DEPARTAMENTO DE FISIOLOGÍA

FACULTAD DE MEDICINA

UNIVERSIDAD DE GRANADA

Influencia del Status Socioeconómico en la Condición Física de Adolescentes Europeos. Repercusión Endocrino-metabólica del Nivel de Condición Física

Influence of Socioeconomic Status on Physical Fitness in European Adolescents. Implications of Physical Fitness Level on Metabolic Hormones

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DAVID JIMÉNEZ PAVÓN

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“A Isa, mis padres, hermanos y a toda mi familia

con especial recuerdo para aquellos que se fueron”

“To Isa, my parents, brothers and the whole family

with special memory to those who left”

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Que la Tesis Doctoral titulada *“Influencia del Status Socioeconómico en la Condición Física de Adolescentes Europeos. Repercusión Endocrino-metabólica del Nivel de Condición Física”* que presenta D. **DAVID JIMÉNEZ PAVÓN** al superior juicio del Tribunal que designe la Universidad de Granada, ha sido realizada bajo mi dirección durante los años 2005-2010, siendo expresión de la capacidad técnica e interpretativa de su autor en condiciones tan aventajadas que le hacen merecedor del Título de Doctor con mención Europea, siempre y cuando así lo considere el citado Tribunal.

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Fdo. Jonatan Ruiz Ruiz

En Granada, 5 de Enero de 2010

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RESEARCH PROJECTS

The present PhD thesis is primarily based on data from the HELENA study but data from the AVENA study have also been used.

1. **The Healthy Lifestyle in Europe by Nutrition in Adolescence Cross study (HELENA study)** (2005-2008). The HELENA study is an EU-funded project conducted in some 3000 adolescents aged 12.5-17.5 years from 10 different European cities. The HELENA study aims to provide a broad picture of the nutritional status and lifestyle of the European adolescents, including objectively measured physical activity and a range of health-related fitness tests.
   Web site available: **www.helenastudy.com**
   Coordinator: Luis Moreno
   Responsible for physical fitness assessment: Manuel J. Castillo
   Responsible for physical activity assessment: Michael Sjöström
   Responsible for hormonal assessment: Marcela González-Gross
   Implication of the PhD candidate: participation in all workshops related to HELENA project, being part of the groups in charge of the physical fitness and hormonal assessment. The PhD candidate was also involved in part of the field work carried out in Zaragoza (Spain). Finally, the PhD candidate has been working in the data analysis and writing of scientific papers.

2. **Alimentación y Valoración del Estado Nutricional de los Adolescentes / Feeding and assessment of nutritional status of Spanish Adolescents (The AVENA Study)** (2000-2003). The AVENA study was conducted in around 3000 Spanish adolescents aged 13-18.5 years. Factors related with the adolescent´s physiological and psychological health status were assessed as well as a battery of health related fitness tests.

   Web site available: **www.estudioavena.com**
   Coordinator: Ascension Marcos
   Responsible for chemical pathology, fitness and physical activity assessments: Manuel J. Castillo
   Implication of the PhD candidate: the PhD candidate has been working in data analysis and writing of scientific papers.

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The AVENA study was funded by the Spanish Ministry of Health (FIS nº 00/0015) and grants form Panrico S.A. Madaus S.A. and Procter and Gamble S.A.

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LIST OF PUBLICATIONS

The present PhD Thesis is based on the following scientific manuscripts:

I. Jiménez-Pavón 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 Jun 26:1-16.

II. Jiménez-Pavón D, Ruiz JR, Ortega FB, Artero EG, España-Romero V, Castro-Piñero J, Gutiérrez A, Castillo MJ. Physical activity, fitness and fatness in children and adolescents. En: Epidemiology of Obesity in Children and Adolescents Prevalence and Aetiology. Coord: Luis Moreno Aznar. Ed: Springer International, Nueva York. *In press.*

III. Jiménez-Pavón D, Ortega FB, Ruiz JR, Chillón P, Castillo R, Artero EG, Martinez-Gómez D, Vicente-Rodríguez G, Rey-López JP, Gracia LA, Noriega MJ, Moreno LA, González-Gross M. Influence of socioeconomic factors on fitness and fatness in urban Spanish adolescents: The AVENA study. Int J Pediatr Obes. *In press*.

IV. Jiménez-Pavón D, Ortega FB, Ruiz JR, España-Romero V, Artero EG, Moliner-Urdiales D, Gómez-Martínez S, Vicente-Rodríguez G, Manios Y, Béghin L, Repasy J, Sjöström M, Moreno LA, González-Gross M, Castillo MJ. Associations of socioeconomic status and physical fitness in European adolescents independently of total body fat and physical activity; The HELENA Study. Nutr Hosp. *In press.*

V. Jiménez-Pavón D, Castillo MJ, Moreno L, Kafatos A, Manios Y, Kondaki K, Béghin L, Zaccaria M, De Henauw S, Widhalm K, Molnár D, Sjöström M, González-Gross M, Ruiz JR. Fitness and fatness are independently associated with markers of insulin resistance in European adolescents; The HELENA Study. *Submitted.*

VI. Jiménez-Pavón D, Ortega FB, Artero EG, Vicente-Rodríguez G, Huybrechts I, Moreno LA, Manios Y, Béghin L, Polito A, De Henauw S, Sjöström M, Castillo MJ, González-Gross M, Ruiz JR. Physical activity, fitness and serum leptin concentrations in adolescents: The HELENA Study. *Submitted.*

RESUMEN

El nivel de condición física y el grado de adiposidad que presentan los adolescentes europeos puede estar influenciado por diversos factores ligados al estilo de vida tales como la actividad física que realizan, pero también por aspectos socio-culturales como el status socioeconómico familiar.

El objetivo general de esta Tesis Doctoral Europea ha sido en primer lugar, analizar la evidencia científica disponible que relaciona la actividad física, la condición física y el grado de adiposidad durante la infancia y la adolescencia. En segundo lugar, estudiar la relación entre el status socioeconómico y el nivel de condición física de los adolescentes europeos, controlando por importantes factores de confusión entre los que se incluyen actividad física y adiposidad, ambas medidas o. En tercer lugar, determinar el papel que la condición física tiene sobre dos hormonas claves para la fisiología del tejido adiposo como son la insulina y la leptina.

Los adolescentes estudiados en la presente Tesis Doctoral estaban incluidos en los estudios AVENA y HELENA. La muestra está formada por 2474 adolescentes procedentes de cinco ciudades Españolas (Estudio AVENA) y por 2567 adolescentes procedentes de diez ciudades de nueve países Europeos (Estudio HELENA).

Los resultados indican que a) Tras revisar sistemáticamente la literatura científica, se constata que una elevada actividad física y un alto nivel de condición física están relacionados con un menor grado de adiposidad en niños y adolescentes. b) Un mayor nivel socioeconómico se asocia con una mejor condición física independientemente del nivel de actividad física y del grado de adiposidad. c) En adolescentes europeos, el exceso de grasa corporal se asocia a una menor sensibilidad a la insulina. Una buena condición física atenúa este efecto, disminuyendo la resistencia a la insulina. d) Una buena condición física se asocia con menores niveles de leptina, incluso tras controlar por la adiposidad y actividad física, medidas objetivamente.

En conclusión, existe una fuerte evidencia de que altos niveles de actividad física y condición física están asociados con un menor grado de adiposidad en niños y adolescentes. El status socioeconómico, independientemente de la actividad física y la adiposidad, influye positivamente en la condición física, y ésta a su vez tiene un efecto favorable sobre la sensibilidad a la insulina y los niveles de leptina.

ABSTRACT

The levels of physical fitness and adiposity of European adolescents can be influenced by several factors linked to lifestyle, among these factors, physical activity can be highlighted, but socio-cultural factors, including the familiar socioeconomic status, may be also be important.

The main aim of the PhD thesis was first, to analyze the evidence regarding the association of physical activity and fitness and with body fat in children and adolescents. Second, to study the association between socioeconomic status and the level of physical fitness in European adolescents after controlling for potential confounders including objectively measured physical activity and adiposity; and finally, to examine the independent role of physical fitness on two adiposity-related hormones, namely insulin and leptin.

The participants studied in the present PhD Thesis were gathered from the AVENA and HELENA studies. The sample comprised with a total of 2474 adolescents from five different Spanish cities (the AVENA study) and 2567 adolescents from ten cities of nine European countries (the HELENA study).

The findings indicate that a) After a systematic review of the literature, higher levels of objectively measured physical activity and fitness are associated with lower fatness. b) A high socioeconomic status is associated with a better physical fitness, independiently of physical activity and adiposity. c) The excess of body fat is associated with lower insulin sensitivity in European adolescents. High levels of physical fitness attenuate this effect, by decreasing insulin resistance. d) Higher levels of physical fitness are associated with lower serum leptin levels, even after controlling for the levels of adiposity and objectively measured physical activity.

In conclusion, there is strong evidence that higher levels of physical activity and fitness are associated with lower adiposity in children and adolescents. The socioeconomic status positively influences physical fitness regardless of physical activity and adiposity. Physical fitness has a favorable effect on insulin sensitivity and leptin levels.

ABBREVIATIONS

ABF	Abdominal body fat
ALPHA	Assessing Levels of Physical Activity
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
AVENA	Alimentación y Valoración del Estado Nutricional de los Adolescentes (Feeding and assessment of nutritional status of Spanish adolescents)
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CD	Compact disc
CDAH	Childhood Determinants of Adult Health
CRF	Cardiorespiratory fitness
CV	Curriculum Vitae
CVD	Cardiovascular disease
DXA	Dual-energy X-ray absorptiometry
EFFECTS	Evaluación Funcional y Fisiológica del Ejercicio. Ciencia y Tecnología de la Salud
ELISA	Enzyme-Linked InmunoSorbent Assay
EU	European Union
EUROFIT	Council of Europe Committee for the Development of Sport Test Battery
EYHS	European Youth Heart Study

FAS	Family Affluence Scale
FEDER	Fondo Europeo de Desarrollo Regional
FFM	Fat-free mass
FFMI	Fat free mass index
FITNESSGRAM	Fitness program (test battery)
FM	Fat mass
FMI	Fat mass index
FPU	Formación de Profesorado Universitario
HDL-c	High density lipoprotein cholesterol (Colesterol unido a lipoproteína de alta densidad)
HR	Heart rate
HELENA	Healthy Lifestyle in Europe by Nutrition in Adolescence
HOMA	Homeostasis model assessment
HTFM	High trunk fat mass
LDL-c	Low density lipoprotein cholesterol [Colesterol unido a lipoproteína de baja densidad]
MET	Metabolic equivalents
MPA	Moderate physical activity
MVPA	Moderate to Vigorous physical activity
NHANES	National Health and Nutrition Examination Survey
NS	Non significant
NTFN	Normal trunk fat mass
PA	Physical activity

PAL	Physical activity levels
PEPA	Play-equipment physical activity
SAT	Subcutaneous abdominal adipose
SD	Standard deviation
SEM	Standard error of the measure
SES	Socioeconomic status
SIG	Significant
SLJ	Standing long jump
SPSS	Statistical package for social sciences
ROC	Receiver operating characteristics
TBF	Total body fat
TC	Total cholesterol
TEM	Technical error of measurement
VAT	Visceral adipose tissue
VO_{2max}	Maximal oxygen consumption
VPA	Vigorous physical activity
WBF	Whole body fat
WC	Waist circumference
WHO	World Health Organization
% BF	Percentage body fat
4x10m SRT	4 x 10 meters shuttle run test
20m-SRT	20 meters shuttle run test

INTRODUCTION

Physical fitness is an important health marker both in adulthood (1) and adolescence (2-4). Recent evidence suggests that, in adults, low fitness level is also an important risk factor for cardiovascular disease being even considered as a predictor of cardiovascular and all-causes mortality (1). In adolescents, low physical fitness has been associated to higher levels of body fat and several cardiovascular risk factors (2, 3). This is important because cardiovascular disease (a typical adult condition) is the leading cause of death in European countries.

Adolescence is a crucial period in life. Physical fitness status is influenced by many factors, such as sexual maturation and growth. In addition, changes in body fat content and distribution as well as dynamic changes in various metabolic systems (including hormonal regulation) are known to occur during puberty (5). Lifestyle and many healthy/unhealthy behaviours are established during these years, and may remain for the rest of the life (6, 7). It is well known that an important component of a healthy lifestyle is physical activity (PA), which may influence body composition and fitness level in this crucial period of life. The socioeconomic status can also play an important and modulating role but little information is available regarding European adolescents.

Since the majority of non-communicable diseases present in European adults seem to have its origins in the first decades of life (8), societies and governments need to take responsibilities in order to assess the health status of European adolescents and to study the influence of lifestyle. In this context, two multicenter studies were carried out. One was performed in Spain, the AVENA study (2000-2002) (9). The other took place at European level, the HELENA study (20006-2007) (10). Both projects aimed to provide a broad picture of the nutritional status and lifestyle of the Spanish and European adolescents, respectively, including the measurement of PA, fitness and hormone profile, among others.

Conceptual definitions

Physical activity

Physical Activity is defined as any bodily movement produced by the contraction of skeletal muscles that increases energy expenditure above a basal level (11). During the last decades this concept has acquired great relevance in all populations' age groups but especially in children and adolescents because of its positive influence on several health-related factors.

There is evidence supporting a relationship between PA, overweight and obesity-related CVD risk factors and all-cause mortality in adults (12, 13), yet, studies focusing on children and adolescents are limited.

The measurement of PA is complex and existing methods can be grouped in three main categories, namely direct observation, subjective and objective methods. The first one is the direct observation through doubly labeled water and indirect calorimetry which is used as method of reference. However, PA has commonly been measured by subjective methods, such as self-reported questionnaires, interviewer questionnaires, and so on. These subjective methods allow assessing large numbers of adolescents with a low cost and little time compared with others methods more sophisticated such as the doubly labeled water. However, these techniques must be used cautiously in the pediatric population that has difficulty recalling such information. Recently, technologies have become available that allow the objective measurement of PA and its intensity. Devices such as heart rate, pedometers and accelerometers have been used as objective methods to measure PA having the advantages that it can be used in large sample studies and avoid the overestimation laid to subjective techniques in pediatric populations (14, 15). Especially, accelerometry has been the more widely used during the last decades allowing the researches to measure objectively the total amount of PA and the time spent at different intensities. Objectively measured PA levels seem to be negatively associated with insulin resistance and both total and central body fat in children and adolescents (16).

Physical fitness

Physical fitness is a set of attributes that people have or achieve that relates to the ability to perform PA. Another related term is *Health-related physical fitness* which refers to those components of physical fitness that have a relationship with health (3). These components are favorably or unfavorably affected by PA habits and are related to the health status. Health-related fitness is characterized by an ability to perform daily activities with vigor, and by traits and capacities that are associated with a low risk for the development of chronic diseases and premature death (3).

Physical fitness is considered an important health-related marker already in children and adolescents and its main components are muscular strength, speed-agility and cardiorespiratory fitness (CRF) (2, 3). High levels of CRF provides strong and independent prognostic information about the overall risk of illness and death, especially that from cardiovascular causes (1-3).

Less is known regarding the association between other fitness components (i.e.; muscular strength and motor fitness) and health-related outcomes. Results from cross-sectional studies in children and adolescents showed a negative relationship between muscular strength and obesity-related CVD risk factors such as blood lipids and insulin resistance (17-19). A recent systematic review concluded that due to a limited number of studies, there is inconclusive evidence for a relationship between muscular strength or motor fitness and CVD risk factors in young people (3).

Fatness (adiposity)

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems (20). It is not only the total amount of fat that is associated with poor health status, but also the distribution of fat in the body (21). In fact, abdominal fatness instead of total fatness, is nowadays used as a key component in the definition of the metabolic syndrome in both adults (22, 23) and young people (24).

Socioeconomic Status

Socioeconomic status is the combined economic and social position of a family (or individual) relative to others. Socioeconomic status is commonly measured by self-reported occupational social class but also income and educational attainment are used in both adults and adolescents (25, 26) and it has tipically been classed into three categories: low, middle and high. The use of this information in studies focused on adolescents seems to have several conceptual and methodological difficulties (27). Thereby, a new measure called "Family Affluence Scale" (FAS) was developed and started to be used in young population based studies (27).

Socioeconomic status may influence present and future health and wellbeing. Several health-related factors, such as birth weight, height, risk of metabolic syndrome and obesity, among other, have been reported to be associated to socioeconomic status in young and adult people (25, 28-30). Furthermore, several studies reported that low socioeconomic status in childhood may lead to higher morbidity, including CVD later in life (31-33).

Regarding the relationship between socioeconomic status and physical fitness in young people, the literature is scarce and the results are so far contradictory (26, 34-36). Whereas some studies (34) reported that young people from the low socioeconomic status group performed better in muscular and CRF, others observed that adolescents with higher socioeconomic status had higher CRF than those with lower socioeconomic status (35). A longitudinal study (36) observed that high socioeconomic status was associated with increases in activity and fitness from childhood to adulthood (36). Concerning the association between socioeconomic status and fatness, several studies (26, 37-40), but not all (25), showed that children in the most deprived families or low social class had higher risk of overweight and obesity.

It is important to highlight that both social and cultural contexts are often country and region-specific. Consequently, large population studies analyzing adolescents from different countries could be useful to provide an overall picture of the relationships between socioeconomic status, fitness and fatness in young people.

Fat-related hormones

Fat metabolism is influenced by several hormones. One of the most important and traditionally studied hormones is insulin (5, 41-47). More recently, other hormones such as leptin have gained relevance due to its key role in the regulation of fat metabolism (48-59).

Insulin

Insulin is a polypeptide hormone synthesized by beta-cells of the islets of Langerhans in the pancreas. It is a hormone that has extensive effects on metabolism and other body functions. Insulin is essential for blood glucose homeostasis but also for fat and protein metabolism. An increase in circulating insulin levels determines glucose uptake by insulin-sensitive tissues (among which is muscle) and promote glycogen deposition in liver and muscle cells, and vice-versa. Insulin also promotes lipogenesis, prevents lipolysis and induces fat accumulation, among other actions. Insulin action is impaired, to a variable extent, in some conditions such as obesity, type 2 diabetes and metabolic syndrome. The phenomenon is known as insulin resistance. Insulin resistance can be measured using different approaches, a simple one only takes into account fasting insulin and plasma glucose levels, and this is the preferred method for large epidemiological studies.

It is well known that insulin resistance is associated with adiposity not only in adults but also in children and adolescents (43). More recently, insulin resistance has also shown to be inversely associated with CRF (46) and PA (45). Longitudinal studies also pointed a negative association between fitness and insulin resistance (41, 42), yet a recent systematic review concluded that due to the limited number of studies, there is inconclusive evidence indicating that changes in CRF are associated with diabetes (3). Given the global increase in the prevalence of obesity, type 2 diabetes, and the metabolic syndrome (47), there is a need to further investigate how markers of insulin resistance are influenced by potentially modifiable factors, such as fatness and fitness in the European population.

Leptin

The adipose tissue is today recognized as an endocrine organ that secretes peptides known as adipokines. One adipokine which may function as modulators of metabolism is leptin (50). A major development in energy balance regulation has come with the discovery in 1994 of leptin. It is synthesized mainly in white adipose tissue in an amount proportional to body fat mass, but also in other tissues (i.e. stomach, intestines, placenta, testicles) (48, 59). The initial concept was that leptin informs the brain about the abundance of body fat (48), however, leptin has been associated with many others functions such as control of appetite and energy expenditure through hypothalamic pathways; direct effects on lipolysis, insulin secretion and sensitivity (*adipoinsular axis*) (50, 53). Leptin is also implicated in sexual maturation in adolescence (60).

Several studies have shown that PA, measured by questionnaire, was inversely associated with leptin in adolescents (51, 57, 58), whereas others found no association between objectively measured PA and leptin concentrations (51, 54). On the other hand, despite physical fitness is considered an important health-related marker already in children and adolescents, there are no studies examining the role of the main physical fitness components on leptin concentrations in adolescents. Several intervention studies showed that long or intense single bouts of exercise as well as physical training reduced leptin concentrations in children (49) and adults (52, 55, 56).

The main aim of the PhD thesis was first, to analyze the evidence regarding the association of physical activity and fitness and with body fat in children and adolescents. Second, to study the association between socioeconomic status and the level of physical fitness in European adolescents after controlling for potential confounders including objectively measured physical activity and adiposity; and finally, to examine the independent role of physical fitness on two adiposity-related hormones, namely insulin and leptin.

The relationships between the main concepts studied in this thesis and the correspondent papers in which those were treated, are displayed in Figure 1.

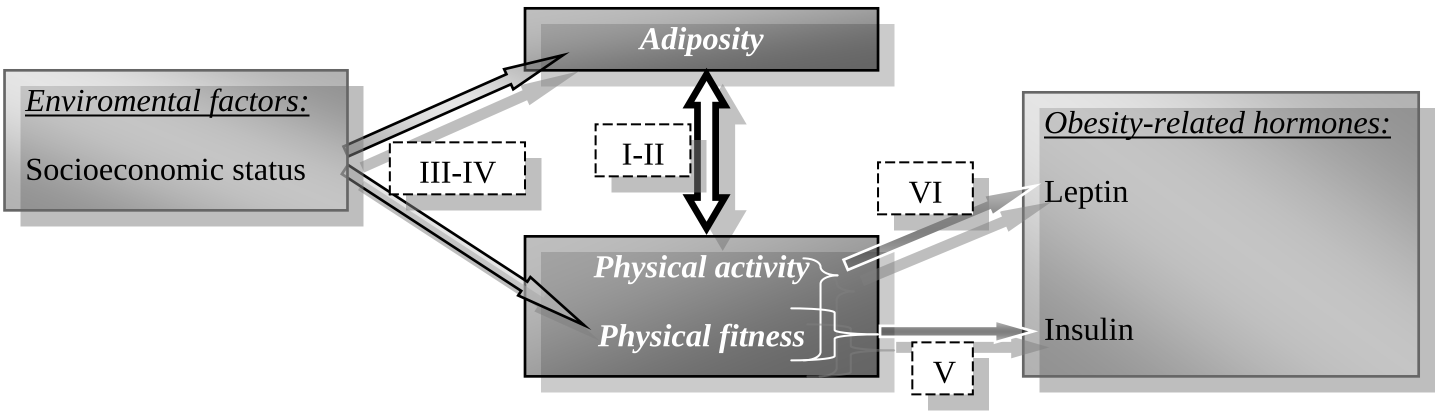

Figure 1. Main concepts and papers (from paper I to VI).

REFERENCES

1. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N, Sone H. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*. 2009 May 20;301(19):2024-35.

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

3. Ruiz JR, Castro-Pinero J, Artero EG, Orgeta FB, Sjostrom M, Suni J, Castillo MJ. Predictive Validity of Health-Related Fitness in Youth: A Systematic Review. *Br J Sports Med*. 2009 Jan 21.

4. Ruiz JR, Espana-Romero V, Ortega FB, Sjostrom M, Castillo MJ, Gutierrez A. Hand span influences optimal grip span in male and female teenagers. *J Hand Surg Am*. 2006 Oct;31(8):1367-72.

5. Ball GD, Shaibi GQ, Cruz ML, Watkins MP, Weigensberg MJ, Goran MI. Insulin sensitivity, cardiorespiratory fitness, and physical activity in overweight Hispanic youth. *Obes Res*. 2004 Jan;12(1):77-85.

6. Puska P. Possibilities of a preventive approach to coronary heart disease starting in childhood. *Acta Paediatr Scand Suppl*. 1985;318:229-33.

7. Viikari JS, Niinikoski H, Juonala M, Raitakari OT, Lagstrom H, Kaitosaari T, Ronnemaa T, Simell O. Risk factors for coronary heart disease in children and young adults. *Acta Paediatr Suppl*. 2004 Dec;93(446):34-42.

8. Berenson GS, Srinivasan SR, Bao W, Newman WP, 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med*. 1998 Jun 4;338(23):1650-6.

9. Gonzalez-Gross M, Castillo MJ, Moreno L, Nova E, Gonzalez-Lamuno D, Perez-Llamas F, Gutierrez A, Garaulet M, Joyanes M, Leiva A, Marcos A. [Feeding and assessment of nutritional status of spanish adolescents (AVENA study). Evaluation of

risks and interventional proposal. I.Methodology]. *Nutr Hosp*. 2003 Jan-Feb;18(1):15-28.

10. Moreno LA, De Henauw S, Gonzalez-Gross M, Kersting M, Molnar D, Gottrand F, Barrios L, Sjostrom M, Manios Y, Gilbert CC, Leclercq C, Widhalm K, Kafatos A, Marcos A. Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. *Int J Obes (Lond)*. 2008 Nov;32 Suppl 5:S4-11.

11. Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report, 2008. *Washington, DC: US Department of Health and Human Services*. 2008.

12. Oguma Y, Sesso HD, Paffenbarger RS, Jr., Lee IM. Physical activity and all cause mortality in women: a review of the evidence. *Br J Sports Med*. 2002 Jun;36(3):162-72.

13. Lollgen H, Bockenhoff A, Knapp G. Physical activity and all-cause mortality: an updated meta-analysis with different intensity categories. *Int J Sports Med*. 2009 Mar;30(3):213-24.

14. Adamo KB, Prince SA, Tricco AC, Connor-Gorber S, Tremblay M. A comparison of indirect versus direct measures for assessing physical activity in the pediatric population: a systematic review. *Int J Pediatr Obes*. 2009;4(1):2-27.

15. Corder K, Ekelund U, Steele RM, Wareham NJ, Brage S. Assessment of physical activity in youth. *J Appl Physiol*. 2008 Sep;105(3):977-87.

16. Dencker M, Andersen LB. Health-related aspects of objectively measured daily physical activity in children. *Clin Physiol Funct Imaging*. 2008 May;28(3):133-44.

17. Benson AC, Torode ME, Singh MA. Muscular strength and cardiorespiratory fitness is associated with higher insulin sensitivity in children and adolescents. *Int J Pediatr Obes*. 2006;1(4):222-31.

18. Garcia-Artero E, Ortega FB, Ruiz JR, Mesa JL, Delgado M, Gonzalez-Gross M, Garcia-Fuentes M, Vicente-Rodriguez G, Gutierrez A, Castillo MJ. [Lipid and

metabolic profiles in adolescents are affected more by physical fitness than physical activity (AVENA study)]. *Rev Esp Cardiol*. 2007 Jun;60(6):581-8.

19. Ruiz JR, Ortega FB, Warnberg J, Moreno LA, Carrero JJ, Gonzalez-Gross M, Marcos A, Gutierrez A, Sjostrom M. Inflammatory proteins and muscle strength in adolescents: the Avena study. *Arch Pediatr Adolesc Med*. 2008 May;162(5):462-8.

20. Haslam DW, James WP. Obesity. *Lancet*. 2005 Oct 1;366(9492):1197-209.

21. Gutin B, Johnson MH, Humphries MC, Hatfield-Laube JL, Kapuku GK, Allison JD, Gower BA, Daniels SR, Barbeau P. Relationship of visceral adiposity to cardiovascular disease risk factors in black and white teens. *Obesity (Silver Spring)*. 2007 Apr;15(4):1029-35.

22. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome--a new worldwide definition. *Lancet*. 2005 Sep 24-30;366(9491):1059-62.

23. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC, Jr., Spertus JA, Costa F. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005 Oct 25;112(17):2735-52.

24. Jolliffe CJ, Janssen I. Development of age-specific adolescent metabolic syndrome criteria that are linked to the Adult Treatment Panel III and International Diabetes Federation criteria. *J Am Coll Cardiol*. 2007 Feb 27;49(8):891-8.

25. Batty GD, Leon DA. Socio-economic position and coronary heart disease risk factors in children and young people. Evidence from UK epidemiological studies. *Eur J Public Health*. 2002 Dec;12(4):263-72.

26. Parizkova J. Impact of education on food behaviour, body composition and physical fitness in children. *Br J Nutr*. 2008 Feb;99 Suppl 1:S26-32.

27. Currie C, Molcho M, Boyce W, Holstein B, Torsheim T, Richter M. Researching health inequalities in adolescents: the development of the Health Behaviour

in School-Aged Children (HBSC) family affluence scale. *Soc Sci Med*. 2008 Mar;66(6):1429-36.

28. Janssen I, Boyce WF, Simpson K, Pickett W. Influence of individual- and area-level measures of socioeconomic status on obesity, unhealthy eating, and physical inactivity in Canadian adolescents. *Am J Clin Nutr*. 2006 Jan;83(1):139-45.

29. Ramsay SE, Whincup PH, Morris R, Lennon L, Wannamethee SG. Is socioeconomic position related to the prevalence of metabolic syndrome?: influence of social class across the life course in a population-based study of older men. *Diabetes Care*. 2008 Dec;31(12):2380-2.

30. Yarnell J, Yu S, McCrum E, Arveiler D, Hass B, Dallongeville J, Montaye M, Amouyel P, Ferrieres J, Ruidavets JB, Evans A, Bingham A, Ducimetiere P. Education, socioeconomic and lifestyle factors, and risk of coronary heart disease: the PRIME Study. *Int J Epidemiol*. 2005 Apr;34(2):268-75.

31. Brunner E, Shipley MJ, Blane D, Smith GD, Marmot MG. When does cardiovascular risk start? Past and present socioeconomic circumstances and risk factors in adulthood. *J Epidemiol Community Health*. 1999 Dec;53(12):757-64.

32. Power C, Graham H, Due P, Hallqvist J, Joung I, Kuh D, Lynch J. The contribution of childhood and adult socioeconomic position to adult obesity and smoking behaviour: an international comparison. *Int J Epidemiol*. 2005 Apr;34(2):335-44.

33. Regidor E, Banegas JR, Gutierrez-Fisac JL, Dominguez V, Rodriguez-Artalejo F. Socioeconomic position in childhood and cardiovascular risk factors in older Spanish people. *Int J Epidemiol*. 2004 Aug;33(4):723-30.

34. Freitas D, Maia J, Beunen G, Claessens A, Thomis M, Marques A, Crespo M, Lefevre J. Socio-economic status, growth, physical activity and fitness: the Madeira Growth Study. *Ann Hum Biol*. 2007 Jan-Feb;34(1):107-22.

35. Mutunga M, Gallagher AM, Boreham C, Watkins DC, Murray LJ, Cran G, Reilly JJ. Socioeconomic differences in risk factors for obesity in adolescents in Northern Ireland. *Int J Pediatr Obes*. 2006;1(2):114-9.

36. Cleland VJ, Ball K, Magnussen C, Dwyer T, Venn A. Socioeconomic position and the tracking of physical activity and cardiorespiratory fitness from childhood to adulthood. *Am J Epidemiol*. 2009 Nov 1;170(9):1069-77.

37. Moreno LA, Tomas C, Gonzalez-Gross M, Bueno G, Perez-Gonzalez JM, Bueno M. Micro-environmental and socio-demographic determinants of childhood obesity. *Int J Obes Relat Metab Disord*. 2004 Nov;28 Suppl 3:S16-20.

38. Shrewsbury V, Wardle J. Socioeconomic status and adiposity in childhood: a systematic review of cross-sectional studies 1990-2005. *Obesity (Silver Spring)*. 2008 Feb;16(2):275-84.

39. Ness AR, Leary S, Reilly J, Wells J, Tobias J, Clark E, Smith GD. The social patterning of fat and lean mass in a contemporary cohort of children. *Int J Pediatr Obes*. 2006;1(1):59-61.

40. Armstrong J, Dorosty AR, Reilly JJ, Emmett PM. Coexistence of social inequalities in undernutrition and obesity in preschool children: population based cross sectional study. *Arch Dis Child*. 2003 Aug;88(8):671-5.

41. Carnethon MR, Gidding SS, Nehgme R, Sidney S, Jacobs DR, Jr., Liu K. Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. *JAMA*. 2003 Dec 17;290(23):3092-100.

42. Dwyer T, Magnussen CG, Schmidt MD, Ukoumunne OC, Ponsonby AL, Raitakari OT, Zimmet PZ, Blair SN, Thomson R, Cleland VJ, Venn A. Decline in physical fitness from childhood to adulthood associated with increased obesity and insulin resistance in adults. *Diabetes Care*. 2008 Dec 23.

43. Hale DE. Type 2 diabetes and diabetes risk factors in children and adolescents. *Clin Cornerstone*. 2004;6(2):17-30.

44. Karam JG, McFarlane SI. Prevention of type 2 DM: implications for adolescents and young adults. *Pediatr Endocrinol Rev*. 2008 Aug;5 Suppl 4:980-8.

45. Rizzo NS, Ruiz JR, Oja L, Veidebaum T, Sjostrom M. Associations between physical activity, body fat, and insulin resistance (homeostasis model assessment) in adolescents: the European Youth Heart Study. *Am J Clin Nutr*. 2008 Mar;87(3):586-92.

46. Ruiz JR, Rizzo NS, Ortega FB, Loit HM, Veidebaum T, Sjostrom M. Markers of insulin resistance are associated with fatness and fitness in school-aged children: the European Youth Heart Study. *Diabetologia*. 2007 Jul;50(7):1401-8.

47. Stumvoll M, Goldstein BJ, van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. *Lancet*. 2005 Apr 9-15;365(9467):1333-46.

48. Fruhbeck G, Gomez-Ambrosi J, Muruzabal FJ, Burrell MA. The adipocyte: a model for integration of endocrine and metabolic signaling in energy metabolism regulation. *Am J Physiol Endocrinol Metab*. 2001 Jun;280(6):E827-47.

49. Gutin B, Ramsey L, Barbeau P, Cannady W, Ferguson M, Litaker M, Owens S. Plasma leptin concentrations in obese children: changes during 4-mo periods with and without physical training. *Am J Clin Nutr*. 1999 Mar;69(3):388-94.

50. Huerta MG. Adiponectin and leptin: potential tools in the differential diagnosis of pediatric diabetes? *Rev Endocr Metab Disord*. 2006 Sep;7(3):187-96.

51. Ischander M, Zaldivar F, Jr., Eliakim A, Nussbaum E, Dunton G, Leu SY, Cooper DM, Schneider M. Physical activity, growth, and inflammatory mediators in BMI-matched female adolescents. *Med Sci Sports Exerc*. 2007 Jul;39(7):1131-8.

52. Jurimae J, Jurimae T. Leptin responses to short term exercise in college level male rowers. *Br J Sports Med*. 2005 Jan;39(1):6-9.

53. Kieffer TJ, Habener JF. The adipoinsular axis: effects of leptin on pancreatic beta-cells. *Am J Physiol Endocrinol Metab*. 2000 Jan;278(1):E1-E14.

54. Metcalf BS, Jeffery AN, Hosking J, Voss LD, Sattar N, Wilkin TJ. Objectively measured physical activity and its association with adiponectin and other novel metabolic markers: a longitudinal study in children (EarlyBird 38). *Diabetes Care*. 2009 Mar;32(3):468-73.

55. Pasman WJ, Westerterp-Plantenga MS, Saris WH. The effect of exercise training on leptin levels in obese males. *Am J Physiol*. 1998 Feb;274(2 Pt 1):E280-6.

56. Perusse L, Collier G, Gagnon J, Leon AS, Rao DC, Skinner JS, Wilmore JH, Nadeau A, Zimmet PZ, Bouchard C. Acute and chronic effects of exercise on leptin levels in humans. *J Appl Physiol*. 1997 Jul;83(1):5-10.

57. Platat C, Wagner A, Klumpp T, Schweitzer B, Simon C. Relationships of physical activity with metabolic syndrome features and low-grade inflammation in adolescents. *Diabetologia*. 2006 Sep;49(9):2078-85.

58. Romon M, Lafay L, Bresson JL, Oppert JM, Borys JM, Kettaneh A, Charles MA. Relationships between physical activity and plasma leptin levels in healthy children: the Fleurbaix-Laventie Ville Sante II Study. *Int J Obes Relat Metab Disord*. 2004 Oct;28(10):1227-32.

59. Shklyaev S, Aslanidi G, Tennant M, Prima V, Kohlbrenner E, Kroutov V, Campbell-Thompson M, Crawford J, Shek EW, Scarpace PJ, Zolotukhin S. Sustained peripheral expression of transgene adiponectin offsets the development of diet-induced obesity in rats. *Proc Natl Acad Sci U S A*. 2003 Nov 25;100(24):14217-22.

60. Roemmich JN, Clark PA, Lusk M, Friel A, Weltman A, Epstein LH, Rogol AD. Pubertal alterations in growth and body composition. VI. Pubertal insulin resistance: relation to adiposity, body fat distribution and hormone release. *Int J Obes Relat Metab Disord*. 2002 May;26(5):701-9.

OBJETIVOS

General:

El objetivo general de esta Tesis Doctoral Europea ha sido en primer lugar, analizar la evidencia científica disponible que relaciona la actividad física, la condición física y el grado de adiposidad durante la infancia y la adolescencia. En segundo lugar, estudiar la relación entre el status socioeconómico y el nivel de condición física de los adolescentes europeos, controlando por importantes factores de confusión entre los que se incluyen actividad física y adiposidad, ambas medidas de forma objetiva. En tercer lugar, determinar el papel que la condición física tiene sobre dos hormonas claves para la fisiología del tejido adiposo como son la insulina y la leptina.

Específicos:

I.-Revisar de forma sistemática los estudios observacionales que analizan la asociación entre la práctica habitual de actividad física y el nivel de adiposidad en niños y adolescentes **(Artículo I).**

II.-Revisar la evidencia que relaciona actividad física, condición física y adiposidad, así como algunos de sus efectos sobre la salud, en niños y adolescentes **(Artículo II).**

III.-Examinar la asociación entre el estatus socioeconómico, la condición física y la grasa corporal en adolescentes **(Artículos III y IV).**

IV.-Estudiar la asociación de la grasa corporal y capacidad cardiorespiratoria con marcadores de resistencia a la insulina en adolescentes **(Artículo V).**

V.-Examinar la asociación de la actividad física y la condición física con los niveles de leptina en adolescentes **(Artículo VI).**

AIMS

Overall:

The main aim of the PhD thesis was first, to analyze the evidence regarding the association of physical activity and fitness and with body fat in children and adolescents. Second, to study the association between socioeconomic status and the level of physical fitness in European adolescents after controlling for potential confounders including objectively measured physical activity and adiposity; and finally, to examine the independent role of physical fitness on two adiposity-related hormones, namely insulin and leptin.

Specific:

I.-To systematically review the observational studies analysing the association between objectively measured physical activity and the level of adiposity in children and adolescents **(Paper I).**

II.- To review the literature addressing the relationship of physical activity and fitness with adiposity and other health indicators in children and adolescents **(Paper II).**

III.-To examine the association of socioeconomic status with fitness and fatness in adolescents **(Papers III and IV).**

IV.-To study the association of fatness and cardiorespiratory fitness with markers of insulin resistance in adolescents **(Paper V).**

V.-To examine the association of physical activity and fitness with leptin levels in adolescents **(Paper VI).**

MATERIAL AND METHODS

The current PhD Thesis is based on data from the AVENA and HELENA studies. The abstracts from the methodological papers of both studies are provided. A summary of the methodology used in the manuscripts included in the Thesis is presented in **Table 1**.

Alimentación y valoración del estado nutricional de los adolescentes españoles (Estudio AVENA). Evaluación de riesgos y propuesta de intervención. I. Descripción metodológica del proyecto [Feeding and assessment of nutritional status of Spanish adolescents (AVENA study). Evaluation of risks and interventional proposal. I. Methodology].

González-Gross M, Castillo MJ, Moreno L, Nova E, González-Lamuño D, Pérez-Llamas F, Gutiérrez A, Garaulet M, Joyanes M, Leiva A, Marcos A. *Nutr Hosp* 2003; 18(1): 15-28.

BACKGROUND: Adolescence is a decisive period in human life due to the multiple physiological and psychological changes that take place. These changes will condition both nutritional requirements and eating/physical activity behavior. It has been demonstrated that these "adolescence" factors are of significant influence in health status during adult life. Due to its importance and adequate development the project has been granted by the Fondo de Investigación Sanitaria of the Institute of Health Carlos III.

OBJECTIVE: To develop a methodology to evaluate the health and nutritional status of a representative population of Spanish adolescents. Specific attention is paid to three specific health problems: obesity, anorexia nervosa/bulimia, dislipidemia.

METHODOLOGY: The following magnitudes will be studied: 1) dietary intake, food habits and nutrition knowledge; 2) daily physical activity and personal approach; 3) physical condition; 4) anthropometry and body composition; 5) hematobiochemical study: plasma lipid phenotypic and metabolic profile, blood cell counts; 6) genotipic profile of cardiovascular risk lipid factors; 7) immune function profile related to nutritional status; 8) psychological profile.

CONCLUSION: This project includes the co-ordinate activity of five Spanish centers of five different cities (Granada, Madrid, Murcia, Santander, Zaragoza). Each center is specialized in a specific area and will be responsible for the corresponding part of the study. From the data obtained, we will elaborate a specific intervention program in order to improve nutrition and neutralize the risk for nutritional related problems in adolescence. By this, we will contribute to improve the health status of the Spanish population in the new millennium.

Nutritional status and lifestyles of adolescents from a public health perspective. The HELENA Project—Healthy lifestyle in Europe by Nutrition in Adolescence

S De Henauw, F. Gottrand, I. De Bourdeaudhuij, M. González-Gross, C. Leclercq, A. Kafatos, D. Molnar, A. Marcos, MJ. Castillo, J Dallongeville, C. C. Gilbert, P. Bergman, K. Widhalm, Y. Manios, C. Breidenassel, M. Kersting, L. A. Moreno, on behalf of the HELENA Study Group. *J Public Health* 2007; 15: 187-197

The HELENA Project—Healthy Lifestyle in Europe by Nutrition in Adolescence—is a European, collaborative research project financed by the EU Sixth Framework Programme in the area of nutrition-related adolescent health. The basic objective of the HELENA project is to obtain reliable and comparable data from a random sample of European adolescents (boys and girls aged 13–16 years) on a broad battery of relevant nutrition and health-related parameters: dietary intake, food choices and preferences, anthropometry, serum indicators of lipid metabolism and glucose metabolism, vitamin and mineral status, immunological markers, physical activity, fitness and genetic markers. The HELENA project is conceived as a scientific construction with four complementary substudies that are elaborated through 14 well-defined work packages. Sub-studies are focused, respectively, on “a cross-sectional description of lifestyles and indicators of nutritional status (HELENA-CSS)”, “a lifestyle education intervention programme (HELENA-LSEI), “a metabolic study with cross-over design (HELENA-COMS)” and a “study on behaviour, food preferences and food development” (HELENA-BEFO). The project unites 20 research centres from 10 European countries. In addition, the consortium comprises five SMEs (small and medium-sized enterprises) that are actively involved in the research activities. The core of the HELENA project study material is an overall European cohort of 3,000 adolescents, equally recruited in ten cities from nine countries. Standardization of methods among partners is a key issue in the project and is obtained through the development of standard protocols, training sessions, validation sub-studies and pilot projects. Health-related problems have a tendency to evolve in cycles, with ever new problems emerging in ever new contexts that call for appropriate and tailored actions. The HELENA project is expected to offer essential elements for use in the overall machinery of required public health nutrition cycles. It is of the greatest importance for its results to prove useful that it can communicate with other initiatives on the level of science and society.

Table 1. Summary of methodology used in the current PhD Thesis.

Project	Paper	Study design	Participants	Main variables studied	Methods
-	**I**. Associations between objectively measured habitual physical activity and adiposity in children and adolescents: Systematic review	Review	Children and adolescents	Objectively measured physical activity, adiposity (both proxies and more precise measures)	Systematic literature searches and detailed description of the main findings and gaps
-	**II**. Physical activity, fitness and fatness in children and adolescents	Review	Children and adolescents	Physical activity, physical fitness, body fat, CVD risk factors	Review of the literature and detailed description of the main findings and gaps
AVENA	**III**. Influence of socioeconomic factors on fitness and fatness in urban Spanish adolescents: The AVENA study	Cross-sectional	♂: 833 ♀: 962 Age: 12.5-18.5 y	Socioeconomic status, muscular fitness, cardiorespiratory fitness, motor fitness and fatness	Parental educational and professional level, standing long jump, 20mSRT, 4x10m SRT, sum of 6 skinfold thickness and waist circumference
HELENA	**IV**. Socioeconomic status influences physical fitness in European adolescents independently of body fat and physical activity; The HELENA Study	Cross-sectional	♂: 1558 ♀: 1701 Age: 12.5-17.5 y	Socioeconomic status, motor fitness, muscular fitness and cardiorespiratory fitness	Family affluence scale, 4x10m SRT, handgrip, bent arm hang, standing long jump, squat jump, counter movement jump, abalakov jump and 20mSRT

Table 1 (cont)

Project	Paper	Study design	Participants	Main variables studied	Methods
HELENA	**V**. Fitness and fatness are independently associated with markers of insulin resistance in European adolescents; The HELENA Study	Cross-sectional	♂: 499 ♀: 554 Age: 12.5-17.5 y	Cardiorespiratory fitness, total and central body fat and markers of insulin resistance	20mSRT, BMI, sum of 6 skinfold thickness, waist circumference, insulin, HOMA and glucose
HELENA	**VI**. Physical activity, fitness and serum leptin concentrations in adolescents: The HELENA Study	Cross-sectional	♂: 393 ♀: 509 Age: 12.5-17.5 y	Physical activity levels, muscular fitness, motor fitness, cardiorespiratory fitness and leptin concentrations	PA, MPA, VPA, MVPA, standing long jump, 4x10m SRT, 20mSRT and leptin concentrations

AVENA: Alimentación y Valoración del Estado Nutricional de los Adolescentes; BMI: body mass index; CVD: cardiovascular disease; HELENA: Healthy Lifestyle in Europe by Nutrition in Adolescence; HOMA: homeostasis model assessment; MPA: moderate physical activity; MVPA: moderate and vigorous physical activity; PA: physical activity; VPA: vigorous physical activity; SRT: shuttle run test; ♂ boys; ♀ girls.

RESULTS AND DISCUSSION

The results and discussion of the present PhD Thesis are shown as scientific papers. They are enclosed in the form they have been published or submitted.

1.- PHYSICAL ACTIVITY, FITNESS AND OBESITY; REVIEW OF THE LITERATURE

ACTIVIDAD FÍSICA, CONDICIÓN FÍSICA Y OBESIDAD; REVISIÓN DE LA LITERATURA

Papers I and II (Artículos I y II)

I

ASSOCIATION BETWEEN OBJECTIVELY MEASURED HABITUAL PHYSICAL ACTIVITY AND ADIPOSITY IN CHILDREN AND ADOLESCENTS

David Jiménez-Pavón, Joanna Kelly, John J. Reilly

Int J Pediatr Obes

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REVIEW ARTICLE

Associations between objectively measured habitual physical activity and adiposity in children and adolescents: Systematic review

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Abstract
This review examined recent evidence on associations between objectively measured habitual physical activity and adiposity. A search for observational studies was carried out using several electronic databases from June 2004–June 2008. Of 1 255 potentially eligible papers, 47 papers were included, which described 48 studies. Most studies (41/48; 85%) were cross-sectional and 31/48 (65%) used proxies for adiposity, such as body mass index (BMI) or BMI z-score as the outcome measure. Few studies (10%; 5/48) focused on pre-school children. There was consistent evidence of negative associations between objectively measured physical activity and adiposity: significant negative associations were observed in 38/48 (79%) of studies overall. The present review supports the hypothesis that higher levels of habitual physical activity are protective against child and adolescent obesity. However, prospective longitudinal studies are warranted; there is a need for more research on younger children, and for more 'dose-response' evidence.

Key words: *Objectively measured physical activity, adiposity, obesity, overweight, accelerometer, pedometer, heart rate, body mass index*

Introduction

A low level of habitual physical activity is a potentially important and potentially modifiable cause of obesity in children and adolescents (1). Negative associations between level of habitual physical activity and weight status are expected, i.e., higher levels of habitual physical activity are assumed to be protective against obesity. In addition habitual levels of physical activity, when measured objectively, are typically low among children and adolescents (2–4). However, systematic reviews to date have generally found only weak and inconsistent evidence that low levels of physical activity predispose to obesity in children and adolescents (5–7).

Recent systematic reviews (5–7) have concluded that the absence of convincing evidence on the contribution of habitual physical activity to childhood obesity may lie in methodological weaknesses: many older studies used biased and/or imprecise measures of exposure (subjective measurement of physical activity [8]); or imprecise measures of outcome; in some studies proxies for physical activity (e.g., school physical education time) were used as the exposure rather than direct measures of physical activity; many studies were probably underpowered (5–7); and possible heterogeneity in the etiology of childhood obesity (9,10) might mean that an influence of habitual physical activity might be more marked (and more detectable) in some populations (e.g., in certain age groups) than in others (9).

With the increasing availability of quantitative evidence from objective measurements of habitual physical activity in recent studies (8), and a greater awareness of the need to study larger samples, it seemed likely that more definitive evidence on relationships between habitual physical activity and weight status in youth might be available now. The

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primary aim of the present study was therefore to provide a systematic review of recent observational studies that tested for associations between habitual physical activity and adiposity in children and adolescents. A secondary aim was to examine the possibilities that evidence on such associations may vary between groups (e.g., age group or gender, possibly reflecting heterogeneity in etiology), by exposure measure (pedometers vs. heart rate monitors vs. accelerometers), or by outcome measure (in particular differences, arising from use of a proxy for body composition, such as body mass index [BMI] or use of more precise body composition measures).

Methods

Search strategy

An Information Officer (JK) ran systematic literature searches in MEDLINE, EMBASE, CINAHL and The Cochrane Library for the period of June 2004 to June 2008. In addition, manual searching of reference lists was carried out and results combined in EndNote. The start date for the present search was chosen so as to follow on from the previous systematic review of a similar topic by Wareham et al. (6), though in the present review eligibility was restricted to studies that used objective measurement of habitual physical activity.

The search strategy used in MEDLINE is given below:

1. exp exercise/ or exp leisure activities/ or exp physical fitness/
2. exp Exertion/
3. exp Life Style/
4. exp Television/
5. (activ$ adj2 level$).tw.
6. exercis$.tw.
7. exertion$.tw.
8. exp risk factors/
9. sedentar$.tw.
10. (physic$ adj3 (exerc$ or activ$)).tw.
11. or/1–10
12. exp Obesity/
13. exp body weight/ or exp overweight/
14. (obes$ or overweight$).tw.
15. exp body weight changes/ or exp weight gain/ or exp weight loss/
16. (weight$ adj2 (gain$ or chang$ or fluctuat$)).tw.
17. exp "body weights and measures"/ or exp body fat distribution/ or exp body mass index/ or exp body size/ or exp skinfold thickness/ or exp waist-hip ratio/
18. or/12–17
19. 11 and 18
20. limit 19 to yr = "2004–2008"
21. exp Adult/
22. 20 not 21

Similar strategies were run in the other databases. The search yielded several thousand hits, and a preliminary sift was conducted by an Information Officer (JK) to remove the obviously irrelevant material. This left 1 255 potentially eligible papers.

Eligibility criteria

Eligible studies were longitudinal and cross-sectional observational studies of healthy children and adolescents (0–18 years) that tested for the existence of associations between habitual physical activity and adiposity. Studies were only included where they attempted to measure typical or 'habitual', free-living, physical activity: studies that measured physical activity in confined conditions (e.g., within whole body calorimeters) were excluded; studies that took place within short specified periods or settings (e.g., during school or nursery time only) that did not reflect usual physical activity, were also excluded. Community-based (non clinical) studies with a measure of objectively measured habitual physical activity as the exposure variable and with at least one weight-based outcome indicative of adiposity were included. Studies that used subjectively measured physical activity as the exposure (e.g., using questionnaires) were excluded as these are more likely to be biased than studies using objectively measured physical activity (9). There is also a good deal of doubt over the ability of subjective measures to quantify absolute amounts of habitual physical activity in children (8), leaving doubt over the ability of studies based on subjective measures to provide associations that are quantitative. Longitudinal studies in which age at baseline was >16 years were excluded. Studies in clinical populations, not in the English language, or which used only measures of sedentary behavior as the exposure (sedentary behavior is a distinct construct and evidence on associations between sedentary behavior and adiposity in youth has been reviewed elsewhere recently), or proxy measures of habitual physical activity (e.g., physical education time) were also excluded. In addition, duplicate publications were excluded and in all cases of duplicates the first publication was selected for inclusion. Doubts over eligibility of individual papers/studies were resolved by discussion and consensus between the authors. Reasons for excluding papers were noted and are available from the corresponding author upon request.

Data management and extraction

Characteristics of each study were extracted and summarised: the exposure variable (s) used; methodology for measurement of the exposure variable; the outcome variable(s) used; methodology for measurement of the outcome variable(s) (adiposity measure, proxy, or index); sample size, location and characteristics; results and main conclusions relevant to the present review.

Sensitivity analyses

Age of study participants. Studies were stratified by age range of study participants, into pre-school children (≤5.5 years), children (>5.5 to ≤10.5 years) and adolescents (>10.5 to 18 years) in order to examine possible age-dependence of relationships between physical activity and adiposity (11). The precise age categories chosen made little difference to the conclusions of the present review.

Outcome measure(s). A wide variety of different measures of adiposity or indices of adiposity were used in the studies reviewed. The study outcome measures could be subdivided conveniently into two broad categories: studies that used proxies for adiposity (usually absolute BMI or BMI z-score); studies that used more precise measures of adiposity (measures of body composition, such as dual-energy x-ray absorptiometry [DXA], skinfolds, impedance). When both approaches to measurement of outcome were used in the same study it was categorized as being a study with 'more precise measures'.

Exposure measure(s). Three methods were used to measure habitual physical activity in the eligible studies: accelerometry; pedometry; and heart rate monitoring. All three methods measure different dimensions of habitual physical activity and so they were treated both separately and combined when summarising the data in the review.

Sample size. The studies reviewed were characterized by a very wide range of sample sizes. Sample size is likely to determine the ability to detect associations between habitual physical activity and adiposity, and previous reviews have noted that small sample sizes were typical in the older literature (5–8). Publication bias is also possible, and small studies that find no association between physical activity and adiposity are less likely to be published than small studies that find significant associations.

In an attempt to address the influence of sample size on the confidence in any conclusions reached, studies were categorized by sample size in the present review: 'large studies' n > 1 000 participants; 'medium sized studies', n ≥ 100 to 1 000 participants; 'small studies', n < 100 participants. The authors also analysed using a variety of different categories of study sample size.

Consistency of evidence. Sallis et al. (11) proposed a scheme to summarise the consistency of a body of evidence in reviews, and to use the degree of consistency observed in order to infer the degree of confidence in the conclusions of reviews. According to Sallis et al. (11) 'strong evidence' of an association exists when 60%–100% of studies find significant associations in the same direction.

Results

Overall results

Of the 1 255 potentially eligible papers, 47 were included and are summarised in the present review (Figure 1 is a flow diagram describing the search and selection process). One paper described two separate studies, giving 48 studies in 47 papers.

Only 15% (7/48) of eligible studies were longitudinal ([(10),(12–17)]; Table I). Most studies (41/48; 85%) were cross-sectional ([(18)–(57)]; Table II–IV).

Few studies used pedometers (11/48; 23%) or heart rate monitors (5/48; 10%) as the physical activity assessment instrument (exposure variable), most studies used accelerometers (32/48; 67%). Relatively few studies focused on the pre-school

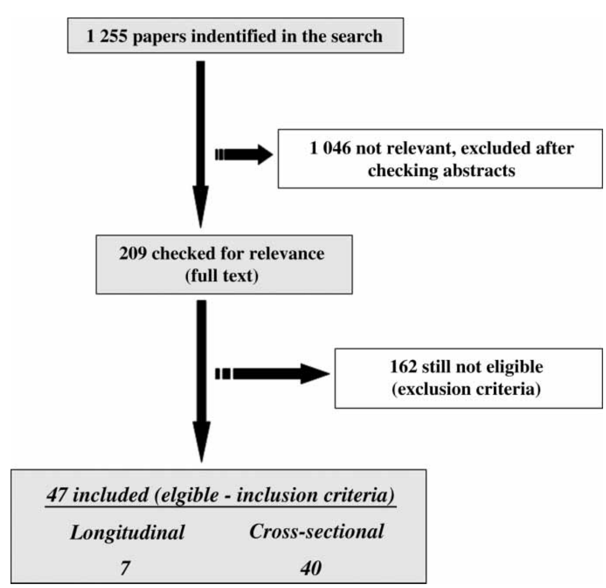

Figure 1. Flow diagram of the literature search and paper selection process. Note: The 47 eligible papers described 48 studies.

Table I. Recent longitudinal studies of associations between objectively assessed physical activity and adiposity in youth.

Study	Exposure variable	Outcome variable	Location/ Participants	Conclusions	Overall result
Physical activity using heart rate					
(10)	- Moderate Vigorous PA (number of minutes with mean heart rates >140 bpm/h) 2–4 days, (heart rate monitoring, Quantum XL telemetry)	**Continuous variable:** - BMI (kg/m^2)	n = not clear; 3–4-year-olds at baseline, followed for 3 years, USA	- Year 1: PA SIG positively associated with BMI - Years 2 and 3: PA SIG negatively associated with BMI (stronger in year 3)	(-)
Physical activity using pedometer					
(17)	- Number of daily steps 4 days (including 2 weekend) (pedometer Yamax Digiwalker, S700)	**Continuous variable:** - BMI (kg/m^2)	n = 22 (9 boys, 13 girls) 6–8-year-olds at baseline 2 years follow up, Australia	SIG negative association between BMI and PA (weekdays r = −0.28; weekend r = −0.32).	(-)
(12)	- z-score of average of daily steps 7 days (pedometer Yamax Digiwalker, S200)	**Categorical variables:** - at baseline: Healthy weight; overweight[a] - at follow up: Healthy weight = BMI <25.	n = 1 594 (815 boys and 779 girls) 9–15 years at baseline and 27–36 at the end, Australia	Younger males and older females at baseline that demonstrated the largest PA increase were 34 and 25% more likely to be healthy weight maintainers at follow-up (nonsignificant in males).	(-)
(14)	- Number of daily steps 4 weekdays (Yamax pedometers; SW200)	**Categorical variables[a]:** - Overweight - Obesity **Continuous variables:** - BMI (kg/m^2)	n = 93 (46 girls, 47 boys) 12–14-year-olds at baseline, 3 years follow-up, Sweden.	Lower BMI levels SIG associated with high PA in boys.	(-)
(13)	- Overall activity (counts minutes^{-1}) - Moderate activity (minutes day^{-1}) - Vigorous activity (minutes day^{-1}) - 5-minute bouts moderate (events day^{-1}) - 5-minute bouts vigorous (events day^{-1}) 3 weekdays +1 weekend day (Actigraph)	**Continuous variable:** Body fat percent (DXA)	n = 378 children (176 boys, 202 girls) 4–6-years-old at baseline 3 years follow-up, USA	Higher overall activity, vigorous activity and 5-minute bouts of vigorous associated with lower quartile %BF (follow-up)	(-)
(16)	- Total physical activity 1 day (Tritrac R3D)	**Categorical variable:** - No-overweight - Overweight[b]	n = 454 children (233 boys, 221 girls)	No-overweight: higher Total PA SIG negative association with lower %BF.	(-)

Table I (*Continued*)

Study	Exposure variable	Outcome variable	Location/ Participants	Conclusions	Overall result
		Continuous variables: - BMI (kg/m^2) - Fat mass (kg) - Fat free-mass (kg)	6–8-years-old at baseline 2–3-years follow-up, USA	Overweight: Total PA significantly association with increases in BMI, fat mass, and fat-free mass (not %BF).	(-)
(15)	- Moderate-vigorous; MVPA (>1 500) - Vigorous, VPA (≥2 600) - MET-weighted MVPA 6 days included weekend days (MTI Actigraph)	**Continuous variables:** - BMI (kg/m^2) - % body fat **	n = 984 girls 10–14-year-old at baseline 2–3 years follow-up USA	There were no statistically significant associations between PA in the sixth grade and incident overweight in the eighth grade	(0)

[a]International age- and sex-specific BMI cut-off points (62).
[b]BMI ≥95th percentile.
*equation: body weight, age, gender, triceps and subscapular skinfolds, bioelectric resistance and reactance.
**equation: −23.39 + 2.27(BMI) + 1.94(triceps skinfold [mm]) −2.95(race [1 = African American, 0 = other]) −0.52(age [years]) −0.52(age [year]) −0.06(BMI × triceps skinfold [mm])
PA: Physical activity, BMI: Body mass index, SIG: Significant, NS: Not Significant. %BF: Percent body fat.
(-): Significant negative association, (+) significant positive association, (0) no significant association.

population (5/48; 10%). In total 65% of studies (31/48) used a simple proxy for body composition as the outcome, rather than more precise measures of body composition, and specifically 46% (22/48) used absolute BMI or BMI z-score as the sole outcome.

The studies reviewed here consistently reported significant and negative associations between objectively measured physical activity and adiposity (38/48; 79%), indicating 'strong evidence' that such an association exists (11) with higher levels of habitual physical activity being associated with lower measures or indices of adiposity. In the cross-sectional studies, 32/41 (78%) of studies found significant negative associations, and in the longitudinal studies, 6/7 (86%) of studies found significant negative associations while the other study found a non-significant trend in the 'expected' direction.

Sensitivity analysis

Results by age group. Significant negative associations between physical activity and adiposity were found in 3/5 (60%) of preschool studies; 17/22 (77%) of studies of primary school-age children, and 18/21 (86%) of studies of adolescents.

Results by outcome measure. Significant negative associations between habitual physical activity and adiposity were found in 25/31 (81%) of studies that used simple proxies for adiposity as the outcome measure, and 13/17 (76%) of studies that used more precise body composition methods as the outcome measure.

Results by exposure measure. Significant negative associations between habitual physical activity and adiposity were found in 23/32 (72%) of studies that used accelerometry, 11/11 (100%) of studies that used pedometry, and 4/5 (80%) of studies that used heart rate monitoring.

Results by sample size. 6/47 (13%) of studies were 'large' (n > 1 000 participants), 25/47 (53%) 'medium size' (n = 100–1 000 participants), and 15/47 (32%) 'small size' (n < 100 participants). In the large studies 5/6 (83%) found significant negative associations, while the corresponding percentage was 80% (20/25 studies) in the medium sized studies, and 73% (11/15) in the small studies. Use of different categories of sample size made little difference to the conclusions. For example, using categories of: small (n ≤250), medium (n > 250 to ≤500), large (n > 500) the percentages of studies that found negative association were 82% (9/11) in the large studies,

Table II. Cross-sectional studies of associations between objectively measured physical activity (heart rate monitoring) and indices of adiposity.

Study	Exposure variable	Outcome variable	Location/Participants	Conclusions	Overall result
(20)	**% time in:** Light-intensity (LI): - Low activity (LI_LA) - High activity (LI-HA) Vigorous-intesity (VI): - Low activity (VI_LA) - High activity (VI-HA) 7 days, (daytime only) (Polar PE3 000)	**Categorical variables[a]:** - Overweight - Obesity **Continuous variables:** **(isotopic dilution):** - Fat mass index (FMI) - Lean mass index (LMI) - Body mass index (BMI; kg/m2)	n = 68 (49 boys, 19 girls). 2 groups according to their risk of future obesity 6–8-year-olds non-obese, Northern Ireland. UK	In nonobese children: Boys who spent more time in Light -intensity had SIG higher FMI than those who spent less time. Not in girls.	(-)
(18)	**% time in:** - Moderate-vigorous PA Two weekdays plus one weekend day	**Continuous variable:** - % Body fat (air displacement plethysmography)	n = 47 (23 boys, 24 girls). 9–11-year-olds, Birmingham UK	NS association between %BF and MVPA.	(0)
(21)	**% time in:** - MVPA as 50% heart rate reserve - VPA as 75% heart rate reserve 1 day (Polar Team System)	**Categorical variables[a]:** - Overweight - Obesity	n = 375 (185 boys, 190 girls) 6–10-year-olds, Northwest of England, UK	Overweight boys were significantly less active than their normal-weight male counterparts; this difference did not hold true for girls.	(-)
(19)	**% time in:** - Under (<flex-HR)* - Over (>flex-HR) the flex-HR.* 1 day Heart rate monitoring (Polar) (12 h per day in adolescents; 8 h in children)	**Continuous variables:** - BMI (kg/m2) - Triceps skinfold	n = 99 children (46 boys, 53 girls) n = 43 girls (Adolescent group) 10–13-year-olds, 15.5-year-old adolescents, Senegal (Africa)	In children no SIG relationship between PA and body composition. In adolescents, body composition was SIG predictor of activity levels.	(-)

[a]International age- and sex-specific BMI cut-off points (62).
*The flex-HR is the critical heart rate value recorded between resting and the lowest value during exercise.
PA: Physical activity, BMI: Body mass index, SIG: Significant, NS: Not significant.
(-): Significant negative association, (+) significant positive association, (0) no significant association.

Table III. Cross-sectional studies of associations between objectively measured physical activity (pedometer) and indices of adiposity.

Study	Exposure variable	Outcome variable	Location/Participants	Conclusions	Overall result
(24)	- Number of daily step counts 3 weekdays and 2 weekend days (Lifestyles NL-2 000)	**Categorical variables[a]:** - Normal weight - Overweight - Obese **Continuous variables:** BMI (kg/m2) - Waist circumference (WC) - % Body Fat (%BF by BIA)	n = 969 children (536 boys, 579 girls) 5–12 (8.5)-year-olds, New Zealand.	Categorical variable: SIG difference in weekend PA among the weight status categories. Continuous variables: SIG negative associations between PA and %BF, BMI and WC. Stronger association with %BF categories.	(-)
(25)	**Step count quartiles:** - I: < 10 000 - II: 10 000 – 12 000 - III:12 000 – 14 000 - IV: > 14 000 7 day (at least 4 days; 3 weekdays and 1 weekend) (Digiwalker 200SW).	**Categorical variables[a]:** - Overweight - Obese **Continuous variables:** - BMI (kg/m2) - Waist Circumference (WC)	n = 608 9.6-year-olds, Midwestern USA	Categorical variables: SIG increase in odds of overweight and obesity and high WC with lower count quartiles. Continuous variables: SIG negative associations between step count, BMI and WC.	(-)
(22)	- Active (> 13 000 steps/day) - Inactive (< 13 000 steps/day) 3 weekdays electronic pedometer (Yamax Digi-walker SW 701)	**Categorical variables[a]:** - Normal weight - Overweight - Obese **Continuous variables:** - BMI (kg/m2) - Triceps and subscapular skinfolds - % predicted body fat* - FM, FFM, FMI and FFMI.	n = 293 8–12 (10)-year-olds, city of Riyadh (Saudi Arabia)	Categorical variables: Obese were significantly less active than normal weight. Continuous variables: SIG difference between active and inactive boys in BMI, triceps and subscapular skinfolds, fat percentage, FMI.	(-)
(26)	-Daily step counts 7 day (at least 4 days; 3 weekdays and 1 weekend) (Pedometer, Yamax SW 700).	**Categorical variables[a]:** - Acceptable weight - Overweight - Obese **Continuous variables:** - BMI (kg/m2) - Normal trunk fat mass (NTFM)[e] - High trunk fat mass (HTFM)[e]	n = 1 539 (752 girls and 787 boys) 7–16-year-olds, Australia	Categorical variable: Participants with acceptable weight had significantly higher PA than overweight/obese (girls p = 0.003, boys p = 0.06). Continuous variables: NS association between BMI and PA. SIG negative associations between Waist girth and PA for boys. Those with high HTFM had lower steps.	(-)

Table III (*Continued*)

Study	Exposure variable	Outcome variable	Location/Participants	Conclusions	Overall result
(28)	- Average of daily steps 6 day (Yamax SW 200)	**Continuous Variables:** - BMI (kg/m2) - % body fat *	n = 296 (163 girls, 129 boys) 11–14 year-olds (grades 5–8), USA	SIG negative association between %BF and PA.	(-)
(57)	- Physical activity levels (STPs) 7 days (uniaxial accelerometry sensor, Japan)	**Categorical variables[d]:** - Normal weight - Overveight **Continuous variables:** - BMI (kg/m2) - Body fat (BIA)	n = 159 10–11-year-olds (grade 5) 13–14-year-olds, (grade 8) Korea and China	NS difference in STPs between weight status categories. STPs SIG negatively correlated with weight, BMI, and % body fat	(-)
(27)	**Number of counts at:** - Slow walk (3 METs) - Fast walk (5 METs) - Run (8 METs) 200 m arenas (New Lifestyles Digiwalker SW-200)	**Categorical variables:** - Normal weight [b] - At risk of being overweight [c,d]	n = 78 boys 11–15-year-olds, Houston, Texas, USA	Participants at risk of being overweight had SIG lower counts than participants of normal weight in slow walk, fast walk and run (at all locations)	(-)
(23)	- Average of daily steps 5-8 days (Yamax Digi-walker SW-701)	**Continuous variable:** - BMI (kg/m^2)	n = 297 13–15-year-olds, Australia.	SIG negative association between BMI and PA.	(-)

[a]International age- and sex-specific BMI cutoff points (62); b(BMI between the 5th and 85th percentiles); c(BMI = 85th and < 95th percentiles); d(BMI = 95th percentile)
[e]based on waist girth using the 80th percentile cut-off.
* estimated from sum of calf and triceps using the equations of Slaughter (63).
PA: Physical activity, BMI: Body mass index, SIG: Significant, NS: Not Significant, FM: Fat mass, FFM: Fat-free mass, FMI: FM index, FFMI: FFM index.
(-): Significant negative association, (+) significant positive association, (0) no significant association .

Table IV. Cross-sectional studies of associations between objectively measured physical activity (accelerometer) and indices of adiposity.

Study	Exposure variables	Outcome variable	Location/Participants	Conclusions	Overall result
(37)	**Accelerometer (counts/min) (mins/d):** - Light (<615) (I) - Moderate (615–2 971) (II) - Vigorous (2 972–5 331) (III) - Very vigorous (>5 331) (IV) **Index (mins/d):** - Active minutes (II+III+IV) - Very active minutes (III+IV) 7 days (Actigraph 7164)	**Categorical variables:** - Non overweight - Overweight (At-risk-for-overweight[b] +overweight[c]) **Continuous variables:** - BMI (kg/m^2)	n =56 (30 girls, 26 boys) 2–5-year-olds, Massachusetts, USA	VPA and VVPA SIG negative associations with overweight (age, sex-,and race-adjusted model) Overweight had significantly lower mean daily very vigorous minutes and mean daily total very active minutes than non-overweight (adjusting for age, sex, and race/ethnicity)	(-)
(36)	- Activity counts (counts/d) 7 days (Actiwatch, model AW16)	**Continuous variables (isotope dilution):** - Lean body mass (kg)** - Fat mass (kg) *(body weight-lean body mass)* - Percentage fat mass (PFM)	n =29 (girls and boys) 4–6-year-olds, Birmingham, UK	Percentage and total fat mass NS associated with average total activity counts (after adjusting for age, body weight, gender, ethnicity and TEE)	(0)
(41)	- Total PA 5 days (including one weekend) (Actigraph, AM 7164-2.2)	**Continuous variable:** - BMI (kg/m^2)	n =205 5–6-year-olds, Germany	BMI and total PA not significantly associated.	(0)
(33)	**Accelerometer (counts/min):** -Moderate PA -Vigorous PA 24 h (MTI accelerometer)	**Continuous variable (BIA):** - Percentage fat mass	n =287 boys 7.3-year-olds, New Zeland	NS association was found between both PA levels and percentage of body fat.	(0)
(32)	**Minutes spent in:** -Moderate PA -Vigorous PA -Hard PA 2 week days and 2 weekend days (Tritrac-R3D)	**Continuous variables:** - BMI (Wt/Ht^2) - Body fat *(from ^{18}O dilution)*	n =47 (23 boys; 24 girls) 5–10.5-year-olds, Australia	- NS association between BMI & PA - SIG negative association %BF & PA (vigorous and hard) - Highest tertile for vigorous and hard showed significantly lower percentage body fat.	(-)
(39)	**PA as (counts/min):** - Sedentary PA (<800) - Light PA (801–3 199) (I) - Moderate PA (3 200–8 199) (II) - Vigorous PA (≥8 200) (III) - Total PA (I+II+III) 5–7 days (Actigraph; AM7164)	**Continuous variables:** - Whole body fat (by DXA) - Visceral adipose tissue (VAT by magnetic resonance) - Subcutaneous abdominal adipose (SAT by magnetic resonance)	n =42 children (21 boys, 21 girls) 8-year-olds, USA.	Total PA significantly negatively associated with VAT (stronger in boys). Total PA negatively association with WBF and SAT (NS)	(-)

Table IV (*Continued*)

Study	Exposure variables	Outcome variable	Location/Participants	Conclusions	Overall result
(34)	**Mean minutes spent daily:** - Light PA - Moderate PA = walking 3 km/h - Vigorous PA = walking 6 km/h - Hard-Vigorous PA = running 9 km/h 4 days (The RT3)	**Continuous variables:** Body mass index (BMI; z score) Waist Circumference	n = 152 (100 girls; 52 boys) 7–10-year-olds, Dublin, Ireland.	In boys, SIG negative correlations between vigorous and moderate PA and waist circumference and between moderate intensity PA and BMI.	(-)
(35)	**Average minutes of:** - Low PA - Moderate/vigorous PA 2 weekdays + 2 weekend days (MTI)	**Continuous variable:** - BMI (kg/m^2)	n = 100 (53 girls, 47 boys) 7–11-year-olds, Texas. USA	- NS association between BMI and PA	(0)
(42)	**Time spent in counts/min:** - Mean accelerometer (cpm) - Light PA (=800 to <3 200) - Moderate PA (>3 200 to =8 200) - Vigorous PA (=8 200) - Moderate-vigorous PA (=3 200) 6–7 day (same week at least 10 h/d) (Actigraph, model MTI 7 164)	**Categorical variables:** - Overweight[c] - % overweight*** **Continuous variable:** - BMI z-score.	n = 56 (34 girls; 31 boys) 8–10-year-olds, New York, USA	SIG correlations between BMI z-score and overall PA	(0)
(40)	**Daily min:** - Moderate to vigorous PA. 7 days (Actigraph, model 7 164)	**Categorical variables[d]:** - Overweight - Obese	n = 177 8–10-year-olds, Colorado, USA	NS difference in PA between groups.	(0)
(38)	**(min/day):** - MVPA (636–1 645 counts/min) - Vigorous PA (>1 645 counts/min) - Total PA (daily counts) 7 days (RT3 accelerometer)	**Continuous variable:** - % body fat (DXA)	n = 76 (38 girls, 38 boys) 8–11-year-olds, California, USA	Total and vigorous PA SIG negatively associated with % body fat.	(-)
(44)	**PA counts/min:** - Light PA (<3 200) - Moderate-Vigorous PA (≤3 200) - Total PA (counts) 5 days (including two weekend days) (Actigraph)	**Categorical variables:** - Nonoverweight[a] - Overweight[b,c]	n = (85 females, 84 males) 9.5-year-olds, North Wales, UK.	Total PA and MVPA SIG lower in the overweight	(-)

Table IV (*Continued*)

Study	Exposure variables	Outcome variable	Location/Participants	Conclusions	Overall result
(56)	**Acivity Time (AT) (min/d):** - <30 - 30–59.9 - 60–89.9 - ≥90 2 days (RT3)	**Continuous variables:** - Body fat **** - Fat free mass = Weight –Body fat. - BMI (kg/m^2)	n = 251 (121 females, 130 males) 8–11-year-olds, Canada	Activity time (AT) SIG inversely related to body composition.	(-)
(45)	- Total PA (counts/min) - Moderate PA (MVPA) (min/d) - Vigorous PA (VPA) (min/d) 3–4 days (included a weekend day), (Actigraph)	**Continuous variables (DXA):** - Total body fat (TBF) - % body fat (% BF) - Abdominal body fat (ABF)	n = 182 8–11-year-olds, Sweden	SIG negative associations of VPA and TBF, % BF and AFM, adjusted for a range of confounders.	(-)
(46)	**PA (counts/min):** - Light (500–1 999) - Moderate and vigorous (≥2 000) - Vigorous (≥3 000) - and Total PA (counts ·min^{-1} · d^{-1}) 3–4 days (MTI Actigraph; 7164)	**Categorical variables[d]:** - Normal weight - Overweight - Obese **Continuous variable:** - Fat mass (FM) (Sum of 5 skinfolds)	n = 1 292 (638 boys; 654 girls) 9–10-year-olds, 4 European Centres	Normal weight SIG more active (MVPA) than obese after adjustment. Total PA, MVPA and VPA were all SIG inversely correlated with FM, after adjustment.	(-)
(54)	- Light PA (<3 METs) - Moderate PA (3 – 5.9 METs) - Hard PA (6 – 8.9 METs) - Very hard PA (>9 METs) - Total minutes of PA 7 day (Actigraph, MTI)	**Categorical variables:** - Normal weight[a] - Overweight[b] - Obese[c]	n = 1 613 Age groups: 8–9; 10–11 and 15–17 years, Canada.	NS associations between BMI categories and activity.	(0)
(48)	- Total PA 3–4 day (1 weekend day) (Tritrac, RT-3)	**Continuous variables:** - Lean group (BMI <25th percentile) - Obese group[d]	n = 54 (50% obese/50% lean) 9–11.5-year-olds, Greece	NS differences between groups in PA	(0)
(50)	**-** Volume of PA (counts/hour) - Minutes of MPA or above (>3METs) 3 weekdays and 1 weekend day (CSA Actigraph)	**Categorical variables[d]:** - Nonobese - Obese	n = 133 (68 boys; 65 girls). 9–11-year-olds, Bristol, UK	Obese SIG less active than nonobese in both PA variables.	

Table IV (*Continued*)

Study	Exposure variables	Outcome variable	Location/Participants	Conclusions	Overall result
(57)	- Physical activity levels (PAL) 7 days (uniaxial accelerometry sensor, Japan)	**Categorical variables[d]:** - Normal weight - Overweight **Continuous variables:** - BMI (kg/m^2) - Body fat (BIA)	n = 159 10–11-year-olds (grade 5) 13–14-year-olds, (grade 8) Korea and China	NS difference in PAL between weight status categories. PAL SIG negatively correlated with weight, BMI, and % body fat	(-)
(43)	- Total PA counts - Moderate-vigorous bouts (5-min bouts/day) 3 full days (Actiwatch, Mini Mitter)	**Categorical variables:** - Nonoverweight - Overweight	n = 897 (424 nonoverweight and 473 overweight) 4–19-year-olds Houston, USA	Total activity counts were influenced by BMI, and significantly higher in nonoverweight. Time in bouts of moderate-vigorous activity was SIG lower in the overweight.	(-)
(55)	- Total PA volume (count/day) 7 consecutive days (accelerometer Tracmor-4)	**Categorical variables[d]:** - Lean - Overweight	n = 29 12-year-olds, Dutch, Germany.	Overweight SIG lower PA than lean group.	(-)
(47)	Light PA (800 to 3 199 counts) - MVPA (≥3 200counts) 3 days (MTI accelerometer)	**Continuous variable:** - BMI (kg/m^2)	n = 210 (boy Scouts) 10–14-year-olds, Houston, USA	BMI SIG negatively associated with minutes of moderate-to-vigorous PA	(-)
(49)	- MVPA (>1 500) - VPA (≥2 600) - MET-weighted MVPA 6 days included weekend days (MTI Actigraph)	**Continuous variables:** - Weight - BMI (kg/m^2) - %Body fat* - Fat free mass - Fat mass - Index 1 or FMI: fat mass kg/ H^2 - Index 2 or FFMI: fat-free mass kg/ H^2	n = 1 553 girls 10–14-year-old girls, USA	PA SIG negatively associated with all body size and composition variables (strongest for BF and FMI) VPA had slightly more negative correlations with each index	(-)
(30)	- Total PA (counts per minute) - MVPA (>3 600 cpm) 7 days (MTI Actigraph AM7164 2.2)	**Continuous variables (DXA):** - BMI (kg/m^2) - Fat mass - Lean mass - Trunk fat mass	n = 5 500 (2 622 boys, 2 878 girls) 12-year-olds, Bristol, England. UK	SIG negative associations between MVPA and FM (after adjustment for total physical activity), stronger in boys. BMI, FM, and trunk fat were negatively associated with total PA. LM was positively associated with total PA.	(-)

Table IV (*Continued*)

Study	Exposure variables	Outcome variable	Location/Participants	Conclusions	Overall result
(31)	**Activity intensity (counts/min):** - Light PA(100 to 900) - Moderate PA (>900 to ≥2 200) - Vigorous PA (≥2 200) - And Total PA 5–6 days (2 weekend days) (Actiwatch, model AW 16)	**Categorical variables:** - Overweight and Obese [c] - Normal weight [a] **Continuous variables (BIA):** - Fat mass - Fat-free mass - % fat	n = 229 (130 girls; 99 boys). 7–19-year-olds, In three age groups: Elementary, Middle and High school, USA	NS differences in PA by groups defined by weight status. In all age groups, SIG negative associations between body fat and light intensity PA. No association for other PA levels.	(-)
(51)	**Minutes/ day:** - Moderate PA (3–5.9 METs) - Vigorous PA (>6 METs) - And Total PA 7 day (Actigraph)	**Categorical variables:** Overweight/Obese [b,c] - Normal weight	n = 878 12–15-year-olds, USA	Significantly greater VPA in normal weight.	(-)
(52)	- Mean daily PA (counts/min) - Play-equivalent PA (PEPA) 5–7, 1-weekend days (Actiwatch)	**Continuous variables:** - BMI (kg/m^2) - BMI z score [2] - Total body fat % (DXA) - Abdominal body fat % (DXA)	n = 56 (34 boys, 22 girls) 11–16-year-olds, Baltimore, Maryland, USA	NS associations between PA and body composition.	(0)
(53)	- Total daytime PA - Before-school PA - During-school PA - After- school PA 7 day (accelerometer Actigraph, Adrsley)	**Categorical variables:** - Normal weight[a] - at risk of overweight[b] - Overweight[c] **Continuous variables:** - BMI (kg/m^2)	n = 172 girls 14–17-year-olds, Houston, Texas, USA	SIG differences in total daytime and after school PA by groups defined by BMI category. SIG inverse associations PA between BMI and total daytime as well as after-school PA.	(-)
(29)	**Intensity of PA:** - Light - Moderate - Vigorous 5 days (MTI Actigraph)	**Continuous variable (DXA):** - % Body fat (BF)	n = 421 (196 males, 125 females) 16-year-olds, Augusta, GA, USA	- SIG negative association between %BF & all the indexes of PA (stronger for VPA). (Bivariate correlation) - Vigorous PA only SIG predictor of %BF. (Regression)	(-)

[a](BMI between the 5th and 85th percentiles); b (BMI =85th and <95th percentiles); c (BMI =95th percentile); d International age- and sex-specific BMI cut-off points (62)
*equation: -23.39 + 2.27(BMI) + 1.94(triceps skinfold [mm])-2.95(race [1 = African American, 0 = other])-0.52(age [years])-0.52(age [year])-0.06(BMI × triceps skinfold [mm]); equation validated by DXA.
**total body water (kg)/ sex-specific hydration Constants.
***BMI-BMI at the 50th BMI percentile)/BMI at the 50th BMI percentile.
****Using the equations of Slaughter (63).
PA: Physical activity, BMI: Body mass index, SIG: Significant, NS: Not significant, BIA: Bioelectrical impedance analysis.
(-): Significant negative association, (+) significant positive association, (0) no significant association.

89% (8/9) in the medium sized studies and 77% (20/26) in the small studies.

Discussion

The studies summarized in the present review represent a large body of evidence that reported significant and negative associations between objectively measured physical activity and adiposity with a high degree of consistency, probably indicating 'strong evidence' that such an association exists (11). The present review therefore supports the view that variation in the level of habitual physical activity in youth is a contributor to variation in weight status.

The present review found a larger and more consistent body of evidence of significant negative associations between habitual physical activity and adiposity than slightly older reviews (5–8), and is more conclusive in support of the hypothesis that higher levels of physical activity than previous reviews could be. The reasons for differences between the present and older reviews are unclear, but may reflect the inclusion and exclusion criteria in the present study, as well as a rapid expansion in the evidence base, such that 47 eligible new papers were identified in a four year literature search period (30,58).

The present review included studies that used three different kinds of exposure measure (accelerometry, pedometry, and heart rate monitoring). The number of pedometer and heart rate monitoring studies was less than the number of accelerometry studies, but there was a high degree of consistency in conclusions between studies that used the three types of exposure measure. Few authors attempted to identify 'dose-response' relationships between physical activity and adiposity. Future studies might usefully address dose-response relationships in longitudinal and/or intervention studies, and devices that combine accelerometry and heart rate monitoring (59) may be particularly helpful in elucidating more quantitative relationships between physical activity (and physical activity energy expenditure) and adiposity.

The present review found that the recent evidence on associations between habitual physical activity and adiposity in youth remains largely from cross-sectional studies, leaving doubt over causality. More longitudinal studies would be helpful, as recommended by Must and Tybor in their critique of earlier evidence (7). Doubts over causality, and the direction of causality, are not always removed entirely by the longitudinal study design (58). Intervention studies can help resolve doubts over causality (9), and the original concept for the present review was to include randomized controlled intervention studies, which used objective measures of habitual physical activity. However, evidence from randomized controlled studies was not helpful in view of the very small number of studies found in initial searches, the fact that most used physical activity promotion as part of a more complex intervention (which usually involved dietary modification and/or changes in sedentary behavior), making interpretation of the contribution of physical activity problematic, and the fact that those studies that remained failed to achieve an increase in objectively measured habitual physical activity and so could not test the hypothesis that increased habitual physical activity would reduce adiposity.

Publication bias may well have influenced the literature on associations between habitual physical activity and adiposity in youth. No formal test for publication bias was performed in the present study, but the conclusions of larger studies ($n > 1\ 000$) reviewed were actually more supportive (83% of studies found significant negative associations) of the hypothesis that higher levels of physical activity protects against high adiposity than the conclusions of smaller studies ($n < 100$; 73% of studies found significant negative associations), and this conclusion was independent of the method used to categorize sample size, as noted above.

A number of other 'gaps' in the published literature were evident from the present review. Relatively few studies tested for associations between habitual physical activity and adiposity in the preschool population. Many studies did not consider differences in associations between the sexes, but it may be noteworthy that the evidence summarised here contained a suggestion that significant negative associations may be found more commonly among boys than girls, and that associations may be stronger in boys than girls. Future research would be required to address the issue of gender differences more conclusively, but boys are usually more physically active than girls, as suggested by many reviews (60,61). Few studies reviewed here considered differences in associations between sub-groups of the population studied, to permit the examination of possible differences in associations between different socio-economic or ethnic groups for example (10). Almost half of the published studies were from the USA and only 3/48 studies were from developing countries. The inclusion of only publications in the English language may have biased the present review against studies from developing countries, but it is likely that few relevant studies from developing countries have been carried out and/or published. Future research should also focus on addressing the gaps in the literature identified here and in the earlier related reviews (5–8).

Conclusions

The present review supports the hypothesis that higher levels of habitual physical activity are protective against higher levels of child and adolescent adiposity. However, prospective longitudinal studies using more precise methods of body composition are warranted; there is a need for more research on younger children, in a wider variety of settings and populations, and for more 'dose-response' evidence.

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References

1. Reilly JJ. Physical activity and obesity in childhood and adolescence. Lancet. 2005;366(9482):268–9.
2. 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):211–2.
3. Metcalf BS, Voss LD, Hosking J, et al. Physical activity at the government-recommended level and obesity-related health outcomes: a longitudinal study (Early Bird 37). Arch Dis Child. 2008;93(9):772–7.
4. Riddoch CJ, Mattocks C, Deere K, et al. Objective measurement of levels and patterns of physical activity. Arch Dis Child. 2007;92(11):963–9.
5. Hawkins SS, Law C. A review of risk factors for overweight in preschool children: a policy perspective. Int J Pediatr Obes. 2006;1(4):195–209.
6. Wareham NJ, van Sluijs EM, Ekelund U. Physical activity and obesity prevention: a review of the current evidence. Proc Nutr Soc. 2005;64(2):229–47.
7. 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;29Suppl 2:S84–96.
8. Reilly JJ, Penpraze V, Hislop J, et al. Objective measurement of physical activity and sedentary behaviour: review with new data. Arch Dis Child. 2008;93(7):614–9.
9. Reilly JJ, Ness AR, Sherriff A. Epidemiological and physiological approaches to understanding the etiology of pediatric obesity: finding the needle in the haystack. Pediatr Res. 2007;61(6):646–52.
10. Jago R, Baranowski T, Baranowski JC, et al. BMI from 3-6 y of age is predicted by TV viewing and physical activity, not diet. Int J Obes (Lond). 2005;29(6):557–64.
11. Sallis JF, Prochaska JJ, Taylor WC. A review of correlates of physical activity of children and adolescents. Med Sci Sports Exerc. 2000;32(5):963–75.
12. Cleland VJ, Dwyer T, Venn AJ. Physical activity and healthy weight maintenance from childhood to adulthood. Obesity (Silver Spring). 2008;16(6):1427–33.
13. Janz KF, Burns TL, Levy SM. Tracking of activity and sedentary behaviors in childhood: the Iowa Bone Development Study. Am J Prev Med. 2005;29(3):171–8.
14. Raustorp A, Mattsson E, Svensson K, et al. Physical activity, body composition and physical self-esteem: a 3-year follow-up study among adolescents in Sweden. Scand J Med Sci Sports. 2006;16(4):258–66.
15. 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):1298–305.
16. Stevens J, Suchindran C, Ring K, et al. Physical activity as a predictor of body composition in American Indian children. Obes Res. 2004;12(12):1974–80.
17. Ziviani J, Macdonald D, Ward H, et al. Physical activity of young children: a two-year follow-up. Phys Occup Ther Pediatr. 2008;28(1):25–39.
18. Al-Nakeeb Y, Duncan MJ, Lyons M, et al. Body fatness and physical activity levels of young children. Ann Hum Biol. 2007;34(1):1–12.
19. Benefice E, Ndiaye G. Relationships between anthropometry, cardiorespiratory fitness indices and physical activity levels in different age and sex groups in rural Senegal (West Africa). Ann Hum Biol. 2005;32(3):366–82.
20. Rennie KL, Livingstone MB, Wells JC, et al. Association of physical activity with body-composition indexes in children aged 6-8 y at varied risk of obesity. Am J Clin Nutr. 2005;82(1):13–20.
21. Stratton G, Ridgers ND, Fairclough SJ, et al. Physical activity levels of normal-weight and overweight girls and boys during primary school recess. Obesity. 2007;15(6):1513–9.
22. Al-Hazzaa HM. Pedometer-determined physical activity among obese and non-obese 8- to 12-year-old Saudi schoolboys. J Physiol Anthropol. 2007;26(4):459–65.
23. Cuddihy T, Michaud-Tomson L, Jones EK, et al. Exploring the relationship between daily steps, body mass index and physical self-esteem in female Australian adolescents. J Exerc Sci Fit. 2006;4(1):25–35.
24. Duncan JS, Schofield G, Duncan EK. Pedometer-determined physical activity and body composition in New Zealand children. Med Sci Sports Exerc. 2006;38(8):1402–9.
25. Eisenmann JC, Laurson KR, Wickel EE, et al. Utility of pedometer step recommendations for predicting overweight in children. Int J Obes (Lond). 2007;31(7):1179–82.
26. Hands B, Parker H. Pedometer-determined physical activity, BMI, and waist girth in 7- to 16-year-old children and adolescents. J Phys Act Health. 2008;5 Suppl 1:S153–65.
27. Jago R, Watson K, Baranowski T, et al. Pedometer reliability, validity and daily activity targets among 10- to 15-year-old boys. J Sports Sci. 2006;24(3):241–51.
28. Rowe DA, Raedeke TD, Wiersma LD, et al. Investigating the youth physical activity promotion model: internal structure and external validity evidence for a potential measurement model. Pediatr Exerc Sci. 2007;19(4):420–35.

29. Gutin B, Yin Z, Humphries MC, et al. Relations of moderate and vigorous physical activity to fitness and fatness in adolescents. Am J Clin Nutr. 2005;81(4):746–50.
30. Ness AR, Leary SD, Mattocks C, et al. Objectively measured physical activity and fat mass in a large cohort of children. PLoS Med. 2007;4(3):e97.
31. Treuth MS, Hou N, Young DR, et al. Accelerometry-measured activity or sedentary time and overweight in rural boys and girls. Obes Res. 2005;13(9):1606–14.
32. Abbott RA, Davies PS. Habitual physical activity and physical activity intensity: their relation to body composition in 5.0-10.5-y-old children. Eur J Clin Nutr. 2004;58(2):285–91.
33. Blair NJ, Thompson JM, Black PN, et al. Risk factors for obesity in 7-year-old European children: the Auckland Birthweight Collaborative Study. Arch Dis Child. 2007; 92(10):866–71.
34. Hussey J, Bell C, Bennett K, et al. 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):311–6.
35. Jago R, Anderson CB, Baranowski T, et al. Adolescent patterns of physical activity differences by gender, day, and time of day. Am J Prev Med. 2005;28(5):447–52.
36. Lopez-Alarcon M, Merrifield J, Fields DA, et al. Ability of the actiwatch accelerometer to predict free-living energy expenditure in young children. Obes Res. 2004;12(11):1859–65.
37. Metallinos-Katsaras ES, Freedson PS, Fulton JE, et al. The association between an objective measure of physical activity and weight status in preschoolers. Obesity (Silver Spring). 2007;15(3):686–94.
38. Rowlands AV, Eston RG, Powell SM. Total physical activity, activity intensity and body fat in 8-11-year-old boys and girls. J Exerc Sci Fit. 2006;4(2):96–102.
39. Saelens BE, Seeley RJ, van Schaick K, et al. Visceral abdominal fat is correlated with whole-body fat and physical activity among 8-y-old children at risk of obesity. Am J Clin Nutr. 2007;85(1):46–53.
40. Shoup JA, Gattshall M, Dandamudi P, et al. Physical activity, quality of life, and weight status in overweight children. Qual Life Res. 2008;17(3):407–12.
41. Toschke JA, von Kries R, Rosenfeld E, et al. Reliability of physical activity measures from accelerometry among preschoolers in free-living conditions. Clin Nutr. 2007; 26(4):416–20.
42. Wrotniak BH, Epstein LH, Dorn JM, et al. The relationship between motor proficiency and physical activity in children. Pediatrics. 2006;118(6):e1758–65.
43. Butte NF, Puyau MR, Adolph AL, et al. Physical activity in nonoverweight and overweight Hispanic children and adolescents. Med Sci Sports Exerc. 2007;39(8):1257–66.
44. Byrd-Williams C, Kelly LA, Davis JN, et al. Influence of gender, BMI and Hispanic ethnicity on physical activity in children. Int J Pediatr Obes. 2007;2(3):159–66.
45. Dencker M, Thorsson O, Karlsson MK, et al. Daily physical activity related to body fat in children aged 8-11 years. J Pediatr. 2006;149(1):38–42.
46. Ekelund U, Sardinha LB, Anderssen SA, et al. Associations between objectively assessed physical activity and indicators of body fatness in 9- to 10-y-old European children: a population-based study from 4 distinct regions in Europe (the European Youth Heart Study). Am J Clin Nutr. 2004;80(3):584–90.
47. Jago R, Baranowski T, Zakeri I, et al. Observed environmental features and the physical activity of adolescent males. Am J Prev Med. 2005;29(2):98–104.
48. Krekoukia M, Nassis GP, Psarra G, et al. Elevated total and central adiposity and low physical activity are associated with insulin resistance in children. Metabolism. 2007;56(2): 206–13.
49. Lohman TG, Ring K, Schmitz KH, et al. Associations of body size and composition with physical activity in adolescent girls. Med Sci Sports Exerc. 2006;38(6):1175–81.
50. Page A, Cooper AR, Stamatakis E, et al. Physical activity patterns in nonobese and obese children assessed using minute-by-minute accelerometry. Int J Obes (Lond). 2005;29(9):1070–6.
51. Patrick K, Norman GJ, Calfas KJ, et al. Diet, physical activity, and sedentary behaviors as risk factors for overweight in adolescence. Arch Pediatr Adolesc Med. 2004;158(4):385–90.
52. Snitker S, Le KY, Hager E, et al. Association of physical activity and body composition with insulin sensitivity in a community sample of adolescents. Arch Pediatr Adolesc Med. 2007;161(7):677–83.
53. Sulemana H, Smolensky MH, Lai D. Relationship between physical activity and body mass index in adolescents. Med Sci Sports Exerc. 2006;38(6):1182–6.
54. Thompson AM, Campagna PD, Rehman LA, et al. Physical activity and body mass index in grade 3, 7, and 11 Nova Scotia students. Med Sci Sports Exerc. 2005;37(11):1902–8.
55. Vogels N, Westerterp KR, Posthumus DL, et al. Daily physical activity counts vs structured activity counts in lean and overweight Dutch children. Physiol Behav. 2007;92(4): 611–6.
56. Wittmeier KD, Mollard RC, Kriellaars DJ. Objective assessment of childhood adherence to Canadian physical activity guidelines in relation to body composition. Appl Physiol Nutr Metab. 2007;32(2):217–24.
57. Yamauchi T, Kim SN, Lu Z, et al. Age and gender differences in the physical activity patterns of urban schoolchildren in Korea and China. J Physiol Anthropol. 2007;26(2):101–7.
58. Ekelund U, Brage S, Besson H, et al. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality? Am J Clin Nutr. 2008;88(3):612–7.
59. Dencker M, Andersen LB. Health-related aspects of objectively measured daily physical activity in children. Clin Physiol Funct Imaging. 2008;28(3):133–44.
60. Seabra AF, Mendonca DM, Thomis MA, et al. [Biological and socio-cultural determinants of physical activity in adolescents]. Cad Saude Publica. 2008;24(4):721–36.
61. Oliver M, Schofield GM, Kolt GS. Physical activity in preschoolers: understanding prevalence and measurement issues. Sports Med. 2007;37(12):1045–70.
62. Cole TJ, Bellizzi MC, Flegal KM, et al. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320(7244):1240–3.
63. Slaughter MH, Lohman TG, Boileau RA, et al. Skinfold equations for estimation of body fatness in children and youth. Hum Biol. 1988;60(5):709–23.

II

PHYSICAL ACTIVITY, FITNESS AND FATNESS IN CHILDREN AND ADOLESCENTS

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Chapter 21

Physical activity, fitness and fatness in children and adolescents

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Outline

1. Introduction

Childhood and adolescence are crucial periods of life since dynamic changes in various metabolic systems, including hormonal regulation, changes in body fat content and body fat distribution, as well as transient changes in insulin sensitivity are known to occur during growth and puberty (Cruz, Shaibi, Weigensberg, Spruijt-Metz, Ball & Goran, 2005). Dramatic psychological changes also occur during this period. Likewise, lifestyle and healthy/unhealthy behaviours are established during these years, which may influence adult behaviour and health status.

A sedentary lifestyle together with a poor diet are the leading causes together with tobacco for the development of cardiovascular disease (CVD) and death (Mokdad, Marks, Stroup & Gerberding, 2004). Obesity is also a major health problem that affects not only adults but also children and adolescents. Increased energy intake together with reduced energy expenditure results in body fat accumulation. The consequences on health of excess of body fat are well known. Adults who were overweight in childhood have higher levels of blood lipids and lipoproteins, blood pressure, and fasting insulin levels, and thus are at increased risk for CVD compared with adults who were thin as children (Freedman, Khan, Dietz, Srinivasan & Berenson, 2001; Steinberger, Moran, Hong, Jacobs & Sinaiko, 2001; Thompson, Obarzanek, Franko, Barton, Morrison, Biro, Daniels & Striegel-Moore, 2007). Moreover, over the long term, childhood overweight is strongly associated with adult obesity. Childhood overweight confers a 5-fold or greater increase in risk for being overweight in early adulthood relative to children who were not overweight at the same age (Steinberger et al., 2001; Guo, Wu, Chumlea & Roche, 2002; Thompson et al., 2007).

The protective effect of intentional physical activity on the above mentioned CVD risk factors has been reported in people of all ages (Strong, Malina, Blimkie, Daniels, Dishman, Gutin, Hergenroeder, Must, Nixon, Pivarnik, Rowland, Trost & Trudeau, 2005; Pedersen & Saltin, 2006). However, these findings are often confined to questionnaire-based assessment of physical activity, which often lack the necessary accuracy, especially in young people (Kohl, Fulton & Caspersen, 2000).

One factor related with physical activity is physical fitness. Physical activity and physical fitness are closely related in that fitness is partially determined by physical activity patterns over recent weeks or months. Cardiorespiratory fitness has received special attention during the last decades. There is increasing evidence that high levels of cardiorespiratory fitness provides strong and independent prognostic information about the overall risk of illness and death, especially that from cardiovascular causes (LaMonte & Blair, 2006; Castillo-Garzon, Ruiz, Ortega & Gutierrez-Sainz, 2007).

In the present chapter, we summarise the latest developments in regard to physical activity, fitness, obesity and obesity-related CVD risk factors in children and adolescents.

2. Physical activity and body fat in children and adolescents: Does the intensity matter?

2.1. Physical activity and total body fat

The prevalence of childhood and adolescence obesity is increasing at alarming rate worldwide. A sedentary lifestyle (i.e., watching television or/and playing computer/video games) as well as reduction of physical activity level seem to be the major determinant implicated in this trend. However, studies performed in children and adolescents show contradictory results, probably due to the inherent difficulties on measuring physical activity, as well as to the different technologies used to assess it. Physical activity has been commonly assessed by using questionnaires. Questionnaires have highly limited accuracy in the measurement of daily physical activity, especially in children and adolescents. More objective methods such as accelerometry, have been shown to provide adequate measures for physical activity in children and adolescents Precise methods of measuring physical activity utilizing objective measurement such as accelerometry are needed to accurately establish the dose-response relationships between physical activity with cardiovascular health outcomes in children and adolescents (Dencker & Andersen, 2008; Steele, Brage, Corder, Wareham & Ekelund, 2008). In the present review, we will mostly refer to studies that used accelerometry to assess physical activity, otherwise, it will be indicated.

Cross-sectional studies examining the relationship between various measures of body fat objectively measured physical activity have usually indicated a negative relationship, between activity levels and body fat. A multicenter study conducted on 1292 European children aged 9-10 years analysed the associations of objectively measured physical activity with indicators of total body fat (i.e., sum of 5 skinfold thicknesses and body mass index) (Ekelund, Sardinha, Anderssen, Harro, Franks, Brage, Cooper, Andersen, Riddoch & Froberg, 2004). The results suggested that accumulated amount of time spent at moderate and vigorous physical activity is related, yet weakly, to total body fat. Wittmeier et al. (Wittmeier, Mollard & Kriellaars, 2007) investigated 251 Canadian children aged 8-11 years, and found that time spent in moderate to vigorous physical activity was inversely correlated with body mass index and skinfold-derived estimate of body fat. However, several studies suggested that vigorous physical activity may be more important in the prevention of obesity in children and adolescents (Rowlands, Eston & Ingledew, 1999; Abbott & Davies, 2004; Ara, Vicente-Rodriguez, Jimenez-Ramirez, Dorado, Serrano-Sanchez & Calbet, 2004; Gutin, Yin, Humphries & Barbeau, 2005; Ruiz, Rizzo, Hurtig-Wennlöf, Ortega, Wärnberg & Sjöström, 2006d; Butte, Puyau, Adolph, Vohra & Zakeri, 2007; Stallmann-Jorgensen, Gutin, Hatfield-Laube, Humphries, Johnson & Barbeau, 2007; Dencker, Thorsson, Karlsson, Linden, Wollmer & Andersen, 2008). Gutin et al. (Gutin et al., 2005) reported that only vigorous physical activity was associated with lower fatness in 421 North-American adolescents aged 16 years. A report of a small study, conducted on 47 children aged 5-10, showed similar finding (Abbott & Davies, 2004). Denker et al. (Dencker et al., 2008) reported a strong relationship between vigorous physical activity and body fat in 225 Swedish children aged 8-11 years. Likewise, Butte et al. (Butte et al., 2007) observed a strong and negative association between vigorous physical activity and percent body fat in 897 children aged 4-19 years. Furthermore, Ruiz et al. (Ruiz et al., 2006d) suggested that physical activity of vigorous intensity may have a greater effect on preventing obesity in children than does physical activity of lower intensity in Estonian and Swedish children participating in the European Youth Heart Study (EYHS) (Figure 1). Finally, a study recently reported that lower levels of body fat were related to greater amount (≥ 1 hour) of vigorous physical activity, but not with moderate physical activity or total energy intake in 661 adolescents aged 8-14 years (Stallmann-Jorgensen et al., 2007). Longitudinal studies also support the idea that youth who participate in relatively high levels of physical activity have less body fat later in life compare to their less active peers (Berkey, Rockett, Field, Gillman, Frazier, Camargo & Colditz, 2000; Ekelund, Aman, Yngve, Renman, Westerterp & Sjostrom, 2002; Moore, Gao, Bradlee, Cupples, Sundarajan-Ramamurti, Proctor, Hood, Singer & Ellison, 2003; Stevens, Suchindran, Ring, Baggett, Jobe, Story, Thompson, Going & Caballero, 2004; Janz, Burns & Levy, 2005; Metcalf, Voss, Hosking, Jeffery & Wilkin, 2008). Experimental studies have been developed to obtain specific information about the influence of regular physical activity on body fat in normal-weight and/or overweight and obese children and adolescents.

In overweight and obese children, beneficial effects in body fat control maybe attained with 30-60 min of moderate physical activity, 3-7 d/wk (Barbeau, Gutin, Litaker, Owens, Riggs & Okuyama, 1999; Owens, Gutin, Allison, Riggs, Ferguson, Litaker & Thompson, 1999; Gutin, Barbeau, Owens, Lemmon, Bauman, Allison, Kang & Litaker, 2002; LeMura & Maziekas, 2002; Klijn, van der Baan-Slootweg & van Stel, 2007). However, obese adolescents who spent more time engaged in vigorous physical activity tended to be those who decreased body fat the most (Barbeau et al., 1999; Gutin et al., 2002). For several reasons, it is reasonable to recommend moderate physical activity for obese children and adolescents until higher intensities can be attained. Moderate physical activity is better tolerated than vigorous physical activity (Barbeau et al., 1999), and tiring physical activity may lead to less physical activity on the following day (Kriemler, Hebestreit, Mikami, Bar-Or, Ayub & Bar-Or, 1999), although it likely depends on the type of exercise performed (Owens et al., 1999). Therefore, for obese children and those who have been physically inactive, an incremental approach to the 45-60 min/d goal of moderate physical activity 5 or more days per week is recommended (Strong et al., 2005). However, these programs do not influence body fatness in normal-weight children and adolescents (Rowland, Martel, Vanderburgh, Manos & Charkoudian, 1996; Tolfrey, Campbell & Batterham, 1998; Owens et al., 1999; Eliakim, Scheett, Allmendinger, Brasel & Cooper, 2001; Tolfrey, Jones & Campbell, 2004). Limited evidences suggest that more intensive and longer sessions (≥ 80 min/d) are needed to reduce percentage body fat in normal-weight youth (Eliakim, Makowski, Brasel & Cooper, 2000; Yin, Gutin, Johnson, Hanes, Moore, Cavnar, Thornburg, Moore & Barbeau, 2005; Barbeau, Johnson, Howe, Allison, Davis, Gutin & Lemmon, 2007). Finally, Gutin et al. (Gutin, Yin, Johnson & Barbeau, 2008) have recently reported the effect of a 3-year after-school physical activity intervention on aerobic fitness and percent body fat. The intervention included 40 min of academic enrichment activities, during which healthy snacks were provided, and 80 min of moderate-to-vigorous physical activity. They showed a favourable effects on cardiorespiratory fitness and fatness during the school years when the children were exposed to the intervention. However, during the summers following the first and second years of intervention, the favourable effects on cardiorespiratory fitness and percentage body fat were lost, which shows the importance of maintaining exposure to vigorous physical activity.

The current literature above mentioned agrees in a fairly consistent manner that association between physical activity and obesity is stronger for vigorous physical activity than for moderate physical activity. However, when the adolescent is exercising at a higher intensity, the total energy expenditure associated with that activity is higher than for a similar time effort at moderate intensity. So the question whether is it really the intensity what matters or is the total amount of energy expenditure the responsible for many of the outcomes reported remains to be answered. In other words, whether 30 min of moderate-intensity physical activity and 10 min of vigorous-intensity physical activity (assuming that both would have the same energy cost) have different effects on body composition indexes remains to be elucidated. Strictly, only a well-design control-randomized trial could accurately answer to this question, though some attempts can also be done using observational data.

Future research should pay effort on solving this dilemma by making equivalent the energy expenditure-linked to vigorous physical activity and moderate physical activity, so only the intensity and not the total number of calories spent will differ between these two sub-components of physical activity. The outcomes of such study designs will help to better understand how and to what extent the intensity of physical activity matters regarding obesity management and prevention.

2.2. Physical activity and central body fat

Central body fat has shown to be associated with a range of risk factors for cardiovascular disease already in young people (Gutin, Johnson, Humphries, Hatfield-Laube, Kapuku, Allison, Gower, Daniels & Barbeau, 2007) and is becoming of increasing importance in paediatrics. Although, there are accurate and sophisticated methods to evaluate central body fat, waist circumference is an accurate surrogate for central body fat (Brambilla, Bedogni, Moreno, Goran, Gutin, Fox, Peters, Barbeau, De Simone & Pietrobelli, 2006) and a powerful marker associated with a number of cardiovascular risk factors and metabolic syndrome, both in non-overweight and overweight individuals (Janssen, Katzmarzyk, Srinivasan, Chen, Malina, Bouchard & Berenson, 2005).

We (Ortega, Tresaco, Ruiz, Moreno, Martin-Matillas, Mesa, Warnberg, Bueno, Tercedor, Gutierrez & Castillo, 2007b) did not observe any association between abdominal fat and physical activity assessed by questionnaire in 2859 Spanish adolescents who took part in the AVENA (Alimentación y Valoración del Estado Nutricional en Adolescentes) study. However, another study with 2714 French children aged 12 years, reported a negative relationship between waist circumference and physical activity, which was also assessed by questionnaire (Klein-Platat, Oujaa, Wagner, Haan, Arveiler, Schlienger & Simon, 2005).

More recent findings performed in children and adolescents have shown a negative association between central body fat and physical activity assessed by accelerometers, especially with vigorous physical activity (Hussey, Bell, Bennett, O'Dwyer & Gormley, 2007; Ortega, Ruiz & Sjostrom, 2007a; Saelens, Seeley, van Schaick, Donnelly &

O'Brien, 2007; Dencker et al., 2008; Sardinha, Andersen, Anderssen, Quiterio, Ornelas, Froberg, Riddoch & Ekelund, 2008) (Figure 2). Moreover, some of them suggest that time spent in sedentary activities, such us viewing television or/and playing computer/video games is strongly related with the increasing of central body fat (Hussey et al., 2007; Ortega et al., 2007a; Dencker et al., 2008).

Whether cardiorespiratory fitness modifies the association between physical activity and abdominal fat is another matter of interest. We (Ortega, Ruiz, Hurtig-Wennlof, Vicente-Rodriguez, Rizzo, Castillo & Sjostrom, 2008) have addressed the first study examining how cardiorespiratory fitness can influence the associations between objectively measured physical activity and abdominal fat in 1075 Swedish children and adolescents from the EYHS. We showed that the associations between physical activity and abdominal fat differ by fitness levels. In low fit children and adolescents, time spent in vigorous physical activity seems to be the key component linked to abdominal body fat. Unexpectedly, we also observed that in high fit children and adolescents, physical activity was positively associated with waist circumference. Further research examining genetic and dietary factors, in addition to objectively measured physical activity and cardiorespiratory fitness are still needed for a better understanding of the associations between physical activity and body fat in young people.

Finally, evidence from intervention studies support that physical activity in children and adolescents reduces central body fat, as well as we have mentioned for total body fat (Owens et al., 1999; Eliakim et al., 2000; Gutin et al., 2002; Barbeau et al., 2007; Klijn et al., 2007). It seems that 30-60 min of moderate physical activity for 3-7 d/wk may have beneficial effects to control and reduce waist central body fat in obese children (Owens et al., 1999; Gutin et al., 2002; Klijn et al., 2007). However, in normal-weight children, sessions of at least 80 min/d of vigorous physical activity might be needed in order to reduce it (Eliakim et al., 2000; Barbeau et al., 2007).

3. Physical activity and obesity-related cardiovascular disease risk factors

There is extensive evidence on the relationship between physical activity and obesity-related CVD risk factors. In adults, it has been shown an association of physical activity with slower progression towards the metabolic syndrome independently of body fatness (Ekelund, Franks, Sharp, Brage & Wareham, 2007b). However, population studies focusing on these relationships in children and adolescents are limited.

Recently, habitual physical activity levels have been associated with many obesity-related CVD risk factors such as blood pressure, total cholesterol (TC), low density lipoprotein cholesterol (LDLc), triglycerides and insulin resistance (Brage, Wedderkopp, Ekelund, Franks, Wareham, Andersen & Froberg, 2004; Andersen, Harro, Sardinha, Froberg, Ekelund, Brage & Anderssen, 2006; Ekelund, Anderssen, Froberg, Sardinha, Andersen & Brage, 2007a; Hurtig-Wennlof, Ruiz, Harro & Sjostrom, 2007; Rizzo, Ruiz, Oja, Veidebaum & Sjostrom, 2008). This negative association was stronger for moderate and vigorous physical activity levels (Andersen et al., 2006; Hurtig-Wennlof et al., 2007; Rizzo et al., 2008; Sardinha et al., 2008) than for light or sedentary activity levels (Sardinha et al., 2008). In this sense, we showed that total, moderate, and vigorous physical activity were inversely correlated with insulin resistance in Swedish adolescents from the EYHS (Rizzo et al., 2008) (Figure 3). In a study conductedin 2,201 children from 3 different countries, found that a graded decrease in metabolic risk across five levels of physical activity (Andersen et al., 2006). Children that were in the lowest activity level had an odds ratio of clustered risk around 3 compared with the most active children. The authors concluded that to prevent clustering of cardiovascular disease risk factors, the total accumulate physical activity level should be 90 min of daily activity. This would also prevent insulin resistance, which seems to be the central feature for clustering of cardiovascular disease risk factors.

Whether the association between physical activity and markers of cardiovascular health is mediated or confounded by body fat is controversial. The degree to which adjustment for body fat attenuates or modifies the association between physical activity and metabolic risk varies across studies. In some studies, when level of body fat is excluded from the risk score and adjusted for as a covariate, the magnitude of the association between physical activity and the non-obesity CVD risk tends remain unchanged (Brage et al., 2004; Ekelund et al., 2007a), whereas in others studies this association is attenuated (Rizzo, Ruiz, Hurtig-Wennlof, Ortega & Sjostrom, 2007). Sardinha et al. found that physical activity was associated with insulin resistance independent of total and central body fat in children (Sardinha et al., 2008).

Attenuation may suggest a mediating effect of body fat, because this factor may lie on the causal pathway between physical activity and metabolic health. For example, physical activity may detectably impact on variables such as fasting glucose and blood lipids, whereas no effect would be observed for body fat, which is likely to be the result of long-term balance or imbalance between energy expenditure and intake. However, long-term effects of physical activity on other risk factors could plausibly exist. Different degrees of measurement precision in the assessment of body fat and physical activity may also explain attenuation of results and variation between studies.

4. Physical fitness and body fat in children and adolescents

Childhood obesity is associated with a variety of adverse consequences both at early age and later in life, therefore, it is of relevance to thoroughly study the association between fatness and modifiable lifestyle-inherent factors potentially related with body fat, such as physical fitness. Not only the total fat amount may influence the youths' health status, but also how that fat is distributed in the body. In this section both total and central body fat and their relationships with physical fitness in children and adolescents are discussed.

4.1. Physical fitness and total body fat

Nowadays, children spent less time practicing sports or physical activities (Oehlschlaeger, Pinheiro, Horta, Gelatti & San'Tana, 2004), and more time watching television and/or playing video games (Andersen, Crespo, Bartlet, Cheskin & Pratt, 1998). These behavioural changes may lead to decreases in daily energy expenditure, what in turns could explain, at least partially, the increasing trends in childhood obesity (Rey-Lopez, Vicente-Rodriguez & Moreno, 2007). Despite its well known limitation to discriminate between fat and lean tissue, body mass index is internationally used to define overweight and obese in children and adolescents (Cole, Bellizzi, Flegal & Dietz, 2000), though other anthropometrics such as skinfold thicknesses are often used in the literature as surrogates of total body fat. Several studies have been conducted to study the associations between physical fitness and fatness measures in young people.

Data from the Swedish part of the EYHS, a school based, cross-sectional study of risk factors for future CVD in a sample of children (9-10 years old) and adolescents (15-16 years old) (Poortvliet, Yngve, Ekelund, Hurtig-Wennlof, Nilsson, Hagstromer & Sjostrom, 2003), indicate that those individuals having a high cardiorespiratory fitness level also have significantly lower total body fat, as measured by skinfold thicknesses (Ortega, Ruiz, Castillo, Moreno, Warnberg, Tresaco, Gonzalez-Gross, Perez, Garcia-

Fuentes & Gutierrez, 2006). When total fatness was assessed by a reference method, such as Dual Energy X-ray Absorptiometry in Spanish (Ara et al., 2004) and North American (Lee & Arslanian, 2007) children, similar inverse associations were found. Cardiorespiratory fitness has shown a stronger association with total body fat, as measured by skinfold thicknesses, than other physical fitness components such as muscular fitness, speed/agility, flexibility or motor coordination (Ara, Moreno, Leiva, Gutin & Casajus, 2007). Even in overweight or obese children, those children who had a higher cardiorespiratory fitness have shown a lower overall body fat (Nassis, Psarra & Sidossis, 2005). Longitudinal data have shown a significant relationship between adolescent cardiorespiratory fitness and later body fatness, so that the higher the cardiorespiratory fitness levels the lower the body fat levels (Eisenmann, Wickel, Welk & Blair, 2005; Ara, Vicente-Rodriguez, Perez-Gomez, Jimenez-Ramirez, Serrano-Sanchez, Dorado & Calbet, 2006).

4.2. Physical fitness and central body fat

The study of fat distribution among children and adolescents is complex because there are marked changes in circumferences and skinfold thickness during growth and development (Ruiz, Ortega, Tresaco, Warnberg, Mesa, Gonzalez-Gross, Moreno, Marcos, Gutierrez & Castillo, 2006c). Waist circumference has shown to be an accurate marker of abdominal fat accumulation (Taylor, Jones, Williams & Goulding, 2000) and visceral fat (Brambilla, Bedogni, Moreno, Goran, Gutin, Fox & 2006) in young people. In addition, waist circumference seems to explain the variance in a range of CVD risk factors to a similar extent as measures derived from high-technology techniques, including DXA and Magnetic Resonance Imaging (Ara et al., 2007). Therefore, the use of waist circumference as a surrogate of abdominal fat, and as a powerful index associated with metabolic risk in young people, seems to be appropriate for epidemiological studies.

Data from the AVENA study showed that both moderate to high levels of cardiorespiratory fitness are associated with lower abdominal fat, as measured by waist circumference (Ortega et al., 2007b). These results are in accordance with those found in 224 Irish children aged 7-10 years (Hussey et al., 2007). Similar associations have also been reported when physical fitness was measured as lower limb explosive strength, abdominal endurance strength or speed/agility instead of cardiorespiratory fitness in 1,140 Canadian children (591 boys and 549 girls) aged 7-10 years (Brunet, Chaput & Tremblay, 2007). In those studies the abdominal fat was also measured by waist circumference. The same inverse association with cardiorespiratory fitness was observed when visceral and abdominal subcutaneous adipose tissue were measured using computed tomography or magnetic imaging resonance instead of waist circumference (Winsley, Armstrong, Middlebrooke, Ramos-Ibanez & Williams, 2006; Lee & Arslanian, 2007).

Several studies showed that cardiorespiratory fitness at childhood and adolescence is a predictor of excess of overall and central body fat later in life (Johnson, Figueroa-Colon, Herd, Fields, Sun, Hunter & Goran, 2000; Twisk, Kemper & van Mechelen, 2000; Boreham, Twisk, Neville, Savage, Murray & Gallagher, 2002; Hasselstrom, Hansen, Froberg & Andersen, 2002; Janz, Dawson & Mahoney, 2002b; Twisk, Kemper & van Mechelen, 2002b; Koutedakis & Bouziotas, 2003; Andersen, Hasselstrom, Gronfeldt, Hansen & Karsten, 2004b; Psarra, Nassis & Sidossis, 2005; Byrd-Williams, Shaibi, Sun, Lane, Ventura, Davis, Kelly & Goran, 2008). In contrast, there is one study showing that cardiorespiratory fitness at the age of 16 is not associated with markers of overall and central body fat at the age of 34 (Barnekow-Bergkvist, Hedberg, Janlert & Jansson, 2001).

5. Physical fitness and obesity-related cardiovascular disease risk factors

There is compelling evidence that the precursors of cardiovascular disease (CVD) have their origin in childhood and adolescence (Berenson, Srinivasan, Bao, Newman, Tracy & Wattigney, 1998). CVD risk factors such as TC, LDLc, high density lipoprotein cholesterol (HDLc), triglycerides, insulin resistance, inflammatory proteins, blood pressure and total and central body fat in childhood have been shown to track into adulthood (Raitakari, Juonala, Kahonen, Taittonen, Laitinen, Maki-Torkko, Jarvisalo, Uhari, Jokinen, Ronnemaa, Akerblom & Viikari, 2003; Andersen, Hasselstrøm, Gronfeldt, Hansen & Froberg, 2004a).

Cardiorespiratory fitness and obesity-related cardiovascular disease risk factors

Higher levels of cardiorespiratory fitness have been associated with a healthier cardiovascular profile in children and adolescents (Mesa, Ortega, Ruiz, Castillo, Hurtig-Wennlöf, Sjöstrom & Gutierrez, 2006a; Mesa, Ortega, Ruiz, Castillo, Tresaco, Carreno, Moreno, Gutierrez & Bueno, 2006b; Mesa, Ruiz, Ortega, Warnberg, Gonzalez-Lamuno, Moreno, Gutierrez & Castillo, 2006c; Ruiz, Ortega, Gutierrez, Meusel, Sjöström & Castillo, 2006a; Ruiz, Ortega, Meusel, Harro, Oja & Sjöström, 2006b; Ruiz et al., 2006d; Garcia-Artero, Ortega, Ruiz, Mesa, Delgado, Gonzalez-Gross, Garcia-Fuentes, Vicente-Rodriguez, Gutierrez & Castillo, 2007; Hurtig-Wennlof et al., 2007; Lobelo & Ruiz, 2007; Ortega et al., 2007b; Rizzo et al., 2007; Ruiz, Ortega, Loit, Veidebaum & Sjostrom, 2007b; Ruiz, Ortega, Meusel & Sjostrom, 2007c; Ruiz, Ortega, Rizzo, Villa, Hurtig-Wennlöf, Oja & Sjöström, 2007d; Ruiz, Ortega, Warnberg & Sjostrom, 2007e; Ruiz, Rizzo, Ortega, Loit, Veidebaum & Sjostrom, 2007f; Ruiz, Sola, Gonzalez-Gross, Ortega, Vicente-Rodriguez, Garcia-Fuentes, Gutierrez, Sjöström, Pietrzik & Castillo, 2007g; Ruiz, Castro-Pinero, Artero, Ortega, Sjostrom, Suni & Castillo, 2009). This association seems to be independent of sex, age, ethnicity, and grade of obesity. Results from the AVENA study indicate that high levels of cardiorespiratory fitness are associated with a more favourable metabolic profile (computed from age and sex specific standardized values of triglycerides, LDLc, HDLc and fasting glycaemia) in both overweight and non-overweight Spanish adolescents (Mesa et al., 2006c). The same association was also found between cardiorespiratory fitness and a clustering of CVD risk factors, as well as with individual CVD risk factors in Swedish and Estonian children and adolescents participating in the EYHS (Hurtig-Wennlof et al., 2007; Rizzo et al., 2007; Ruiz et al., 2007d). Data from the 1999-2002 rounds of the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the non-institutionalized U.S. adolescents (Centers for Disease Control and Prevention, ; Centers for Disease Control and Prevention), also revealed that higher levels of cardiorespiratory fitness were associated with a more favorable cardiovascular profile (Lobelo, Pate, Dowda, Liese & Ruiz, In press).

Given the importance of cardiorespiratory fitness as a powerful marker of health in childhood and adolescence, sex-specific cut-offs for a healthy cardiorespiratory fitness level in childhood and adolescence have been proposed by several institutions and worldwide recognized organizations such as the Cooper Institute or the European Group of Pediatric Work Physiology (Table 1) (Bell, Macek, Rutenfranz & Saris, 1986. p. 39-42.; Cureton & Warren, 1990; The Cooper Institute for Aerobics Research, 2004. p. 38-39.; Ruiz et al., 2007d). The health-related cardiorespiratory fitness thresholds suggested by the FITNESSGRAM (Cureton & Warren, 1990; The Cooper Institute for Aerobics Research, 2004. p. 38-39.) are similar to those proposed by the European

Group of Pediatric Work Physiology (Bell et al., 1986. p. 39-42.) and also to those associated with an increased risk for metabolic disease, calculated by others (Ruiz et al., 2007d; Lobelo et al., In press) (Table 1). It is noteworthy that the approaches used to calculate these cardiorespiratory fitness health-related thresholds were different in these studies, as were age, race, nationality, environmental and cultural and social factors of the participants studied. However, the consistency in the findings support the existence of a hypothetical cardiorespiratory fitness value linked to a more favorable cardiovascular profile, which seems to range between 40 and 42 ml/min/kg in boys and between 35 and 38 ml/min/kg in girls.

Cardiorespiratory fitness has also been inversely associated with relatively other obesity-related CVD risk factors such as low grade inflammatory markers and homocysteine in young people (Wärnberg, Ruiz, Sjöström, Ortega, Moreno, Moreno, Rizzo & Marcos, 2006b; Ruiz et al., 2007e; Ruiz et al., 2007g). Low-grade inflammation seems to play a role in the development of cardiovascular disease from an early age (Jarvisalo, Harmoinen, Hakanen, Paakkunainen, Viikari, Hartiala, Lehtimaki, Simell & Raitakari, 2002; Hansson, 2005). It has been observed an increased low-grade inflammation in overweight adolescents compared with their non-overweight counterparts (Wärnberg, Nova, Moreno, Romeo, Mesana, Ruiz, Ortega, Sjöström, Bueno & Marcos, 2006a). We (Ruiz et al., 2007e) showed that the levels of C-reactive protein and C3 were inversely associated with cardiorespiratory fitness in prepubertal Swedish children from the EYHS, which is consistent with other studies of young people (Halle, Berg, Northoff & Keul, 1998; Isasi, Deckelbaum, Tracy, Starc, Berglund & Shea, 2003; Cooper, Nemet & Galassetti, 2004). Similarly, data from the AVENA study showed that overweight and unfit adolescents are more likely to have high levels of C-reactive protein, C3 and C4 compared to non overweight and fit peers (Wärnberg et al., 2006b). It has been shown (Halle, Korsten-Reck, Wolfarth & Berg, 2004) that low grade inflammation was negatively associated with cardiorespiratory fitness in normal weight and overweight children aged 12 years. They reported that IL-6 levels were as low for obese and fit as for lean and unfit children, while the higher IL-6 levels were found in the obese and unfit group. In contrast, they also showed that TNF-α seemed to be primarily dependent on cardiorespiratory fitness but not obesity as similar levels were found for non obese as well as obese children with a low cardiorespiratory fitness.

Epidemiologic and clinical evidence show that hyperhomocysteinaemia is an independent, modifiable risk factor for atherosclerosis and cardiovascular disease (McCully, 2005; Castro, Rivera, Blom, Jakobs & Tavares de Almeida, 2006). The amount of body fat has been associated with homocysteine levels in obese children and adolescents (Gallistl, Sudi, Mangge, Erwa & Borkenstein, 2000). Insulin resistance has been implicated in the relationship, since insulin levels are strongly correlated with body fat (Gallistl et al., 2000). In contrast, we did not find an association between body fatness (as expressed as skinfold thickness or as body mass) and homocysteine levels, even when the analyses were performed separately for normal-weight or overweight-obese categories (Ruiz, Hurtig-Wennlöf, Ortega, Patersson, Nilsson, Castillo & Sjöström, 2007a). Studies examining the association between cardiorespiratory fitness and homocysteine levels in young people are scarce, and the results published so far are contradictory. We have found conflicting results in Spanish adolescents (Ruiz et al., 2007g) and Swedish children and adolescents (Ruiz et al., 2007a) after controlling for different potential confounders including age, puberty, birth weight, smoking, socioeconomic status, skinfold thickness and methylenetetrahydrofolate reductase 677C>T genotype. Cardiorespiratory fitness was inversely and significantly associated in female Spanish adolescents (Ruiz et al., 2007g), which concur with the results reported by others (Kuo, Yen & Bean, 2005) in adult women. In contrast, we did not observed an association between cardiorespiratory fitness and homocysteine levels in Swedish children and adolescents (Ruiz et al., 2007a). These results should encourage discussion on whether the metabolism of homocysteine could be one way in which the benefits of high cardiorespiratory fitness are exerted.

Cardiorespiratory fitness and later obesity-related cardiovascular disease risk factors

The relationships between health-related physical fitness in youths and obesity-related CVD risk factors later in life have been examined. Several studies have showed that cardiorespiratory fitness at childhood and adolescence is a predictor of obesity-related CVD risk factors, such as abnormal blood lipids (Johnson et al., 2000; Twisk et al., 2000; Boreham et al., 2002; Hasselstrom et al., 2002; Janz et al., 2002b; Twisk et al., 2002b; Carnethon, Gidding, Nehgme, Sidney, Jacobs & Liu, 2003; Ferreira, Twisk, Stehouwer, van Mechelen & Kemper, 2003; Andersen et al., 2004b; Ferreira, Henry, Twisk, van Mechelen, Kemper & Stehouwer, 2005), high blood pressure (Hasselstrom et al., 2002; Twisk, Kemper & van Mechelen, 2002a; Carnethon et al., 2003; Andersen et al., 2004b), excess of overall and central body fat (Johnson et al., 2000; Twisk et al., 2000; Boreham et al., 2002; Hasselstrom et al., 2002; Janz et al., 2002b; Twisk et al., 2002b; Koutedakis & Bouziotas, 2003; Andersen et al., 2004b; Psarra et al., 2005; Byrd-Williams et al., 2008), metabolic syndrome (Carnethon et al., 2003; Ferreira et al., 2005) and arterial stiffness (Ferreira et al., 2003; Boreham, Ferreira, Twisk, Gallagher, Savage & Murray, 2004) later in life.

Musculoskeletal fitness and obesity-related cardiovascular disease risk factors

In addition to cardiorespiratory fitness, the role of muscular fitness in the performance of exercise and activities of daily living, as well as in preventing disease has become increasingly recognized (Jurca, Lamonte, Barlow, Kampert, Church & Blair, 2005; Wolfe, 2006). Data from the AVENA study showed that there is an inverse association between muscular fitness, as defined by an index computed from the standardized scores of maximal handgrip strength, explosive strength and endurance strength, and a CVD risk score (an average value from the standardized triglycerides, LDLc, HDLc, and glucose) in female adolescents (Garcia-Artero et al., 2007). In addition, it was reported that for a given cardiorespiratory fitness level, an increased level of muscular fitness was associated with a lower CVD risk score (Figure 4). Findings from the same cohort indicate that muscular fitness is inversely associated with C-reactive protein, C3 and ceruloplasmin (Ruiz, Ortega, Warnberg, Moreno, Carrero, Gonzalez-Gross, Marcos, Gutierrez & Sjostrom, 2008).

Results from cross-sectional studies in children and adolescents have reported a negative relationship between muscular strength and obesity-related CVD risks factors such as triglycerides, total cholesterol, high density lipoprotein cholesterol, LDLc, glucose (Garcia-Artero et al., 2007), C-reactive protein (Ruiz et al., 2008) and insulin resistance (Benson, Torode & Singh, 2006). Upper body muscular strength showed to be an independent predictor of insulin resistance in 126 boys and girls aged 10-15 years (Benson et al., 2006). In addition, those children in the highest third of absolute upper body muscular strength were 98% less likely to have high insulin resistance than those with the lowest strength, after adjusting for maturation, waist circumference, body mass and cardiorespiratory fitness (Benson et al., 2006). The same authors designed a study which can be considered the first randomized controlled trial of resistance training (i.e., any exercise training that uses a resistance to the force of muscular contraction, also called strength training) in children and adolescents, and reported that isolated high-intensity progressive resistance training significantly improves central and total body fat in association with muscle strength in normal-weight and overweight children and adolescents (Benson, Torode & Fiatarone Singh, 2008).

Musculoskeletal fitness and later obesity-related cardiovascular disease risk factors

There is strong evidence suggesting that increases in muscular strength in childhood and adolescence are associated with decreases in overall body fat later in life, and *viceversa* (decreases in muscular strength are associated with increases in overall body fat) (Twisk et al., 2000; Janz, Dawson & Mahoney, 2002a). This association is less evident for markers of central body fat (Hasselstrom et al., 2002; Janz et al., 2002b). In contrast, there is inconclusive evidence that muscular strength changes (increases or decreases) in childhood and adolescence are associated with changes (decreases or increases) in CVD risk factors later in life (Hasselstrom et al., 2002; Janz et al., 2002b).

5.1. Cardiovascular consequences of being fat but fit

There are reasons to believe that there might be potential interactions between fitness and fatness in relation to CVD risk. Regarding cardiorespiratory fitness and traits of paediatric type-II diabetes, data from the Swedish and Estonian part of the EYHS indicate that cardiorespiratory fitness explains a significant proportion of the HOMA (homeostasis model assessment, a surrogate marker of insulin resistance) and fasting insulin variance in those children with relatively high levels (i.e., the highest third) of body fat and waist circumference (Ruiz et al., 2007f). Likewise, cardiorespiratory fitness was inversely associated with C-reactive protein in those children with high levels of body fat, therefore, attenuating the negative effect of body fat on C-reactive protein (Figure 5). Data from the same cohort also revealed that in girls with low levels of cardiorespiratory fitness, a higher total and central body fat were significantly associated with higher systolic blood pressure (Ruiz et al., 2007b). In contrast, none of the markers of total and central body fat were significantly associated with blood pressure in girls with high levels of cardiorespiratory fitness (Ruiz et al., 2007b). Results from the AVENA study indicate that high levels of cardiorespiratory fitness are associated with a more favourable metabolic profile in non-overweight but also in overweight Spanish adolescents (Mesa et al., 2006c) (Figure 6).

It has been suggested that children and adolescents with high percent body fat and high cardiorespiratory fitness have better metabolic risk profiles than those classified as high fat but low cardiorespiratory fitness (Eisenmann, Welk, Ihmels & Dollman, 2007). It has been reported a significant difference in metabolic risk scores across four fitness-fatness groups in male adolescents and a trend for significance in females (Eisenmann, Welk, Wickel & Blair, 2007). High cardiorespiratory fitness did not completely remove the risk associated with high body mass index (BMI) on clustered metabolic risk, yet the study showed an attenuation of the association between BMI and clustered risk after adjustment for cardiorespiratory fitness. These result concur with others showing that clustered metabolic risk varied across fitness-fatness groups, where high cardiorespiratory fitness appeared to attenuate the metabolic risk score within BMI categories (DuBose, Eisenmann & Donnelly, 2007). Likewise, Halle et al. (Halle et al., 1998) reported that interleukin-6 levels were as low for obese and fit as for lean and unfit children, while the highest serum interleukin-6 concentrations were found in the obese and unfit group. Regarding muscular fitness, data from the AVENA study revealed that C-reactive protein and transthyretin are inversely associated with muscular fitness in overweight adolescents after controlling for different confounders, including cardiorespiratory fitness (Ruiz et al., 2008).

Collectively, these findings suggest that having moderate to high levels of physical fitness may attenuate the deleterious consequences ascribed to high levels of total and central body fat in children and adolescents.

6. Concluding remarks

The available literature suggests that:

- Cross-sectional studies using objective measures of physical activity support that a high level of physical activity, particularly vigorous physical activity, is associated with a lower total and central body fat in children and adolescents. The same associations have been suggested between activity levels during childhood/adolescence and overall or central body fat later in life. However, the role of the intensity in these longitudinal associations has not been examined.
- Experimental studies suggest that 45-50 min of moderate-vigorous physical activity 5 or more days a week lead to significant body fat reduction in overweight or obese youths. Studies conducted in normal-weight individuals suggest that higher doses (e.g. ≥80min moderate-vigorous physical activity) are required to decrease total body fat. The same doses of physical activity have been found useful for decreasing central body fat.
- Moderate and vigorous physical activity rather than light activity or inactivity, seems to be independently associated with clustered CVD risk in normal weight children and adolescents.
- Regarding physical fitness, both cross-sectional and longitudinal studies have found an inverse association of physical fitness in childhood and adolescence and total and abdominal body fat at these ages and later in life.
- A high physical fitness level, especially cardiorespiratory and muscular fitness, is associated with more favorable levels of traditional and novel CVD risk factors in children and adolescents. The current evidence suggests that both cardiorespiratory and muscular fitness may have a combined and accumulative effect on the cardiovascular system from an early age (i.e., childhood and adolescence).

-There is evidence of the existence of a hypothetical cardiorespiratory fitness threshold associated with a more favorable cardiovascular profile, which seems to range between 40 and 42 ml/min/kg in boys and between 35 and 38 ml/min/kg in girls.

- The deleterious consequences ascribed to high fatness could be counteracted by having high levels of cardiorespiratory fitness and/or muscular fitness. This implies that interventions to prevent states of unfavorable cardiovascular profiles should focus not only on weight reduction but also on enhancing cardiorespiratory and muscular fitness.

- Finally, the need of future research perspectives has been identified. A) The effects of the intensity itself and the effects of energy expenditure should be separately examined or controlled in relation to body fat and obesity-related CVD risk at childhood/adolescence and later in life. B) Whether physical fitness can modify the associations between physical activity and body fat or CVD risk, remains to be elucidated. C) The associations between physical fitness and fatness or CVD risk are fairly consistent in the literature, but the effect of changes in fitness levels during childhood/adolescence on body fat or CVD risk need to be studied.

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7. References

Abbott RA & Davies PS (2004) Habitual physical activity and physical activity intensity: their relation to body composition in 5.0-10.5-y-old children. *Eur J Clin Nutr 58*, 285-291.

Andersen L, Hasselstrøm H, Gronfeldt V, Hansen S & Froberg K (2004a) The relationship between physical fitness and clustered risk, and tracking of clustered risk from adolescence to young adulthood: eight years follow-up in the Danish Youth and Sport Study. *Int J Behav Nutr Phys Act 1:6*.

Andersen LB, Harro M, Sardinha LB, Froberg K, Ekelund U, Brage S & Anderssen SA (2006) Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). *Lancet 368*, 299-304.

Andersen LB, Hasselstrom H, Gronfeldt V, Hansen SE & Karsten F (2004b) The relationship between physical fitness and clustered risk, and tracking of clustered risk from adolescence to young adulthood: eight years follow-up in the Danish Youth and Sport Study. *Int J Behav Nutr Phys Act 1*, 6.

Andersen RE, Crespo CJ, Bartlet SJ, Cheskin LJ & Pratt M (1998) Relationship of physical activity and television watching with body weight and level of fatness among children: results from de Third National Health and Nutrition Examination Survey. *JAMA*, 938-942.

Ara I, Moreno LA, Leiva MT, Gutin B & Casajus JA (2007) Adiposity, physical activity, and physical fitness among children from Aragon, Spain. *Obesity (Silver Spring) 15*, 1918-1924.

Ara I, Vicente-Rodriguez G, Jimenez-Ramirez J, Dorado C, Serrano-Sanchez JA & Calbet JA (2004) Regular participation in sports is associated with enhanced physical fitness and lower fat mass in prepubertal boys. *Int J Obes Relat Metab Disord 28*, 1585-1593.

Ara I, Vicente-Rodriguez G, Perez-Gomez J, Jimenez-Ramirez J, Serrano-Sanchez JA, Dorado C & Calbet JA (2006) Influence of extracurricular sport activities on body composition and physical fitness in boys: a 3-year longitudinal study. *Int J Obes (Lond) 30*, 1062-1071.

Barbeau P, Gutin B, Litaker M, Owens S, Riggs S & Okuyama T (1999) Correlates of individual differences in body-composition changes resulting from physical training in obese children. *Am J Clin Nutr 69*, 705-711.

Barbeau P, Johnson MH, Howe CA, Allison J, Davis CL, Gutin B & Lemmon CR (2007) Ten months of exercise improves general and visceral adiposity, bone, and fitness in black girls. *Obesity (Silver Spring) 15*, 2077-2085.

Barnekow-Bergkvist M, Hedberg G, Janlert U & Jansson E (2001) Adolescent determinants of cardiovascular risk factors in adult men and women. *Scand J Public Health 29*, 208-217.

Bell RD, Macek M, Rutenfranz J & Saris W (1986. p. 39-42.) Health indicators and risk factors of cardiovascular diseases during childhood and adolescence. In: Rutenfranz J, Mocelin R, Klimt F(eds). *Children and Exercise XII*.

Benson AC, Torode ME & Fiatarone Singh MA (2008) The effect of high-intensity progressive resistance training on adiposity in children: a randomized controlled trial. *Int J Obes (Lond) 32*, 1016-1027.

Benson AC, Torode ME & Singh MA (2006) Muscular strength and cardiorespiratory fitness is associated with higher insulin sensitivity in children and adolescents. *Int J Pediatr Obes 1*, 222-231.

Berenson GS, Srinivasan SR, Bao W, Newman WP, 3rd, Tracy RE & Wattigney WA (1998) Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *New England Journal of Medicine 338*, 1650-1656.

Berkey CS, Rockett HR, Field AE, Gillman MW, Frazier AL, Camargo CA, Jr. & Colditz GA (2000) Activity, dietary intake, and weight changes in a longitudinal study of preadolescent and adolescent boys and girls. *Pediatrics 105*, E56.

Boreham C, Twisk J, Neville C, Savage M, Murray L & Gallagher A (2002) Associations between physical fitness and activity patterns during adolescence and cardiovascular risk factors in young adulthood: the Northern Ireland Young Hearts Project. *Int J Sports Med 23 Suppl 1*, S22-26.

Boreham CA, Ferreira I, Twisk JW, Gallagher AM, Savage MJ & Murray LJ (2004) Cardiorespiratory fitness, physical activity, and arterial stiffness: the Northern Ireland Young Hearts Project. *Hypertension 44*, 721-726.

Brage S, Wedderkopp N, Ekelund U, Franks PW, Wareham NJ, Andersen LB & Froberg K (2004) Features of the metabolic syndrome are associated with objectively measured physical activity and fitness in Danish children: the European Youth Heart Study (EYHS). *Diabetes Care 27*, 2141-2148.

Brambilla P, Bedogni G, Moreno LA, Goran MI, Gutin B, Fox KR & (2006) Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. *Int J Obes (Lond) 30*, 23-30.

Brambilla P, Bedogni G, Moreno LA, Goran MI, Gutin B, Fox KR, Peters DM, Barbeau P, De Simone M & Pietrobelli A (2006) Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. *Int J Obes (Lond) 30*, 23-30.

Brunet M, Chaput JP & Tremblay A (2007) The association between low physical fitness and high body mass index or waist circumference is increasing with age in children: the 'Quebec en Forme' Project. *Int J Obes (Lond) 31*, 637-643.

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

Byrd-Williams CE, Shaibi GQ, Sun P, Lane CJ, Ventura EE, Davis JN, Kelly LA & Goran MI (2008) Cardiorespiratory Fitness Predicts Changes in Adiposity in Overweight Hispanic Boys. *Obesity (Silver Spring)*.

Carnethon MR, Gidding SS, Nehgme R, Sidney S, Jacobs DR, Jr. & Liu K (2003) Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. *Jama 290*, 3092-3100.

Castillo-Garzon M, Ruiz JR, Ortega FB & Gutierrez-Sainz A (2007) A mediterranean diet is not enough for health: physical fitness is an important additional contributor to health for the adults of tomorrow. *World Rev Nutr Diet 97*, 114-138.

Castro R, Rivera I, Blom HJ, Jakobs C & Tavares de Almeida I (2006) Homocysteine metabolism, hyperhomocysteinaemia and vascular disease: an overview. *J Inherit Metab Dis 29*, 3-20.

Centers for Disease Control and Prevention National Center for Health Statistics. National Health and Nutrition Examination Survey 1999-2000 Data [Internet]. Hyattsville, Md: US Dept of Health and Human Services, Centers for Disease Control and Prevention; 2004; [cited 2007 September 21]. Available from: http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm

Centers for Disease Control and Prevention National Center for Health Statistics. National Health and Nutrition Examination Survey 2001-2002 Data [Internet]. Hyattsville, Md: US Dept of Health and Human Services, Centers for Disease Control and Prevention; 2004; [cited 2007 September 21]: Available from: http://www.cdc.gov/nchs/about/major/nhanes/nhanes01-02.htm.

Cole TJ, Bellizzi MC, Flegal KM & Dietz WH (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. *Bmj 320*, 1240-1243.

Cooper DM, Nemet D & Galassetti P (2004) Exercise, stress, and inflammation in the growing child: from the bench to the playground. *Curr Opin Pediatr 16*, 286-292.

Cruz ML, Shaibi GQ, Weigensberg MJ, Spruijt-Metz D, Ball GD & Goran MI (2005) Pediatric obesity and insulin resistance: chronic disease risk and implications for treatment and prevention beyond body weight modification. *Annu Rev Nutr 25*, 435-468.

Cureton KJ & Warren GL (1990) Criterion-referenced standards for youth health-related fitness tests: a tutorial. *Res Q Exerc Sport 61*, 7-19.

Dencker M & Andersen LB (2008) Health-related aspects of objectively measured daily physical activity in children. *Clin Physiol Funct Imaging 28*, 133-144.

Dencker M, Thorsson O, Karlsson MK, Linden C, Wollmer P & Andersen LB (2008) Daily physical activity related to aerobic fitness and body fat in an urban sample of children. *Scand J Med Sci Sports*.

DuBose KD, Eisenmann JC & Donnelly JE (2007) Aerobic fitness attenuates the metabolic syndrome score in normal-weight, at-risk-for-overweight, and overweight children. *Pediatrics 120*, e1262-1268.

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

Eisenmann JC, Welk GJ, Wickel EE & Blair SN (2007) 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 2*, 66-72.

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

Ekelund U, Aman J, Yngve A, Renman C, Westerterp K & Sjostrom M (2002) Physical activity but not energy expenditure is reduced in obese adolescents: a case-control study. *Am J Clin Nutr 76*, 935-941.

Ekelund U, Anderssen SA, Froberg K, Sardinha LB, Andersen LB & Brage S (2007a) Independent associations of physical activity and cardiorespiratory fitness with metabolic risk factors in children: The European youth heart study. *Diabetologia 50*, 1832-1840.

Ekelund U, Franks PW, Sharp S, Brage S & Wareham NJ (2007b) Increase in physical activity energy expenditure is associated with reduced metabolic risk independent of change in fatness and fitness. *Diabetes Care 30*, 2101-2106.

Ekelund U, Sardinha LB, Anderssen SA, Harro M, Franks PW, Brage S, Cooper AR, Andersen LB, Riddoch C & Froberg K (2004) Associations between objectively assessed physical activity and indicators of body fatness in 9- to 10-y-old

European children: a population-based study from 4 distinct regions in Europe (the European Youth Heart Study). *Am J Clin Nutr 80*, 584-590.
Eliakim A, Makowski GS, Brasel JA & Cooper DM (2000) Adiposity, lipid levels, and brief endurance training in nonobese adolescent males. *Int J Sports Med 21*, 332-337.
Eliakim A, Scheett T, Allmendinger N, Brasel JA & Cooper DM (2001) Training, muscle volume, and energy expenditure in nonobese American girls. *J Appl Physiol 90*, 35-44.
Ferreira I, Henry RM, Twisk JW, van Mechelen W, Kemper HC & Stehouwer CD (2005) The metabolic syndrome, cardiopulmonary fitness, and subcutaneous trunk fat as independent determinants of arterial stiffness: the Amsterdam Growth and Health Longitudinal Study. *Arch Intern Med 165*, 875-882.
Ferreira I, Twisk JW, Stehouwer CD, van Mechelen W & Kemper HC (2003) Longitudinal changes in VO2max: associations with carotid IMT and arterial stiffness. *Med Sci Sports Exerc 35*, 1670-1678.
Freedman DS, Khan LK, Dietz WH, Srinivasan SR & Berenson GS (2001) Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. *Pediatrics 108*, 712-718.
Gallistl S, Sudi K, Mangge H, Erwa W & Borkenstein M (2000) Insulin is an independent correlate of plasma homocysteine levels in obese children and adolescents. *Diabetes Care 23*, 1348-1352.
Garcia-Artero E, Ortega FB, Ruiz JR, Mesa JL, Delgado M, Gonzalez-Gross M, Garcia-Fuentes M, Vicente-Rodriguez G, Gutierrez A & Castillo MJ (2007) [Lipid and metabolic profiles in adolescents are affected more by physical fitness than physical activity (AVENA study)]. *Rev Esp Cardiol 60*, 581-588.
Guo SS, Wu W, Chumlea WC & Roche AF (2002) Predicting overweight and obesity in adulthood from body mass index values in childhood and adolescence. *Am J Clin Nutr 76*, 653-658.
Gutin B, Barbeau P, Owens S, Lemmon CR, Bauman M, Allison J, Kang HS & Litaker MS (2002) Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. *Am J Clin Nutr 75*, 818-826.
Gutin B, Johnson MH, Humphries MC, Hatfield-Laube JL, Kapuku GK, Allison JD, Gower BA, Daniels SR & Barbeau P (2007) Relationship of visceral adiposity to cardiovascular disease risk factors in black and white teens. *Obesity (Silver Spring) 15*, 1029-1035.
Gutin B, Yin Z, Humphries MC & Barbeau P (2005) Relations of moderate and vigorous physical activity to fitness and fatness in adolescents. *Am J Clin Nutr 81*, 746-750.
Gutin B, Yin Z, Johnson M & Barbeau P (2008) Preliminary findings of the effect of a 3-year after-school physical activity intervention on fitness and body fat: the Medical College of Georgia Fitkid Project. *Int J Pediatr Obes 3 Suppl 1*, 3-9.
Halle M, Berg A, Northoff H & Keul J (1998) Importance of TNF-alpha and leptin in obesity and insulin resistance: a hypothesis on the impact of physical exercise. *Exercise Immunology Review 4*, 77-94.
Halle M, Korsten-Reck U, Wolfarth B & Berg A (2004) Low-grade systemic inflammation in overweight children: impact of physical fitness. *Exerc Immunol Rev 10*, 66-74.
Hansson GK (2005) Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med 352*, 1685-1695.

Hasselstrom H, Hansen SE, Froberg K & Andersen LB (2002) Physical fitness and physical activity during adolescence as predictors of cardiovascular disease risk in young adulthood. Danish Youth and Sports Study. An eight-year follow-up study. *Int J Sports Med 23 Suppl 1*, S27-31.

Hurtig-Wennlof A, Ruiz JR, Harro M & Sjostrom M (2007) Cardiorespiratory fitness relates more strongly than physical activity to cardiovascular disease risk factors in healthy children and adolescents: the European Youth Heart Study. *Eur J Cardiovasc Prev Rehabil 14*, 575-581.

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

Isasi CR, Deckelbaum RJ, Tracy RP, Starc TJ, Berglund L & Shea S (2003) Physical fitness and C-reactive protein level in children and young adults: the Columbia University BioMarkers Study. *Pediatrics 111*, 332-338.

Janssen I, Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C & Berenson GS (2005) Combined influence of body mass index and waist circumference on coronary artery disease risk factors among children and adolescents. *Pediatrics 115*, 1623-1630.

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

Janz KF, Dawson JD & Mahoney LT (2002a) Increases in physical fitness during childhood improve cardiovascular health during adolescence: the Muscatine Study. *International Journal of Sports Medicine 23 Suppl 1*, S15-21.

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

Jarvisalo MJ, Harmoinen A, Hakanen M, Paakkunainen U, Viikari J, Hartiala J, Lehtimaki T, Simell O & Raitakari OT (2002) Elevated serum C-reactive protein levels and early arterial changes in healthy children. *Arterioscler Thromb Vasc Biol 22*, 1323-1328.

Johnson MS, Figueroa-Colon R, Herd SL, Fields DA, Sun M, Hunter GR & Goran MI (2000) Aerobic fitness, not energy expenditure, influences subsequent increase in adiposity in black and white children. *Pediatrics 106*, E50.

Jurca R, Lamonte MJ, Barlow CE, Kampert JB, Church TS & Blair SN (2005) Association of muscular strength with incidence of metabolic syndrome in men. *Med Sci Sports Exerc 37*, 1849-1855.

Klein-Platat C, Oujaa M, Wagner A, Haan MC, Arveiler D, Schlienger JL & Simon C (2005) Physical activity is inversely related to waist circumference in 12-y-old French adolescents. *Int J Obes (Lond) 29*, 9-14.

Klijn PH, van der Baan-Slootweg OH & van Stel HF (2007) Aerobic exercise in adolescents with obesity: preliminary evaluation of a modular training program and the modified shuttle test. *BMC Pediatr 7*, 19.

Kohl HW, Fulton JE & Caspersen CJ (2000) Assessment of physical activity among children and adolescents: a review and synthesis. *Prev Med 31*, S54-S76.

Koutedakis Y & Bouziotas C (2003) National physical education curriculum: motor and cardiovascular health related fitness in Greek adolescents. *Br J Sports Med 37*, 311-314.

Kriemler S, Hebestreit H, Mikami S, Bar-Or T, Ayub BV & Bar-Or O (1999) Impact of a single exercise bout on energy expenditure and spontaneous physical activity of obese boys. *Pediatr Res 46*, 40-44.

Kuo HK, Yen CJ & Bean JF (2005) Levels of homocysteine are inversely associated with cardiovascular fitness in women, but not in men: data from the National Health and Nutrition Examination Survey 1999-2002. *J Intern Med 258*, 328-335.
LaMonte MJ & Blair SN (2006) Physical activity, cardiorespiratory fitness, and adiposity: contributions to disease risk. *Curr Opin Clin Nutr Metab Care 9*, 540-546.
Lee SJ & Arslanian SA (2007) Cardiorespiratory fitness and abdominal adiposity in youth. *Eur J Clin Nutr 61*, 561-565.
LeMura LM & Maziekas MT (2002) Factors that alter body fat, body mass, and fat-free mass in pediatric obesity. *Med Sci Sports Exerc 34*, 487-496.
Lobelo F, Pate RR, Dowda M, Liese AD & Ruiz JR (In press) Validity of Cardiorespiratory Fitness Criterion-referenced Standards for Adolescents. *Med Sci Sports Exerc*.
Lobelo F & Ruiz JR (2007) Cardiorespiratory fitness as criterion validity for health-based metabolic syndrome definition in adolescents. *J Am Coll Cardiol 50*, 471.
McCully KS (2005) Hyperhomocysteinemia and arteriosclerosis: historical perspectives. *Clin Chem Lab Med 43*, 980-986.
Mesa JL, Ortega FB, Ruiz JR, Castillo MJ, Hurtig-Wennlöf A, Sjöstrom M & Gutierrez A (2006a) The importance of cardiorespiratory fitness for healthy metabolic traits in children and adolescents: the AVENA study. *J Public Health 14*, 178-180.
Mesa JL, Ortega FB, Ruiz JR, Castillo MJ, Tresaco B, Carreno F, Moreno LA, Gutierrez A & Bueno M (2006b) Anthropometric Determinants of a Clustering of Lipid-Related Metabolic Risk Factors in Overweight and Non-Overweight Adolescents - Influence of Cardiorespiratory Fitness. The AVENA Study. *Ann Nutr Metab 50*, 519-527.
Mesa JL, Ruiz JR, Ortega FB, Warnberg J, Gonzalez-Lamuno D, Moreno LA, Gutierrez A & Castillo MJ (2006c) Aerobic physical fitness in relation to blood lipids and fasting glycaemia in adolescents: Influence of weight status. *Nutr Metab Cardiovasc Dis 16*, 285-293.
Metcalf BS, Voss LD, Hosking J, Jeffery AN & Wilkin TJ (2008) Physical activity at the government-recommended level and obesity-related health outcomes: a longitudinal study (EarlyBird 37). *Arch Dis Child*.
Mokdad AH, Marks JS, Stroup DF & Gerberding JL (2004) Actual causes of death in the United States, 2000. *Jama 291*, 1238-1245.
Moore LL, Gao D, Bradlee ML, Cupples LA, Sundarajan-Ramamurti A, Proctor MH, Hood MY, Singer MR & Ellison RC (2003) Does early physical activity predict body fat change throughout childhood? *Prev Med 37*, 10-17.
Nassis GP, Psarra G & Sidossis LS (2005) Central and total adiposity are lower in overweight and obese children with high cardiorespiratory fitness. *Eur J Clin Nutr 59*, 137-141.
Oehlschlaeger MH, Pinheiro RT, Horta B, Gelatti C & San'Tana P (2004) [Prevalence of sedentarism and its associated factors among urban adolescents]. *Rev Saude Publica 38*, 157-163.
Ortega FB, Ruiz JR, Castillo MJ, Moreno LA, Warnberg J, Tresaco B, Gonzalez-Gross M, Perez F, Garcia-Fuentes M & Gutierrez A (2006) Cardiorespiratory Fitness is Associated with a Favorable Lipid Profile Independent of Abdominal Fat in Male Adolescents: 10:30AM-10:45AM: 611. *Med Sci Sports Exerc 38*, S7-S8.

Ortega FB, Ruiz JR, Hurtig-Wennlof A, Vicente-Rodriguez G, Rizzo NS, Castillo MJ & Sjostrom M (2008) Cardiovascular fitness modifies the associations between physical activity and abdominal adiposity in children and adolescents. The European Youth Heart Study. *Br J Sports Med*.

Ortega FB, Ruiz JR & Sjostrom M (2007a) Physical activity, overweight and central adiposity in Swedish children and adolescents: the European Youth Heart Study. *Int J Behav Nutr Phys Act 4*, 61.

Ortega FB, Tresaco B, Ruiz JR, Moreno LA, Martin-Matillas M, Mesa JL, Warnberg J, Bueno M, Tercedor P, Gutierrez A & Castillo MJ (2007b) Cardiorespiratory fitness and sedentary activities are associated with adiposity in adolescents. *Obesity (Silver Spring) 15*, 1589-1599.

Owens S, Gutin B, Allison J, Riggs S, Ferguson M, Litaker M & Thompson W (1999) Effect of physical training on total and visceral fat in obese children. *Med Sci Sports Exerc 31*, 143-148.

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

Poortvliet E, Yngve A, Ekelund U, Hurtig-Wennlof A, Nilsson A, Hagstromer M & Sjostrom M (2003) The European Youth Heart Survey (EYHS): an international study that addresses the multi-dimensional issues of CVD risk factors. *Forum Nutr 56*, 254-256.

Psarra G, Nassis GP & Sidossis LS (2005) Short-term predictors of abdominal obesity in children. *Eur J Public Health*.

Raitakari OT, Juonala M, Kahonen M, Taittonen L, Laitinen T, Maki-Torkko N, Jarvisalo MJ, Uhari M, Jokinen E, Ronnemaa T, Akerblom HK & Viikari JS (2003) Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA 290*, 2277-2283.

Rey-Lopez JP, Vicente-Rodriguez G & Moreno LA (2007) Sedentary behaviors and obesity development in children and adolescents. *Nutrition, Metabolism & Cardiovascular Diseases*, In press.

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

Rizzo NS, Ruiz JR, Oja L, Veidebaum T & Sjostrom M (2008) Associations between physical activity, body fat, and insulin resistance (homeostasis model assessment) in adolescents: the European Youth Heart Study. *Am J Clin Nutr 87*, 586-592.

Rowland TW, Martel L, Vanderburgh P, Manos T & Charkoudian N (1996) The influence of short-term aerobic training on blood lipids in healthy 10-12 year old children. *Int J Sports Med 17*, 487-492.

Rowlands AV, Eston RG & Ingledew DK (1999) Relationship between activity levels, aerobic fitness, and body fat in 8- to 10-yr-old children. *J Appl Physiol 86*, 1428-1435.

Ruiz JR, Castro-Pinero J, Artero EG, Ortega FB, Sjostrom M, Suni J & Castillo MJ (2009) Predictive Validity of Health-Related Fitness in Youth: A Systematic Review. *Br J Sports Med*.

Ruiz JR, Hurtig-Wennlöf A, Ortega FB, Patersson E, Nilsson TK, Castillo MJ & Sjöström M (2007a) Homocysteine levels in children and adolescents are associated with the methylenetetrahydrofolate reductase 677C > T genotype, but

not with physical activity, fitness or fatness: The European Youth Heart Study. *Brit J Nutr 96*, 255-262.
Ruiz JR, Ortega FB, Gutierrez A, Meusel D, Sjöström M & Castillo MJ (2006a) Health-related fitness assessment in childhood and adolescence; A European approach based on the AVENA, EYHS and HELENA studies *J Public Health 14*, 269-277.
Ruiz JR, Ortega FB, Loit HM, Veidebaum T & Sjostrom M (2007b) Body fat is associated with blood pressure in school-aged girls with low cardiorespiratory fitness: The European Youth Heart Study. *J Hypertens 25*, 2027-2034.
Ruiz JR, Ortega FB, Meusel D, Harro M, Oja P & Sjöström M (2006b) Cardiorespiratory fitness is associated with features of metabolic risk factors in children. Should cardiorespiratory fitness be assessed in a European health monitoring system? The European Youth Heart Study. *J Public Health 14*, 94-102.
Ruiz JR, Ortega FB, Meusel D & Sjostrom M (2007c) Traditional and Novel Cardiovascular Risk Factors in School-aged Children: Call for the Further Development of Public Health Strategies with Emphasis on Fitness. *J Public Health 15*, 171-177.
Ruiz JR, Ortega FB, Rizzo NS, Villa I, Hurtig-Wennlöf A, Oja L & Sjöström M (2007d) High Cardiovascular Fitness Is Associated with Low Metabolic Risk Score in Children: The European Youth Heart Study. *Pediatr Res 61*, 350-355.
Ruiz JR, Ortega FB, Tresaco B, Warnberg J, Mesa JL, Gonzalez-Gross M, Moreno LA, Marcos A, Gutierrez A & Castillo MJ (2006c) Serum lipids, body mass index and waist circumference during pubertal development in Spanish adolescents: the AVENA Study. *Horm Metab Res 38*, 832-837.
Ruiz JR, Ortega FB, Warnberg J, Moreno LA, Carrero JJ, Gonzalez-Gross M, Marcos A, Gutierrez A & Sjostrom M (2008) Inflammatory proteins and muscle strength in adolescents: the AVENA study. *Arch Pediatr Adolesc Med 162*, 462-468.
Ruiz JR, Ortega FB, Warnberg J & Sjostrom M (2007e) Associations of low-grade inflammation with physical activity, fitness and fatness in prepubertal children; the European Youth Heart Study. *Int J Obes (Lond) 31*, 1545-1551.
Ruiz JR, Rizzo NS, Hurtig-Wennlöf A, Ortega FB, Wärnberg J & Sjöström M (2006d) Relations of total physical activity and intensity to fitness and fatness in children: the European Youth Heart Study. *Am J Clin Nutr 84*, 299-303.
Ruiz JR, Rizzo NS, Ortega FB, Loit HM, Veidebaum T & Sjostrom M (2007f) Markers of insulin resistance are associated with fatness and fitness in school-aged children: the European Youth Heart Study. *Diabetologia 50*, 1401-1408.
Ruiz JR, Sola R, Gonzalez-Gross M, Ortega FB, Vicente-Rodriguez G, Garcia-Fuentes M, Gutierrez A, Sjöström M, Pietrzik K & Castillo MJ (2007g) Cardiovascular Fitness Is Negatively Associated With Homocysteine Levels in Female Adolescents. *Arch Pediatr Adolesc Med 161*, 166-171.
Saelens BE, Seeley RJ, van Schaick K, Donnelly LF & O'Brien KJ (2007) Visceral abdominal fat is correlated with whole-body fat and physical activity among 8-y-old children at risk of obesity. *Am J Clin Nutr 85*, 46-53.
Sardinha LB, Andersen LB, Anderssen SA, Quiterio AL, Ornelas R, Froberg K, Riddoch CJ & Ekelund U (2008) 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 31*, 569-575.
Stallmann-Jorgensen IS, Gutin B, Hatfield-Laube JL, Humphries MC, Johnson MH & Barbeau P (2007) General and visceral adiposity in black and white adolescents

and their relation with reported physical activity and diet. *Int J Obes (Lond) 31*, 622-629.
Steele RM, Brage S, Corder K, Wareham NJ & Ekelund U (2008) Physical activity, cardiorespiratory fitness, and the metabolic syndrome in youth. *J Appl Physiol 105*, 342-351.
Steinberger J, Moran A, Hong CP, Jacobs DR, Jr. & Sinaiko AR (2001) Adiposity in childhood predicts obesity and insulin resistance in young adulthood. *J Pediatr 138*, 469-473.
Stevens J, Suchindran C, Ring K, Baggett CD, Jobe JB, Story M, Thompson J, Going SB & Caballero B (2004) Physical activity as a predictor of body composition in American Indian children. *Obes Res 12*, 1974-1980.
Strong WB, Malina RM, Blimkie CJ, Daniels SR, Dishman RK, Gutin B, Hergenroeder AC, Must A, Nixon PA, Pivarnik JM, Rowland T, Trost S & Trudeau F (2005) Evidence based physical activity for school-age youth. *J Pediatr 146*, 732-737.
Taylor RW, Jones IE, Williams SM & Goulding A (2000) Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3-19 y. *Am J Clin Nutr 72*, 490-495.
The Cooper Institute for Aerobics Research (2004. p. 38-39.) *FITNESSGRAM test administration manual*. 3rd ed. Champaign, Ill: Human Kinetics.
Thompson DR, Obarzanek E, Franko DL, Barton BA, Morrison J, Biro FM, Daniels SR & Striegel-Moore RH (2007) Childhood overweight and cardiovascular disease risk factors: the National Heart, Lung, and Blood Institute Growth and Health Study. *J Pediatr 150*, 18-25.
Tolfrey K, Campbell IG & Batterham AM (1998) Exercise training induced alterations in prepubertal children's lipid-lipoprotein profile. *Med Sci Sports Exerc 30*, 1684-1692.
Tolfrey K, Jones AM & Campbell IG (2004) Lipid-lipoproteins in children: an exercise dose-response study. *Med Sci Sports Exerc 36*, 418-427.
Twisk JW, Kemper HC & van Mechelen W (2000) Tracking of activity and fitness and the relationship with cardiovascular disease risk factors. *Med Sci Sports Exerc 32*, 1455-1461.
Twisk JW, Kemper HC & van Mechelen W (2002a) Prediction of cardiovascular disease risk factors later in life by physical activity and physical fitness in youth: general comments and conclusions. *Int J Sports Med 23 Suppl 1*, S44-49.
Twisk JW, Kemper HC & van Mechelen W (2002b) The relationship between physical fitness and physical activity during adolescence and cardiovascular disease risk factors at adult age. The Amsterdam Growth and Health Longitudinal Study. *Int J Sports Med 23 Suppl 1*, S8-14.
Wärnberg J, Nova E, Moreno LA, Romeo J, Mesana MI, Ruiz JR, Ortega FB, Sjöström M, Bueno M & Marcos A (2006a) Inflammatory proteins are related to total and abdominal adiposity in a healthy adolescent population: the AVENA Study. *Am J Clin Nutr 84*, 505-512.
Wärnberg J, Ruiz JR, Sjöström M, Ortega FB, Moreno A, Moreno LA, Rizzo NS & Marcos A (2006b) Association of fitness and fatness to low-grade systemic inflammation in adolescents. The AVENA study. *Med Sci Sports Exerc [abstract] 38*, S8.
Winsley RJ, Armstrong N, Middlebrooke AR, Ramos-Ibanez N & Williams CA (2006) Aerobic fitness and visceral adipose tissue in children. *Acta Paediatr 95*, 1435-1438.

Wittmeier KD, Mollard RC & Kriellaars DJ (2007) Objective assessment of childhood adherence to Canadian physical activity guidelines in relation to body composition. *Appl Physiol Nutr Metab 32*, 217-224.

Wolfe RR (2006) The underappreciated role of muscle in health and disease. *Am J Clin Nutr 84*, 475-482.

Yin Z, Gutin B, Johnson MH, Hanes J, Jr., Moore JB, Cavnar M, Thornburg J, Moore D & Barbeau P (2005) An environmental approach to obesity prevention in children: Medical College of Georgia FitKid Project year 1 results. *Obes Res 13*, 2153-2161.

Table 1. Health criterion-referenced standards for cardiorespiratory fitness in children and youth.

Study/Institution	Methodology	Sex	Age (years)	CRF values (mL/kg/min)
FITNESSGRAM (Cureton & Warren, 1990; The Cooper Institute for Aerobics Research, 2004. p. 38-39.)	Linked to adult mortality/chronic disease risk.	Males	12-19	42
		Females	12	37
			13	36
			≥14	35
European Group of Paediatric Work (Bell et al., 1986. p. 39-42.)	Expert judgment	Males	Adolescents	40
		Females	Adolescents	35
European Youth Heart Study (Ruiz et al., 2007d)	ROC curve	Males	9-10	42
		Females	9-10	37
NHANES 1999-2002 (Lobelo et al., In press)	ROC curve	Males	12-15	44
			16-19	40
		Females	12-15	36
			16-19	36

ROC indicates receiver operating characteristic; CRF, cardiorespiratory fitness.

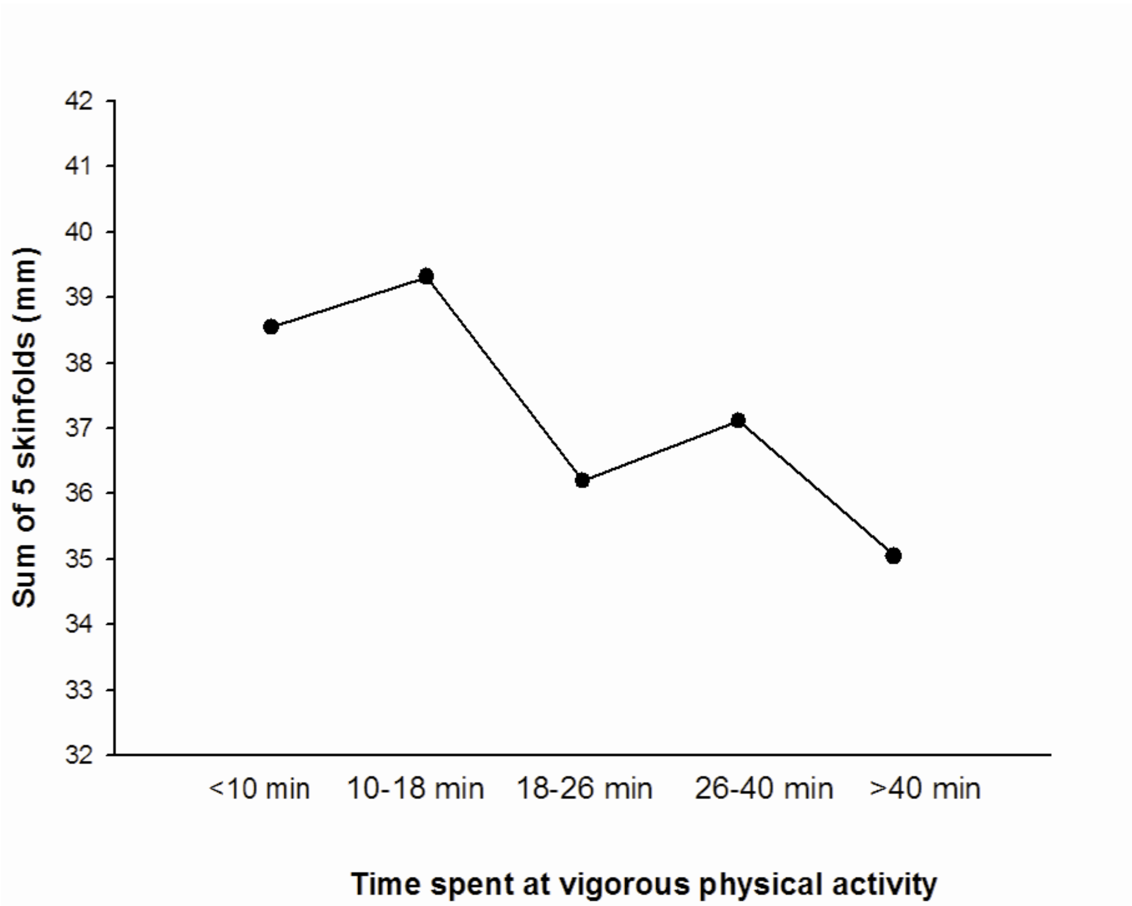


Figure 1. Body fat (mean sum of five skinfolds) stratified (in fifths) by time spent at vigorous physical activity in children (n=780). Modified from (2006d).

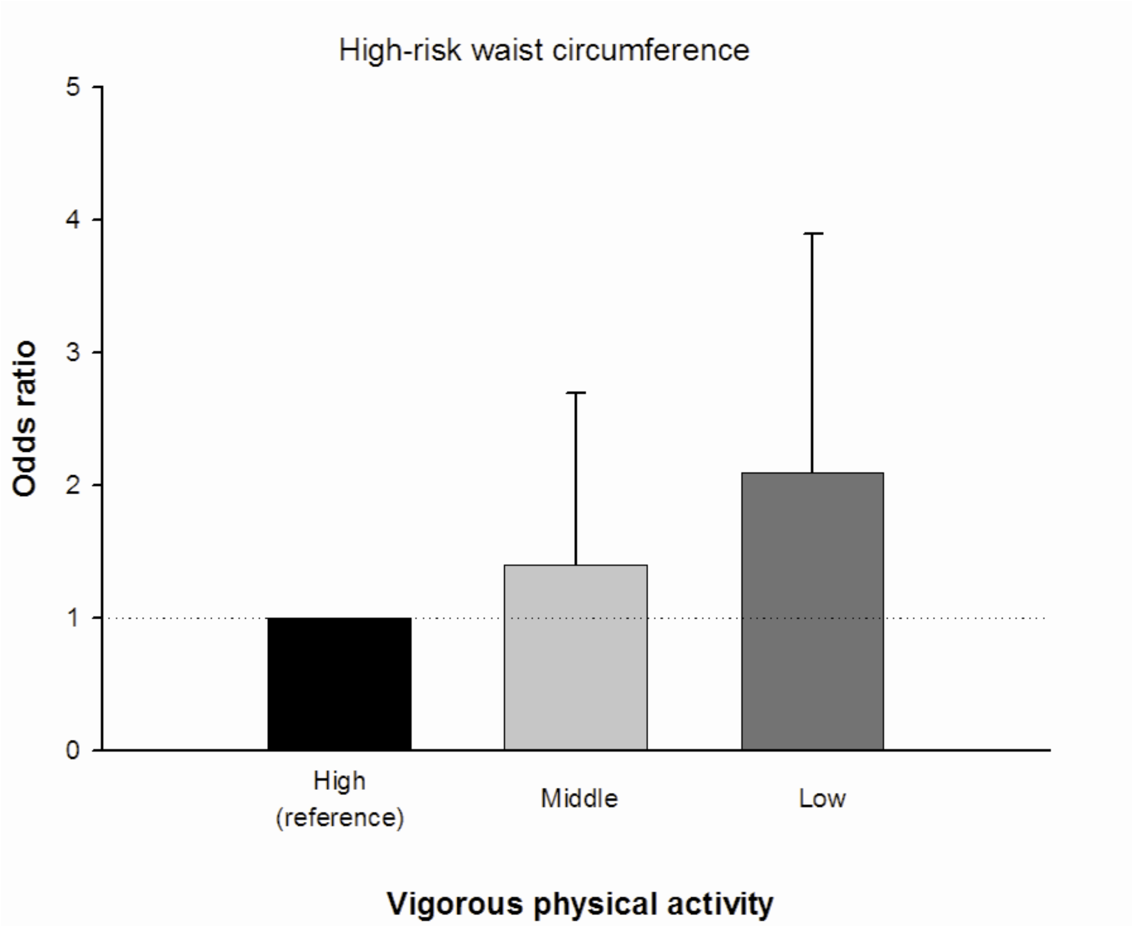
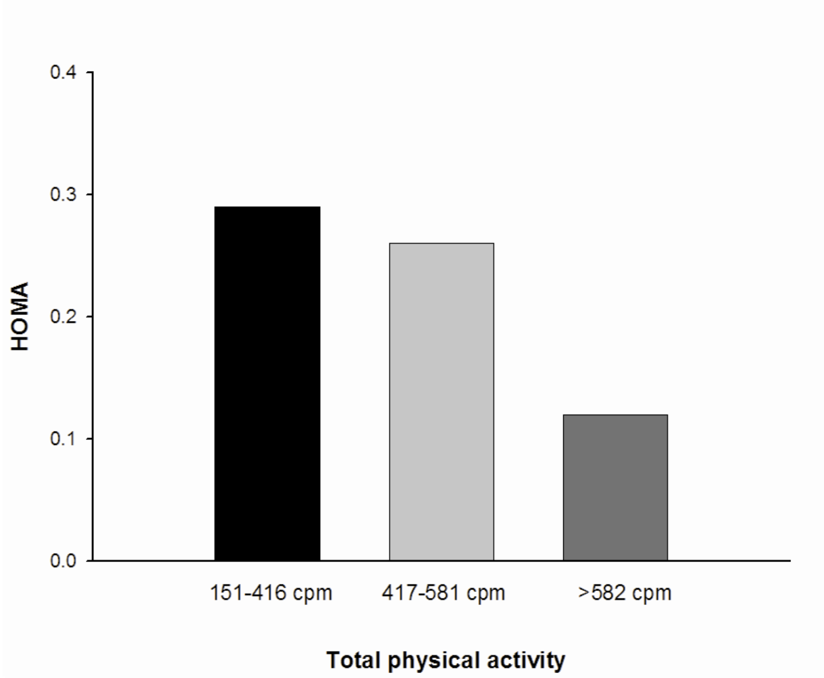
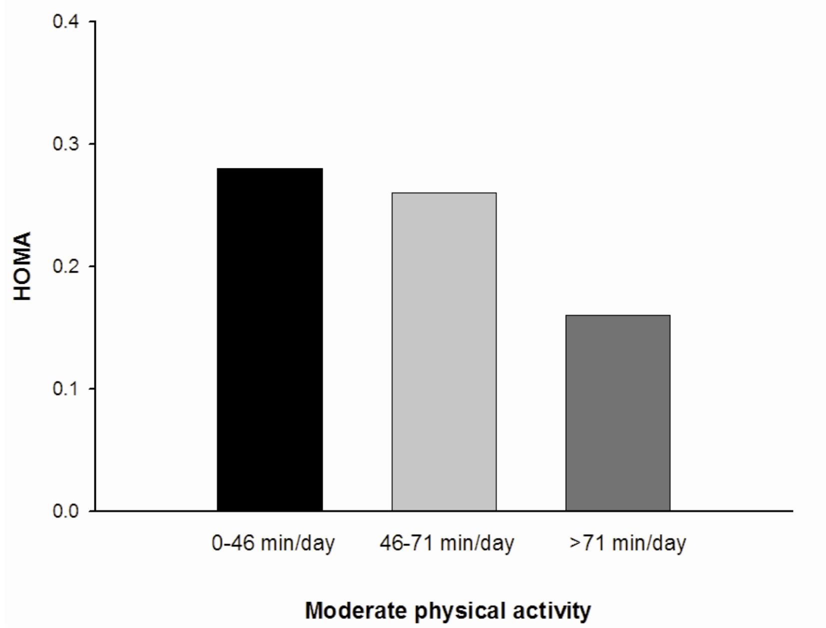


Figure 2. High-risk waist circumference according to thirds of vigorous physical activity in children and adolescents (n=1074). Adapted from Ortega et al. (2007a).


0.4
0.3
0.2
0.1
0.0
HOMA
151-416 cpm
417-581 cpm
>582 cpm
Total physical activity


0.4
0.3
0.2
0.1
0.0
HOMA
0-46 min/day
46-71 min/day
>71 min/day
Moderate physical activity

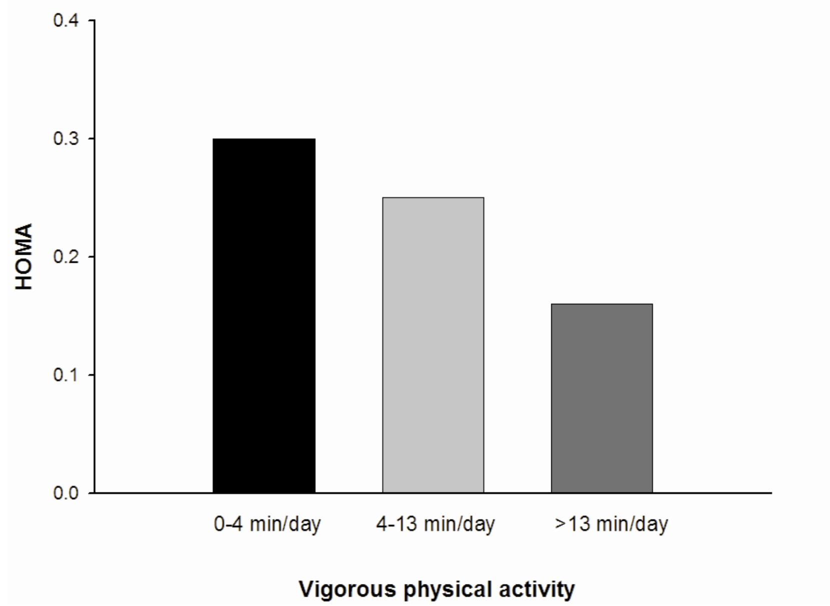

0.4
0.3
0.2
0.1
0.0
HOMA
0-4 min/day
4-13 min/day
>13 min/day
Vigorous physical activity

Figure 3. Association between HOMA (homeostasis model assessment, a surrogate marker of insulin resistance) and thirds of total, moderate and vigorous physical activity in adolescents (n=613). Modified from Rizzo et al. (2008).

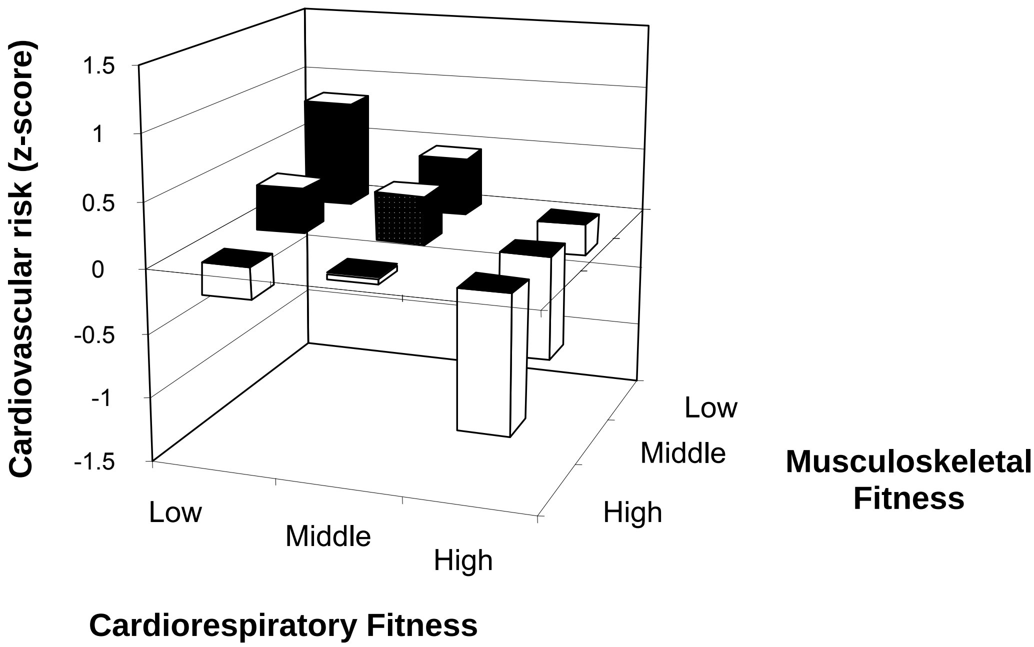


Figure 4. Joint effects of cardiorespiratory fitness (low, middle and high) and musculoskeletal fitness (low, middle and high) on cardiovascular risk score (an average value from the standardised triglycerides, LDLc, HDLc and glucose) in adolescents (n=460). Adapted from García-Artero et al. (2007).

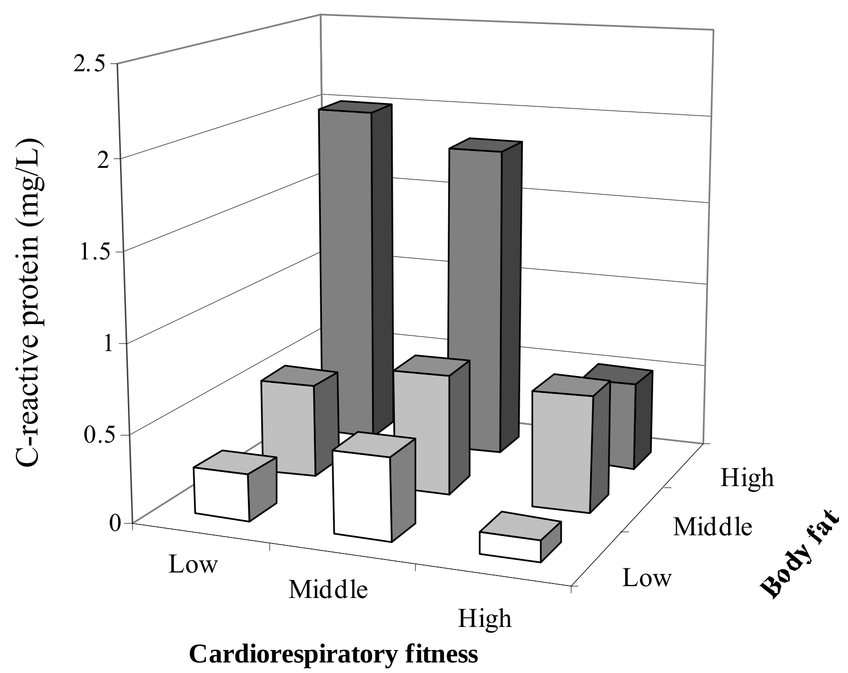


Figure 5. Joint associations between cardiorespiratory fitness (low, middle and high) and body fat mass (low, middle and high of sum of 5 skinfold thickness) in children aged 9-10 years (n=142). Adapted from Ruiz et al. (2007e).

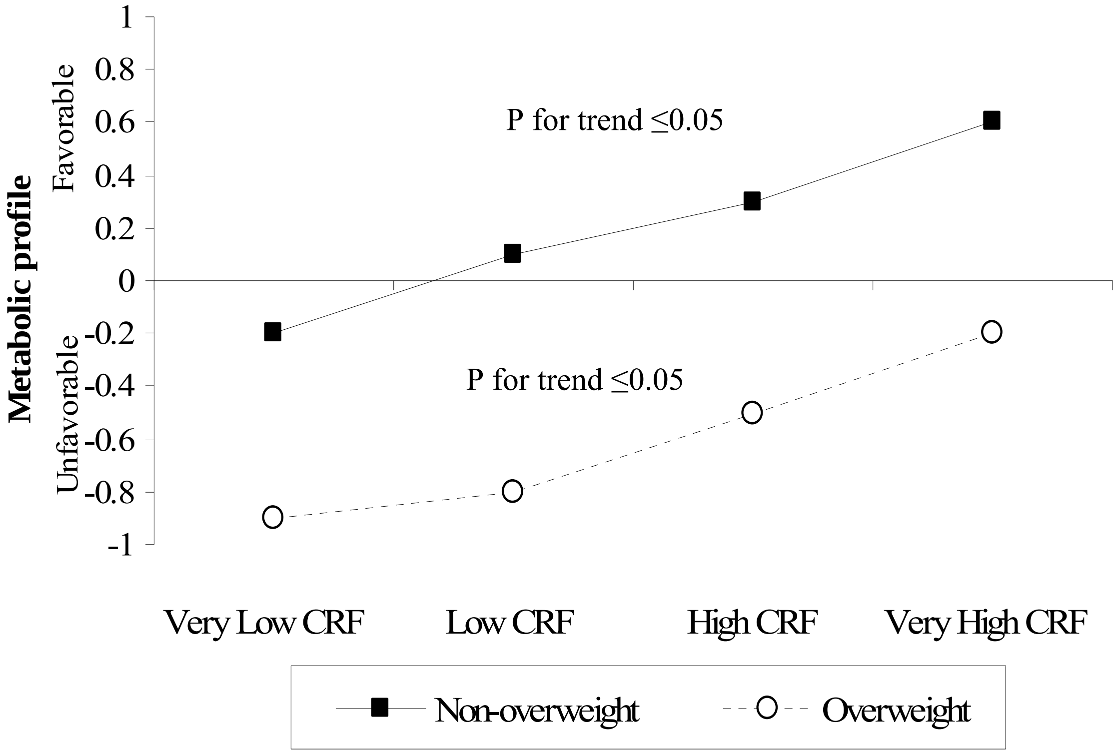


Figure 6. Associations between cardiorespiratory fitness (CRF) and metabolic profile (computed with age- gender specific standardized values of triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol and fasting glycaemia) in non-overweight and overweight young healthy adolescents. Modified from Castillo-Garzon et al. (2007).

2.- SOCIOECONOMIC FACTORS AND PHYSICAL FITNESS

FACTORES SOCIOECONÓMICOS Y CONDICIÓN FÍSICA

Papers III and IV (Artículos III y IV)

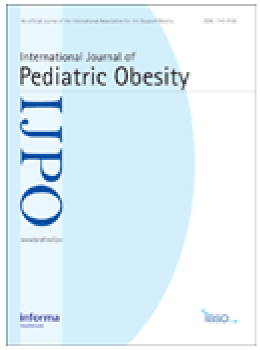
III

INFLUENCE OF SOCIOECONOMIC FACTORS ON FITNESS AND FATNESS IN SPANISH ADOLESCENTS: THE AVENA STUDY

David Jiménez-Pavón, Francisco B. Ortega, Jonatan R. Ruiz, Palma Chillón, Ruth Castillo, Enrique G. Artero, David Martínez-Gómez, German Vicente-Rodriguez, Juan P. Rey-López, Luis A. Gracia, María J. Noriega, Luis A. Moreno, Marcela González-Gross

Int J Pediatr Obes

In press



Influence of socioeconomic factors on fitness and fatness in Spanish adolescents: The AVENA study.

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Abstract:

The purpose of this study was to examine the influence of socioeconomic status on fitness and fatness in Spanish adolescents. A total of 1795 adolescents (833 boys) aged 12.5-18.5 years from the AVENA study participated in this study. The following physical fitness components were assessed: muscular strength (standing long jump), speed-agility (4x10m shuttle run) and cardiorespiratory fitness (20m shuttle run). Total and central body fat was assessed using skinfold thickness and waist circumference, respectively. Both parents reported their educational and professional level. Girls with higher paternal educational level and boys with higher either maternal or paternal professional level had higher muscular strength levels (all $P<0.05$). Speed-agility and cardiorespiratory fitness were not associated with parental educational or professional levels in boys. In contrast, girls with higher paternal educational level or higher parental professional level had higher levels in both fitness components (all $P<0.05$). A higher maternal educational level was associated with lower total and central body fat in boys (all $P<0.05$), but not in girls. We observed a small effect size (*Cohen´s d*~0.2) in most of these associations. Our results suggest modest associations of high socioeconomic status with better fitness and fatness levels in Spanish adolescents. These associations greatly depend on the socioeconomic status and fitness parameters studied.

Key words: Socioeconomic status; fitness; fatness; obesity; adolescents

Introduction

Physical fitness is an important health marker in children and adolescents, and the main health-related fitness components are cardiorespiratory fitness, muscular fitness, speed-agility and body composition (1, 2). Physical fitness is partially determined by genetic endowment, yet it is highly modified by environmental factors (3). Socioeconomic status (SES) has been shown to influence several health-related factors such as birth weight, height, metabolic syndrome, malnutrition and obesity (4-7). Furthermore, several studies reported that low SES in childhood may lead to higher morbidity, including cardiovascular disease later in life (8-10).

Several studies reported the association of SES with fitness and fatness in European youth, and the results are contradictory (11-13). Freitas et al.(11) studied children from the Madeira Growth Study aged 8-18 years old. Physical fitness was assessed using the Eurofit test battery. The authors found that boys from the low SES group performed better for muscular and aerobic endurance whereas girls from the high SES group performed better for power(11). By contrast, a cross-sectional survey conducted by Mutunga et al. in adolescents aged 12 and 15 years from Northern Ireland, observed that adolescents with higher SES (family affluence) had higher cardiorespiratory fitness than those with lower SES (12). Regarding the association between SES and fatness, Armstrong et al. showed that Scottish children in the most deprived families had a 30% higher risk of obesity (14), which concurs with others (13, 15, 16), but not all (6). Likewise, Ness et al. observed that even in children higher fat mass assessed by Dual energy X-ray absorptiometry (DXA) was associated with lower social class although no association with lean mass or central adiposity were found (17). It is important to highlight that both social and cultural contexts are often country-specific. To the best of our knowledge, the effect of SES on both physical fitness and fatness has not been studied in Spanish adolescents. Therefore, the present study aimed to examine the influence of SES on fitness and fatness in a sample of Spanish adolescents

.

Methods

Study sample and design

The data presented in this paper were gathered as a part of the AVENA study (Alimentación y Valoración del Estado Nutricional de los Adolescentes / Feeding and assessment of nutritional status of Spanish adolescents). The complete methodology has been published elsewhere (18). Participants of the AVENA study were urban adolescents aged 12.5–18.5 years. Sampling was multi-staged and stratified by city of origin (Madrid, Granada, Santander, Zaragoza and Murcia), gender and age. Data collection was carried out between 2000 and 2002. A total of 2100 subjects were deemed necessary for the full study to be representative of the population, yet a greater number of subjects were measured to avoid problems of drop-out and consequent data loss. The response rate was >90%.

All the adolescents meeting the general AVENA inclusion criteria (18, 19) and with valid data for age and sex were included in this report. Consequently, sample sizes vary for the different models, the average number of adolescents involved 819 boys and 931 girls. These subjects were equally distributed by gender and age in the study cities. The study sample was considered urban, since all the subjects lived in cities.

Parents and school supervisors were informed by letter about the nature and purpose of the study and written informed consent was required. The study protocol was designed and followed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki (amended in Hong-Kong in 1989 and in Edinburgh in 2000), and was approved by the Review Committee for Research Involving Human Subjects of the Hospital Universitario Marqués de Valdecilla (Santander, Spain).

Physical Fitness

The physical fitness components, i.e. muscular fitness, speed-agility and aerobic capacity, were assessed by the physical fitness tests described below. All the tests were performed twice and the best score was retained, except the 20m shuttle run test, which was performed only once. The scientific rationale for the selection of all of these tests, as well as the validity and reliability in young people, was published elsewhere (20-22).

1.- Standing long jump test (muscular strength): The participant stands behind the starting line and was instructed to push off vigorously and jump as far as possible. The distance is measured from the take-off line to the point where the back of the heel nearest to the take-off line lands on the mat. The result was recorded in centimeters (cm).

2.- 4x10m shuttle run test (speed-agility): The adolescent runs as fast as possible from the starting line to the other line and returns to the starting line (10m apart), crossing each line with both feet every time. This is performed twice, covering a distance of 40 m (4 x 10 m). Every time the adolescent crosses any of the lines, he/she should pick up (the first time) or exchange (second and third times) a sponge, previously placed behind the lines. The time taken to complete the test was recorded to the nearest tenth of a second.

3.- 20m shuttle run test (cardiorespiratory fitness): Adolescents run back and forth between two lines set 20 m apart. Running pace was determined by audio signals, emitted from a pre-recorded cassette tape. The initial speed was 8.5 km·h^{-1}, increasing by 0.5 km·h^{-1} every minute (1 minute equals 1 stage). Participants were instructed to run in a straight line, to pivot upon completing a shuttle and to pace themselves in accordance with the time intervals. The test was finished when the adolescent failed to reach the end lines concurrent with the audio signals on two consecutive occasions. Otherwise, the test ends when the adolescent stops because of fatigue. The final score was computed as the number of stages completed (precision of 0.5 stages).

Physical examination

The description of the anthropometric procedures used in the AVENA study, as well as the reference values can be found elsewhere (19, 23, 24). In brief, weight and height were measured and body mass index was calculated as weight/height squared (kg/m^2). Waist circumference was measured using an inelastic tape (range 0-150 cm; precision 1 mm), horizontally midway between the lowest rib margin and the iliac crest, at the end of a gentle expiration. Skinfold thicknesses were measured to the nearest 0.2 mm in the left side of the body at biceps, triceps, subscapular, suprailiac, thigh, and medial calf using a Holtain skinfold caliper (range, 0 to 40 mm; precision, 0.2 mm). The sum of six skinfold thickness was computed. Overall the technical error of measurement (TEMs) intra-observer for skinfold thickness was smaller than 1 mm. Likewise, the TEMs inter-observer ranged from 1 to 2 mm for the six skinfold thicknesses measured. Pubertal stage was estimated following the Tanner and Whitehouse' method (25).

Socioeconomic factors

Parental educational level

Detailed information about socioeconomic assessment in the AVENA study as well as the representatively of the AVENA participants in terms of parental educational and professional level has been previously described (26).

Both parents were asked to fill in a questionnaire about their educational level, and the possible answers were: primary school, secondary school/technical training or university training. The minimum training period in the Spanish education system was 8 years for primary school, 4 years for secondary school/technical training and 3 years for university training. These three categories shall be referred to as primary, secondary and university, respectively.

Parental professional level

Parents also answered several questions concerning their current occupation. The questions were adapted from, and classified according to, the recommendations of the Spanish Society of Epidemiology (27). Three categories of parental professional levels were established: unskilled worker/ unemployed, skilled worker and managerial. These three categories shall be referred to as low, medium and high professional level, respectively.

Statistical analysis

Data are presented as mean ± standard deviation, standard error of the mean or percentages. All the variables showed a Normal distribution, except for the sum of skinfold thickness that showed a borderline Normal distribution. We calculated the log skinfold and run the statistical analyses using both log data and raw data. The results were rather similar, so we decided to show the raw data to facilitate the interpretation. Differences in fitness and fatness according to SES (education and professional level) groups were examined by one-way analysis of covariance (ANCOVA), with parental educational and professional levels as fixed factors and fitness or fatness as dependent variables. Age, height and sum of skinfold thickness were entered as covariates. Effect size statistics is a measure of the magnitude of effect and in this study was assessed using Cohen´s *d* (standardized mean difference) (28). Taking into account the cut-off established by Cohen the effect size (Cohen´d) can be small (~0.2), medium (~0.5) or large (~0.8). The analyses were performed using the Statistical Package for Social Science (SPSS, v. 15.0 for Windows; SPSS Inc., Chicago, IL) and the level of significance was set to 0.05.

Results

Table 1 shows descriptive characteristics of the study sample.

Differences in fitness and fatness across parental educational and professional levels are displayed in tables 2 and 3, respectively. Girls with either a higher paternal educational level or maternal professional level showed higher muscular strength (all P<0.05). Likewise, boys with higher paternal professional level showed higher muscular strength (P=0.01). Speed-agility and cardiorespiratory fitness were not associated with parental neither educational nor professional levels in boys, whereas girls with higher paternal educational level or higher parental professional level had higher levels in these physical fitness components (all P<0.01). Higher maternal educational level was associated with lower total and central body fat in boys (all P<0.05), but not in girls. The associations of SES with speed-agility and cardirespiratory fitness remained significant after adjusting for multiple comparisons (29).

Additional adjustments for pubertal stage instead of age did not modify the results. In table 2, we observed small effect sizes (Cohen´s *d* =0.2 and 0.3 for boys and girls, respectively) for the previous analyses with significant differences. Likewise, in table 3, we observed small effect sizes (Cohen´s *d* =0.2 and 0.3 for boys and girls, respectively) and medium effect size (Cohen´s *d* =0.6 for girls regarding paternal professional level).

Discussion

The results from the present study suggest that the association between SES and fitness differ depending on which SES or fitness component is analyzed. Overall, SES showed a stronger influence on fitness in girls than in boys. Paternal educational level was positively associated with muscular strength, speed-agility and cardiorespiratory fitness in girls. Similarly, both maternal and paternal professional levels were positively associated with speed agility and cardiorespiratory fitness in girls. Muscular strength was also positively associated with paternal professional level in boys and maternal professional level in girls.

Few studies have deepened on the influence of SES on physical fitness, and the findings are so far contradictory (11, 12). Freitas et al. found a negative association of SES (parental occupation, education, income and housing) with lower-body muscular strength (standing long jump) and cardiorespiratory fitness (12 min walk-run) in boys (11). In addition, they found a positive association between SES and speed-agility performance (5 x 10m shuttle run test). In contrast, we observed a positive association between SES and lower-body muscular strength (standing long jump) in boys, and no association of SES with speed-agility (4 x 10m shuttle run test) or cardiorespiratory fitness (20m shuttle run test). Freitas et al. also reported positive associations between SES and lower-body muscular strength and speed-agility performance in girls, while they did not observe an association between SES and cardiorespiratory fitness (11). These findings concur with our results in the association observed in girls with high SES and lower-body muscular strength or speed-agility performance. Another study observed higher cardiorespiratory fitness (VO_{2max} estimated from 20m shuttle run test) in both boys and girls with high SES (mother occupational level) (12). Discrepancies among studies could be due to the specific social and cultural contexts of each country together with the different methodologies used to assess fitness and SES factors.

The present study also examined the association between SES and adiposity in adolescents. Our data suggest that a high maternal educational level was the main SES factor associated with low levels of both total and central adiposity in boys. High paternal educational level was also associated with low lower central body fat in boys, whereas no association was observed between SES and adiposity in girls. This finding agrees with previous research suggesting maternal educational status as one of the main determinants of adiposity both in youth and adults (13, 15, 16, 30). It has been suggested in several recent reviews the increasing prevalence of obesity during growth and development is related to the education not only of the children but also to that of parents who are influencing food intake and physical activity from the first decade of life (13, 15). Indeed, mother´s nutrition and physical activity habits seems to influence their children's habits (13). Maternal educational level can influence children´s adiposity already from pregnancy through putting more attention on the selection of the appropriate diet during this period and also with regard to the duration of breast-feeding (13, 15).

We did not find any empirical evidence to justify the stronger association observed in girls, compared to boys, in the association between SES and fitness. However, we can hypothesize about it. The different social and cultural roles attributed to boys and girls may at least partially explain this finding. Girls from a low SES environment may have a role more related with home tasks or indoor entertainment activities; while boys in this same SES environment spend more time doing outdoor activities such as running, jumping, playing football, etc. On the other hand, high SES families may have a higher awareness about healthy lifestyle, physical activity and fitness, and promote these behaviors equally in both daughters and sons. This may result in bigger differences in fitness between girls from different SES than between boys from different SES, and explain therefore the stronger association between SES and fitness observed in girls.

We studied the association of maternal educational level with total and central (waist circumference) body fat in Swedish children and adolescents, and observed a borderline association between maternal educational level and the risk of being overweight (31). In agreement with our results a previous study showed that Scottish children in the most deprived families had a 30% higher risk of obesity (14). In contrast, others concluded that there was little evidence on the association between adiposity and SES in children (6).

The small effect size observed for the associations of SES with fitness and fatness could be due to the multifactorial aetiology of adolescent fitness and fatness status. Cross-sectional designs usually do not allow stating the direction of the associations. However, in the current work is not likely that adolescent's fitness and fatness levels could influence their parents' educational or professional level. So, the results from this study can be interpreted as the influence of SES on fitness and fatness, rather than the other way around. Another limitation of the present study was the use of proxy measures for fatness instead of using more accurate methods such as DXA. In fitness field tests participant´s motivation can skew the final performance, so in the present study researchers strongly encouraged the adolescents during the tests in order to avoid this effect. The relatively large sample of adolescents from southern, central and northern Spain studied in this work provides an overall picture of the relationships between SES, fitness and fatness in Spanish adolescent population.

In conclusion, the results suggest that a high socioeconomic level seems to positively influence health-related parameters such as fitness and fatness in Spanish adolescents, yet these associations vary depending on the SES and fitness parameters studied. Concerning fitness, a stronger association was observed in girls, while the association with fatness is present only in boys.

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References

1. Ruiz JR, Castro-Pinero J, Artero EG, et al. Predictive Validity of Health-Related Fitness in Youth: A Systematic Review. Br J Sports Med. 2009 Jan 21.
2. Ortega FB, Ruiz JR, Castillo MJ, et al. Physical fitness in childhood and adolescence: a powerful marker of health. Int J Obes (Lond). 2008 Jan;32(1):1-11.
3. Bray MS, Hagberg JM, Perusse L, et al. The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update. Med Sci Sports Exerc. 2009 Jan;41(1):35-73.
4. Ramsay SE, Whincup PH, Morris R, et al. Is socioeconomic position related to the prevalence of metabolic syndrome?: influence of social class across the life course in a population-based study of older men. Diabetes Care. 2008 Dec;31(12):2380-2.
5. Janssen I, Boyce WF, Simpson K, et al. Influence of individual- and area-level measures of socioeconomic status on obesity, unhealthy eating, and physical inactivity in Canadian adolescents. Am J Clin Nutr. 2006 Jan;83(1):139-45.
6. Batty GD, Leon DA. Socio-economic position and coronary heart disease risk factors in children and young people. Evidence from UK epidemiological studies. Eur J Public Health. 2002 Dec;12(4):263-72.
7. Yarnell J, Yu S, McCrum E, et al. Education, socioeconomic and lifestyle factors, and risk of coronary heart disease: the PRIME Study. Int J Epidemiol. 2005 Apr;34(2):268-75.
8. Brunner E, Shipley MJ, Blane D, et al. When does cardiovascular risk start? Past and present socioeconomic circumstances and risk factors in adulthood. J Epidemiol Community Health. 1999 Dec;53(12):757-64.
9. Power C, Graham H, Due P, et al. The contribution of childhood and adult socioeconomic position to adult obesity and smoking behaviour: an international comparison. Int J Epidemiol. 2005 Apr;34(2):335-44.
10. Regidor E, Banegas JR, Gutierrez-Fisac JL, et al. Socioeconomic position in childhood and cardiovascular risk factors in older Spanish people. Int J Epidemiol. 2004 Aug;33(4):723-30.
11. Freitas D, Maia J, Beunen G, et al. Socio-economic status, growth, physical activity and fitness: the Madeira Growth Study. Ann Hum Biol. 2007 Jan-Feb;34(1):107-22.
12. Mutunga M, Gallagher AM, Boreham C, et al. Socioeconomic differences in risk factors for obesity in adolescents in Northern Ireland. Int J Pediatr Obes. 2006;1(2):114-9.
13. Parizkova J. Impact of education on food behaviour, body composition and physical fitness in children. Br J Nutr. 2008 Feb;99 Suppl 1:S26-32.
14. Armstrong J, Dorosty AR, Reilly JJ, et al. Coexistence of social inequalities in undernutrition and obesity in preschool children: population based cross sectional study. Arch Dis Child. 2003 Aug;88(8):671-5.
15. Moreno LA, Tomas C, Gonzalez-Gross M, et al. Micro-environmental and socio-demographic determinants of childhood obesity. Int J Obes Relat Metab Disord. 2004 Nov;28 Suppl 3:S16-20.
16. Shrewsbury V, Wardle J. Socioeconomic status and adiposity in childhood: a systematic review of cross-sectional studies 1990-2005. Obesity (Silver Spring). 2008 Feb;16(2):275-84.
17. Ness AR, Leary S, Reilly J, et al. The social patterning of fat and lean mass in a contemporary cohort of children. Int J Pediatr Obes. 2006;1(1):59-61.

18. Gonzalez-Gross M, Castillo MJ, Moreno L, et al. [Feeding and assessment of nutritional status of spanish adolescents (AVENA study). Evaluation of risks and interventional proposal. I.Methodology]. Nutr Hosp. 2003 Jan-Feb;18(1):15-28.
19. Moreno LA, Joyanes M, Mesana MI, et al. Harmonization of anthropometric measurements for a multicenter nutrition survey in Spanish adolescents. Nutrition. 2003 Jun;19(6):481-6.
20. Ortega FB, Artero EG, Ruiz JR, et al. Reliability of health-related physical fitness tests in European adolescents. The HELENA Study. Int J Obes (Lond). 2008 Nov;32 Suppl 5:S49-57.
21. Ruiz JR, Ortega FB, Gutierrez A, et al. Health-related fitness assessment in childhood and adolescence: a European approach based on the AVENA, EYHS and HELENA studies. J Public Health. 2006;14(5):269-77.
22. Castro-Piñero J, Artero EG, Espana-Romero V, et al. Criterion-related validity of field-based fitness tests in youth: A systematic review. Br J Sports Med. 2009 Apr 12.
23. Moreno LA, Mesana MI, Gonzalez-Gross M, et al. Anthropometric body fat composition reference values in Spanish adolescents. The AVENA Study. Eur J Clin Nutr. 2006 Feb;60(2):191-6.
24. Moreno LA, Mesana MI, Gonzalez-Gross M, et al. Body fat distribution reference standards in Spanish adolescents: the AVENA Study. Int J Obes (Lond). 2007 Dec;31(12):1798-805.
25. Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child. 1976 Mar;51(3):170-9.
26. Chillon P, Ortega FB, Ruiz JR, et al. Socio-economic factors and active commuting to school in urban Spanish adolescents: the AVENA study. Eur J Public Health. 2009 Jun 17.
27. Álvarez-Dardet C, Alonso J, Domingo A, et al. La medición de la clase social en ciencias de la salud. Informe de un grupo de trabajo de la Sociedad Española de Epidemiología [The measurement of social class in health sciences. Report of a working group of the Spanish Society of Epidemiology]. Barcelona: S G Editores. 1995.
28. Nakagawa S, Cuthill IC. Effect size, confidence interval and statistical significance: a practical guide for biologists. Biol Rev Camb Philos Soc. 2007 Nov;82(4):591-605.
29. Holm S. A simple sequentially rejective multiple test procedure. Scand J Statist. 1997;6:65-70.
30. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. Circulation. 1993 Oct;88(4 Pt 1):1973-98.
31. Ortega FB, Ruiz JR, Sjostrom M. Physical activity, overweight and central adiposity in Swedish children and adolescents: the European Youth Heart Study. Int J Behav Nutr Phys Act. 2007;4:61.

Table 1. Descriptive characteristics of Spanish adolescents.

	All	Boys	Girls
Age (years)	15.3 ± 1.3	15.2 ± 1.3	15.4 ± 1.4
Pubertal stage (I/II/III/IV/V)*	0/3/12/44/41	0/4/14/38/44	0/1/10/50/39
Weight (kg)	60.0 ± 11.9	63.8 ± 12.9	56.4 ± 9.5
Height (m)	166.2 ± 8.7	170.9 ± 8.6	161.8 ± 6.2
Body mass index (kg/m^2)	21.6 ± 3.4	21.8 ± 3.6	21.5 ± 3.3
Body mass index z-scores	-2.0E-15 ± 1.0	0.03 ± 1.1	-0.03 ± 1.0
Standing long jump (cm)	169.1 ± 32.9	190.0 ± 28.8	149.3 ± 22.7
4x10m shuttle run test (s)	12.3 ± 1.5	11.7 ± 1.4	12.9 ± 1.4
20m shuttle run (stage)	5.6 ± 2.6	7.0 ± 2.5	4.2 ± 1.8
Sum of 6 skinfold thickness (mm)	87.4 ± 35.8	74.6 ± 36.4	99.5 ± 30.7
Waist circumference (cm)	73.8 ± 9.1	76.6 ± 9.4	71.1 ± 7.8
Waist z-scores	-5.6E-15 ± 1.0	0.31 ± 1.0	-0.29 ± 0.9
Fat Mass Slaughter (%)	22.6 ± 8.6	19.5 ± 9.6	25.5 ± 6.2
Fat Free Mass Slaughter (kg)	45.9 ± 7.8	50.6 ± 7.8	41.5 ± 4.7
Overweight*	18.1	20.2	16.1
Obese*	4.3	5.8	2.9
Maternal educational level (P/S/U)*	36/18/46	35/19/46	37/18/45
Paternal educational level (P/S/U)*	31/18/51	30/19/51	31/18/51
Maternal professional level (L/M/H)*	53/31/17	51/31/19	54/31/15
Paternal professional level (L/M/H)*	4/63/33	5/62/33	4/64/32

All values are means± standard deviation or percentages(*). P: Primary; S: Secondary; U: University; L: Low; M: Medium; H: High.

Table 2. Associations of maternal and paternal educational level with fitness and fatness in adolescents, after adjusting for age and height.

		Maternal					Paternal				
		n	Primary	Secondary	University	P	*n*	Primary	Secondary	University	P
Boys	Standing long jump (cm)[a]	873	188.1 (1.5)	188.9 (2.0)	193.0 (1.3)	0.62	860	187.9 (1.6)	190.2 (2.0)	192.5 (1.2)	0.19
	4x10m shuttle run test (s)[a]	862	11.6 (0.1)	11.8 (0.1)	11.7 (0.1)	0.13	849	11.7 (0.1)	11.7 (0.1)	11.7 (0.1)	0.91
	20m shuttle run (stage)[a]	788	6.8 (0.1)	7.1 (0.1)	7.2 (0.2)	0.15	774	6.7 (0.2)	7.2 (0.2)	7.1 (0.1)	0.06
	Sum of 6 skinfold thickness (mm)	908	76.7 (2.0)	78.7 (2.6)	71.0[§§] (1.7)	0.02	895	75.4 (2.1)	77.7 (2.7)	71.8 (1.7)	0.14
	Waist circumference (cm)	920	76.4 (0.5)	77.8 (0.7)	75.9[§§] (0.4)	0.01	906	76.6 (0.5)	77.7 (0.7)	75.6[§] (0.4)	0.04
Girls	Standing long jump (cm)[a]	1001	147.4 (1.1)	149.5 (1.6)	151.7 (1.0)	0.11	970	146.2 (1.2)	150.8 (1.5)	151.5[††] (1.0)	0.02
	4x10m shuttle run test (s)[a]	968	13.0 (0.1)	12.9 (0.1)	12.8 (0.1)	0.16	946	13.1 (0.1)	13.0 (0.1)	12.7[†††] (0.1)	0.001
	20m shuttle run (stage)[a]	854	4.2 (0.1)	4.3 (0.1)	4.4 (0.1)	0.32	830	3.9 (0.1)	4.6[**] (0.1)	4.4[††] (0.1)	0.001
	Sum of 6 skinfold thickness (mm)	1075	99.5 (1.5)	98.6 (2.2)	97.9 (1.3)	0.72	1043	100.8 (1.7)	97.2 (2.2)	98.6 (1.3)	0.39
	Waist circumference (cm)	1093	71.1 (0.4)	70.6 (0.6)	70.6 (0.3)	0.57	1062	71.6 (0.4)	70.3 (0.6)	70.8 (0.3)	0.15

Values are mean (standard error of the mean). [a] adjusting for age, height and skinfold thickness.
[*] Differences Secondary vs Primary. [§] Differences University vs Secondary. [†] Differences University vs Primary.
One symbol indicates P<0.05, two symbols indicates P<0.01 and three symbols indicates P<0.001.

Table 3. Associations of maternal and paternal professional level with fitness and fatness in adolescents, after adjusting for age and height.

		Maternal								Paternal							
			Low		Medium		High		P		Low		Medium		High		P
		n								*n*							
Boys	Standing long jump (cm)[a]	807	187.2	(1.3)	191.8	(1.7)	193.6	(2.1)	0.06	746	183.9	(4.1)	186.9	(1.2)	194.6§§	(1.5)	0.01
	4x10m shuttle run test (s)[a]	800	11.8	(0.1)	11.7	(0.1)	11.6	(0.1)	0.54	739	11.7	(0.2)	11.7	(0.1)	11.7	(0.1)	0.94
	20m shuttle run (stage)[a]	722	6.9	(0.1)	6.9	(0.1)	7.2	(0.2)	0.62	668	6.8	(0.4)	6.8	(0.1)	7.2	(0.2)	0.39
	Sum of 6 skinfold thickness (mm)	838	76.7	(1.7)	73.5	(2.3)	71.6	(2.9)	0.26	777	74.2	(6.1)	75.2	(1.6)	74.0	(2.3)	0.91
	Waist circumference (cm)	851	76.5	(0.4)	76.4	(0.6)	76.2	(0.7)	0.95	787	75.4	(1.5)	75.6	(0.4)	75.9	(0.6)	0.55
Girls	Standing long jump (cm)[a]	940	148.2	(1.0)	150.4	(1.2)	154.6†	(1.7)	0.03	804	143.6	(3.6)	148.6	(1.0)	151.6	(1.3)	0.28
	4x10m shuttle run test (s)[a]	926	13.0	(0.1)	12.9	(0.1)	12.6††	(0.1)	<0.01	795	13.0	(0.3)	13.0	(0.1)	12.6§§	(0.1)	<0.01
	20m shuttle run (stage)[a]	800	4.2	(0.1)	4.1	(0.1)	4.6§§	(0.2)	<0.01	679	3.7	(0.2)	4.2	(0.1)	4.7§§††	(0.1)	<0.01
	Sum of 6 skinfold thickness (mm)	1010	100.3	(1.3)	97.4	(1.7)	98.7	(2.5)	0.41	864	96.3	(5.2)	99.6	(1.3)	96.7	(1.8)	0.41
	Waist circumference (cm)	1030	71.0	(0.3)	70.8	(0.4)	71.1	(0.6)	0.94	881	71.5	(1.3)	71.1	(0.3)	70.3	(0.5)	0.33

Values are mean (standard error of the mean). [a] adjusting for age, height and skinfold thickness. § Differences High vs Medium. † Differences High vs Low. One symbol means P<0.05, two symbols mean P<0.01 and three symbols mean P<0.001.

SOCIOECONOMIC STATUS INFLUENCES PHYSICAL FITNESS IN EUROPEAN ADOLESCENTS INDEPENDIENTLY OF BODY FAT AND PHYSICAL ACTIVITY. THE HELENA STUDY

David Jiménez-Pavón, Francisco B. Ortega, Jonatan R. Ruiz, Vanesa España-Romero, Enrique G. Artero, Diego Moliner-Urdiales, Sonia Gómez-Martínez, German Vicente-Rodriguez, Yannis Manios, Laurent Béghin, Judit Répásy, Michael Sjöström, Luis A. Moreno, Marcela González-Gross, Manuel J. Castillo on behalf of the HELENA study group

IV

Nutr Hosp

In press

Titulo: El estatus socioeconómico influencia la condición física en adolescentes Europeos. El Estudio HELENA.

Title: Socioeconomic status influences physical fitness in European adolescents independently of body fat and physical activity; The HELENA Study.

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Número total de palabras: 1710

ABSTRACT

Introduction: The influence of socioeconomic status on health-related fitness is not clear. **Aim:** To examine the influence of socioeconomic status on health-related fitness in adolescents. **Methods:** A total of 3259 adolescents (15.0±1.3y) from the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study (HELENA-CSS) participated in the study. Socioeconomic status was assessed by the family affluence scale (FAS). Speed-agility, muscular strength and cardiorespiratory fitness were assessed. Covariates included total body fat, physical activity and pubertal status. **Results:** Adolescents with high FAS had significantly higher fitness levels than their peers of lower FAS categories except for speed-agility and handgrip in boys. Overall, the associations observed presented a medium to large effect size. **Conclusion:** These results suggest that socioeconomic status is positively associated with physical fitness in European adolescents independently of total body fat and habitual physical activity.

Keywords: Socioeconomic status, physical fitness, physical activity, total body fat

RESUMEN

Introducción: La influencia del estatus socioeconómico sobre la condición física en relación con la salud no está clara. **Objetivo:** Examinar la influencia del estatus socioeconómico sobre la condición física en relación con la salud en adolescentes. **Metodología:** Un total de 3259 adolescentes (15.0±1.3 años) del "Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study" (HELENA-CSS) participaron en el estudio. El estatus socioeconómico fue medido con una escala de riqueza familiar "family affluence scale (FAS)". Se midieron velocidad-agilidad, fuerza muscular y capacidad aeróbica. Las covariables incluidas fueron grasa corporal total, actividad física y estadio madurativo. **Resultados:** Los adolescentes con alto FAS tuvieron significativamente mayores niveles de condición física que aquellos con bajo FAS exceptuando los tests de velocidad-agilidad y fuerza de prensión manual en chicos. En general, las asociaciones observadas presentaron un efecto del tamaño de la muestra (effect size) entre medio y largo. **Conclusión:** Estos resultados sugieren que el estatus socioeconómico esta positivamente asociado con la condición física en adolescentes Europeos independientemente de la grasa corporal total y el nivel de actividad física.

Palabras clave: Estatus socioeconómico, condición física, actividad física y grasa corporal total.

INTRODUCTION

Speed-agility, muscular fitness, and cardiorespiratory fitness (CRF) are considered important health-related markers already in youth[1, 2]. Genetics greatly determines physical fitness[3], but there is little doubt that environmental factors also play an important role. Socioeconomic status is associated with several health outcomes (e.g., birth weight, obesity, diet, etc.) [4, 5] and with mortality[6]. To better understand the specific role of different indicators of socioeconomic status on health-related fitness markers will enable a more efficient physical fitness promotion. In this regard, the association between socioeconomic status and fitness was investigated in Portuguese[7] and Irish[8] youth with contradictory results. In Portuguese adolescents, the socioeconomic status was inversely associated with fitness in boys but positively in girls[7]. However, in Irish youth there was a positive association of socioeconomic status with fitness[8]. These previous findings highlight that both social and cultural contexts are often country-specific, so studies from a widespread vision and including populations from different countries are required to facilitate a better understanding.

The Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study (HELENA-CSS) used harmonised and well standardised methods of measurement in nine European countries and previous workshops were organised in order to guarantee this process. Therefore the HELENA-CSS provides a good opportunity to explore the relationship between socioeconomic status and physical fitness in European adolescents (see annex 2). The aim of this study was to examine the influence of socioeconomic status on health-related physical fitness (speed-agility, muscular fitness, and CRF) in urban European adolescents.

METHODS

The HELENA-CSS study is a multi-centre study aiming to obtain reliable data from European adolescents aged 12.5 to 17.5 years about nutritional habits and patterns, body composition and levels of physical activity and fitness (see annex 2). The total sample of the HELENA-CSS was 3528 adolescents and the present work comprised 3259 (1558 boys and 1701 girls) adolescents with valid data on socioeconomic status and at least one physical fitness test. More details about the sampling procedures, preparation of the field teams, pilot study and reliability of the data can be found elsewhere (see annex 2).

Ten cities in nine different European countries were chosen due to an existing network of research groups and a rough geographical balance across Europe; Stockholm (Sweden), Athens (Greece), Heraklion (Greece), Rome (Italy), Zaragoza (Spain), Pecs (Hungary), Ghent (Belgium) Lille (France), Dortmund (Germany) and Vienna (Austria). Signed informed consent was obtained from all participants and their parents, and the protocol was approved by the Human Research Review Committees of the involved centres (see annex 2).

Socioeconomic status

The Family Affluence Scale (FAS) is based on the concept of material conditions in the family to base the selection of items. Currie et al. [9] chose a set of items which reflected family expenditure and consumption that were relevant to family circumstances. Possessing these items was considered to reflect affluence and their lack, on the other hand, material deprivation. FAS was used in the present study as an index of socioeconomic status[10], which includes 4 questions answered by the adolescent: Do you have your own bedroom?; How many cars are there in your family?; How many PCs are there in your home?; Do you have internet access at home? We defined low, medium and high socioeconomic status based on the final score obtained from the four questions. That is, we give a numerical value to each possible answer in the four questions. Then we summed the final score from all the questions being ranged from 0 to 8. Finally, we grouped these scores in three levels: low (from 0 to 2), medium (from 3 to 5) and high (from 6 to 8).

Physical fitness

Speed-agility was assessed with the 4x10m shuttle run test. Upper-body muscular strength was assessed with the handgrip strength and the bent arm hang tests. Lower-body muscular strength was assessed with the standing long jump, the squat jump, the counter movement jump and the Abalakov jump tests. The Infrared Platform ERGO JUMP Plus – BOSCO SYSTEM (Byomedic, S.C.P., Barcelona, Spain) was used for the jump assessment. CRF was assessed by the 20m shuttle run test. More detailed information about the fitness testing protocol has been published elsewhere (see annex 2).

Covariates

Following standard procedures (see annex 2), weight was measured in underwear and without shoes with an electronic scale (Type SECA 861) to the nearest 0.05 kg, and height was measured barefoot in the Frankfort plane with a telescopic height measuring instrument (Type SECA 225) to the nearest 0.1 cm. Skinfold thickness was measured to the nearest 0.2 mm in triplicate in the left side at biceps, triceps, subscapular, suprailiac, thigh, and medial calf with a Holtain Caliper (Crymmych, UK)[11]. The Actigraph accelerometer (Actigraph MTI, model GT1M, Manufacturing Technology Inc., Fort Walton Beach, FL, USA) was used to assess physical activity and expressed as counts/min[12]. Adolescents were asked to wear the accelerometer during the daytime for 7 consecutive days, except during water based activities. The criterion for inclusion was to record at least 8 h per day, for at least 3 days[13]. A total of 2208 (68% of the total) adolescents (1192 girls) reported valid data of accelerometry. Pubertal status was assessed by a medical doctor according to Tanner stages[14].

Statistical analysis

The data are presented as means (standard deviation). To achieve normality in the residuals, handgrip, bent arm hang, squat jump, counter movement jump, Abalakov jump, and sum of skinfold thickness were transformed to the natural logarithm. The associations between FAS and physical fitness were assessed by one-way analysis of covariance with FAS entered as fixed factor and the fitness tests as dependent variables. Age, height, total body fat and physical activity were entered as covariates. Effect size statistics is a measure of the magnitude of effect and in this study was assessed using Cohen´s *d* (standardized mean difference) and 95% confidence interval[15]. Taking into account the cut-off established by Cohen, the effect size (Cohen´d) can be small (~0.2), medium (~0.5) or large (~0.8). We analysed possible differences in age, weight, height and BMI (variables available for the whole study sample) between adolescents with complete valid data (1411) and missing data. No differences were observed in the variables studied. The analyses were performed using the Statistical Package for Social Science (SPSS, v. 15.0 for Windows; SPSS Inc., Chicago, IL) and the level of significance was set at 0.05.

RESULTS

Table 1 shows the associations between FAS and physical fitness by sex. In boys, those with high FAS performed better in bent arm hang, standing long jump, squat jump, counter movement jump, Abalakov jump or 20m shuttle run test (all $P \leq 0.05$). FAS was not associated with the 4x10m shuttle run test or handgrip strength. Small effect sizes were observed for the standing long jump test in boys with high FAS compared to those with low FAS, whereas medium to large effect sizes were observed for the bent arm hang, squat jump, Abalakov jump, counter movement jump and 20m shuttle run tests.

Girls with high FAS performed significantly better in all fitness tests (all $P<0.05$) compared to their peers of lower FAS level. Medium effect sizes were found for the bent arm hang, 4x10m shuttle run test, standing long jump, counter movement jump and Abalakov jump in girls with high FAS compared to those with low FAS. We observed large effect sizes for the squat jump and 20m shuttle run tests. Additional adjustments for pubertal status instead of age did not modify the results (data not shown). The result did not change when body mass index or waist circumference was used instead of skinfold thickness. Likewise, the results remained the same when parental educational level was used instead of FAS (data not shown).

DISCUSSION

The results from the present study suggest that there is a strong positive association between socioeconomic status and physical fitness in European adolescents independently of total body fat and objectively assessed physical activity. Overall, the associations observed presented a medium to large effect size. These findings could be interpreted as an overall influence of socioeconomic status on the physical fitness performance. A higher socioeconomic status could allow the adolescents to have more facilities to practice exercise in terms of sport equipments acquisition, extracurricular sport sessions as well as a major awareness of their parents regarding the importance of having a healthy fitness.

These findings do not concur with a previous study[7] in which negative associations were observed between socioeconomic status and CRF (12 min walk-run) and muscular strength (standing long jump and bent arm hang) in boys[7]. Moreover, Freitas et al. reported a positive association between socioeconomic status and speed-agility performance (5 x 10m shuttle run test). They also reported a higher upper-body muscular strength (handgrip) in those boys with medium socioeconomic status compared to those with lower socioeconomic status[7]. In contrast, our findings showed positive associations between socioeconomic status and CRF (20m shuttle run test), lower-body muscular strength (standing long jump, squat jump, counter movement jump, Abalakov jump) and one upper-body muscular strength test (bent arm hang), while no associations for speed-agility (4x10m shuttle run test) and other upper-body muscular strength (handgrip) were found. In girls, Freitas et al. found positive associations between socioeconomic status and lower-body muscular strength and speed-agility performance, but no association for CRF and upper-body muscular strength[7], which partially concur with our results. However, we also found positive associations for CRF and upper-body muscular strength. Our data also concur with the results observed by Mutunga et al.[8] They reported higher CRF (20m shuttle run test) in boys and girls with higher socioeconomic status compared to those with lower socioeconomic status[8]. Discrepancies among studies could be due to the specific social and cultural contexts of each country, together with the different methodologies used to assess socioeconomic status and physical fitness.

The direction of the associations cannot be established from cross-sectional designs. However, in the current study, it is not likely that adolescent physical fitness level determines the affluence of their families. The relatively large sample of adolescents studied from nine European countries (ten cities) provides a good overview of the relationships between socioeconomic status and physical fitness in European adolescent population.

In conclusion, these results suggest that high socioeconomic status, as assessed by family affluence, positively influences physical fitness in urban European adolescents independently of total body fat and habitual physical activity.

ANNEX

Annex 1: HELENA Study Group

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Annex 2: Methodological references of HELENA-CSS in relation with this paper.

- Moreno L. A., De Henauw S., Gonzalez-Gross M., et al. Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. *Int J Obes (Lond)*. 2008;**32 Suppl 5**:S4-11.
- Moreno L. A., Gonzalez-Gross M., Kersting M., et al. Assessing, understanding and modifying nutritional status, eating habits and physical activity in European adolescents: the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) Study. *Public Health Nutr*. 2008;**11**:288-99.
- Ortega F. B., Artero E. G., Ruiz J. R., et al. Physical fitness levels among European adolescents: The HELENA study. *Br J Sports Med*. 2009.
- Ortega F. B., Artero E. G., Ruiz J. R., et al. Reliability of health-related physical fitness tests in European adolescents. The HELENA Study. *Int J Obes (Lond)*. 2008;**32 Suppl 5**:S49-57.
- Beghin L., Castera M., Manios Y., et al. Quality assurance of ethical issues and regulatory aspects relating to good clinical practices in the HELENA Cross-Sectional Study. *Int J Obes (Lond)*. 2008;**32 Suppl 5**:S12-8.
- Ruiz J. R., Ortega F. B., Gutierrez A., et al. Health-related fitness assessment in childhood and adolescence: a European approach based on the AVENA, EYHS and HELENA studies. *J Public Health*. 2006;**14**:269-77.

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REFERENCES

1. Ruiz JR, Castro-Pinero J, Artero EG, Orgeta FB, Sjostrom M, Suni J, Castillo MJ. Predictive Validity of Health-Related Fitness in Youth: A Systematic Review. *Br J Sports Med*. 2009 Jan 21.

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

3. Bray MS, Hagberg JM, Perusse L, Rankinen T, Roth SM, Wolfarth B, Bouchard C. The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update. *Med Sci Sports Exerc*. 2009 Jan;41(1):35-73.

4. Ramsay SE, Whincup PH, Morris R, Lennon L, Wannamethee SG. Is socioeconomic position related to the prevalence of metabolic syndrome?: influence of social class across the life course in a population-based study of older men. *Diabetes Care*. 2008 Dec;31(12):2380-2.

5. Moreno LA, Tomas C, Gonzalez-Gross M, Bueno G, Perez-Gonzalez JM, Bueno M. Micro-environmental and socio-demographic determinants of childhood obesity. *Int J Obes Relat Metab Disord*. 2004 Nov;28 Suppl 3:S16-20.

6. Berkman LF. Tracking social and biological experiences: the social etiology of cardiovascular disease. *Circulation*. 2005 Jun 14;111(23):3022-4.

7. Freitas D, Maia J, Beunen G, Claessens A, Thomis M, Marques A, Crespo M, Lefevre J. Socio-economic status, growth, physical activity and fitness: the Madeira Growth Study. *Ann Hum Biol*. 2007 Jan-Feb;34(1):107-22.

8. Mutunga M, Gallagher AM, Boreham C, Watkins DC, Murray LJ, Cran G, Reilly JJ. Socioeconomic differences in risk factors for obesity in adolescents in Northern Ireland. *Int J Pediatr Obes*. 2006;1(2):114-9.

9. Currie CE, Elton RA, Todd J, Platt S. Indicators of socioeconomic status for adolescents: the WHO Health Behaviour in School-aged Children Survey. *Health Educ Res*. 1997 Sep;12(3):385-97.

10. Currie C, Molcho M, Boyce W, Holstein B, Torsheim T, Richter M. Researching health inequalities in adolescents: the development of the Health Behaviour in School-Aged Children (HBSC) family affluence scale. *Soc Sci Med*. 2008 Mar;66(6):1429-36.

11. Lohman TG, Roche AF, Martorell R. Anthropometric Standardization Reference Manual. *Human Kinetics Books: Champaign, Illinois*. 1988.

12. Hagstromer M, Bergman P, De Bourdeaudhuij I, Ortega FB, Ruiz JR, Manios Y, Rey-Lopez JP, Phillipp K, von Berlepsch J, Sjostrom M. Concurrent validity of a modified version of the International Physical Activity Questionnaire (IPAQ-A) in European adolescents: The HELENA Study. *Int J Obes (Lond)*. 2008 Nov;32 Suppl 5:S42-8.

13. Trost SG, Pate RR, Freedson PS, Sallis JF, Taylor WC. Using objective physical activity measures with youth: how many days of monitoring are needed? *Med Sci Sports Exerc*. 2000 Feb;32(2):426-31.

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

15. Nakagawa S, Cuthill IC. Effect size, confidence interval and statistical significance: a practical guide for biologists. *Biol Rev Camb Philos Soc*. 2007 Nov;82(4):591-605.

Table 1. Association between family affluence scale and physical fitness, after adjusting for age, height, skinfold thickness and physical activity.

		Family affluence scale				Effect size		
Fitness Tests	*n*	*Low (L)*	*Medium (M)*	*High (H)*	*P*	*L - M*	*M - H*	*L - H*
Boys								
4x10m shuttle run test (s)	921	11.6 (0.9)	11.4 (0.9)	11.4 (0.9)	0.207	0.2 (0.04;0.45)	0.0 (-0.14;0.14)	0.2 (0.01;0.39)
Handgrip (kg)[a]	942	69.6 (12.0)	70.8 (12.0)	70.7 (12.0)	0.352	0.1 (-0.05;0.26)	0.1 (-0.04;0.23)	0.0 (-0.18;0.21)
Bent arm hang (s)[a]	902	18.4 (16.0)	21.9 (15.9)	24.8[†§] (16.0)	**< 0.001**	0.4 (0.23;0.55)	0.1 (-0.02;0.25)	0.5 (0.31;0.71)
Standing long jump (cm)	933	179.1 (26.2)	185.1 (26.1)	186.5[†] (26.2)	**0.05**	0.2 (0.02;0.38)	0.1(-0.08;0.19)	0.3 (0.09;0.48)
Squat Jump (cm)[a]	868	22.5 (7.0)	24.9* (7.0)	26.9[†§] (7.0)	**< 0.001**	0.3 (0.19;0.51)	0.3 (0.13;0.41)	0.6 (0.41;0.83)
Counter Movement Jump (cm)[a]	868	24.5 (6.7)	28.0* (6.7)	29.8[†§] (6.7)	**< 0.001**	0.5 (0.35;0.68)	0.3 (0.13;0.41)	0.8 (0.56;0.99)
Abalakov Jump (cm)[a]	867	30.6 (7.1)	34.2* (7.0)	35.0[†§] (7.0)	**< 0.001**	0.4 (0.21;0.54)	0.3 (0.12;0.40)	0.6 (0.43;0.85)
20m shuttle run (stage)	820	5.8 (2.6)	6.8* (2.6)	7.2[†§] (2.6)	**< 0.001**	0.4 (0.24;0.48)	0.2 (0.01;0.30)	0.6 (0.35;0.78)
Girls								
4x10m shuttle run test (s)	1060	13.4 (1.2)	12.8* (1.2)	12.8[†§] (1.2)	**< 0.001**	0.5 (0.33;0.62)	0.3 (-0.13;0.39)	0.7 (0.55;0.92)
Handgrip (kg)[a]	1093	51.3 (8.5)	50.8 (8.4)	52.3[§] (8.5)	**< 0.05**	0.1 (-0.08;0.20)	0.2 (-0.05;0.31)	0.1 (-0.06;0.30)
Bent arm hang (s)[a]	1048	7.3 (14.5)	8.5 (14.4)	9.8 (14.5)	**< 0.001**	0.3 (0.16;0.46)	0.3 (0.16;0.43)	0.6 (0.42;0.79)
Standing long jump (cm)	1085	139.1 (25.0)	144.4 (24.8)	153.1[†§] (25.1)	**< 0.001**	0.2 (0.07;0.36)	0.3(-0.23;0.48)	0.6 (0.38;0.74)
Squat Jump (cm)[a]	974	16.0 (5.6)	18.8* (5.5)	21.2[†§] (5.6)	**< 0.001**	0.5 (0.35;0.65)	0.4 (0.29;0.57)	0.9 (0.73;1.12)
Counter Movement Jump (cm)[a]	971	19.3 (6.1)	21.1* (6.0)	23.7[†§] 6.1)	**< 0.001**	0.3 (0.15;0.45)	0.4 (0.28;0.56)	0.7 (0.52;0.91)
Abalakov Jump (cm)[a]	967	23.2 (5.6)	24.9* (5.5)	27.2[†§] (5.6)	**< 0.001**	0.3 (0.17;0.47)	0.4 (0.28;0.55)	0.7 (0.53;0.92)
20m shuttle run (stage)	942	3.1 (1.9)	3.8* (1.9)	4.6[†§] (1.9)	**< 0.001**	0.4 (0.22;0.53)	0.4 (0.29;0.57)	0.8 (0.61;1.00)

Values are mean (standard deviation). Effects size statistics are expressed as *Cohen's d* (95% Confidence interval).
*P<0.01 for differences in Medium vs Low. [§]P<0.01 for differences in High vs Medium. [†]P<0.01 for differences in High vs Low. [a]Non-transformed data are presented in the table, but analyses were performed on log-transformed data.

3.- RELATIONSHIP OF FITNESS WITH FAT-RELATED HORMONES (INSULIN AND LEPTIN)

RELACIÓN DE LA CONDICIÓN FÍSICA CON HORMONAS RELACIONADAS CON LA ADIPOSIDAD (INSULINA Y LEPTINA)

Papers V and VI (Artículos V y VI)

FITNESS AND FATNESS ARE INDEPENDENTLY ASSOCIATED WITH MARKERS OF INSULIN RESISTANCE IN EUROPEAN ADOLESCENTS; THE HELENA STUDY

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V

Submitted

Title: Fitness and fatness are independently associated with markers of insulin resistance in European adolescents; The HELENA Study

Running title: Fitness, fatness and insulin resistance

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Abstract

The purpose of this study was to examine the association of markers of insulin resistance with total and central body fat after controlling for cardiorespiratory fitness in European adolescents. We also examined the association between markers of insulin resistance and cardiorespiratory fitness at differing levels of total and central body fat. We conducted a cross sectional study (the HELENA-CSS) which comprised 1053 (12.5-17.5 years) adolescents from ten European cities. Weight, height, waist circumference and skinfold thickness were measured, and body mass index (BMI) was calculated. Cardiorespiratory fitness was measured by the 20-meter shuttle run test. Markers of insulin resistance were fasting insulin and glucose, and homeostasis model assessment (HOMA). HOMA and insulin were positively associated with BMI, skinfolds and waist circumference after controlling for country, age, pubertal status and cardiorespiratory fitness (all $P \leq 0.01$). HOMA and insulin were negatively associated with cardiorespiratory fitness in adolescents with moderate to high levels of total and central body fat (all $P \leq 0.01$). In conclusion, HOMA and insulin were associated with total and central body fat in European adolescents. Moreover, cardiorespiratory fitness explained a significant proportion of the HOMA and insulin variance in those adolescents with moderate to high levels of total and central body fat.

Keywords: Insulin, glucose, HOMA, Cardiorespiratory fitness, total and central body fat.

Abbreviations:

BMI: Body Mass Index

HOMA: Homeostasis Model Assessment

HELENA-CSS: Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional

Introduction

The prevalence of type 2 diabetes has increased among children and adolescents (1). One of the causes might be the increased prevalence of obesity, which is one of the primary risk factors for type 2 diabetes (2). Insulin resistance is strongly associated with obesity in adults as well as in children and adolescents (3). Likewise, both total and central adiposity are negatively associated with cardiorespiratory fitness in young people (4, 5).

We observed that cardiorespiratory fitness is inversely associated with insulin resistance in children aged 9-10 years with high levels (third tertile) of total and central body fat (6). High levels of cardiorespiratory fitness seems to attenuate the negative consequences attributed to fatness regarding blood pressure (7) inflammatory proteins (8) and blood lipids (9). A systematic review analysing the predictive validity of cardiorespiratory fitness in children and adolescents concluded that there is strong evidence indicating that higher levels of cardiorespiratory fitness at childhood and adolescence are associated with healthier cardiovascular profile later in life (10).

Given the global increase in the prevalence of obesity, type 2 diabetes, and the metabolic syndrome (11) there is a need to further understand how markers of insulin resistance are influenced by potentially modifiable factors, such as fatness and fitness in the European population. To our knowledge, there are no studies that examined the influences of fatness and cardiorespiratory fitness on markers of insulin resistance in a cohort of European adolescents using harmonised and standardised methodology.

The purpose of the present study was to examine the association of markers of insulin resistance with total and central body fat after controlling for several potential confounders, including cardiorespiratory fitness, in European adolescents from ten cities participating in the HELENA-CSS (Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional) study. We also examined the association between markers of insulin resistance and cardiorespiratory fitness at differing levels of total and central body fat.

Methods

The HELENA cross-sectional study is a multi-centre study aiming to obtain reliable data from European adolescents aged 12.5 to 17.5 years about nutritional habits and patterns, body composition and levels of physical activity and fitness (12, 13). The total sample of the HELENA study was 3528 adolescents with a subset of 1089 of them with blood sample. The present work is confined to a sample of 1053 adolescents (554 females and 499 males), with complete data on at least glucose and insulin and body weight and height.

Ten cities in nine different European countries were chosen due to an existing network of research groups and a rough geographical balance across Europe; Stockholm (Sweden), Athens (Greece), Heraklion (Greece), Rome (Italy), Zaragoza (Spain), Pecs (Hungary), Ghent (Belgium) Lille (France), Dortmund (Germany) and Vienna (Austria) (12). Data collection took place between October 2006 and December 2007. The study was performed following the ethical guidelines of the Declaration of Helsinki 1961 (revision of Edinburgh 2000), the Good Clinical Practice, and the legislation about clinical research in humans in each of the participating countries. The protocol was approved by the Human Research Review Committees of the involved centres (14).

Physical examination

The anthropometric methods followed in the HELENA-CSS study were described in detail by Nagy (15). Weight was measured in underwear and without shoes with an electronic scale (Type SECA 861) to the nearest 0.05 kg, and height was measured barefoot in the Frankfort plane with a telescopic height measuring instrument (Type SECA 225) to the nearest 0.1 cm. Body mass index was calculated as body weight (kg) divided by the height (m) squared (kg/m^2). Skinfold thickness was measured to the nearest 0.2 mm in triplicate in the right side at biceps, triceps, subscapular, suprailiac, thigh, and medial calf with a Holtain Caliper (Crymmych, UK) (16). The sum of 6 skinfold thickness was used as an indicator of total body fat. In every city, the same trained investigator made all skinfold thickness measurements, and the intraobserver technical errors of measurement were smaller than 1 mm and reliability greater than 95%. Waist circumference was measured in triplicate at the midpoint between the lowest rib and the iliac crest with an anthropometric tape SECA 200 (16), and was used as a surrogate marker of central body fat. In every city, the same trained investigator made all measurements, and reliability was greater than 95%. Inter-observer reliability for skinfold and circumferences were higher than 90% (15). Pubertal stage was assessed by a medical doctor according to Tanner and Whitehouse (17).

Blood samples

A detailed description of the blood analysis has been reported elsewhere (18). Serum concentrations of glucose and insulin were measured after an overnight fast. The homeostasis model assessment (HOMA) was calculated (19) as fasting insulin (µlU/mL)×fasting glucose (mmol/l)/22.5 (to convert insulin values in µlU/mL to pmol/l multiply by 6.945).

Cardiorespiratory fitness

Cardiorespiratory fitness was measured by the progressive 20-m shuttle run test (20). This test required subjects to run back and forth between two lines set 20 m apart. Running pace was determined by audio signals, emitted from a pre-recorded CD. The initial speed was 8.5 $km \cdot h^{-1}$, increasing by 0.5 $km \cdot h^{-1}$ every minute (1 minute equals 1 stage). Subjects were instructed to run in a straight line, to pivot upon completing a shuttle and to pace themselves in accordance with the time intervals. The test was finished when the subject failed to reach the end lines concurrent with the audio signals on two consecutive occasions. The test was done once and the final score was computed as the number of stages completed (precision of 0.5 stages). VO_{2max} ($ml\ min^{-1}\ kg^{-1}$) was estimated using the equation reported by Léger (20).

Statistical analysis

The data are presented as mean±SD, unless otherwise stated. To achieve normality in the residuals, insulin, waist circumference, sum of skinfold thickness and cardiorespiratory fitness were transformed to the natural logarithm, and HOMA was raised to the power of 1/3. Sex differences were assessed by one-way analysis of variance.

Bivariate correlation analyses were performed to examine the association between the outcome and exposure variables. The association between markers of insulin resistance and total (BMI categories and sum of skinfold thickness) and central (waist circumference) body fat was assessed by one-way analysis of covariance with BMI, skinfold thickness, and waist circumference as fixed factors, and HOMA, insulin and glucose as dependent variables. Country, age, pubertal status and cardiorespiratory fitness, were entered as covariates. Both skinfold thickness and waist circumference were recorded into thirds to be entered into the models, whereas BMI was categorised into four categories according to the BMI international cut-off values: underweight, normal weight, overweight and obese (21, 22).

We used multiple regressions to study the association between markers of insulin resistance and cardiorespiratory fitness after controlling for age, pubertal status and country. Regression analysis was performed separately by BMI categories (underweight, normal weight, overweight and obese) (21, 22), and thirds of skinfold thickness and waist circumferences (low, middle and high equals first, second and third, respectively). The analyses were performed using the Statistical Package for Social Science (SPSS, v. 15.0 for Windows; SPSS Inc., Chicago, IL) and the level of significance was set to 0.05.

Results

A set of valid data for cardiorespiratory fitness, skinfold thickness, waist circumference and BMI were available in 68% (n=718/1053), 83% (n=873/1053), 88% (n=926/1053) and 89% (n=937/1053) adolescents, respectively. Table 1 shows the descriptive characteristics of the study sample. Females had significantly higher body fat than males, while males had significantly higher waist circumference, glucose and cardiorespiratory fitness levels than females. HOMA and insulin mean levels were similar between the sexes.

Bivariate correlations between HOMA, insulin, glucose, fatness parameters and cardiorespiratory fitness are displayed in Table 2. All the fatness-related parameters were positively correlated (all P<0.01) with HOMA and insulin in both females and males and with glucose in males. Cardiorespiratory fitness was negatively correlated with HOMA, insulin and glucose, as well as with body fat parameters in both females and males (all P<0.01), except for glucose in females.

The associations of HOMA, fasting insulin and glucose with BMI, skinfold thickness and waist circumference are shown in Figure 1. HOMA and fasting insulin were positively associated (all P≤0.01) with BMI, skinfold thickness and waist circumference in both females and males after controlling for country, age, pubertal status and cardiorespiratory fitness. Glucose was not significantly associated with any of the studied markers of total and central body fat (all P>0.1).

The results of the linear regression models showing the association of HOMA, fasting insulin and glucose with cardiorespiratory fitness stratified by BMI categories, and thirds of skinfolds and waist circumference are presented in Table 3. HOMA and fasting insulin were negatively associated with cardiorespiratory fitness in normal weight females and in those with middle to high levels of skinfold thickness (all P≤0.001). In addition, both HOMA and insulin were negatively associated with cardiorespiratory fitness for all levels of waist circumference but a higher percentage of variance was explained in females with middle to high waist circumference. Likewise, fasting glucose was negatively associated with cardiorespiratory fitness in normal weight and overweight females, as well as in those with high levels of skinfold thickness and waist circumference (all $P \leq 0.05$).

In males, HOMA and fasting insulin were negatively associated with cardiorespiratory fitness in those males with middle to high levels of total or central body fat, that is, those who were overweight ($P \leq 0.01$), those with high levels of skinfold thickness ($P<0.01$), or those with high levels of waist circumference ($P<0.001$). Glucose was negatively associated with fitness in those classified as underweight and normal weight, with low skinfold thickness or with low waist circumference (first third). For the other relationships where waist circumference was involved, additionally controlling for height or skinfold thickness did not modify the results.

The analyses were repeated using the numbers of stages completed or the equation reported by Ruiz et al. (23) instead of using the equation reported by Léger et al. (20) and the results did not materially change (data not shown).

Discussion

The results of the present study indicate that HOMA and fasting insulin are positively associated with total and central body fat in European adolescents. In addition, cardiorespiratory fitness explained a significant proportion of the HOMA and fasting insulin variance in those adolescents with middle to high levels of total and central body fat, which suggests that high levels of cardiorespiratory fitness may have a protective effect against the deleterious consequences ascribed to high fatness. Overall, these findings suggest that interventions oriented to prevent insulin resistance studies in youth should focus not only on decreasing fatness but also on enhancing cardiorespiratory fitness.

Our results show that BMI, skinfold thickness (total adiposity) and waist circumference (central adiposity) were significantly associated with HOMA and fasting insulin variance after adjusting for potential confounders including cardiorespiratory fitness, which concurs with other studies (24-26). Raman et al. (26) in 8- 10-year-old African-American children with BMI greater than the 85th percentile showed that children with higher waist circumference had higher insulin resistance after adjusting for age, sex, pubertal stage, socioeconomic index, and family history of diabetes. Others showed that waist circumference in children and adolescents is an independent predictor of insulin resistance, lipids levels and blood pressure (25). Likewise, Bacha et al. (24) reported that adolescents with severe insulin resistance had higher visceral adiposity than pair-matched moderately insulin-resistant subjects (24).

We observed in a previous study on younger populations that cardiorespiratory fitness explained a significant proportion of the HOMA and fasting insulin variance in both girls and boys with high levels of body fat and waist circumference (6). In contrast, findings from the Study of Latino Adolescents at Risk for Diabetes revealed that insulin sensitivity or secretion was not independently associated with cardiorespiratory fitness in a relatively small sample of overweight Hispanic children aged 8-13 years with a family history of type 2 diabetes (27). In the present study, HOMA and fasting insulin were significantly associated with cardiorespiratory fitness in those females who were normal weight and with middle to high levels of skinfold thickness or waist circumference. In males, HOMA and fasting insulin were negatively associated with fitness in those with moderate to high levels of total and central body fat. Additionally, glucose was negatively associated with fitness in those males with low total or central body fat and those females with moderate to high total or central body fat. Differences in subject characteristics, methodologies and maturity of some metabolic systems such as hormonal regulation, may partially explain the different glucose behaviour between gender and studies. Moreover, the HELENA study involved only adolescents who were apparently healthy and without any diagnosed cardiovascular pathologies.

In a recent systematic review Ruiz et al. (10) concluded that due to a limited number of studies, there is inconclusive evidence indicating that changes in cardiorespiratory fitness are associated with diabetes. Carnethon et al. (28) analyzed the relationship between changes in cardiorespiratory fitness and diabetes over 7 and 15 years, and they reported that adolescents with low cardiorespiratory fitness were 3- to 6-fold more likely to develop diabetes than adolescents with high cardiorespiratory fitness. They also reported that improved cardiorespiratory fitness over 7 years was associated with a reduced risk of developing diabetes but the strength and significance of this association were reduced after accounting for changes in body weight.

The Childhood Determinants of Adult Health (CDAH) study which is a prospective cohort study (29) showed that a decline in fitness from childhood to adulthood is associated with obesity and insulin resistance in adulthood. In their study, the effect of a longitudinal fitness decrease on insulin resistance persisted after adjustment for child BMI, adult BMI or adult obesity status, suggesting that the effect of a decline in fitness on insulin resistance is not merely due to a lower adult BMI but a direct implication of muscle metabolism might underlay as a possible cause. In fact, exercise has been suggested to induce alterations in skeletal muscle substrate metabolism by way of some specific adaptations into the skeletal muscle such as an increased mitochondrial volume and density and oxidative enzyme capacity and an increased GLUT-4 concentration which in turn lead to improvements in glucose metabolism as well as increases in VO_{2max} (30).

The present study has several limitations. Owing to its cross-sectional design, we cannot infer that our observed associations reflect causal relationships. As strength, this study was addressed in a heterogeneous sample of European adolescents and using harmonised and standardised methodology.

In conclusion, the present study showed that HOMA and fasting insulin were significantly associated with total and central body fat in European adolescents. In addition, cardiorespiratory fitness explained a significant proportion of the HOMA and fasting insulin variance in those adolescents with moderate to high levels of total and central body fat. Collectively, the findings suggest that the deleterious consequences ascribed to high fatness could be counteracted to some degree by having high levels of cardiorespiratory fitness. The assessment of the effect of an exercise intervention focused on reducing fatness and improving fitness is warranted. Programs aimed at improving childhood and adolescence cardiorespiratory fitness, through moderate and vigorous physical activity, may have the potential to prevent insulin resistance.

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References

1. Karam JG, McFarlane SI 2008 Prevention of type 2 DM: implications for adolescents and young adults. Pediatr Endocrinol Rev 5 Suppl 4:980-988.

2. Hale DE 2004 Type 2 diabetes and diabetes risk factors in children and adolescents. Clin Cornerstone 6:17-30.

3. Srinivasan SR, Myers L, Berenson GS 2002 Predictability of childhood adiposity and insulin for developing insulin resistance syndrome (syndrome X) in young adulthood: the Bogalusa Heart Study. Diabetes 51:204-209.

4. Ruiz JR, Rizzo NS, Hurtig-Wennlof A, Ortega FB, Warnberg J, Sjostrom M 2006 Relations of total physical activity and intensity to fitness and fatness in children: the European Youth Heart Study. Am J Clin Nutr 84:299-303.

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

6. Ruiz JR, Rizzo NS, Ortega FB, Loit HM, Veidebaum T, Sjostrom M 2007 Markers of insulin resistance are associated with fatness and fitness in school-aged children: the European Youth Heart Study. Diabetologia 50:1401-1408.

7. Ruiz JR, Ortega FB, Loit HM, Veidebaum T, Sjostrom M 2007 Body fat is associated with blood pressure in school-aged girls with low cardiorespiratory fitness: the European Youth Heart Study. J Hypertens 25:2027-2034.

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

9. Mesa JL, Ortega FB, Ruiz JR, Castillo MJ, Tresaco B, Carreno F, Moreno LA, Gutierrez A, Bueno M 2006 Anthropometric determinants of a clustering of lipid-related metabolic risk factors in overweight and non-overweight adolescents--influence of cardiorespiratory fitness. The Avena study. Ann Nutr Metab 50:519-527.

10. Ruiz JR, Castro-Piñero J, Artero EG, Ortega FB, Sjostrom M, Suni J, Castillo MJ 2009 Predictive Validity of Health-Related Fitness in Youth: A Systematic Review. Br J Sports Med.

11. Stumvoll M, Goldstein BJ, van Haeften TW 2005 Type 2 diabetes: principles of pathogenesis and therapy. Lancet 365:1333-1346.

12. Moreno LA, De Henauw S, Gonzalez-Gross M, Kersting M, Molnar D, Gottrand F, Barrios L, Sjostrom M, Manios Y, Gilbert CC, Leclercq C, Widhalm K, Kafatos A, Marcos A 2008 Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. Int J Obes (Lond) 32 Suppl 5:S4-11.

13. Moreno LA, Gonzalez-Gross M, Kersting M, Molnar D, de Henauw S, Beghin L, Sjostrom M, Hagstromer M, Manios Y, Gilbert CC, Ortega FB, Dallongeville J, Arcella D, Warnberg J, Hallberg M, Fredriksson H, Maes L, Widhalm K, Kafatos AG, Marcos A 2008 Assessing, understanding and modifying nutritional status, eating habits and physical activity in European adolescents: the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) Study. Public Health Nutr 11:288-299.

14. Beghin L, Castera M, Manios Y, Gilbert CC, Kersting M, De Henauw S, Kafatos A, Gottrand F, Molnar D, Sjostrom M, Leclercq C, Widhalm K, Mesana MI, Moreno LA, Libersa C 2008 Quality assurance of ethical issues and regulatory aspects relating to good clinical practices in the HELENA Cross-Sectional Study. Int J Obes (Lond) 32 Suppl 5:S12-18.

15. Nagy E, Vicente-Rodriguez G, Manios Y, Beghin L, Iliescu C, Censi L, Dietrich S, Ortega FB, De Vriendt T, Plada M, Moreno LA, Molnar D 2008 Harmonization process and reliability assessment of anthropometric measurements in a multicenter study in adolescents. Int J Obes (Lond) 32 Suppl 5:S58-65.

16. Lohman TG, Roche AF, Martorell R 1988 Anthropometric Standardization Reference Manual. Human Kinetics Books: Champaign, Illinois.

17. Tanner JM, Whitehouse RH 1976 Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child 51:170-179.

18. Gonzalez-Gross M, Breidenassel C, Gomez-Martinez S, Ferrari M, Beghin L, Spinneker A, Diaz LE, Maiani G, Demailly A, Al-Tahan J, Albers U, Warnberg J, Stoffel-Wagner B, Jimenez-Pavon D, Libersa C, Pietrzik K, Marcos A, Stehle P 2008 Sampling and processing of fresh blood samples within a European multicenter nutritional study: evaluation of biomarker stability during transport and storage. Int J Obes (Lond) 32 Suppl 5:S66-75.

19. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC 1985 Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28:412-419.

20. Leger L, Lambert J, Goulet A, Rowan C, Dinelle Y 1984 [Aerobic capacity of 6 to 17-year-old Quebecois--20 meter shuttle run test with 1 minute stages]. Can J Appl Sport Sci 9:64-69.

21. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH 2000 Establishing a standard definition for child overweight and obesity worldwide: international survey. Bmj 320:1240-1243.

22. Cole TJ, Flegal KM, Nicholls D, Jackson AA 2007 Body mass index cut offs to define thinness in children and adolescents: international survey. Bmj 335:194.

23. Ruiz JR, Ramirez-Lechuga J, Ortega FB, Castro-Pinero J, Benitez JM, Arauzo-Azofra A, Sanchez C, Sjostrom M, Castillo MJ, Gutierrez A, Zabala M 2008 Artificial neural network-based equation for estimating VO2max from the 20 m shuttle run test in adolescents. Artif Intell Med 44:233-245.

24. Bacha F, Saad R, Gungor N, Arslanian SA 2006 Are obesity-related metabolic risk factors modulated by the degree of insulin resistance in adolescents? Diabetes Care 29:1599-1604.

25. Lee S, Bacha F, Arslanian SA 2006 Waist circumference, blood pressure, and lipid components of the metabolic syndrome. J Pediatr 149:809-816.

26. Raman A, Fitch MD, Hudes ML, Lustig RH, Murray CB, Ikeda JP, Fleming SE 2008 Baseline correlates of insulin resistance in inner city high-BMI African-American children. Obesity (Silver Spring) 16:2039-2045.

27. Ball GD, Shaibi GQ, Cruz ML, Watkins MP, Weigensberg MJ, Goran MI 2004 Insulin sensitivity, cardiorespiratory fitness, and physical activity in overweight Hispanic youth. Obes Res 12:77-85.

28. Carnethon MR, Gidding SS, Nehgme R, Sidney S, Jacobs DR, Jr., Liu K 2003 Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. Jama 290:3092-3100.

29. Dwyer T, Magnussen CG, Schmidt MD, Ukoumunne OC, Ponsonby AL, Raitakari OT, Zimmet PZ, Blair SN, Thomson R, Cleland VJ, Venn A 2008 Decline in physical fitness from childhood to adulthood associated with increased obesity and insulin resistance in adults. Diabetes Care.

30. Shaibi GQ, Ball GD, Cruz ML, Weigensberg MJ, Salem GJ, Goran MI 2006 Cardiovascular fitness and physical activity in children with and without impaired glucose tolerance. Int J Obes (Lond) 30:45-49.

Figure Legend

Figure 1. Associations of markers of insulin resistance with total and central body fat adjusting for country, age, pubertal status and cardiorespiratory fitness. **A**. Associations of HOMA, insulin and glucose with BMI categories for females and males. **B**. Associations of HOMA, insulin and glucose with skinfold thickness thirds for females and males. **C**. Associations of HOMA, insulin and glucose with waist circumference thirds for females and males. Data are mean and standard error of the mean.

APPENDIX

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Table 1. Descriptive characteristics of European adolescents.

	All (n=1053)	Females (n=554)	Males (n=499)	*P* value
Age (years)	14.9 ± 1.2	14.9 ± 1.2	14.9 ± 1.3	0.716
Puberal status (I/II/III/IV/V)[a]	1/6/20/44/29	0/5/21/44/30	2/8/20/42/28	
Weight (kg)	58.9 ± 12.4	56.0 ± 10.2	62.1 ± 14.0	<0.001
Height (m)	1.7 ± 0.1	1.6 ± 0.1	1.7 ± 0.1	<0.001
BMI (kg/m^2)	21.4 ± 3.6	21.3 ± 3.4	21.4 ± 3.8	0.845
BMI categories (U/N/OV/O)[a,b]	5 / 72 /17 / 6	6 / 75 / 15 / 4	5 / 69 / 18 / 8	
Skinfold thickness (mm)[c]	90.2 ± 39.6	102.8 ± 35.7	76.0 ± 39.2	<0.001
Waist circumference (cm)[c]	72.4 ± 8.8	70.6 ± 8.0	74.5 ± 9.1	<0.001
HOMA[d]	2.3 ± 1.9	2.3 ± 1.6	2.3 ± 2.2	0.786
Insulin (µlU/mL)[c]	10.1 ± 7.6	10.2 ± 6.4	10.1 ± 8.7	0.019
Glucose (mmol/L)	5.1 ± 0.4	5.0 ± 0.4	5.2 ± 0.4	<0.001
Cardiorespiratory fitness by Leguer (ml min^{-1} kg^{-1})[c]	40.1 ± 7.8	36.2 ± 5.5	44.3 ± 7.8	<0.001
Cardiorespiratory fitness (stage)	4.8 ± 2.8	3.4 ± 1.8	6.3 ± 2.8	<0.001

All values are means±SD, or [a]percentages
[b]BMI categories: underweight (U); normal weight (N); overweight (OV); obese (O). BMI indicates body mass index; HOMA, homeostasis model assessment.
Non-transformed data are presented in this table, but analyses were performed on [c]log-transformed data or [d]data transformed to the power of 1/3.

Table 2. Person correlations between markers of insulin resistance, body composition and cardiorespiratory fitness in female and male adolescents.

	Insulin[a]		HOMA[b]		Glucose		Cardiorespiratory fitness[a,c]	
	Females	Males	Females	Males	Females	Males	Females	Males
Body mass index	0.28†	0.44†	0.23†	0.42†	-0.06	0.12*	-0.40†	-0.45†
Skinfold thickness[a]	0.29†	0.44†	0.23†	0.42†	-0.00	0.15†	-0.34†	-0.42†
Waist circumference[a]	0.27†	0.39†	0.23†	0.37†	-0.04	0.10*	-0.32†	-0.42†
Cardiorespiratory fitness[a,c]	-0.21†	-0.23†	-0.18†	-0.23†	-0.02	-0.13†		

Analyses were performed on [a]log-transformed data or [b]data transformed to the power of 1/3. Values are bivariate correlation (Pearson coefficient).
[c] by Leguer (ml min^{-1} kg^{-1})
*$P<0.05$, †$P<0.01$

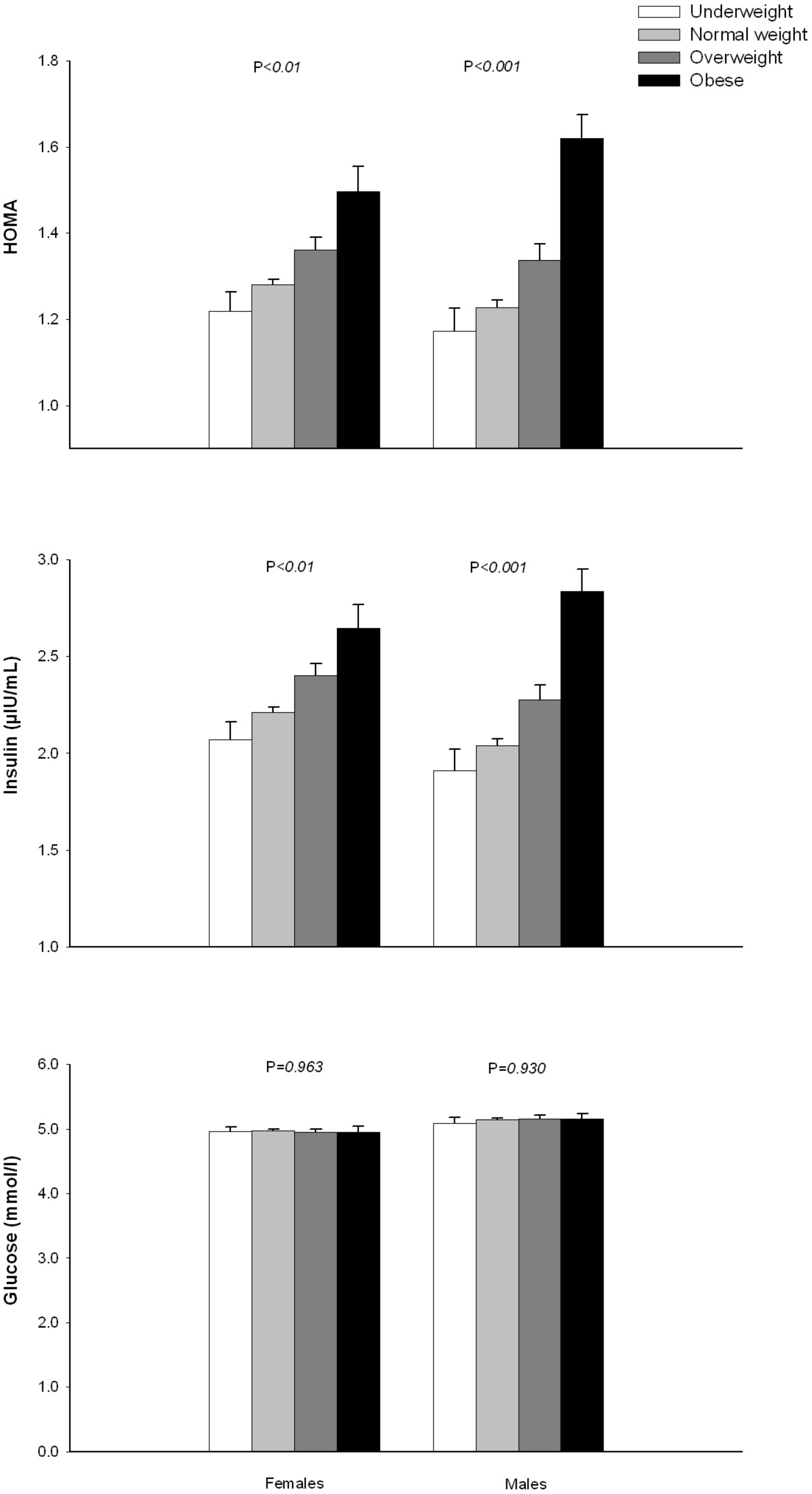
Table 3. Multiple regression coefficients (β) and coefficient of determination (R^2), examining the association between markers of insulin resistance and cardiorespiratory fitness separately by body mass index (BMI) categories, and thirds of skinfold thickness and circumference in females and male adolescents.

Outcome		Females			Males		
		β	*P*	R^2	β	*P*	R^2
By BMI categories							
HOMA	Underweight	-0.317	0.321	0.094	-0.319	0.192	0.224
	Normal weight	-0.319	<0.001	0.089	-0.085	0.191	0.040
	Overweight	-0.081	0.541	0.251	-0.761	<0.01	0.254
	Obese	-0.426	0.436	0.280	-0.105	0.629	0.117
Insulin	Underweight	-0.305	0.335	0.106	-0.264	0.228	0.193
	Normal weight	-0.341	<0.001	0.106	-0.079	0.220	0.043
	Overweight	-0.054	0.689	0.219	-0.439	<0.01	0.272
	Obese	-0.517	0.352	0.266	-0.143	0.510	0.118
Glucose	Underweight	-0.040	0.894	0.180	-0.567	<0.05	0.448
	Normal weight	-0.156	<0.05	0.047	-0.138	<0.05	0.021
	Overweight	-0.283	<0.05	0.372	-0.059	0.721	0.047
	Obese	-0.037	0.942	0.357	-0.015	0.944	0.112
By thirds of skinfold thickness							
HOMA	Low	-0.171	0.328	0.034	-0.040	0.594	0.025
	Middle	-0.522	0.001	0.109	-0.244	0.112	0.178
	High	-0.521	<0.001	0.182	-0.628	<0.01	0.157
Insulin	Low	-0.135	0.442	0.016	-0.031	0.683	0.035
	Middle	-0.529	<0.001	0.141	-0.263	0.234	0.199
	High	-0.401	0.001	0.173	-0.714	<0.01	0.173
Glucose	Low	-0.116	0.482	0.135	-0.355	<0.05	0.018
	Middle	-0.245	0.123	0.067	-0.151	0.756	0.027
	High	-0.205	<0.05	0.150	-0.060	0.656	0.054
By thirds of waist circumference							
HOMA	Low	-0.280	<0.01	0.078	-0.183	0.102	0.066
	Middle	-0.360	0.001	0.209	-0.021	0.823	0.049
	High	-0.333	0.001	0.235	-0.335	<0.001	0.171
Insulin	Low	-0.304	0.001	0.088	-0.156	0.164	0.052
	Middle	-0.356	0.001	0.195	-0.027	0.772	0.060
	High	-0.312	<0.01	0.233	-0.335	<0.001	0.183
Glucose	Low	-0.188	<0.05	0.125	-0.281	<0.05	0.078
	Middle	-0.087	0.442	0.110	-0.093	0.337	0.030
	High	-0.283	<0.01	0.244	-0.112	0.212	0.039

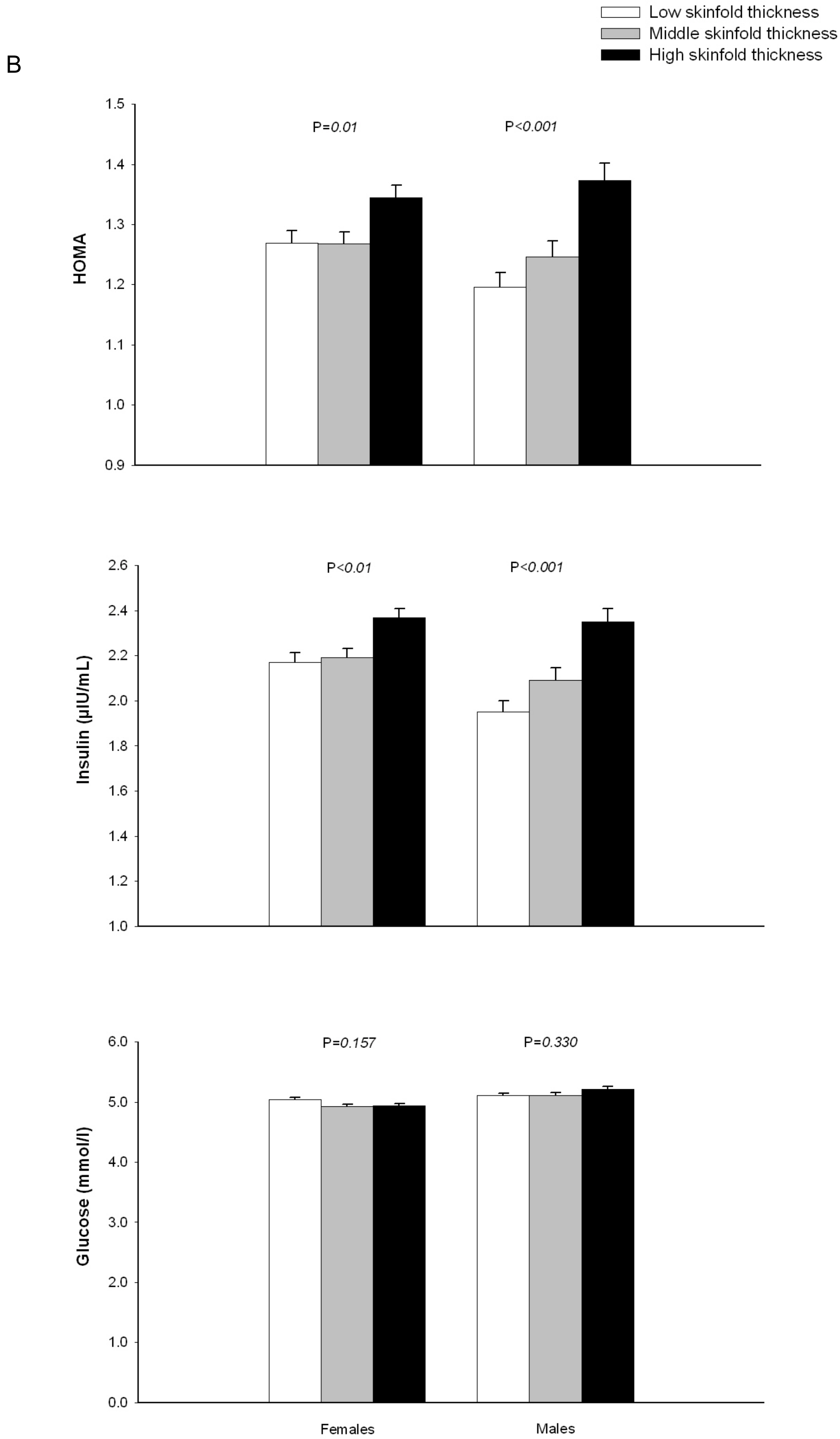
Analysis controlled for age, country and pubertal status.

Figure 1

A

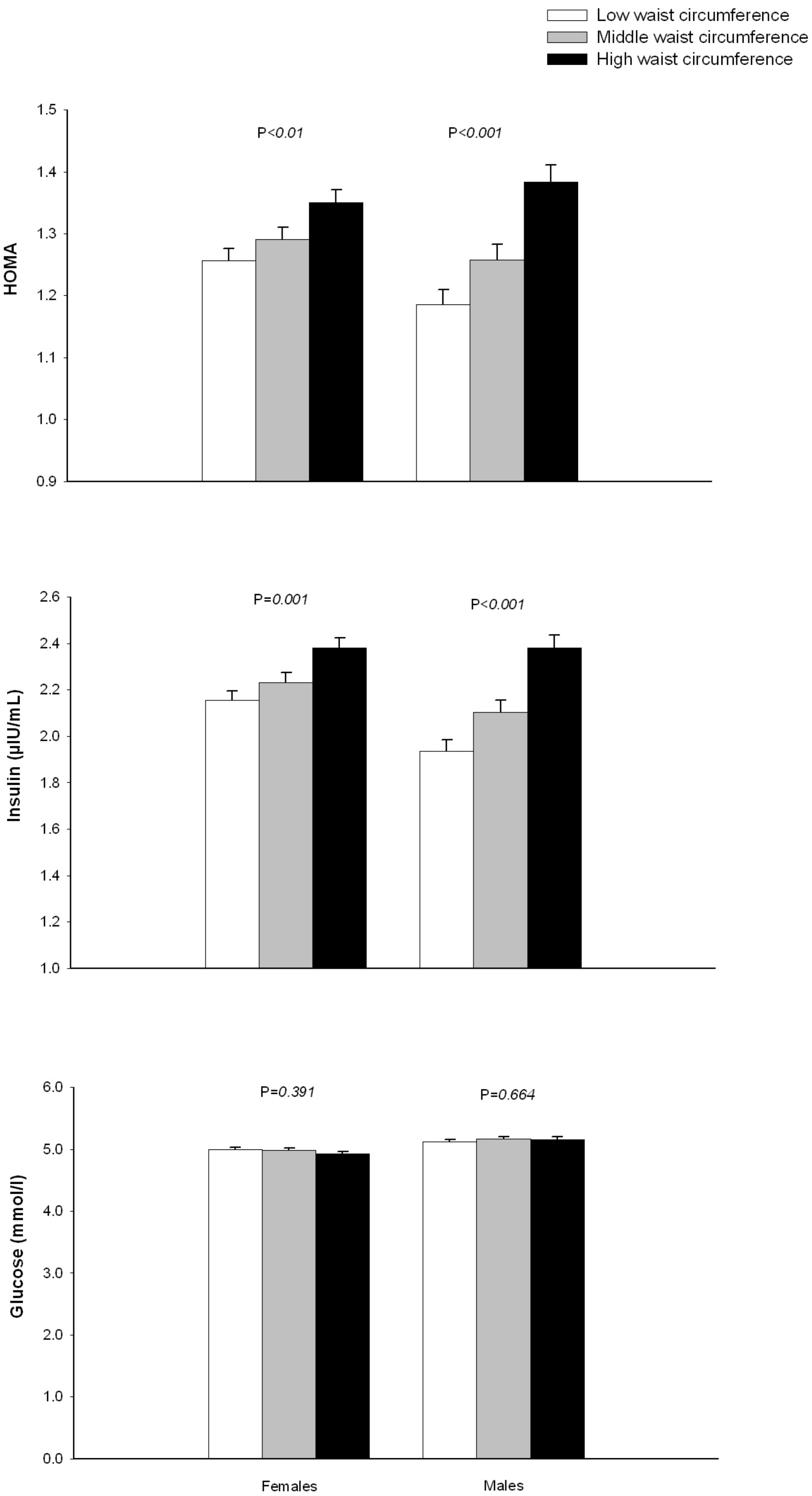


Underweight
Normal weight
Overweight
Obese
1.8
1.6
1.4
1.2
1.0
HOMA
P<0.01
P<0.001
3.0
2.5
2.0
1.5
1.0
Insulin (µIU/mL)
P<0.01
P<0.001
6.0
5.0
4.0
3.0
2.0
1.0
0.0
Glucose (mmol/l)
P=0.963
P=0.930
Females
Males



Low skinfold thickness
Middle skinfold thickness
High skinfold thickness
B
HOMA
P=0.01
P<0.001
Insulin (µIU/mL)
P<0.01
P<0.001
Glucose (mmol/l)
P=0.157
P=0.330
Females
Males

C


Low waist circumference
Middle waist circumference
High waist circumference
HOMA
1.5
1.4
1.3
1.2
1.1
1.0
0.9
P<0.01
P<0.001
Insulin (µIU/mL)
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
P=0.001
P<0.001
Glucose (mmol/l)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
P=0.391
P=0.664
Females
Males

PHYSICAL ACTIVITY, FITNESS AND SERUM LEPTIN CONCENTRATIONS IN ADOLESCENTS; THE HELENA STUDY

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Submitted

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ABSTRACT

Context: Given the role of leptin concentrations in the energy metabolism and its association with insulin resistance and type 2 diabetes in children. There is a need to further understand the relationship of physical activity and/or fitness with leptin in adolescents.

Objective: To examine the association of physical activity and fitness with leptin concentrations in European adolescents.

Design and setting: We conducted a cross sectional study at school setting (the HELENA-CSS).

Participants: The present study included 902 (509 girls) adolescents aged 12.5-17.5 years from the HELENA-CS study.

Primary Outcome Measure: Weight, height and total body fat (sum of 6 skinfold thickness) were measured, and fat free-mass was calculated. Physical activity was assessed by accelerometry. Physical fitness was assessed by the handgrip, standing long jump, 4x10m shuttle run, and 20m shuttle run tests. Serum leptin, insulin and glucose concentrations were measured, and homeostasis model assessment (HOMA) was computed.

Results: Both average and vigorous physical activity were negatively associated with leptin, independently of several potential confounders including total body fat and HOMA. Likewise, the physical fitness tests were negatively associated with leptin independently of several potential confounders including total body fat and HOMA. The association of both physical activity and fitness with leptin remained significant after further controlling for all the fitness and physical activity variables, respectively.

Conclusions: The results suggest that physical activity (particularly average and vigorous physical activity) and physical fitness (particularly muscular strength and cardiorespiratory fitness) were negatively associated with leptin concentrations, regardless of relevant confounders including total body fat.

Introduction

Leptin is a cytokine primarily expressed by adipose tissue and product of the obese (ob) gene, which was described as an important regulator of food intake and energy expenditure by means of informing the brain about the body´s energy store (1). Increased serum leptin concentrations are prominent in obese youth (2, 3). Leptin concentrations are associated with cardiovascular disease risk factors, insulin resistance and type 2 diabetes in children (3, 4) and is an independent risk factor for coronary heart disease in adults (5).

Physical activity seems to attenuate the negative influence of fatness on several cardiovascular disease risk factors in adolescents such as blood pressure, insulin resistance, low-grade inflammatory proteins and blood lipids (6-10). The association between physical activity and leptin in adolescents is contradictory. Several studies showed that physical activity assessed by questionnaire was inversely associated with leptin in adolescents (11-13), whereas others found no association between objectively assessed physical activity and leptin concentrations (11, 14).

Physical fitness is considered an important health-related marker already in children and adolescents (15, 16). We observed negative associations between cardiorespiratory fitness and insulin resistance, blood pressure, and low-grade inflammatory proteins in youth with relatively high levels of total and central body fat (10, 17, 18). However, there are no studies in the literature about the role of the main physical fitness components (muscular strength, speed-agility and cardiorespiratory fitness) on leptin concentrations in adolescents.

Physical activity emerges as the main tool to improve cardiovascular health through increasing physical fitness levels. Likewise, the association between physical fitness and leptin in adolescents is not known. It is of clinical and public health interest to better understand whether physical activity and/or fitness are associated with leptin in adolescents, as well as to know the role of body fat in these associations.

The aim of the present study was to examine the association of physical activity and fitness with leptin concentrations in a cohort of European adolescents, after taking into account several potential confounders including total body fat.

Methods

The Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study (HELENA-CSS) is a multi-centre study aiming to obtain reliable data from European adolescents aged 12.5 to 17.5 years about nutritional habits and patterns, body composition and levels of physical activity and fitness (19). The total sample of the HELENA-CSS study included 3528 adolescents with a subset of 1089 of them with blood sample. The present study is confined to a sample of 902 adolescents, with complete data on leptin and at least one physical fitness test.

Ten cities in nine different European countries included in the HELENA-CSS were chosen to get a rough geographical balance across Europe; Stockholm (Sweden), Athens (Greece), Heraklion (Greece), Rome (Italy), Zaragoza (Spain), Pecs (Hungary), Ghent (Belgium) Lille (France), Dortmund (Germany) and Vienna (Austria) (19). Data collection took place between October 2006 and December 2007. Parents and adolescents given their written informed consent to participate in the research. The study was performed following the ethical guidelines of the Declaration of Helsinki 1961 (revision of Edinburgh 2000), the Good Clinical Practice, and the legislation about clinical research in humans in each of the participating countries. The protocol was approved by the Human Research Review Committees of the involved centres (20).

Physical examination

The anthropometrical measurements protocols followed in the HELENA study were described in detail by Nagy et al. (21). Skinfold thicknesses were measured to the nearest 0.2 mm in triplicate in the left side at biceps, triceps, subscapular, suprailiac, thigh, and medial calf with a Holtain Caliper (Crymmych, UK) (22). The sum of 6 skinfold thickness was used as an indicator of total body fat (hereinafter called total body fat). We calculated body fat percentage using skinfold thickness from Slaughter's equation (23), and fat free-mass (kg) (FFM) was derived by subtracting fat mass from total body weight. In every city, the same trained investigator made all skinfold thickness measurements. For all the skinfold thickness measurements, intraobserver technical errors of measurement were smaller than 1 mm and reliability greater than 95%. Inter-observer reliability for skinfold was higher than 90% (21).

Pubertal status was assessed by a medical doctor according to Tanner and Whitehouse (24). Birth weight was reported by the parents, according to information obtained in the neonatal health booklet, and systolic blood pressure was measured with an automatic oscillometric device (M6, HEM-7001-E, Omron).

Blood samples

A detailed description of the blood analysis has been reported elsewhere (25). Venous blood was obtained by venipuncture after an overnight fast. Serums aliquoted and frozen at 18-25ºC until assays were performed. Concentration of serum leptin (ng/mL) was measured using the RayBio® Human Leptin ELISA (Enzyme-Linked Immunosorbent Assay) kit. The sensitivity of leptin assay was less than 6 pg/mL, with intra and inter-assay coefficients of variation of <10% and <12%. The homeostasis model assessment (HOMA) was calculated as fasting insulin (µlU/mL)×fasting glucose (mmol/l)/22.5 (26).

Physical activity levels

The Actigraph accelerometer (Actigraph MTI, model GT1M, Manufacturing Technology Inc., Fort Walton Beach, FL, USA) was used to assess physical activity. The Actigraph is a small, robust, lightweight and unobtrusive monitor, worn at the lower back (secured by an elastic waistband). Prior to data collection, the adolescents were instructed on how to handle the accelerometer. Adolescents were asked to wear the accelerometer during the daytime for 7 consecutive days, except during water based activities. The criterion for inclusion was to record at least 8 h per day, for at least 3 days (27).

In this study, the time sampling interval (epoch) was set at 15 seconds. A measure of average volume of activity (hereafter called average physical activity) was expressed as the sum of recorded counts divided by total daily registered time expressed in minutes (counts/min). The time engaged in moderate and vigorous physical activity was calculated and presented as the average time per day during the complete registration. The time engaged at moderate physical activity [3-6 metabolic equivalents (METs)] was calculated based upon a cut-off of 2000-3999 counts per minute. The lower cut-off for moderate activity (2000 counts/min) is equivalent to walking at 3 km/h (28). The time engaged at vigorous physical activity (>6 METs) was calculated based upon a cut-off of ≥4000 counts per minute. Also, we calculated the time spent in at least moderate intensity level (>3 METs) as the sum of time spent in moderate plus vigorous physical activity (MVPA).

Physical fitness

The scientific rationale for the selection of the fitness tests, as well as their validity and reliability in young people was published elsewhere (29-31). All the tests were performed twice and the best score was retained, except the 20m shuttle run test, which was performed only once. Physical fitness was assessed by the tests described below.

1.- Handgrip test (Maximum handgrip strength): A hand dynamometer with adjustable grip was used (TKK 5101 Grip D; Takey, Tokio Japan). This dynamometer has shown to be more valid and reliable than other dynamometers when compared with calibrated known weights (32). The adolescent squeezes gradually and continuously for at least two seconds, performing the test with the right and left hand alternatively, using the optimal grip-span. The optimal grip-span was calculated according to hand size using an equation that we developed specifically for adolescents (33). The maximum score in kilograms for each hand was recorded. The sum of the maximum scores achieved by left and right hands was used in the analysis.

2.- Standing long jump test (lower body explosive strength): The participant stands behind the starting line and was instructed to push off vigorously and jump as far as possible. The distance is measured from the take-off line to the point where the back of the heel nearest to the take-off line lands on the mat. The result was recorded in centimeters (cm).

3.- 4x10m shuttle run test (speed-agility): The adolescent runs as fast as possible from the starting line to the other line and returns to the starting line (10m apart), crossing each line with both feet every time. This is performed twice, covering a distance of 40m (4x10m). Every time the adolescent crosses any of the lines, he/she picks up (the first time) or exchange a sponge, which has been previously placed behind the lines. The time taken to complete the test was recorded to the nearest tenth of a second.

4.- 20m shuttle run test (cardiorespiratory fitness): Adolescents run back and forth between two lines set 20m apart. Running pace was determined by audio signals, emitted from a pre-recorded CD. The initial speed was 8.5 $km \cdot h^{-1}$, increasing by 0.5 $km \cdot h^{-1}$ every minute (1 minute equals 1 stage). Participants were instructed to run in a straight line, to pivot upon completing a shuttle and to pace themselves in accordance with the time intervals. The test was finished when the adolescent failed to reach the end lines concurrent with the audio signals on two consecutive occasions. Otherwise, the test ends when the adolescent stops because of exhaustion. The final score was computed as the number of stages completed (precision of 0.5 stages).

Statistical analysis

The data are presented as mean ± standard deviation, unless otherwise stated. To achieve normality in the residuals, leptin, sum of skinfold thickness, insulin, 20m shuttle run test, average physical activity, moderate physical activity, vigorous physical activity and MVPA were transformed to the natural logarithm and HOMA was raised to the power of 1/3. Interaction products between gender and both physical activity and fitness were calculated.

Since there were no significant interaction effect in the association of gender and leptin with physical activity and fitness, all the analyses were performed for girls and boys together.

Partial correlation analyses controlling for pubertal status and gender were performed to examine the association of leptin and insulin concentrations with physical activity, fitness, total body fat and other potential confounders.

Linear regression models were used to study the association of both physical activity and fitness with leptin. Regression analysis was performed in four steps: Model 1 included gender, pubertal status and country (entered as dummy variable) as confounders. Model 2 included model 1 plus fat free-mass, HOMA and systolic blood pressure, Model 3 included the confounders involved in Model 2 plus total body fat. The criteria to include these confounders into model 2 were based on the previous significant relationship showed with leptin concentration.

We performed additional models where the physical activity-leptin association was controlled for the physical fitness components; handgrip strength, standing long jump, 4x10m shuttle run and 20m shuttle run tests (one models for each variable). Similarity, the physical fitness-leptin association was additionally controlled for physical activity levels; average, moderate, vigorous and MVPA (one models for each variable). The analyses were performed using the Statistical Package for Social Science (SPSS, v. 15.0 for Windows; SPSS Inc., Chicago, IL) and the level of significance was set to 0.05.

Results

Valid data on handgrip strength, standing long jump, 4x10m shuttle run test, 20m shuttle run test and physical activity was available in 100% (n=902), 99% (n=893), 97% (n=875), 82% (n=744) and 68% (n=612) of the studied adolescents, respectively. Table 1 shows the descriptive characteristics of the study sample. Girls had significantly higher total body fat, body fat percentage and leptin concentrations than boys, while males had significantly higher weight, birth weight, systolic blood pressure, height, fat free-mass, physical activity and fitness levels than girls. HOMA and insulin levels were similar between both genders.

Table 2 shows partial correlations among the study variables after controlling for pubertal status and gender. Leptin was positively associated with total body fat, insulin, HOMA and systolic blood pressure and negatively associated with fat free-mass and birth weight. Moreover, leptin and insulin levels were negatively associated with all the physical activity and fitness variables, except to moderate physical activity and handgrip.

The results of the linear regression models showing the association of physical activity and fitness with leptin concentrations are presented in Tables 3 and 4. Average and vigorous physical activity as well as MVPA were negatively associated with leptin concentrations (all $P<0.05$) after controlling for gender, pubertal status and country (Table 3; Model 1). The results remained significant for vigorous physical activity after further controlling for other potential confounders (Table 3; Model 2). When total body fat was added as confounder average and vigorous physical activity were negatively associated with leptin (Table 3; Model 3). The association between average physical activity and leptin only disappeared after further controlling for 20m shuttle runt test, whereas vigorous physical activity remained significantly associated with leptin concentration after additional controlling for the four different fitness tests (Table 4).

The handgrip strength, standing long jump, 4x10m shuttle run test and 20m shuttle run test performances were negatively associated with leptin (all $P<0.001$, except handgrip $P<0.05$) after controlling for gender, pubertal status and country (Table 3; Model 1), and these associations remained significant after controlling for fat free-mass, HOMA, systolic blood pressure (Table 3; Model 2), total body fat (table 3; Model 3) and physical activity (Table 4). The results did not change when birth weight was added to the model (data not shown). The pattern of the associations was similar when the analyses were repeated separately for boys and girls (data not shown).

Discussion

The results of the present study indicate that physical activity, specifically average and vigorous physical activity, is negatively associated with leptin concentrations after controlling for potential confounders including total body fat in European adolescents. These results are in agreement with previous studies (12, 13), while others failed to find an association between objectively assessed physical activity and leptin (11, 14). Platat et al. showed that total physical activity assessed by questionnaire was inversely associated with leptin after controlling for body fat in adolescents (12). Similarly, Romon et al. found a negative association of physical activity (assessed by both questionnaire and pedometer) with leptin, also after controlling for body fat in girls (13). In contrast, a recent study in children did not find an association of objectively assessed physical activity (average physical activity and MVPA by accelerometry) with leptin concentrations before and after controlling for body fat (14). Likewise, another study performed in female adolescents did not show an association between physical activity (assessed by questionnaire) and leptin concentrations after taking into account body fat (11).

The use of physical activity assessed by questionnaire has shown to have important drawbacks when used in paediatric populations (34, 35). Therefore, the different findings between studies could be due to the use of less accurate measurements of physical activity such as questionnaires (11-13) and the relatively small sample size (11). Another reason could be because the differences in age, pubertal development and hence in the hormone profiles (14).

A major finding in this study was that the association of average physical activity and vigorous physical activity with leptin concentrations remained after further controlling for physical fitness. To our knowledge there are no studies examining the association between physical activity and leptin concentrations after controlling for physical fitness, so these results suggest that physical activity could influence leptin concentrations independently of the physical fitness levels.

We also observed a negative association between physical fitness (particularly muscular strength and cardiorespiratory fitness) and leptin concentrations independently of gender, pubertal status, country, blood pressure, fat free-mass, HOMA, and total body fat. Furthermore, the results persisted after further controlling for physical activity, which suggest that the association of physical activity and fitness with leptin in adolescents are independent of each other. The lack of studies analysing the association between physical fitness and leptin in adolescents hamper further comparisons.

Intervention studies showed that long or intense single bouts of exercise as well as physical training reduced leptin concentrations in children (36) and adults (37-40). Gutin et al. showed that a 4-month physical activity (training) intervention program (heart rate above 150 beats/min) significantly decreased leptin concentrations in obese children (36). The mechanisms by which physical activity or fitness influence leptin concentrations are unknown. Weight loss after an intervention program has shown to be related with increased levels of leptin receptors which cause a decrease in leptin concentrations (41). Whereby, this could be suggested as a possible link between the relationship of physical activity and fitness with leptin concentrations.

Leptin is involved in the metabolic features related to obesity, and it was suggested that increased leptin concentrations could reduce insulin sensitivity (42). Moreover, a bidirectional hormonal feedback loop between insulin and leptin, namely *"the adipoinsular axis"* was described (3). In the present study, leptin was associated with plasma insulin and HOMA, and so was physical activity and fitness. Therefore it is biologically plausible that physical activity or fitness could influence leptin concentrations by increasing insulin sensitivity.

Owing to the cross-sectional design of this study, we cannot state causal relationships. The use of harmonised and standardised methodology in nine different countries as well as the objective assessment of physical activity, physical fitness and several potential confounders including HOMA and total body fat are strengths of our study.

In conclusion, the results suggest that physical activity (particularly average and vigorous physical activity) and physical fitness (particularly muscular strength and cardiorespiratory fitness) are negatively associated with leptin concentrations in adolescents, regardless of relevant confounders including total body fat. Intervention studies are needed in order to show whether increasing the levels of physical activity, fitness or both, may have an influence on leptin concentrations in adolescents.

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References

1. **Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM** 1994 Positional cloning of the mouse obese gene and its human homologue. Nature 372:425-432

2. **Fleisch AF, Agarwal N, Roberts MD, Han JC, Theim KR, Vexler A, Troendle J, Yanovski SZ, Yanovski JA** 2007 Influence of serum leptin on weight and body fat growth in children at high risk for adult obesity. J Clin Endocrinol Metab 92:948-954

3. **Huerta MG** 2006 Adiponectin and leptin: potential tools in the differential diagnosis of pediatric diabetes? Rev Endocr Metab Disord 7:187-196

4. **Retnakaran R, Zinman B, Connelly PW, Harris SB, Hanley AJ** 2006 Nontraditional cardiovascular risk factors in pediatric metabolic syndrome. J Pediatr 148:176-182

5. **Wallace AM, McMahon AD, Packard CJ, Kelly A, Shepherd J, Gaw A, Sattar N** 2001 Plasma leptin and the risk of cardiovascular disease in the west of Scotland coronary prevention study (WOSCOPS). Circulation 104:3052-3056

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

7. **Leary SD, Ness AR, Smith GD, Mattocks C, Deere K, Blair SN, Riddoch C** 2008 Physical activity and blood pressure in childhood: findings from a population-based study. Hypertension 51:92-98

8. **Rizzo NS, Ruiz JR, Oja L, Veidebaum T, Sjostrom M** 2008 Associations between physical activity, body fat, and insulin resistance (homeostasis model assessment) in adolescents: the European Youth Heart Study. Am J Clin Nutr 87:586-592

9. **Ruiz JR, Ortega FB** 2009 Physical Activity and Cardiovascular Disease Risk Factors in Children and Adolescents. Current Cardiovascular Risk Reports 3:281-287

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

11. **Ischander M, Zaldivar F, Jr., Eliakim A, Nussbaum E, Dunton G, Leu SY, Cooper DM, Schneider M** 2007 Physical activity, growth, and inflammatory mediators in BMI-matched female adolescents. Med Sci Sports Exerc 39:1131-1138

12. **Platat C, Wagner A, Klumpp T, Schweitzer B, Simon C** 2006 Relationships of physical activity with metabolic syndrome features and low-grade inflammation in adolescents. Diabetologia 49:2078-2085

13. **Romon M, Lafay L, Bresson JL, Oppert JM, Borys JM, Kettaneh A, Charles MA** 2004 Relationships between physical activity and plasma leptin levels in healthy children: the Fleurbaix-Laventie Ville Sante II Study. Int J Obes Relat Metab Disord 28:1227-1232

14. **Metcalf BS, Jeffery AN, Hosking J, Voss LD, Sattar N, Wilkin TJ** 2009 Objectively measured physical activity and its association with adiponectin and other novel metabolic markers: a longitudinal study in children (EarlyBird 38). Diabetes Care 32:468-473

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

16. **Ruiz JR, Castro-Pinero J, Artero EG, Orgeta FB, Sjostrom M, Suni J, Castillo MJ** 2009 Predictive Validity of Health-Related Fitness in Youth: A Systematic Review. Br J Sports Med

17. **Ruiz JR, Rizzo NS, Ortega FB, Loit HM, Veidebaum T, Sjostrom M** 2007 Markers of insulin resistance are associated with fatness and fitness in school-aged children: the European Youth Heart Study. Diabetologia 50:1401-1408

18. **Ruiz JR, Ortega FB, Loit HM, Veidebaum T, Sjostrom M** 2007 Body fat is associated with blood pressure in school-aged girls with low cardiorespiratory fitness: the European Youth Heart Study. J Hypertens 25:2027-2034

19. **Moreno LA, De Henauw S, Gonzalez-Gross M, Kersting M, Molnar D, Gottrand F, Barrios L, Sjostrom M, Manios Y, Gilbert CC, Leclercq C, Widhalm K, Kafatos A, Marcos A** 2008 Design and implementation of the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study. Int J Obes (Lond) 32 Suppl 5:S4-11

20. **Beghin L, Castera M, Manios Y, Gilbert CC, Kersting M, De Henauw S, Kafatos A, Gottrand F, Molnar D, Sjostrom M, Leclercq C, Widhalm K, Mesana MI, Moreno LA, Libersa C** 2008 Quality assurance of ethical issues and regulatory aspects relating to good clinical practices in the HELENA Cross-Sectional Study. Int J Obes (Lond) 32 Suppl 5:S12-18

21. **Nagy E, Vicente-Rodriguez G, Manios Y, Beghin L, Iliescu C, Censi L, Dietrich S, Ortega FB, De Vriendt T, Plada M, Moreno LA, Molnar D** 2008 Harmonization process and reliability assessment of anthropometric measurements in a multicenter study in adolescents. Int J Obes (Lond) 32 Suppl 5:S58-65

22. **Lohman TG, Roche AF, Martorell R** 1988 Anthropometric Standardization Reference Manual. Human Kinetics Books: Champaign, Illinois

23. **Slaughter MH, Lohman TG, Boileau RA, Horswill CA, Stillman RJ, Van Loan MD, Bemben DA** 1988 Skinfold equations for estimation of body fatness in children and youth. Hum Biol 60:709-723

24. **Tanner JM, Whitehouse RH** 1976 Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child 51:170-179

25. **Gonzalez-Gross M, Breidenassel C, Gomez-Martinez S, Ferrari M, Beghin L, Spinneker A, Diaz LE, Maiani G, Demailly A, Al-Tahan J, Albers U, Warnberg J, Stoffel-Wagner B, Jimenez-Pavon D, Libersa C, Pietrzik K, Marcos A, Stehle P** 2008 Sampling and processing of fresh blood samples within a European multicenter nutritional study: evaluation of biomarker stability during transport and storage. Int J Obes (Lond) 32 Suppl 5:S66-75

26. **Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC** 1985 Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28:412-419

27. **Trost SG, Pate RR, Freedson PS, Sallis JF, Taylor WC** 2000 Using objective physical activity measures with youth: how many days of monitoring are needed? Med Sci Sports Exerc 32:426-431

28. **Puyau MR, Adolph AL, Vohra FA, Butte NF** 2002 Validation and calibration of physical activity monitors in children. Obes Res 10:150-157

29. **Castro-Piñero J, Artero EG, Espana-Romero V, Ortega FB, Sjostrom M, Suni J, Ruiz JR** 2009 Criterion-related validity of field-based fitness tests in youth: A systematic review. Br J Sports Med

30. **Ortega FB, Artero EG, Ruiz JR, Vicente-Rodriguez G, Bergman P, Hagstromer M, Ottevaere C, Nagy E, Konsta O, Rey-Lopez JP, Polito A, Dietrich S, Plada M, Beghin L, Manios Y, Sjostrom M, Castillo MJ** 2008 Reliability of health-related physical fitness tests in European adolescents. The HELENA Study. Int J Obes (Lond) 32 Suppl 5:S49-57

31. **Ruiz JR, Ortega FB, Gutierrez A, Meusel D, Sjostrom M, Castillo MJ** 2006 Health-related fitness assessment in childhood and adolescence: a European approach based on the AVENA, EYHS and HELENA studies. J Public Health 14:269-277

32. **España-Romero V, Ortega FB, Vicente-Rodriguez G, al. e** in press Elbow position affects handgrip strength in adolescents; Validity and reliability of Jamar, DynEx and TKK dynamometers. J Strength Cond Res

33. **Ruiz JR, Espana-Romero V, Ortega FB, Sjostrom M, Castillo MJ, Gutierrez A** 2006 Hand span influences optimal grip span in male and female teenagers. J Hand Surg Am 31:1367-1372

34. **Sirard JR, Pate RR** 2001 Physical activity assessment in children and adolescents. Sports Med 31:439-454

35. **Hagstromer M, Bergman P, De Bourdeaudhuij I, Ortega FB, Ruiz JR, Manios Y, Rey-Lopez JP, Phillipp K, von Berlepsch J, Sjostrom M** 2008 Concurrent validity of a modified version of the International Physical Activity Questionnaire (IPAQ-A) in European adolescents: The HELENA Study. Int J Obes (Lond) 32 Suppl 5:S42-48

36. **Gutin B, Ramsey L, Barbeau P, Cannady W, Ferguson M, Litaker M, Owens S** 1999 Plasma leptin concentrations in obese children: changes during 4-mo periods with and without physical training. Am J Clin Nutr 69:388-394

37. **Jurimae J, Jurimae T** 2005 Leptin responses to short term exercise in college level male rowers. Br J Sports Med 39:6-9

38. **Perusse L, Collier G, Gagnon J, Leon AS, Rao DC, Skinner JS, Wilmore JH, Nadeau A, Zimmet PZ, Bouchard C** 1997 Acute and chronic effects of exercise on leptin levels in humans. J Appl Physiol 83:5-10

39. **Pasman WJ, Westerterp-Plantenga MS, Saris WH** 1998 The effect of exercise training on leptin levels in obese males. Am J Physiol 274:E280-286

40. **Landt M, Lawson GM, Helgeson JM, Davila-Roman VG, Ladenson JH, Jaffe AS, Hickner RC** 1997 Prolonged exercise decreases serum leptin concentrations. Metabolism 46:1109-1112

41. **Reinehr T, Kratzsch J, Kiess W, Andler W** 2005 Circulating soluble leptin receptor, leptin, and insulin resistance before and after weight loss in obese children. Int J Obes (Lond) 29:1230-1235

42. **Moreno LA, Pineda I, Rodriguez G, Fleta J, Giner A, Juste MG, Sarria A, Bueno M** 2002 Leptin and metabolic syndrome in obese and non-obese children. Horm Metab Res 34:394-399

Table 1. Descriptive characteristics of the study participants.

	All (n=902)	Girls (n=509)	Boys (n=393)	*P* value
Age (years)	15.0 ± 1.2	15.0 ± 1.2	15.0 ± 1.3	0.976
Pubertal status (I/II/III/IV/V) (%)	1/6/20/44/29	0/5/21/44/30	2/8/20/42/28	
Height (m)	1.7 ± 0.1	1.6 ± 0.1	1.7 ± 0.1	<0.001
Weight (kg)	59.3 ± 12.7	56.2 ± 10.1	62.7 ± 14.3	<0.001
Birth Weight (kg)	3.3 ± 0.6	3.3 ± 0.6	3.4 ± 0.6	<0.001
Systolic blood pressure (mmHg)	120.4 ± 13.4	116.5 ± 11.5	125 ± 13.9	<0.001
Total body fat (mm)[a]	90.2 ± 39.8	103.1 ± 35.9	75.5 ± 38.9	<0.001
Body fat percentage (%)	23.6 ± 9.4	26.4 ± 7.0	20.0 ± 10.8	<0.001
Fat free mass (kg)	44.6 ± 8.2	40.9 ± 5.2	75.5 ± 38.9	<0.001
Insulin (µlU/mL)[a]	10.1 ± 7.6	10.2 ± 6.4	10.1 ± 8.7	0.783
HOMA[b]	2.3 ± 1.9	2.3 ± 1.6	2.3 ± 2.2	0.531
Leptin (ng/mL)[a]	19.7 ± 22.5	28.5 ± 24.6	9.3 ± 13.8	<0.001
Average physical activity (cpm)[a]	439.1 ± 156.5	387.0 ± 123.1	503.6 ± 169.1	<0.001
Moderate physical activity (min/day)[a]	40.5 ± 14.5	37.6 ± 13.0	44.0 ± 15.3	<0.001
Vigorous physical activity (min/day)[a]	19.0 ± 14.3	13.9 ± 10.9	25.2 ± 15.5	<0.001
MVPA (min/day)[a]	59.4 ± 24.4	51.5 ± 20.5	69.2 ± 25.2	<0.001
Handgrip strength (kg)	61.6 ± 18.1	52.0 ± 9.9	72.7 ± 19.1	<0.001
Standing long jump (cm)	163.1 ± 35.3	144.7 ± 25.7	184.5 ± 32.9	<0.001
4 x 10m shuttle run (s)	12.2 ± 1.3	12.8 ± 1.2	11.5 ± 1.1	<0.001
20m shuttle run (stage)[a]	4.8 ± 2.8	3.4 ± 1.8	6.3 ± 2.8	<0.001

All values are mean ± standard deviation, or percentages (pubertal status)
HOMA, homeostasis model assessment. MVPA, moderate and vigorous physical activity
Non-transformed data are presented in this table, but analyses were performed on [a]Log-transformed data or [b] power of 1/3-transformed data

Table 2. Partial correlations of serum leptin and insulin concentrations with physical activity, physical fitness and potential confounders, controlling for pubertal status and gender.

	Physical activity				Physical Fitness				Confounders					
	Average PA[a]	MPA[a]	VPA[a]	MVPA[a]	Handgrip	SLJ	4x10m SRT	20m SRT[a]	TBF[a]	FFM	Insulin[a]	HOMA[b]	Birth weight	Systolic blood pressure
Leptin (ng/mL)[a]	-0.125*	0.002	-0.234*	-0.109**	0.014	-0.472*	0.415*	-0.368*	0.74*	-0.268**	0.418*	0.397*	-0.105**	0.243*
Insulin (μIU/mL)[a]	-0.106*	-0.037	-0.097*	-0.139*	0.058	-0.218*	0.220*	-0.276*	0.347*	0.114**	---	0.973*	-0.024	0.221*

PA, physical activity; MPA, moderate physical activity; VPA, vigorous physical activity; MVPA, moderate to vigorous physical activity; SLJ, standing long jump; TBF, total body fat; FFM, fat free-mass; HOMA, homeostasis model assessment

*P <0.01, **P<0.05

[a]Log-transformed data. [b] power of 1/3-transformed data

Table 3. Linear regression models showing the association of physical activity and physical fitness with leptin levels in adolescents.

	Model 1			Model 2			Model 3		
Predictor variables	β	R^2	P	β	R^2	P	β	R^2	P
Physical Activity									
Average physical activity[a]	-0.083	0.497	**0.019**	-0.053	0.559	0.084	-0.054	0.742	**0.021**
Moderate physical activity[a]	-0.007	0.491	0.808	0.011	0.557	0.708	-0.022	0.740	0.335
Vigorous physical activity[a]	-0.165	0.513	**<0.001**	-0.121	0.569	**<0.001**	-0.055	0.742	**0.023**
MVPA[a]	-0.09	0.498	**0.011**	-0.055	0.560	0.074	-0.044	0.741	0.071
Physical Fitness									
Handgrip strength	-0.088	0.461	**0.020**	-0.203	0.543	**<0.001**	-0.146	0.737	**<0.001**
Standing long jump	-0.374	0.526	**<0.001**	-0.332	0.583	**<0.001**	-0.090	0.732	**0.002**
4 x 10m shuttle run test[b]	0.339	0.523	**<0.001**	0.274	0.574	**<0.001**	0.052	0.732	**0.048**
20m shuttle run test[a]	-0.384	0.517	**<0.001**	-0.331	0.569	**<0.001**	-0.075	0.745	**0.008**

β, standardised regression coefficients; R^2, coefficients of determination. [a]Log-transformed data. [b]Higher scores mean worse performance
Confounders in Model 1: gender, pubertal status and country
Confounders in Model 2: Model 1 + fat free-mass, homeostasis model assessment and systolic blood pressure
Confounders in Model 3: Model 2 + total body fat
MVPA indicates moderate and vigorous physical activity

Table 4. Linear regression models showing the association of physical activity and physical fitness with serum leptin concentrations in adolescents, after controlling for each other

Predictor variables	β	R^2	P	β	R^2	P	β	R^2	P	β	R^2	P
Physical Activity	Model 3 + handgrip strength			Model 3 + Standing long jump			Model 3 + 4x10m shuttle run test			Model 3 + 20m shuttle run test		
Average physical activity[a]	-0.057	0.745	**0.017**	-0.048	0.745	**0.048**	-0.053	0.740	**0.029**	-0.037	0.759	0.148
Moderate physical activity[a]	-0.023	0.743	0.312	-0.017	0.744	0.464	-0.019	0.738	0.416	-0.052	0.758	0.958
Vigorous physical activity[a]	-0.059	0.745	**0.017**	-0.052	0.745	**0.038**	-0.056	0.740	**0.026**	-0.058	0.760	**0.032**
MVPA[a]	-0.046	0.744	0.057	-0.038	0.744	0.113	-0.042	0.739	0.086	-0.026	0.758	0.311
Physical Fitness	Model 3 + average physical activity			Model 3 + moderate physical activity			Model 3 + vigorous physical activity			Model 3 + MVPA		
Handgrip strength	-0.146	0.745	**<0.001**	-0.147	0.743	**<0.001**	-0.144	0.737	**0.001**	-0.146	0.744	**<0.001**
Standing long jump	-0.138	0.745	**<0.001**	-0.143	0.744	**<0.001**	-0.138	0.745	**<0.001**	-0.140	0.744	**<0.001**
4 x 10m shuttle run test[b]	0.060	0.740	0.058	0.64	0.738	**0.044**	0.059	0.740	0.065	0.62	0.739	0.054
20m shuttle run test[a]	-0.082	0.759	**0.019**	-0.088	0.758	**0.012**	-0.078	0.760	**0.027**	-0.085	0.758	**0.016**

β, standardised regression coefficients; R^2, coefficients of determination. [a]Log-transformed data. [b]Higher scores mean worse performance

Confounders in Model 3: gender, pubertal status, country, fat free-mass, homeostasis model assessment, systolic blood pressure and total body fat

MVPA indicates moderate and vigorous physical activity

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CONCLUSIONES

I.- Niveles elevados tanto de actividad física (particularmente de intensidad moderada y vigorosa) como de condición física (en concreto la capacidad aeróbica y la fuerza muscular) se asocian negativamente con la adiposidad así como con diversos factores de riesgo de enfermedad cardiovascular en jóvenes (Artículos I y II).

II.- En adolescentes, un alto status socioeconómico familiar se asocia positivamente con una mejor condición física independientemente del nivel de actividad física y de adiposidad (Artículos III y IV).

III.- En adolescentes europeos, el exceso de grasa corporal se asocia a una menor sensibilidad a la insulina. Una buena condición física atenúa este efecto, es decir disminuye la resistencia a la insulina (Artículo V).

IV.- El nivel de condición física (fuerza muscular y capacidad aeróbica) se asocia con menores niveles de leptina independientemente del nivel de actividad física y adiposidad en adolescentes Europeos. Además, el nivel de actividad física (actividad física total y de intensidad vigorosa) se asocia también de manera inversa con los niveles de leptina (Artículo VI).

Conclusión general:

Existe una fuerte evidencia de que altos niveles de actividad física y condición física están asociados con un menor grado de adiposidad en niños y adolescentes. El status socioeconómico, independientemente de la actividad física y la adiposidad, influye positivamente en la condición física, y ésta a su vez tiene un efecto favorable sobre la sensibilidad a la insulina y los niveles de leptina.

CONCLUSIONS

I.- High levels of physical activity (specially of moderate and vigorous intensities) and physical fitness (specially cardiorespiratory and muscular fitness) are associated with lower total and central body fat as well as with several obesity-related CVD risk factors in children and adolescents (Papers I y II).

II.- A high familiar socioeconomic level is positively associated with a better fitness and lower fatness in adolescents regardless of physical activity and adiposity (Papers III y IV).

III.- The excess of body fat is associated with lower insulin sensitivity in European adolescents. High levels of physical fitness attenuate this effect, in other words, a high fitness decreases insulin resistance (Paper V).

IV.- Physical fitness (particularly muscular strength and cardiorespiratory fitness) are associated with serum leptin, regardless of the physical activity and adiposity levels in European adolescents. Likewise, physical activity (particularly average and vigorous physical activity) is also inversely associated with leptin levels (Paper VI).

Overall conclusion:

There is strong evidence that higher levels of physical activity and fitness are associated with lower adiposity in children and adolescents. The socioeconomic status positively influences physical fitness regardless of physical activity and adiposity. Physical fitness has a favorable effect on insulin sensitivity and leptin levels.

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Estancias

- Estancia de investigación en el Instituto Karolinska (PrevNut), Estocolmo, Suecia (Agosto - Diciembre 2009).
- Estancia de investigación en el Departamento de Nutrición Humana, Universidad de Glasgow, Escocia (Agosto - Diciembre 2008).

Docencia

- **Docencia Oficial** en la Facultad de Ciencias de la Actividad Física y del Deporte (INEF). Universidad Politécnica de Madrid.
  - Bases Fisiológicas del Ejercicio. Curso 2009-2010. 6 créditos.
- **Ponente invitado** al "X Seminario: Problemas emergentes en Nutrición y Alimentación"; mesa sobre *"Idoneidad de la cerveza en la recuperación del metabolismo de los deportistas"*. Organizado por la Universidad Internacional Menéndez Pelayo (Cuenca) del 14 al 16 de Octubre de 2009.
- **Ponencia** en la "Annual Conference of the International Society of Behavioral Nutrition and Physical Activity (ISBNPA). Título: *"Associations between objectively measured habitual physical activity and adiposity in children and adolescents"*. Lisboa, 17-20 Junio 2009. ISBN: 978-972-735-165-7.
- **Profesor colaborador/ayudante** en la Asignatura de 3º curso *"Fisiología del Ejercicio"*. Facultad de Ciencias de la Actividad Física y del Deporte (INEF). Universidad Politécnica de Madrid. Durante el curso 2008-2009.
- **Conferencia "Alcohol y Salud"** en la asignatura de 5º curso *"Nutrición y ayudas ergogénicas en el deporte"*. Facultad de Ciencia de la Actividad Física y del Deporte (INEF). Universidad Politécnica de Madrid. 16 de Enero de 2008.
- **Ponente Invitado** en el "III Encuentro sobre Investigación en Actividad Física y Salud. Titulo: *"Condición física en la actividad deportiva". Ponente invitado"*. Delegación de Deportes de Puente Genil y COLEF de Andalucía. 20 de Octubre de 2007.
- **Ponencia** en las Jornadas de Intercambio de Experiencias Motrices en virtud del Plan Anual de Formación Permanente de del Centro de Enseñanza de Profesores de la Junta de Andalucía. Titulo: *"Evaluación de la condición física para la correcta intervención en educación física en secundaria"*. Córdoba, España, 20-22, Abril, 2007.
- **Profesor externo** en el "Curso Educación física y salud en primaria". Organizado por FUNDECOR y la Universidad de Córdoba. Profesora responsable Dra. Marta Dominguez. Córdoba 2007.

- **<u>Profesor colaborador</u>** en el "Curso de entrenamiento Personal" Impartido por la Federación Española de Aeróbic y Fitness. 90 horas. Edición 2006.

Participación en proyectos de investigación

1.- Assessing Levels of Physical Activity in Europe. (**ALPHA Project**)" 2007-2009. Proyecto financiado por la Unión Europea: Public Health Executive Agency, DG SANCO, Health Information Strand (Ref. 2006120). www.thealphaproject.eu.

2.- Healthy Lifestyle in Europe by Nutrition in Adolescence. (**HELENA).** Financiado por la Unión Europea (FP6-2003-Food-2-A, FOOD-CT-2005-007034) 2004 - 2008. http://www.helenastudy.com

3.- Red de investigación en ejercicio físico y salud para poblaciones especiales (**EXERNET**)". Acción Estratégica sobre Deporte y Actividad Física de la convocatoria del Plan Nacional de I+D+I 2004-2007. Ministerio de Educación y Ciencia (DEP2005-00046/ACTI) 2006-2008. http://www.spanishexernet.com/.

4.- Laboratorio ergonómico para el desarrollo y validación de un protocolo integral de valoración de la calidad de vida en poblaciones adultas y mayores. (**ERGOLAB**)". 2006.

5.- Utilidad de la cerveza en la recuperación del metabolismo mineral, hormonal e inmunológico de deportistas tras realizar un esfuerzo físico. 2005 – 2006.

6.- Alimentación y Valoración del Estado Nutricional de los Adolescentes españoles (**AVENA**). Fondo de Investigaciones Sanitarias. Ministerio de Sanidad y Consumo. Ref.00/0015-3. www.estudioavena.com

Publicaciones científicas

<u>Internacionales</u>

1.- Ortega FB, Artero EG, Ruiz JR, España-Romero V, **<u>Jimenez-Pavón D,</u>** Vicente-Rodríguez G, Moreno LA, Manios Y, Béghin L, Ottevaere C, Ciarapica D, Sarri K, Dietrich S, Blair SN, Kersting M, Molnar D, González-Gross M, Gutierrez A, Sjostrom M, Castillo MJ. Physical fitness levels among European adolescents: The HELENA study. Br J Sports Med. 2009 Aug 20.

2.- **<u>Jiménez-Pavón D,</u>** Kelly J, Reilly JJ. Associations between objectively measured habitual physical activity and adiposity in children and adolescents: Systematic review. Int J Pediatr Obes. 2009 Jun 26:1-16.

3.- Gómez-Martinez S, Martín A, Romeo J, Castillo MJ, Mesena M, Baraza JC, **<u>Jiménez-Pavón D,</u>** Redondo C, Zamora S, Marcos A. Is soft drink consumption associated with body composition? A cross-sectional study in Spanish adolescents. Nutr Hosp. 2009 Jan-Feb;24(1):97-102.

4.- España-Romero V, Ortega Porcel FB, Artero EG, **<u>Jiménez-Pavón D,</u>** Gutiérrez Sainz A, Castillo Garzon MJ, Ruiz JR. Climbing time to exhaustion is a determinant of climbing performance in high-level sport climbers. Eur J Appl Physiol. 2009 Aug 14.

5.- Artero EG, España-Romero V, Ortega FB, **Jiménez-Pavón D,** Ruiz JR, Vicente-Rodríguez G, Bueno M, Marcos A, Gómez-Martínez S, Urzanqui A, González-Gross M, Moreno LA, Gutiérrez A, Castillo MJ. Health-related fitness in adolescents: underweight, and not only overweight, as an influencing factor. The AVENA study. Scand J Med Sci Sports. 2009 Jun 23.

6.- Romeo J, **Jiménez-Pavón D,** Cervantes-Borunda M, Warnberg J, Gómez-Martínez S, Castillo MJ, Marcos A. Immunological changes after a single bout of moderate-intensity exercise in a hot environment. J Physiol Biochem. 2008 Sep;64(3):197-204.

7.- Gonzólez-Gross M, Breidenassel C, Gómez-Martínez S, Ferrari M, Béghin L, Spinneker A, Diaz LE, Maiani G, Demailly A, Al-Tahan J, Albers U, Warnberg J, Stoffel-Wagner B, **Jiménez-Pavón D,** Libersa C, Pietrzik K, Marcos A, Stehle P. Sampling and processing of fresh blood samples within a European multicenter nutritional study: evaluation of biomarker stability during transport and storage. Int J Obes (Lond). 2008 Nov;32 Suppl 5:S66-75.

8.- Artero EG, España-Romero V, Ortega FB, **Jiménez-Pavón D,** Carreño-Gálvez F, Ruiz JR, Gutiérrez A, Castillo MJ. Use of whole-body vibration as a mode of warming up before counter movement jump. J Sports Sci Med 2007; 6: 574-5.

9.- **Jiménez-Pavón D,** Ruiz JR, Ortega FB, España-Romero V, Moliner D, Artero EG, Gómez-Martínez S, Vicente-Rodríguez G, Repasy J, Béghin L, Manios Y, Moreno LA, González-Gross M, Castillo MJ. Socioeconomic status is associated with physical fitness in European adolescents independently of total body fat and physical activity; The HELENA Study. Nutr Hosp. *In press.*

10.- **Jiménez-Pavón D,** Ortega FB, Ruiz JR, Chillón P, Castillo R, Artero EG, Martínez-Gómez D, Vicente-Rodríguez G, Rey-López JP, Gracia LA, Noriega MJ, Moreno LA, González-Gross M. Influence of socioeconomic factors on fitness and fatness in urban Spanish adolescents: The AVENA study. Int J Pediatr Obes. *In press.*

11.- Vicente-Rodríguez G, Rey-Lopez JP, Ruiz JR, **Jiménez-Pavón D,** Rey-López, J.P., Bergman P, Ciarapica D, Heredia JM, Molnar D, Gutiérrez A, Moreno LA, Ortega FB. Inter-rater Reliability and Time Measurement Validity of Speed-Agility Field Tests in Adolescents. . J Strength Cond Res *(revised version submitted).*

12.- España-Romero V, Artero EG, **Jiménez-Pavón D,** Cuenca-García M, Ortega FB, Castro-Piñero J, Sjöstrom M, Castillo MJ, Ruiz JR. Assessing health-related fitness tests in the school setting: reliability, feasibility and safety; The ALPHA study. Int J Sports Med. *(revised version submitted).*

13.- Gracia-Marco L, Tomás C, Vicente-Rodríguez G, **Jiménez-Pavón D,** Rey-López JP, Ortega FB, Lanza-Saiz R, Moreno LA. Extra-curricular participation in sports and socio-demographic factors in Spanish adolescents. The AVENA study. J Sports Sci *(revised version submitted).*

14.- Rey-López JP, Tomas C, Gracia-Marco L, Vicente-Rodriguez G, **Jiménez-Pavón D,** Pérez-Llamas F, Redondo C, De Bourdeaudhuij I, Sjöström M, Marcos A, Chillón P, Moreno LA. Sedentary behaviours and socio-economic status in Spanish adolescents: The AVENA study. *Submitted.*

15.- Moliner-Urdiales D, Ruiz JR, Ortega FB, **Jiménez-Pavón D,** Vicente-Rodríguez G, Rey-Lopez JP, Martínez-López D, Casajús JA, Mesana MI, Marcos A, Noriega-Borge MJ, Sjöström M, Castillo MJ, Moreno LA. Secular trends in health-related physical fitness in Spanish adolescents; The AVENA & HELENA Studies. *Submitted.*

16.- **Jiménez-Pavón D,** Romeo J, Cervantes-Borunda M, Ortega FB, Ruiz JR, Marcos A, Castillo MJ. Effects of dehydration and the optimal rehydration solution for healthy children and adolescent athletes. *Submitted.*

17.- **Jiménez-Pavón D,** Castillo MJ, Moreno L, Kafatos A, Manios Y, Kondaki K, Béghin L, Zaccaria M, De Henauw S, Widhalm K, Molnár D, Sjöström M, González-Gross M, Ruiz JR. Fitness and fatness are independently associated with markers of insulin resistance in European adolescents; The HELENA Study. *Submitted.*

18.- **Jiménez-Pavón D,** Ortega FB, Artero EG, Vicente-Rodríguez G, Huybrechts I, Moreno LA, Manios Y, Béghin L, Polito A, De Henauw S, Sjöström M, Castillo MJ, González-Gross M, Ruiz JR. Physical activity, fitness and serum leptin concentrations in adolescents: The HELENA Study. *Submitted.*

19.- Artero EG, España-Romero V, Castro-Piñero J, Ruiz JR, **Jiménez-Pavón D,** Aparicio VA, Gatto-Cardia MC, Baena PA, Vicente-Rodríguez G, Castillo MJ, Ortega FB. Criterion-related validity of field-based muscular fitness tests in youth. *Submitted.*

20.- Labayen I, Ruiz JR, Meirhaegue A, Ortega FB, **Jiménez-Pavón D**, Castillo MJ, De Henauw S, González-Gross M, Bueno G, Molnar D, Kafatos A, Esperanza L and Moreno LA. Association between the FTO rs9939609 polymorphism and leptin in European. *Submitted.*

Nacionales

21.- España-Romero V, Artero EG, Ortega FB, **Jiménez-Pavón D**, Gutiérrez A, Castillo MJ, Ruiz JR. Fisiología de la Escalada Deportiva. Rev Int Med Cienc Act Fís Deporte.*2009*;9(35):264-98.
Http://cdeporte.rediris.es/revista/revista35/artescalada129.htm.

22.- Moreno, LA. González-Gross, M. Marcos, A. **Jiménez-Pavón, D.** Sánchez, MJ. Mesana, MI. Gómez, S. Vicente Rodríguez, G. Díaz, LE. Castillo, MJ. en representación del grupo HELENA. Promoción de un estilo de vida saludable en adolescentes europeos mediante la actividad física y la nutrición: El proyecto HELENA. Selección: Revista Española e Iberoamericana de Medicina de la Educación Física y el Deporte.2007;16 (1)13-17.

23.- Carreño-Gálvez F, Artero EG, España-Romero V, **Jiménez-Pavón D,** Ortega FB, Ruiz JR, Gutiérrez A. “Economía de carrera. Análisis de la metodología para su evaluación y tratamientol". Selección: Revista Española e Iberoamericana de Medicina de la Educación Física y el Deporte. 2007; 16(2): 91-7.

24.- Pedrero-Chamizo R, **Jiménez-Pavón D**, González-Gross M. Effects of dehydration and the optimal rehydration solution for healthy children and adolescent athletes. *Submitted*.

Premios recibidos, comunicaciones y eventos

Premios

- **Jiménez-Pavón. D.** Tercer Premio Nacional Fin de Carrera de Educación Universitaria. Curso Académico 2004-2005. Ministerio de Educación y Cultura y Deporte. Entrega 2006.
- **Jiménez-Pavón D,** Gálvez A, Mesa JL, Gutiérrez A. 1er Premio a la Mejor comunicación oral. Nivel de afectación del tiempo de reacción simple y discriminativo durante la utilización de telefonía móvil comparado con la alcoholemia. *II Jornadas Científicas de Ciencias de la Salud. Escuela universitaria de Ciencias de la Salud*, Granada (España) **2005.**

Comunicaciones y eventos

- El doctorando ha participado como autor y coautor en más de 40 congresos internacionales y nacionales.
- El doctorando ha sido secretario de la organización y miembro del comité científico en varios simposios de carácter nacional.

Capítulos de Libros y Monografías

1. **Jiménez-Pavón,** D. Romeo J, Cervantes-Borunda M, Marcos A, Castillo MJ. *Monografía*: Idoneidad de la cerveza en la recuperación del metabolismo de los deportistas. Ed. Centro de Información Cerveza y Salud (CICS). ISBN: 978-84-613-2592-4. Febrero 2009
2. **Jiménez-Pavón, D.** y Ortega Porcel, FB. Capítulo: Evaluación De La Condición Física En Niños Y Adolescentes. Importancia y Métodos. En: *Actividad física, deporte, ejercicio y salud en niños y adolescentes*. Eds: Redondo, Figuero C, González Gross M, Moreno Aznar L, García Fuentes M. Asociación Española de Pediatría, 2009. In press.
3. **Jiménez-Pavón D**, Ruiz JR, Ortega FB, Artero EG, España-Romero V, Castro-Piñero J, Gutiérrez A, Castillo MJ. Physical activity, fitness and fatness in children and adolescents. En: *Epidemiology of Obesity in Children and Adolescents Prevalence and Aetiology In press*; Coord: Luis Moreno Aznar. Ed: Springer International, Nueva York.
4. **Jiménez-Pavón, D.** España-Romero, Vanesa. Ortega Porcel, FB. "Condición Física En La Actividad Deportiva". En: Ciencia Salud y Actividad Física. Por: De La Rosa, Francisco J. B., Baltanas Zurera, Francisco., Manzano Moreno, Ignacio., Aires Rosales, Antonio. Editado por Colegio Oficial de Licenciados en Educación Física I.S.B.N. 978-84-611-9704-0. D.L. CO-1397-2007.