations between fitness and CV risk by gender may be not only because of different biological changes in sex hormone levels during puberty, but also because of different societal experiences and expectations for boys vs. girls. Kwon *et al*.[115] reported a gender difference in the fitness effect on CV risk; fitness had a beneficial effect on CV risk factors, particularly in boys, after controlling for weight status in a representative sample of U.S. adolescents 12 to 19 years of age (National Health and Nutrition Examination Survey (NHANES) 1999-2002).

A few studies have investigated the independent effect of fitness and adiposity on CV risk during puberty, accounting for age, sexual maturity status, and gender. Ekelund *et al*.[114] examined an independent cross-sectional association between fitness and metabolic risk among 1,092 children 9 to 10 years of age and 829 adolescents 15 to 16 years of age participating in the European Youth Heart Study (EYHS). Fitness was assessed during an incremental ergometer cycle test to exhaustion and expressed as watts per kilogram fat-free mass per min (W kg FFM^{-1} min^{-1}). Sexual maturity was assessed using the five-stage Tanner scale[130] for breast development in girls and pubic hair in boys.

They found that fitness was inversely associated with metabolic risk, adjusted for adiposity, age, and gender. The magnitude of the association did not change after further adjustment for maturity.

The Muscatine Heart Study is one of the first studies to examine CV risk in children. A four-year follow-up sub-study within the Muscatine Heart Study was conducted from 1991 to 1995 in order to characterize the growth of the heart related to changes in blood pressure (BP), body size, physical fitness, and physical activity through puberty. Using data from the sub-study, Janz *et al.*[131] previously demonstrated that change in fitness over four years (from approximately 10 to 14 years of age) was inversely associated with the ratio of TC to HDL-C, low-density lipoprotein cholesterol (LDL-C), and waist circumference, after adjustment for age, gender, fat-free mass, and pubertal stage. However, the potential effect of adiposity was not accounted for in this analysis. Here, we aimed to examine whether fitness is associated with CV risk factors during puberty, after accounting for adiposity. Identifying the independent effects of adiposity and fitness on CV risk would help establish their causal relationships and inform intervention strategies for CV risk reduction in children and adolescents.

2.2 Methods

2.2.1 Participants

Existing datasets from a four-year follow-up sub-study of the Muscatine Heart Study were used to achieve the study aim. More details for the sub-study can be found elsewhere.[131-133] But briefly, 150 potential participants who were likely to be prepubertal based on age were first identified from 925 school survey participants and contacted for this four-year follow-up sub-study. Informed consent was obtained from 130 participants. Based on a parent's report on pubertal development or a physician's physical examination, 126 children were confirmed as prepubertal or in early puberty (stage 1 or 2 in the Tanner scale).[130] Thus, 126 prepubertal Caucasian children were enrolled in the

study. The study was approved by the University of Iowa Institutional Review Board (Human Subjects).

2.2.2 Exposure Measurements

Maximal oxygen uptake (VO_2 max) was obtained from maximal graded exercise testing with direct determination of VO_2. Maximal graded exercise tests were conducted yearly using a cycle ergometer and the Medgraphics System CPX metabolic cart (Medical Graphics Corp., St. Paul, MN). The protocol for the graded exercise test consisted of a 1-minute warm up and three 3-minute submaximal stages followed by a series of 30-second stages until participants reached exhaustion. Pedal frequency throughout the test was 60 revolutions (rev)/min. The test was terminated when a participant could no longer maintain a pedal cadence of at least 40 rev/min and had a respiratory exchange ratio (RER) of more than 1.0 or was within 95% of his/her predicted maximal heart rate. VO_2 was collected breath-by-breath. VO_2 max was calculated by averaging all breath-by-breath VO_2 during the last 30-second stage. VO_2 max measured using this protocol was reported to have high reliability in this study sample ($r = 0.96$).[134]

Skinfold thickness was measured quarterly by Muscatine Heart Study field staff members who attended yearly formal training sessions. Skinfold thickness was taken on the right side of the body at six sites (tricep, bicep, subscapular, abdominal, suprailiac, and calf). Two measures were obtained at each site and averaged. If the measurements varied more than 1 mm, additional measurements were taken until the difference was less than 1 mm.

2.2.3 Outcome Measurements

Blood pressure (BP) was measured quarterly using a random-zero sphygmomanometer (Hawksley Gelman, Copiague, NY). Three resting BPs were recorded for each participant by the field staff, following a five-minute seated rest. The mean of the three measures of the first and the fourth Korotkoff sounds were recorded as SBP and DBP, respectively. The fifth Karotkoff sound was not recorded. After a 12-hour

fast, 15 mL of blood was drawn from the antecubital vein using a venipuncture technique at study years 1 (baseline), 2 (first-year follow-up), and 5 (fourth-year follow-up). Plasma TC, TG, and HDL-C levels were measured using standard protocols; LDL-C levels were calculated (LDL = TC - HDL - TG/5).[135]

2.2.4 Covariates

Height and weight were measured quarterly by the field staff. Height without shoes was measured to the nearest 0.1 cm using the IOWA anthropometric plane and square (University of Iowa Department of Medical Engineering, Iowa City, IA). Weight was measured to the nearest 0.1 kg using a Seca 770 digital metric scale (Seca, Columbia, MD) calibrated daily with standardized weights. Pubertal stage was estimated yearly by trained pediatricians using the five-stage Tanner scale (genital development in boys and breast development in girls).[130] Age, height, weight, and pubertal stage were considered as covariates.

2.2.5 Statistical Analysis

Gender-specific analysis was conducted using SAS version 9.2 (Cary, NC). For the quarterly-measured variables, BP and skinfold thickness, the mean value of the four measurements taken each year was used for analysis. Descriptive analyses, including estimation of summary descriptive measures and distributions, were conducted. An absolute rate in liter of VO_2 max per minute (L/min) was used as a measure of fitness. The sum of six skinfold measurements (cm) represented adiposity level. Pearson correlation coefficients of the sum of skinfolds measures and VO_2 max measures between baseline and follow-ups were calculated to test stability of adiposity and fitness levels over time. Age-adjusted least-squares means of the sum of skinfolds and VO_2 max were calculated according to pubertal stage in the SAS MIXED procedures. Gender-, age-, and height-specific SBP and DBP percentiles were calculated for each participant based on the U.S. national standard (by National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents).[136] Because of

non-normal distributions of CV risk factor variables, these variables were transformed using the Box-Cox transformation method.

Individual growth curve models were estimated to predict CV risk factor variables using mixed model approaches. Both the exposure and outcome variables were treated as continuous variables. Age was centered at the grand mean of age. The intercept and centered age were fit as random effects so that an intercept and a slope (the degree of linear change over time) for an individual were accounted for. VO_2 max (L/min), the sum of skinfolds (cm), centered age (yr), height (cm), weight (kg), and pubertal stage (stages 1 to 4) were fit as fixed effects. Because BP percentile variables were age- and height-adjusted variables, BP percentile prediction models did not include centered age and height as fixed effects. Interactions among fitness, adiposity, age, and maturity were considered. An interaction effect with a *P*-value of less than 0.20 was included in a final model. The pattern of growth (linear or quadratic models, or models which grouped the variance-covariance matrix on Tanner stage subgroup) and the variance of the individual growth estimates (intercept and slope) were appropriately identified based on Akaike's Information Criterion (AIC) for goodness of fit. The structure of the working correlation matrix was also determined based on AIC. An unstructured variance-covariance matrix was chosen because it allowed for an assumption of higher variance for measures at study year 5 with the within-person covariance. When the within-person error covariance matrix specification was combined with the model where the intercept and slope were considered as random effects, if the new model did not converge, the specification of the within-person error matrix was not included for a final model fitting. The significance level was set at 0.05.

2.3 Results

Sixty-one boys and 62 girls completed assessments at study year 1; 57 boys (93%) and 57 girls (92%) at study year 2; and 47 boys (77%) and 52 girls (84%) at study year 5. Those who dropped out were not significantly different from those who

completed the fourth-year follow-up (study year 5) assessment in terms of age, the sum of skinfolds, VO_2 max, TC, TG, HDL-C, LDL-C, SBP, or DBP at baseline.

Table 2.1 presents the characteristics of participants by study year and gender. This study sample had a relatively low HDL-C level (Table 2.2). Girls had higher TC, TG, and LDL-C than boys. No participants were identified as being in Tanner stage 5 until study year 5. The stability of VO_2 max (L/min) levels from baseline to follow-ups was moderate to high ($r = 0.71$ to 0.58 in boys and $r = 0.83$ to 0.46 in girls, $P < 0.05$). The sum of skinfolds from baseline to follow-ups were highly stable ($r = 0.98$ to 0.85 in boys and $r = 0.96$ to 0.80 in girls, $P < 0.05$). The age-adjusted mean of VO_2 max (L/min) tended to increase with increasing Tanner stage in both boys and girls (Table 2.3). The age-adjusted mean of the sum of skinfolds did not change with advance in Tanner stage among girls, while it was the highest in Tanner stage 2 and tended to decrease afterwards among boys.

Table 2.4 summarizes the mixed model analysis results describing the associations of the sum of skinfolds and VO_2 max with transformed CV risk factor outcomes, adjusted for age, height, weight, and pubertal stage, among boys and girls over the four-year follow-up period. Among boys, when a model included both the sum of skinfolds and VO_2 max simultaneously, SBP percentile, TC, TG, and LDL-C levels were positively associated with the sum of skinfolds ($P < 0.05$), but not with VO_2 max. DBP percentile and HDL-C level were not significantly associated with either the sum of skinfold or VO_2 max. No significant sum of skinfolds × VO_2 max interaction effect was observed for any CV risk factor variables. Among girls, when a model included both the sum of skinfolds and VO_2 max simultaneously, SBP percentile, DBP percentile, TC, TG, and LDL-C levels were positively associated with the sum of skinfolds ($P < 0.05$), but not with VO_2 max. HDL-C level was not significantly associated with either the sum of skinfold or VO_2 max. No interaction effects of fitness and adiposity were identified.

2.4 Discussion

This study examined whether fitness is associated with CV risk factors during puberty after accounting for adiposity, chronological age, gender, and pubertal stage. It confirmed that adiposity is positively associated with CV risk factors, such as plasma lipids and blood pressure, during puberty, after accounting for fitness, age, and pubertal stage in both boys and girls. However, the fitness effect on CV risk factors was mostly attenuated after accounting for adiposity, age, and pubertal stage in both boys and girls.

Several studies have demonstrated that, to some degree, the association between fitness and a favorable CV risk profile is retained even after controlling for the possible mediating effect of adiposity in children and adolescents.[109-115,118] However, other studies have shown no effect of fitness after controlling for adiposity.[116-118] Such inconsistent results may be explained partially by the distribution of CV risk factors in the study sample. For example, lack of association between SBP and fitness in the current study may be due to the study sample being relatively healthy; only two boys and two girls had elevated SBP (gender-, age-, and height-specific SBP percentile $\geq 90^{th}$ percentile)[136] at least once. Nielsen *et al.*[137] reported that only the lowest quintile of fitness level had a higher mean SBP as compared to the other four quintiles, and the mean SBP was not different among the other four quintiles in a group of adolescents. In exploratory work, we dichotomized four components of the metabolic syndrome; the cut-points of the components were gender- and age-specific waist circumference $\geq 90^{th}$ percentile,[138] TG $\geq$ 150 mg/L, HDL-C $<$ 40 mg/L, and gender-, age-, and height-specific SBP $\geq 90^{th}$ percentile.[136] A glucose or insulin component was not examined because these measures were not available. The analysis revealed that only approximately 4% of observations (10 observations from 10 girls and 13 observations from 12 boys) had two or more risk factors. No association was observed between VO_2 max (L/min) and having two or more risk factors after adjusting for the sum of skinfolds, age, height, weight, and pubertal stage. A low prevalence of two or more risk factors in this sample may have limited the

ability to detect a significant association between VO_2 max and having two or more risk factors. We also examined the relationship between VO_2 max and a composite CV risk score using a continuous CV risk Z-score method,[139] where Z-scores were calculated based on gender- and age-specific means and standard deviations for waist circumference, TG, and HDL-C from the NHANES III (1988-1994), and were based on the national standard for SBP.[140] This analysis showed no significant association between VO_2 max and the composite CV risk score, after adjusting for the sum of skinfolds, height, weight, and pubertal stage ($P > 0.30$ for both boys and girls).

The inconsistent results on the relationship of fitness and adiposity with CV risk are also possibly due to the differences of measures used to describe fitness and adiposity across studies. In this study, we used an absolute rate of VO_2 max as a fitness indicator. One may argue that body weighted-adjusted VO_2 max (mL/kg/min) is more commonly used; however, because high correlations between the sum of skinfolds and body weight-adjusted VO_2 max (mL/kg/min) were observed in this sample ($r = -0.59$ to -0.82), we chose an absolute rate of VO_2 max (mL/min) to avoid over-adjustment by body weight. At the same time, we included body weight as a covariate in statistical models to avoid overestimation of fitness level in heavy participants. When we examined associations between body weight-adjusted VO_2 max and CV risk factors in exploratory work, similar results to those of the current report were produced (data not shown). We chose the sum of skinfolds over body mass index (BMI) as an adiposity indicator, because BMI is not a good indicator of adiposity for normal-weight children (gender- and age-specific BMI < 85th percentile).[20,23,141] Fat mass can be estimated using prediction equations from skinfolds, but the standard error of estimation (SEE) of fat mass estimated based on skinfolds is considerable (3-5%).[19] Therefore, the sum of skinfolds was thought to be a better measure than fat mass estimated based on skinfolds for ranking adiposity level in this sample.

This study supports interventions aimed at obesity prevention to improve CV health among healthy adolescents during puberty. Body fat can be used as an appropriate outcome to evaluate the effectiveness of interventions for CV health improvement. A high fitness level was negatively associated with a low adiposity level, and fitness was not associated with CV risk factors after accounting for adiposity. This may suggest that adiposity plays a role in the mechanism underlying the effect of fitness on CV health. In addition, we observed some confounding effects of sexual maturity status in associations of adiposity and fitness with TC, LDL-C, and HDL-C levels; however, there was no (positive or negative) consistent trend in change of CV risk factors with advance in pubertal stage (data not shown). Considering sexual maturity status appears to be significant in understanding the roles of adiposity and fitness in determining CV health for adolescents.

One limitation of this study is a relatively small sample size. All participants were white, which is a lower risk population for childhood obesity than the Hispanic or African American populations. However, homogeneity of ethnicity and living-environment can be an advantage because unknown confounders are less likely to exist. Skinfold measurement is known to be vulnerable to measurement error; however, by using the mean of four sums of skinfold thicknesses, which were quarterly assessed, variability should have been reduced and reliability increased. Unmeasured potential confounding factors, such as genetic predisposition, were not considered. The fourth Korotkoff sound was recorded as DBP because, at the time of data collection, this was the standard procedure, although the fifth Korotkoff sound is currently accepted to predict DBP more accurately in children.[142]

Nonetheless, this study is one of few longitudinal studies that have examined the effects of fitness on CV risk factors during puberty, while considering significant factors such as adiposity, sexual maturity, and individual growth difference. The use of individual growth curve models allowed us to take into account change in CV risk factors

over time not only at a sample level, but also at an individual level. A low attrition rate (approximately 20% over four years) should have helped reduce selection bias. In conclusion, we found that adiposity, but not fitness, is independently associated with CV risk factors during puberty among healthy adolescents. Adiposity may more strongly influence CV risk factors than fitness during puberty. Adiposity may play a role in the mechanism underlying the effect of fitness on CV health during puberty. Adolescents experience dramatic biological changes during puberty. The fitness effect may become manifest after puberty, particularly among boys who experience an increase of muscle mass and fitness levels during puberty. Investigations of change of fitness effects on CV health throughout adolescence should follow.

2.5 Summary of Findings

The aim of this study was to examine whether fitness is associated with cardiovascular (CV) risk factors during puberty after accounting for adiposity. Study participants were 126 prepubertal Caucasian children participating in a longitudinal four-year follow-up study. Fitness level was determined by VO_2 max (L/min) obtained from maximal graded exercise testing and adiposity level was determined by the sum of skinfolds. Pubertal stage was estimated using the Tanner criteria. Gender-specific individual growth curve models, including both VO_2 max and the sum of skinfolds simultaneously, were fit to predict CV risk factor variables. Models also included covariates such as age, height, weight, and pubertal stage. In boys, systolic blood pressure percentile, total cholesterol, triglyceride, and LDL-C levels were positively associated with the sum of skinfolds ($P < 0.05$), but not with VO_2 max. Similary in girls, systolic and diastolic blood pressure percentiles, total cholesterol, triglyceride, and LDL-C levels were positively associated with the sum of skinfolds ($P < 0.05$), but not with VO_2 max. In conclusion, cardiorespiratory fitness was not associated with CV risk factors, after adjusting for adiposity, among healthy adolescents. This study suggests that cardiorespiratory fitness may influence CV health mostly through adiposity effects.

Table 2.1 Participant characteristics according to study year and gender

	Year 1	Year 2	Year 3	Year 4	Year 5
No. of participants					
Boys	61	57	56	56	47
Girls	62	57	59	56	52
Age (years)					
Boys	10.8 ± 1.0	11.8 ± 1.0	12.9 ± 0.9	13.8 ± 1.0	14.4 ± 0.9
Girls	10.3 ± 1.0	11.3 ± 1.0	12.4 ± 1.0	13.3 ± 1.0	14.1 ± 1.0
Height (cm)					
Boys	143.8 ± 7.3	149.5 ± 7.9	157.4 ± 9.5	164.1 ± 9.5	168.3 ± 8.2
Girls	140.7 ± 8.4	146.8 ± 8.7	153.3 ± 7.1	157.3 ± 6.3	160.0 ± 6.0
Weight (kg)					
Boys	39.3 ± 10.8	44.2 ± 12.8	50.9 ± 15.6	56.0 ± 14.0	60.6 ± 15.7
Girls	37.9 ± 9.5	44.2 ± 11.8	49.9 ± 12.3	55.0 ± 13.5	58.3 ± 12.5
Tanner stage[a]					
Boys	G1 (87%)	G1 (61%)	G1 & G2 (76%)	G3 & G4 (60%)	G4 (85%)
Girls	B1 (61%)	B1 & B2 (81%)	B2 & B3 (68%)	B3 & B4 (68%)	B4 (72%)
VO_2 max (L/min)					
Boys	1.86 ± 3.00	2.03 ± 3.52	2.18 ± 0.43	2.58 ± 0.53	2.73 ± 4.90
Girls	1.48 ± 3.45	1.67 ± 3.44	1.81 ± 0.34	2.02 ± 0.37	1.91 ± 2.93
VO_2 max (mL/kg/min)					
Boys	48.9 ± 8.2	47.4 ± 8.0	44.3 ± 7.3	46.9 ± 6.5	46.2 ± 7.5
Girls	39.7 ± 6.7	38.7 ± 5.9	37.2 ± 6.5	37.8 ± 6.6	33.5 ± 5.4
Sum of skinfolds (cm)[b]					
Boys	7.3 ± 4.2	8.3 ± 4.8	8.8 ± 5.1	8.2 ± 4.6	7.5 ± 4.5
Girls	8.8 ± 3.4	10.2 ± 4.3	10.6 ± 4.4	11.2 ± 4.9	11.0 ± 4.2

Note: G1 to G4 represent Tanner stages of genital development in boys. B1 to B4 represent Tanner stages of breast development in girls.

Mean ± SD.

[a]The distributions of Tanner stage are presented in Appendix C.

[b]Mean of measurements obtained quarterly during the year.

Table 2.2 Descriptive analyses of cardiovascular risk factors according to study year and gender

	Year 1	Year 2	Year 3	Year 4	Year 5
No. of participants					
Boys	61	57	56	56	47
Girls	62	57	59	56	52
SBP (mmHg) [a]					
Boys	98 ± 8	97 ± 7	101 ± 9	103 ± 11	106 ± 11
Girls	98 ± 7	99 ± 7	102 ± 7	103 ± 8	105 ± 8
DBP (mmHg) [a]					
Boys	61 ± 7	62 ± 6	61 ± 6	62 ± 6	63 ± 6
Girls	63 ± 7	63 ± 6	64 ± 5	64 ± 6	63 ± 6
TC (mg/dL)					
Boys	159 ± 23	160 ± 22	--	--	138 ± 18
Girls	165 ± 24	169 ± 26	--	--	153 ± 22
TG (mg/dL)					
Boys	73 ± 32	63 ± 25	--	--	75 ± 23
Girls	80 ± 37	89 ± 50	--	--	86 ± 37
HDL-C (mg/dL)					
Boys	46 ± 11	38 ± 10	--	--	48 ± 13
Girls	42 ± 8	33 ± 8	--	--	48 ± 9
LDL-C (mg/dL)					
Boys	97 ± 8	107 ± 21	--	--	73 ± 18
Girls	107 ± 21	119 ± 24	--	--	87 ± 21

Note: DBP = diastolic blood pressure, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, TC = total cholesterol, TG = triglyceride.

Mean ± SD.

[a]Mean of measurements obtained quarterly during the year.

Table 2.3 Age-adjusted least-squares means of VO_2 max and the sum of skinfolds according to gender and pubertal stage

	Boys (n=61)				Girls (n=62)			
Pubertal stage	G1 (Ob=111)	G2 (Ob=60)	G3 (Ob=30)	G4 (Ob=57)	B1 (Ob=67)	B2 (Ob=83)	B3 (Ob=61)	B4 (Ob=60)
VO_2 max (L/min)	2.08 ± 0.04	2.13 ± 0.04	2.34 ± 0.05	2.56 ± 0.05	1.66 ± 0.05	1.75 ± 0.04	1.83 ± 0.04	1.84 ± 0.05
VO_2 max (mL/kg/min)	45.0 ± 1.0	45.6 ± 1.0	48.0 ± 1.2	50.78 ± 1.3	38.2 ± 1.0	39.0 ± 0.8	37.4 ± 0.9	36.0 ± 1.0
Sum of skinfolds (cm)	8.1 ± 0.6	8.4 ± 0.6	7.8 ± 0.6	7.2 ± 0.6	10.3 ± 0.6	10.1 ± 0.5	10.3 ± 0.6	10.3 ± 0.6

Note: Ob = the number of observations (each participants represents one or more observations).

G1 to G4 represent Tanner stages of genital development in boys. B1 to B4 represent Tanner stages of breast development in girls.

Least-squares mean ± SE.

Least-squares means of VO_2 max and the sum of skinfolds were calculated according to Tanner stage in mixed models, accounting for repeated measures.

Table 2.4 Associations of the sum of skinfolds and VO_2 max with cardiovascular risk factors in boys and girls

	Boys (n=61)						Girls (n=62)					
	Sum of skinfolds (cm)			VO_2 max (L/min)			Sum of skinfolds (cm)			VO_2 max (L/min)		
	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value
SBP (pct)	1.28	0.45	<0.01	2.68	2.77	0.33	1.88	0.61	<0.01	0.18	3.91	0.96
DBP (pct)	0.80	0.64	0.21	-0.55	4.06	0.89	3.03	0.66	<0.0001	6.27	4.34	0.15
TC (mg/dl)	1.57	0.48	<0.01	0.30	2.77	0.91	1.73	0.48	<0.001	-1.57	2.97	0.60
TG (mg/dl)	0.57	0.24	<0.05	-2.21	1.34	0.10	4.16	0.91	<0.0001	1.22	6.00	0.84
HDL-C (mg/dl)	-0.08	0.05	0.12	0.18	0.32	0.58	-0.27	0.17	0.13	0.10	1.19	0.40
LDL-C (mg/dl)	0.26	0.08	<0.01	-0.31	0.48	0.53	1.83	0.54	<0.01	0.02	3.34	0.99

Note: β = parameter coefficient, DBP = diastolic blood pressure, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, pct = percentile, SBP = systolic blood pressure, SE = standard error, TC = total cholesterol, TG = triglyceride.

Individual growth curve models were fit, including both VO_2 max and the sum of skinfolds simultaneously, adjusted for the fixed effects, centered age, height, weight, and pubertal stage, as well as the random effects, centered age and the intercept. Transformed TC, TG, HDL-C, and LDL-C variables were used as outcome variables.

Complete mixed models are provided in Appendix C.

CHAPTER 3

THE EFFECT OF ADIPOSITY ON PHYSICAL ACTIVITY DURING CHILDHOOD: THE IOWA BONE DEVELOPMENT STUDY

3.1 Introduction

Physical inactivity is known to increase adiposity level in children. However, a relationship between physical activity (PA) and adiposity may be bi-directional. That is, not only may physical inactivity be a contributor to body fat gain, but also adiposity status may influence PA behaviors (reverse causation[81,82] hypothesis). Although cross-sectional studies have demonstrated an inverse association between PA and adiposity levels in children,[143] a review of prospective studies[144] concluded that low levels of baseline PA were only weakly or not associated with body fat gain. It is conceivable that the reported inverse cross-sectional relation may be due to a reduction of PA as a consequence of a high level of adiposity.

A high level of adiposity may negatively influence PA participation by children, presumably through psychological, societal, and physical functioning, such as low self-efficacy, poor body image, fear of being teased by peers, low athletic proficiency, and discomfort from heaviness (Figure 3.1). There is some evidence that obese youth are likely to be less active because of weight stigma.[145] Storch *et al.*[146] showed that peer victimization among overweight youth are linked to lower levels of PA. Faith *et al.*[147] also showed that weight criticism during sports and PA is associated with negative attitudes about sports and lower participation in PA among overweight students. Must and Tybor[81] have suggested that, given the fact that PA in children often occurs as part of organized sport, overweight children may be less likely to want to participate in PA, either due to fears of being teased or because they are “less athletic.”

Five prospective, adult population-based cohort studies[86-90] have consistently demonstrated that obesity is inversely associated with PA level later in life. To our knowledge, no study to date has explicitly addressed the reverse causation hypothesis in

children. Testing this reverse causation hypothesis may provide evidence to promote PA at an early age before excess body fat is accumulated. If obesity leads to a reduction of PA later in life, specific intervention strategies for overweight children to promote PA would be warranted. The aim of this study was to examine whether early adiposity level is inversely associated with subsequent PA behaviors during childhood.

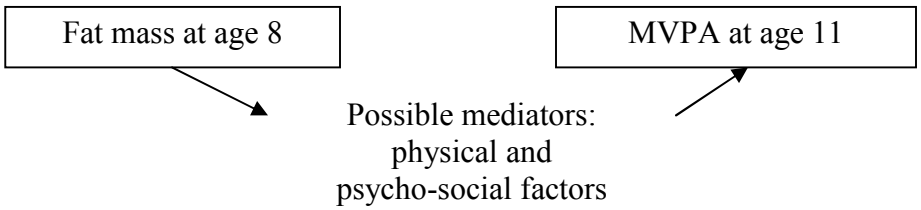


Figure 3.1 Conceptual model of the reverse causation hypothesis between early adiposity and subsequent physical activity

Note: MVPA = moderate- to vigorous-intensity physical activity.

3.2 Methods

3.2.1 Participants

Study participants were a cohort of children participating in the Iowa Bone Development Study which is an ongoing longitudinal study of bone health during childhood. The study participants are a sub-set of Midwestern children recruited during 1998 to 2001 from a cohort of 890 families participating in the Iowa Fluoride Study. Detailed information about the study design and demographic characteristics of participants can be found elsewhere.[64,148,149] Accelerometer and dual energy X-ray absorptiometry (DXA) measurements were conducted three times per child at approximately 5, 8, and 11 years of age (4.3 to 6.8 years of age range at the first examination, 7.6 to 10.8 years at the second examination, and 10.5 to 12.4 years at the third examination). Even if a cohort member did not participate in the age 5 examination, s/he was invited to participate in the age 8 and 11 examinations. If a time interval

between accelerometer measurement and DXA scanning was larger than 1.5 years for each age examination, the data were excluded. Four hundred thirty-six children completed both accelerometer and DXA examinations at the age 5 examination from Feb. 1998 to Nov. 2000; 502 at the age 8 examination from Sep. 2000 to Dec. 2004; and 454 at the age 11 examination from Oct. 2003 to Sep. 2006. Five hundred seventy-seven children (51% girls) completed at least one examination and 326 (56% girls) completed all three examinations. Those 326 children (95% white) served as the study sample for this report. We examined an association between adiposity at age 8 and PA at age 11 for the aim (Figure 3.1), so that data obtained at the age 5 examination could be used to account for the preceding change of PA and adiposity. The study was approved by the University of Iowa Institutional Review Board (Human Subjects). Written informed consent was provided by the parents of the children and assent was obtained from the children.

3.2.2 Adiposity Measurements

At the age 5 and 8 examinations, whole body scans using a Hologic QDR 2000 DXA (Hologic, Waltham, MA) were conducted with software version 7.20B in the fan-beam mode. At the age 11 examination, the Hologic QDR 4500 DXA (Delphi upgrade) with software version 12.3 and fan-beam mode was used for scan acquisition. Quality control scans were performed daily using the Hologic phantom. To adjust for the difference of the two DXA machines, translational equations from 4500 DXA measures to 2000 DXA measures for age 11 records were used. The translational equations (linear regression equations) were developed specifically for the two scanners in a pilot study where 60 of the children (32 boys, 28 girls) aged 9.9 to12.4 years (mean = 11.4 years, SD = 0.4 years) were scanned on each machine in random order during one clinic visit.[64] Fat mass (kg) was derived from the DXA scan images. Percent body fat (BF%) was calculated as fat mass (kg) divided by body weight (kg).

3.2.3 Physical Activity Measurements

Actigraph uniaxial accelerometers (model number 7164, Pensacola, FL) were used to measure PA level. The procedure for PA measurement has been described elsewhere.[150,151] Accelerometer movement counts were collected in a one-minute interval (one-minute epoch). At the time of the age 5 and 8 examinations, children were asked to wear the monitors during waking hours for 4 consecutive days, including one weekend day, during the fall season (Sep. through Nov.). At the time of the age 11 examination, they were asked to wear the monitors during waking hours for 5 consecutive days, including both weekend days during the fall season. In the accelerometer data reduction process, an interval of 20 or more consecutive minutes of zero accelerometer counts was considered as not wearing the monitor and invalid data.[152] The two inclusion criteria for accelerometer data were having valid data for more than 8 hours per day and wearing the monitor for 3 or more of the days. Intensity-weighted moderate- to vigorous-intensity PA (IW-MVPA) was defined as the daily sum of accelerometer counts derived during moderate- to vigorous-PA (MVPA) determined by 3,000 or greater accelerometer movement counts per minute ($ct \cdot min^{-1}$).[40,44]

3.2.4 Covariate Measurements

At each DXA visit, research nurses trained in anthropometry measured the child's height and weight. Sitting height was measured at age 11 to calculate maturity offset (year from peak height velocity) using predictive equations established by Mirwald and colleagues.[56] The equations have been developed in white Canadian children and adolescents and cross-validated in a different Canadian and a Flemish sample.[56] To estimate physical maturity status, the maturity offset variable was dichotomized as pre-peak height velocity (pre-mature) or post-peak height velocity (mature).

Family income and parental education level data were obtained from a mailed family demographic questionnaire completed by each child’s parents in 2007. Family income level was dichotomized into less than $40,000/year and $40,000/year or more for

data analysis. Education levels of mothers and fathers were also dichotomized into some college or lower and college graduate or higher. The modified Baecke Physical Activity Questionnaire[153] is administered to the child's mother and father at the child's age 8 examination. The questionnaire was one of the most widely used tools for assessing PA in adults at the time of data collection.[154,155] It was developed to evaluate a person's PA in three domains: work activity, sports activity, and leisure activity. PA levels of parents were estimated using the active living index (leisure activity) and the simple sport score (sports activity) from the questionnaire.

3.2.5 Statistical Analysis

Gender-specific analyses were conducted using SAS version 9.2 (Cary, NC). Descriptive analyses, including frequency distributions and estimation of summary descriptive measures, were conducted. If the IW-MVPA variable at age 11 was not normally distributed, a Box-Cox power transformation of the IW-MVPA variable (labeled 'transformed IW-MVPA') at age 11 was performed using the SAS TRANSREG procedures. Bivariate analyses were performed to identify a set of covariates included during the model development process; Pearson correlation analyses between transformed IW-MVPA at age 11 and continuous covariates and two-sample t-tests for IW-MVPA at age 11 and categorical covarites were performed. Potential covariates considered are presented in Tables 3.2 and 3.3. If the *P*-value was less than 0.10, the variable was considered to be included in a final model. The BF% and IW-MVPA data from the age 5 examination were used to account for the changes in BF% and IW-MVPA between the first two examinations (ages 5 and 8). Because the error terms of BF% at ages 5 and 8 were not independent (autocorrelated), the BF% residualized change score variable, which was defined as the residual of regression of yearly change of the measure from age 5 to age 8 on the measure at age 8, was created using the SAS AUTOREG procedure. The IW-MVPA residualized change score variable was also created in the same method.

Gender-specific generalized linear models were fit in the SAS GENMOD procedures. The main exposure variable was BF% at age 8 and the main outcome variable was transformed IW-MVPA at age 11. Models included covariates which could possibly confound a relationship between IW-MVPA and BF% based on bivariate analysis results. Several nested models were fit to examine how a parameter estimate for the exposure variable behaved when an additional covariate was included one by one. The likelihood ratio test was performed to compare the fit of the nested models. After model fitting, model diagnostics were conducted. For categorical data analysis, BF% level at age 8 was dichotomized into low BF% (< 25% for boys and < 32% for girls) or high BF% (≥ 25% for boys and ≥ 32% for girls).[156,157] IW-MVPA levels at 11 were divided into tertiles. Odds ratios and their 95% confidence intervals (CIs) were calculated to examine associations between BF% levels at age 8 and IW-MVPA levels at age 11, using logistic regressions. The significance level was set at 0.05.

3.3 Results

Table 3.1 presents means and 95% CIs of study variables. Fat mass increased approximately 5.1 kg for boys and 5.3 kg for girls from age 8 to 11. Participants, on average, wore accelerometers for more than 12 hours per day. IW-MVPA was higher in boys than in girls. IW-MVPA tended to increase with age among boys, but not among girls. Table 3.2 shows results of descriptive analyses of potential categorical covariates and t-tests for the significance of the mean difference of IW-MVPA at age 11 between categories of those potential covariates. Less than a fifth of the study sample reported lower than $40,000/year of family income. Approximately two-thirds of parents reported college graduate or higher education levels. At age 11, all boys were classified as pre-peak height velocity (pre-mature), whereas 20% of girls were classified as post-peak height velocity (mature). In t-test results, IW-MVPA at age 11 was positively associated with mother's education level and father's education level for boys ($P < 0.10$). IW-

MVPA at age 11 was positively associated with family income and negatively associated with maturity for girls ($P < 0.10$).

Based on the Box-Cox transformation, the IW-MVPA variable at age 11 was square root-transformed for boys ($\lambda = 0.5$) and log-transformed for girls ($\lambda = 0$). Results of Pearson correlation analyses between transformed IW-MVPA at age 11 and BF% at age 8 and between transformed IW-MVPA at age 11 and potential covariates are presented in Table 3.3. A significant negative correlation between transformed IW-MVPA at age 11 and BF% at age 8 was observed in both boys and girls ($P < 0.05$). IW-MVPA at age 8 was significantly positively correlated with IW-MVPA at age 11 in both boys and girls ($P < 0.05$). Transformed IW-MVPA at age 11 was positively correlated with a time interval between the age 8 and 11 examinations and negatively correlated with residualized change scores of BF% and IW-MVPA only among boys ($P < 0.10$). Age, mother's PA, and father's PA were not significantly correlated with transformed IW-MVPA at age 11 for either boys or girls. Finally, for boys, IW-MVPA at age 8, an interval between the age 8 and 11 examinations, residualized change scores of BF% and IW-MVPA, and mother's education were selected as covariates for a final model. Because of a fair agreement between mother's education level and father's education level (kappa = 0.37, P for chi-square test < 0.0001), only mother's education level was included. For girls, IW-MVPA at age 8, family income, and physical maturity were selected as covariates for a final model.

Several nested models were fit to predict transformed IW-MVPA at age 11 based on BF% at age 8. Because full models provided the better fit to the data than reduced models in both boys and girls based on the likelihood ratio test, the full models are presented in Table 3.4. Two boys and two girls identified as outliers in model diagnostics were excluded from the final model. After adjusted for IW-MVPA at age 8, an interval between the age 8 and 11 examinations, residualized change scores of BF% and IW-MVPA, and mother's education, BF% at age 8 was significantly inversely associated

with IW-MVPA at age 11 among boys ($P < 0.05$). After adjusted for IW-MVPA at age 8, family income, and physical maturity, BF% at age 8 was significantly inversely associated with IW-MVPA at age 11 among girls ($P < 0.05$).

In categorical data analysis, 23% of boys and 26% of girls were identified as being high BF% (≥ 25% BF for boys and ≥ 32% BF for girls) at age 8. In a fully-adjusted logistic regression model, boys and girls with high BF% at age 8 were more likely to be in the lowest tertile of IW-MVPA at age 11 than their counterparts with low BF% at age 8 (OR: 4.38, 95% CI: 1.05, 18.24 for boys, OR: 4.48, 95% CI: 1.35, 14.85 for girls, reference group: the highest tertile of IW-MVPA at age 11, Table 3.5).

3.4 Discussion

The aim of this study was to examine whether early adiposity status is inversely associated with subsequent PA behaviors in childhood (the reverse causation hypothesis). This study found that, in continuous data analysis, BF% at age 8 was inversely associated with IW-MVPA at age 11 in both boys and girls. Categorical data analysis also showed that boys and girls with high BF% at age 8 were more likely to have low PA levels at age 11 than those with lower BF% age 8. These findings are consistent with those of five adult population studies,[86-90] where obesity was a significant predictor of PA level later in life. However, the current study results are inconsistent with Sallis' study,[91] which reported no association between skinfold category at baseline and total activity accelerometer counts measured for one day at a 20-month follow-up among 732 children who were fourth graders at baseline.

In exploratory work, we examined the association between early adiposity and later PA using other PA indicators. BF% at age 8 was significantly inversely associated with total activity (≥ 100 $ct \cdot min^{-1}$) at age 11 in both boys and girls ($P < 0.05$). When time spent in MVPA (Time MVPA) was used as a PA indicator, the inverse association between Time MVPA at age 11 and BF% at age 8 was significant among girls ($P < 0.05$) and suggestive among boys ($P < 0.10$). Considering that there was a significant inverse

association between BF% at age 8 and IW-MVPA at age 11 among boys, these results may imply that boys with low BF% are more likely to engage in higher intensity PA than those with high BF%. From an energy expenditure perspective, IW-MVPA was expected to better represent PA level than Time MVPA in establishing a relationship between adiposity and PA. PA intensity may be critical particularly for boys. However, researchers should be cautious because the use of IW-MVPA may amplify measurement error, which is derived from the difference of relative intensities between individuals when absolute intensity is given.

The current study findings indicate that adiposity status may be a determinant of PA behavior in childhood. Godin *et al.*[83] suggested a theoretical model of the reverse causation hypothesis based on Ajzen's Theory of Planned Behavior (TPB).[84] According to this model, adiposity may impact PA behaviors by influencing cognition such as intention (motivation) and perceived behavioral control (ease or difficulty in engaging in the behavior, e.g., social barriers). Although we assumed that obesity-related psychological, societal, and physical functioning may negatively influence PA participation, we were not able to examine whether these are mediating factors in an association between early adiposity and subsequent PA because those potentially mediating variables were not measured in the Iowa Bone Development Study.

The current study suggests at least two significant points in terms of public health implications. First, this study suggests that a new perspective is necessary to develop intervention strategies to promote PA and to prevent obesity in children. This study suggests weight status-specific intervention strategies for PA promotion, since overweight children may have different barriers to PA participation. Given the childhood obesity epidemic, it would be critical to identify specific barriers for overweight children and develop strategies to overcome these barriers. Second, the study results support PA promotion interventions from an early age, before excess fat is accumulated. Once excess fat is accumulated in early childhood possibly due to a low level of PA, it may lead to

low PA participation. In turn, lack of PA may exacerbate fat accumulation. This assumption is supported by Valerio's study[158] showing that overweight and obese children 7 years of age had a higher BMI increase at three-year follow-up than normal-weight children. PA interventions from an early age are recommended to prevent excess fat accumulation throughout childhood and later in life.

Several limitations of this study should be acknowledged. We included only data from those who completed all three examinations. Loss to follow-up may have caused selection bias; but, IW-MVPA and BF% levels at age 8 were comparable between those who completed all three examinations and those who did not. The study sample was not randomly selected; it would also have lead to selection bias. Therefore, an association between early adiposity and subsequent PA observed in this sample may not represent that in the general child population. Caution should be taken in generalizing the results to the general child population. In the participant cohort, approximately 95% were white, which is a lower risk population for childhood obesity than the Hispanic or African American population. However, homogeneity of ethnicity and living-environment can be an advantage because unknown confounders are less likely to exist. Genetic predisposition was not considered. This observational study cannot eliminate error by residual and unmeasured confounding factors.

Nonetheless, to our knowledge, this study is the first prospective cohort study in a fairly large childhood sample to explicitly examine the reverse causation hypothesis. The use of objective and accurate measures for both PA and adiposity helped reduce measurement error and increase the confidence of internal validity. Three time-point examinations allowed accounting for the preceding changes in adiposity and PA during the first two examinations.

In conclusion, this study showed that children with low adiposity were more likely to be active at three-year follow-up than their counterpart with high adiposity. Adiposity may be a determinant of PA behavior in childhood. Regarding future research,

more evidence should be accumulated to support the reverse causation hypothesis in childhood. Research is required to understand the mechanism underlying the effect of adiposity status on PA behaviors. It would be valuable to test the hypothesis that obesity-related psychological, societal, and physical functioning are mediating factors in an association between early adiposity and subsequent PA, using existing datasets containing PA, adiposity, and related psycho-societal measurement data.

3.5 Summary of Findings

The aim of this study was to examine whether early adiposity level is inversely associated with subsequent physical activity (PA) behaviors in childhood. Study participants were 326 children participating in the Iowa Bone Development Study. PA and fat mass were measured using accelerometers and dual energy X-ray absorptiometry (DXA) at approximately 5, 8, and 11 years of age. Data for relevant variables such as parents' education and PA levels and family income were also collected. Gender-specific generalized linear models were fit to examine the association between percent body fat (BF%) at age 8 and intensity-weighted moderate- to vigorous-intensity PA (IW-MVPA) at age 11. After adjusting for IW-MVPA at age 8, an interval between the age 5 and 8 examinations, residualized change scores of BF% and IW-MVPA from age 5 to 8 and mother's education level, BF% at age 8 was inversely associated with IW-MVPA at age 11 among boys ($P < 0.05$). After adjusting for IW-MVPA at age 8, physical maturity, and family income, BF% at age 8 was inversely associated with IW-MVPA at age 11 among girls ($P < 0.05$). Categorical analysis also showed that the odd of being in the lowest quartile relative to the highest quartile of IW-MVPA at three-year follow-up for boys and girls with high BF% was approximately four times higher than the odd for those with low BF% ($P < 0.05$). This study suggests that adiposity levels may be a determinant of PA behavior. Specific intervention strategies for overweight children may be needed to promote PA.

Table 3.1 Description (means and 95% confidence intervals) of participants

	Age 5		Age 8		Age 11	
	Boys (n=142)	Girls (n=184)	Boys	Girls	Boys	Girls
	Mean (95% CI)		Mean (95% CI)		Mean (95% CI)	
Age (years)	5.2 (5.2, 5.3)	5.3 (5.2, 5.3)	8.7 (8.6, 8.8)	8.7 (8.6, 8.8)	11.2 (11.2, 11.3)	11.3 (11.2, 11.3)
Height (m)	1.12 (1.11, 1.13)	1.11 (1.10, 1.12)	1.34 (1.33, 1.35)	1.33 (1.32, 1.34)	1.49 (1.48, 1.50)	1.49 (1.48, 1.50)
Body weight (kg)	20.4 (19.8, 21.0)	20.0 (19.5, 20.6)	32.4 (31.0, 33.8)	31.8 (30.5, 33.0)	44.5 (42.4, 46.6)	44.6 (42.8, 46.4)
Time MVPA (min/d)	31 (28, 34)	24 (22, 26)	40 (36, 43)	25 (23, 27)	41 (38, 44)	23 (21, 25)
IW-MVPA ($\times 10^3$ ct/d)	143 (128, 159)	116 (103, 129)	188 (168, 208)	124 (112, 137)	204 (184, 224)	108 (97, 119)
Monitor-wearing time (hr/d)	12.1 (12.0, 12.2)	12.1 (12.0, 12.2)	12.5 (12.4, 12.6)	12.4 (12.3, 12.5)	12.4 (12.2, 12.5)	12.3 (12.2, 12.4)
Fat mass (kg)	3.8 (3.4, 4.1)	4.6 (4.2, 4.9)	7.6 (6.6, 8.5)	9.1 (8.3, 10.0)	12.7 (11.2, 14.3)	14.4 (13.1, 15.6)
Percent body fat (%)	17.9 (17.1, 18.8)	22.0 (21.2, 22.8)	21.5 (20.1, 22.9)	26.8 (25.5, 28.0)	26.0 (24.2, 27.9)	30.0 (28.6, 31.4)

Note: CI = confidence interval, IW-MVPA = the daily sum of accelerometer movement counts derived during moderate- to vigorous-intensity physical activity, Time MVPA = daily minutes spent in moderate- to vigorous-intensity physical activity.

Table 3.2 Comparisons of the means of IW-MVPA at age 11 between potential covariate categories

		Boys (n=142)		Girls (n=184)	
Variable	Category	Percentage	Mean (95% CI) ($\times 10^3$ ct/d)	Percentage	Mean (95% CI) ($\times 10^3$ ct/d)
Physical maturity[a]	Mature	0%	--[b]	20%	88 (67, 109)[c]
	Pre-mature	100%	204 (184, 224)	80%	113 (100, 126)
Family income	< $40,000/yr	9%	197 (102, 292)	16%	88 (65, 111)[c]
	≥ $40,000/yr	74%	206 (184, 229)	69%	116 (102, 130)
Mother's education	< college graduate	31%	178 (141, 215)[c]	33%	103 (86, 119)
	≥ college graduate	69%	216 (192, 241)	67%	111 (96, 126)
Father's education	< college graduate	38%	182 (157, 206)[c]	44%	105 (85, 124)
	≥ college graduate	61%	220 (191,250)	55%	112 (98, 125)

Note: CI = confidence interval, IW-MVPA = the daily sum of accelerometer movement counts during moderate- to vigorous-intensity physical activity.

[a]Physical maturity was determined by year from peak height velocity and categorized into pre- and post-peak height velocity (pre-mature vs. mature).

[b]All boys were categorized as pre-peak height velocity (pre-mature).

[c]$P < 0.10$.

Table 3.3 Associations between IW-MVPA at age 11 and the exposure variable and potential covariates

Variable	Boys (n=142)	Girls (n=184)
	coefficient *r* (95% CI)	coefficient *r* (95% CI)
Exposure variable		
BF% at age 8	-0.30 (-0.45, -0.15)	-0.23 (-0.37, -0.09)
Potential covariate		
Age	0.11 (-0.05, 0.27)	-0.08 (-0.22, 0.07)
Interval between age 8 and 11 examinations	0.18 (0.01, 0.33)[a]	0.05 (-0.10, 0.19)
IW-MVPA at age 8	0.42 (0.27, 0.55)[a]	0.27 (0.13, 0.40)[a]
IW-MVPA residualized change score from age 5 to 8	-0.16 (-0.31, 0.01)[b]	0.01 (-0.13, 0.16)
BF% residualized change score from age 5 to 8	-0.15 (-0.31, 0.01)[b]	0.04 (-0.10, 0.19)
Monitor-wearing time at age 11	0.11 (-0.06, 0.27)	0.04 (-0.10, 0.18)
Mother's sport score	0.07 (-0.10, 0.24)	0.02 (-0.13, 0.16)
Mother's active living index	-0.02 (-0.19, 0.15)	0.08 (-0.07, 0.23)
Father's sport score	0.07 (-0.11, 0.24)	0.06 (-0.11, 0.23)
Father's active living index	-0.12 (-0.30, 0.05)	0.02 (-0.14, 0.19)

Note: BF% = percent body fat, CI = confidence interval, IW-MVPA = the daily sum of accelerometer movement counts during moderate- to vigorous-intensity physical activity.

Transformed IW-MVPA at age 11 was used.

Pearson correlation coefficients are presented.

Scattor plots of transformed MVPA at age 11 versus BF% at age 8 are presented in Appendix D.

[a] $P < 0.05$.

[b] $P < 0.10$.

Table 3.4 Generalized linear models of IW-MVPA at age 11 predicted by BF% at age 8

Boys (n=140)[a]			Girls (n=153)[b]		
Parameter	β (95% CI)	*P*-value	Parameter	β (95% CI)	*P*-value
BF% at age 8	-2.47 (-4.37, -0.57)	<0.05	BF% at age 8	-1.36 (-2.53, -0.19)	<0.05
IW-MVPA at age 8	0.37 (0.23, 0.51)	<0.0001	IW-MVPA at age 8	0.16 (0.05, 0.26)	<0.01
Mother's education	31.5 (-1.9, 64.9)	0.06	Family income	23.6 (0.7, 46.7)	<0.05
Interval between the age 8 and 11 examinations	-23.5 (-49.1, 3.0)	0.08	Physical maturity	0.29 (-25.8, 26.3)	0.98
BF% residualized change score	-33.7 (-52.3, -15.1)	<0.001	Intercept	242 (203, 281)	<0.0001
IW-MVPA residualized change score	-0.001 (-0.001, -0.0002)	<0.05	--	--	--
Intercept	348 (249, 447)	<0.0001	--	--	--

Note: β = parameter estimate, BF% = percent body fat, CI = confidence interval, IW-MVPA = the daily sum of accelerometer movement counts during moderate- to vigorous-intensity physical activity.

Transformed IW-MVPA ($\times 10^3$ ct/d) at age 11 was used. In Box-Cox transformations, λ was 0.5 for boys and 0 for girls.

[a]Because of two outliers, 140 boys were included for a final model.

[b]Because of missing data for physical maturity (missing n = 2) and family income (missing n = 28, missing data for both physical maturity and family income in one girl) and two outliers, 153 girls were included for a final model.

Table 3.5 Odds of being in the lowest tertile relative to the highest tertile of IW-MVPA at age 11 for boys and girls with high[a] vs. low percent body fat at age 8

	Boys[b] (n=142)	Girls (n=155)[c]
IW-MVPA at age 11	Odds ratio (95% CI)	Odds ratio (95% CI)
The lowest tertile	4.38 (1.05, 18.24)	4.48 (1.35, 14.85)
The middle tertile	1.89 (0.40, 8.97)	2.40 (0.82, 6.07)
The highest tertile	Reference	Reference
P for trend	<0.05	<0.05

Note: CI = confidence interval, IW-MVPA = the daily sum of accelerometer movement counts during moderate- to vigorous-intensity physical activity.

[a]High percent body fat was defined as ≥ 25% for boys and ≥ 32% for girls, resulting in 23% of boys and 26% of girls being categorized into high percent body fat.

[b]Adjusted for IW-MVPA at age 8, BF% residualized change score from age 5 to 8, IW-MVPA residualized change score from age 5 to 8, mother's education, and an interval between the age 8 and 11 examinations.

[c]Adjusted for IW-MVPA at age 8, physical maturity at age 11, and family income. Because of missing data for physical maturity (missing n = 2) and family income (missing n = 28, missing data for both physical maturity and family income in one girl), 155 girls were included for a final model.

CHAPTER 4

AN ASSOCIATION BETWEEN LIGHT-INTENSITY PHYSICAL ACTIVITY AND ADIPOSITY DURING CHILDHOOD: THE IOWA BONE DEVELOPMENT STUDY

4.1 Introduction

Although the health benefits of regular moderate- to vigorous-intensity physical activity (MVPA), particularly in preventing obesity, is well acknowledged by the public, the majority of Americans do not meet MVPA recommendations.[31] The effect of MVPA on adiposity is mainly explained by energy expenditure associated with MVPA. Light-intensity PA (LPA) such as slow walking, despite its less energy expenditure than MVPA, involves more energy expenditure than sedentary behavior. Therefore, it is conceivable that daily LPA may have a beneficial effect on obesity prevention.

Exercise studies have traditionally focused on MVPA, which has often been measured by self-report PA recall questionnaires. Because LPA tends to be performed frequently in daily life, it is more difficult to accurately quantify LPA than MVPA when using PA questionnaires.[74] The development of accelerometry as an objective measure of PA provides new possibilities for objectively assessing the full range of PA intensities, from sedentary to vigorous, in free-living subjects over a number of days, and for studying the health effects of all PA intensity levels.[73]

Recently, several studies[75-80] have examined the association between accelerometer-measured daily LPA and adiposity in children. Two cross-sectional studies[75,76] demonstrated an inverse association between accelerometer-measured time spent in LPA (Time LPA) and adiposity indicators, such as body mass index (BMI) percentile, fat mass, and percent body fat (BF%), among children and adolescents. But, others[77-80] have reported no association between Time LPA and BMI level. At this time, limited research and evidence exist on the effects of LPA on adiposity among children.

The purpose of this study was to examine whether accelerometer-measured daily LPA is inversely associated with adiposity during childhood. Previous studies have often used Time LPA as a LPA indicator. From an energy expenditure perspective, however, not only duration of LPA, but also its intensity is assumed to be a significant factor in establishing a relationship between adiposity and LPA. Fat mass is expected to better indicate an actual body fat level than BMI in children. Therefore, we examined the cross-sectional association between accelerometer-measured intensity-weighted LPA (IW-LPA) and dual energy X-ray absorptiometry (DXA)-derived fat mass during childhood. If daily LPA is proved to have a preventive effect against adiposity, promoting LPA can be an alternative strategy to prevent childhood obesity.

4.2 Methods

4.2.1 Participants

The study sample was a cohort of children participating in the Iowa Bone Development Study which is an ongoing longitudinal study of bone health during childhood. The study participants are a sub-set of Midwestern children recruited during 1998 to 2001 from a cohort of 890 families participating in the Iowa Fluoride Study. Detailed information about the study design and demographic characteristics of participants can be found elsewhere.[64,148,149] Accelerometer and DXA measurements were conducted at approximately 5, 8, and 11 years of age (4.3 to 6.8 years of age range at the first examination, 7.6 to 10.8 years at the second examination, and 10.5 to 12.4 years at the third examination). Even if a cohort member did not participate in the age 5 examination, s/he was invited to participate in the age 8 and 11 examinations. If a time interval between accelerometer measurement and DXA scanning was larger than 1.5 years for each age examination, the data were excluded. Of the cohort, 436 children completed both accelerometer and DXA examinations at the age 5 examination from Feb. 1998 to Nov. 2000; 502 at the age 8 examination from Sep. 2000 to Dec. 2004; and 454 at the age 11 examination from Oct. 2003 to Sep. 2006. A total of 577 children (51% girls,

95% white) who completed at least one of those three examinations were included for data analysis. The study was approved by the University of Iowa Institutional Review Board (Human Subjects). Written informed consent was provided by the parents of the children and assent was obtained from the children.

4.2.2 Physical Activity Measurements

Actigraph uniaxial accelerometers (model number 7164, Pensacola, FL) were used to measure PA level. The procedure for PA measurement has been described in detail elsewhere.[150,151] Accelerometer movement counts were collected in a one-minute interval (one-minute epoch). At the age 5 and 8 examinations, children were asked to wear the monitors during waking hours for 4 consecutive days, including one weekend day, during the fall season (Sep. through Nov.). At the age 11 examination, they were asked to wear the monitor during waking hours for 5 consecutive days, including both weekend days, during the fall season.

In the data reduction process, an interval of 20 or more consecutive minutes of zero accelerometer counts was considered as not wearing the monitor and invalid data.[152] The two inclusion criteria for accelerometer data for data analysis were having valid data for more than 8 hours per day and wearing the monitor for 3 or more of the days. Moderate to vigorous intensity was defined as 3,000 or greater accelerometer movement counts per minute ($ct \cdot min^{-1}$).[40,44] Intensity-weighted MVPA (IW-MVPA) was determined as the daily sum of accelerometer counts derived during MVPA defined as ≥ 3000 $ct \cdot min^{-1}$. There is no consensus on an accelerometer count cut-point to define being sedentary for children. Two cut-points which have been suggested in previous studies were applied: 99 $ct \cdot min^{-1}$ [40,159] and 1,099 $ct \cdot min^{-1}$.[46] Light intensity was determined by accelerometer counts between being sedentary and MVPA: 100 to 2,999 $ct \cdot min^{-1}$ or 1,100 to 2,999 $ct \cdot min^{-1}$. The latter light intensity range was named high-LPA in this report. IW-LPA was determined as the daily sum of accelerometer counts during LPA (100 to 2,999 $ct \cdot min^{-1}$). Intensity-weighted high-LPA (IW-HLPA) was determined as the daily sum of

accelerometer counts during high-LPA (1,100 to 2,999 $ct \cdot min^{-1}$). Total activity was defined as the daily sum of accelerometer counts during LPA and MVPA ($\geq$ 100 $ct \cdot min^{-1}$).

4.2.3 Body Fat Mass Measurements

At the age 5 and 8 examinations, whole body scans using a Hologic QDR 2000 DXA (Hologic, Waltham, MA) were conducted with software version 7.20B and fan-beam mode. At the age 11 examination, the Hologic QDR 4500 DXA (Delphi upgrade) with software version 12.3 and fan-beam mode was used for scan acquisition. Quality control scans were performed daily using the Hologic phantom. To adjust for the difference of the two DXA machines, translational equations from 4500 DXA measures to 2000 DXA measures for age 11 records were used. The translational equations (linear regression equations) were developed specifically for the two scanners in a pilot study where 60 of the children (32 boys, 28 girls) aged 9.9 to12.4 years (mean = 11.4 years, SD = 0.4 years) were scanned on each machine in random order during one clinic visit.[64] Total body fat mass (kg) was derived from the scan images. Fat-free mass (kg) was calculated as the sum of bone-free soft tissue and bone mineral content.

4.2.4 Covariate Measurements

At each DXA visit, research nurses trained in anthropometry measured the child's height and weight. Sitting height was measured at age 11 to calculate maturity offset (year from peak height velocity) using predictive equations established by Mirwald and colleagues.[56] To estimate physical maturity status, the maturity offset variable was dichotomized as pre-peak height velocity (pre-mature) or post-peak height velocity (mature). Dietary assessment was conducted using the 3-day food diary at the age 5 examination and the Block Kid's Food Frequency Questionnaire (the Block Kid's FFQ)[160] at the age 8 and 11 examinations. Approximately 40% of the age 5 population completed the 3-day food diary, and 94% of the age 8 population and 98% of the age 11 population completed the Block Kid's FFQ, respectively. Birth weight data were obtained from the original Fluoride Study.

4.2.5 Statistical Analysis

Gender-specific analyses were performed using SAS version 9.2 (Cary, NC). Descriptive analyses, tests for normal distribution, and bivariate analyses between PA variables, were conducted. The distribution of times spent in different intensities of activity during waking hours was calculated. IW-LPA and IW-HLPA were used as indicators of LPA. Fat mass was used as an indicator of adiposity. Because the fat mass variable was not normally distributed, a Box-Cox power transformation of the variable (named 'transformed fat mass') was performed using the SAS TRANSREG procedures. Age-, height-, and fat-free mass-adjusted partial correlation coefficients between the LPA variables and the transformed fat mass variable were calculated.

Gender-specific individual growth curve models were estimated to examine an association between LPA and transformed fat mass using the SAS MIXED procedures. Age and the intercept were fit as random effects. Age, IW-LPA (or IW-HLPA), birth weight, height, fat-free mass, physical maturity, calorie intake, and IW-MVPA were fit as fixed effects. In this model, age was found to be a modifier of an association between LPA and transformed fat mass. Therefore, examination time point- and gender-specific multivariable linear regression models were fit. To test an association between transformed fat mass and IW-LPA (or IW-HLPA), age, birth weight, height, fat-free mass, calorie intake, and IW-MVPA were included as covariates in regression models. Physical maturity status was additionally included as a covariate in models for girls at age 11. After model fitting, model diagnostics were performed to test whether data met the assumptions of linear regression. If an observation significantly changed the estimate of coefficients (influence, residuals exceeding +3 or -3), the observation was excluded. Linearity, normality of residuals, and heteroscedasticity were tested. For the collinearity assumption, if a tolerance value was lower than 0.1, the variable was considered as a linear combination of other predictor variables. The significance level was set at 0.05.

4.3 Results

Table 4.1 presents the characteristics of participants according to gender and examination time point. The mean fat mass increased 9.3 kg in boys and 9.5 kg in girls over six years. The range of fat mass distribution became wider with age (Figure 4.1). As illustrated in Figure 4.2, time spent being sedentary tended to increase and Time LPA tended to decrease with age. The proportion of Time MVPA during waking hours was minimal. Bivariate analyses showed that IW-LPA was more strongly correlated with total activity than with IW-MVPA (Table 4.2). Similarly, the correlations of IW-HLPA with total activity were high, but the correlations of IW-HLPA with IW-MVPA were low. As presented in Table 4.3, age-, height-, and fat-free mass-adjusted Pearson correlation coefficients between transformed fat mass and IW-LPA and between transformed fat mass and IW-HLPA were significant at ages 8 and 11 ($P < 0.05$), but not at age 5, among either boys or girls.

We here present multivariate linear regression model results from excluding calorie intake for three main reasons. First, when a multivariable linear regression model was fit including daily calorie intake as a covariate, the calorie intake effect did not change the direction and magnitude of the association between LPA and fat mass (data not shown). Second, in the Block Kid's FFQ validation study using the current study sample,[160] the calorie intake data from the Block Kid's FFQ was found to have a low validity (a weighted kappa statistic and a correlation coefficient of daily calorie intake data from the Block Kid's FFQ were 0.15 and 0.26, respectively, compared to the data from the 3-day food diary). Third, the sample size would significantly decrease if calorie intake is included as a covariate because of a low completion rate of dietary assessment at age 5 (40%). In addition, because all boys were identified as pre-mature at age 11, physical maturity status was included in a final regression model only for girls at age 11. Based on model diagnositics, one boy at age 5, three boys at age 8, and two boys and three girls at age 11 were excluded.

Table 4.4 shows the results of multivariable linear regression model estimates to examine cross-sectional associations between IW-LPA (or IW-HLPA) and transformed fat mass according to gender and examination time point, adjusted for age, birth weight, height, fat-free mass, IW-MVPA, and physical maturity only for girls. Among boys, both IW-LPA and IW-HLPA were significantly inversely associated with transformed fat mass at age 11 ($P < 0.01$), but not at ages 5 and 8. Among girls, IW-HLPA was significantly inversely associated with transformed fat mass at age 11 ($P < 0.05$). The inverse association between IW-LPA and transformed fat mass at age 11 among girls was suggestive ($P < 0.10$). IW-LPA and IW-HLPA were significantly inversely associated with transformed fat mass at age 8 ($P < 0.05$), but not at age 5.

4.4 Discussion

The purpose of this study was to examine whether LPA is inversely associated with adiposity during childhood. This study found that LPA was inversely associated with fat mass in children at age 11, but not at age 5. The inverse association between LPA and fat mass at age 8 was observed only among girls. A few studies have been conducted to examine accelerometer-measured Time LPA and adiposity in youth. Two cross-sectional studies[75,76] demonstrated a significant inverse association between Time LPA and adiposity. Treuth *et al.*[76] examined a cross-sectional relationship between several adiposity indicators (BMI, fat mass, and BF%) and Actiwatch accelerometer-measured Time LPA in 229 elementary, middle, and high school boys and girls. They found that Time LPA was inversely associated with adiposity indicators in all three school levels among girls, but not among boys. In this sample, time spent in moderate-intensity PA and vigorous-intensity PA were not associated with adiposity. Butte *et al.*[75] examined a cross-sectional relationship between DXA-measured BF% and Actiwatch accelerometer-measured Time LPA among 897 children 4 to 19 years of age. Time LPA was inversely associated with BF%, adjusted for gender and age. Furthermore, the association was stronger than an association between time spent in moderate-intensity PA

and BF%. On the other hand, four other cross-sectional studies[77-80] have shown no association between Time LPA and BMI level. For example, Thompson *et al*.[80] found no difference in Time LPA among healthy-weight, overweight, and obese groups of 790 boys and girls at grades 3 and 7. Montgomery *et al*.[67] reported that time spent in sedentary behaviors and Time LPA, but not Time MVPA, were significant predictors of PA energy expenditure in a multivariable linear regression model among 104 children (median of 5.4 year of age). This result may imply that the proportion of time distributed between sedentary behaviors and LPA determines daily PA energy expenditure, given a minor contribution of MVPA to daily PA energy expenditure: this study sample spent much less time in MVPA (4% of waking hours) than in LPA (20% of waking hours). The current study also demonstrated that children spend most waking hours in sedentary behaviors and LPA and spend least in MVPA.

It is not feasible to compare study results directly between studies, because different types of accelerometer and different cut-points were used across studies. There is no consensus on accelerometer count cut-point to define LPA in children. Here, we reported analysis results of applying two different lower thresholds to define LPA, which previous studies have used: 100 $ct \cdot min^{-1}$ [40,159,161] and 1,100 $ct \cdot min^{-1}$.[46,67,77,162-165] The analysis results produced from these two cut-points were fairly consistent. Previous studies have often used Time LPA as LPA indicator. In exploratory analyses, we found that fat mass was more strongly inversely associated with IW-LPA ($P < 0.05$ for boys and $P < 0.10$ for girls) than with Time LPA ($P > 0.10$ for boys and $P > 0.70$ for girls) at age 11. These findings suggest that not only LPA duration, but also its intensity should be considered in investigating a relationship between LPA and adiposity. However, researchers should be cautious because the use of IW-LPA may amplify measurement error, which is derived from the difference of relative intensities between individuals when absolute intensity is given. Previous studies did not take into account MVPA and birth weight, which were found to be significant confounding factors in the current study.

Controlling for possible confounding factors is critical for the internal validity of study results. For example, in the current study, an age-, height-, and fat-free mass-adjusted correlation coefficient between IW-HLPA and fat mass at age 8 among boys was significant, but multivariable regression analysis revealed that IW-HLPA was not associated with fat mass, after further adjustment for birth weight and IW-MVPA. In future research to examine the role of LPA in determining adiposity, such factors, particularly MVPA, should be taken into account as potential confounding factors. In addition, monitor-wearing time could also be a potential confounding factor. However, when we additionally examined a relationship between average IW-LPA (IW-LPA divided by monitor-wearing time) and fat mass, the analysis results were also similar to those of this report.

This study has several public health implications for childhood obesity prevention. First, the study supports the current PA recommendations focusing on MVPA. LPA seems to have some beneficial effect on adiposity among older children, but no effect among younger children, whereas the beneficial effect of MVPA on adiposity is consistent throughout childhood. Therefore, promoting MVPA would be an appropriate recommendation for obtaining a health benefit of PA. Second, this study suggests that the effect of LPA on adiposity may become apparent with age throughout childhood. The promotion of LPA, such as slow walking and playing active electronic games,[166] may be an alternative intervention strategy for obesity prevention in older children. It would be a realistic and practical strategy for inactive children to gradually increase PA, by moving from being sedentary to LPA and to MVPA. Promoting LPA may be particularly meaningful for girls who are likely to engage in less MVPA than boys.

Several limitations of this study should be noted. Because this study examined a cross-sectional relationship between LPA and adiposity, a temporal relationship cannot be established. The study sample was not randomly selected; selection bias may have occurred. Therefore, an association between LPA and adiposity observed in this sample

may not represent that in the general child population and caution should be taken in generalizing the results to the general child population. In the participant cohort, 95% were white, which is a lower risk population for childhood obesity than the Hispanic or African American population. Genetic predisposition to body composition was not accounted for. This observational study cannot eliminate error by residual and unmeasured confounding factors.

Nonetheless, to our knowledge, this study is the first longitudinal study to examine an association between accelerometer-measured LPA and DXA-derived fat mass during childhood. The use of objective and accurate measures for both PA and adiposity helped reduce measurement error and increase the confidence of internal validity. Considering potential confounders such as MVPA and birth weight also helped protect study results against threats to internal validity. In conclusion, this study suggests that LPA may have a preventive effect against adiposity in older children. More research is required to examine a beneficial effect of LPA on obesity prevention among adolescents.

4.5 Summary of Findings

The purpose of this study was to examine whether accelerometer-measured daily light-intensity physical activity (LPA) is inversely associated with dual energy X-ray absorptiometry (DXA)-derived body fat mass during childhood. The study sample was 577 children participating in the longitudinal Iowa Bone Development Study. Fat mass and PA were measured at approximately 5, 8, and 11 years of age. Data for relevant variables such as height, physical maturity, and birth weight were also obtained. Two intensity-weighted LPA indicators were used, applying two accelerometer count cut-points: the daily sum of accelerometer counts during LPA (IW-LPA) and the daily sum of accelerometer counts during high-LPA (IW-HLPA). Examination time point- and gender-specific multivariable linear regression models were fit to predict fat mass based on IW-LPA and IW-HLPA, including covariates, such as age, birth weight, fat-free mass, height,

intensity-weighted moderate- to vigorous-intensity PA, and physical maturity only for girls. Among boys, both IW-LPA and IW-HLPA were inversely associated with fat mass at age 11 ($P < 0.05$), but not ages 5 and 8. Among girls, both LPA variables were inversely associated with fat mass at ages 8 and 11 ($P < 0.10$ for IW-LPA at age 11, $P < 0.05$ for others), but not at age 5. In conclusion, this study suggests that LPA may have a preventive effect against adiposity among older children.

Table 4.1 Descriptive characteristics of study participants by gender and examination time point

	Boys			Girls		
	Age 5 (n=204)	Age 8 (n=245)	Age 11 (n=218)	Age 5 (n=232)	Age 8 (n=257)	Age 11 (n=236)
	Mean (95% CI)			Mean (95% CI)		
Age (years)	5.2 (5.2, 5.3)	8.8 (8.7, 8.9)	11.2 (11.2, 11.3)	5.3 (5.2, 5.4)	8.8 (8.7, 8.8)	11.2 (11.2, 11.3)
Height (m)	1.12 (1.11, 1.13)	1.35 (1.34, 1.36)	1.49 (1.48, 1.50)	1.11 (1.10, 1.12)	1.33 (1.32, 1.34)	1.49 (1.48, 1.50)
Body weight (kg)	20.5 (20.0, 21.1)	33.8 (32.6, 35.1)	45.3 (43.5, 47.0)	20.0 (19.5, 20.5)	31.9 (30.8, 32.9)	44.5 (42.9, 46.0)
IW-LPA ($\times 10^3$ ct/d)	416 (406, 425)	351 (342, 360)	315 (307, 324)	397 (388, 406)	333 (324, 341)	291 (283, 298)
IW-HLPA ($\times 10^3$ ct/d)	253 (245, 261)	214 (206, 221)	190 (184, 197)	228 (221, 235)	190 (184, 197)	160 (154, 166)
IW-MVPA ($\times 10^3$ ct/d)	150 (137, 164)	181 (167, 196)	216 (189, 224)	114 (104, 125)	129 (116, 141)	109 (99, 120)
Monitor-wearing time (hr/d)	12.1 (12.0, 12.2)	12.5 (12.4, 12.6)	12.4 (12.2, 12.5)	12.1 (12.0, 12.2)	12.4 (12.3, 12.5)	12.3 (12.2, 12.4)
Fat mass (kg)	3.9 (3.6, 4.3)	8.4 (7.6, 9.1)	13.1 (11.8, 14.3)	4.5 (4.2, 4.8)	9.2 (8.5, 9.9)	14.0 (12.9, 15.1)

Note: CI = confidence interval, IW-HLPA = the daily sum of accelerometer counts during high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, IW-LPA = the daily sum of accelerometer counts during light-intensity physical activity defined as 100 to 2,999 $ct \cdot min^{-1}$, IW-MVPA = the daily sum of accelerometer counts during moderate- to vigorous-intensity physical activity defined as $\geq$ 3,000 $ct \cdot min^{-1}$.

Table 4.2 Pearson correlation coefficients between physical activity variables by gender and examination time point

		Boys			Girls		
		Age 5 (n=204)	Age 8 (n=245)	Age 11 (n=218)	Age 5 (n=232)	Age 8 (n=257)	Age 11 (n=236)
		r (95% CI)			*r* (95% CI)		
IW-LPA	IW-MVPA	0.22 (0.08, 0.35)	0.22 (0.10, 0.34)	0.29 (0.17, 0.41)	0.30 (0.18, 0.42)	0.20 (0.08, 0.32)	0.33 (0.21, 0.44)
IW-LPA	Total activity	0.68 (0.59, 0.74)	0.64 (0.56, 0.71)	0.62 (0.53, 0.70)	0.76 (0.70, 0.81)	0.66 (0.58, 0.72)	0.75 (0.69, 0.80)
IW-HLPA	IW-MVPA	0.34 (0.21, 0.45)	0.34 (0.23, 0.45)	0.37 (0.25, 0.48)	0.36 (0.25, 0.47)	0.30 (0.19, 0.42)	0.42 (0.31, 0.52)
IW-HLPA	Total activity	0.74 (0.67, 0.80)	0.71 (0.65, 0.77)	0.67 (0.59, 0.74)	0.78 (0.72, 0.82)	0.71 (0.65, 0.77)	0.79 (0.74, 0.83)

Note: CI = confidence interval, IW-HLPA = the daily sum of accelerometer counts during high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, IW-LPA = the daily sum of accelerometer counts during light-intensity physical activity defined as 100 to 2,999 $ct \cdot min^{-1}$, IW-MVPA = the daily sum of accelerometer counts during moderate- to vigorous-intensity physical activity defined as ≥ 3,000 $ct \cdot min^{-1}$, total activity = the daily sum of ≥ 100 $ct \cdot min^{-1}$.

Table 4.3 Age-, height-, and fat-free mass-adjusted Pearson partial correlation coefficients between IW-LPA and IW-HLPA and fat mass by gender and examination time point

	Boys			Girls		
	Age 5 (n=203)	Age 8 (n=242)	Age 11 (n=216)	Age 5 (n=232)	Age 8 (n=257)	Age 11 (n=233)
		r (95% CI)			*r* (95% CI)	
IW-LPA	-0.04 (-0.18, 0.09)	-0.14 (-0.27, -0.02)	-0.27 (-0.39, -0.14)	-0.11 (-0.24, 0.02)	-0.17 (-0.29, -0.05)	-0.20 (-0.32, -0.07)
IW-HLPA	-0.07 (-0.21, 0.07)	-0.20 (-0.31, -0.07)	-0.32 (-0.43, -0.19)	-0.12 (-0.24, 0.01)	-0.21 (-0.32, -0.09)	-0.25 (-0.36, -0.12)

Note: CI = confidence interval, IW-HLPA = the daily sum of accelerometer counts during high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, IW-LPA = the daily sum of accelerometer counts during light-intensity physical activity defined as 100 to 2,999 $ct \cdot min^{-1}$.

Transformed fat mass was used.

Table 4.4 Regression parameter estimates of IW-LPA and IW-HLPA in multivariable linear regression models to predict fat mass based on IW-LPA and IW-HLPA

		Age 5			Age 8			Age 11		
	Exposure variable	β	*SE*	*P*	β	*SE*	*P*	β	*SE*	*P*
Boys	IW-LPA ($\times 10^3$ ct/d)	0.38	0.96	0.69	-2.27	2.31	0.33	-13.91	4.85	<0.01
	IW-HLPA ($\times 10^3$ ct/d)	0.38	1.12	0.74	-2.96	3.08	0.34	-20.79	6.13	<0.01
Girls	IW-LPA ($\times 10^3$ ct/d)	-0.25	1.09	0.82	-5.41	2.60	<0.05	-8.93	4.88	0.07
	IW-HLPA ($\times 10^3$ ct/d)	0.03	1.32	0.98	-8.14	3.34	<0.05	-16.12	6.61	<0.05

Note: β = regression parameter estimate, IW-HLPA = the daily sum of accelerometer counts during high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, IW-LPA = the daily sum of accelerometer counts during light-intensity physical activity defined as 100 to 2,999 $ct \cdot min^{-1}$, IW-MVPA = the daily sum of accelerometer counts during moderate- to vigorous-intensity physical activity defined as $\geq$ 3,000 $ct \cdot min^{-1}$, SE = standard error of the estimate.

Multivariable linear regression model: transformed fat mass (g) = exposure variable + age (year) + birth weight (g) + fat-free mass (g) + height (cm) + IW-MVPA ($\times 10^3$ ct/d). Physical maturity was included in a model only for girls at age 11.

For boys, n = 203 at age 5, n = 242 at age 8, and n = 216 at age 11.

For girls, n = 232 at age 5, n = 257 at age 8, and n = 233 at age 11.

Complete multivariable linear regression models to predict IW-HLPA are presented in Appendix E.

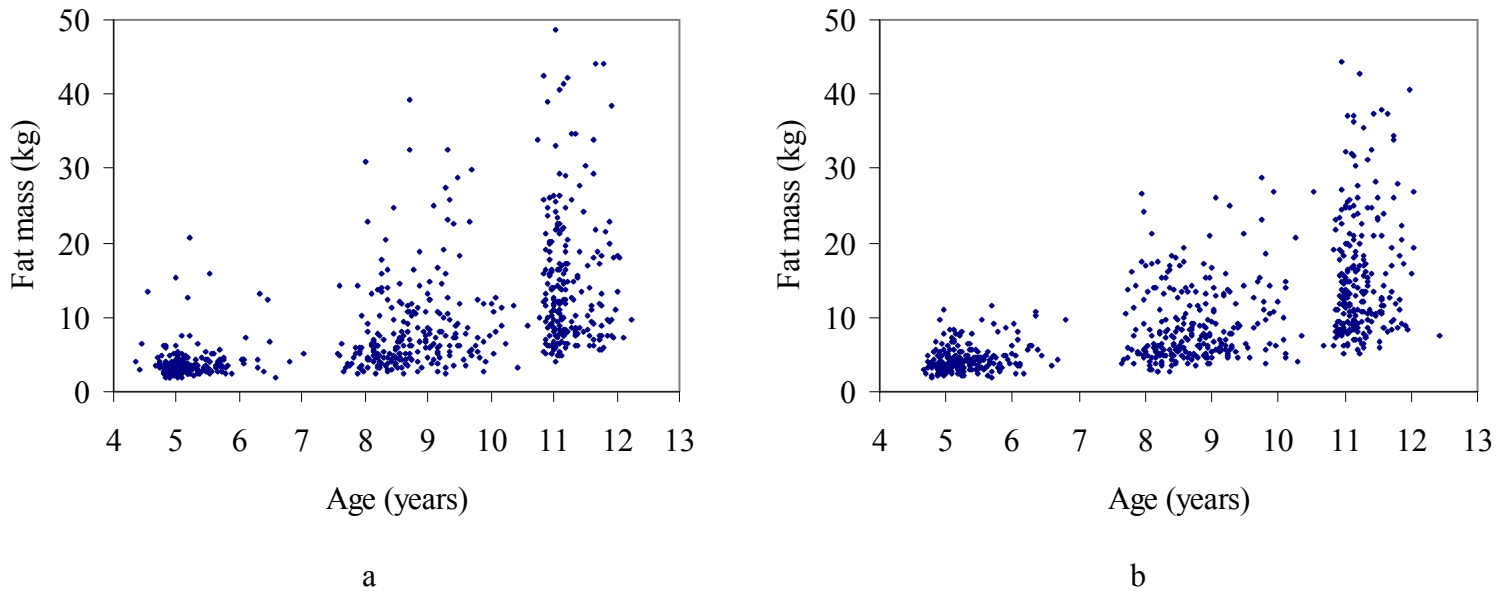


Figure 4.1 Scatter plots of fat mass over age in boys and girls
(a) Boys (n = 204 at age 5, n = 245 at age 8, and n = 218 at age 11)
(b) Girls (n = 232 at age 5, n = 257 at age 8, and n = 236 at age 11)

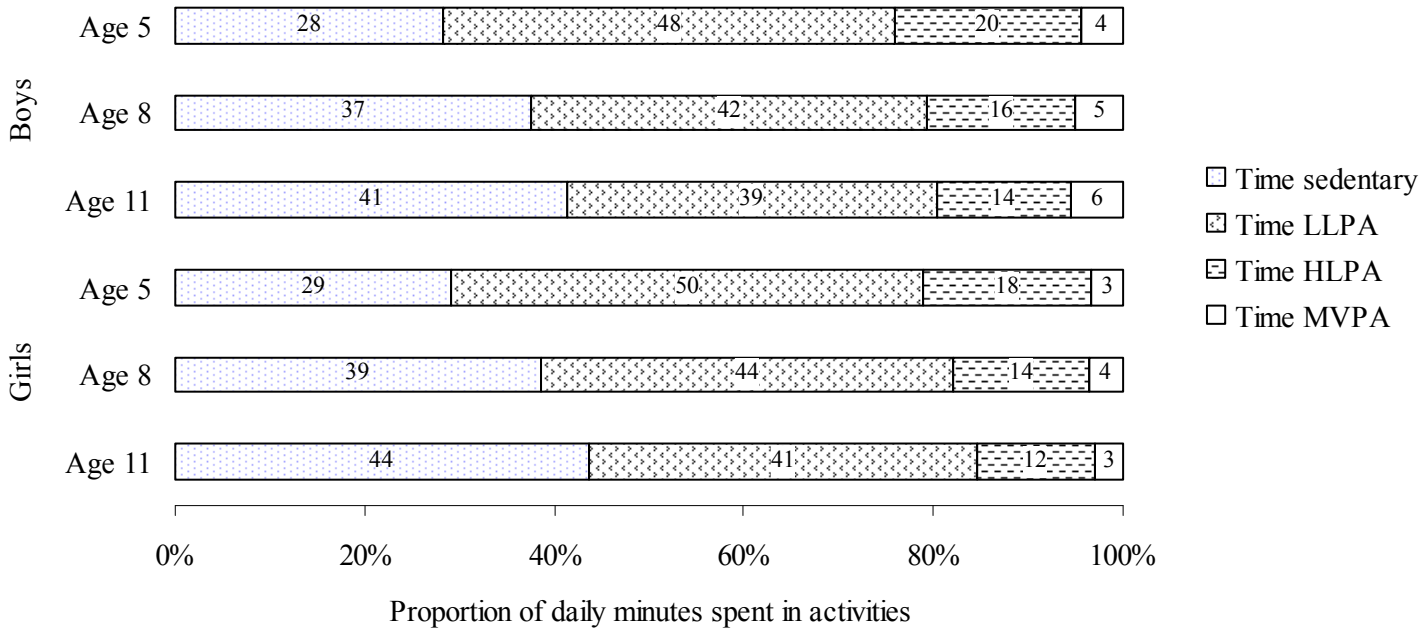


Figure 4.2 Daily time allocation for physical activity intensities according to gender and examination time point

Note: Time HLPA = the amount of daily time spent in high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, Time LLPA = the amount of daily time spent in low-light-intensity physical activity defined as 100 to 1,099 $ct \cdot min^{-1}$, Time MVPA = the amount of daily time spent in moderate- to vigorous-intensity physical activity defined as ≥ 3,000 $ct \cdot min^{-1}$, Time sedentary = the amount of daily time spent in sedentary behavior defined as < 100 $ct \cdot min^{-1}$.

For boys, n = 204 at age 5, n = 245 at age 8, and n = 218 at age 11.

For girls, n = 232 at age 5, n = 257 at age 8, and n = 236 at age 11.

CHAPTER 5

CONCLUSIONS

5.1 Overall Findings of Research

The goal of this dissertation research was to better understand relationships among PA, cardiorespiratory fitness, adiposity, and CV health in children and adolescents. The first paper titled "Associations of cardiorespiratory fitness and adiposity with cardiovascular risk factors during puberty" aimed to determine whether cardiorespiratory fitness is associated with CV risk factors during puberty after accounting for adiposity. Data from 123 children participating in a sub-study of the Muscatine Heart Study were analyzed to achieve this aim. Adiposity was positively associated with CV risk factors during puberty after accounting for cardiorespiratory fitness, age, and sexual maturity status in both boys and girls. However, a beneficial effect of cardiorespiratory fitness on CV risk factors was not apparent after accounting for adiposity, age, and sexual maturity status in both boys and girls.

The aim of the second paper titled "The effect of adiposity on physical activity during childhood" was to determine whether early adiposity level is inversely associated with subsequent PA behaviors during childhood (the reverse causation hypothesis). Analysis of data from 326 children participating in the Iowa Bone Development Study demonstrated that BF% at age 8 was inversely associated with IW-MVPA at age 11 among both boys and girls. Boys and girls with high levels of adiposity were more likely to have low PA levels at three-year follow-up, compared to their counterparts with low levels of adiposity. These findings suggest that adiposity status may be a determinant of PA behavior in childhood.

The third paper titled "An association between light-intensity physical activity and adiposity during childhood" aimed to determine whether LPA is inversely associated with body fat mass during childhood. Data analysis showed that at 11 years of age, but not at 5 years of age, LPA was inversely associated with fat mass in 577 children

participating in the Iowa Bone Development Study. The inverse association was also significant at age 8 among girls, but not among boys. These cross-sectional inverse associations were independent of MVPA. This study suggests that LPA may have a preventive effect against adiposity in older children.

5.2 Additional Findings and Discussion

5.2.1 Indicators of Physical Activity Level

There are some aspects of the research which were not discussed in the second and third papers in detail, but are worthy of further consideration. Previous studies have often used time spent in PA, such as Time MVPA and Time LPA, as an indicator of PA level. However, this research used intensity-weighted PA, such as IW-MVPA and IW-LPA, because PA intensity is a significant dimension of PA in determining energy expenditure and therefore adiposity. It would be worthy to compare the results of using different indicators for the same data. When Time MVPA was used as a PA indicator to examine an association between BF% at baseline and PA at three-year follow-up, the inverse association did not reach statisitical significance in boys ($P < 0.10$, Table 5.1). Considering that there was a significant inverse association between BF% at baseline and IW-MVPA at three-year follow-up among boys, these results may imply that boys with low BF% are more likely to engage in higher intensity PA than those with high BF%. In addition, when total activity was used as a PA indicator, the association was significant among both boys and girls ($P < 0.05$). Table 5.2 presents analysis results of examining associations of Time LPA and Time HLPA with fat mass. Time LPA was not associated with fat mass in any of three age groups of boys or girls ($P > 0.10$ for boys and $P > 0.40$ for girls). Time HLPA was associated with fat mass only at age 11 among boys ($P < 0.05$). Considering that there were inverse associations between both IW-LPA and IW-HLPA and fat mass at age 11 among boys and at ages 8 and 11 among girls, PA intensity appears to be an important factor to estimate PA level and predict adiposity. Overall,

these results support that PA intensity should be considered in establishing a relationship between PA and adiposity.

5.2.2 Indicators of Adiposity Level

Gender- and age-specific BMI percentile is widely used as an obesity indicator for children in epidemiologic studies. But, BMI is not a measure of adiposity. Unlike BMI, fat mass, BF%, and FMI are constructed from direct measurements of adiposity. The second paper used BF% as an adiposity indicator. In exploratory work, additional generalized linear models were fit to examine an association between early adiposity and subsequent PA using different adiposity indicators. Among girls, the use of height- and fat-free mass-adjusted fat mass did not produce a significant association with any of PA variables (IW-MVPA, Time MVPA, and total activity), whereas BF% was significantly inversly associated with each of IW-MVPA, Time MVPA, and total activity (Table 5.1). One may assume that because children with high body fat are likely to have high fat-free mass, height- and fat-free mass-adjusted fat mass may have over-adjusted for body size. When analyses were repeated using height-adjusted fat mass residual, the same results were found: no associations between height-adjusted fat mass at baseline and three PA variables (IW-MVPA, Time MVPA, and total activity) at follow-up ($P > 0.05$, data not shown). The inverse association between FMI at age 8 and IW-MVPA and Time MVPA at age 11 was significant among girls ($P < 0.05$). Future research is required to answer the questions on which indicator is the best measure of adiposity for children and why different adiposity indicators suggest different magnitudes of the association between adiposity and PA.

5.2.3 Energy Intake as a Predictor of Adiposity

Energy intake and energy expenditure are two major determinants of adiposity status. Energy intake would be a significant potential confounding factor in predicting fat mass based on PA. However, for several reasons, analysis results which did not account for energy intake were presented in the third paper titled “An association between light-

intensity physical activity and adiposity during childhood": (1) only 40% of the study participants completed dietary assessment at age 5, (2) the Block Kid's FFQ, which was used to assess dietary intake at ages 8 and 11, has a low validity to estimate energy intake (a weighted kappa statistic and a correlation coefficient of daily energy intake data from the Block Kid's FFQ were 0.15 and 0.26, respectively, compared to the data from the 3-day food diary),[160] and (3) the analysis results from considering energy intake were consistent with those from not considering it (Table 5.3). Although the *P*-value of the regression parameter estimate of energy intake was close to being significant at age 8 among girls ($P = 0.05$), the energy intake effect did not change the magnitude of the association between IW-HLPA and fat mass. The *P*-values for regression parameter estimates of energy intake were closer to significance level in girls than in boys. However, because of a low validity of energy intake data from the Block Kid's FFQ, it is questionable if these results reflect a true relationship between energy intake and fat mass. Dietary intake is often a concern in research on PA effects on adiposity. Assessing dietary intake is burdensome for study participants and involves measurement error. More effort is required to assess dietary intake accurately.

5.3 Research Findings and Hypotheses

These three research papers provide pieces of evidence to support or not support the research hypotheses suggested in Chapter 1. This dissertation research confirmed that high body fat has a negative impact on CV health in adolescents. However, it does not support the first hypothesis that cardiorespiratory fitness influences CV health in children and adolescents after accounting for adiposity (pathway A in Figure 5.1). A temporal inverse association between early adiposity level and subsequent PA behaviors during childhood was found, which supports the second hypothesis that a high level of adiposity negatively influences PA participation in children (pathway B in Figure 5.1). A cross-sectional association between LPA and adiposity was found among older children. This

finding suggests that LPA may have a preventive effect against adiposity at least in older children (pathway C in Figure 5.1).

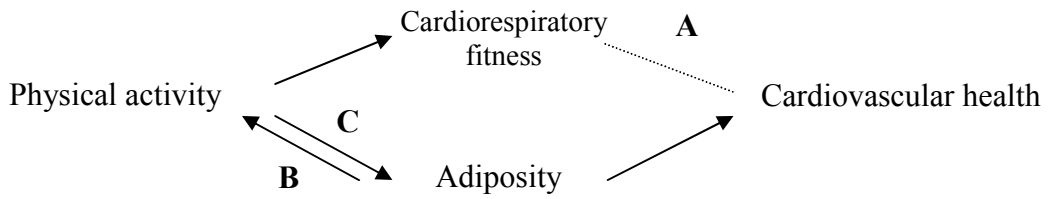


Figure 5.1 Hypothetical model of relationships among physical activity, cardiorespiratory fitness, adiposity, and cardiovascular health

5.4 Public Health Implications

The epidemic of childhood obesity is a significant public health concern worldwide. Scientific evidence is necessary to develop effective interventions and suggest recommendations. This research provides scientific evidence to support specific intervention strategies to promote PA, prevent obesity, and improve CV health in children and adolescents.

Cardiorespiratory fitness is assumed to be positively associated with CV health. In the first paper, however, cardiorespiratory fitness was not inversely associated with CV risk factors after accounting for adiposity during puberty. This suggests that adiposity may play a role in the mechanism underlying the effect of fitness on CV health. Adiposity was positively associated with CV risk factors after accounting for cardiorespiratory fitness. This result supports interventions aimed at obesity prevention to improve CV health among healthy adolescents in puberty. Adiposity level can be used as an appropriate outcome to evaluate the effectiveness of interventions for CV health improvement. It is noteworthy that an increased PA is a proven strategy to reduce adiposity levels.

The second paper suggests a new perspective for developing intervention strategies to promote PA and prevent obesity in children. First, it suggests weight status-specific intervention strategies for PA promotion. Overweight children may have different barriers to participation in PA. Given the childhood obesity epidemic, it would be significant to identify specific barriers for overweight children and develop strategies to overcome the barriers. Second, the study results support PA promotion interventions from an early age, before excess body fat is accumulated. Once excess fat is accumulated in early childhood possibly due to a low level of PA, it may lead to low PA participation. In turn, lack of PA may exacerbate fat accumulation. PA from an early age is recommended to prevent excess fat accumulation throughout childhood and later in life.

The third paper supports the current PA recommendations focusing on MVPA. While a beneficial effect of MVPA on adiposity is consistent throughout childhood, LPA seems to have a beneficial effect on adiposity only among older children, but no effect among younger children. This lays emphasis on relatively higher intensity PA, such as MVPA, in early childhood. Promoting MVPA, not LPA, would be an appropriate recommendation for obtaining a health benefit of PA for younger children. However, given the practical difficulty of increasing the level of MVPA, promoting LPA such as slow walking and playing active electronic games can be an alternative intervention strategy for preventing obesity in older children. It may be a realistic and practical strategy for inactive children to gradually increase PA, by moving from the sedentary state to LPA and to MVPA. LPA may be particularly meaningful for girls who are likely to engage in less MVPA than boys.

5.5 Future Research Directions

Future research is expected to confirm findings and examine hypotheses generated by this research. We failed to find an effect of cardiorespiratory fitness on CV risk factors among adolescents during puberty after accounting for adiposity. However, a beneficial effect of fitness on CV health may occur post-puberty, given the dramatic

change on body composition and fitness levels during puberty. Particularly, boys experience an increase of muscle mass and fitness level. The effects of cardiorespiratory fitness on CV health throughout adolescence should be further investigated. Some confounding effects of sexual maturity status on the associations of adiposity and fitness with total cholesterol, LDL-C, and HDL-C levels were identified; however, there is no (positive or negative) consistent trend in change of fitness level with advance in pubertal stage. In future studies, sexual maturity status should be considered in understanding roles of adiposity and cardiorespiratory fitness in determining CV health for adolescents.

The reverse causation hypothesis that adiposity status influences PA behaviors is considered to be a fairly new idea. Evidence to support the reverse causation hypothesis in childhood should be accumulated. It was assumed that obesity-related psychological, societal, and physical functioning may mediate low PA participation. Because psychological and societal and physical functioning data were not collected in the Iowa Bone Development Study, the assumption (these factors are mediating factors in an association between early adiposity and subsequent PA behaviors) could not be tested. Researchers should investigate the mechanism underlying the effect of adiposity status on PA behaviors. It would be valuable to test the hypothesis using existing datasets containing PA, adiposity, and related psycho-societal measure data.

Traditionally, MVPA has been the focus in obesity research. This research suggests that LPA may also have a preventive effect against obesity in older children. A beneficial effect of LPA on adiposity may become apparent in adolescence due to decreased MVPA. More research is required to examine the hypothesis that LPA has a beneficial impact on adiposity among adolescents. Furthermore, time spent in PA is often used to represent PA level. However, intensity was found to be significant in determining PA level and predicting adiposity. For future research, it is recommended to consider PA intensity. However, researchers should take caution because the use of the sum of

accelerometer movement counts may amplify measurement error, which is derived from the difference of relative intensities between individuals when absolute intensity is given.

Lastly, there is no universally agreed indicator to determine adiposity level for children. BMI percentile, BF%, FMI, and fat mass are commonly used in obesity research. Different results produced from the use of different adiposity indicators make it difficult to interpret results and suggest public health implications. For example, IW-MVPA at age 11 was significantly inversely associated with BF% at age 8 ($P < 0.05$), but not with height- and fat-free mass-adjusted fat mass at age 8 ($P > 0.10$), among girls. These seeming contradictions require in-depth discussion to identify an appropriate indicator of adiposity for children.

In conclusion, this research suggests fairly new ideas on adiposity as a determinant of PA, the potential effect of LPA on adiposity, and the use of intensity-weighted PA to predict adiposity. The future research is recommended to develop these ideas and provide evidence to support them.

Table 5.1 Maximum likelihood parameter estimates of adiposity indicators at age 8 in generalized linear models to predict physical activity indicators at age 11 based on adiposity indicator at age 8

		Boys (n=142)		Girls (n=153)	
Outcome variable	Exposure variable	β (95% CI)	*P*	β (95% CI)	*P*
IW-MVPA at age 11 ($\times 10^3$ ct/d)	Fat mass residual at age 8	-4.58 (-8.35, -0.81)	<0.05	-2.18 (-4.88, 0.51)	0.11
IW-MVPA at age 11 ($\times 10^3$ ct/d)	BF% at age 8	-2.47 (-4.37, -0.57)	<0.05	-1.36 (-2.53, -0.19)	<0.05
IW-MVPA at age 11 ($\times 10^3$ ct/d)	FMI at age 8	-5.26 (-1.12, 0.76)	0.09	-3.70 (-7.47, 0.07)	0.05
Time MVPA at age 11 (min/d)	Fat mass residual at age 8	-0.0005 (-0.001, 0.0002)	0.15	-0.0004 (-0.0009, 0.0001)	0.08
Time MVPA at age 11 (min/d)	BF% at age 8	-0.31 (-0.67, 0.04)	0.09	-0.25 (-0.45, -0.04)	<0.05
Time MVPA at age 11 (min/d)	FMI at age 8	-0.61 (-1.67, 0.44)	0.25	-0.66 (-1.32, -0.005)	<0.05
Total activity at age 11 ($\times 10^3$ ct/d)	Fat mass residual at age 8	-4.69 (-9.94, 0.55)	0.07	-2.22 (-7.05, 2.61)	0.37
Total activity at age 11 ($\times 10^3$ ct/d)	BF% at age 8	-2.59 (-5.14, -0.05)	<0.05	-2.38 (-4.46, -0.29)	<0.05
Total activity at age 11 ($\times 10^3$ ct/d)	FMI at age 8	-6.00 (-14.19, 2.17)	0.15	-5.77 (-12.49, 0.95)	0.09

Note: β = regression parameter estimate, BF% = percent body fat, CI = confidence interval, fat mass residual = height- and fat-free mass-adjusted residual of fat mass, FMI = fat mass index, IW-MVPA = the daily sum of accelerometer counts derived during moderate- to vigorous-intensity physical activity, Time MVPA = daily minutes spent in moderate- to vigorous-intensity physical activity, total activity = the daily sum of $\geq$ 100 $ct \cdot min^{-1}$.

Transformed outcome variables were used if they were not normally distributed.

For boys, models were adjusted for the PA variable at age 8, an interval between the age 8 and 11 examinations, the residualized change score of the PA variable from age 5 to age 8, the residualized change score of the adiposity variable from age 5 to age 8, and mother's education. To predict total activity at age 11, monitor-wearing time was additionally included as a covariate.

Table 5.1 continued

For girls, models were adjusted for the PA variable at age 8, physical maturity at age 11, and family income. To predict total activity at age 11, monitor-wearing time was additionally included as a covariate.

Table 5.2 Parameter estimates of time spent in light-intensity physical activity in multivariable linear regression models to predict fat mass based on time spent in light-intensity physical activity

		Age 5			Age 8			Age 11		
	Exposure variable	*β*	*SE*	*P*	*β*	*SE*	*P*	*β*	*SE*	*P*
Boys	Time LPA (min/d)	0.37	1.17	0.75	-0.64	2.41	0.79	-7.15	5.16	0.17
	Time HLPA (min/d)	3.16	2.24	0.16	-2.00	5.78	0.73	-30.29	12.46	<0.05
Girls	Time LPA (min/d)	-0.89	1.32	0.50	-2.04	2.75	0.46	-1.30	4.73	0.78
	Time HLPA (min/d)	2.84	2.71	0.30	-3.87	6.56	0.56	-16.62	13.12	0.21

Note: β = regression parameter estimate, Time HLPA = time spent in high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, Time LPA = time spent in light-intensity physical activity defined as 100 to 2,999 $ct \cdot min^{-1}$, Time MVPA = time spent in moderate- to vigorous-intensity physical activity defined as ≥ 3,000 $ct \cdot min^{-1}$, SE = standard error of the estimate.

Multivariable linear regression model: transformed fat mass (g) = exposure variable + age (year) + birth weight (g) + fat-free mass (g) + height (cm) + Time MVPA (min/d).

For boys, n=203 at age 5, n=242 at age 8, and n=216 at age 11.

For girls, n=232 at age 5, n=257 at age 8, and n=233 at age 11.

Table 5.3 Multivariable linear regression models to predict fat mass based on energy intake and IW-HLPA

		Age 5			Age 8			Age 11		
	Exposure variable	*β*	*SE*	*P*	*β*	*SE*	*P*	*β*	*SE*	*P*
Boys	Energy intake (kcal/d)	0.08	0.19	0.70	0.05	0.30	0.86	-0.55	0.58	0.34
	IW-HLPA ($\times 10^3$ ct/d)	0.02	1.24	0.99	-2.94	3.17	0.35	-20.85	6.22	<0.01
Girls	Energy intake (kcal/d)	0.42	0.28	0.13	0.56	0.29	0.05	0.88	0.58	0.13
	IW-HLPA ($\times 10^3$ ct/d)	1.31	1.69	0.44	-8.50	3.52	<0.05	-16.20	6.78	<0.05

Note: β = regression parameter estimate, IW-HLPA = the daily sum of accelerometer counts during high-light-intensity physical activity defined as 1,100 to 2,999 $ct \cdot min^{-1}$, IW-MVPA = the daily sum of accelerometer counts during moderate- to vigorous-intensity physical activity defined as ≥ 3,000 $ct \cdot min^{-1}$, SE = standard error of the estimate.

Multivariable linear regression model: transformed fat mass (g) = energy intake (kcal/d) + IW-HLPA ($\times 10^3$ ct/d) + age (year) + birth weight (g) + fat-free mass (g) + height (cm) + IW-MVPA ($\times 10^3$ ct/d).

For boys, n=122 at age 5, n=229 at age 8, and n=211 at age 11.

For girls, n=139 at age 5, n=241 at age 8, and n=227 at age 11.

APPENDIX A

ACCELEROMETER DATA

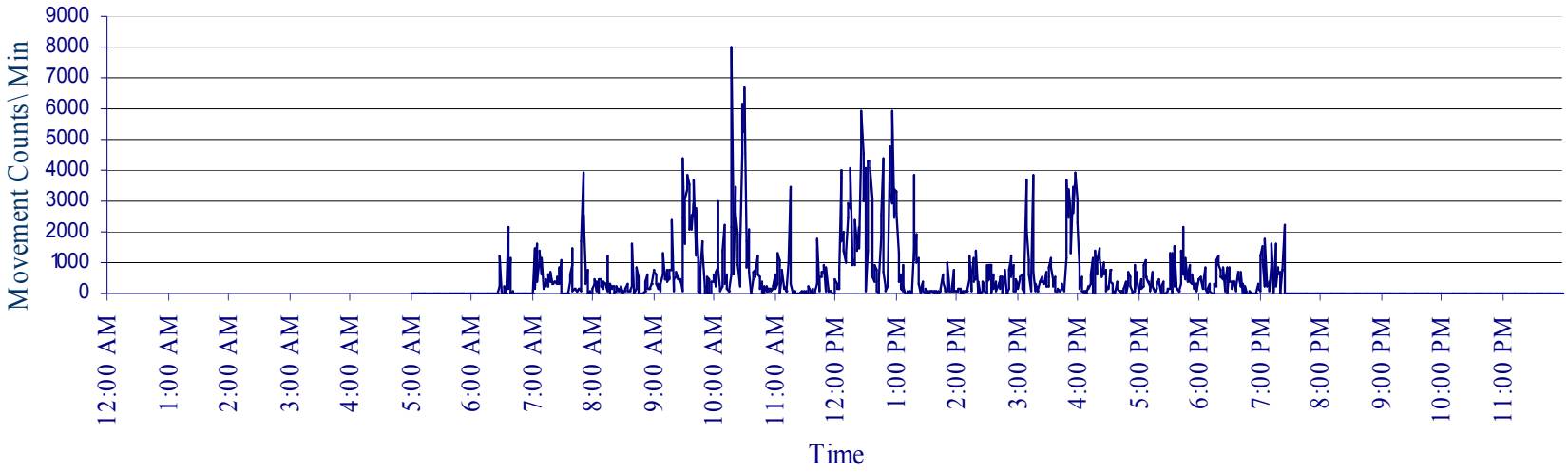


Figure A1. Example of accelerometer data of one day for a five-year-old child

APPENDIX B

LIGHT-INTENSITY PHYSICAL ACTIVITY STUDY REVIEW

Table B1. Calibration studies suggesting accelerometer count cut-points for categorization of physical activity intensity

First author, year (Ref. no)	Study participants, age	Inactivity cut-point ($ct \cdot min^{-1}$)	LPA range ($ct \cdot min^{-1}$)
Actigraph			
*Sirard, 2005 [38]	269 children, 3-5 yr	<1206 for age 3 <1455 for age 4 <1595 for age 5	1206-<2459 for age 3 1455-<3247 for age 4 1595-<3563 for age 5
†Treuth, 2004 [40]	74 girls, 13-14 yr	<100	100-<3000
*Evenson, 2008 [167]	33 children, 5-8 yr	<100	101-2292
Reilly, 2003 [46]	30 children, 3-4 yr	<1100	None
Puyau, 2002 [44]	26 children, 6-16 yr	<800	800-<3200
Actiwatch			
Puyau, 2004 [48]	32 children, 7-18 yr	<50	50-<700
Puyau, 2002 [44]	26 children, 6-16 yr	<100	100-<900
Actical			
*Evenson, 2008 [167]	33 children, 5-8 yr	<44	45-2028
Puyau, 2004 [48]	32 children, 7-18 yr	<100	100-<1500
RT3			
Chu, 2007 [168]	35 children, 8-12 yr	<420	420-1860

Note: $ct \cdot min^{-1}$ = accelerometer movement counts per minute, LPA = light-intensity physical activity.

Studies were sorted by the type of accelerometer and the number of participants (descending).

*15 second-epoch, †30 second-epoch, 1 minute-epoch if not otherwise indicated,

Table B2. Descriptive studies of accelerometer-measured daily inactivity and light-intensity physical activity

First author, year (Ref. no)	Study participants	Results	Monitoring days,[1)] minimum monitoring h/d[2)]	Inactivity cut-point ($ct \cdot min^{-1}$)	LPA range ($ct \cdot min^{-1}$)
Actigraph					
Janz, 1995 [169]	30 children (50% girls) aged 7-15 yr	Inactivity: 53% vs. 58% of the mean monitoring time of 12.2 h/d in boys vs. girls.	6 d, 10 h/d	<25	None
Wickel, 2007 [170]	113 boys aged 6-12 yr (>95% Caucasian)	Inactivity: 50%, LPA: 37% of 13.5 h/one day when participating in an after-school organized youth sport (sport day). In a subsample of 38 boys, Time inactivity was greater in a sport day than in a non-sport day. Time LPA was not different.	1 d	≤2 METs in Age-specific MET equation[171]	2<- 4 METs
Matthew, 2008 [159]	386 children aged 6-11 yr, 466 adolescents aged 12-15 yr, and 429 adolescents aged 12-19 yr from the NHANES 2003-2004	Monitoring time-adjusted inactivity: 6 h/d for 6-11 yr, 7.5 h/d for 12-15 yr, 8h/d for 16-19 yr.[3)] Time inactivity was 10-20 min greater in girls than in boys. Mexican Americans aged 16-19 yr spent 25 min less in inactivity than Whites. Black girls aged 6-11 yr spent 10-20 min less in inactivity than White or Mexican American girls.	7 d, 10 h/d	<100	None
†Pate, 2006 [161]	1,578 6th grade girls from the TAAG	Inactivity: 56%, LPA: 41%, of the mean monitoring time of 13.8 h/d.	6 d, data imputation for 12 h/d	≤100	101-<3000
*Williams, 2008 [172]	198 children (50% girls) aged 3-4 yr from the CHAMPS	Inactivity: 55%, LPA: 33%, of the mean monitoring time of 12.7 h/d.	7 d, 5 h/d	<150	150-<1680

Table B2. continued

Mitchell, 2009 [173]	5,434 children (52% girls) aged 11-12 yr from the ALSPAC	Inactivity: 55% of the mean monitoring time of 13 h/d. Time inactivity was 20 min greater in girls than in boys.	7 d, 10 h/d	<200	200-<3600
Sardinha, 2008 [174]	308 Portugal children (48% girls) aged 9-10 yr	Inactivity: 40%, LPA: 37%, of the mean monitoring time of 13 h/d. Girls spent 20 min more in LPA and 30 min less in MVPA than boys.	4 d, 10 h/d	<500	500-<2000
Jago, 2006 [175]	473 Huston Boy Scouts aged 10-14 yr	Inactivity: 83%, LPA: 13%, of the mean monitoring time of 18 h/d at the baseline.	3 d, 13.3 h/d	<800	800-<3200
Byrd-Williams, 2007 [78]	169 4th grade children in Los Angeles area	Inactivity: 77%, LPA: 20%, of the mean monitoring time of 12.5 h/d. Boys spent less time in inactivity than girls. No difference in LPA by gender. No difference in Time inactivity and Time LPA by ethnicity (Hispanic vs. non-Hispanic).	5 d, 6 h/d	<800	800-<3200
Wrotniak, 2006 [79]	65 New York children (54% girls) aged 8-10 yr	Inactivity: 73%, LPA: 22%, of the mean monitoring time of 11.6 h/d. No difference in Time inactivity and Time LPA between boys and girls	7 d, 10 h/d	<800	800-<3200
Houwen, 2009 [176]	48 pairs of Dutch children with and without visual impairment (VI) aged 6-12 yr	Of the mean monitoring time of 12.2h/d, inactivity: 81% vs. 78%, LPA: 16% vs. 19% in children with VI vs. without VI.	8 d, 10 h/d	<800	800-<3200
Fisher, 2005 [162]	394 Scottish children (47% girls) aged 3-5 yr	Inactivity: 76%, LPA: 20%, of the mean monitoring time of 56 h. Time inactivity was less in boys. Time LPA was greater in boys.	6 d, 9 h/d	<1100	1100-3200

Table B2. continued

Hughes, 2006 [77]	116 obese and 53 age- and gender-matched non-obese Scottish children aged 5-11 yr	Of the mean monitoring time of 10 h/d, Inactivity: 81% vs. 80%, LPA: 16% vs. 17% in obese children vs. non-obese children.	7 d, 6 h/d	<1100	1100-3200
Montgomery, 2004 [67]	104 Scottish children (50% girls) aged 2.6-6.9 yr	Inactivity: 73% vs. 79%, LPA: 23% vs. 18% of 6-13 h/d in boys vs. girls.	3 d, 6 h/d	<1100	1100-3200
Reilly, 2004 [163]	78 U.K. children (49% girls) aged 3 yr from the SPARKLE	Of the mean monitoring time of 9.8 h/d at baseline, inactivity: a median of 76% vs. 81% in boys vs. girls, LPA: 18%. Of the mean monitoring time of 10.9 h/d at 2-yr follow-up, inactivity: 73% vs. 78% in boys vs. girls, LPA: 20%.	3 d at baseline, 7 d at follow-up	<1100	1100-<3200
Kelly, 2007 [165]	A subcohort of 42 participants of Reilly's study [163]	Low tracking of inactivity over 2 yr (r=-0.15 in boys, r=0.35 in girls).	3 d at baseline, 7 d at follow-up, 6 h/d	<1100	1100-<3200
Kelly, 2005 [164]	41 rural Irish children (53% girls) aged 4-6 yr	Inactivity: 74% vs. 82%, LPA: 20% vs. 16% in boys vs. girls.	7 d, 6 h/d	<1100	1100-<3200
Moller, 2009 [177]	589 3rd grade children in 1997/1998 and 709 3rd grade children in 2003/2004 (ages 8-10)	Inactivity+LPA: 76% vs. 80% of 14 h/d[4)] in boys vs. girls. PA did not decrease during the two time points.	5 d, 10 h/d	None	<1000
§Baquet, 2007 [178]	26 French children (50%) aged 8-10 yr	Inactivity+LPA: 70% of the mean monitoring time of 14 h/d.	7 d, almost all day[5)]	None	<1950

Table B2. continued

Actiwatch					
Butte, 2007 [75]	897 Hispanic children and adolescents (62% girls) aged 4-19 yr	Of the mean monitoring time of 23.5 h/d, inactivity: 34% vs. 41% in NO vs. OW boys, 35% vs. 40% in NO vs. OW girls, LPA: 55% vs. 50% in NO vs. OW boys, 56% vs. 52% in NO vs. OW girls. Time inactivity increased with age. Time LPA decreased with age.	24 h for 3 d, 16.7 h/d	<50	50-<700
Treuth, 2005 [76]	229 children and adolescents (56% girls) aged 7-19 yr in rural Maryland	Of the mean monitoring time of 16 h/d, inactivity: 47%, 51%, and 56%, LPA: 46%, 43%, and 39% for elementary, middle, and high school students.	6 d, 11.7 h/d	<100	100-<900
RT3					
Hussey, 2007 [179]	152 Dublin children (62% girls) aged 7-10 yr	Time inactivity+Time LPA: 85% vs. 88% of the mean monitoring time of 18.3 h/d in boys vs. girls.	4 d, not reported	100-970	100-970
Parfitt, 2009 [180]	57 U.K. children (60% girls) aged 9-10 yr	Very LPA+LPA: 5.7 h/d.	7 d, 10 h/d for a weekday and 8 h/d for a weekend day	None	Very LPA: 100-470 LPA: 470.1-976.8

Note: ALSPAC = Avon Longitudinal Study of Parents and Children, CHAMPS = Children's Activity and Movement in Preschool Study, $ct \cdot min^{-1}$ = accelerometer movement counts per minutes, NHANES = National Health and Nutrition Examination Survey, LPA: light-intensity physical activity, MET = metabolic equivalent, MVPA = moderate- to vigorous-intensity physical activity, NO = non-overweight, OW = overweight, PA = physical activity, SPARKLE = Study of Preschool Activity, Lifestyle and Energetics, TAGG = Trial of Activity for Adolescent Girls, Time inactivity = time spent being sedentary, Time LPA = time spent in light-intensity physical activity, VHPA = very high physical activity, VI = visual impairment.

Table B2. continued

Studies were sorted by the type of accelerometer, a lower threshold of LPA (ascending), and the number of participants (descending).

Proportions of hours spent in inactivity and LPA to the mean accelerometer monitoring hours are presented. If time spent in inactivity and LPA or their proportions were reported alone without the mean monitoring time in original articles, they are presented without indication of the mean monitoring time.

[1)]The number of days on which participants were asked to wear accelerometers.

[2)]Minimum monitoring hours/day required for inclusion in data analysis.

[3)]The mean monitoring time in adults and children from the NAHES 2003-2004 was 13.9h/d.

[4)]Time inactivity and Time LPA were adjusted for 14 waking hours/d.

[§]2 second-epoch, *15 second-epoch, [†]30 second-epoch, 1 minute-epoch if not otherwise indicated.

Table B3. Association studies of accelerometer-measured daily inactivity and light-intensity physical activity with health outcomes

First author, year (Ref. no)	Study participants	Covariates considered	Results	Accelerometer, monitoring days,[1)] minimum monitoring h/d[2)]	Inactivity cut-point ($ct \cdot min^{-1}$)	LPA range ($ct \cdot min^{-1}$)
Obesity						
Mitchell, 2009 [173]	5,434 children (52% girls) aged 11-12 yr from ALSPAC	MVPA, gender, social factors,[‡] early life sleep and TV viewing habits, pubertal status	A significant association between obesity and Time inactivity (OR=1.3) was negated after adjustment for MVPA (OR=1.1).	Actigraph, 7 d, 10 h/d	<200	200-<3600
Butte, 2007 [75]	897 Hispanic children and adolescents (62% girls) aged 4-19 yr	Age, gender	Time inactivity was positively correlated with %BF (r=0.28) and Z-BMI-adjusted WC (r=0.14). Time LPA was inversely correlated with %BF (r=-0.30) and Z-BMI-adjusted WC (r=-0.15).	Actiwatch, 24 h for 3 d, 16.7 h/d	<50	50-<700
Treuth, 2005 [76]	229 children and adolescents (56% girls) aged 7-19 yr in rural Maryland	Gender- and school age group-specific analysis	Obesity measures (BMI for age, fat mass, and %BF) were correlated with inactivity (r=0.42 to 0.54) and LPA (r=-0.40 to -0.51), but not with MPA and VPA in girls. No association in boys.	Actiwatch, 6 d, 11.7 h/d	<100	100-<900

Table B3. continued

Hughes, 2006 [77]	116 obese and 53 matched non-obese Scottish children aged 5-11 yr	Matched for age and gender	No difference in Time inactivity (p=0.10) and Time LPA (p=0.10) between the obese and non-obese groups.	Actigraph, 7 d, 6 h/d	<1100	1100-3200
Byrd-Williams, 2007 [78]	169 4th grade children in Los Angeles area	Gender- and ethnicity-specific analysis	No difference in Time inactivity (p=0.5) and Time LPA (p=0.9) between overweight and non-overweight children.	Actigraph, 5 d, 6 h/d	<800	800-<3200
Hussey, 2007 [179]	152 Dublin children (62% girls) aged 7-10 yr	Age, gender	Z-BMI and WC were not significant predictors of Time inactivity+Time LPA.	RT3, 4 d, not reported	100-970	100-970
Wrotniak, 2006 [79]	65 New York children (54% girls) aged 8-10 yr	None	Inactivity (r=0.28) and MVPA (r=0.30), but not LPA (r=-0.18), were correlated with Z-BMI.	Actigraph, 7 d, 10 h	<800	800-3200
Houwen, 2009 [176]	48 pairs of Dutch children with and without visual impairment (VI) aged 6-12 yr	Age, gender, degree of VI	BMI was correlated with inactivity (r=0.30) and LPA (r=-0.30) in children with VI. No correlation in children without VI.	Actigraph, 8 d, 10 h/d	<800	800-<3200
Insulin resistance						
Butte, 2007 [75]	897 Hispanic children and adolescents (62% girls) aged 4-19 yr	Age, gender, Z-BMI	Serum insulin was correlated with Time inactivity (r=0.13) and Time LPA (r=-0.12).	Actiwatch, 24 h for 3 d, 16.7 h/d	<50	50-<700

Table B3. continued

Sardinha, 2008 [174]	308 Portugal children (48% girls) aged 9-10 yr	Monitoring time, MVPA, gender, age, physical maturity, birth weight, fat mass, central fat mass, total PA, fat mass, central fat mass,	In a regression model, inactivity (p=0.01), but not LPA (p=0.76), was significant predictors of insulin resistance.	Actigraph, 4 d, 10 h/d	<500	500-<2000
Bone Health						
Tobias, 2007 [181]	4,457 children (52% girls) aged 11-12 yr from the ALSPAC	Age, gender, height, lean mass, fat mass, socio-economic factors	Time inactivity +Time LPA was positively associated with lower limb BMC, bone area, and BMD	Actigraph, 7 d, 10 h/d	none	<3600
Motor skills						
Fisher, 2005 [162]	394 Scottish children (47% girls) aged 3-5 yr	None	No correlation between fundamental movement skills and Time LPA (r=0.02).	Actigraph, 6 d, 9 h/d	<1100	1100-3200
*Williams, 2008 [172]	198 children (50% girls) aged 3-4 yr	Gender, age, race, BMI, parent education	A high locomotor score was associated with low Time inactivity, but not with Time LPA	Actigraph, 7 d, 5 h/d	<150	150-<1680

Table B3. continued

Houwen, 2009 [176]	48 pairs of Dutch children with and without visual impairment (VI) aged 6-12 yr	Age, gender, degree of VI, BMI	In children with VI, locomotor scores were correlated with Time inactivity (r=-0.31) and Time LPA (r=0.30), but not Time MVPA (r=0.19), and objective control skills were correlated with Time inactivity (r=0.37). No correlation between motor skills and inactivity and LPA in children without VI.	Actigraph, 8 d, 10 h/d	<800	800-<3200
Wrotniak, 2006 [79]	65 New York children (54% girls) aged 8-10 yr	None	Inactivity (r=-0.31) and MVPA (r=0.30), but not LPA (r=0.22), were correlated with motor proficiency.	Actigraph, 7 d, 10 h/d	<800	800-<3200
Psychological health						
Parfitt, 2009 [180]	57 U.K. children (60% girls) aged 9-10 yr	%BF	Very LPA was correlated with anxiety (r=0.33), depression (r=0.28), global self-worth (r=-0.3), scholastic competence (r=-0.29), physical appearance (r=-0.28), and physical self-worth (r=-0.27).	RT3, 7 d, 10 h/d for a weekday and 8 h/d for a weekend day	None	Very LPA: 100-470 LPA: 470.1-976.8

Table B3. continued

Note: ALSPAC = Avon Longitudinal Study of Parents and Children, BMC = bone mineral content, BMD = done mineral density, BMI = body mass index, $ct \cdot min^{-1}$ = accelerometer movement counts per minutes, LPA = light-intensity physical activity, MPA: moderate-intensity physical activity, MVPA = moderate- to vigorous-intensity physical activity, NO = non-overweight, OR = odds ratio, OW = overweight, PA = physical activity, Time inactivity = time spent being sedentary, Time LPA = time spent in light-intensity physical activity, Time MVPA = time spent in moderate- to vigorous-intensity physical activity, VPA = vigorous-intensity physical activity, WC = waist circumference, %BF = percent body fat.

Studies were sorted by health outcome and the number of participants (descending).

[1)]The number of days on which participants were asked to wear accelerometers.

[2)]Minimum monitoring hours/day required for inclusion in data analysis.

*15 second-epoch, [†]30 second-epoch, 1 minute-epoch if not otherwise indicated.

[‡]Social factors include social class, mother's education, maternal smoking status during pregnancy, mother's weight status, birth weight, and gestational age.

APPENDIX C

CARDIORESPIRATORY FITNESS AND CARDIOVASCULAR RISK FACORS

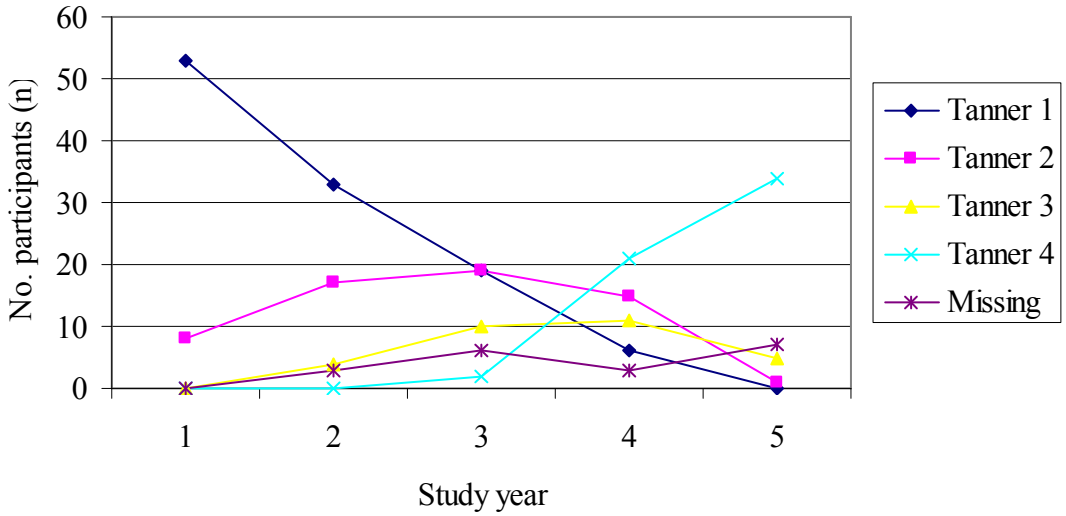


Figure C1. Distribution of Tanner stage according to study year among boys

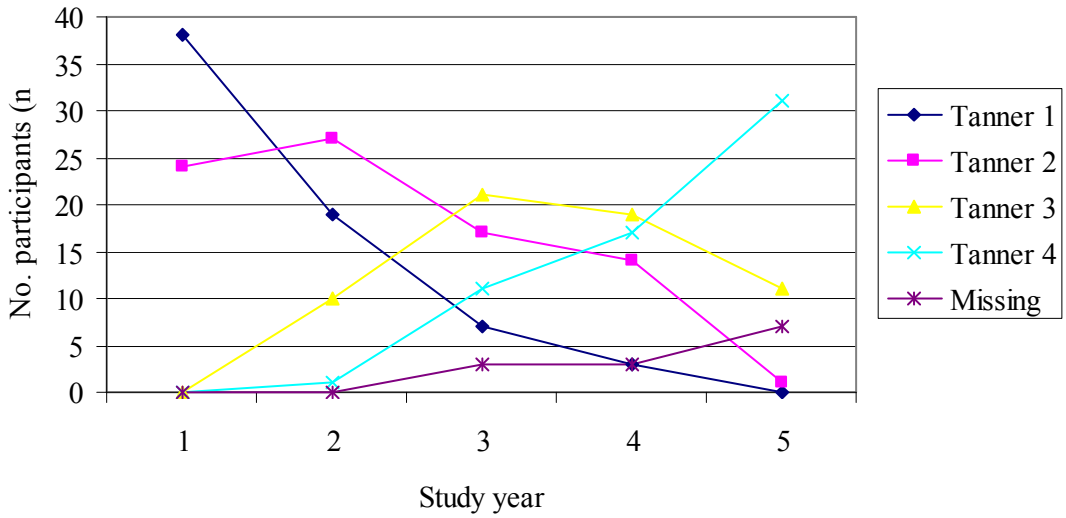


Figure C2. Distribution of Tanner stage according to study year among girls

Table C1. Mixed models to predict systolic blood pressure percentile

	Boys (λ=0.5)			Girls (λ=0.5)		
	β	SE	*P*-value	*β*	SE	*P*-value
Intercept	24.63	7.83	<0.01	28.03	8.43	<0.01
Tanner 1	1.57	3.29	0.63	2.79	4.05	0.49
Tanner 2	-1.41	2.62	0.59	0.24	3.05	0.94
Tanner 3	-2.56	2.02	0.21	3.41	2.31	0.14
Weight (kg)	0.00	0.17	0.98	-0.02	0.24	0.95
Sum of skinfolds (cm)	1.28	0.45	<0.01	1.88	0.61	<0.01
VO_2 max (L/min)	2.68	2.77	0.33	0.18	3.91	0.96

Note: Transformed systolic blood pressure percentile was used as an outcome variable. Tanner stage 4 was used as a reference group.

Table C2. Mixed models to predict diastolic blood pressure percentile

	Boys (λ=0.5)			Girls (λ=1.0)		
	β	SE	*P*-value	*β*	SE	*P*-value
Intercept	47.99	10.75	<0.0001	50.28	9.21	<0.0001
Tanner stage 1	1.58	4.87	0.75	-2.29	4.45	0.61
Tanner stage 2	-0.58	3.99	0.89	-2.26	3.39	0.51
Tanner stage 3	-1.94	3.22	0.55	-1.72	2.59	0.51
Weight (kg)	0.03	0.24	0.89	-0.85	0.27	<0.01
Sum of skinfolds (cm)	0.80	0.64	0.21	3.03	0.66	<0.0001
VO_2 max (L/min)	-0.55	4.06	0.89	6.27	4.34	0.15

Note: Transformed diastolic blood pressure percentile was used as an outcome variable. Tanner stage 4 was used as a reference group.

Table C3. Mixed models to predict total cholesterol

	Boys (λ=1.0)			Girls (λ=0)		
	β	SE	*P*-value	*β*	SE	*P*-value
Intercept	461.58	35.28	<0.0001	438.00	25.53	<0.0001
Centered age (yr)	-0.02	1.32	0.99	-0.77	0.88	0.39
Tanner stage 1	3.63	4.33	0.41	0.31	3.78	0.93
Tanner stage 2	4.46	3.82	0.25	3.27	2.98	0.28
Tanner stage 3	6.80	3.51	0.06	1.79	2.28	0.44
Weight (kg)	-0.16	0.19	0.41	-0.46	0.21	<0.05
Height (cm)	-0.23	0.24	0.35	0.25	0.20	0.21
Sum of skinfolds (cm)	1.57	0.48	<0.01	1.73	0.48	<0.001
VO_2 max (L/min)	0.30	2.77	0.91	-1.57	2.96	0.60

Note: Transfomed total cholesterol (mg/dL) was used as an outcome variable. Tanner stage 4 was used as a reference group.

Table C4. Mixed models to predict triglyceride

	Boys (λ=1.0)			Girls (λ=0)		
	β	SE	*P*-value	*β*	SE	*P*-value
Intercept	259.85	13.98	<0.0001	468.15	46.51	<0.0001
Centered age (yr)	-0.28	0.80	0.73	-1.76	1.62	0.28
Tanner stage 1 (T1)	-2.18	2.05	0.29	-1.61	7.77	0.84
Tanner stage 2 (T2)	-2.44	1.96	0.22	-0.92	6.15	0.88
Tanner stage 3 (T3)	-5.55	3.08	0.08	3.50	4.83	0.47
Centered age × T1	-0.36	0.79	0.65	--	--	--
Centered age × T2	1.39	1.10	0.21	--	--	--
Centered age × T3	4.09	2.40	0.09	--	--	--
Weight (kg)	-0.09	0.12	0.44	-0.99	0.42	<0.05
Height (cm)	0.01	0.10	0.90	0.80	0.36	<0.05
Sum of skinfolds (cm)	0.57	0.24	<0.05	4.16	0.91	<0.0001
VO_2 max (L/min)	-2.21	1.34	0.10	1.22	6.00	0.84

Note: Transformed triglyceride (mg/dL) was used as an outcome variable. Tanner stage 4 was used as a reference group.

Table C5. Mixed models to predict high-density lipoprotein cholesterol

	Boys (λ=0)			Girls (λ=0.5)		
	β	SE	*P*-value	*β*	SE	*P*-value
Intercept	260.30	3.35	<0.0001	79.77	9.48	<0.0001
Centered age (yr)	-0.12	0.13	0.36	0.09	0.47	0.84
Tanner stage 1 (T1)	-0.83	0.48	0.09	-5.68	1.82	<0.01
Tanner stage 2 (T2)	-0.78	0.43	0.07	-5.00	1.55	<0.01
Tanner stage 3 (T3)	-0.33	0.42	0.43	-5.13	1.62	<0.01
Centered age × T1	--	--	--	-0.34	0.66	0.61
Centered age × T2	--	--	--	0.03	0.64	0.97
Centered age × T3	--	--	--	2.10	0.73	<0.01
Weight (kg)	0.00	0.02	0.97	-0.01	0.08	0.95
Height (cm)	0.01	0.02	0.80	-0.03	0.07	0.62
Sum of skinfolds (cm)	-0.08	0.05	0.12	-0.27	0.17	0.13
VO_2 max (L/min)	0.18	0.32	0.58	1.01	1.19	0.40

Note: Transformed high-density lipoprotein cholesterol (mg/dL) was used as an outcome variable. Tanner stage 4 was used as a reference group.

Table C6. Mixed models to predict low-density lipoprotein cholesterol

	Boys (λ=0)			Girls (λ=1.0)		
	β	SE	*P*-value	*β*	SE	*P*-value
Intercept	117.24	6.07	<0.0001	99.11	28.23	<0.001
Centered age (yr)	0.16	0.21	0.45	-1.11	0.97	0.25
Tanner stage 1	0.75	0.74	<0.05	6.93	4.32	0.11
Tanner stage 2	1.82	0.65	<0.01	9.29	3.39	<0.01
Tanner stage 3	1.47	0.59	<0.05	3.65	2.57	0.16
Weight (kg)	-0.07	0.04	0.10	-0.42	0.24	0.08
Height (cm)	0.01	0.04	0.86	0.24	0.22	0.28
Sum of skinfolds (cm)	0.26	0.08	<0.01	1.83	0.54	<0.01
VO_2 max (L/min)	-0.31	0.48	0.53	0.02	3.34	0.99

Note: Transformed low-density lipoprotein cholesterol (mg/dL) was used as an outcome variable. Tanner stage 4 was used as a reference group.

APPENDIX D

ADIPOSITY AND SUBSEQUENT PHYSICAL ACTIVITY

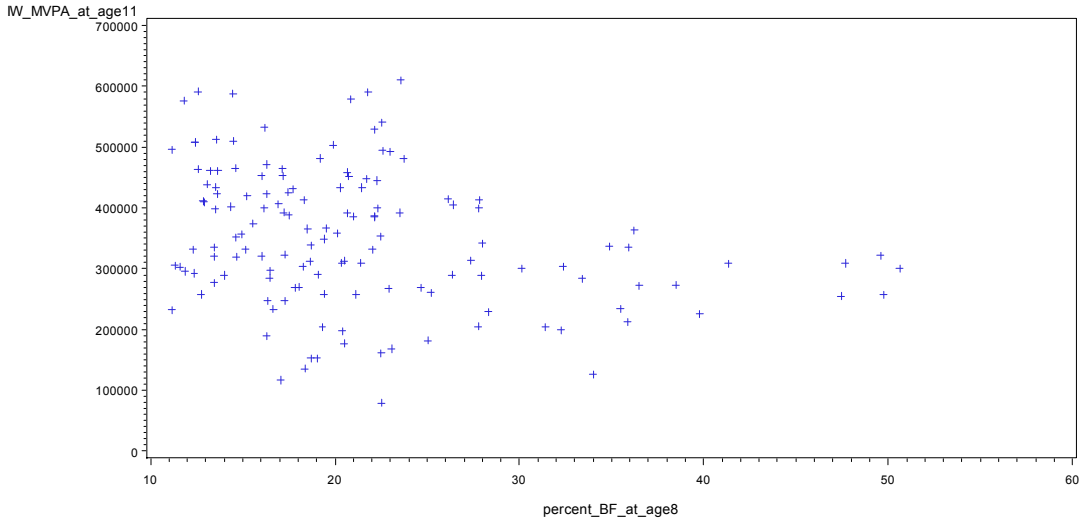


Figure D1. Scattor plots of transformed IW-MVPA at age 11 and percent body fat at age 8 among boys (n=142)

Note: IW-MVPA = intensity-weighted moderate- to vigorous-intensity physical activity, BF = body fat.

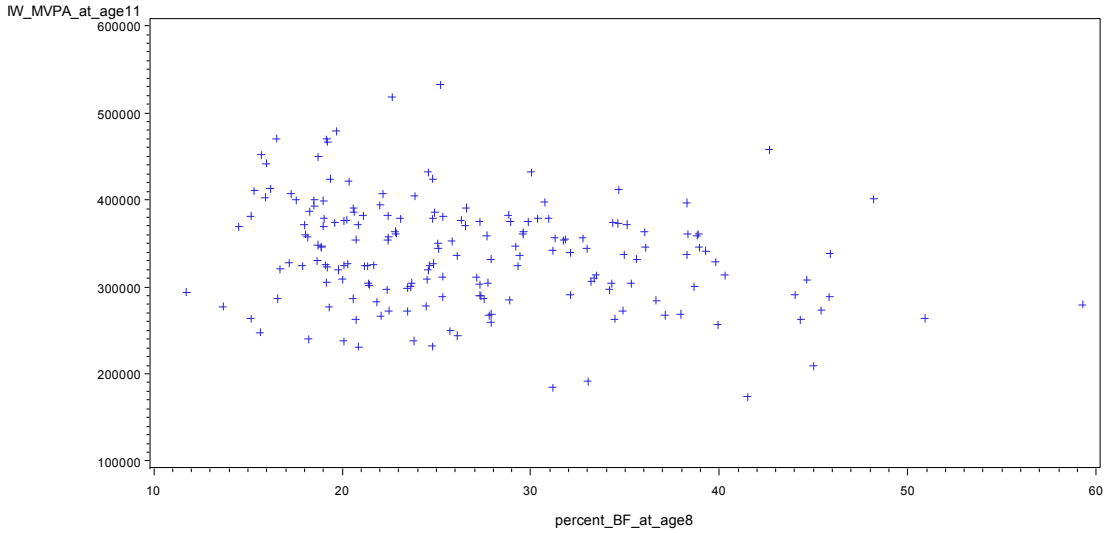


Figure D2. Scattor plots of transformed IW-MVPA at age 11 and percent body fat at age 8 among girls (n=184)

Note: IW-MVPA = intensity-weighted moderate- to vigorous-intensity physical activity, BF = body fat.

APPENDIX E

LIGHT-INTENSITY PHYSICAL ACTIVITY AND ADIPOSITY

Table E1. Multivariable linear regression models to predict fat mass based on IW-LPA among boys

	Age 5 (n=203)			Age 8 (n=242)			Age 11 (n=216)		
Exposure variable	*β*	*SE*	*P*	*β*	*SE*	*P*	*β*	*SE*	*P*
Intercept	1.2×10^{7}	1,807	<0.0001	2.1×10^{5}	4,608	<0.0001	1.5×10^{5}	11,914	<0.0001
Age (yr)	-519	179	<0.01	-588	275	<0.05	-2,743	908	<0.01
Fat-free mass (g)	0.32	0.06	<0.0001	0.67	0.07	<0.0001	1.25	0.09	<0.0001
Height (cm)	15.0	22.2	0.50	32.0	43.3	0.46	-194.3	62.4	<0.01
Birth weight (g)	0.16	0.12	0.17	0.001	0.29	1.00	0.03	0.51	0.96
IW-MVPA ($\times10^{3}$ ct/d)	-0.002	0.001	<0.01	-0.009	0.001	<0.0001	-0.01	0.002	<0.0001
IW-LPA ($\times10^{3}$ ct/d)	0.37	0.96	0.69	-2.27	2.31	0.33	-13.91	4.85	<0.01

Table E2. Multivariable linear regression models to predict fat mass based on IW-LPA among girls

	Age 5 (n=232)			Age 8 (n=257)			Age 11 (n=233)		
Exposure variable	*β*	*SE*	*P*	*β*	*SE*	*P*	*β*	*SE*	*P*
Intercept	5.2×10^{5}	2,171	<0.0001	2.5×10^{5}	4,891	<0.0001	1.5×10^{5}	13,283	<0.0001
Age (yr)	-75	201	0.71	-376	305	0.22	-21	1,027	0.98
Fat-free mass (g)	0.54	0.07	<0.0001	0.89	0.09	<0.0001	1.35	0.11	<0.0001
Height (cm)	-7.6	28.5	0.80	2.6	49.9	0.96	-384.3	66.1	<0.0001
Birth weight (g)	-0.03	0.13	0.80	0.26	0.34	0.43	1.08	0.56	0.06
IW-MVPA ($\times10^{3}$ ct/d)	-0.004	0.001	<0.0001	-0.005	0.002	<0.01	-0.01	0.004	<0.05
Physical maturity	--	--	--	--	--	--	843	1,072	0.43
IW-LPA ($\times10^{3}$ ct/d)	-0.25	1.09	0.82	-5.41	2.60	<0.05	-8.93	4.88	0.07

Note: *β* = regression parameter estimate, IW-LPA = intensity-weighted light-intensity physical activity, IW-MVPA = intensity-weighted moderate- to vigorous-intensity physical activity, SE = standard error. Transformed fat mass (g) was used as an outcome variable.

Table E3. Multivariable linear regression models to predict fat mass based on IW-HLPA among boys

	Age 5 (n=203)			Age 8 (n=242)			Age 11 (n=216)		
Exposure variable	*B*	*SE*	*P*	*B*	*SE*	*P*	*B*	*SE*	*P*
Intercept	1.2×10^{7}	1764	<0.0001	2.1×10^{5}	4643	<0.0001	1.5×10^{5}	11745	<0.0001
Age (yr)	-520	178	<0.01	-684	278	<0.05	-2,775	901	<0.01
Fat-free mass (g)	0.32	0.06	<0.0001	0.70	0.07	<0.0001	1.27	0.09	<0.0001
Height (cm)	15.0	22.2	0.50	18.4	44.2	0.68	-200.8	62.0	<0.01
Birth weight (g)	0.16	0.12	0.17	-0.11	0.29	0.70	0.04	0.51	0.94
IW-MVPA ($\times10^{3}$ ct/d)	-0.002	0.001	<0.01	-0.01	0.001	<0.0001	-0.01	0.002	<0.001
IW-HLPA ($\times10^{3}$ ct/d)	0.38	1.12	0.74	-2.96	3.08	0.34	-20.79	6.13	<0.001

Table E4. Multivariable linear regression models to predict fat mass based on IW-HLPA among girls

	Age 5 (n=232)			Age 8 (n=257)			Age 11 (n=233)		
Exposure variable	*B*	*SE*	*P*	*B*	*SE*	*P*	*B*	*SE*	*P*
Intercept	5.3×10^{5}	2113	<0.0001	2.5×10^{5}	4788	<0.0001	1.5×10^{5}	13133	<0.0001
Age (yr)	-68	201	0.74	-362	304	0.23	-23	1020	0.98
Fat-free mass (g)	0.54	0.07	<0.0001	0.90	0.09	<0.0001	1.35	0.11	<0.0001
Height (cm)	-6.7	28.4	0.81	1.6	49.7	0.97	-387.6	65.8	<0.0001
Birth weight (g)	-0.03	0.13	0.81	-0.29	0.34	0.39	1.05	0.56	0.06
IW-MVPA ($\times10^{3}$ ct/d)	-0.004	0.001	<0.0001	-0.004	0.002	<0.05	-0.01	0.004	<0.05
Physical maturity	--	--	--	--	--	--	860	1,066	0.42
IW-HLPA ($\times10^{3}$ ct/d)	0.03	1.32	0.98	-8.14	3.33	<0.05	-16.12	6.61	<0.05

Note: β = regression parameter estimate, IW-HLPA = intensity-weighted light-intensity physical activity, IW-MVPA = intensity-weighted moderate- to vigorous-intensity physical activity, SE = standard error. Transformed fat mass (g) was used as an outcome variable.

REFERENCES

1. Strauss RS, Pollack HA. Epidemic increase in childhood overweight, 1986-1998. *JAMA*. 2001;286(22):2845-2848.

2. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA*. 2002;288(14):1728-1732.

3. Thomson Reuters. Trend tracker: Rising pediatric obesity has strong implications for healthcare providers. http://provider.thomsonhealthcare.com/News/view/?id=1467. Updated 2007. Sep.10, 2008.

4. Must A, Strauss RS. Risks and consequences of childhood and adolescent obesity. *Int J Obes Relat Metab Disor*d. 1999;23 Suppl 2:S2-11.

5. Center for Disease Control and Prevention. Overweight and obesity. http://www.cdc.gov/nccdphp/dnpa/obesity/index.htm. Updated July 28, 2008. Accessed Sep.10, 2008.

6. Jolliffe CJ, Janssen I. Vascular risks and management of obesity in children and adolescents. *Vasc Health Risk Mana*g. 2006;2(2):171-187.

7. Nwobu CO, Johnson CC. Targeting obesity to reduce the risk for type 2 diabetes and other co-morbidities in African American youth: a review of the literature and recommendations for prevention. *Diab Vasc Dis Re*s. 2007;4(4):311-319.

8. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatric*s. 1998;101(3 Pt 2):518-525.

9. Williams J, Wake M, Hesketh K, Maher E, Waters E. Health-related quality of life of overweight and obese children. *JAM*A. 2005;293(1):70-76.

10. Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. *JAM*A. 2003;289(14):1813-1819.

11. Dietz WH, Gortmaker SL. Preventing obesity in children and adolescents. *Annu Rev Public Healt*h. 2001;22:337-353.

12. Bell CG, Walley AJ, Froguel P. The genetics of human obesity. *Nat Rev Gene*t. 2005;6(3):221-234.

13. van Vliet-Ostaptchouk JV, Hofker MH, van der Schouw YT, Wijmenga C, Onland-Moret NC. Genetic variation in the hypothalamic pathways and its role on obesity. *Obes Re*v. 2009;10(6):593-609.

14. Dietz WH. Periods of risk in childhood for the development of adult obesity--what do we need to learn? *J Nut*r. 1997;127(9):1884S-1886S.

15. Rogers I, EURO-BLCS Study Group. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. *Int J Obes Relat Metab Disor*d. 2003;27(7):755-777.

16. Rogers IS, Ness AR, Steer CD, et al. Associations of size at birth and dual-energy X-ray absorptiometry measures of lean and fat mass at 9 to 10 y of age. *Am J Clin Nut*r. 2006;84(4):739-747.

17. Pintauro SJ, Nagy TR, Duthie CM, Goran MI. Cross-calibration of fat and lean measurements by dual-energy X-ray absorptiometry to pig carcass analysis in the pediatric body weight range. *Am J Clin Nut*r. 1996;63(3):293-298.

18. Sopher AB, Thornton JC, Wang J, Pierson RN,Jr, Heymsfield SB, Horlick M. Measurement of percentage of body fat in 411 children and adolescents: a comparison of dual-energy X-ray absorptiometry with a four-compartment model. *Pediatric*s. 2004;113(5):1285-1290.

19. Physical Activity Guidelines Advisory Committee. *Physical activity guidelines advisory committee report.* Washington, DC: U.S. Department of Health and Human Services; 2008.

20. Freedman DS, Ogden CL, Berenson GS, Horlick M. Body mass index and body fatness in childhood. *Curr Opin Clin Nutr Metab Car*e. 2005;8(6):618-623.

21. Schaefer F, Georgi M, Wuhl E, Scharer K. Body mass index and percentage fat mass in healthy German schoolchildren and adolescents. *Int J Obes Relat Metab Disor*d. 1998;22(5):461-469.

22. Bray GA, DeLany JP, Harsha DW, Volaufova J, Champagne CC. Evaluation of body fat in fatter and leaner 10-y-old African American and white children: the Baton Rouge Children's Study. *Am J Clin Nut*r. 2001;73(4):687-702.

23. Freedman DS, Wang J, Maynard LM, et al. Relation of BMI to fat and fat-free mass among children and adolescents. *Int J Obes (Lond*). 2005;29(1):1-8.

24. Wickramasinghe VP, Cleghorn GJ, Edmiston KA, Murphy AJ, Abbott RA, Davies PS. Validity of BMI as a measure of obesity in Australian white Caucasian and Australian Sri Lankan children. *Ann Hum Bio*l. 2005;32(1):60-71.

25. Daniels SR, Khoury PR, Morrison JA. The utility of body mass index as a measure of body fatness in children and adolescents: differences by race and gender. *Pediatric*s. 1997;99(6):804-807.

26. Gallagher D, Visser M, Sepulveda D, Pierson RN, Harris T, Heymsfield SB. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemio*l. 1996;143(3):228-239.

27. Sarria A, Garcia-Llop LA, Moreno LA, Fleta J, Morellon MP, Bueno M. Skinfold thickness measurements are better predictors of body fat percentage than body mass index in male Spanish children and adolescents. *Eur J Clin Nut*r. 1998;52(8):573-576.

28. Gutin B. Child obesity can be reduced with vigorous activity rather than restriction of energy intake. *Obesity (Silver Spring*). 2008;16(10):2193-2196.

29. Lee S, Kuk JL, Katzmarzyk PT, Blair SN, Church TS, Ross R. Cardiorespiratory fitness attenuates metabolic risk independent of abdominal subcutaneous and visceral fat in men. *Diabetes Car*e. 2005;28(4):895-901.

30. U.S. Department of Health and Human Services. Physical activity guidelines for Americans. http://www.health.gov/paguidelines/. Updated 2008. Accessed Jan. 10, 2009.

31. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exer*c. 2008;40(1):181-188.

32. Sallis JF, Prochaska JJ, Taylor WC. A review of correlates of physical activity of children and adolescents. *Med Sci Sports Exer*c. 2000;32(5):963-975.

33. Howell J. The 1996 surgeon general's Report on Physical Activity and Health. *Nurse Pract Foru*m. 1996;7(3):104.

34. Seabra AF, Mendonca DM, Thomis MA, Anjos LA, Maia JA. Biological and socio-cultural determinants of physical activity in adolescents. *Cad Saude Public*a. 2008;24(4):721-736.

35. Welk GJ. *Physical activity assessment for health related research.* Champaign,IL: Human Kinetics Publishers; 2002.

36. Goran MI. Measurement issues related to studies of childhood obesity: assessment of body composition, body fat distribution, physical activity, and food intake. *Pediatric*s. 1998;101(3 Pt 2):505-518.

37. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. *Res Q Exerc Spor*t. 2000;71(2 Suppl):S1-14.

38. Sirard JR, Pate RR. Physical activity assessment in children and adolescents. *Sports Me*d. 2001;31(6):439-454.

39. Troiano RP. A timely meeting: objective measurement of physical activity. *Med Sci Sports Exer*c. 2005;37(11 Suppl):S487-9.

40. Treuth MS, Schmitz K, Catellier DJ, et al. Defining accelerometer thresholds for activity intensities in adolescent girls. *Med Sci Sports Exer*c. 2004;36(7):1259-1266.

41. Hendelman D, Miller K, Baggett C, Debold E, Freedson P. Validity of accelerometry for the assessment of moderate intensity physical activity in the field. *Med Sci Sports Exer*c. 2000;32(9 Suppl):S442-9.

42. Levine JA, Baukol PA, Westerterp KR. Validation of the Tracmor triaxial accelerometer system for walking. *Med Sci Sports Exer*c. 2001;33(9):1593-1597.

43. Midorikawa T, Tanaka S, Kaneko K, et al. Evaluation of low-intensity physical activity by triaxial accelerometry. *Obesity (Silver Spring*). 2007;15(12):3031-3038.

44. Puyau MR, Adolph AL, Vohra FA, Butte NF. Validation and calibration of physical activity monitors in children. *Obes Re*s. 2002;10(3):150-157.

45. Freedson PS, Sirard J, Debold E, et al. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exer*c. 1997;29(5):S45.

46. Reilly JJ, Coyle J, Kelly L, Burke G, Grant S, Paton JY. An objective method for measurement of sedentary behavior in 3- to 4-year olds. *Obes Re*s. 2003;11(10):1155-1158.

47. Trost SG, Ward DS, Moorehead SM, Watson PD, Riner W, Burke JR. Validity of the computer science and applications (CSA) activity monitor in children. *Med Sci Sports Exer*c. 1998;30(4):629-633.

48. Puyau MR, Adolph AL, Vohra FA, Zakeri I, Butte NF. Prediction of activity energy expenditure using accelerometers in children. *Med Sci Sports Exer*c. 2004;36(9):1625-1631.

49. Mattocks C, Leary S, Ness A, et al. Calibration of an accelerometer during free-living activities in children. *Int J Pediatr Obe*s. 2007;2(4):218-226.

50. Mattocks C, Ness A, Leary S, et al. Use of accelerometers in a large field-based study of children: protocols, design issues, and effects on precision. *J Phys Act Health*. 2008;5 Suppl 1:S98-111.

51. Rowland TW. Evolution of maximal oxygen uptake in children. *Med Sport Sc*i. 2007;50:200-209.

52. Armstrong N, Welsman JR. Aerobic fitness: what are we measuring? *Med Sport Sc*i. 2007;50:5-25.

53. Loomba-Albrecht LA, Styne DM. Effect of puberty on body composition. *Curr Opin Endocrinol Diabetes Obe*s. 2009;16(1):10-15.

54. Cumming SP, Standage M, Gillison F, Malina RM. Sex differences in exercise behavior during adolescence: is biological maturation a confounding factor? *J Adolesc Healt*h. 2008;42(5):480-485.

55. Neinstein LS, Kaufman FR. *Adolescent Health Care: A Practical Guide.* 4th edition ed. Baltimore:MD: Lippincott Williams and Wilkins; 2002.

56. Mirwald RL, Baxter-Jones AD, Bailey DA, Beunen GP. An assessment of maturity from anthropometric measurements. *Med Sci Sports Exer*c. 2002;34(4):689-694.

57. Mota J, Guerra S, Leandro C, Pinto A, Ribeiro JC, Duarte JA. Association of maturation, sex, and body fat in cardiorespiratory fitness. *Am J Hum Bio*l. 2002;14(6):707-712.

58. Thompson AM, Baxter-Jones AD, Mirwald RL, Bailey DA. Comparison of physical activity in male and female children: does maturation matter? *Med Sci Sports Exer*c. 2003;35(10):1684-1690.

59. Kwiterovich PO,Jr, Barton BA, McMahon RP, et al. Effects of diet and sexual maturation on low-density lipoprotein cholesterol during puberty: the Dietary Intervention Study in Children (DISC). *Circulatio*n. 1997;96(8):2526-2533.

60. Altwaijri YA, Day RS, Harrist RB, Dwyer JT, Ausman LM, Labarthe DR. Sexual maturation affects diet-blood total cholesterol association in children: Project HeartBeat! *Am J Prev Med*. 2009;37(1 Suppl):S65-70.

61. Niinikoski H, Lagstrom H, Jokinen E, et al. Impact of repeated dietary counseling between infancy and 14 years of age on dietary intakes and serum lipids and lipoproteins: the STRIP study. *Circulation*. 2007;116(9):1032-1040.

62. Morrow JR, Freedson PS. Relationship between habitual physical activity and aerobic fitness in adolescents. *Pediatr Exerc Sci*. 1994;6:315-329.

63. Goran MI, Treuth MS. Energy expenditure, physical activity, and obesity in children. *Pediatr Clin North Am*. 2001;48(4):931-953.

64. Janz KF, Kwon S, Letuchy EM, et al. Sustained effect of early physical activity on body fat mass in older children. *Am J Prev Med*. 2009;37(1):35-40.

65. Levine JA, Vander Weg MW, Klesges RC. Increasing non-exercise activity thermogenesis: a NEAT way to increase energy expenditure in your patients. *Obes Manag*. 2006;1:146-151.

66. Donahoo WT, Levine JA, Melanson EL. Variability in energy expenditure and its components. *Curr Opin Clin Nutr Metab Care*. 2004;7(6):599-605.

67. Montgomery C, Reilly JJ, Jackson DM, et al. Relation between physical activity and energy expenditure in a representative sample of young children. *Am J Clin Nutr*. 2004;80(3):591-596.

68. Levine JA, Eberhardt NL, Jensen MD. Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science*. 1999;283(5399):212-214.

69. Levine JA, Schleusner SJ, Jensen MD. Energy expenditure of nonexercise activity. *Am J Clin Nutr*. 2000;72(6):1451-1454.

70. Levine JA. Non-exercise activity thermogenesis (NEAT). *Best Pract Res Clin Endocrinol Metab*. 2002;16(4):679-702.

71. Levine JA. Non-exercise activity thermogenesis. *Proc Nutr Soc*. 2003;62(3):667-679.

72. Levine JA. Non-exercise activity thermogenesis (NEAT). *Nutr Rev*. 2004;62(7 Pt 2):S82-97.

73. Pate RR, O'Neill JR, Lobelo F. The evolving definition of "sedentary". *Exerc Sport Sci Rev*. 2008;36(4):173-178.

74. Shephard RJ. Limits to the measurement of habitual physical activity by questionnaires. *Br J Sports Med*. 2003;37(3):197-206; discussion 206.

75. Butte NF, Puyau MR, Adolph AL, Vohra FA, Zakeri I. Physical activity in nonoverweight and overweight Hispanic children and adolescents. *Med Sci Sports Exerc*. 2007;39(8):1257-1266.

76. Treuth MS, Hou N, Young DR, Maynard LM. Accelerometry-measured activity or sedentary time and overweight in rural boys and girls. *Obes Res*. 2005;13(9):1606-1614.

77. Hughes AR, Henderson A, Ortiz-Rodriguez V, Artinou ML, Reilly JJ. Habitual physical activity and sedentary behaviour in a clinical sample of obese children. *Int J Obes (Lond)*. 2006;30(10):1494-1500.

78. Byrd-Williams C, Kelly LA, Davis JN, Spruijt-Metz D, Goran MI. Influence of gender, BMI and Hispanic ethnicity on physical activity in children. *Int J Pediatr Obes*. 2007;2(3):159-166.

79. Wrotniak BH, Epstein LH, Dorn JM, Jones KE, Kondilis VA. The relationship between motor proficiency and physical activity in children. *Pediatrics*. 2006;118(6):e1758-65.

80. Thompson AM, Campagna PD, Durant M, Murphy RJ, Rehman LA, Wadsworth LA. Are overweight students in Grades 3, 7, and 11 less physically active than their healthy weight counterparts? *Int J Pediatr Obes*. 2009;4(1):28-35.

81. Must A, Tybor DJ. Physical activity and sedentary behavior: a review of longitudinal studies of weight and adiposity in youth. *Int J Obes (Lond)*. 2005;29 Suppl 2:S84-96.

82. Hu FB. Physical activity, sedentary behaviors, and obesity. In: Hu FB, ed. *Obesity Epidemiology.* New York:NY: Oxford University Press; 2008:301-319.

83. Godin G, Belanger-Gravel A, Nolin B. Mechanism by which BMI influences leisure-time physical activity behavior. *Obesity (Silver Spring)*. 2008;16(6):1314-1317.

84. Ajzen I. The theory of planned behavior. *Organ Behav Hum Decis Process*. 1991;50:179-211.

85. Henderson M, Daneman D, Hux J, Hanley A. Exercise interventions in obese youth: are they effective? *J Pediatr Endocrinol Metab*. 2008;21(9):823-826.

86. Petersen L, Schnohr P, Sorensen TI. Longitudinal study of the long-term relation between physical activity and obesity in adults. *Int J Obes Relat Metab Disord*. 2004;28(1):105-112.

87. Bak H, Petersen L, Sorensen TI. Physical activity in relation to development and maintenance of obesity in men with and without juvenile onset obesity. *Int J Obes Relat Metab Disord*. 2004;28(1):99-104.

88. Mortensen LH, Siegler IC, Barefoot JC, Gronbaek M, Sorensen TI. Prospective associations between sedentary lifestyle and BMI in midlife. *Obesity (Silver Spring)*. 2006;14(8):1462-1471.

89. Weiss DR, O'Loughlin JL, Platt RW, Paradis G. Five-year predictors of physical activity decline among adults in low-income communities: a prospective study. *Int J Behav Nutr Phys Act*. 2007;4:2.

90. Ekelund U, Brage S, Besson H, Sharp S, Wareham NJ. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality? *Am J Clin Nutr*. 2008;88(3):612-617.

91. Sallis JF, Alcaraz JE, McKenzie TL, Hovell MF. Predictors of change in children's physical activity over 20 months. Variations by gender and level of adiposity. *Am J Prev Med*. 1999;16(3):222-229.

92. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. *Arch Pediatr Adolesc Med*. 2003;157(8):821-827.

93. Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. *Pediatrics*. 2004;114(2):e198-205.

94. Celik T, Iyisoy A, Yuksel UC. Pediatric metabolic syndrome: A growing threat. *Int J Cardiol*. In press.

95. Nguyen NT, Magno CP, Lane KT, Hinojosa MW, Lane JS. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the National Health and Nutrition Examination Survey, 1999 to 2004. *J Am Coll Surg*. 2008;207(6):928-934.

96. De Ferranti SD, Osganian SK. Epidemiology of paediatric metabolic syndrome and type 2 diabetes mellitus. *Diab Vasc Dis Res*. 2007;4(4):285-296.

97. Morrison JA, Friedman LA, Gray-McGuire C. Metabolic syndrome in childhood predicts adult cardiovascular disease 25 years later: the Princeton Lipid Research Clinics Follow-up Study. *Pediatrics*. 2007;120(2):340-345.

98. Morrison JA, Friedman LA, Wang P, Glueck CJ. Metabolic syndrome in childhood predicts adult metabolic syndrome and type 2 diabetes mellitus 25 to 30 years later. *J Pediatr*. 2008;152(2):201-206.

99. Srinivasan SR, Bao W, Wattigney WA, Berenson GS. Adolescent overweight is associated with adult overweight and related multiple cardiovascular risk factors: the Bogalusa Heart Study. *Metabolism*. 1996;45(2):235-240.

100. Gutin B, Islam S, Manos T, Cucuzzo N, Smith C, Stachura ME. Relation of percentage of body fat and maximal aerobic capacity to risk factors for atherosclerosis and diabetes in black and white seven- to eleven-year-old children. *J Pediatr*. 1994;125(6 Pt 1):847-852.

101. Katzmarzyk PT, Malina RM, Bouchard C. Physical activity, physical fitness, and coronary heart disease risk factors in youth: the Quebec Family Study. *Prev Med*. 1999;29(6 Pt 1):555-562.

102. Carnethon MR, Gulati M, Greenland P. Prevalence and cardiovascular disease correlates of low cardiorespiratory fitness in adolescents and adults. *JAMA*. 2005;294(23):2981-2988.

103. Shaibi GQ, Cruz ML, Ball GD, et al. Cardiovascular fitness and the metabolic syndrome in overweight latino youths. *Med Sci Sports Exerc*. 2005;37(6):922-928.

104. Anderssen SA, Cooper AR, Riddoch C, et al. Low cardiorespiratory fitness is a strong predictor for clustering of cardiovascular disease risk factors in children independent of country, age and sex. *Eur J Cardiovasc Prev Rehabil*. 2007;14(4):526-531.

105. Janssen I, Cramp WC. Cardiorespiratory fitness is strongly related to the metabolic syndrome in adolescents. *Diabetes Care*. 2007;30(8):2143-2144.

106. Ruiz JR, Ortega FB, Rizzo NS, et al. High cardiovascular fitness is associated with low metabolic risk score in children: the European Youth Heart Study. *Pediatr Res*. 2007;61(3):350-355.

107. Ortega FB, Ruiz JR, Castillo MJ, Sjostrom M. Physical fitness in childhood and adolescence: a powerful marker of health. *Int J Obes (Lond)*. 2008;32(1):1-11.

108. Imperatore G, Cheng YJ, Williams DE, Fulton J, Gregg EW. Physical activity, cardiovascular fitness, and insulin sensitivity among U.S. adolescents: the National Health and Nutrition Examination Survey, 1999-2002. *Diabetes Care*. 2006;29(7):1567-1572.

109. Eisenmann JC, Katzmarzyk PT, Perusse L, Tremblay A, Despres JP, Bouchard C. Aerobic fitness, body mass index, and CVD risk factors among adolescents: the Quebec family study. *Int J Obes (Lond)*. 2005;29(9):1077-1083.

110. Eisenmann JC, Welk GJ, Wickel EE, Blair SN. Combined influence of cardiorespiratory fitness and body mass index on cardiovascular disease risk factors among 8-18 year old youth: The Aerobics Center Longitudinal Study. *Int J Pediatr Obes*. 2007;2(2):66-72.

111. Eisenmann JC, Welk GJ, Ihmels M, Dollman J. Fatness, fitness, and cardiovascular disease risk factors in children and adolescents. *Med Sci Sports Exerc*. 2007;39(8):1251-1256.

112. DuBose KD, Eisenmann JC, Donnelly JE. Aerobic fitness attenuates the metabolic syndrome score in normal-weight, at-risk-for-overweight, and overweight children. *Pediatrics*. 2007;120(5):e1262-8.

113. Andersen LB, Sardinha LB, Froberg K, Riddoch CJ, Page AS, Anderssen SA. Fitness, fatness and clustering of cardiovascular risk factors in children from Denmark, Estonia and Portugal: the European Youth Heart Study. *Int J Pediatr Obes*. 2008;3 Suppl 1:58-66.

114. Ekelund U, Anderssen SA, Froberg K, et al. Independent associations of physical activity and cardiorespiratory fitness with metabolic risk factors in children: the European youth heart study. *Diabetologia*. 2007;50(9):1832-1840.

115. Kwon S, Burns TL, Janz KF. Associations of Cardiorespiratory Fitness and Fatness with Cardiovascular Risk Factors among Adolescents: the NHANES 1999-2002. *J Phys Act Health*. In press.

116. Boreham C, Twisk J, Murray L, Savage M, Strain JJ, Cran G. Fitness, fatness, and coronary heart disease risk in adolescents: the Northern Ireland Young Hearts Project. *Med Sci Sports Exerc*. 2001;33(2):270-274.

117. Rizzo NS, Ruiz JR, Hurtig-Wennlof A, Ortega FB, Sjostrom M. Relationship of physical activity, fitness, and fatness with clustered metabolic risk in children and adolescents: the European youth heart study. *J Pediatr*. 2007;150(4):388-394.

118. Ondrak KS, McMurray RG, Bangdiwala SI, Harrell JS. Influence of aerobic power and percent body fat on cardiovascular disease risk in youth. *J Adolesc Health*. 2007;41(2):146-152.

119. Thomas NE, Cooper SM, Williams SP, Baker JS, Davies B. Relationship of fitness, fatness, and coronary-heart-disease risk factors in 12- to 13-year-olds. *Pediatr Exerc Sci*. 2007;19(1):93-101.

120. Ruiz JR, Ortega FB, Warnberg J, Sjostrom M. Associations of low-grade inflammation with physical activity, fitness and fatness in prepubertal children; the European Youth Heart Study. *Int J Obes (Lond)*. 2007;31(10):1545-1551.

121. McMurray RG, Bangdiwala SI, Harrell JS, Amorim LD. Adolescents with metabolic syndrome have a history of low aerobic fitness and physical activity levels. *Dyn Med*. 2008;7:5.

122. Harrell JS, McMurray RG, Gansky SA, Bangdiwala SI, Bradley CB. A public health vs a risk-based intervention to improve cardiovascular health in elementary school children: the Cardiovascular Health in Children Study. *Am J Public Health*. 1999;89(10):1529-1535.

123. Ferreira I, Twisk JW, van Mechelen W, Kemper HC, Stehouwer CD. Development of fatness, fitness, and lifestyle from adolescence to the age of 36 years: determinants of the metabolic syndrome in young adults: the amsterdam growth and health longitudinal study. *Arch Intern Med*. 2005;165(1):42-48.

124. Eisenmann JC, Wickel EE, Welk GJ, Blair SN. Relationship between adolescent fitness and fatness and cardiovascular disease risk factors in adulthood: the Aerobics Center Longitudinal Study (ACLS). *Am Heart J*. 2005;149(1):46-53.

125. Ortega FB, Ruiz JR, Castillo MJ, et al. Health-related physical fitness according to chronological and biological age in adolescents. The AVENA study. *J Sports Med Phys Fitness*. 2008;48(3):371-379.

126. Kimm SY, Barton BA, Obarzanek E, et al. Obesity development during adolescence in a biracial cohort: the NHLBI Growth and Health Study. *Pediatrics*. 2002;110(5):e54.

127. Barlow CE, Kohl HW,3rd, Gibbons LW, Blair SN. Physical fitness, mortality and obesity. *Int J Obes Relat Metab Disord*. 1995;19 Suppl 4:S41-4.

128. Lee CD, Blair SN, Jackson AS. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr*. 1999;69(3):373-380.

129. Melanson KJ, McInnis KJ, Rippe JM, Blackburn G, Wilson PF. Obesity and cardiovascular disease risk: research update. *Cardiol Rev*. 2001;9(4):202-207.

130. Tanner JM, Whitchouse. R.H., Marshall WA. *Assessment of skeletal maturity and prediction of adult height.* London: Academic Press; 1975.

131. Janz KF, Dawson JD, Mahoney LT. Increases in physical fitness during childhood improve cardiovascular health during adolescence: the Muscatine Study. *Int J Sports Med*. 2002;23 Suppl 1:S15-21.

132. Janz KF, Mahoney LT. Two year follow-up on the impact of physical fitness and boy fatness on children's heart growth and rising blood pressure. *Pediatr Exerc Sci*. 1995;7:364-378.

133. Janz KF, Dawson JD, Mahoney LT. Predicting heart growth during puberty: the Muscatine Study. *Pediatrics*. 2000;105:E631-E638.

134. Golden JC, Janz KF, Clarke WR, Mahoney LT. New protocol for submaximal and peak exercise values for children and adolescents:The Muscatine study. *Pediatr Exerc Sci*. 1991;2(129):140.

135. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18(6):499-502.

136. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114(2 Suppl 4th Report):555-576.

137. Nielsen GA, Andersen LB. The association between high blood pressure, physical fitness, and body mass index in adolescents. *Prev Med*. 2003;36(2):229-234.

138. Fernandez JR, Redden DT, Pietrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. *J Pediatr*. 2004;145(4):439-444.

139. Eisenmann JC. On the use of a continuous metabolic syndrome score in pediatric research. *Cardiovasc Diabetol*. 2008;7:17.

140. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106(25):3143-3421.

141. Freedman DS, Sherry B. The validity of BMI as an indicator of body fatness and risk among children. *Pediatrics*. 2009;124 Suppl 1:S23-34.

142. Roy LP. Measurement of blood pressure in children. *J Paediatr Child Health*. 1997;33(6):477-478.

143. Jimenez-Pavon D, Kelly J, Reilly JJ. Associations between objectively measured habitual physical activity and adiposity in children and adolescents: Systematic review. *Int J Pediatr Obes*. 2009:1-16.

144. Wareham NJ, van Sluijs EM, Ekelund U. Physical activity and obesity prevention: a review of the current evidence. *Proc Nutr Soc*. 2005;64(2):229-247.

145. Brownell KD, Schwartz MB, Puhl RM, Henderson KE, Harris JL. The need for bold action to prevent adolescent obesity. *J Adolesc Health*. 2009;45(3 Suppl):S8-17.

146. Storch EA, Milsom VA, Debraganza N, Lewin AB, Geffken GR, Silverstein JH. Peer victimization, psychosocial adjustment, and physical activity in overweight and at-risk-for-overweight youth. *J Pediatr Psychol*. 2007;32(1):80-89.

147. Faith MS, Leone MA, Ayers TS, Heo M, Pietrobelli A. Weight criticism during physical activity, coping skills, and reported physical activity in children. *Pediatrics*. 2002;110(2 Pt 1):e23.

148. Janz KF, Levy SM, Burns TL, Torner JC, Willing MC, Warren JJ. Fatness, physical activity, and television viewing in children during the adiposity rebound period: the Iowa Bone Development Study. *Prev Med*. 2002;35(6):563-571.

149. Janz KF, Burns TL, Levy SM, Iowa Bone Development Study. Tracking of activity and sedentary behaviors in childhood: the Iowa Bone Development Study. *Am J Prev Med*. 2005;29(3):171-178.

150. Janz KF, Burns TL, Torner JC, et al. Physical activity and bone measures in young children: the Iowa bone development study. *Pediatrics*. 2001;107(6):1387-1393.

151. Janz KF, Gilmore JM, Burns TL, et al. Physical activity augments bone mineral accrual in young children: The Iowa Bone Development study. *J Pediatr*. 2006;148(6):793-799.

152. Cliff DP, Reilly JJ, Okely AD. Methodological considerations in using accelerometers to assess habitual physical activity in children aged 0-5 years. *J Sci Med Sport*. 2009;12(5):557-567.

153. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr*. 1982;36(5):936-942.

154. Pols MA, Peeters PH, Bueno-De-Mesquita HB, et al. Validity and repeatability of a modified Baecke questionnaire on physical activity. *Int J Epidemiol*. 1995;24(2):381-388.

155. Ono R, Hirata S, Yamada M, Nishiyama T, Kurosaka M, Tamura Y. Reliability and validity of the Baecke physical activity questionnaire in adult women with hip disorders. *BMC Musculoskelet Disord*. 2007;8:61.

156. Williams DP, Going SB, Lohman TG, et al. Body fatness and risk for elevated blood pressure, total cholesterol, and serum lipoprotein ratios in children and adolescents. *Am J Public Health*. 1992;82(3):358-363.

157. Stevens J, Murray DM, Baggett CD, et al. Objectively assessed associations between physical activity and body composition in middle-school girls: the Trial of Activity for Adolescent Girls. *Am J Epidemiol*. 2007;166(11):1298-1305.

158. Valerio G, D'Amico O, Adinolfi M, Munciguerra A, D'Amico R, Franzese A. Determinants of weight gain in children from 7 to 10 years. *Nutr Metab Cardiovasc Dis*. 2006;16(4):272-278.

159. Matthews CE, Chen KY, Freedson PS, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. *Am J Epidemiol*. 2008;167(7):875-881.

160. Marshall TA, Eichenberger Gilmore JM, Broffitt B, Stumbo PJ, Levy SM. Relative validity of the Iowa Fluoride Study targeted nutrient semi-quantitative questionnaire and the block kids' food questionnaire for estimating beverage, calcium, and vitamin D intakes by children. *J Am Diet Assoc*. 2008;108(3):465-472.

161. Pate RR, Stevens J, Pratt C, et al. Objectively measured physical activity in sixth-grade girls. *Arch Pediatr Adolesc Med*. 2006;160(12):1262-1268.

162. Fisher A, Reilly JJ, Kelly LA, et al. Fundamental movement skills and habitual physical activity in young children. *Med Sci Sports Exerc*. 2005;37(4):684-688.

163. Reilly JJ, Jackson DM, Montgomery C, et al. Total energy expenditure and physical activity in young Scottish children: mixed longitudinal study. *Lancet*. 2004;363(9404):211-212.

164. Kelly LA, Reilly JJ, Grant S, Paton JY. Low physical activity levels and high levels of sedentary behaviour are characteristic of rural Irish primary school children. *Ir Med J*. 2005;98(5):138-141.

165. Kelly LA, Reilly JJ, Jackson DM, Montgomery C, Grant S, Paton JY. Tracking physical activity and sedentary behavior in young children. *Pediatr Exerc Sci*. 2007;19(1):51-60.

166. Maddison R, Mhurchu CN, Jull A, Jiang Y, Prapavessis H, Rodgers A. Energy expended playing video console games: an opportunity to increase children's physical activity? *Pediatr Exerc Sci*. 2007;19(3):334-343.

167. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. *J Sports Sci*. 2008:1-9.

168. Chu EY, McManus AM, Yu CC. Calibration of the RT3 accelerometer for ambulation and nonambulation in children. *Med Sci Sports Exerc*. 2007;39(11):2085-2091.

169. Janz KF, Witt J, Mahoney LT. The stability of children's physical activity as measured by accelerometry and self-report. *Med Sci Sports Exerc*. 1995;27(9):1326-1332.

170. Wickel EE, Eisenmann JC. Contribution of youth sport to total daily physical activity among 6- to 12-yr-old boys. *Med Sci Sports Exerc*. 2007;39(9):1493-1500.

171. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. *Med Sci Sports Exerc*. 2005;37(11 Suppl):S523-30.

172. Williams HG, Pfeiffer KA, O'Neill JR, et al. Motor skill performance and physical activity in preschool children. *Obesity (Silver Spring)*. 2008;16(6):1421-1426.

173. Mitchell JA, Mattocks C, Ness AR, et al. Sedentary Behavior and Obesity in a Large Cohort of Children. *Obesity (Silver Spring)*. 2009;17(8):1596-1602.

174. Sardinha LB, Andersen LB, Anderssen SA, et al. Objectively measured time spent sedentary is associated with insulin resistance independent of overall and central body fat in 9- to 10-year-old Portuguese children. *Diabetes Care*. 2008;31(3):569-575.

175. Jago R, Baranowski T, Baranowski JC, et al. Fit for Life Boy Scout badge: outcome evaluation of a troop and Internet intervention. *Prev Med*. 2006;42(3):181-187.

176. Houwen S, Hartman E, Visscher C. Physical activity and motor skills in children with and without visual impairments. *Med Sci Sports Exerc*. 2009;41(1):103-109.

177. Moller NC, Kristensen PL, Wedderkopp N, Andersen LB, Froberg K. Objectively measured habitual physical activity in 1997/1998 vs 2003/2004 in Danish children: the European Youth Heart Study. *Scand J Med Sci Sports*. 2009;19(1):19-29.

178. Baquet G, Stratton G, Van Praagh E, Berthoin S. Improving physical activity assessment in prepubertal children with high-frequency accelerometry monitoring: a methodological issue. *Prev Med*. 2007;44(2):143-147.

179. Hussey J, Bell C, Bennett K, O'Dwyer J, Gormley J. Relationship between the intensity of physical activity, inactivity, cardiorespiratory fitness and body composition in 7-10-year-old Dublin children. *Br J Sports Med*. 2007;41(5):311-316.

180. Parfitt G, Pavey T, Rowlands AV. Children's physical activity and psychological health: the relevance of intensity. *Acta Paediatr*. 2009;98(6):1037-1043.

181. Tobias JH, Steer CD, Mattocks CG, Riddoch C, Ness AR. Habitual levels of physical activity influence bone mass in 11-year-old children from the United Kingdom: findings from a large population-based cohort. *J Bone Miner Res*. 2007;22(1):101-109.