ELSIE COSTA DE OLIVEIRA FORKERT

Obesidade abdominal e sua associação com fatores socioeconômicos e de estilo de vida em adolescentes: um estudo multicêntrico

Abdominal obesity and its association with socioeconomic and lifestyle factors in adolescents: a multicenter study

Tese apresentada à Faculdade de Medicinada Universidade de São Paulo para obtenção do título de Doutor em Ciências

São Paulo

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Programa de Medicina Preventiva
Orientador: Prof. Dr. Heráclito Barbosa de Carvalho
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DEDICATION

Aos meus ***Queridos Pais***!!

Que me ensinaram a ser uma pessoa do bem. Estimulando e incentivando sempre a aprender mais, buscando todas as oportunidades que a vida nos oferece; e a tudo que fizer, fazê-lo com Amor, dedicação, e dar o seu melhor!

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"All men naturally desire to know,
but what avails knowledge without the fear of God?"
Aristotle

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RESUMO

Forkert ECO. **Obesidade abdominal e sua associação com fatores socioeconômicos e de estilo de vida em adolescentes: um estudo multicêntrico** [Tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2017.

Nas últimas décadas a prevalência mundial de sobrepeso/obesidade duplicou entre adolescentes, especialmente nos países de baixa média-renda. Como indicador de obesidade total amplamente utilizado em estudos, temos o índice de massa corporal (IMC). Entretanto, danos prematuros à saúde reconhecidamente pioram, quando o excesso de gordura local está presente, como ocorre na obesidade abdominal (AO). Circunferência da cintura (CC) e relação cintura/estatura (RCE) são índices antropométricos utilizados com alta sensibilidade para definir a OA. Sendo esta um componente da síndrome metabólica (MetS), em adolescentes apresenta associações positivas mais precisas com fatores de risco cardiovascular, do que o IMC. Identificar principais fatores de risco associados a obesidade total/abdominal torna-se primordial na implementação de estratégias educativas/preventivas. O objetivo deste estudo é avaliar se existem associações entre fatores socioeconômicos e de estilo de vida com a obesidade total/abdominal em adolescentes. Dados de dois estudos transversais de base-escolar foram utilizados, um multicêntrico europeu (HELENA-CSS: *Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study*) e um brasileiro (BRACAH *study*: *Brazilian Cardiovascular Adolescent Health*). Adolescentes de escolas privadas e públicas de áreas urbanas foram selecionados por amostragem aleatória, em estágios múltiplos. O HELENA-CSS envolveu 3528 adolescentes (52,3% meninas; 12,5-17,5anos) de 10 cidades europeias, e o brasileiro 991 adolescentes (54,5% meninas; 14-18anos) da cidade de Maringá (PR). Os desfechos foram a obesidade total mensurada pelo IMC e a OA mensurada por dois indicadores: CC e RCE. As variáveis independentes analisadas foram os indicadores socioeconômicos [condição socioeconômica familiar, nível de educação dos pais, nível de ocupação dos pais (este apenas no HELENA-CSS)], e variáveis do estilo de vida (comportamentos sedentários, atividade física, tempo de sono, consumo do café da manhã). Associações entre os desfechos e variáveis independentes foram analisadas utilizando regressão linear multinível sendo estratificadas por estudo, sexo e tempo de sono; e ajustadas por confundidoras. A significância foi fixada em α=5%. Análises ajustadas mostram associação inversa entre o nível educacional dos pais e o nível de ocupação paterno com os indicadores de OA, nas meninas europeias. Entre os meninos europeus há associação significativa com estes dois desfechos, e o nível de ocupação materna. A RCE associa-se negativamente com a condição socioeconômica familiar e ocupação materna entre as meninas europeias, e com o nível educacional dos pais entre os meninos europeus. Entre adolescentes brasileiros não há associação significativa. Pular o café da manhã está associado positivamente com indicadores de obesidade total e abdominal entre adolescentes europeus. Entre meninos brasileiros a obesidade total associa-se inversamente as horas de sono. Após a análise estratificada pelo tempo de sono observa-se associação entre os desfechos e pular o café da manhã em adolescentes europeus, e meninos brasileiros. Excesso de comportamento sedentário (≥2h/dia) mostra associação positiva com os indicadores de OA em meninas europeias, mesmo as que relatam

dormir adequadamente (≥8h/dia). Conclui-se que o nível educacional dos pais e principalmente o materno associa-se com a obesidade abdominal em adolescentes europeus, e não consumir o café da manhã é um importante fator de risco para obesidade total/abdominal entre adolescentes europeus e meninos brasileiros.

Descritores: obesidade abdominal; estado nutricional; fatores socioeconômicos; estilo de vida; adolescente; fatores de risco cardiometabólicos; estudo multicêntrico; fatores de risco.

SUMMARY/ABSTRACT

Forkert ECO. **Abdominal obesity and its association with socioeconomic and lifestyle factors in adolescents: a multicenter study** [Tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2017.

In the last decades, the worldwide prevalence of overweight / obesity has doubled among adolescents, especially in low middle-income countries. As an indicator of total obesity widely used in studies, we have the body mass index (BMI). However, premature health damage is known to worsen when local excess fat is present, as occurs in abdominal obesity (AO). Waist circumference (WC) and waist-to-height ratio (WHtR) are anthropometric indices used with high sensitivity to define AO. Being a component of the metabolic syndrome (MetS) in adolescents it presents more positive associations with cardiovascular risk factors than BMI. Identifying the main risk factors associated with total / abdominal obesity becomes paramount in the implementation of educational / preventive strategies. The aims of this study are to evaluate if there are associations between socioeconomic and lifestyle factors with total / abdominal obesity in adolescents. Data from two school-based cross-sectional studies were used, a European multicenter (HELENA-CSS: *Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study*) and a Brazilian (BRACAH study: *Brazilian Cardiovascular Adolescent Health*). Adolescents from private and public schools in urban areas were selected by random sampling, in multiple stages. The HELENA-CSS involved 3528 adolescents (52.3% girls, 12.5-17.5 years) from 10 European cities and the Brazilian study included 991 adolescents (54.5% girls, 14-18 years) from the city of Maringá (PR). The outcomes were total obesity measured by BMI and AO measured by two indicators: WC and WHtR. The independent variables analyzed were socioeconomic indicators [socioeconomic family status, parental education level, parental occupation level (this only in HELENA-CSS)], and lifestyle variables (sedentary behaviors, physical activity, sleep time, breakfast consumption). Associations between outcomes and independent variables were analyzed using multilevel linear regression being stratified by study, sex, and sleep time; and adjusted by confounders. The significance was set at $\alpha = 5\%$. Adjusted analyzes show an inverse association between parental education level and father's occupation level with indicators of AO in European girls. Among European boys, there are a significant association with these two outcomes, and maternal occupation level. The WHtR is negatively associated with socioeconomic family status and maternal occupation among European girls, and with parental educational level among European boys. Among Brazilian adolescents, there is no significant association. Skipping breakfast is positively associated with indicators of total and abdominal obesity in European adolescents. Among Brazilian boys, total obesity is inversely associated with sleep time. After the analysis stratified by sleep time, we observed an association between the outcomes and skip breakfast in European adolescents, and Brazilian boys. Excess sedentary behavior (≥2h / day) shows a positive association between indicators of AO in European girls, even those reporting adequate sleep (≥8h / day). In conclusion, the educational level of parents and especially the maternal level are associated with AO in

European adolescents, and skipping breakfast is an important risk factor for total / abdominal obesity among European adolescents and Brazilian boys.

Descriptors: abdominal obesity; nutritional status; socioeconomic factors; lifestyle; adolescent; cardiometabolic risk factors; multicenter study; risk factors.

1. INTRODUCTION

Concerning child growth, in the last thirty years, the worldwide prevalence of overweight/obesity rose substantially (47.1% between 1980 and 2013) (1). Although it still high in developed countries, a stability has been observed, while in low middle-income countries is increasing unrelentingly (2). Using measured height and weight, data from 2013-2014 (National Health and Nutrition Examination Survey) showed that the prevalence of obesity in American children decreased since 2004, but among adolescents it increased since 1988 (10.5% to 20.6%), being also influenced by the lower degree of household head education, pointed as an indicator of socioeconomic status (SES) (3). Europe experienced as well, an increase prevalence of obesity childhood about 6 to 31% among boys and from 5 to 21% among girls, presenting in southern European countries, the highest prevalence of overweight (4). Regarding obesity of Brazilian children/adolescents, an overall 14.1% prevalence is showed (16.1% for boys and among girls14.9%), placing the South region ahead the others (5).

Childhood obesity is associated with metabolic complications (insulin resistance, glucose intolerance, hypertension), constitutes an important current global health problem for the individual and the community. Besides, is a strong predictor of adult obesity associating comorbidities to cardiovascular diseases(CVD) and type 2 diabetes(6),which adds sums to national health budgets (7).

The distribution of the excess body fat deserves special attention when visceral adiposity as abdominal obesity (AO) is involved, because it has linked to early metabolic changes, constituting cardiometabolic risk factors in young population, more than overweight or total obesity (8).In adolescents, the prevalence of AO is higher in low middle-income countries, varying from 3.8 to 51.7 %, than in high-income countries (8.7 to 33.2 %) (9).

Even in developed countries chronic diseases and metabolic syndrome (MetS), a cluster of atherogenic abnormalities that compound the risk factors for cardiovascular diseases and type2 diabetes, are a concern. Prevalence rate of their risks rise among children and adolescents, getting worse when the predominant risk factor is AO, which

is influenced by SES as parental education level and family income (10). Throughout decades, substantial evidences support an inverse relation between SES and CVD, where persistent socioeconomic inequalities may lead to unhealthy weight gain, for vulnerable children and adolescents (11). In one hand, economic growth brings prosperity, especially for low middle-income countries on the other hand forces, mainly children and adolescents to a high consumption of energy-dense foods in an increasingly obesogenic environment, where choices have been easily affected by marketing (12).

Epidemiological approaches are still needed to better understand the causes of obesity, which include interactions of environmental, behavioral, genetic, physiological, social and economic factors. These factors when alienate the individual from a healthy purpose; promote increased caloric intake and sedentary lifestyle (13). Behaviors are the result of a learning history through biological influences (age, sex, genetic and psychological factors) and environmental influences, which in turn will influence the energy balance (14). There is a general consensus that lifestyle factors conduct to the obesity epidemic (15). In this behalf, not only genetic factors such as lifestyle adopted by the individual, contribute to the level of CVD risk. At an early age, healthy behaviors can be acquired and followed, and will often perpetuate throughout life by avoiding or postponing metabolic disorders that predict CVD (16).

In this sense, literature has shown associations between energy-balance related behaviors (EBRBs) with increase of the prevalence of overweight / obesity among school-children and adolescents. Behaviors related to the etiology of obesity, when drive to a healthy lifestyle, may be important allies in the prevention of obesity (17). These EBRBs comprise dietary habits, regular physical activity, sedentary behaviors among others: inadequate sleep time (18,19) and skipping breakfast (20) are as well of great importance. Identifying the occurrence of such behavior is relevant in preventing obesity in this population, since the occurrence of several EBRBs is more prevalent than the prevalence of isolated behaviors (21).

Considering the importance of identifying behavioral and social components that are harmful to cardiovascular health from early age, this work was developed with approach at children and adolescents based on three articles. The first article is a review

that approaches the existing knowledge regarding the association of abdominal obesity with the main associated cardiometabolic risk factors in children and adolescents. The second one addresses abdominal obesity and evaluates its association with indicators of socioeconomic status, in adolescents from different contexts. Finally, the third article aimed to assess energy-balance related behaviors (EBRBs) associated with markers of obesity in adolescents, and the role of sleep duration in the association between lifestyle behaviors and obesity.

1.1 PRESENTATION OF THE DOCTORAL THESIS

This work will be presented in the form of compilation of articles, based on the norms defined by the Program of Postgraduate Committee of the University of São Paulo related to the article 8º of the Postgraduate Regiment (Resolution 6542 of April 18th 2013). Initially, an Introduction was presented taking into account general aspects of the study. Following the norms, the text will be presented in English as the language used in the articles, developed and submitted to international scientific journals.

Subsequently, the Research Project, as approved in the Research Ethics Committee - English version - followed by a text presenting the adjustments (i.e., presenting the changes that occurred during the process, both those that are naturally incorporated during this work and those suggested by the qualification exam). After that, the thesis' Articles, Discussion and Conclusion, and finally the References (pertinent to introduction and discussion) and Appendix.

1.2 REGULATIONS OF THE POSTGRADUATE COMMITTEE

Included below are the rules for submission of Master dissertation and Thesis in the form of a compilation of articles, regulated by the Postgraduate Committee (CPG) at the School of Medicine, University of São Paulo (FMUSP).

1) At the discretion of the Program Coordinating Committee, dissertations and theses may be accepted based on Article/Paper compilations;

2) The master dissertation should contain at least one paper accepted for publication;

3) The doctoral thesis shall contain at least two articles accepted for publication;
4) The date of article submission must occur after the student‘s registration in the Program;
5) The paper that is accepted or published should contain the stated purpose of the Research Project approved by the Ethics Committee on Research Involving Human Participants of the FMUSP and sent to CPG;
6) The student must be the first author of the article;
7) The supervisor must be a co-author of the article;
8) The indexing of the journal that accepted or published the article should be according to the Program rules concerning procedures for delivering dissertations and theses;

The presentation:
Theses and dissertations should include the following mandatory items:

1) Delivering a correlated volume containing the Research Project approved by the Ethics Committee on Research Involving Human Participants of the FMUSP with presentation and critical analysis, written in Portuguese or English;
2) Insert the manuscript that was accepted or published;
3) The contributions of the paper are analyzed, discussed and summarized as the same language as the articles did.

2. RESEARCH PROJECT APPROVED BY CAPPESQ

FACULDADE DE MEDICINA DA UNIVERSIDADE DE SÃO PAULO

DEPARTAMENTO DE MEDICINA PREVENTIVA

PROJETO DE DOUTORADO

Socioeconomic and microenvironmental factors related to abdominal obesity in adolescents: a multicenter study

ELSIE COSTA DE OLIVEIRA FORKERT

Prof. Dr. Heráclito Barbosa de Carvalho

São Paulo

2013

ABSTRACT

Abdominal obesity (AO) has as an important role as risk factor for cardiometabolic diseases. Identifying and preventing the development of AO at an early age will promote the prevention of health risks and complications in both childhood and adulthood. The objectives of this study will be to evaluate the socioeconomic and micro-environmental factors related to AO in adolescents, with a specific focus on the lifestyle factors related to physical activity and eating habits. **Method**: This project is a component of the "**High blood pressure and aggregation of risk factors in adolescents: a multicenter study**" and will use data from two high school-based cross-sectional studies of students aged 12.5 to 18 years in Brazil and in nine European countries; each of these studies used standardized probabilistic sampling, recruitment and data collection methodologies. The Brazilian data will be derived from the study entitled "Cardiovascular Risk Factors: Biological and Behavioral Indicators," and data from the European countries will be obtained from the "Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study". AO will be the outcome of interest in this study, as indicated by waist circumference (WC). The following independent variables will be analyzed: city, sex, age, household structure, parental education, parental employment status, familial socioeconomic status, physical activity, sedentary behaviors and food habits. To analyze the magnitude of the associations between the outcome and the independent variables, prevalence ratios with 95% confidence intervals will be calculated using Poisson regression with robust variance.

1. INTRODUCTION

Currently, dyslipidemia, diabetes, hypertension and obesity are diseases that are highly prevalent among the young population in developed and developing countries and important risk factors for mortality and cardiovascular and metabolic diseases (Prentice 2006; Ramachandran et al., 2002). A recent epidemiological study conducted in the United States showed that 50% of the 2,456 included adolescents presented at least one of these cardiovascular risk factors (Johnson et al., 2009), and comparable

results have been identified in Australia. Similar but lower results have been recognized in Europe, which has also reported the prevalence of overweight and obesity in children and adolescents (Moreno et al., 2000;Kalies et al., 2002). The prevalence of childhood obesity has increased substantially over the last several decades, and the condition is now considered an epidemic (Lobstein et al., 2004). Public health data regarding overweight and obesity are worrisome since the affected pediatric population may be more vulnerable to increased morbidity and early mortality due to cardiovascular diseases in adulthood (Raitakari et al., 2003; Baker et al., 2007), particularly because these conditions are difficult to control (Ebbeling et al., 2002).

According to Egger and Swinburn (1997), obesity occurs due to a confluence of biological and behavioral risk factors that are influenced by socioeconomic, educational, and cultural conditions in the home, school and community settings. These authors proposed an ecological model of obesity, within which they classified environments into the following categories: macro environment, which affect and are determinants of the prevalence of obesity within the general population. In addition, microenvironments are characterized by their proximity to the individual; these include home, school and community environments, which typically involves food and physical activity. Lastly, behavioral and biological influences also help to determine whether an individual will be obese. Familial patterns of adiposity have indicated that there is likely a genetic component to weight gain; however, this factor becomes irrelevant when an individual is exposed to an environment in which he or she has increased energy intake and reduced of energy expenditure, thereby leading to a caloric nutritional imbalance and weight increase (Moreno et al., 2004).

Other factors such as educational and socioeconomic status may affect the probability of obesity. When impoverished individuals have poor educational attainment, the opportunities for them to increase their knowledge of health and the nutritional value of food is decreased; this knowledge may help these individuals to selected foods of better quality with lower energy density such as fruits, vegetables and whole grains and engage in leisure and exercise activities (Sobal and Stunkard 1989; WHO 2000). Previous studies have reported that childhood obesity begins to develop in the domestic environment (Strauss and Knight, 1999). Many families exhibit

obesogenic behavior, wherein dietary patterns are altered (increased) and physical activity patterns are reduced, leading to serious health consequences. Within this context, the educational level of parents and, more specifically, the level of maternal education have been identified as determinants of overweight in children and adolescents (Moreno et al., 2004). Additionally, paternal obesity has been shown to be associated with a fourfold in the risk of obesity among male and female adolescents; furthermore, maternal obesity was associated with 8 times greater risk of obesity among daughters (Burke et al., 2001). Conversely, individuals of higher socioeconomic status were more likely to have the knowledge and the opportunities that are preventive against becoming obese than poorer individuals (WHO,2003).

Studies have reported obesity to be inversely associated with socioeconomic level Monteiro et al., 2004), being twice as high in developing than developed countries (Janewa et al., 2012). On the other hand, evidence has suggested that improvements in socioeconomic status in low- and middle-income classes, which are usually accompanied by urbanization and migration to urban agglomerates, may lead to a rapid and inadequate nutritional transitions, including dietary changes and reduced physical activity, both of which have been identified as risk factors for obesity and diabetes (Fall, 2001; Gutiérrez-Fisac et al., 2002; Wang et al., 2002). The socioeconomic inequalities associated with individual and environmental aspects also have a direct influence on engagement in physical activity, with evidence suggesting that less physical activity may occur in the environments of lower socioeconomic status; therefore, familial socioeconomic status has been identified one of the main determinants of engaging in physical activity in childhood (De Cocker et al., 2012). Studies have identified associations between the risk of becoming obesity and physical inactivity (Martinez-Gomez et al., 2010) and time spent on sedentary behavior (Rey-López et al., 2008). According to Klein-Platat (2005), an inverse link may exist between physical activity and abdominal obesity. Few studies have reported the effects of a combination of physical inactivity and sedentary behaviors or analyzed to associations between different socioeconomic indicators and overweight and obesity in adolescents. Obesity can be measured using anthropometric measurements, including body mass index (BMI), which, despite being found to have low sensitivity in identifying adiposity and

excess body fat (Okorodudu et al., 2010), has been well-accepted, is frequently used in epidemiological investigations, and has been recommended by pediatric obesity committee specialists. As an alternative, waist circumference (WC) has been used to assess abdominal obesity, which is one of the components of the metabolic syndrome, according to the criteria of the National Cholesterol Education Program of the Adult Treatment Panel III and the International Diabetes Federation. WC is an anthropometric index with higher sensitivity and specificity for identifying cardiovascular risk than BMI. The prevalence of abdominal obesity has been reported to be high among adolescents and associated with different eating habits, and this relationship may be mediated by the family socioeconomic context (de Moraes e Falcão, 2013). Studies conducted by our group have shown that adolescents who devote many hours to technology use (e.g., computers, television) have less healthy eating habits (Rey-Lopéz et al.,2011). In light of the aforementioned literature, the purpose of this study will be to identify socioeconomic and environmental factors (domiciliary, school and community) that influence eating habits and physical activity and may stimulate the development of abdominal obesity in adolescents. To do so, we will use data from two European and Brazilian studies.

1.1 JUSTIFICATION

In this study, we analyzed data obtained from the database of a European multicenter study and the database of a local study conducted in the city of Maringá to identify environmental factors (domiciliary, school and community) and socioeconomic factors that may affect adolescents' abdominal obesity, and determine the roles that physical activity and dietary habits play in this process. Determining to what extent socioeconomic and environmental differences may be associated with overweight and abdominal obesity can help to facilitate the development public health policies with intervention measures directed toward preventing overweight and obesity during childhood.

1.2 GENERAL OBJECTIVES

A) To evaluate whether physical activity is associated with abdominal obesity in Brazilian and European adolescents.

B) To verify if there is an association between eating habits and abdominal obesity in Brazilian and European adolescents.

C) To assess if there is an association between socioeconomic status and abdominal obesity in Brazilian and European adolescents.

2. METHODS

This project is a component of the "High Blood Pressure and Aggregation of Risk Factors in Adolescents: A Multicenter Study" and will use data from two high school-based cross-sectional studies. HELENA study (*Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study*) from Europe and the Brazilian, BRACAH study (*Brazilian Cardiovascular Adolescent Health*), which were carried out with adolescents aged 12.5 to 18 years from 11 cities in the following ten different countries: Brazil (Maringá), Austria (Vienna), Belgium (Ghent), France (Lille), Germany (Dortmund), Greece (Athens and Heraklion), Hungary (Pécs), Italy (Rome), Spain (Zaragoza) and Sweden (Stockholm). Data from the European countries were retrieved from the HELENA Study, which was coordinated by Professor Luis A. Moreno Aznar, University School of Health Sciences of the University of Zaragoza (Spain).The study was approved by the Research Ethics Committees for data collection (2) and followed the ethical principles of the Helsinki Declaration (Association WM, 2000).

In Brazil, this study was submitted for approval by the Research Ethics Committee (CEP) of the Faculty of Medicine of the University of São Paulo

2.1 SAMPLE SIZE

2.1.1 HELENA study

A total of 3,000 adolescents aged 12.5 to 17.5 were randomly selected from all

the colleges in the 10 participating cities: Vienna (Austria), Ghent (Belgium), Lille (France), Dortmund (Germany), Athens and Heraklion (Greece), Pécs (Hungary), Rome (Italy), Zaragoza (Spain), Stockholm (Sweden). The sample size was estimated based on the study variable that presented the highest variation (BMI) within each sex and age group. A 95% confidence intervals and error of ± 0.3 were used to calculate the sample size. Ten schools from each participating city were included, with the exception of Pécs (Hungary), where only 8 schools participated. Multiple random sampling was applied after stratification by district or region to ensure the cultural and socioeconomic diversity of the sample, and schools in different regions in each participating city were initially used as the unit of selection; subsequently, the classrooms within the schools were identified. Classrooms were considered for inclusion if they included at least 20 students and demonstrated a similar age and sex distribution. More detailed information on the design and development of the study was published (Moreno et al., 2008a; Moreno et al., 2008b). A total of 3528 (1683 boys and 1845 girls) adolescents met the general inclusion criteria in terms of age, non-participation in another clinical study and not suffering from any acute infectious disease during the week prior to inclusion in the study.

2.1.2 BRACAH study

Maringá is located northwest of the state of Paraná in the southern region of Brazil and has approximately 335,000 inhabitants. The city has a high human development index (HDI = 0.84, while the HDI for Brazil as a whole is 0.79) (UN 2007). The participants included in this study were students of both sexes between 14 and 18 years old who were enrolled (n = 16301 high school students) in the public and private school networks in 2007, as verified by data of the State Secretariat of Education of Paraná (Secretaria,2007).The following parameters were used to calculate the sample size: 95% confidence level, 80% power, estimated prevalence of 50% (± 5 percentage points) and design effect of 2. Based on these parameters, the authors estimated that it would be necessary to collect data from 734 adolescents. Because it was a major research study on the health of adolescents, we added 10% to the sample for possible

losses and refusals and 15% for the use of multivariate analyses, resulting in a total sample of 991 adolescents required for data collection. Sampling was performed in the following two stages: school type (primary sample unit) and classrooms. First, the number of schools that had students within the studied age range (n = 38 schools, including 26 public and 12 private schools) was determined; then, schools were randomly and systematically selected with consideration of size and type proportionality (public or private). Ultimately, eight public and four private schools were selected. In the second stage, the classes within each school were selected using simple random sampling with consideration of the proportion of students in each grade (1st to 3rd grade). All schoolchildren in the selected classes on the day of data collection were considered eligible to participate in the study. The exclusion criteria were as follows: adolescents with orthopedic conditions that impeded anthropometric assessments, pregnant adolescents and parental non-consent. In the two studies, all the participating students had consent written provided by the parents or guardians, and verbal consent provided by the adolescent him- or herself.

2.2 STUDY VARIABLES

Abdominal obesity will be the outcome of interest in this study, which was evaluated based on waist circumference (WC). WC was measured using an inextensible tape measure and measured in duplicate at the mid-distance between the iliac crest and the last rib in duplicates; then, the two measures were averaged, and the procedure was repeated in cases in which a maximum variation of 0.5 cm was exceeded (accuracy of 0.1 cm) (WHO, 1995). The adolescents participating in the two studies were classified into non-obese and obese according to the sex- and age-specific cut-off values (Taylor et al., 2000). The independent variables investigated were as follows: socio-demographic, socioeconomic and behavioral variables. These variables will be described in detail below.

Sociodemographic indicators

Cities: Vienna, Ghent, Lille, Dortmund, Athens and Heraklion, Pécs, Rome, Zaragoza, Stockholm, and Maringá.

Sex: male and female;

Age: determined as the difference between the date of birth reported by the adolescents themselves and the date of data collection;

Socioeconomic indicators

HELENA study

Family Affluence Scale (*FAS*): The adolescents answered a questionnaire that evaluated the goods present in the domicile, such as the number of cars and computers, if they had access to the internet and if they had their own room. The FAS was developed based on the model proposed by Currie (Currie et al., 2008) and was adapted by replacing the item: "having holidays" with "Internet access at home". Scores on this scale range from 0 to 8, with 0 being very low level and 8 being very high socioeconomic status;

Family structure: adolescents reported living with parents or with only one parent and their number of sisters/half-sisters and brothers/half-brothers;

Employment status of parents: adolescents reported whether both parents worked all day, worked part-time, or did not work or if least one parent worked and the other stayed at home;

Parental education level: the highest level of education achieved by each parent was considered, and the adolescents responded by selecting one of the following levels:

1) primary studies (first degree);
2) secondary studies (second degree);
3) technical studies;
4) university education;

BRACAH study

Family structure: adolescents living with parents (yes or no, which included living with grandparents, alone, in a boarding house, or with a husband and/or wife);

Parental employment status: both work, none work or at least one works and the other stays at home;

Parental education level: university level (high) or medium and fundamental level (medium/low);

Behavioral indicators

Sedentary behavior

Information through a self-reported questionnaire regarding the time (in hours) spent watching TV, using computer and playing video game (Rey-López et al., 2011).

Physical activity

Information regarding the practice of daily physical activities will be obtained through the *International Physical Activity Questionnaire* (IPAQ) modified and validated for adolescents- *International Physical Activity Questionnaire for Adolescents*(IPAQ-A)with reference to the last week (Guedes et al., 2005; Hagströmer et al., 2008).

Eating habits

The Food Frequency Questionnaire (FFQ), which was previously used in the international study entitled Health Behavior in School-Aged Children (HBSC), was applied to investigate the health habits of a large number of schoolchildren. The questionnaire was translated and modified for the eating habits of each country (Vereecken et al., 2009) after being assessed for reliability among Brazilian (Romanzini et al., 2008) and European students (Vereecken et al., 2008). For example, the question, "How many times in the last week have you ingested fruit?" evaluated the consumption of fruit within a usual week. The questionnaire was self-reported in the classroom under the supervision of a researcher, and the questions addressed the following five food

groups: 1) vegetables; 2) fruits; 3) refrigerated foods; 4) fried foods; and 5) sweets (high energy density foods such as cakes, biscuits and chocolates). Inadequate food consumption was classified as eating fried foods, cakes, biscuits and sweets 4 days a week and fruits and vegetables four days a week. The amount of each food ingested was not collected. The questionnaire also measured the number of meals served (breakfast, morning snack, lunch, afternoon coffee, afternoon snack, dinner and supper) and which were consumed at home.

3. DATA ANALYSIS

Initially, continuous variables will be presented as the mean and 95% confidence interval (95% CI), and qualitative variables will be presented as percentages (%). Additionally, the Shapiro-Wilk test will be used to verify the normality of the data. Subsequently, the t-test for unpaired samples and the Mann-Whitney U test will be applied to analyze gender differences in the evaluated variables. To identify differences between categorical variables, the chi-square test with Yates correction will be employed for dichotomous independent variables and the chi-square test for linear tendency will be employed for ordinal or nominal categorical variables. Then, prevalence ratios (PRs) with 95% confidence intervals (95% CIs) will be calculated using the Poisson regression to quantify the unadjusted and adjusted association between the outcome and the independent variables (Coutinho et al., 2008). The adjusted analysis will be performed based a hierarchical model divided into the following three levels, as previously described: 1) sociodemographic indicators; 2) socioeconomic indicators; and 3) behavioral indicators. In this type of analysis, the variables included in the same level or higher levels will be adjusted for in the model (Victora et al., 1997). Variables with p value ≤ 0.20 will be adopted as significance level required for maintenance in the model. Wald tests will be used to evaluate heterogeneity across dichotomous or nominal variables, and linear trends will be used to assess heterogeneity across ordinal categorical variables. For all statistical analyses, the Stata software version 11.0 (Stata Corporation, College Station, TX, USA) will be used, and the statistical significance criterion will be 5%.

4. SCHEDULE OF ACTIVITIES AND ARTICLES

The activities will be developed jointly with a postdoctoral student of the Department of Preventive Medicine, Tara Rendo-Urteaga, and under the supervision and guidance of Prof. Dr. Heráclito Barbosa de Carvalho.

First and Second Semesters

1) Literature review

2) Internship at the University of Zaragoza (Spain) to inform the compilation of the databases

3) Analysis of data from the two studies

4) Elaboration upon a previous report and composition of a manuscript entitled, "Association between physical activity and sedentary behavior and abdominal obesity in adolescents".

Third and Fourth Semesters

1) Update literature review

2) Disciplinary compliance

3) Analysis of data from the two studies

4) Elaboration upon a previous report and composition of a manuscript entitled, "Association among eating habits and abdominal obesity in adolescents"

5) Doctorate qualification exam

Fifth and Sixth Semesters

1) Update literature review

2) Disciplinary compliance

3) Analysis of data from the two studies

4) Composition of doctoral thesis and a scientific article: "Socioeconomic factors and abdominal obesity in adolescents: data from two European and Brazilian observational studies"

5) Defense of Doctoral Thesis

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3. RESEARCH PROJECT: ADJUSTMENTS

Adjustments are presented relative of the modifications that occurred naturally during the study process, from the initial Research Project approved by CAPPesq, and the Qualification Project. Suggestions were incorporated after Qualification Exam as well as those that led to the elaboration of the articles carried out on this work.

1. A ***theoretical conceptual model*** (Appendix-Qualification Project, page 100) was proposed, through which it was sought to guide and demonstrate better the hierarchical relationship between the determinants (independent variables) of the disease and its influence on the outcome. From then on the specific objectives were set up idealizing the construction of the articles that make up this thesis.

2. **Changing the variables of dietary habits:** Initially, the variables chosen to evaluate adolescents' behavior regarding dietary habits were the consumption of fruits, vegetables, sweetened beverages. However, the literature has extensively explored this exposition being others so important and of current interest in the relationship with obesity, which can lead to cardiometabolic risks, such as sleep time and breakfast consumption. In addition, we decided to evaluate whether sleep time influences the others behaviors, related to the adolescents' lifestyle.

3. **Modification of the proposed statistical analysis:** Cluster analysis idealized initially did not provide an adequate division of the groups, which compromised the analysis, choosing to develop it in a second moment based on a more adequate statistical technique (Canonical Analysis).

4. ARTICLES

4.1 Article 1

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Nutrire

REVIEW Open Access

Abdominal obesity and cardiometabolic risk in children and adolescents, are we aware of their relevance?

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Abstract

Obesity prevalence has increased worldwide over the last decades and has reached alarming rates in low middle-income countries. Childhood has been affected by this epidemic, leading to premature dramatic health problems. Adipose tissue is currently considered as an endocrine organ modulating an inflammatory state and important metabolic processes (insulin resistance, hypertension, glucose intolerance) leading to consequences of the cardiovascular system. This situation may be worst if the excess of body fat distribution such as abdominal obesity (AO) is involved because it is associated with a more atherogenic risk profile determining the cardiometabolic risks mainly in children and adolescents.

Hence, the knowledge regarding the association between AO and cardiometabolic factors aims to prevent and treat the obesity in this young population, avoiding early harmful consequences of adulthood health.

Keywords: Abdominal obesity, Adolescents, Children, Cardiometabolic risks, Prevalence

Background

Obesity is characterized by excessive accumulation of total body fat related to health problems and reduced quality of life in adults and children [1]. Besides, this condition adds greatly to the national health-care budgets [2].

The prevalence of obesity has increased in alarming rates in developing countries. In 2013, 42 million of children under the age of 5 were overweight or obese and the rate of increase was 30 % higher in low middle-income countries than that in developed countries (where no increase was observed after around 2000). If the trends continue by 2025, this rate may raise 70 million of patients worldwide [1].

Obesity per se, rather than the associated risk factors, is an independent predictor of some adverse cardiovascular events [3, 4] increasing threefold the mortality rate when compared with normal weight subjects [5]. In children and adolescents, obesity is associated with cardiometabolic risk factors such as dyslipidemia and type 2 diabetes, which are related with atherosclerosis development [6, 7]. High cardiovascular risk (assessed by Pathobiological Determinants of Atherosclerosis in Youth score) was associated with carotid intima-media thickening in obese adolescents with a fourfold higher risk of atherosclerosis [8]. The presence of overweight in adolescence was also associated with an increased risk of mortality from coronary heart disease in adulthood (women and men) regardless of the individual's weight in adulthood [9].

Otherwise, one of the most prevalent topics of discussion regarding excess body fat is the question of visceral fat depot or abdominal obesity (AO), also known as central obesity, central fat deposition, visceral obesity, visceral adiposity, visceral fat, truncal obesity, truncal fat, intra-abdominal fat, and its early effects on the metabolic changes in young populations [10]. Of note, cardiometabolic risk factors are more prevalent in children and adolescents with AO than those with overweight or general obesity [11]. So, it is important to estimate the association

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between AO and cardiovascular risk factors, especially in children and adolescents [9].

Abdominal obesity contribute to an inflammatory state and may cause abnormalities in health, triggering deleterious reactions related to insulin resistance (IR). Together with other factors as lipid abnormalities, fibrinolysis, oxidative stress, hypertension, hyperglycemia, or type 2 diabetes are positively associated with endothelial dysfunction, leading to early atherosclerosis [12].

Knowing the disorders related to excessive AO, which surround childhood and translate into chronic diseases in adulthood, it is urgent to approach them and to identify vulnerable points that could be addressed in prevention strategies. Therefore, the purpose of this paper is to review the existing knowledge regarding the association of AO with the main associated cardiometabolic risk factors such as disorders of glucose metabolism, lipid abnormalities, hypertension, and the metabolic syndrome (MetS) in children and adolescents.

Obesity prevalence and risks in children and adolescents

The worldwide prevalence of overweight and obesity among children and young adults has increased in the last years. In children under 5 years, the prevalence of overweight and obesity in 1990 was 4.2 %, increasing to 6.7 % in 2010, and in 2020, it could reach 9.1 % [13]. Among adolescents, the rate of increase of obesity was about 12 % (from 1980 to 2000) [14]. The scenario recently changed, because in low middle-income countries, the tendency of childhood overweight and obesity seems to rise quickly, especially in urban areas, reaching about 30 % more when compared with developed countries [15, 16].

Thereby, from around 2005, Latin America has shown trends of increase in overweight/obesity similar to those previously observed in Western Europe and North America, where a plateau level was reached [17]. Thus, currently the prevalence of overweight in children from Latin America is over 25 %,whereas in adults, it is higher than 50 %.The prevalence of obesity in children also reached more than 3 % (exception in Peru where for preschool children it is less than 2 %), and in adults, this prevalence is higher than 25 % [18]. In Brazilian children, overweight prevalence ranged from 25 to 40 % and among adolescents, it is 22 % in boys and 19.4 % in girls [18]. Recently, a meta-analysis conducted in Brazil showed that the overall prevalence of obesity among children/adolescents was 14.1 %. Among boys, it was 16.1 % and for girls, it was 15 %, showing the highest prevalence in the southeastern regions, mainly in the South region [19].

Concerning childhood overweight/obesity in European countries (2009–2010), Norway showed the lowest prevalence (15 %), while Italy the highest prevalence (36 %) [17]. In the majority of the countries (except Italy, Czech Republic, and Slovenia), the prevalence was higher in females than that in males. In the USA, data from 2009–2010 showed that 34 % of children aged 5–17 years were affected by this epidemic [14, 17].

According to Zhang et al., the prevalence of obesity is increasing among children and adolescents from rural area as well, alerting for an urban-rural disparity ever closer [20]. In children and adolescents from low middle-income countries, obesity carries on a problem, especially to those with fairly high socioeconomic status [21]. In contrast, developed economies with children in lower socio-economic status tend to show a higher prevalence of obesity [17]. Despite efforts applied to recognize this epidemic and to deal with, there is no decrease noted in its occurrence, but at least a leveling off in its prevalence [14]. Although, a stability of obesity in this young population from developed countries is supported by Rokholm et al. [22], it must be kept in mind that the prevalence is higher than ever before.

Nowadays, it is known that the adipose tissue is an essential endocrine organ [10]. It takes an important place in the body related with the destination of excess dietary lipids, which might determine body homeostasis maintenance or the production and regulation of certain hormones, modulating an inflammatory state and important metabolic processes (insulin resistance, atherogenesis (endothelial dysfunction)), leading to detrimental consequences of the cardiovascular system [23].

Overweight/obese children show early changes on left cardiac structures that were not explained by blood pressure [24] besides significant impairment of vascular function as arterial wall stiffness [25]. That supports an attainable cumulative cardiovascular effect of childhood obesity on adult cardiovascular outcomes. Thus, overweight and obesity during childhood and adolescence increase the risk of long-term obesity, leading to chances of harmful consequences [23, 26].

Abdominal obesity and cardiometabolic risk factors

The pathophysiologic mechanisms linking childhood obesity to cardiovascular abnormalities have not been clearly established. Body fat distribution plays an important role on the endothelial damage because obese subjects are more prone to such dysfunction. Particularly, AO has been identified as a determinant of arteriosclerosis development [27].

Abdominal obesity is associated with a more atherogenic risk profile (Fig. 1) because it increases the cardiometabolic risk factors (lipid profile, systolic hypertension, and abnormal fasting blood glucose) both in children and adolescents [28–31]. Furthermore, approximately 16 to 18 % of children and adolescents have AO [32]. In adolescents, the prevalence of AO is higher in low middle-income countries, varying from 3.8 to 51.7 %, than in high-income countries (8.7 to 33.2 %) [33], as it was also noticed in American children and adolescents [34].

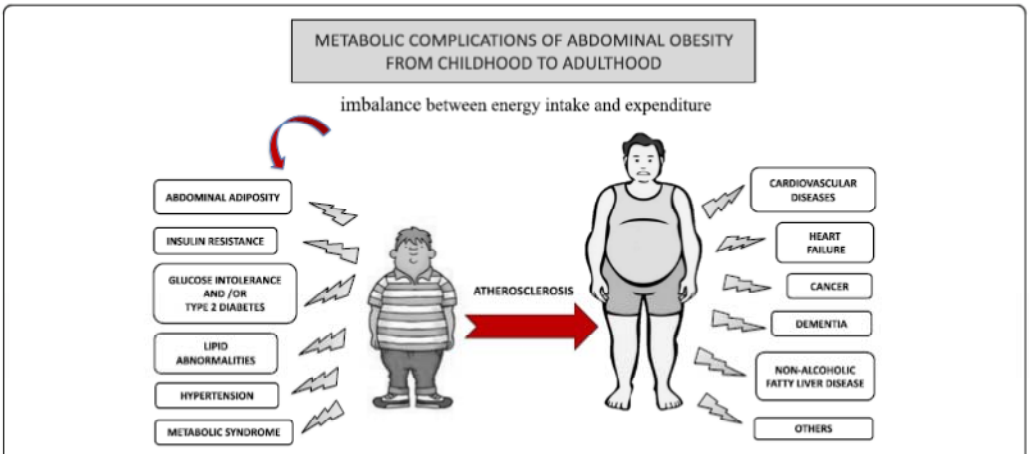

Fig. 1 Metabolic disorders associated with abdominal adiposity speeds up morbidity-mortality in adulthood

Hence, the association between general obesity and AO with cardiometabolic risk factors is different [35]. The excessive amount of visceral adipose tissue plays a role in the development of several metabolic disorders in pediatric population [36]. The importance of examining AO using low-cost anthropometric indices may contribute to identify cardiometabolic risk factors from adolescence through adulthood [34]. Thereby, simple anthropometric measures of AO, such as waist circumference (considering ethnicity, sex, and age) [37, 38], waist to hip ratio, and waist to height ratio (independent of age, gender or race/ethnicity), could be considered as predictors of AO [11, 39]. In this sense, a number of studies have shown that surrogate markers of AO are independent risk factors for type 2 diabetes mellitus, dyslipidemia, hypertension, and coronary artery disease [28, 40].

Disorders of glucose metabolism

Studies have shown that a high degree of obesity, especially AO, in children and adolescents is detrimental to glucose metabolism, regardless of the ethnic background, leading to a high prevalence of impaired glucose tolerance [41].

Considering glucose metabolism, it is important to clarify some definitions. *Insulin resistance* is a condition in which there is a low uptake of glucose by the tissues in response to insulin action. *Glucose intolerance* is a risk factor for future diabetes and/or adverse outcomes [42] in which an individual has higher than normal levels of glucose in the blood upon fasting or following a carbohydrate-rich meal, being an inability to properly metabolize glucose. *Type 2 diabetes* is an array of dysfunctions characterized by hyperglycemia, resulting from the combination of varying degrees of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion [43]. These metabolic abnormalities result in an inflammatory state, triggering cardiovascular risks to the individual.

In obese individuals, mainly with AO, hypertrophy of adipose tissue releases high quantities of preinflammatory markers (cytokines) as tumor necrosis factor alpha (TNF-alpha) and interleukin-6 (IL-6), producing lipotoxicity and triggering a resistance to the action of insulin by damaging the insulin receptor substrate (IRS-1). Thus, there will be a reduced capacity to transport and uptake glucose into the intracellular space. In case of a high fat diet, there is a widening in adipocyte size (hypertrophy), enhancing lipolysis, and releasing free fatty acids (FFA) to the circulation [44]. These particles will be deposited on the insulin-sensitive organs (lean tissues): muscle, liver, and heart, leading to an inflammatory state [45]. The described inflammatory state may produce other undesirable effects such as endothelial-vasomotor dysfunction [46].

Summing up, in obese people, initially, IR appears in adipose tissue and then in other tissues, leading to glucose intolerance. As a consequence, pancreatic β cells try to produce more and more insulin to reverse this situation, which does not occur, following up the resistance to them. The persistence of long-term hyperglycemia leads to the onset of type 2 diabetes [47].

In children and adolescents, epidemiological studies show an association between AO with such disorders, driving important and premature cardiometabolic risk in adulthood. The homeostatic model assessment (HOMA) index is a method to quantify IR, calculated as the product of fasting plasma insulin level (microU/ml) and fasting plasma glucose level (mmol/L), divided by 22.5 [48]. There is no widely agreed cutoff to define IR in children and adolescents; however, some values have been

proposed [49] that should be specific for age, sex, and pubertal development [50].

Once IR appears the foremost to development of MetS [51] in the pediatric population, associated with the other manifestations of the MetS. Although, the impact by which AO affects MetS risk in children and adolescents is unclear, studies have shown that the strongest metabolic impact of AO is IR [52].Moreover, the prevalence of glucose intolerance among children and adolescents was higher among girls (4.2 %) as compared with boys (3.2 %) and was even higher when AO was present in girls (12.7 %) [53].

Lipid abnormalities

Several chronic conditions such as obesity and diabetes may exacerbate the development of atherosclerosis [54], a process that begins as early as the first years of life [6, 55–57]. Atherogenesis has been associated with dyslipidemia, being an important risk factor for atherosclerosis and cardiovascular diseases, also in the pediatric population [58].

Atherogenic dyslipidemia is one of the metabolic abnormalities that define the MetS and is characterized by hypertriglyceridemia, increased levels of very-low-density lipoprotein (VLDL) and small dense low-density lipoprotein (LDL) particles, and reduced levels of high-density lipoprotein (HDL) [59]. General obesity is strongly associated with atherogenic dyslipidemia in youth [60]. Several studies show an association between AO and abnormal lipid profile in children and adolescents [11, 35, 58, 61–66], especially associated with high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), and hypertriglyceridemia at all ages [67–70].

Moreover, AO promote a cluster of atherogenic risk factors [71, 72].

During the last decade, the atherogenic dyslipidemia prevalence is increasing in children and adolescents with obesity [73, 74]. Data from the Third National Health and Nutrition Examination Survey (NHANES III) indicate that 25 % of adolescents are characterized by high triglyceride (TG) concentrations and 40 % by low HDL cholesterol concentrations [60, 75]. The AVENA (*Alimentación y Valoración del Estado Nutricional en Adolescentes*) study, in Spanish adolescents, found a deleterious effect of both abdominal and truncal obesity on the lipid profile [76]. In the Bogalusa Heart Study, overweight schoolchildren were 2.4 to 7.1 times more likely to have elevated total cholesterol (TC), LDL cholesterol, and TG than their lean counterparts [60, 77].

The "portal free fatty acid" theory [78] was the first hypothesis explaining the close relationship between AO and metabolic complications. Due to its close proximity to the liver and drained by the portal circulation, excess visceral adipose tissue could alter lipoprotein metabolism mainly by inducing an overproduction of large triglyceride-rich lipoproteins, VLDLs [23]. Non-esterified FFAs released from the visceral adipose tissue are transformed into VLDLs enriched with TGs which leads to the formation of TG-rich LDL particles, which become remodeled into small and dense LDL particles, the most atherogenic form of dyslipidemia [79]. Thus, a high proportion of small and dense LDL has been associated with an increased risk of coronary heart disease.

Atherogenic dyslipidemia is associated with other components of the MetS and is an important risk factor for cardiovascular diseases [59, 73, 80]. Accordingly, AO represent one of the most important factors of its progression in children with obesity [81]. Currently, the literature shows novel merged dyslipidemic patterns in children and adolescents associated with obesity that consist in a moderate-to-severe elevation in TGs and non-HDL-C, mild elevation in LDL-C, and reduced HDL-C, showing a high atherogenic pattern [74]. This pattern of combined dyslipidemia is represented as both an increase in small, dense LDL and in overall LDL particle number and a reduction in total HDL-C and in large HDL particles [82–84].

In adults, children, and also in adolescents, AO may be associated with compositional changes in HDL particles, making them less efficient regarding their protective action on cholesterol efflux [85]. It is well known that low levels of HDL are associated with an increased risk of developing cardiovascular diseases [86]; however, high levels of HDL may not always be protective, since in a context of chronic inflammation, HDL particles may be less functional [87].

The association between AO and dyslipidemia is a complex trait that is associated with several metabolic diseases (e.g., insulin resistance, non-alcoholic fatty liver disease, chronic inflammation) during life [74], suggesting an integrated pathophysiological response to excessive weight gain.

Hypertension

Blood pressure (BP) is an easy and common measurement in health surveys, and it is well established that high BP can be identified in children and adolescents [88, 89]. In several epidemiological studies, hypertension prevalence has significantly increased among this young population over the recent years [90–96]. Numerous studies show that both overweight and obesity were associated with elevated BP in children and adolescents [91, 94, 97]. Moreover, data from clinical studies on high BP in childhood show that primary hypertension is commonly associated with other cardiovascular risk factors as well as obesity [98].

Regarding AO, a previous study assessing the association between fat distribution and cardiovascular risk in children showed that visceral fat (as well as total fat) is

associated to high BP in Italian children [99]. This association has also been established by several researchers [28, 61, 94, 100–106]. Some of these studies showed that this association was stronger in boys than in girls [104–106], and the association of AO with systolic hypertension have been seen more frequently than with diastolic hypertension [107, 108]. In a recent systematic review by Kelishadi et al., they found only one study showing that total body fat is a stronger predictor of elevated BP than AO in children and adolescents [28, 109].

Abdominal obesity plays a more important role in the occurrence of hypertension than subcutaneous adiposity [110]. The anatomical location may be the answer about functional differences between visceral and subcutaneous adipocytes. The accumulation of visceral fat promotes a greater activation of sympathetic nervous system (SNS) than subcutaneous fat [111], producing more proinflammatory cytokines (TNF-alpha and IL-6) and less adiponectin, resulting in insulin resistance. Further, hyperinsulinemia may result in the raise of sodium reabsorption (hypervolemia) and an increase of SNS (vasoconstriction) activity, contributing to hypertension [110, 112].

Metabolic syndrome

In 2005, the International Diabetes Federation (IDF) defined MetS in adults "as a cluster of risk factors for cardiovascular diseases and type 2 diabetes mellitus, including AO, atherogenic dyslipidemia (high TGs and low HDL-cholesterol, elevated apolipoproteina B (Apo B), small-dense LDL particles, and small HDL particles; all of these abnormalities are individually atherogenic) [113], impaired glucose tolerance and hypertension" [114]. MetS could be also defined as a grouping of abnormalities resulting from IR and the excess of AO [113]. Thus, two potential causative factors in the pathogenesis of MetS stand out: IR and AO.

In the South region of Brazil, a high prevalence of MetS among adolescents with AO and IR was observed [115]. Weiss et al. stated that, in children and adolescents, MetS is far more common than formerly reported and its prevalence increases directly with the degree of obesity [116]. In a systematic review, Friend et al. [117] found that the prevalence of MetS in the general population of children and adolescents worldwide was 3.3 % (range 0–19.2 %); in overweight, 11.9 % (2.8–29.3 %) and it was 29.2 % (10.0–66.0 %) in the obese population. For non-obese, non-overweight children and adolescents was lower than 1 %.

Waist circumference is an independent predictor of cardiovascular risk in adults and children and an indicator of IR, dyslipidemia, and hypertension. Waist circumference measurement is easy and cheap, and it is considered a clinical parameter to infer the degree of abdominal adiposity [118] but it may vary depending on the ethnic group. In addition, there is no consensus in the literature on the standard cutoff points, for classification of AO in children and adolescents [119].

Subjects with MetS usually manifest a proinflammatory state (elevated high sensitive C-reactive protein (CRP), elevated unhealthy cytokines (TNF-alpha, IL-6), decrease adiponectin plasma concentrations) and a prothrombotic state (fibrinolytic factors—plasminogen activator inhibitor-1 (PAI-1)) [114]. Individuals with MetS in which diabetes is not already present have five times more risk of developing type 2 diabetes [120]. Nevertheless, the identification of MetS in children and adolescents through clinical and metabolic factors should be done earlier to allow risk stratification on the onset of type 2 diabetes and cardiovascular diseases in this population [118].

Concerning the pediatric population, based on previous studies [75, 116, 121–123], the IDF suggested modified adult criteria to be applied in children and adolescents. In addition, MetS should not be diagnosed in children younger than 10 years, but in those with AO (90th percentile as a cutoff for waist circumference), they should "work on weight reduction," with healthy changes on lifestyle. For children aged 10 years till 16 years old, MetS can be determined by the presence of AO and two or more clinical risk factors such as high triglycerides (≥150 mg/dl), low HDL-cholesterol(<40 mg/dl), high blood pressure(95th percentile), or high fasting plasma glucose(>100 mg/dl). For adolescents aged 16 years or more, the IDF adult criteria can be used [124]. However, considering children and adolescents, some studies have proposed scientific evidence's items to evaluate and characterize this population with metabolic risk factors, since there is not an updated and precise definition. These items include personal and family history, pubertal status, metabolic abnormalities, and clinical feature [125, 126].

Defining body composition or metabolic abnormalities in children through single cutoff points is difficult because they change with age, sex, and pubertal development, but this is not been taken into account duly, once current definitions have considered the age rather than the pubertal status. In accordance, studies have shown a high prevalence of MetS, not only in pubertal but also in prepubertal obese children [127, 128].

Prepubertal obese children [129] showed an elevation of proinflammatory factors (TNF-alpha, IL-6, CPR, PAI-1), and markers of endothelial dysfunction which contribute to early increase of cardiovascular diseases later in life. Likewise, serum myeloperoxidase (MPO) level was elevated in prepubertal obese children [129]. MPO is an enzyme which has bactericidal action and plays an important role in the onset and progression of acute and chronic inflammatory diseases.

Conclusions

According to the literature, children and adolescents with obesity are more likely to develop cardiovascular risk factor and MetS. Abdominal obesity plays an important role on the pathophysiological process, linking obesity to atherosclerosis and cardiovascular diseases, clearly involving a chronic inflammatory state. Abdominal obesity leads to insulin resistance and the development of type 2 diabetes.

The goal should be to focus on the prevention and treatment of obesity in childhood and young adulthood, since its complications are harmful to health, leading to serious outcomes in later life. Hence, it becomes of great importance the awareness on individuals at high risk of overweight and obesity, mainly children and adolescents. The attention on their lifestyle is urgent, considering the quality of dietary habits and avoiding "obesogenic" environments, encouraging and increasing physical activity in groups, and adequate sedentary behavior to reduce it mostly during leisure time. Understand and build up an early behavior of healthy habits would be the basis for a future life with more health and wellness.

Abbreviations

AO: Abdominal obesity; Apo B: Apolipoproteina B; BP: Blood pressure; CRP: C-reactive protein; FFAs: Free fatty acids; HDL-C: High-density lipoprotein cholesterol; HOMA: Homeostatic model assessment; IDF: International Diabetes Federation; IL-6: Interleukin-6; IR: Insulin resistance; IRS-1: Insulin receptor substrate; LDL-C: Low-density lipoprotein cholesterol; MetS: Metabolic syndrome; MPO: Myeloperoxidase; PAI-1: Plasminogen activator inhibitor-1; SNS: Sympathetic nervous system; TG: Triglycerides; TNF-alpha: Tumor necrosis factor alpha; VLDL: Very-low-density lipoprotein

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Authors' contributions

EF participated in the design the work and drafted and revised the manuscript. TU helped to draft the manuscript and revised the manuscript. MF and AM revised the manuscript. LM conceived, designed, and revised the work that led to the submission of the manuscript. HC designed and revised the work that led to the submission of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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4.2 Article 2

Abdominal obesity and its association with socioeconomic factors among adolescents from different living environments

Running title – Abdominal obesity and socioeconomic status

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Abstract

Objectives: To evaluate the association between different socioeconomic indicators such as parental education and occupation, and socioeconomic status with abdominal obesity (AO) in adolescents from two observational studies; Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study (HELENA-CSS) and Brazilian Cardiovascular Adolescent Health (BRACAH) study.

Methods: European (n=3192 aged 12.5-17.5y, with 53.1% girls from HELENA-CSS) and Brazilian (n= 991aged 14-18y, with 54.5% girls from BRACAH study) adolescents from two cross-sectional studies, were included in this analysis. Complete data on waist circumference (WC), height, socioeconomic status indicators and several confounders were collected. Socioeconomic indicators were measured using a self-reported questionnaire in order to assess the family social status of the adolescents. Multilevel linear regression models were used to examine associations, and results were adjusted for potential confounders.

Results: Adjusted results showed inverse associations between mother's and father's education levels ($p<0.001$) and father's occupation level ($p<0.001$) with waist to height ratio (WHtR) and WC in HELENA-CSS girls. Similarly, in European girls, socioeconomic indicators by socioeconomic status and maternal occupation level were associated with WHtR. In HELENA-CSS boys, the same significant association was found between WHtR and WC with maternal occupation level. Moreover, in European boys WHtR was also associated with parental education. In Brazilian adolescents, both indicators of abdominal obesity did not remain associated with the independents variables, after adjustment for potential confounders.

Conclusions: Abdominal obesity was associated with socioeconomic indicators in higher income countries, but this association was not observed in a lower-middle income country.

Keyword: Abdominal obesity, adolescents, risk factors, socioeconomic status.

Introduction

In developing countries, the prevalence of obesity in childhood and adolescence has gradually increased over the past decades (1). However, in developed countries such as USA, Australia, Japan and most of Europe, a clear indication of stability or leveling off has been observed (2). In developing countries, social and economic changes were very fast, leading children and adolescents to choose energy dense foods of low nutritional value, combined with low levels of physical activity, increasing the likelihood of developing overweight(3).

Obesity in childhood is associated with an increased risk of developing cardiovascular and metabolic diseases in adulthood. Abdominal obesity is a better indicator of many chronic diseases such as hypertension, type 2 diabetes, metabolic syndrome and cardiovascular diseases than total obesity (4). Recent studies underline the importance of examining abdominal obesity levels using low cost measurements of anthropometric indices, which can strongly prevent the occurrence of cardiometabolic risk in adolescence through adulthood (5).

Waist circumference (WC) and waist-to-height ratio (WHtR) are anthropometric indices used for defining abdominal obesity. Despite body mass index being widely used as a measure to evaluate the impact of obesity on cardiovascular and metabolic risk factors, both in children and adults, it does not relate to central obesity, because it has

high specificity but low sensitivity to identify excess adiposity of children(6), and cannot differentiate muscle mass, from fat mass(7). As body mass index, WC is not an ideal tool for mass screening either because diagnostic references are age-specific and, they are age-dependent indices (8). However, WHtR is independent of age, gender or race/ethnicity and has been considered as a simple anthropometric index of abdominal obesity, being reported as a good indicator of the risk for cardiovascular disease(9). Several studies have reported the prevalence of abdominal obesity among children and adolescents throughout the world. In Shandong, China the prevalence rates defined by WHtR≥0.5, reached 16,45% for boys and 7,80% for girls, in 2010(10). In American children and adolescents, the prevalence of abdominal obesity leveled off from 2003-2004 to 2011-2012, although it still remains high, about 33% defined by WHtR and 19% defined by WC(11).

Regardless of the association between indicators of socioeconomic status (SES), in most developed countries, there is an inverse gradient between SES and adult overweight and obesity. This strong association has also been observed with low SES in early life and, overweight and obesity in adulthood(12). In children and adolescents, wealth and other socioeconomic indicators have shown some association with abdominal obesity(13).

The aim of this study was to assess how abdominal obesity in adolescents is distributed according to different indicators of SES, including parental education, parental occupation and socioeconomic level (*Family Affluence Scale*) (14), from two observational studies: the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study(HELENA-CSS) and the Brazilian Cardiovascular Adolescent Health (BRACAH) study.

Methods

Studies design

Data from two cross-sectional studies, one European and one Brazilian were obtained. The European study, which was carried out from2006 to 2007, HELENA-CSS is a cross-sectional multi-centre examination of the nutritional and lifestyle status of adolescents in ten cities from nine European countries: Dortmund (Germany), Stockholm (Sweden), Athens (Greece), Heraklion (Greece), Rome (Italy), Zaragoza (Spain), Pecs (Hungary), Ghent (Belgium) Lille (France), and Vienna (Austria), which stratified 3528 adolescents, 52.3% girls, (aged 12.5 -17.5 years) by age, geographic location and SES.

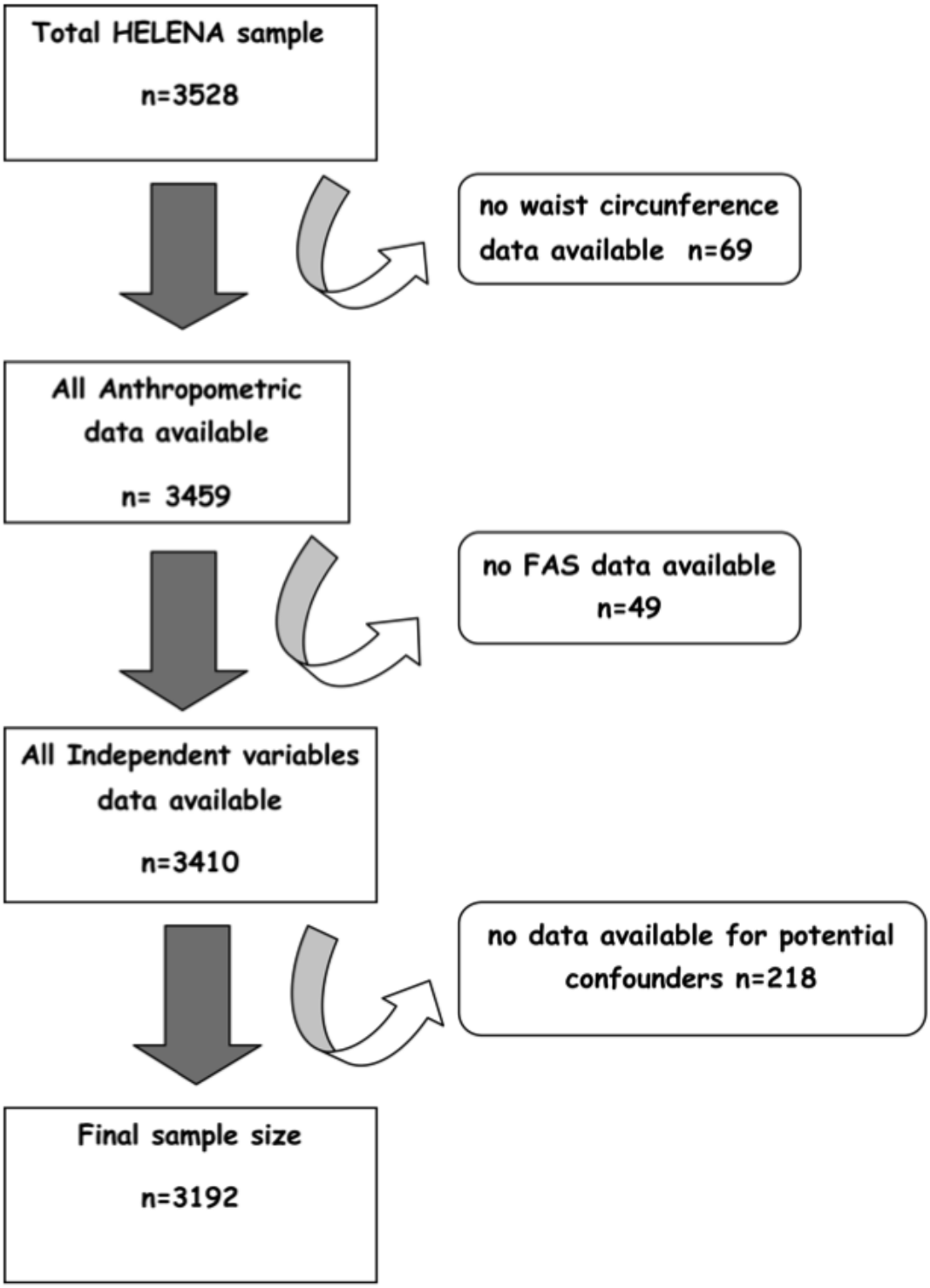
From the total number (n=3528) of adolescents studied in the HELENA-CSS, we included in this analysis n=3192, (53.1% girls), because for the 336 of the participants there were no available data for variables used, (see the *Supplementary material*). The harmonization and methodology from HELENA-CSS has been described in detail elsewhere (15).

Parents/guardians and adolescents provided a written informed consent, and the study was approved by Research Ethics Committee of the centres involved (for most,

this was the countries' Minister of Health) and was performed following the ethical guidelines of Declaration of Helsinki, 1961(revision of Edinburgh, 2000) (16).

The Brazilian study, BRACAH study, was conducted in 2007, in the city of Maringá (PR), southern region of Brazil, with a population of approximately 330,000 people. A total of 991 adolescents, 54.5%girls, (aged 14-19 years) after random selection from public and private schools, were evaluated according to cardiovascular risk factors as well as healthy behavior parameters.

A parental consent was obtained. The study was approved by the Ethics Committee on Research Involving Human Participants of the University Center of Maringá and authorized by the Ethics Committee on Research Projects of the University of São Paulo, in accordance with Brazilian laws(17). In both studies the inclusion criteria were met, being the participants included in the analysis.



Supplementary file: File sample size flowchart

Outcomes

Anthropometric measurements

In this study, anthropometric indicators such as WC and WHtR defined abdominal obesity. WC was measured in both studies using a non-elastic tape to the nearest 0.1cm in the midpoint between the lowest border of the rib cage and the upper border of iliac crest at minimal respiration, when the participant was in a standing position. Height was measured barefoot in the Frankfort plane, using a telescope height measuring instrument (Type SECA 225), to the nearest 0.1cm (18). WHtR was calculated as waist size divided by height, both in centimeters (cm) (9).

Independent variables

Socioeconomic status (SES)

Socioeconomic status was considered a socioeconomic indicator and was assessed by a self-reported questionnaire and sorted in both studies in three levels: low, medium and high.

In the HELENA-CSS the SES was measured by an affluence index - *Family Affluence Scale (FAS)*. This index measures the socioeconomic adolescent circumstances' reflect expenditure and consumption based on material conditions of the adolescent family, indicating affluence or material deprivation(19). The scale consists of four questions: *Do you have your own bedroom?, How many cars are there in your family?, How many PCs are there in your home?*;and *Do you have internet access at home?* After the final score was computed based on summing the numerical value of each question answered, the final score ranged 0-8. Finally, the scores were grouped into three levels of socioeconomic status: low (from 0 to 2), medium (from 3 to 5) and high (from 6 to 8). The scale has been used in previous HELENA studies (20, 21), as well as in large epidemiologic studies(14).

In the BRACAH study, the Brazil Criterion of Economic Classification was applied (22). These criteria consider parents' education level, presence/absence and number of domestic appliances, vehicles and rooms in the adolescent's home. Through a specific score (range 0–46) attributed by the questionnaire, the family was classified into one of seven categories (A_1 [the wealthiest], A_2, B_1, B_2, C, D and E [the poorest]). In BRACAH these categories were grouped into three levels as well: low (D and E), medium (B_2 and C)and high (A_1, A_2 and B_1)(22)

Parental education

A self-reported questionnaire regarding parental education included four categories: lower education, lower secondary education, higher secondary education and university degree (21).

Parental occupation

This was only assessed in the European adolescents. Regarding parental occupation, 12 categories were assessed by questionnaire: legislators, senior officials or managers,

professionals, technicians and associate professionals, clerks, service workers and shop and market sales workers, skilled agricultural and fishery worker, craft and related workers, plant and machine operators and assemblers, unskilled occupations, armed forces, other namely and does not work. Finally, these categories were grouped in four levels in order to homogenize the samples in each group: low occupation level, medium-high occupation level, high occupation level and undefined class. The category-undefined class was excluded from the analyses due to the large number of responses with low frequency in each (21).

Potential Confounders

Confounders were analyzed:

*Age (years): calculated from birthday and medical examination day.

*Center (HELENA-CSS only)

Statistical Analysis

All the analyses were stratified by sex and study. Descriptive analyses were presented as means (quantitative variables), percentages (qualitative variables) and 95% confidence intervals (CI95%). Trends in mean WC and WHtR across SES variables were examined by using multilevel linear regression models, with consideration of age and gender. In the univariate analysis for maintenance of confounding variables in the multivariate model, we adopted the significance level, a value of $p \leq 0.20$. Each independent variable was introduced separately, and the analyses were stratified by sex. Significance was set at p-values < 0.05, after controlling for multiple testing using the Bonferroni correction. Statistical analysis was performed by using Stata12 (Stata Corp., College Station, TX, USA).

Results

The main characteristics of the adolescents, studied in both studies, are presented in *Table 1*. Significant differences were observed in weight and height when European boys with Brazilian boys were compared, and WC and WHtR when the comparison was done between European adolescents with Brazilian adolescents. Another significant difference was found for parents' education level, where parents of European adolescents are more numerous at the university degree and parents of Brazilian adolescents in high secondary education. Considering the mother´s occupation level, we observed that medium high occupation level represented the higher percentage of

European adolescents. Nevertheless, among European girls, we found fathers in the lowest level of occupation, and among European boys, the father's occupation level was the highest.

*Tables S1*and *S2* present unadjusted data, showing that parental education level was inversely associated with abdominal obesity (WC andWHtR) in European adolescents, while this association was observed considering father's occupation level, only in European girls. An inverse association was also observed in Brazilian girls between father's education level and WHtR, and there was a positive association in Brazilian boys between mother's education level with WC and WHtR.

On the other hand, as shown in *TablesS1*and*S2,* socioeconomic level showed a significant association only with WHtR in European adolescents, and also in girls from the BRACH study with WC and WHtR. However, these associations in Brazilian adolescents were not significant when analysis was adjusted for potential confounders. Further to the aforementioned, after adjustment for confounders, *Table 2* shows the associations among SES indicators and abdominal obesity - related with WC's variable. Education of mothers ***(p=0.001)*** and fathers ***(p<0.001)*** was negatively associated with WC in European girls, as well as father's occupation level ***(p<0.001)*.**Mother's occupation level ***(p=0.022)*** also showed an inverse association with WC in European boys.

Table 3 shows that significant associations were found among SES indicators such as socioeconomic status ***(p=0.006),*** parental education ***(p<0.001)*** and occupation ***(p<0.05)****,* with abdominal obesity - related with waist-to-height's variable, in HELENA-CSS girls. Similarly, a negative association was observed in European boys with mother's ***(p=0.039)*** and father's education ***(p=0.027)*** and mothers' occupation level ***(p=0.001)*** with WHtR. Among Brazilian adolescents, no significant association was found.

Table 1: Main characteristics of the studied adolescents from the HELENA-CSS and BRACAH studies

	Girls		Boys	
	HELENA mean (CI95%)	**BRACAH mean (CI95%)**	**HELENA mean (CI95%)**	**BRACAH mean (CI95%)**
Age (years)	14.7(14.6 – 14.8)	16.2 (16.2 –16.3)	14.8 (14.7 – 14.8)	16.4 (16.3 – 16.5)
Weight (kg)	56.0(55.5 – 56.5)	56.3(55.5 – 57.1)	62.5 (61.8 – 63.2)	67.2(66.0 – 68.5)
Height (cm)	162.0(161.7-162.4)	162.7(162.2-163.2)	169.9(169.5-170.4)	175.2(174.6-175.8)
BMI (kg/m²)	21.3 (21.1 – 21.5)	21.3(21.0 – 21.6)	21.5(21.3 -21.7)	21.8(21.5-22.2)
Waist (cm)	70.2(69.8 – 70.6)	77.3(76.5 – 78.1)	74.4(73.9 - 74.9)	80.4(79.5 – 81.4)
Waist/Height	0.43(0.43 - 0.44)	0.48(0.47 - 0.48)	0.44(0.44 - 0.44)	0.46(0.45 - 0.46)
Socioeconomic status	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Low_SES	255 (14.9)	42 (7.8)	180 (11.6)	18 (4.0)
Medium_SES	953 (55.8)	424 (78.5)	887 (57.2)	367 (81.4)
High_SES	500 (29.3)	74 (13.7)	483 (31.2)	66 (14.6)
Education mother	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Low education	142 (8.67)	45 (8.44)	121 (8.24)	29 (6.46)
Low secondary education	418 (25.53)	132 (24.77)	402 (27.38)	113 (25.17)
High secondary education	528 (32.25)	228 (42.78)	454 (30.93)	192 (42.76)
University degree	549 (33.54)	128 (24.02)	491 (33.45)	115 (25.61)
Education father	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Low education	130 (8.31)	42 (7.97)	101 (7.03)	28 (6.41)
Low secondary education	474 (30.31)	141 (26.76)	429 (29.87)	110 (25.17)
High secondary education	427 (27.30)	240 (45.54)	403 (28.06)	206 (47.14)
University degree	533 (34.08)	104 (19.73)	503 (35.03)	93 (21.28)
Occupation Mother	**n (%)**		**n (%)**	
Low occupation level	289 (16.4)		240 (15.2)	
Medium high occupation level	688 (39.0)		578 (36.6)	
High occupation level	285 (16.2)		292 (18.5)	
Occupation Father	**n (%)**		**n (%)**	
Low occupation level	501 (29.6)		380 (24.5)	
Medium high occupation level	472 (27.9)		441 (28.4)	
High occupation level	446 (26.3)		462 (29.8)	

HELENA-CSS (Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study) **BRACAH study** (Brazilian Cardiovascular Adolescent Health)

Table S1. Unadjusted association between socioeconomic indicators and abdominal obesity (waist circumference) in European and Brazilian adolescents

	Girls		Boys	
	HELENA	BRACAH	HELENA	BRACAH
	mean (95%CI)	mean (95%CI)	mean (95%CI)	mean (95%CI)
Education mother	**(n=1697)**	**(n=540)**	**(n=1548)**	**(n=451)**
Low education	**71.8 (70.3 – 73.3)**	77.9 (75.1 – 80.6)	**75.3 (73.4 – 77.2)**	**80.0 (76.5 – 83.6)**
Low secondary education	**71.3 (70.5 - 72.0)**	77.5 (75.9 – 79.0)	**76.2 (75.2 – 77.3)**	**78.6 (76.9 –80.2)**
High secondary education	**70.3 (69.6– 71.0)**	77.7 (76.7 – 78.9)	**74.4 (73.6 – 75.3)**	**79.9 (78.6 – 81.3)**
University degree	**68.9 (68.3– 69.5)**	76.1 (74.1 – 78.1)	**72.7 (72.0 – 73.4)**	**83.2 (80.8 – 85.6)**
p for trend	**p= 0.0000**	p= 0.2273	**p= 0.0000**	**p= 0.0039**
Education father	**(n=1697)**	**(n=540)**	**(n=1548)**	**(n=451)**
Low education	**72.6 (71.0 – 74.3)**	78.5 (75.7 – 81.4)	**76.0 (73.8 – 78.2)**	80.5 (76.1 – 84.9)
Low secondary education	**71.1 (70.3 - 71.8)**	77.0 (75.3 – 78.8)	**75.8 (74.7 – 76.8)**	79.9 (77.9 –81.9)
High secondary education	**70.2 (69.4 – 71.0)**	78.0 (76.9 – 79.1)	**74.0 (73.1 – 74.9)**	79.8 (78.5 – 81.1)
University degree	**68.8 (68.2 – 69.4)**	75.1 (73.5 – 76.7)	**73.0 (72.3 – 73.7)**	82.6 (80.0 – 85.1)
p for trend	**p= 0.0000**	p= 0.0920	**p= 0.0000**	p= 0.1579
Socioeconomic status	**(n=1697)**	**(n=540)**	**(n=1548)**	**(n=451)**
Low_SES	70.5 (69.5 – 71.6)	**77.1 (74.5 – 79.9)**	74.9 (73.4 – 76.6)	79.7 (75.2 – 84.2)
Medium_SES	70.3 (69.8 – 70.8)	**77.9 (76.9 – 78.8)**	74.1 (73.5 – 74.8)	80.2 (79.1– 81.3)
High_SES	69.9 (69.2 – 70.5)	**74.5 (72.6 – 76.3)**	74.4 (73.5 – 75.2)	81.8 (79.4 – 84.2)
p for trend	p= 0.2244	**p= 0.0451**	p= 0.7097	p= 0.2528
Occupation mother	**(n=1813)**		**(n=1646)**	
Low occupation level	71.2 (70.2 - 72.1)		75.5 (74.2 – 76.8)	
Med-high occupation level	70.5 (69.9 - 71.1)		73.8 (73.1 – 74.5)	
High occupation level	69.1 (68.2 –70.0)		72.8 (71.9 -73.7)	
p for trend	P=0.0542		P=0.2208	
Occupation father	**(n=1813)**		**(n=1646)**	
Low occupation level	**71.3 (70.5 –72.0)**		74.8(73.7 –75.8)	
Med- high occupation level	**70.4 (69.7- 71.1)**		74.5 (73.7 -75.4)	
High occupation level	**68.7 (68.1- 69.4)**		73.6 (72.9 -74.4)	
p for trend	**P=0.0048**		P=0.8090	

Significant associations are in bold.

Table S2. Unadjusted association between socioeconomic indicators and abdominal obesity (waist to height) in European and Brazilian adolescents

	Girls		Boys	
	HELENA	BRACAH	HELENA	BRACAH
	mean (95%CI)	mean (95%CI)	mean (95%CI)	mean (95%CI)
Education mother	**(n=1697)**	**(n=540)**	**(n=1548)**	**(n=451)**
Low education	**0.45 (0.44 –0 .46)**	0.48 (0.46 – 0.50)	**0.45 (0.44 – 0.46)**	**0.46 (0.44 – 0.48)**
Low secondary education	**0.44 (0.44 - 0.45)**	0.48 (0.47 – 0.49)	**0.45 (0.44 – 0.46)**	**0.45 (0.44 – 0.46)**
High secondary education	**0.44 (0.43 – 0.44)**	0.48 (0.47 – 0.49)	**0.44 (0.43 – 0.44)**	**0.46 (0.45 – 0.46)**
University degree	**0.42 (0.42 – 0.43)**	0.47 (0.45 –0.48)	**0.43 (0.42 – 0.43)**	**0.47 (0.46 – 0.49)**
p for trend	**p= 0.0000**	p= 0.2346	**p= 0.0000**	**p= 0.0221**
Education father	**(n=1697)**	**(n=540)**	**(n=1548)**	**(n=451)**
Low education	**0.46 (0.45 – 0.47)**	**0.48 (0.47 – 0.50)**	**0.45 (0.44 – 0.47)**	0.46 (0.44 – 0.50)
Low secondary education	**0.44 (0.43 - 0.44)**	**0.48 (0.47 – 0.49)**	**0.45 (0.44 – 0.45)**	0.46 (0.45 – 0.47)
High secondary education	**0.44 (0.43 – 0.44)**	**0.48 (0.47 – 0.49)**	**0.44 (0.43 – 0.44)**	0.46 (0.45 – 0.46)
University degree	**0.42 (0.42 – 0.43)**	**0.46 (0.45 – 0.47)**	**0.43 (0.42 – 0.43)**	0.47 (0.46 – 0.48)
p for trend	**p= 0.0000**	**p= 0.0303**	**p= 0.0000**	p= 0.2532
Socioeconomic status	**(n=1697)**	**(n=540)**	**(n=1548)**	**(n=451)**
Low_SES	**0.44 (0.43 – 0.45)**	**0.48 (0.46 –0 .50)**	**0.45 (0.44 – 0.45)**	0.46 (0.43 –0.48)
Medium_SES	**0.43 (0.43 – 0.44)**	**0.48 (0.47 – 0.49)**	**0.44 (0.43 – 0.44)**	0.46 (0.45 – 0.46)
High_SES	**0.43 (0.42 – 0.43)**	**0.45 (0.44 – 0.46)**	**0.43 (0.43 –0 .44)**	0.47 (0.46 – 0.48)
p for trend	**p= 0.0003**	**p= 0.0031**	**p= 0.0299**	p= 0.1207
Occupation mother	**(n=1813)**		**(n=1646)**	
Low occupation level	0.44 (0.44 - 0.45)		0.45 (0.44 - 0.45)	
Med-high occupation level	0.43 (0.43 - 0.44)		0.43 (0.43 - 0.44)	
High occupation level	0.42 (0.42 - 0.43)		0.43(0.42 - 0.43)	
p for trend	P=0.3001		P=0.2111	
Occupation father	**(n=1813)**		**(n=1646)**	
Low occupation level	**0.44 (0.44 -0 .45)**		0.44 (0.44 - 0.45)	
Med-high occupation level	**0.43 (0.43 -0.44)**		0.44 (0.43 -0 .44)	
High occupation level	**0.42 (0.42 - 0.43)**		0.43 (0.43 - 0.44)	
p for trend	**P= 0.0003**		P=0.3905	

Significant associations are in bold.

Table 2: Adjusted* association between socioeconomic indicators and abdominal obesity (waist circumference) in European and Brazilian adolescents

	Girls				Boys			
	HELENA	***p for trend***	**BRACAH**	***p for trend***	**HELENA**	***p for trend***	**BRACAH**	***p for trend***
	mean (95%CI)		**mean (95%CI)**		**mean (95%CI)**		**mean (95%CI)**	
Education mother	**(n=1610)**	**0.001**	**(n=533)**	0.751	**(n=1441)**	0.448	**(n=449)**	0.195
Low education	**71.7 (70.4 – 73.1)**		77.3 (74.4 – 80.2)		74.5 (72.8 – 76.1)		80.2 (76.4 – 84.0)	
Low secondary education	**70.9 (70.1 - 71.8)**		77.1 (75.2 – 79.0)		75.5 (74.5 – 76.4)		78.6 (76.6 –80.7)	
High secondary education	**70.3 (69.5 – 71.1)**		77.6 (76.1 – 79.2)		74.1 (73.3 – 74.9)		79.8 (78.1 – 81.4)	
University degree	**69.2 (68.4– 69.9)**		76.8 (74.9 – 78.7)		73.8 (72.9 – 74.6)		83.0 (81.0 – 85.1)	
Education father	**(n=1538)**	**<0.001**	**(n=527)**	0.287	**(n=1412)**	0.292	**(n=437)**	0.454
Low education	**72.2 (70.8 – 73.5)**		78.0 (75.0 – 81.0)		75.0 (73.3 – 76.8)		80.6 (76.7 – 84.6)	
Low secondary education	**70.9 (70.1 - 71.7)**		76.6 (74.7 – 78.4)		75.1 (74.2 – 76.0)		79.8 (77.7 –82.0)	
High secondary education	**70.0 (69.2 – 70.9)**		78.0 (76.4 – 79.5)		73.6 (72.7 – 74.5)		79.7 (78.0 – 81.3)	
University degree	**69.1 (68.3 – 69.8)**		76.1 (74.0 – 78.3)		74.0 (73.2 – 74.8)		82.4 (80.0 – 84.7)	
Socioeconomic status (SES)	**(n=1678)**	0.132	**(n=540)**	0.541	**(n=1521)**	0.825	**(n=451)**	0.510
Low_SES	70.8 (69.8 – 71.9)		76.7 (73.6 – 79.8)		74.7 (73.3 – 76.1)		79.7 (74.7 – 84.7)	
Medium_SES	70.2 (69.5 – 70.8)		77.7 (76.4 – 79.0)		74.1 (73.4 – 74.8)		80.1 (78.7– 81.5)	
High_SES	69.9 (69.1 – 70.7)		75.5 (73.1 – 78.0)		74.5 (73.6 – 75.4)		81.6 (78.8 – 84.3)	
Occupation mother	**(n=1243)**	0.084			**(n=1089)**	**0.022**		
Low occupation level	70.9 (69.9 - 71.9)				**75.0 (73.9 – 76.1)**			
Med-high occupation level	70.3 (69.6 - 71.0)				**73.7 (73.0 – 74.4)**			
High occupation level	69.8 (68.8 –70.8)				**73.3 (72.3 -74.3)**			
Occupation father	**(n=1397)**	**<0.001**			**(n=1261)**	0.650		
Low occupation level	**71.3 (70.6 –72.0)**				74.4(73.5 –75.4)			
Med-high occupation level	**69.9 (69.2- 70.7)**				74.2 (73.4 -75.1)			
High occupation level	**69.2 (68.5- 70.0)**				74.2 (73.3 -75.0)			

*Adjusted by potential confounders: Center (only HELENA-CSS) and Age. **Significant associations are in bold.** BRACAH, Brazilian Cardiovascular Adolescent Health; CI, confidence interval; HELENA-CSS, Healthy Lifestyle in Europe by Nutrition in Adolescence cross-sectional study; SES, socioeconomic status.

Table 3: Adjusted* association between socioeconomic indicators and abdominal obesity (waist-to-height) in European and Brazilian adolescents

	Girls				Boys			
	HELENA	***p for trend***	**BRACAH**	***p for trend***	**HELENA**	***p for trend***	**BRACAH**	***p for trend***
	mean (95%CI)		**mean (95%CI)**		**mean (95%CI)**		**mean (95%CI)**	
Education mother	**(n=1610)**	**<0.001**	**(n=533)**	0.843	**(n=1441)**	**0.039**	**(n=449)**	0.324
Low education	**0.45 (0.44 –0.46)**		0.47 (0.45 – 0.49)		**0.44 (0.43 – 0.45)**		0.46 (0.44 – 0.48)	
Low secondary education	**0.44 (0.44 - 0.45)**		0.47 (0.46 – 0.49)		**0.45 (0.44 – 0.45)**		0.45 (0.44 – 0.46)	
High secondary education	**0.43 (0.43 – 0.44)**		0.48 (0.47 – 0.49)		**0.44 (0.43 – 0.44)**		0.45 (0.45 – 0.46)	
University degree	**0.42 (0.42 – 0.43)**		0.47 (0.46 –0.49)		**0.43 (0.43 – 0.44)**		0.47 (0.46 – 0.48)	
Education father	**(n=1446)**	**<0.001**	**(n=527)**	0.396	**(n=1412)**	**0.027**	**(n=437)**	0.770
Low education	**0.45 (0.44 – 0.46)**		0.48 (0.46 – 0.50)		**0.45 (0.44 – 0.46)**		0.46 (0.44 – 0.49)	
Low secondary education	**0.44 (0.43 - 0.44)**		0.47 (0.46 – 0.48)		**0.44 (0.44 – 0.45)**		0.46 (0.44 – 0.47)	
High secondary education	**0.43 (0.43 – 0.44)**		0.48 (0.47 – 0.49)		**0.43 (0.43 – 0.44)**		0.46 (0.45 – 0.46)	
University degree	**0.42 (0.42 – 0.43)**		0.47 (0.45 – 0.48)		**0.43 (0.43 – 0.44)**		0.47 (0.46 – 0.48)	
Socioeconomic status (SES)	**(n=1678)**	**0.006**	**(n=540)**	0.386	**(n=1521)**	0.384	**(n=451)**	0.403
Low_SES	**0.44 (0.43 – 0.45)**		0.47 (0.45 –0 .49)		0.44 (0.43 – 0.45)		0.46 (0.43 –0.48)	
Medium_SES	**0.43 (0.43 – 0.44)**		0.48 (0.47 – 0.49)		0.44 (0.43 – 0.44)		0.46 (0.45 – 0.46)	
High_SES	**0.43 (0.42 – 0.44)**		0.46 (0.45 – 0.48)		0.44 (0.43 –0 .44)		0.47 (0.45 – 0.48)	
Occupation mother	**(n=1243)**	**0.016**			**(n=1089)**	**0.001**		
Low occupation level	**0.44 (0.43 - 0.45)**				**0.44 (0.44 - 0.45)**			
Med-high occupation level	**0.43 (0.43 - 0.44)**				**0.43 (0.43 - 0.44)**			
High occupation level	**0.43 (0.42 - 0.44)**				**0.43(0.42 - 0.43)**			
Occupation father	**(n=1397)**	**<0.001**			**(n=1261)**	0.050		
Low occupation level	**0.44 (0.44 -0 .45)**				0.44 (0.44 - 0.45)			
Med-high occupation level	**0.43 (0.43 -0.44)**				0.44 (0.43 -0 .44)			
High occupation level	**0.43 (0.42 - 0.43)**				0.43 (0.43 - 0.44)			

*Adjusted by potential confounders: Center (only HELENA-CSS) and Age. **Significant associations are in bold.**
BRACAH, Brazilian Cardiovascular Adolescent Health; CI, confidence interval; HELENA-CSS, Healthy Lifestyle in Europe by Nutrition in Adolescence cross-sectional study; SES, socioeconomic status.

Discussion

The association between abdominal obesity and affluence socioeconomic indicators measured by socioeconomic level (SES), parental education and occupation was assessed from adolescents of two observational studies. The findings in the current study indicate that socioeconomic level is associated with abdominal obesity (WC and WHtR) in European adolescents after adjustment for potential confounders – age and center (HELENA-CSS only). Results showed that parental education and father's

occupation level in European girls and mother's occupation level in European boys are significantly associated with abdominal obesity in both dependent variables analyzed. In Brazilian girls and boys, unadjusted analysis proved a significant association between parental education and waist-to-height ratio. However, after adjusting for age, this association did not retain significant. This is indicative of the fact that age is an important determinant in the development of obesity in adolescents. Several studies have linked obesity with age (4); relevant studies have attributed this event to the adolescents who have had unhealthy behaviors (lower physical activity level; higher consumption of sugar sweetened beverages) (23) than younger adolescents.

On the other hand, anthropometric and body composition changes are influenced by pubertal phenomena. Thus, early pubertal stage is a risk in the development and growth in adolescence reflecting the health of this population (e.g. distribution of body fat). As we did not evaluate this variable in our study, we have employed age as a proxy pubertal stage, because in general, the adolescents have a normal pubertal development.

In agreement with our findings, assessing SES by father's employment level indicated that girls whose father has lower level with employment showed higher prevalence of abdominal obesity when compared with others whose father had high employment status (24). In contrast, and in accordance with the findings reported regarding many low-middle-income countries, higher maternal education and employment level has been related with significantly higher odds of overweight or obesity among children and adolescents (25).Thus, in relation to children in low-middle-income countries, the high economic level relates to a gradual increase in the prevalence of overweight and obesity(26). The obesity epidemic is a complex public health problem. Eating behavior and lifestyles established in childhood often track into adulthood resulting in healthy or unhealthy conditions. Inequalities in health are usually established early in life, and socioeconomic status is the main determinant of these inequalities. Income inequality has increased steadily in recent years, increasing social and economic inequality, which reflects in a precarious health. This has also been perceived by increased prevalence of overweight among adolescents girls from low-middle-income countries in both urban and rural areas (27). Nevertheless, the increase in the income inequality observed lately have worsened the health of adolescents in general, since this is affected by social factors at personal, family, community and national level(28)

An important point that should be taken into consideration is the differences between being of low socioeconomic class in Brazil and being of low socioeconomic class in Europe, but it was not possible to measure in this study, (eg. purchasing power). However, we believe this to be a small limitation, because the self-reported questionnaires that measured the family SES were divided into three levels in both studies. In the context of this study, it is likely that the validity of criteria and tools used varied for each characteristic of the adolescents studied (29).

Because some methodological differences between the HELENA-CSS and the BRACAH study were present (e.g., age range and geographic region) data from both studies were analyzed separately. In order to control the influence (country specific) of contextual variables, multilevel analysis was applied to strengthen our present study.

Limitations

As mother's employment may be a modulator of the family environment, having a direct influence on lifestyle, physical activity and general behaviors of children, this variable was not measured in the sample of Brazilian adolescents; thus, this may be characterized as a limitation of our study.

In addition, it was not possible to adjust the analysis of other factors potentially associated with abdominal obesity in either of the two samples, such as physical activity and sedentary behavior because they are in the causative variables line.

Moreover, it was not possible to adjust the analysis for other potential abdominal obesity-associated factors such as genetics, intrauterine development or pubertal status in either of the two samples, but we developed an adjusted analysis for important potential confounders, and we stratified it by study and gender.

This study adds more evidence to the existing literature about predictors of abdominal obesity risk in adolescents. Thus, our report added scientific consistency, because we included data and described results from two different pediatrics populations (Hill's principles) (30).

Conclusions

Abdominal obesity was associated with socioeconomic indicators in higher income countries, but this association was not observed in a lower-middle-income country.

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4.3 Article 3

Skipping breakfast is associated with adiposity markers especially when sleep time is adequate in adolescents

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Abstract

Background: Adolescence as a critical stage of development an important influence has in energy balance-related behaviors (EBRBs). When they are associated with obesity lead to increased cardiometabolic risk.

Objectives: (**i**)to assess if EBRBs adopted by adolescents are associated to markers of total and abdominal adiposity in a multicenter European study and a Brazilian study, and (**ii**)to assess whether sleep duration influence the association between skipping

breakfast, physical activity(PA) and sedentary behaviors(SB), with total and abdominal obesity(AO).

Methods: Subsamples included adolescents from two cross-sectional studies: the *Healthy Lifestyle in Europe by Nutrition in Adolescence Study* (HELENA-CSS; 2371, *54.8%girls*) and the *Brazilian Cardiovascular Adolescent Health* (BRACAH) study (991, *54.5%girls*). Multilevel linear regression models using fixed and random intercepts analyzed the association between markers of obesity [body mass index (BMI), waist circumference (WC), waist-to-height (WHtR)] and EBRBs, stratified by sleep time, sex and study. Age, maternal education level and centre were used as confounders.

Results: Among European boys who slept less, the association with obesity markers did not remain after adjustment, suggesting the importance of the mother's educational level beyond age and where the adolescent lives. In addition, less sleep among Brazilian boys was protective for total obesity [β = -0.93kg/m^2; 95% confidence intervals (95%CI:-1.80; -0.07)].Skipping breakfast was the prevalent behavior in association with total and abdominal obesity among European and Brazilian boys besides European girls, remaining even after stratification by sleep time. Moreover, European boys who slept properly skip breakfast increased on average 2.83cm in WC and 0.02 in WHtR. As1.69kg/m2 in BMI in Brazilian boys. Similarly, among European girls the association showed an increase on average of 1.20cm in WC when they were more sedentary.

Conclusion: Skipping breakfast was associated with total and abdominal obesity in adolescents independently of sleep duration. Furthermore, sedentary behaviors for girls were also associated with abdominal obesity, especially for those who reported sleep adequately.

Keyword: Youth, Anthropometric, Abdominal obesity, Obesity, Energy balance-related behaviors, Cross-sectional study.

Introduction

Overweight/obesity represents a growing problem because they seriously affect health, leading to impaired quality of life for both, children and adults (1). The worldwide prevalence of childhood overweight and obesity rose from 4.2% to 6.7% between1990 to 2010. In this way, the expected trend is to reach 60million (9.1%) by 2020 (2). Regarding abdominal obesity(AO) it has been identified as atherosclerosis' determinant in young adults, independent of traditional risk factors [eg.BMI, adiponectin levels, and markers of insulin resistance(IR)] (3). Furthermore, in children and adolescents it is associated with cardiometabolic risk factors, such as IR, leading to the development of *type-2* diabetes (4).

Several energy balance-related behaviors (EBRBs) are associated with adiposity and are influenced by the environment and biological factors, and then they should be examined within a global strategy (5). Though the majority of the literature has focused on each behavior separately, analyzing the co-occurrence of several EBRBs could help identify subgroups at an increased risk of developing obesity (6). Combinations of behaviors as a set of several EBRBs are more prevalent than expected based on the

prevalence of each behavior separately (7). As adolescence is a critical period for the acquisition of healthy behaviors, they should be encouraged and well absorbed to prevent (or postpone) the onset of non-communicable diseases (8).

Among adolescents, scientists point out the role of behavioral factors in the etiology of obesity, especially dietary habits, PA and SB (9). However, other EBRBs have been identified as important, such as inadequate sleep time (10) and skipping breakfast (11). Sleep restriction through different mechanisms, plays an important role on adiposity, since it may influence the healthy-lifestyle (increasing SB and decreasing physical activity) (12). In the past decades there was an accelerated growth on skipping of breakfast at least among US children and adolescents, especially in older adolescents, mainly associated to behavioral changes (13).

In this context, the purposes of this study were**(i)**to assess if EBRBs adopted by adolescents are associated to markers of total and abdominal obesity of a multicenter European study and a Brazilian study, and (**ii**)to assess whether sleep time influence the association between skipping breakfast, physical activity and sedentary behaviors, with total and abdominal obesity.

Methods

Study design and sampling

The current study includes data from two school-based cross-sectional studies, one European and other Brazilian. In both studies, male and female adolescents from private and public schools in urban areas were eligible. The European study, *Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study* (HELENA-CSS), which was carried out from 2006 to 2007,is a multi-center study performed in 3528 adolescents(52.3 % girls; aged 12.5-17.5 years), stratified by age, sex, region and socio-economic status. In ten cities from nine European countries: Athens (Greece), Dortmund (Germany), Ghent (Belgium), Heraklion (Greece), Lille (France), Pecs (Hungary), Rome (Italy), Stockholm (Sweden),Vienna (Austria),Zaragoza(Spain),their nutritional status and lifestyle behavior were analyzed. The methodological aspects and standardization, harmonization and analysis strategies were described thoroughly elsewhere (14).Participants who met the following criteria were included: correct age range, not participating simultaneously in another clinical trial, and being free of any acute infection in the previous week. From the total sample, this analysis included 2371 adolescents (54.8 % girls) having available data from the used variables (*Supplementary material-1*).

Parents/guardians and adolescents signed the written consent form after receiving complete information about the study. The study was approved by the Research Ethics Committee of the centers involved, and was accomplished following the ethical principles of the Declaration of Helsinki, 1964 (revision of Edinburgh,Scotland2000) (15).

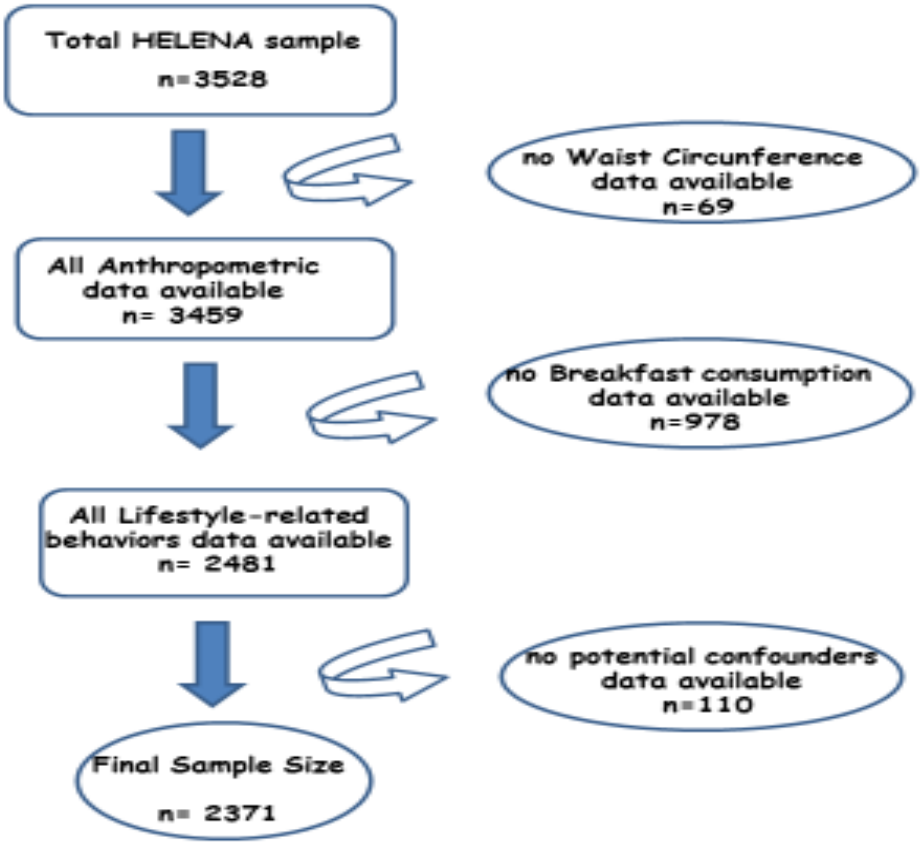
The Brazilian study, *Brazilian Cardiovascular Adolescent Health* (BRACAH) study data were collected in 2007, in a city of southern region of Brazil –*Maringá (PR)*

with a population of about330,000 inhabitants. After random selection, a total of 991adolescents (54.5% girls, aged 14-18years) were included and evaluated regarding to cardiovascular risk factors and health-related behaviors. The complete methodology and sample size of this study has been described elsewhere(16).Adolescents with orthopedic problems preventing anthropometric assessments, pregnancy or no parental consent met the exclusion criteria.

Parental informed consent was obtained and the adolescents agreed to participate in the study through their assent. The Ethics Committee on Research Involving Human Participants of the University Center of *Maringá* approved the study, which was authorized by the Ethics Committee on Research Projects of the University of São Paulo in accordance with Brazilian laws.

For the present study, adolescents from HELENA-CSS and BRACAH study were included since they had complete data on age, sex, weight, height and WC. Mother education level and EBRBs as PA,SB, sleep time and breakfast consumption were also the variables used in this study, which are described in detail below.

Supplementary material-1



Flowchart : included sample size of the *HELENA Study*

Outcomes

Anthropometric measurements

Weight was measured with an electronic scale (*Type SECA861*) in underwear and without shoes. For *height*, a telescopic height-measuring instrument (*Type SECA225*) was used to the nearest 0.1cmfor barefoot measurement in the Frankfort plane. The body mass index (BMI) was calculated through body weight(kg) divided by height(m) squared(17). Obesity (including overweight) was defined using the international BMI cutoffs suggested by Cole et al, which are based on the populations of several countries. They provide age and sex-specific, centile curves that at age 18 years passed through cutoff points of BMI for adult overweight and obesity as 25 and 30 kg/m^2,respectively(18). Abdominal obesity was defined using *waist circumference* (WC) and *waist-to-height ratio* (WHtR). WC was measured in both studies using a non-elastic tape (*TypeSECA200*) to the nearest 0.1cm in the midpoint between the lowest border of the rib cage and the upper border of iliac crest. Adolescents were in a standing position, abdomen relaxed and at the end of a normal expiration (17). WHtR was calculated as WC divided by height, both in centimeters (cm) and was categorized as the presence or absence of abdominal obesity when WHtR ≥ 0.5 or WHtR< 0.5, respectively(20).

Independent variables

Energy balance–related behaviors were measured and evaluated through a self-reported questionnaire in both studies.

Physical activity (PA) moderate–to-vigorous physical activity(MVPA) levels were assessed using the *International Physical Activity Questionnaire for Adolescents (*IPAQ-A),which was adapted and validated to adolescents from the long version of IPAQ(22). The IPAQ-A examined PA in different domains such as school (physical education classes and breaks), transport, home or garden and leisure time. The questionnaire was validated with the accelerometers in the adolescents from the HELENA-CSS (R^2=0.81), and in the BRACAH study this questionnaire showed an excellent agreement and reproducibility (*kappa-values*=0.91). Adolescents who accumulated at least 60min/day of moderate-to-vigorous physical activity were classified as active, following physical activity recommendations for school-age youth (23,24). In the present study the variable was categorized considering moderate-to-vigorous PA ≥60min/day (physically active) or <60min/day (insufficiently active).

Sedentary behaviors (SB) were examined over a structured questionnaire, which requested for habitual screen-time spent in front of television, computer and/or playing video games."*During weekdays, how many hours do you usually spend watching television*?";"*During weekdays, how many hours do you usually spend on computers*?"; "*During weekdays, how many hours do you usually spend playing video games*?".The same questions about weekend days were also inquired. Total SB time was calculated by summing hours in week and weekend days and classified according to: 0–2 h/d; >2–4 h/d; ≥4 h/d (25). The questionnaire was translated and adapted to each participating city, and its reproducibility and reliability were tested: *k-values*= 0.81 in the HELENA-

CSS(26) and *k-values*= 0.79 in the BRACAH study. In the current study this variable was dichotomized as ≤ 2hours/day (low) or >2hours/day (high).

Skipping breakfast: The "*Food Choices and Preferences*"(FCP) questionnaire (27) explored attitudes and concern issues regarding food choices, preferences, healthy eating and lifestyle among adolescents, and also it was used to assess breakfast consumption. Based on the agreement with the statement: *"I often skip breakfast"* participants answered with 7 categories varying from *strongly disagree* (1) to *strongly agree* (7) being the category 4 placed as neither agree, nor disagree categorizing the variables breakfast non-skipper (1to3) and breakfast skipper (5to7) (28). In the BRACAH study consumption of breakfast as well as the other main meals were evaluated by having them whether at home or not (29). So, the variable was also categorized as not skipping breakfast and skipping breakfast.

Sleep time was estimated through habitual sleep duration by questions:"*During weekdays how many hours (or minutes) do you usually sleep?"* and *"During weekend days how many hours (or minutes) do you usually sleep?"*A subsample of 183 adolescents (13-18 years) answered the questionnaire twice, one week apart to evaluate the reliability and reproducibility of these questions. Excellent agreement showed by the *Cohen's weighted kappa* of 0.81 during weekdays and 0.96 during weekend days (30, 31).In the final HELENA study sample this subsample did not participate, but also did not differ in age, ethnicity or socioeconomic status. In the present study sleep time was dichotomized as ≥ 8hours/day (adequate) or < 8hours/day (inadequate) (32).

Potential Confounders

Confounders were analyzed:
*Age (years): calculated from birthday and medical examination day
*Centre (cities participants only in the HELENA-CSS)
*Maternal education level: a self-reported questionnaire on the socioeconomic status was applied and assessed information on education level (used as a socioeconomic marker). It encloses four categories: elementary education, lower secondary education, higher secondary education and university degree (33).

Statistical analysis

Descriptive analyses were presented as means (quantitative variables) and percentages (qualitative variables) and 95% confidence intervals.
Multilevel linear regression models using fixed and random intercepts (school as contextual factors) stratified by sleep time, sex and study were used to investigate associations between EBRBs (independent variables) with total and abdominal obesity (outcomes). Age, maternal education level and centre entered as confounders. The magnitude of these associations was expressed in unadjusted and adjusted β-coefficients and their specific 95%confidencial intervals.
In order to clarify the distal and proximal determinants related to the outcomes, in the adjusted analyses, a conceptual framework has been created to shows the hierarchical relationship between these determinants, positioned at a contextual and individual level.

Centre (only HELENA-CSS) and school entered as contextual variable (distal exposure). Regarding the individual level, socio-demographic factors such as age, socioeconomic status (mother education level) were the intermediate exposures, and EBRBs to the adolescents constituted the proximal (34) (*supplementary material-2)*.
In the unadjusted analysis, each independent and confounder variable was introduced separately. A potential confounder was retained in the multivariate model, when significance level in the unadjusted analysis was *p-values*≤ 0.20 or any change of 10% in the β-coefficient. In multivariate analysis that followed the hierarquical conceptual model, according to the levels mentioned above, the significance was set at *p-values*<0.05. All the statistical analyses were stratified by sex and performed by using Stata12 (*Stata Corp., College Station, TX, USA*).

Supplementary material-2

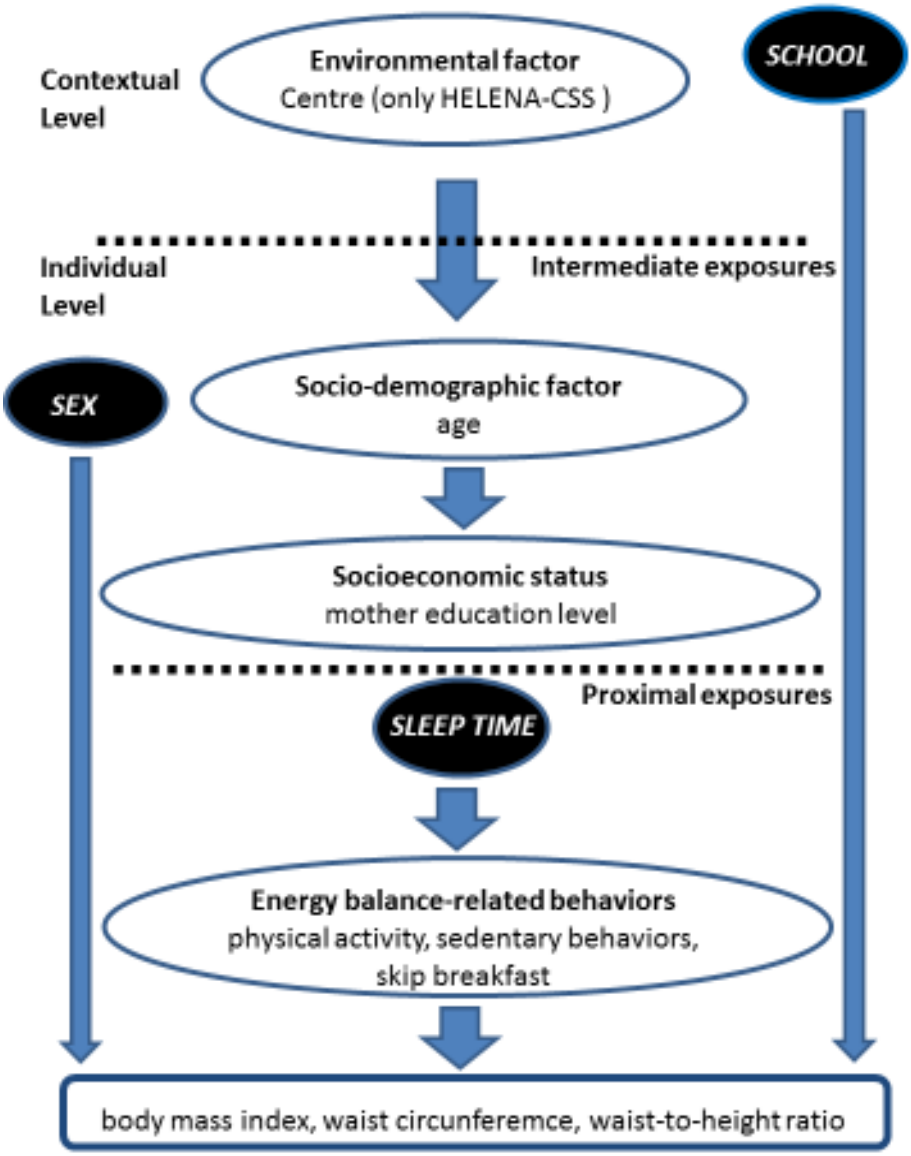


Figure1. Theoretical conceptual model for analysis of determinants of adiposity indicators

Results

Table1 presents the main characteristics of adolescents studied. Boys were heavier and taller than girls in both studies and had Brazilian boys had a larger WC. Otherwise, considering another visceral fat marker, Brazilian girls presented a higher WHtR than other adolescents. Related to EBRBs, European girls had lower prevalence on sedentary behaviors (>2h/day), but in counterpart they were less physically active than European boys, although more active (PA≥60min/day) than Brazilian adolescents. What concerns Brazilian adolescents, girls were more sedentary (>2h/day) than boys. Regarding breakfast consumption and sleep time, European and Brazilian boys had lower prevalence of skipping breakfast and adequate sleep time (≥8h/day) than girls. The association between EBRBs (independent variables) and outcomes (total and abdominal obesity) without adjustments (unadjusted analysis) are presented in *Table S1* (*supplementary material-3*).There was a positive association between skipping breakfast and SB with BMI and AO (WC and WHtR) among European girls. In European boys skip breakfast and sleep less than 8h/day, was associated with an increase of all adiposity indicators. On the contrary, among Brazilian boys, sleep less showed a negative association with indicators of adiposity.

After adjusted by potential confounders the significant association of skipping breakfast and SB with adiposity indicators was maintained in European girls. In boys from both studies, skip breakfast was the prevailing behavior, showing a positive association with the indicators of obesity (BMI, WC and WHtR), being highest with WC, and among Brazilian boys who slept less than 8h/day remained a negative association with BMI. On other hand, physical activity did not present any association with obesity, even after adjustments by the confounders (*Table2*).

Table3 shows the influence of sleeping time on the association between the studied EBRBs and the body composition outcomes. European girls even sleeping adequately (≥8h/day) experienced an increase on the indicators of total and abdominal obesity when they skipped breakfast and had higher SB (>2h/day).Concerning the duration of sleeping on European boys, both for adequate (≥8h/day) and inadequate duration (<8h/day), the positive association with obesity indicators happened when adolescents skipped breakfast. Likewise, in Brazilian boys when they skipped breakfast, there was an increase in average of 1.69kg/m^{2}in BMI and 0.02 in WHtR even when they slept properly. Regarding to the risk for obesity this behavior of skipping breakfast apparently had association indeed on this population.

Table1. Main characteristic of the studied adolesecents from HELENA-CSS and BRACAH studies

	Girls				Boys			
		HELENA		BRACAH		HELENA		BRACAH
	n	mean or % (95%CI)	n	mean or % (95%CI)	n	mean or % (95%CI)	n	mean or % (95%CI)
Age (years)	1372	14.7 (14.6 - 14.8)	540	16.2 (16.2 - 16.3)	1154	14.8 (14.7 - 14.8)	451	16.4 (16.3 - 16.5)
Weight (kg)		56.3 (55.8 -56.9)		56.3 (55.5 -57.1)		62.5 (61.7 - 63.3)		67.2 (66.0 - 68.5)
Height (cm)		162.3 (162.0 - 162.7)		162.7 (162.2 - 163.2)		170.2 (169.7 - 170.8)		175.2 (174.6 - 175.8)
BMI (kg/m²)		21.3 (21.2 - 21.5)		21.3 (21.0 - 21.6)		21.4 (21.2 - 21.7)		21.8 (21.5 - 22.2)
Waist circunference (cm)	1347	70.4 (70.0 - 70.8)	540	77.3 (76.5 - 78.1)	1134	74.2 (73.7 - 74.8)	451	80.4 (79.5 - 81.4)
Waist_height		0.43 (0.43 - 0.44)		0.48 (0.47 - 0.48)		0.44 (0.43 - 0.44)		0.46 (0.45 - 0.46)
Sleep time	1350		390		1121		331	
≥ 8 hours /day		66.2 (63.7 - 68.7)		51.3 (46.0 - 56.0)		67.2 (64.4 - 70.0)		57.1 (52.0 - 62.0)
< 8 hours /day		33.8 (31.3 - 36.3)		48.7 (44.0 - 54.0)		32.8 (30.1 - 35.6)		42.9 (38.0 - 48.0)
Skip breakfast	1372		540		1154		451	
no		55.5 (52.8 - 58.1)		62.2 (58.0 - 66.0)		64.1 (61.4 - 67.0)		65.4 (61.0 - 70.0)
yes		44.5 (42.0 - 47.2)		37.8 (34.0 - 42.0)		35.9 (33.1 - 38.6)		34.6 (30.0 -39.0)
Sedentary behavior	1372		540		1154		451	
≤ 2 hours /day		42.4 (39.8 - 45.0)		3.0 (2.0 - 4.0)		21.7 (19.3 - 24.0)		5.3 (3.0 - 7.0)
> 2 hours /day		57.6 (55.0 - 60.2)		97.0 (96.0 - 98.0)		78.3 (76.0 - 80.7)		94.7 (93.0 - 97.0)
Physical activity	1372		540		1154		451	
≥ 60 min /day		83.9 (82.0 - 85.8)		30.6 (27.0 - 34.0)		85.3 (83.2 - 87.3)		31.7 (27.0 - 36.0)
< 60 min /day		16.1 (14.2 - 18.1)		69.4 (66.0 - 73.0)		14.7 (12.7 - 16.8)		68.3 (64.0 - 73.0)
Education mother	1322		533		1091		449	
Low education		7.3 (5.9 - 8.7)		8.4 (6.1 - 10.8)		7.6 (6.0 - 9.2)		6.5 (4.2 - 8.7)
Secondary low education		24.1 (21.7 - 26.4)		24.8 (21.1 - 28.4)		25.6 (23.0 - 28.2)		25.2 (21.1 - 29.2)
Secondary high education		33.4 (30.8 - 36.0)		42.8 (38.6 - 47.0)		31.3 (28.6 - 34.1)		42.8 (38.2 - 47.4)
University degree		35.3 (32.7 - 38.0)		24.0 (20.4 - 27.7)		35.5 (32.6 - 38.3)		25.6 (21.6 - 29.7)

HELENA-CSS: Healthy Lifestyle in Europe by Nutrition in Adolescence cross-sectional study, BRACAH study: Brazilian Cardiovascular Adolescent Health study, BMI: body mass index

Table S1. Unadjusted association between EBRBs with adiposity indicators, among adolescents from HELENA-CSS and BRACAH study

	GIRLS				BOYS			
				BMI				
EBRBs		**HELENA**		**BRACAH**		**HELENA**		**BRACAH**
	n	**coef β (95%CI)**	**n**	**coef β (95%CI)**	**n**	**coef β (95%CI)**	**n**	**coef β (95%CI)**
Sleep time	1350	**(p=0.02)**	390	(p=0.883)	1121	**(p<0.001)**	331	**(p=0.033)**
≥8h/day		Ref.		Ref.		Ref.		Ref.
<8h/day		**0.47 (0.07;0.87)**		-0.05(-0.72 ; 0.62)		**0.93(0.44 ;1.42)**		**-0.93(-1.79 ; -0.08)**
Skip breakfast	1372	**(p<0.001)**	540	(p=0.649)	1154	**(p<0.001)**	451	**(p=0.002)**
no		Ref.		Ref.		Ref.		Ref.
yes		**0.88(0.50 ; 1.26)**		-0.14(-0.73 ; 0.46)		**1.60(1.13 ; 2.06)**		1.17(0.41 ; 1.92)
Sedentary behavior	1372	**(p=0.015)**	540	(p=0.759)	1154	(p=0.061)	451	(p=0.432)
≤2h/day		Ref.		Ref.		Ref.		Ref.
>2h/day		**0.47 (0.09 ; 0.85)**		0.27(-1.45 ; 1.98)		0.53 (-0.03 ; 1.08)		-0.65(-2.27 ; 0.97)
Physical activity	1372	(p= 0.80)	540	(p=0.225)	1154	(p= 0.674)	451	(p=0.805)
≥60min/day		Ref.		Ref.		Ref.		Ref.
<60min/day		0.06(-0.45 ; 0.58)		0.40(-0.25 ; 1.04)		-0.14(-0.78 ; 0.51)		-0.10(-0.89 ; 0.69)
				Waist Circunference				
EBRBs		**HELENA**		**BRACAH**		**HELENA**		**BRACAH**
	n	**coef β (95%CI)**	**n**	**coef β (95%CI)**	**n**	**coef β (95%CI)**	**n**	**coef β (95%CI)**
Sleep time	1325	(p=0.250)	390	(p=0.463)	1101	**(p=0.002)**	331	**(p=0.042)**
≥8h/day		Ref.		Ref.		Ref.		Ref.
<8h/day		0.52(-0.37 ; 1.42)		-0.72(-2.65 ; 1.21)		**1.83(0.66 ; 3.00)**		**-2.34(-4.59 ; -0.09)**
Skip breakfast	1347	**(p=0.006)**	540	(p=0.417)	1134	**(p<0.001)**	451	**(p=0.026)**
no		Ref.		Ref.		Ref.		Ref.
yes		**1.19(0.35 ; 2.04)**		0.67(-0.95 ; 2.29)		**3.21(2.09 ; 4.33)**		2.28(0.28 ; 4.29)
Sedentary behavior	1347	**(p=0.002)**	540	(p=0.534)	1134	(p=0.193)	451	(p=0.929)
≤2h/day		Ref.		Ref.		Ref.		Ref.
>2h/day		**1.34(0.49 ; 2.19)**		1.49(-3.20 ; 6.18)		0.87(-0.44 ; 2.18)		-0.20(-4.49 ; 4.10)
Physical activity	1347	(p=0.51)	540	(p=0.929)	1134	(p=0.784)	451	(p=0.368)
≥60min/day		Ref.		Ref.		Ref.		Ref.
<60min/day		0.39 (-0.75 ; 1.52)		0.08(-1.68 ; 1.84)		0.21 (-1.32 ; 1.75)		-0.98(-3.11 ; 1.15)
				Waist to Height				
EBRBs		**HELENA**		**BRACAH**		**HELENA**		**BRACAH**
	n	**coef β (95%CI)**		**coef β (95%CI)**	**n**	**coef β (95%CI)**	**n**	**coef β (95%CI)**
Sleep time	1325	(p=0.21)	390	(p=0.759)	1101	(p=0.559)	331	**(p=0.068)**
≥8h/day		Ref.		Ref.		Ref.		Ref.
<8h/day		0.00 (-0.00 ; 0.01)		-0.00(-0.01 ; 0.01)		0.00 (-0.01 ; 0.01)		**-0.01(-0.02 ; 0.00)**
Skip breakfast	1347	**(p<0.001)**	540	(p=0.850)	1134	**(p<0.001)**	451	**(p=0.003)**
no		Ref.		Ref.		Ref.		Ref.
yes		**0.01(0.01 ; 0.02)**		0.00(-0.01 ; 0.01)		**0.02 (0.01 ; 0.02)**		**0.02(0.01 ; 0.03)**
Sedentary behavior	1347	**(p<0.001)**	540	(p=0.317)	1134	**(p=0.087)**	451	(p=0.818)
≤2h/day		Ref.		Ref.		Ref.		Ref.
>2h/day		**0.01(0.01; 0.02)**		0.02(-0.01 ; 0.04)		**0.01(-0.00; 0.01)**		-0.00(-0.03 ; 0.02)
Physical activity	1347	(p=0.696)	540	(p=0.311)	1134	(p=0.252)	451	(p=0.863)
≥60min/day		Ref.		Ref.		Ref.		Ref.
<60min/day		0.00(-0.01 ; 0.02)		0.01(-0.01 ; 0.02)		-0.01(-0.01 ; 0.00)		-0.00(-0.01 ; 0.01)

Significant association are in bold. EBRBs: energy balance-related behaviors,BMI: body mass index, HELENA-CSS :Healthy Lifestyle in Europe by Nutrition in Adolescence cross-sectional study, BRACAH study:Brazilian Cardiovascular Adolescent Health study, 95%CI: confidence interval, coef β: beta coeficiente.

Table 2. Adjusted* association between EBRBs with total and abdominal obesity, among adolescents studied from HELENA-CSS and BRACAH study

	Girls					
	HELENA			BRACAH		
	n	coef β (95%CI)	p	n	coef β (95%CI)	p
BMI						
Sleep time	1301	0.20 (-0.21 ; 0.61	0.337	385	0.02(-0.63 ; 0.68)	0.941
Skip breakfast	1322	**0.70 (0.32 ; 1.08)**	**<0.001**	533	-0.10(-0.69 ; 0.49)	0.743
Sedentary behavior	1322	0.30(-0.09 ; 0.69)	0.129			
Physical activity	1322	-0.11(-0.63 ; 0.40)	0.666	540	0.33(-0.33 ; 0.98)	0.330
Waist circunference						
Sleep time	1325	-0.02(-0.92 ; 0.88)	0.97	385	-0.57(-2.49 ; 1.35)	0.560
Skip breakfast	1300	**0.98(0.12 ; 1.83)**	**0.025**	533	0.86(-0.76 ; 2.47)	0.298
Sedentary behavior	1300	**1.19(0.32 ; 2.06)**	**0.007**			
Physical activity	1347	-0.05(-1.19 ; 1.08)	0.93	540	-0.03(-1.83 ; 1.78)	0.978
Waist to Height						
Sleep time						
Skip breakfast	1300	**0.01(0.00 ; 0.01)**	**0.001**			
Sedentary behavior	1300	**0.01(0.00 ; 0.02)**	**<0.001**			
Physical activity						

	Boys					
	HELENA			BRACAH		
	n	coef β (95%CI)	p	n	coef β (95%CI)	p
BMI						
Sleep time	1062	0.43 (-0.08 ; 0.93)	0.100	330	**-0.93(-1.80 ; -0.07)**	**0.035**
Skip breakfast	1091	**1.27 (0.79 ; 1.75)**	**<0.001**	449	**1.11 (0.35 ; 1.87)**	**0.004**
Sedentary behavior	1091	0.29(-0.26 ; 0.83)	0.302	449	-0.73(-2.39 ; 0.93)	0.392
Physical activity	1091	-0.43(-1.08 ; 0.22)	0.195	449	-0.05(-0.83 ; 0.74)	0.910
Waist circunference						
Sleep time	1042	0.55(-0.65 ; 1.74)	0.369	330	-2.17(-4.43 ; 0.09)	0.060
Skip breakfast	1071	**2.61(1.47 ; 3.74)**	**<0.001**	449	**2.13(0.12 ; 4.15)**	**0.038**
Sedentary behavior	1071	0.60(-0.68 ; 1.88)	0.358	449	-0.73(-5.09 ; 3.63)	0.744
Physical activity	1071	-0.63(-2.16 ; 0.90)	0.418	449	-0.77(-2.87 ; 1.33)	0.472
Waist to Height						
Sleep time				330	-0.01(-0.02 ; 0.00)	0.091
Skip breakfast	1071	**0.02(0.01 ; 0.03)**	**<0.001**	449	**0.02 (0.01 ; 0.03)**	**0.005**
Sedentary behavior	1071	0.00(-0.00 ; 0.01)	0.320	449	-0.01(-0.03 ; 0.02)	0.71
Physical activity	1071	-0.01(-0.01 ; 0.00)	0.270			

Adjusted by potention confounders: center(only in HELENA-CSS),age and education mother. Significant association are in bold. EBRBs: energy balance-related behaviors,BMI: body mass index, HELENA-CSS :Healthy Lifestyle in Europe by Nutrition in Adolescence cross-sectional study, BRACAH study:Brazilian Cardiovascular Adolescent Health study, 95%CI: confidence interval, coef β: beta coeficiente.

Table 3. Adjusted* association between EBRBs and general and abdominal obesity stratified by sleep time among adolescents girls studied from HELENA-CSS and BRACAH study

	Sleep time ≥ 8 h/day						Sleep time < 8 h/day					
	HELENA			BRACAH			HELENA			BRACAH		
	n	coef β (95%CI)	p	n	coef β (95%CI)	p	n	coef β (95%CI)	p	n	coef β (95%CI)	p
BMI												
Skip breakfast	862	**1.13 (0.64 ; 1.61)**	**<0.001**	197	0.27 (-0.70 ; 1.24)	0.580	439	-0.19 (-0.81 ; 0.44)	0.560	188	0.26 (-0.73 ; 1.24)	0.605
Sedentary behavior	862	0.27 (-0.22 ; 0.77)	0.274				439	0.44 (-0.21 ; 1.09)	0.182			
Physical activity	862	-0.13 (-0.80 ; 0.54)	0.702	200	0.10 (-0.99 ; 1.18)	0.862	439	-0.31 (-1.11 ; 0.50)	0.459	190	0.24 (-0.78 ; 1.27)	0.641
Waist circunference												
Skip breakfast	851	**1.97 (0.90 ; 3.03)**	**<0.001**	197	1.96 (-0.92 ; 4.85)	0.182	428	-1.61 (-2.63 ; 0.30)	0.120	188	1.73 (-0.99 ; 4.44)	0.211
Sedentary behavior	851	**1.20 (0.12 ; 2.27)**	**0.029**				428	1.22 (-0.31 ; 2.74)	0.117			
Physical activity	881	0.01 (-1.42 ; 1.44)	0.989	200	-1.14 (-4.34 ; 2.05)	0.482	444	-0.19 (-2.05 ; 1.68)	0.845	190	0.66 (-2.18 ; 3.50)	0.646
Waist to height												
Skip breakfast	851	**0.02 (0.01 ; 0.02)**	**< 0.001**				428	-0.01 (- 0.01 ; 0.00)	0.235			
Sedentary behavior	851	**0.01 (0.00 ; 0.02)**	**0.010**				428	**0.01 (0.00 ; 0.02)**	**0.041**			
Physical activity												

Adjusted by potention confounders: center(only in HELENA-CSS),age and education mother. Significant association are in bold. EBRBs: energy balance-related behaviors,BMI: body mass index, HELENA-CSS :Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-sectional study, BRACAH study:Brazilian Cardiovascular Adolescent, CI: confidence interval, coef β: beta coeficiente.

Table 3. Adjusted* association between EBRBs and general and abdominal obesity stratified by sleep time among adolescents boys studied from HELENA-CSS and BRACAH study

	Sleep time ≥8 h/day						Sleep time <8 h/day					
	HELENA			BRACAH			HELENA			BRACAH		
	n	coef β (95%CI)	p	n	coef β (95%CI)	p	n	coef β (95%CI)	p	n	coef β (95%CI)	p
BMI												
Skip breakfast	712	**1.29 (0.70 ; 1.88)**	**<0.001**	189	**1.69 (0.43 ; 2.94)**	**0.009**	350	**1.31 (0.47 ; 2.15)**	**0.002**	141	0.95 (-0.28 ; 2.17)	0.130
Sedentary behavior	712	-0.06 (-0.69 ; 0.57)	0.855	189	0.25 (-2.35 ; 2.86)	0.849	350	0.86 (-0.20 ; 1.93)	0.112	141	-1.35 (-4.62 ; 1.91)	0.416
Physical activity	712	-0.36 (-1.17 ; 0.45)	0.379	189	-0.66 (- 1.96 ; 0.65)	0.323	350	-0.28 (-1.41 ; 0.86)	0.635	141	-0.04 (-1.28 ; 1.19)	0.944
Waist circunference												
Skip breakfast	701	**2.83 (1.35 ; 4.31)**	**<0.001**	189	3.16 (-0.12 ; 6.45)	0.059	341	**2.36 (0.56 ; 4.17)**	**0.010**	141	2.43 (-0.84 ; 5.69)	0.146
Sedentary behavior	701	-0.08 (-1.66 ; 1.49)	0.919	189	2.82 (-3.89 ; 9.54)	0.410	341	1.76 (-0.50 ; 4.03)	0.127	141	-2.35 (-11.03 ; 6.33)	0.596
Physical activity	701	-0.16 (-2.16 ; 1.83)	0.871	189	- 0.90 (-4.21 ; 2.41)	0.595	341	-1.04 (-3.48 ; 1.40)	0.404	141	-0.73 (-4.02 ; 2.55)	0.662
Waist to height												
Skip breakfast	701	**0.02 (0.01 ; 0.03)**	**< 0.001**	189	**0.02 (0.00 ; 0.04)**	**0.020**	341	**0.02 (0.01 ; 0.03)**	**0.004**	141	0.02 (-0.00 ; 0.04)	0.056
Sedentary behavior	701	-0.00 (-0.01 ; 0.01)	0.892	189	0.01 (-0.03 ; 0.04)	0.698	341	0.01 (-0.01 ; 0.02)	0.264	141	-0.02 (-0.06 ; 0.03)	0.519
Physical activity	701	-0.00 (-0.01 ; 0.01)	0.949				341	-0.01 (-0.02 ; 0.01)	0.296			

Adjusted by potention confounders: center(only in HELENA-CSS), age and education mother. Significant association are in bold. EBRBs: energy balance-related behaviors, BMI: body mass index, HELENA-CSS :Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-sectional study, BRACAH study:Brazilian Cardiovascular Adolescent Health study, CI: confidence interval, coef β: beta coeficiente.

DISCUSSION

In this study, we observed how inappropriate EBRBs in a sample of adolescents from Europe and Brazil were associated with total and abdominal adiposity. Moreover, how sleep time may acts on these behaviors leading to obesity. Studies have reported the association between short sleep duration with PA, SB and food intake related to weight gain, compromising healthy development (35).The present study evaluates how sleep predicts not only these behaviors, as well as influence how skipping breakfast is associated with obesity, and the literature has not explored this approach among adolescents. The current study indicate that skipping breakfast is associated with adiposity markers in adolescents independent of sleeping time and sex, being the main finding of our study. Conversely, sleep time did not present a direct relationship with favorable measures for obesity.

Regarding sleep duration the association between obesity in children as in adolescents has been previously observed (36), and may be more stronger among boys than among girls, being probably also explained by the difference of pubertal stage between sexes (changes in body composition) (37). Some studies tried to identify associations between sleeping duration and caloric intake as well as physical inactivity, but were not successful (36).

Our study found no direct association between short sleep time and adiposity among adolescents studied after adjusting by covariates (*Table2*), which illustrate the influence of maternal education level. Thus, this lack of association is in agreement with longitudinal studies in adolescents, unlike those presented in cross-sectional studies when associations can be more easily observed (38). A cohort study places the importance of adjustment by important confounders as MVPA and depression (associated with sleep abnormalities such as insomnia) to explain or not, the still-discrete association of sleep time with adiposity among adolescents (39). Another sample of HELENA study did not show a relationship between sleeping time and obesity even adjusting for MVPA (40).Moreover, in our study we agree it was not possible to adjust the analysis in either of two samples, to this factor potentially associated with AO, as physical activity, since it is in the causative variable line.

Sleeping time does not seem to be the main predictor of obesity in this population; in addition, we do not also evaluate its pattern and quality, which would allow a greater comprehension of its real role. Another point to question refers to the reliability of subjective measures (self-reported questionnaires) such as those used in the current study, though they have been shown strong validation performance comparable to objective measures (accelerometers) (41).

In accordance with our findings, Brazilian boys who slept<8h/day showed a decrease in total obesity (*Table 2*),a large sample of adolescents evaluated longitudinally after adjusting for covariates, the effect of short sleep duration did not predict obesity (*WaveII*), but this association occurred with increased risk due SB (37%) and presence of depression (84%).The association was observed between depressed adolescents who tended to sleep-less than non-depressed one (*WavesI,II*) (42). Nonetheless, adequate sleep may reduce obesity risk by preserving vitality and attenuating fatigue, thus enhancing PA levels.

Sedentary behaviors among European girls were also associated with an increase in 1.19cm of WC.As showed in a systematic review, different types of SB may have different impacts on health, as screen time and TV viewing can be the worst associated with body composition and cardiometabolic risk factors (43).

Although we did not find associations between PA with obesity, the SB were associated with abdominal adiposity. Spending more daily hours in SB from infancy to adolescence, 6years later an increase in all BMI percentiles was observed, being the highest at the 90th percentile. Spending less time in MVPA and sleep did not explain this association, besides other covariates (44).

Since behaviors are not isolated a combination of health-related behaviors could have a stronger influence on obesity development. In a prospective study (follow-up 200-days) combinations of health-related behaviors were associated with measures of adiposity and cardiometabolic health in children and adolescents(12).Danish children who had healthy changes on the combinations of these two behaviors (increase in MVPA and sleep time, or reduced SB), improved their MetS score than children with reduced MVPA and sleep, and increased SB (45).

Breakfast should provide 25% of daily recommended energy intake (46)and skipping breakfast may influence an unbalanced diet and energy intake during the day, which can make adolescents vulnerable to weight gain. The beneficial influence of breakfast consumption on adiposity markers may even improve for male adolescents with low PA levels (47).

As our results suggest, skipping breakfast among adolescents (which was more prevalent among boys than among girls) increased total and abdominal obesity, regardless where they live, sleep duration and sex. Adolescents at 16 years of age who usually skipped breakfast, after 27 years of follow-up, showed a significant increase in the prevalence of MetS in adulthood (predicted by AO and high fasting glucose) despite BMI, have another meal in the day or unhealthy lifestyle habits(48). In addition, skipping breakfast over time during childhood as well as in adulthood, may lead damage of cardiometabolic health (larger WC, higher HOMA score and BMI) besides harmful behaviors (49).

Children have different reasons for skipping breakfast than adults, and parental influence has great importance. Maternal education, especially on the choice of healthy behaviors among adolescents seems to be an important ally. Previous longitudinal studies revealed that approximately 20% of adolescents skip breakfast each day, and the consumption of better patterns of foods like fruits, vegetables and dairy happens in adolescents with better-educated parents than those with less-educated parents(50).Adolescents who most consumed breakfast are associated with mothers with higher schooling and those with lower family income, but this behavior' prevalence tends to decrease with age, which could be explained by the gradual decrease in parental influences (51).

Normal weight children who skipped breakfast were associated with a greater weight gain over time than adolescents who ate breakfast. Otherwise, overweight children who skipped breakfast were leading to a decrease in BMI over time due to lower daily energy intake (52).In a large Australian cohort children were more likely to skip breakfast when their mother had overweight/obesity showing an association between mothers' skipping breakfast and children' greater BMI (53).

A strength of our study, despite its cross-sectional design, was to provide a considerable and diverse sample of adolescents with data available equally for all behaviors. In addition, cultural and geographic differences and age range among European and Brazilian adolescents, besides some methodological differences between the studies, placed data to be assessed separately.

Conclusion

Our results suggest that among European boys, skipping breakfast was associated with total and abdominal obesity independent of sleeping duration. However, in European girls and Brazilian boys the association between skipping breakfast and obesity was observed only among those sleeping more. Likewise, European girls who reported a longer sleep time showed an association between sedentary behaviors and abdominal obesity.

Abbreviations

AO: Abdominal obesity; BMI: Body mass index; EBRBs: Energy balance-related behaviors; MetS: Metabolic syndrome; MVPA: Moderate-to-vigorous physical activity; PA: Physical activity; SB: Sedentary behaviors; WC: Waist circumference; WHtR: Waist-to-height ratio; HOMA: Homeostatic model assessment

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5. CRITICAL ANALYSIS

Socioeconomic indicators were significantly associated with abdominal obesity in European adolescents, which did not show such association when referring to Brazilian adolescents. Older adolescents by generally assume less healthy behaviors. Thus, a more likely important determinant of obesity in this non-association could be the age of the adolescent.

In 30 years of following-up observed a significant increase on the prevalence rates of AO, a marker of cardiometabolic risks, among Australians children and mainly among adolescents, reaching about twice the prevalence of general obesity, where the lowest socioeconomic level influenced this outcome (22). These findings may suggest a probable epigenetic mechanism, where obesogenic environment through behaviors might influence the expression of gene, as to distribution of body fat (22). Although, it is unknown to what extent an increased genetic risk can be offset by a healthy lifestyle, analysis of prospective and cross-sectional studies show that genetic and lifestyle factors, independently associated with risk factors for coronary disease, individuals at high genetic risk and a healthy lifestyle reduced the risks for coronary disease by 50%, than those with unhealthy lifestyle behaviors (16).

Recent systematic review and meta-analysis showed inconsistent effects on the causal relationship between sleep restriction and body composition and weight, in adolescents and children through randomized control trials (RCTs) (23). Another meta-analysis, trials involving behavioral interventions with a sleep component, effective changes in children's BMI, did not occur besides a discrete improve on adolescents eating habits. This can be face as a good change since the literature points out less healthy behaviors in older adolescents, where the parental influence becomes less attended (24). Examining EBRBs among Finnish adolescents, sleep restriction did not show risk for overweight among girls. However, a greater risk was found in those who presented higher screen time (high TV viewing and computer use) (25), which is in agreement with our findings, being sedentary lifestyle an important prevalent behavior

among European girls for the risk of obesity, regardless of sleep restriction. In addition, our group has observed an increased incidence to high blood pressure among European children, pointing out the sedentary lifestyle, as a primary risk factor.

On the other hand, another behavior that involves adolescents, and can generate a risk is skip breakfast. Its consumption has decrease through the last decades. Thus, adolescents who consume breakfast have been associated with decreased metabolic risks and chronic diseases (20).

6. CONCLUSIONS

The adipose tissue has been looked upon with great interest, being considered an endocrine organ influences the inflammatory state and metabolic processes leading to harmful cardiovascular consequences.

Behaviors assumed in childhood can last for adulthood, collaborating early with the quality of the individual's health, which leads to future gains.

Moreover, socioeconomic indicators showed an important association of risk with abdominal obesity among the European adolescents from developed countries, and the maternal educational level is an important ally in the construction and follow of healthy lifestyle behavior for children.

In this sense, much has been said about the importance of healthy behaviors in the life of an individual and especially of children. And from there on, the influence of one behavior on others, increasing and translating the prevalence for a given disease when evaluated together and not individually. Hereupon, we observed that the influence of sleeping time on the adolescents did not interfere in the association with obesity markers in presence of skipping breakfast. What points out the increased importance of this behavior in the total and abdominal obesity among this young population.

Hence, investing in obesity prevention through a healthy lifestyle is the best way to go starting in childhood.

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APPENDIX

APENDIX1

Statement of Project Approval - Ethics Committee for Research-CEP

MEDICINA
USP
COMITÊ DE ÉTICA EM PESQUISA

Ao

Prof. Dr. Heráclito Barbosa de Carvalho

Departamento de Medicina Preventiva

O Comitê de Ética em Pesquisa da Faculdade de Medicina da Universidade de São Paulo, em sessão de **04.06.2014** tomou conhecimento que o Protocolo de Pesquisa nº **066/12** intitulado: **"Pressão arterial elevada e agregação de fatores de risco em adolescentes: um estudo multicêntrico",** contempla o **sub-projeto** intitulado: "***Fatores Socioeconômicos e micro ambientais relacionados à obesidade abdominal em adolescentes: um estudo multicêntrico***", que será executado pela aluna de Doutorado **Elsie Costa de Oliveira Forkert** .

CEP-FMUSP, 06 de junho de 2014.

Prof. Dr. Paulo Eurípedes Marchiori
Vice-Coordenador
Comitê de Ética em Pesquisa

Comitê de Ética em Pesquisa
Faculdade de Medicina da Universidade de São Paulo

APPENDIX 2

First page of Published Articleas first author- *Pediatric Obesity*

Receipt of Manuscript submitted - by *International Journal of Obesity*

***Pediatric Obesity* (Article published, 2016)**

"Abdominal obesity and its association with socioeconomic factors among adolescents from different living environments"

***International Journal of Obesity* (Article submitted, 2017)**

"Skipping breakfast is associated with adiposity markers especially when sleep time is adequate in adolescents"

PEDIATRICOBESITY
ORIGINALRESEARCH
doi:10.1111/ijpo.12116

Abdominal obesity and its association with socioeconomic factors among adolescents from different living environments

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Summary

Background: Socioeconomic status has been associated with obesity in children and adolescents. This association may be dependent according with where adolescents lives.

Objective: The aim of this study was to evaluate the association between different socioeconomic indicators such as parental education and occupation and socioeconomic status with abdominal obesity in adolescents from two observational studies: the Healthy Lifestyle in Europe by Nutrition in Adolescence cross-sectional study (HELENA-CSS) and the Brazilian Cardiovascular Adolescent Health (BRACAH) study.

Methods: European ($n = 3192$, aged 12.5–17.5 years, with 53.1% girls from HELENA-CSS) and Brazilian ($n = 991$, aged 14–18 years, with 54.5% girls from BRACAH study) adolescents from two cross-sectional studies were included in this analysis. Complete data on waist circumference (WC), height, socioeconomic status indicators and several confounders were collected. Socioeconomic indicators were measured using a self-reported questionnaire in order to assess the family social status of the adolescents. Multilevel linear regression models were used to examine associations, and results were adjusted for potential confounders.

Results: Adjusted results showed inverse associations between mother's and father's education levels ($p < 0.001$) and father's occupation level ($p < 0.001$) with waist-to-height ratio (WHtR) and WC in HELENA-CSS girls. Similarly in European girls, socioeconomic indicators by socioeconomic status and maternal occupation level were associated with WHtR. In HELENA-CSS boys, the same significant association was found between WHtR and WC with maternal occupation level. Moreover, in European boys WHtR was also associated with parental education. In Brazilian adolescents, both indicators of abdominal obesity did not remain associated with the independents variables, after adjustment for potential confounders.

Conclusions: Abdominal obesity was associated with socioeconomic indicators in higher-income countries, but this association was not observed in a lower-middle-income country.

Keywords: Abdominal obesity, adolescents, risk factors, socioeconomic status.

Detailed Status Information

Manuscript #	2017IJO01010
Current Revision #	0
Submission Date	14th Jun 17
Current Stage	Editors Decision
Title	Skipping breakfast is associated with adiposity markers especially when sleep time is adequate in adolescents
Running Title	skipping breakfast, sleep and adiposity in youth
Manuscript Type	Original Article
Special Section	N/A
Category	*Pediatric (This option must be selected for ALL Pediatric articles)
Word Count	3,195
Corresponding Author	Mrs. Elsie Forkert (elsie@usp.br) (University of Sao Paulo, School of Medicine)
Contributing Authors	Prof. Augusto Cesar De Moraes , Prof. Heráclito Carvalho , Prof. Yannis Manios , Dr. Kurt Widhalm , Prof. Marcela González-Gross , Prof. Angel Gutierrez , Dr. Anthony Kafatos , Dr. Laura Censi , Dr. Stefaan De Henauw , Prof. Luis Moreno
Abstract	Background: Adolescence as a critical stage of development an important influence has in energy balance-related behaviors (EBRBs). When they are associated with obesity lead to increased cardiometabolic risk. Objectives: (i)to assess if EBRBs adopted by adolescents are associated to markers of total and abdominal adiposity in a multicenter European study and a Brazilian study, and (ii)to assess whether sleep duration influence the association between skipping breakfast, physical activity(PA) and sedentary behaviors(SB), with total and abdominal obesity(AO). Methods: Subsamples included adolescents from two cross-sectional studies: the Healthy Lifestyle in Europe by Nutrition in Adolescence Study (HELENA-CSS; 2371,54.8%girls) and the Brazilian Cardiovascular Adolescent Health (BRACAH study; 991,54.5%girls). Multilevel linear regression models using fixed and random intercepts analyzed the association between markers of obesity [body mass index(BMI), waist circumference(WC), waist-to-height(WHtR)]and EBRBs, stratified by sleep time, sex and study. Age, maternal education level and centre were used as confounders. Results: Among European boys who slept less, the association with obesity markers did not remain after adjustment, suggesting the importance of the mother's educational level beyond age and where the adolescent lives. In addition, less sleep among Brazilian boys was protective for total obesity [β = -0.93kg/m2; 95% confidence intervals (95%CI:-1.80; -0.07)].Skipping breakfast was the prevalent behavior in association with total and abdominal obesity among European and Brazilian boys besides European girls, remaining even after stratification by sleep time. Moreover, European boys who slept properly skip breakfast increased on average 2.83cm in WC and 0.02 in WHtR. As1.69kg/m2 in BMI in Brazilian boys. Similarly, among European girls the association showed an increase on average of 1.20cm in WC when they were more sedentary. Conclusion: Skipping breakfast was associated with total and AO in adolescents independently of sleep duration. Furthermore, sedentary behaviors for girls were also associated with AO, especially for those who reported sleep adequately.
Associate Editor	Assigned
Techniques	Not Applicable;
Subject Terms	Health sciences/Risk factors Health sciences/Diseases/Cardiovascular diseases
Conflict of Interest Statement	There is **NO** conflict of interest to disclose
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Stage	Start Date
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APPENDIX 3

First page of Published Articles as co-author – *Current Obesity Reports / ActaPaediatrica*

***Current Obesity Reports* (Article Published, 2014)**
"Obesity Prevention in Latin America"

***Acta Paediatrica* (Article Published, 2016)**
"Cross-sectional, school-based study of 14–19 year olds showed that raised blood pressure was associated with obesity and abdominal obesity"

Curr Obes Rep (2014) 3:150–155
DOI 10.1007/s13679-014-0097-8

OBESITY PREVENTION (A MUST, SECTION EDITOR)

Obesity Prevention in Latin America

Juliana Kain · Sonia Hernández Cordero · Diana Pineda · Augusto Ferreira de Moraes · Daniel Antiporta · Tatiana Collese · Elsie Costa de Oliveira Forkert · Laura González · Juan Jaime Miranda · Juan Rivera

Published online: 4 March 2014

Abstract In Latin American countries, obesity prevalence has increased significantly as a result of rapid urbanization and an improvement in socioeconomic conditions. We report the prevalence of overweight and/or obesity and prevention efforts in five countries: Mexico, Colombia, Brazil, Peru, and Chile. In children, the highest and lowest rates of obesity are found in Chile (23 % in 6-year-olds) and Peru (1.8 % in those <5 years), respectively. In adults, Mexico and Chile present similar high rates of obesity (around 35 %), whereas in Brazil and Colombia, the rates are around 20 % and 16.5 %, respectively. In general, the highest prevalence occurs in low-income women. Every country has developed initiatives to target obesity, from the government to the private sector and academia, mainly at the health sector and school settings. Food labeling is being addressed, but has not been implemented yet. Two interventions are described, a community-based in Mexico and a school-based in Chile. Because the increase in chronic diseases, especially diabetes, has paralleled that of obesity, effective prevention efforts are urgently needed.

Keywords Obesity · Prevention · Latin America

Introduction

During the past three decades, people living in Latin American countries have experienced extensive demographic, epidemiologic, and socioeconomic changes, showing improvements in overall health and educational indicators [1]. These processes, known as epidemiologic transition, have occurred at a different pace from country to country and are closely related to increasing urbanization and a reduction in poverty levels, producing changes in dietary and physical activity patterns in all age groups. These changes have been directly

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REGULAR ARTICLE

Cross-sectional, school-based study of 14–19 year olds showed that raised blood pressure was associated with obesity and abdominal obesity

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Keywords
Abdominal obesity, Adolescents, High blood pressure, Obesity, Overweight

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ABSTRACT

Aim: Gaining weight has been directly associated with an increased probability of developing high blood pressure (HBP) and metabolic abnormalities. We examined the independent and combined effects of overweight, obesity and abdominal obesity on blood pressure in adolescents.

Methods: This cross-sectional school-based study evaluated 869 adolescents (53.4% girls) from 14 to 19 years of age, and the data were collected in 2013 in the city of Imperatriz, Maranhão, Brazil. The outcome was HBP. The independent variables were overweight and obesity classified by body mass index, abdominal obesity classified by the waist-to-height ratio and the combination of obesity and overweight and abdominal obesity. The potential confounding variables were age, the socio-economic status of the family, parental education, type of school and physical activity levels.

Results: The prevalence ratios of HBP were higher when male and female adolescents were overweight (1.61–3.11), generally obese (3.20–4.70), had abdominal obesity (2.18–3.02) and were both generally obese and had abdominal obesity (3.28–5.16) compared with normal weight adolescents.

Conclusion: Obesity or abdominal obesity increased the risk of HBP in adolescents aged 14–19. However, adolescents who were both generally obese and had abdominal obesity showed an even higher risk of having HBP.

INTRODUCTION

The prevalence of childhood obesity has increased worldwide over the last decade (1), but may be levelling among children and adolescents (2). Nevertheless, this outcome still represents a major public health problem (1), as gaining weight has been directly associated with an increased probability of developing high blood pressure (HBP) and metabolic abnormalities (3–5), which is an established major risk factor for stroke, coronary heart disease and aortic stiffening in adulthood (6,7). Early detection and subsequent targeted prevention and intervention may reduce the life course burden associated with HBP (7).

Abbreviations

95% CI, 95% Confidence interval; BMI, Body mass index; BP, Blood pressure; cm, Centimetres; HBP, High blood pressure; IPAQ-A, International physical activity questionnaire for adolescents; Kg, Kilograms; k, Kappa; MHO, Metabolic healthy obesity; m, Metres; PR, Prevalence ratio; SD, Standard deviation; WHtR, Waist-to-height ratio.

Key Notes

- We examined the independent and combined effect of general obesity and abdominal obesity on the blood pressure of a cross-sectional, school-based study of 869 adolescents aged 14–19 years of age.
- Our results showed that general obesity and abdominal obesity were both strong predictors of high blood pressure when considered separately.
- However, the combination of general and abdominal obesity increased the risk of developing high blood pressure in adolescents.

APPENDIX 4

FACULDADE DE MEDICINA DA UNIVERSIDADE DE SÃO PAULO

DEPARTAMENTO DE MEDICINA PREVENTIVA

PROJETO DE DOUTORADO

FATORES SOCIOECONÔMICOS E MICROAMBIENTAIS RELACIONADOS À OBESIDADE ABDOMINAL EM ADOLESCENTES: UM ESTUDO MULTICÊNTRICO

Aluna: ELSIE COSTA DE OLIVEIRA FORKERT
Orientador: Prof. Dr. Heráclito Barbosa Carvalho

São Paulo
2015

RESUMO

A obesidade abdominal (OA) tem um papel importante como fator de risco para doenças cardiometabólicas. Identificar e prevenir sua ocorrência na tenra idade promove a prevenção de riscos e complicações à saúde, tanto da criança quanto do adulto. O objetivo deste estudo será avaliar a associação dos fatores socioeconômicos e de estilo de vida (consumo semanal de frutas, legumes e bebidas açucaradas, duração do sono, comportamentos sedentários e atividade física) com indicadores antropométricos da OA em adolescentes. **Método**: Este estudo utilizará o banco de dados de dois estudos transversais de base populacional escolar, com processos padronizados de amostragem, recrutamento e coleta de dados. Foram realizados estudos transversais de base escolar com amostragem probabilística de adolescentes estudantes do ensino médio de áreas urbanas, com idades compreendidas entre 12.5 a 18 anos em 9 países Europeus e no Brasil. Os dados dos países europeus são do *"Healthy Lifestyle in Europe b Nutrition in Adolescence Cross-Sectional tudy"*(HELENA-CSS) e os dados brasileiros são provenientes da pesquisa: *"Brazilian Cardiovascular Adolescent Health"* (BRACAH *study*). A OA será o desfecho desse estudo, construída a partir da mensuração da circunferência da cintura (CC) e da relação cintura/estatura (RCE). As variáveis independentes consideradas são: cidade, sexo, idade, escolaridade dos pais, status de emprego dos pais (somente no HELENA-CSS), nível socioeconômico da família e variáveis do estilo de vida (consumo semanal de frutas, legumes e bebidas açucaradas, duração do sono, comportamentos sedentários e atividade física). Para analisar a magnitude das associações entre os desfechos e as variáveis independentes, serão utilizados modelos de regressão linear com intervalo de 95% de confiança, por meio de modelos multinível.

ABSTRACT

Abdominal Obesity (AO) plays an important role on cardiometabolic diseases. Identifying and prevent its occurrence at young age promotes the prevention of the risk and aggravating health circumstances, either in children and adults. The aim of this study will be to evaluate the association of socioeconomic and lifestyle factors (weekly consumption of fruits, vegetables and sugary drinks, sleep duration, sedentary behaviors and physical activity) with anthropometric indicators of AO in adolescents. **Method**: This study will employ a database of two cross sectional studies based on the school community through standardized sampling, recruitment and data collection. There have been realized cross sectional studies in school communities through probabilistic sampling on adolescent high school students in urban areas, with ages ranging between 12.5 and 18 years; in Brazil and in 9 European countries. The data from European countries were obtained from the *"Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional Study"* (HELENA-CSS) and Brazilian data, from the survey: *"Brazilian Cardiovascular Adolescent Health"* (BRACAH *study*). The AO will be the outcome of this study, based on the measurement of waist circumference (WC), as well as the waist-to-height ratio (WHtR). The independent variables to be consider are: city, gender, age, parental education, parental employment status (only in the HELENA-CSS), socioeconomic status of the family and lifestyle variables (weekly consumption of fruits, vegetables and sugary drinks, sleep duration, sedentary behaviors and physical activity). In order to analyze the magnitude of the associations between outcomes and independent variables there will be applied linear regression models with 95% confidence intervals through multilevel models.

1. INTRODUÇÃO

Atualmente a obesidade é uma doença altamente prevalente na população pediátrica em países de alta e de média-baixa renda, sendo importante fator de risco para doenças cardiovasculares e metabólicas, assim como de mortalidade precoce (antes dos 50 anos) (Ramachandran et al., 2002; Prentice, 2006;). Em recente revisão sistemática verificou-se que a prevalência de excesso de peso (sobrepeso + obesidade) da infância a adolescência em países de alta renda é inversamente proporcional ao nível socioeconômico, sendo encontrada em 51.1% dos estudos, e que o indicador nesta relação mais importante é a educação dos pais (Barriuso et al., 2015).Decorrente a estas crescentes prevalências não somente em países desenvolvidos como nos de média-baixa renda, Lobstein et al. (2004) já consideravam a obesidade infantil como uma epidemia. Esses dados são preocupantes, uma vez que o desenvolvimento da obesidade na infância e/ou adolescência aumenta o risco de mortalidade precoce por doenças cardiovasculares/metabólicas na idade adulta em 19% para os com excesso de peso, e em 64% para os obesos (Baker et al., 2007; Hirko et al., 2015). Além do impacto no tratamento, se mostrando muitas vezes ineficiente, gerando alto custo para o sistema público de saúde (Ebbeling et al.,2002).

Segundo Egger e Swinburn (1997), a obesidade origina-se pela presença de fatores de riscos biológicos e comportamentais que são influenciados por condições socioeconômicas, educacionais e culturais nos diversos ambientes: domiciliar, escolar e comunitário. Estes autores propõem um modelo ecológico para entender a obesidade, dentro do qual classificam os ambientes em: macroambiente relativo a uma ampla população, e que determinará a prevalência da obesidade nesta população. E microambiente, caracterizado pela proximidade ao indivíduo – ambiente doméstico, escolar e comunitário, que tipicamente envolve a alimentação e a atividade física, e por influências comportamentais e biológicas determinam se o indivíduo é obeso.

Padrões familiares de adiposidade indicam que há contribuição genética de ganho de gordura, entretanto esse fator contribui significativamente quando o indivíduo é exposto a um ambiente de aumento da ingestão energética e redução do gasto

energético o que leva a um desequilíbrio nutricional calórico, e aumento de peso até a obesidade (Moreno et al., 2004).

Associado ao ambiente, fatores educacionais e socioeconômicos podem interferir adversamente. Uma vez que a informação incrementa o conhecimento sobre algo e este sendo precário ou ausente, impede o indivíduo de realizar escolhas adequadas para suas necessidades, é através da educação que este nível satisfatório de informação para tomada de decisão em saúde, poderá ser atingido (Thiede and McIntyre, 2008). Da mesma forma o baixo nível de educação é determinante ao baixo acesso a prevenção em saúde (Sanders et al., 2009), bem como a renda familiar que interfere diretamente na qualidade de acesso aos alimentos, (BRASIL, 2006).

Portanto, o nível educacional entre os indivíduos de nível socioeconômico mais baixo está negativamente associado com oportunidades de conhecimento sobre a própria saúde e sobre o valor nutritivo dos alimentos. Assim, escolhas de padrões alimentares de melhor qualidade e de menor teor energético como frutas, verduras e cereais integrais, bem como opções de lazer e prática de exercícios serão afetadas (WHO, 2000; Bau et al., 2011).

No ambiente doméstico, o hábito alimentar de crianças e adolescentes é dependente das escolhas dos pais. Muitas famílias apresentam um comportamento obesogênico, caracterizado por dieta hipercalórica e baixos níveis de atividade física, trazendo graves consequências à saúde (Schremptf et al., 2015). Dentro deste contexto, o nível educacional dos pais e particularmente o materno, é um fator determinante de maior probabilidade de sobrepeso nas crianças e adolescentes (Fernández-Alvira et al., 2013). Logo, mostrou-se que a obesidade paterna foi associada a um aumento de risco para obesidade em quatro vezes mais sobre filhos do sexo masculino e feminino em idade de 18 anos (adolescentes mais velhos), e este risco aumenta para oito vezes mais sobre as filhas, se as mães forem obesas (Burke et al., 2001).Certamente, ter os dois pais obesos ou com sobrepeso é mais “obesogênico” do que ter apenas um, uma vez que há dupla carga genética e/ou um ambiente de maior exposição aos hábitos não-saudáveis (Wang et al., 2017).

Contrariamente, entre os indivíduos com nível socioeconômico mais alto, o conhecimento e a oportunidade de resistir a crescentes ambientes obesogênicos, pode

ser maior quando comparados aos indivíduos com nível socioeconômico mais baixo (WHO, 2003).

Desigualdades socioeconômicas coincidentes com distribuições distintas de renda entre ricos e pobres, tem comprometido em muitos domínios a saúde do adolescente, relatando tendências no desequilíbrio da saúde em adultos e mortalidade infantil (Elgar et al., 2015). Estudos mostram que o sobrepeso é inversamente associado ao nível socioeconômico sendo até três vezes maior em países de média-baixa renda quando comparados com países de alta renda (Janewa et al., 2012). Por outro lado, há evidências que a melhora do nível socioeconômico de classes de média-baixa renda, geralmente acompanhadas de urbanização e de migração a aglomerados urbanos, pode levar a uma rápida e inadequada transição nutricional com mudanças alimentares, além de redução da atividade física; ambos fatores de risco para a obesidade e o diabetes (Fall, 2001; Gutiérrez-Fisac et al., 2002; Wang et al., 2002). Uma possível explicação desse maior risco para os desfavorecidos, é que as desigualdades socioeconômicas também apresentam associação negativa com os níveis de atividade física, com evidências de menor dispêndio energético em ambientes de menor nível socioeconômico, onde as oportunidades e possibilidades de acesso são mais escassas, determinando uma possível interação entre o nível socioeconômico familiar e a prática de atividade física na infância (De Cocker et al., 2012).

Estudos mostram associações entre a obesidade e a inatividade física (Martinez-Gomez et al., 2010), e com o tempo dedicado a comportamentos sedentários (Rey-López et al., 2012b). Considerando a adiposidade visceral, Grigorakis et al. (2015) apontam a existência de uma ligação inversa entre a prática de atividade física e a obesidade abdominal (AO), com uma frequente participação em atividades sedentárias. Entretanto, há poucos estudos que mostram os efeitos da combinação de inatividade física e de condutas sedentárias, assim como análise de associações entre diferentes indicadores socioeconômicos com sobrepeso e obesidade em adolescentes de diferentes ambientes.

Avaliando a obesidade na infância/adolescência, outros comportamentos como o tempo de sono devem ser examinados com atenção diante deste desfecho. Evidencias em estudos epidemiológicos têm indicado que a curta duração crônica do sono associa-

se a um maior risco de ganho de peso e obesidade nesta população por diminuição da sensibilidade insulínica e intolerância a glicose, além de alterações endócrinas e comportamentais (Van Cauterand Knutson, 2008).

Geralmente, a obesidade é mensurada por meio do índice de massa corporal (IMC). Apesar de amplamente utilizada em crianças e adultos, possui baixa sensibilidade na identificação de adiposidade para o excesso de gordura corporal (Okorodudu et al., 2010). Entretanto o IMC é aceito e utilizado em investigações epidemiológicas, sendo recomendado por especialistas do comitê de obesidade pediátrica porque é um ótimo preditor de doenças cardiovasculares (Gracia-Marco et al., 2015). Contudo, a circunferência da cintura (CC) se apresenta como um indicador mais sensível e específico para gordura central, uma vez que o IMC não diferencia massa muscular de massa gorda e óssea, sendo por isso um pobre preditor da gordura corporal (Gracia-Marco et al., 2015).

A CC é recomendada pelas associações científicas internacionais: *National Cholesterol Education Program do Adult Treatment Panel III* e *International Diabetes Federation* para avaliar a OA, sendo um dos componentes da síndrome metabólica. Por outro lado, a relação cintura/estatura (RCE) tem sido relatada como melhor indicador de risco para doenças cardiometabólicas do que CC e/ou IMC, por ser um índice antropométrico de simples mensuração, independente da idade, sexo ou raça. Seu ajuste pela altura permite estabelecer um ponto de corte único aplicável a população (Ashwell and Hsieh, 2005). Assim é apontada como uma medida para avaliar associações entre variáveis de risco cardiometabólico e OA (Mokha et al., 2010).

Em uma revisão sistemática verificou-se que a prevalência de OA varia entre 3,8% a 51,7% em adolescentes de países de média-baixa renda, e com variação menor em adolescentes de países de alta renda, 8,7% a 33,2% (de Moraes1 et al., 2011b). Além disso, a AO está associada a diferentes hábitos alimentares, sendo esta relação mediada pelo contexto socioeconômico familiar (de Moraes e Falcão, 2013b). Diante do exposto pressupõe-se que os indicadores de OA (circunferência da cintura e relação cintura/estatura) estão associados com fatores socioeconômicos e de estilo de vida (consumo semanal de frutas, legumes e bebidas açucaradas, duração do sono, comportamentos sedentários e atividade física) em adolescentes europeus e brasileiros,

e que tais associações podem ser dependentes de onde o adolescente vive.

1.1 JUSTIFICATIVA

A obesidade é um problema de saúde pública, contudo sua etiologia é complexa e multifatorial, apresentando associações com fatores biológicos e comportamentais que são influenciados por condições socioeconômicas, educacionais e culturais, além do ambiente. Portanto, faz-se necessário compreender nesta população, quais variáveis agem de forma mais significativa no desenvolvimento deste fenômeno. A análise de dois estudos - um multicêntrico Europeu e outro Brasileiro desenvolvido na cidade de Maringá - justifica-se pela necessidade em contribuir para a identificação de fatores ambientais tais como os domiciliares, escolares e os comunitários que afetam a obesidade abdominal de adolescentes, e qual o papel da atividade física, do comportamento sedentário, da duração do sono, do hábito alimentar e do aspecto socioeconômico neste processo. Com isto, espera-se auxiliar ensaios clínicos/comunitários, de tratamento e de prevenção da obesidade abdominal em populações pediátricas.

1.2 HIPÓTESE CENTRAL DE INVESTIGAÇÃO

Há associação entre exposição a condições ambientais, estilo de vida e fatores socioeconômicos, com indicadores da obesidade abdominal em adolescentes?

2. OBJETIVOS

2.1 OBJETIVO GERAL

Avaliar se existe associação entre fatores socioeconômicos e comportamentais com a obesidade abdominal em adolescentes.

2.2 OBJETIVOS ESPECÍFICOS

a) avaliar se há associações entre fatores socioeconômicos (exposição distal) e obesidade abdominal em adolescentes (Artigo 1): ***"Abdominal obesityand its associationwithsocioeconomicfactorsamongadolescentsfromdifferent living environments"***

b) avaliar a associação entre comportamentos do estilo vida (exposição proximal) nos adolescentes com obesidade abdominal (Artigo 2);

c) identificar quais as contribuições que fatores mediadores têm no desenvolvimento da obesidade abdominal dos adolescentes, nos dois contextos (Artigo 3).

3. MÉTODOS

3.1 DELINEAMENTO DO ESTUDO

Trata-se de um estudo observacional com delineamento transversal multicêntrico que utilizará os bancos de dados de dois estudos transversais (I e II) de base populacional escolar, com estudantes de áreas urbanas do ensino médio, compreendendo idades entre 12.5 e 18anos. Sendo o Estudo I - um estudo randomizado multicêntrico Europeu que analisou o estado nutricional e de estilo de vida de adolescentes por região geográfica, antecedente cultural, condição socioeconômica, idade e sexo dentre as 10 cidades de nove países Europeus participantes: Áustria (Vienna), Bélgica (Ghent), França (Lille), Alemanha (Dortmund), Grécia (AthensandHeraklion), Hungria (Pécs), Itália (Rome), Espanha (Zaragoza) e Suécia (Stockholm), e tendo como dados o "*HealthyLifestyle in EuropebyNutrition in Adolescence Cross-SectionalStudy*" (HELENA-CSS). Este estudo foi coordenado pelo Professor Dr. Luis A. Moreno Aznar da Escola Universitária de Ciências da Saúde da Universidade de Zaragoza (Espanha).

E o Estudo II – um estudo Brasileiro, o qual também investigou determinantes de hábitos saudáveis do estilo de vida do adolescente, tendo como base de dados o "*Brazilian Cardiovascular Adolescent Health"* (BRACAH *study*) realizado na cidade de Maringá – PR (Brasil). Este estudo foi coordenado pelo Dr. Augusto César Ferreira de Moraes e como coordenador científico o Professor Dr. Felipe F. Reichert, Universidade Estadual de Londrina e atualmente professor da Universidade Federal de Pelotas.

3.2 ASPECTOS ÉTICOS

O Protocolo de Pesquisa para análise dos dados para o presente estudo foi submetido e aprovado pelo Comitê de Ética em Pesquisa (CEP) da Faculdade de Medicina da Universidade de São Paulo, sob o nº 066/12, **(ANEXOS)**.

3.3COMPOSIÇÃO DAS AMOSTRAS

3.3.1 HELENA-CSS

Estudo transversal com participantes adolescentes selecionados por amostra aleatorizadas dentre aqueles matriculados nos colégios que se encontravam nas 10 cidades Europeias: Vienna (Áustria), Ghent (Bélgica), Lille (França), Dortmund (Alemanha), Athens e Heraklion (Grécia), Pécs (Hungria), Rome (Itália), Zaragoza (Espanha) e Stockholm (Suécia). Essas cidades foram escolhidas de acordo com a população, por apresentarem mais de 100.000 habitantes, estarem localizadas em regiões geograficamente separadas na Europa (N/S/L/O), e possuírem uma referência cultural e situação socioeconômica semelhantes.

O tamanho da amostra foi estimado a partir da variável do estudo que apresentasse a maior variação (IMC) para cada sexo e grupo de idade. Para o cálculo do tamanho da amostra foi utilizado um intervalo de 95% de confiança (95%CI) e um erro de ±0.3.

Dez escolas de cada cidade participante foram envolvidas, com exceção de Pécs (Hungria), onde apenas oito escolas participaram por não possuir mais escolas na cidade. A amostragem foi realizada em dois estágios, após ocorrer estratificação das escolas por distrito ou região de localização, com isso pretendeu-se garantir a diversidade da amostra em aspectos culturais e socioeconômicos. As escolas de diferentes regiões de cada cidade participante foram utilizadas como unidades de seleção, e posteriormente as salas de aula (classes) das escolas obtidas. Também as classes foram selecionadas aleatoriamente, após estratificação por séries. A classe era considerada elegível se a frequência de participação fosse ao menos de 70%. Foi considerada uma sala de aula escolar, aquela formada por no mínimo 20 estudantes, e

que apresentasse uma distribuição parecida entre idade e sexo. Por outro lado, se uma escola selecionada se recusasse a participar, uma segunda lista de escolas substitutas já estaria organizada.

O número médio de adolescentes estimados a participar foi de 300 e não mais do que 350 por cidade. Descrições detalhadas do HELENA-CSS quanto ao sistema de gestão do estudo, recrutamento, amostragem, harmonização, manual de padronização dos procedimentos coleta de dados e controle de qualidade das atividades estão publicados (Moreno et al., 2008). Um manual completo e detalhado relacionado às operações e atividades do estudo foi cuidadosamente lido pelos pesquisadores envolvidos antes do início da coleta de dados.

Assim, um total de 3528 adolescentes sendo 1683 meninos (47,7%) e 1845 meninas (52,3%), com idade média de 12.5 a 17.5anos, cumpriram os critérios gerais de inclusão no estudo quanto a: idade, não participar de outro estudo clínico e não padecer de nenhuma doença infecciosa aguda durante a semana prévia à inclusão no estudo. Deveriam possuir no mínimo medidas antropométricas de peso e altura, e ao menos terem realizado 75% dos outros testes.

No estudo HELENA-CSS a coleta de dados foi realizada no período entre outubro/2006 e dezembro/2007. Para a coleta de dados o estudo foi aprovado pelos Comitês de Ética em Pesquisa de cada cidade envolvida (sendo que para maioria foi o Ministério da Saúde do país) seguindo as diretrizes da Declaração de Helsinki, 1964 (revisão de Edinburgh, 2000) (Béghin et al., 2008).

3.3.2 BRACAH *study*

A cidade de Maringá, está localizada a noroeste do estado do Paraná, região Sul do Brasil, apresentava condições semelhantes às cidades europeias nos quesitos cultural e populacional, com aproximadamente 330.000 habitantes segundo dados do Instituto Brasileiro de Geografia e Estatística (IBGE) 2007. De acordo com o Índice de Desenvolvimento Humano (IDH), o qual é estimado pelos indicadores de saúde, educação e renda populacional, a cidade de Maringá apresentava um elevado índice em 2007(IDH = 0,84), enquanto o IDH para o Brasil como um todo, era de 0.81 (PNUD 2007).

A população desta investigação foi composta por alunos do ensino médio, sexo masculino e feminino entre 14 e 18 anos de idade, regularmente matriculados nas redes públicas e privadas no ano de 2007, verificados a partir dos dados da Secretaria Estadual de Educação do Paraná e da União das Escolas Particulares de Maringá, PR.

Para o cálculo do tamanho da amostra foram utilizados os seguintes parâmetros: intervalo de 95% de confiança e um poder de teste de 80%. A prevalência estimada de excesso de peso (sobrepeso + obesidade, mensurada pelo IMC) foi de 50% (± 5 pontos percentuais) (desfecho primário) e um efeito do desenho de 2. Baseado nesses parâmetros estimou-se que seria necessário coletar dados em 734 adolescentes. Em função de ser uma grande pesquisa sobre a saúde dos adolescentes, acrescentou-se na amostragem 10% prevendo eventuais perdas e recusas, e mais 15% para as análises multivariadas, totalizando a necessidade em coletar no mínimo dados de 918 adolescentes.

A amostragem foi obtida em dois estágios: tipo da escola (unidade amostral primária) e salas de aula. Primeiramente contabilizou-se o número de escolas que possuíam alunos dentro da faixa etária estudada (n = 38 escolas, sendo públicas n=26 e privadas n=12) e então, selecionou-se aleatória e sistematicamente as escolas, respeitando a proporcionalidade de tamanho e tipo (pública ou privada). Finalizando em oito escolas públicas e quatro particulares. No segundo estágio, foram selecionadas as classes de cada escola por amostragem aleatória simples, de modo que a proporção de estudantes em cada série (1ª à 3ª do ensino médio) fosse respeitada. Todos os escolares das classes sorteadas presentes no dia da coleta foram considerados elegíveis para participar do estudo.

Desta maneira, foram selecionados 774 e 492 alunos de escolas públicas e privadas, respectivamente (1266 adolescentes no total). Ocorreram 92 perdas, alunos que se ausentaram nos dias de coleta de dados, sendo 76,1% estudantes de escolas públicas (n=70) e 183 recusas, aqueles que não entregaram o termo de consentimento ou não consentiram em participar, destes 82% estudantes de escolas privadas (n=150). Portanto, ao final a amostra foi constituída de 991 adolescentes escolares, com 67,7% de estudantes de escolas públicas (n=671). O tamanho da amostra obtido, permitiu detectar razões de prevalência de 1,3 como estatisticamente significativo ao nível de 5% e com

poder de 80% para exposições com prevalência de 50% (de Moraes et al. 2011a).

As coletas de dado do BRACAH *study* compreenderam o período entre agosto/2007 e outubro/2007. Os critérios de exclusão foram: adolescentes com problemas ortopédicos que impedissem as avaliações antropométricas e adolescentes grávidas. O não consentimento foi considerado como recusa em participar do estudo. O estudo foi aprovado pelo Comitê de Ética em Pesquisa envolvendo Seres Humanos do Centro da Universidade de Maringá, e autorizado pelo Comitê de Ética em Projetos de Pesquisa da Universidade de São Paulo, de acordo com as leis Brasileiras.

Tanto no estudo HELENA-CSS quanto no BRACAH *study* todos os estudantes participantes, tiveram previamente o consentimento escrito/assinados pelos pais ou responsáveis, e o assentimento verbal pelo próprio adolescente.

3.4 VARIÁVEIS DO ESTUDO

Será considerada desfecho (variável dependente) assim como descrita nos dois estudos que deram origem ao atual, os indicadores antropométricos de obesidade abdominal: *relação cintura/estatura (RCE) e a circunferência da cintura (CC).*

Para mensuração da CC foi utilizada uma fita métrica inextensível (*Type SECA 200*) estando o participante na posição em pé, abdômen relaxado, braços ao longo do corpo, pés juntos. Foram tomadas duas medidas, compreendidas entre o ponto médio da última costela e a borda superior da crista ilíaca. Assim, calculou-se a média destas medidas sendo admitida uma variação máxima de 0,5 cm entre as duas repetindo-se o procedimento no caso de ultrapassar essa variação (precisão de 0,1 cm) (WHO, 1995; Nagi et al., 2008).

A estatura (medida realizada em posição vertical, entendida pela distância entre a parte mais alta da cabeça e a sola dos pés), foi mensurada utilizando-se um instrumento telescópico de medição de altura (*Type SECA 225*, entre 60-200 cm e com precisão de 0,1cm). Os adolescentes se posicionaram em pé, corretamente apoiados no solo, em posição reta, com os pés descalços e roupas leves. Mantendo os pés paralelos, braços relaxados ao longo do corpo, joelhos estendidos e a parte posterior da cabeça, escápulas, nádegas, panturrilhas e calcanhares tocando o suporte vertical. Foi posicionada a cabeça, em paralelo aos pés, sendo traçada uma "linha horizontal

imaginária do canal auditivo externo até a órbita inferior do olho" (ou seja, o plano de *Frankfurt*) (WHO, 1995; De Onis, 2004; Nagi et al., 2008).

Considerando as variáveis independentes investigadas temos: as sociodemográficas, as socioeconômicas e as comportamentais, sendo descritas a seguir.

Indicadores Sóciodemográficos

Sexo: adolescentes do sexo masculino e feminino;

Idade: determinada com base na diferença entre a data de nascimento relatada pelos próprios adolescentes, e a data da coleta de dados;

Indicadores Socioeconômicos

HELENA-CSS

Nível socioeconômico

Foi mensurado através da Escala de Riqueza Familiar (*Family AffluenceScale - FAS*) sendo um indicador para circunstâncias socioeconômicas e de materiais dos adolescentes. Estes responderam a um questionário pertinente a presença de bens que possuíam no domicílio quanto: ao número de carros e computadores, se tinham acesso a internet em casa, bem como se possuíam um dormitório próprio. A *FAS* foi baseada no modelo proposto por Currie et al., (2008), tendo sido adaptado mediante a substituição do item: *"ter férias"* por *"acesso a Internet em casa"*. Esta escala varia de 0 a 8, sendo que 0 significa um nível muito baixo e 8 um nível socioeconômico muito alto. A qual foi categorizada em 3 níveis socioeconômicos: baixo, médio e alto.

Ocupação dos pais

Avaliado somente no HELENA-CSS, onde através de um questionário auto respondido que continha 12 categorias de ocupações, estas foram categorizadas e agrupadas ao final, em 3 níveis: baixo (agricultor, pescador - trabalho que abriga um maior esforço físico e baixo grau de formação), médio-alto (trabalho administrativo, serviços de negócios) e alto (ocupações que requerem um maior desenvolvimento intelectual/científico, diretores de empresas, professores universitários).

BRACAH *study*

Nível socioeconômico

Classificado de acordo com o critério da Associação Brasileira de Empresas de Pesquisa (ABEP, 2003) em classes A_1 (mais alta), A_2, B_1 B_2, C, D ou E (mais baixa) a qual leva em conta a presença de bens de consumo no domicílio, presença de empregada mensalista e grau de instrução do chefe da família. Recebe-se uma pontuação, referente a presença ou não dos itens, e a somatória dos pontos definirá o critério classificando a categoria. No BRACAH *study* estas categorias foram agrupadas em 3 níveis sendo: baixo (classes D e E), médio (classes B_2, C) e alta (classes A_1, A_2 e B_1).

Nível de escolaridade dos pais: **(avaliado em ambos estudos)**

Nos dois estudos considerou-se o nível educacional mais alto do pai e da mãe, sendo este também avaliado através de um questionário de auto-relato.

Posteriormente os níveis foram classificados em quatro (equivalentes a cada país):

1) Educação mais baixa (correspondente ao Ensino Fundamental I)
2) Ensino secundário inferior (correspondente ao Ensino Fundamental II)
3) Ensino secundário superior (correspondente ao Ensino Médio/Técnico)
4) Universitário (correspondente a Educação Universitária)

Indicadores Comportamentais (avaliado em ambos estudos)

Comportamento sedentário

Os adolescentes responderam um questionário estruturado, relatando informações referentes ao tempo despendido em horas por dia assistindo TV, utilizando computador e jogando vídeo game. Perguntas como, "*Durante a semana quantas horas você frequentemente gasta assistindo TV?"*-"*Durante a semana quantas horas você frequentemente gasta utilizando o computador?"* - "*Durante a semana quantas horas você frequentemente gasta jogando vídeo game?"* As mesmas perguntas foram feitas também, versando sobre os finais de semana. O comportamento sedentário foi classificado de acordo com as seguintes categorias: 0–2 h/d; >2–4 h/d; ≥4 h/d (Dunstan

et al., 2010). O questionário foi traduzido e adequado para cada cidade, e posteriormente foi testado sua reprodutibilidade e confiabilidade, apresentando *k*-values = 0,81 no HELENA-CSS (Rey-López JP et al. 2012a; Rey-López JP et al. 2011), e *k*-values = 0,79 no BRACAH *study*(de Moraes1 et al. 2013a).

Atividade física

Informações referentes à prática de atividade física diária foram obtidas por intermédio do Questionário Internacional de Atividade Física (*International Physical Activity Questionnaire* – IPAQ) que foi desenvolvido para medir a atividade física que melhora a saúde da população adulta. Este em sua versão longa foi modificado e validado para adolescentes, (*International Physical Activity Questionnaire for Adolescents* – IPAQ-A), (Hagströmer M et al.,2008; Guedes et al., 2005), o qual avalia o nível de atividade física (de moderada a vigorosa). Este questionário foi validado com o acelerômetro nos adolescentes do estudo HELENA- CSS (R^2= 0.81) e no estudo BRACAH *study* realizado a confiabilidade dos questionários (coeficiente de Kappa = 0.91) (de Moraes et al., 2009).

Hábitos alimentares

Foi aplicado um questionário de frequência de consumo alimentar (FFQ), utilizado no estudo internacional: *Health Behavior in School-Aged Children* (HBSC), o qual objetivou monitorar e melhorar o entendimento do comportamento relativo à saúde, e o estilo de vida dos jovens, investigando hábitos de saúde entre um grande número de escolares. O questionário foi traduzido e modificado para os hábitos alimentares de cada país (Vereecken et al., 2009), depois de ter sido submetido a um estudo de confiabilidade entre os adolescentes estudantes brasileiros (Romanzini et al., 2008) e europeus (Vereecken et al., 2008). Por exemplo, a pergunta *"Quantas vezes na última semana você ingeriu frutas?"*avaliou o consumo de frutas, tendo como referência uma semana habitual.

O questionário foi auto-respondido em sala de aula sob a supervisão de um pesquisador e versava sobre cinco grupos de alimentos: 1) verduras; 2) frutas; 3) refrigerante; 4) frituras; 5) doces (alimentos de alta densidade energética como: bolos,

bolachas e chocolates). O consumo alimentar inadequado foi classificado em comer: 4 dias/semana frituras, bolos, bolachas e doces e 4dias/semana para frutas e verduras. A quantidade de cada alimento ingerida não foi coletada. O questionário também mensurou número de refeições realizadas na semana (café da manhã, lanche da manhã, almoço, café da tarde, lanche da tarde, jantar e ceia) e quais foram às realizadas em casa. Os resultados observados de reprodutibilidade e confiabilidade dos questionários foram altos, *k*-values = 0.83 no HELENA-CSS e *k*-values = 0.85 (de Moraes et al.,2012), quando avaliado no BRACAH *study*.

Hábito de sono

O tempo frequente de sono foi estimado por meio de um questionário, através do qual se perguntou aos participantes*: "Durante a semana, quantas horas (e minutos) você costuma dormir?"*e "*Durante os dias de final de semana, quantas horas (e minutos) você costuma dormir?"* Adolescentes entre 14 e 18 anos responderam este questionário por duas vezes com um intervalo entre eles de uma semana. Em 183 desses adolescentes a confiabilidade destas perguntas foi estudada, e questões utilizadas para estimar o tempo de sono apresentaram boa reprodutibilidade e confiabilidade. No estudo Europeu o Cohen'sweighted *Kappa* apresentou concordâncias quase que perfeita (0.81 e 0.96 durante os dias de semana e nos dias de final de semana, respectivamente), (Réy-Lopez et al., 2014; de Moraes et al., 2016).

3.5 ANÁLISE ESTATÍSTICA

Inicialmente, as variáveis contínuas serão apresentadas em média e intervalo 95% de confiança (IC95%) e as variáveis qualitativas, em percentuais (%). Para verificar se os dados da amostra estão normalmente distribuídos, aplicar-se-á o teste de Shapiro-Wilk. Posteriormente, para analisar as diferenças entre os sexos nas variáveis será empregado o teste t para amostras com distribuição paramétricas e para as variáveis com distribuição não paramétricas, o teste de Mann-Whitney.

A fim de identificar grupos de participantes relacionados aos comportamentos do estilo de vida como: dieta, atividade física, comportamento sedentário e hábitos de sono semelhantes, uma combinação de agrupamento hierárquico e não hierárquico será

aplicada, (Haerens L et al.,2010; Fernández-Alvira JM et al.,2013). As análises de *cluster* para os comportamentos de estilo de vida serão estratificadas por sexo em cada estudo, devido a diferença significativa entre os gêneros nos agrupamentos destes comportamentos**.** O z-score será calculado para todas as variáveis a fim de padronizar os dados, antes do agrupamento. Com isto, impede-se que variáveis medidas em intervalos maiores, contribuam para um agrupamento em extensão maior do que as variáveis com um intervalo menor.

Os *outliers* maior que 3 desvios padrões serão removidos. Escolhemos o método de Wald´s na aplicação de uma análise de agrupamento hierárquico, com base no quadrado das distâncias Euclidianas (Everitt et al., 2001). Assim, será realizada uma comparação de vários possíveis agrupamentos. Usaremos a distribuição *centroids* resultantes da estimação dos *clusters* e para ajustar ainda mais o modelo hierárquico preliminar, a análise não-hierárquica de *cluster* de *médias-k*será aplicada.

Os testes ANOVA e post hoc Bonferroni serão usados para analisar as diferenças entre cada agrupamento em todas as variáveis. As possíveis associações entre os desfechos e cada variável independente serão analisadas por meio de modelos de regressão linear multinível, usando modelos fixos ou randômicos, que previamente serão testados para cada desfecho através do teste de Durbin-Wu-Hausman (Snijders and Bosker, 1999; Diez-Roux, 2008).

Nas análises ajustadas serão aplicados modelos conceituais hierárquicos. A construção de um modelo conceitual teórico permite a organização de determinantes distais e proximais, que estarão dispostos de forma hierárquica em relação aos desfechos estudados. Desta maneira, os determinantes mais distais podem exercer influência aos mesiais, aos determinantes proximais e ao desfecho, (Victora et al.,1997). Assim neste estudo, organizamos as variáveis em quatro níveis: **(i)** variáveis ambientais, contextuais (centros – somente no estudo HELENA-CSS); **(ii)**variável demográfica, individual (idade); **(iii)** variáveis socioeconômicas, individuais (nível socioeconômico,educação dos pais e ocupação dos pais, este último avaliado somente no estudo HELENA-CSS); **(iv)** variáveis comportamentais, individual (atividade física, comportamento sedentário, consumo de frutas e verduras, bebidas açucaradas e hábitos de sono), **(Figura1)**.

A escola será utilizada como variável contextual nas análises multinível. Homocedasticidade será avaliada graficamente em todos os modelos de regressão como critério de análise. O *p*-valor de $\leq$0.20 ou alterações de 10% no coeficienteβserá adotado nas análises não ajustadas, para incluir as variáveis na análise multivariada que seguirá o modelo conceitual hierárquico, de acordo com os níveis acima mencionados.

Todas as análises serão ajustadas para a natureza em *cluster* da amostra usando o *"svy"* conjunto de comandos, e estratificada por sexo, uma vez que encontramos interações entre os desfechos estudados e o sexo (p <0,001). Todas as análises estatísticas serão também estratificadas por estudo, porque de acordo com as regras do estudo europeu HELENA-CSS não é permitido concatenar os dados deste com outros estudos epidemiológicos similares. Para as análises estatísticas estão sendo utilizado o software *Stata* versão 12.0 (*Stata Corporation, College Station,* TX, E.U.A.) e o critério de significância estatística estabelecido é o de 5%.

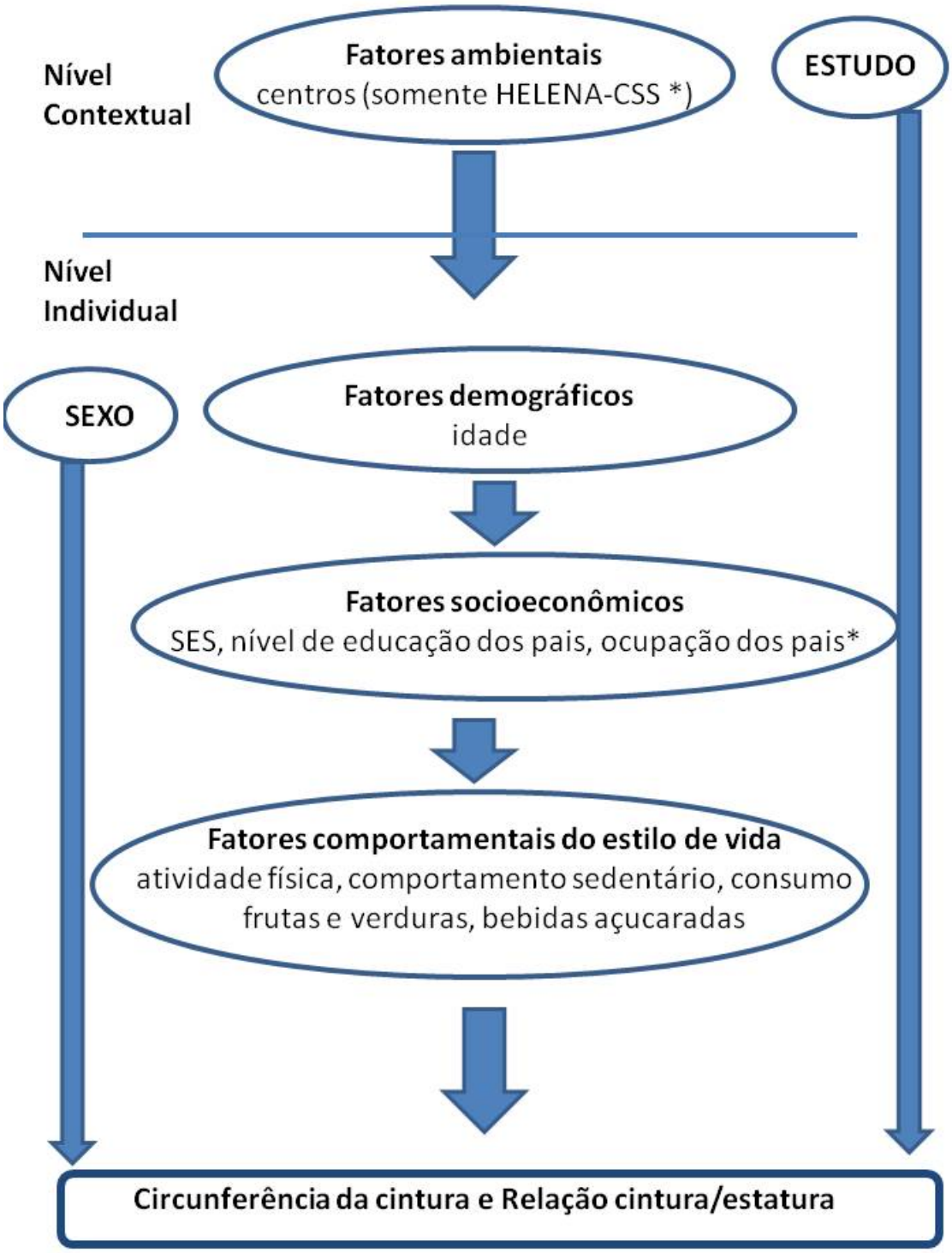

Figura 1. Modelo conceitual teórico para análise de determinantes dos indicadores antropométricos da obesidade abdominal

4. CRONOGRAMA DAS ATIVIDADES / ARTIGOS

As atividades serão desenvolvidas em conjunto como pós-doutorando do Departamento de Medicina Preventiva Dr. Augusto César Ferreira de Moraes, sob supervisão e orientação do Prof. Dr. Heráclito Barbosa de Carvalho.

Primeiro e Segundo Semestres– já realizado

1) Levantamento Bibliográfico

2) Estágio para compilação do banco de dados na Universidade de Zaragoza (Espanha)

3) Análise de dados dos dois estudos (HELENA-CSS e BRACAH *study)*

4) Elaboração de relatório e um artigo científico: ***"Abdominal obesityand its association with socioeconomic factors among adolescents from diferente living environments"***

Submetido a *Pediatric Obesity* (Fator de Impacto= 4,573).

Terceiro e Quarto Semestres – em desenvolvimento

1) Atualização bibliográfica

2) Cumprimento de disciplinas

3) Análise de dados dos dois estudos (HELENA-CSS e BRACAH s*tudy)*

4) Elaboração de relatório e do segundo artigo científico da tese a ser definido em conjunto com Orientador e Co-orientador após a qualificação.

5) Qualificação de Doutorado

Quinto e Sexto Semestres – a ser desenvolvido

1) Atualização bibliográfica

2) Finalização de cumprimento de disciplinas

3) Análise de dados dos dois estudos (HELENA-CSS e BRACAH *study)*

4) Elaboração da tese de doutorado e terceiro artigo científico da tese, a ser definido em conjunto com Orientador e Co-orientador após a qualificação.

5) Defesa de Tese de Doutorado

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APPENDIX 5

Carta-resposta à Ata de Exame de Qualificação

São Paulo, 27 de outubro de 2015.

Aluna: Elsie Costa de Oliveira Forkert
Orientador: Heráclito Barbosa de Carvalho

Diante das novas regras que hoje norteiam o Programa de Pós-graduação em Medicina Preventiva e, no sentido de colaborar no processo de construção da avaliação de alunos e projetos, estamos encaminhando uma carta anexa, em resposta ao Exame de Qualificação.
Esta carta responde de forma objetiva as recomendações solicitadas pela **Comissão Examinadora** por ocasião do **Exame de Qualificação** realizado na data de **18/08/2015** onde, por decisão desta Comissão, a candidata **não foi aprovada**.
Primeiramente vamos esclarecer alguns tópicos. Visto que inicialmente havíamos decidido apresentar na qualificação o artigo já submetido ao ***Pedriatic Obsesity*** *(Fator de Impacto=4,57)*, intitulado ***Abdominal obesity and its association with socioeconomic factors among adolescents from different living environments*** como um dos artigos desenvolvido a partir do projeto, encontramos uma dificuldade operacional ao nos deparar com o guia de avaliação proposto pela Comissão Coordenadora do Programa (CCP).

Observamos que este guia contém elementos mais focados no Projeto de Pesquisa e se apoia no modelo tradicional de tese de doutorado. Assim, ele exigiu que apresentássemos o projeto aprovado pelo Comitê de Ética com modificações, que mostrassem a evolução da aluna no doutorado. Diante desta situação, apresentamos à Comissão tanto o artigo quanto o projeto, no entanto, nos focamos mais no primeiro.

Desta forma, a Comissão limitou sua avaliação somente ao projeto onde deixou de observar elementos importantes que são rotineiramente solicitados em outros documentos da CCP para os alunos – **Ficha de acompanhamento anual do aluno de pós-graduação em Medicina Preventiva** – (anexa), tais como: elaboração e submissão de artigos científicos, apresentação de trabalhos em congressos, realização de estágios no exterior e reuniões de grupos de pesquisa, cronograma das atividades, entre outras, que são exigidos anualmente durante o curso, e que foram apresentados pela aluna durante sua arguição.

O que nos chama a atenção é que apesar dos inúmeros itens a serem avaliados utilizando o modelo da ata do exame de qualificação, a decisão da Comissão Examinadora apoiou seu parecer na reformulação do Projeto de Pesquisa. Isto levou a uma demanda em criar um documento que ainda não sabemos sobre sua utilidade, uma vez que as normas da Coordenação de Pós-graduação (CPG) exigem que seja apresentado na defesa de doutorado com artigos científicos, o projeto aprovado pela Comissão de Ética em Pesquisa (CEP) sem modificações, juntamente com os artigos

propostos. Dentro do planejamento, esta nova demanda interferiu no desenvolvimento das atividades já planejadas, *a priori* - desenvolvimento do segundo artigo da tese, em colaboração com a professora Michelle Wiest da Universidade de Idaho, USA.
Contudo as tarefas exigidas pela Comissão Examinadora foram realizadas, e aqui apresentadas na ordem como nos foi exigida:

1. **Introdução**

Foi reorganizada quanto ao tamanho dos parágrafos e atualizada quanto às referências mais antigas conforme solicitado.
Não entendemos a solicitação de reformular a descrição do objeto do estudo "obesidade abdominal", uma vez que havia sido delimitado e justificado tanto no Resumo quanto na Introdução, já no projeto anterior. (páginas: 05-09)

O **Modelo Conceitual** foi elaborado considerando os determinantes e os desfechos (Circunferência da cintura – CC e Relação cintura/estatura - RCE) de forma hierárquica – conforme apresentado no corpo do Projeto (Figura 1). (página: 25).
Os Objetivos foram descritos como Geral e Específicos. Os objetivos específicos foram organizados como artigos a serem desenvolvidos, sendo que até o momento, o primeiro artigo já foi submetido. (página: 11).

2. **Métodos**

A descrição dos estudos analisados foi reformulada detalhando: os cálculos do tamanho da amostra; características da cidade, mensuração das variáveis independentes (tais informações já tinham sido descritas anteriormente, com menos detalhes). (páginas: 13-17).

3. **Análise Estatística**

Neste item descrevemos as análises que serão realizadas nos artigos planejados, seguindo o modelo conceitual previamente elaborado. (páginas: 22-24).

4. **Título**

Na forma de artigos o titulo do projeto e da tese deverão ser mantidos conforme aprovação pelo CEP- FMUSP (anexo), e diante de uma necessidade de melhor ajuste, ser trocado mediante aprovação da mesma Comissão. (página: 43).

5. **Limitações secundárias**

Foi solicitada a inclusão da variável "desenvolvimento puberal" como uma variável confundidora. No entanto, esta variável não foi mensurada, o que nos obriga a apresentar esta lacuna como uma das limitações do estudo. Tal argumento esta sendo apresentado na resubmissão do artigo 1, que já está aceito com menores revisões na referida revista.

Desta forma, esperamos além de responder à demanda da Comissão Examinadora, poder acrescentar a este processo de avaliação na Pós-Graduação, críticas que contribuam com uma clareza no processo, crescimento e desenvolvimento do aluno.

APPENDIX 6

MEDICINA
USP
COMITÊ DE ÉTICA EM PESQUISA

Ao

Prof. Dr. Heráclito Barbosa de Carvalho

Departamento de Medicina Preventiva

O Comitê de Ética em Pesquisa da Faculdade de Medicina da Universidade de São Paulo, em sessão de **04.06.2014** tomou conhecimento que o Protocolo de Pesquisa nº **066/12** intitulado: **"Pressão arterial elevada e agregação de fatores de risco em adolescentes: um estudo multicêntrico"**, contempla o **sub-projeto** intitulado: "***Fatores Socioeconômicos e micro ambientais relacionados à obesidade abdominal em adolescentes: um estudo multicêntrico***", que será executado pela aluna de Doutorado **Elsie Costa de Oliveira Forkert** .

CEP-FMUSP, 06 de junho de 2014.

Prof. Dr. Paulo Eurípedes Marchiori
Vice-Coordenador
Comitê de Ética em Pesquisa

Comitê de Ética em Pesquisa
Faculdade de Medicina da Universidade de São Paulo