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Acurácia de variáveis antropométricas e sua associação com marcadores lipídicos para identificar risco para doenças cardiovasculares em população de idade escolar do município de Sapucaia do Sul.

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Dissertação submetida ao Programa de Pós-Graduação em Ciências da Saúde da Fundação Universidade Federal de Ciências da Saúde de Porto Alegre como requisito para a obtenção do grau de Mestre.

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Co-orientadora: Prof. Dra. Liane Nanci Rotta

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DEDICATÓRIA

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SUMÁRIO

LISTA DE ABREVIATURAS

DALY: *Disability-Adjusted Life Year*;

DAC: Doença Arterial Coronariana;

DCNT: Doenças Crônicas não Transmissíveis;

ONU: Organização das Nações Unidas;

IMC: Índice de Massa Corporal;

CC: Circunferência da Cintura;

RCE: Relação cintura/estatura;

P/E: Peso para estatura;

OMS: Organização Mundial da Saúde;

TG: Triglicerídeos;

CT: Colesterol Total;

HDL-c: Lipoproteína de alta densidade;

LDL-c: Lipoproteína de baixa densidade;

IHCIS: *Integrated HealthCare Information Services*;

BHS: *Bogalusa Heart Study*;

HAS: Hipertensão Arterial Sistêmica;

AUC: *Area Under the Curve*;

ROC: *Reciever Operating Characteristic*;

SPSS: Statistical Package for the Social Sciences;

ANOVA: One-way Analysis of Variance.

1.RESUMO

Introdução: Alterações no perfil lipídico desempenham um papel fundamental no desenvolvimento de risco cardiovascular. Ferramentas antropométricas são utilizadas como medidas para identificar excesso de peso e obesidade central, os quais são associados de maneira positiva com essas alterações. No entanto, é necessário um maior esclarecimento sobre a aplicabilidade destas ferramentas de acordo com o sexo e faixas etárias.

Objetivo: Comparar a acurácia do Índice de Massa Corporal (IMC), da circunferência da cintura (CC) e da Relação cintura/estatura (RCE) para identificar o risco para doenças cardiovasculares de uma população em idade escolar de Sapucaia do Sul, Rio Grande do Sul, Brasil.

Métodos: 618 crianças em idade escolar (6-17 anos) de 11 escolas municipais foram coletadas. Dessas, 592 crianças foram usadas para a análise final, divididas em quatro grupos: meninos 6-11 anos; meninos de 12 a 17 anos; meninas de 6 a 11 anos; meninas de 12 a 17 anos. Os desempenhos das ferramentas antropométricas foram avaliados de acordo com área sob a curva (AUC) em *Reciever Operating Characterisct* (ROC) com base em duas ou mais alterações no perfil lipídico (colesterol total, triglicerídeos, HDL-colesterol ou LDL-colesterol). Pontos de corte ótimos foram extraídos à partir do índice de Youden.

Resultados: A AUC para os grupos foram: 6-11 meninos (0,735 ± 0,05 para o IMC, 0,728 ± 0,06 para CC e 0,719 ± 0,06 para RCE) e 12-17 (0,855 ± 0,05 para o IMC, 0,872 ± 0,04 para 0,902 e CC ± 0,04 para RCE); meninas 6-11 (0,704 ± 0,06 para o IMC, 0,661 ± 0,06 para CC e 0,696 ± 0,05 para RCE) e 12-17 (0,635 ± 0,08 para o IMC, 0,712 ± 0,06 para CC e 0,702 ± 0,06 para RCE). De acordo com os melhores desempenhos na AUC, os pontos de corte ótimos foram: meninos 6-11 (0,74 para o IMC e 63,25 para CC) e 12-17 (0,5 para RCE); meninas 6-11 (1,715 para o IMC e 0,49 para RCE) e 12-17 (71,25 por CC e 0,45 por RCE).

Conclusão: As três ferramentas antropométricas foram adequadas para identificar risco cardiovascular em crianças de idade escolar. De maneira geral, RCE é um índice melhor e mais simples.

2.ABSTRACT

Background: Alterations in lipid concentrations play a fundamental role in the development of cardiovascular risk. Anthropometric tools are used as a measure of excessive weight and central obesity, which are positively associated with these alterations. However, applicability of these tools needs more exploration according to sex and age groups.

Aim: Compare the accuracy of Body-mass-index (BMI), Waist Circumference (WC) and Waist to Height Ratio (WHtR) to identify cardiovascular disease risk of a school age population from Sapucaia do Sul, Rio Grande do Sul, Brazil.

Methods: 618 children of school age (6-17 years) from 11 municipal schools were collected, 592 children were used for the final analysis divided into four groups: boys from 6 to 11 years; boys from 12 to 17 years; girls from 6 to 11 years; girls from 12 to 17 years. Anthropometric tools' performance were evaluated according to Area Under the Operating Characteristic Curve (AUC) based on two or more alterations on lipid profile (Total Cholesterol, Triglycerides, HDL-cholesterol, LDL-cholesterol). Optimal cut-off points were extracted using Youden Index.

Results: The AUC for the groups were: boys 6-11 (0.735 ±0.05 for BMI, 0.728 ±0.06 for WC and 0.719 ±0.06 for WHtR) and 12-17 (0.855 ±0.05 for BMI, 0.872 ±0.04 for WC and 0.902 ±0.04 for WHtR); girls 6-11 (0.704 ±0.06 for BMI, 0.661 ±0.06 for WC and 0.696 ±0.05 for WHtR) and 12-17 (0.635 ±0.08 for BMI, 0.712 ±0.06 for WC and 0.702 ±0.06 for WHtR). According to best performances in the AUC, optimal cut-off points were: boys 6-11 (0.74 for BMI and 63.25 for WC) and 12-17 (0.5 for WHtR); girls 6-11 (1.715 for BMI and 0.49 for WHtR) and 12-17 (71.25 for WC and 0.45 for WHtR).

Conclusion: The three anthropometric tools were adequate to identify risk for cardiovascular risk in school age children. Overall, WHtR is a better and simpler index.

3.INTRODUÇÃO

O aumento da prevalência do excesso de peso e da obesidade pode ser descrito como uma pandemia (ROTH *et al.*, 2004; SWINBURN *et al.*, 2011; POPKIN *et al.*, 2012). Em 2010, estimou-se que sobrepeso e obesidade causaram 3-4 milhões de mortes, 4% de anos de vida perdidos e 4% *Disability-Adjusted Life Year* (DALYs – ajuste de anos de vida perdidos correlacionado com anos vividos com incapacidades) (LIM *et al.*, 2012). Mundialmente, a prevalência de sobrepeso e obesidade combinados subiu 27,5% para adultos e 47,1% para crianças entre 1980 e 2013. Em números absolutos, essa população cresceu de 857 milhões para 2,1 bilhões de indivíduos no mesmo período de tempo (NG *et al.*, 2014). Esse cenário atual sugere que, indubitavelmente, o incremento da obesidade pode causar uma queda na expectativa de vida (OLSHANSKY *et al.*, 2005).

No Brasil, esse cenário se apresenta de maneira preocupante, visto que a prevalência do sobrepeso ultrapassa mais de 50% da população, em regiões urbanas. Nas 27 capitais dos estados nacionais, a frequência de excesso de peso é de 50,8%, com maior prevalência em homens (54,7%), do que mulheres (47,4%). Foi encontrada prevalência de excesso de peso em 62% dos homens de Porto Alegre e em 52% das mulheres de Manaus. Nessa mesma amostra, é possível identificar 17,5% de indivíduos com obesidade, com taxas mais elevadas nas cidades de Macapá, para homens (23%), e de Cuiabá, para mulheres (23%)(SAÚDE, 2014).

O sobrepeso e obesidade infantis variam de acordo com a região territorial e faixa etária. No Sul do país, o sobrepeso representa 25,7% de crianças e adolescentes de 6 a 18 anos; enquanto isso, 10,4% dessa população é obesa. Na região Sudeste, 13,7% da população entre 2 e 19 anos apresenta sobrepeso e 15,4% obesidade. No Nordeste do Brasil, foi identificado 15,8% de sobrepeso e 4,3% de obesidade na faixa etária de 6 a 19 anos. O Norte apresenta prevalência de 28,8% de sobrepeso entre 6 e 19 anos. Já a região Central apresenta 16,8% de sobrepeso e 5,3% de obesidade na população de 6 a 10 anos de idade (NIEHUES *et al.*, 2014). O excesso de peso em crianças e adolescentes está em ascendência, principalmente após os 5 anos, em todas as regiões e classes econômicas do país. Na faixa etária dos 5 aos 9 anos, 33,5% das crianças apresentam excesso de peso.

Além disso, 16,6% dos meninos e 11,8% das meninas estão obesos nessa idade (IBGE, 2010).

O excesso de peso e a obesidade estão diretamente associados ao comprometimento cardiovascular, que se apresenta como a principal causa de morte prematura no mundo (PAGIDIPATI & GAZIANO, 2013; GO *et al.*, 2014). O desenvolvimento das doenças cardiovasculares está associado a inúmeros fatores de risco, como o consumo alimentar e níveis lipídicos plasmáticos, com início ainda quando criança (EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR *et al.*, 2011; MORRISON *et al.*, 2012). O hábito alimentar do indivíduo sofre influências na infância e persiste como base para os padrões alimentares na vida adulta (NICKLAUS *et al.*, 2013).

De acordo com Brotons e colaboradores (BERENSON *et al.*, 1998), o nível de colesterol na infância é um fator preditivo do nível de colesterol na vida adulta. O inicio da Doença arterial coronariana (DAC) na infância, pelo aumento do colesterol plasmático, seria potencializado no decorrer da vida pela obesidade e por uma série de outros fatores, como história familiar, inatividade física e hipertensão arterial (MCGILL *et al.*, 2000). A partir desses dados, é possível inferir a necessidade de prevenção dos fatores de risco o mais cedo o possível.

No âmbito nacional, para deter a evolução de fatores de risco associados à obesidade, o Governo Federal lançou em 2011 o Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas não Transmissíveis (DCNT). Essa iniciativa é parte do grande projeto da Organização Mundial da Saúde (OMS), vinculado a países componentes da Organização das Nações Unidas (ONU), com ênfase à Estratégia Global da OMS em Dieta, Atividade Física e Saúde. Essa iniciativa representa a importância do aprimoramento do rastreamento da condição de excesso de peso e obesidade e do desenvolvimento de intervenções frente ao cenário atual brasileiro e mundial.

3.1 Marcadores antropométricos e risco cardiovascular em escolares

O sobrepeso na infância é fator de risco para obesidade mórbida no decorrer da vida (FERRARO *et al.*, 2003). De maneira isolada, a obesidade está associada com morbidade e mortalidade de inúmeras doenças, como doenças cardiovasculares, câncer e diabetes (AMUNDSON *et al.*, 2010).

A mensuração do excesso de peso e a análise de sua repercussão pode ser dar por marcadores antropométricos. A mensuração do excesso de peso e a análise de sua repercussão pode ser dar por marcadores antropométricos. A relação cintura/estatura (RCE) foi proposta por McCarthy e Ashwell, em 2006 (MCCARTHY & ASHWELL, 2006) como uma ferramenta antropométrica alternativa que leva em consideração tanto crescimento longitudinal como adiposidade central. A mensagem central por trás dessa relação é simples: "Mantenha sua circunferência da cintura a menos da metada da sua altura". Esse índice pode ser utilizado para rastrear mudanças relevantes na composição corporal e já foi utilizado para identificar risco para doenças crônicas em adultos e, em alguns casos, em crianças (MAFFEIS *et al.*, 2008; LICHTASH *et al.*, 2013).

Dentre as ferramentas antropométricas, é comum a utilização do Índice de Massa Corporal (IMC) e da circunferência da cintura (CC), não obstante, ainda há a necessidade de esclarecer a acurácia da RCE (KAHN *et al.*, 2005; MCCARTHY & ASHWELL, 2006; FREEDMAN *et al.*, 2007). Os três marcadores apresentam necessidade de padronização de treinamento por parte dos avaliadores para poderem ser comparados, porém requerem baixos recursos financeiros para sua reprodutibilidade (LICHTASH *et al.*, 2013). O IMC, que apresenta incremento em crianças e adultos nos anos recentes, se associa de maneira adequada com o grau de adiposidade e pode ser utilizado como preditor de DAC em jovens adultos (JANSSEN *et al.*, 2005). Por outro lado, não é capaz de diferenciar a adiposidade subcutânea da adiposidade visceral, um fator de predição para doenças crônicas não transmissíveis (BIGAARD *et al.*, 2005).

O IMC nem sempre foi usado para identificar sobrepeso e obesidade em crianças. Inicialmente, estas condições eram definidas usando a relação peso para estatura (P/E) de acordo com escores-Z para idade, com o objetivo de identificar as crianças mais pesadas para uma dada altura e idade (Use and interpretation of anthropometric indicators of nutritional status. WHO Working Group, 1986; Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee, 1995). Essa ferramenta continua a ser utilizada como um indicador mais sensível da obesidade que o IMC (STANOJEVIC *et al.*, 2007). No entanto, a implementação do P/E se demonstrou complicada, uma vez que não há um valor único que pode ser usado para crianças de todas as idades. Além disso, essa abordagem não é utilizada em adultos e é menos familiar do que o IMC, tanto pelos profissionais de saúde como pelo público em geral. Uma medida única, ou índice, ajustado para a altura é preferível, e pesquisadores e clínicos têm utilizado o IMC para facilitar esse processo. Embora os pontos de corte para IMC serem amplamente utilizados nas definições de sobrepeso e obesidade infantil na literatura, apenas recentemente eles foram oficializados pela OMS (DE ONIS & LOBSTEIN, 2010). Historicamente, o IMC foi desenvolvido a partir de uma população de adultos diabéticos, a fim de comparar o peso individual com suas respectivas estaturas, e foi demonstrado como um bom preditor de tecido adipose (DOAK, 2013). Os pontos de corte de 25 e 30 kg/m² foram então atribuídos a partir de uma associação de maior risco de mortalidade a essas condições (ASHWELL, 2011). Devido a possíveis erros de classificação ao utilizar esse índice em crianças, é fundamental avaliar criticamente o uso do IMC para diagnosticar o sobrepeso ou a obesidade.

É possível encontrar diferentes metodologias para mensurar a CC na literatura (RUDOLF *et al.*, 2007). Sendo assim, métodos específicos podem comprometer a comparação dessa medida entre estudos e populações diferentes (MAGALHAES *et al.*, 2014). Por exemplo, é possível encontrar autores como Schwandt (SCHWANDT *et al.*, 2008) e Roswall (ROSWALL *et al.*, 2009), que utilizaram o ponto médio entre a crista ilíaca e a costela inferior, enquanto Taylor (TAYLOR *et al.*, 2008) mediram a CC na menor circunferência entre a crista ilíaca e a caixa torácica. Como esses referenciais antropométricos podem complicar a interpretação dos resultados das medidas individuais de CC, não é claro se essas diferenças podem gerar algum viés sistemático entre os estudos.

Devido à inexistência de um ponto de corte universal para a CC para crianças (WHO, 2008), a RCE se apresenta como marcador antropométrico interessante, com recomendação de valor desejado abaixo de 0,5 (MCCARTHY & ASHWELL, 2006). A RCE foi considerada útil para identificar risco metabólico em crianças com excesso de peso (MAFFEIS *et al.*, 2008), porém estudos nessa população permanecem escassos e necessários para a fundamentação dessa ferramenta (CAMPAGNOLO *et al.*, 2011). Dessa maneira, persiste a dúvida relativa a um marcador antropométrico com adequada sensibilidade e especificidade para avaliar risco para doenças cardiovasculares na idade escolar.

3.2 *Dislipidemia e risco para a saúde em escolares:*

Dislipidemia pode ser caracterizada pelo incremento nos níveis séricos de triglicerídeos (TG) e/ou colesterol total (CT) ou diminuição nos níveis séricos da lipoproteína de alta densidade (HDL-c), que pode levar ao desenvolvimento de aterosclerose. Os critérios para determinação de alterações desses parâmetros, segundo a V Diretriz Brasileira de Dislipidemias e Prevenção de Aterosclerose, preconizam valores elevados de CT, TG e lipoproteína de baixa densidade (LDL-c) em ≥ 170 mg/dL, ≥ 130mg/dL e ≥ 130mg/dL, respectivamente; valores desejáveis de HDL-c são determinados em ≥ 45mg/dL para a idade de 2 – 19 anos (SOCIEDADE BRASILEIRA DE *et al.*, 2013). Em concordância com o aumento da prevalência de excesso de peso em escolares, é possível identificar inadequação desses parâmetros para a mesma idade. Li e colaboradores avaliaram 273.064 crianças americanas com registro de ao menos um desses parâmetros lipídicos na plataforma *Integrated HealthCare Information Services* (IHCIS). Nessa amostra, 22,9% dos indivíduos apresentaram dislipidemia, com elevada trigliceridemia como alteração mais comum (13,2%) (LI *et al.*, 2010). Esse achado está de acordo com o apresentado em outro grande estudo populacional (JOHNSON *et al.*, 2009), capaz de rastrear baixos níveis de HDL-c em adolescentes do sexo masculino quando comparados a meninos mais jovens.

A relevância do rastreamento do perfil lipídico em diferentes faixas etárias é demonstrada no *Bogalusa Heart Study* (BHS): um estudo epidemiológico da história natural de fatores de risco cardiovasculares e ambientais, acompanhados desde a infância. Composto por uma amostra birracial, relativamente estável, de todas as crianças e jovens adultos residentes da região semi rural de Bogalusa, Louisiana, desde 1972 (BERENSON *et al.*, 1982). Mais de 160 estudos foram conduzidos até o momento, com o esclarecimento que fatores de risco cardiovasculares são identificáveis na infância e são preditivos para risco para DAC na idade adulta (BURKE *et al.*, 1986; BERENSON, 2002).

Estudos observacionais demonstram claramente que a maioria das etiologias para doenças cardiovasculares tem seu início da infância. De maneira mais específica, é possível encontrar alterações anatômicas tão precocemente quanto de 5 a 8 anos de idade do indivíduo. Estudos de imagens do coração, das artérias carótida e femoral demonstram que DAC e hipertensão arterial sistêmica (HAS) pode se iniciar precocemente na vida (PAUL *et al.*, 2011) e estudos de autópsia confirmam lesões na aorta e em veias coronárias nessa faixa etária (TRACY *et al.*, 1995). Além disso, indivíduos de raça negra apresentam uma forma mais grave e prevalente de HAS e diabetes (CHEN *et al.*, 2011; NGUYEN *et al.*, 2012), homens brancos podem apresentar DAC de maneira precoce (BERENSON & BOGALUSA HEART STUDY, 2001) e mulheres apresentam um retardamento para desenvolver doenças cardiovasculares (KONES, 2011).

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5.OBJETIVOS

5.1 Objetivo geral:

Avaliar a acurácia de variáveis antropométricas e sua associação com marcadores lipídicos para identificar risco para doenças cardiovasculares de uma população de idade escolar do Município de Sapucaia do Sul.

5.2 Objetivos específicos:

- Avaliar a acurácia do IMC para identificar risco para doenças cardiovasculares em escolares estratificados por idade;
- Avaliar a acurácia da Circunferência da Cintura para identificar risco para doenças cardiovasculares escolares estratificados por idade;
- Avaliar a acurácia da Relação Cintura/Estatura para identificar risco para doenças cardiovasculares escolares estratificados por idade.

6.ARTIGO ORIGINAL

6.1 Cover Letter:

Title:

Waist-to-height Ratio: simpler and better. Accuracy to identify cardiovascular risk in school age children from Brazil.

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Keywords: Body Mass Index, Waist Circumference, Whaist-Height Ratio, Child, Cholesterol. HDL, Lipids, Cardiovascular Diseases, Risk.

Acronyms:

BMI: Body Mass Index

WC: Waist Circumference

WHtR: Waist-to-Height Ratio

AUC: Area Under the Curve

ROC: Receiver Operating Characteristic

DALYs: Disability Adjusted Life Years

CVD: Cardiovascular Disease

6.2 Abstract:

(1) Background and Aims: Significant changes in body composition are used to identify cardiovascular risk. However, applicability of anthropometric tools needs more exploration according to sex and age groups. This study analyzed the accuracy of Body-mass-index (BMI), Waist Circumference (WC) and Waist to Height Ratio (WHtR) to identify cardiovascular disease risk of a school age population from Sapucaia do Sul, Rio Grande do Sul, Brazil.

(2) Methods and Results: 592 children from 11 municipal schools were stratified into: boys 6-11 years; boys 12-17 years; girls 6-11 years; girls 12-17 years. Anthropometric tools' performance were evaluated according to Area Under the Curve (AUC) for Receiver Operating Characteristic (ROC) distribution based on two or more alterations on lipid profile (Total Cholesterol, Triglycerides, HDL-cholesterol, LDL-cholesterol). Optimal cut-off points were extracted using Youden Index.

AUC were: boys 6-11 (0.735 for BMI, 0.728 for WC and 0.719 for WHtR) and 12-17 (0.855 for BMI, 0.872 for WC and 0.902 for WHtR); girls 6-11 (0.704 for BMI, 0.661 for WC and 0.696 for WHtR) and 12-17 (0.635 for BMI, 0.712 for WC and 0.702 for WHtR). Optimal cut-off points were: boys 6-11 (0.74 for BMI and 63.25 for WC) and 12-17 (0.5 for WHtR); girls 6-11 (1.715 for BMI and 0.49 for WHtR) and 12-17 (71.25 for WC and 0.45 for WHtR).

(3) Conclusion: The three anthropometric tools were adequate to identify risk for cardiovascular risk in school age children. Overall, WHtR had a better performance to identify children with lipid profile alterations.

6.3 INTRODUCTION:

The increased prevalence of obesity and overweight is now considered to be a global pandemic (1-3). In 2010, it was estimated that overweight and obesity caused 3-4 million deaths, a loss of 4% loss of life years, and 4% of Disability Adjusted Life Years (DALYs) due to co-morbidities associated with excess body fat mass (4). Globally, the prevalence of overweight and obesity among adults is 27.5% for adults is 47.1% for children. In absolute numbers, this population has increased from 857 million to 2.1 billion people, from 1980 to 2013 (5). Thus, it is clear that obesity and overweight are serious public health problems and it is important to improve our understanding of how excess body weight increases the risk for chronic disease.

Excess body weight and obesity are positively associated with cardiovascular diseases (CVD), the leading cause of death in the world (6, 7). The development of CVDs is associated with a number of risk factors, such as the consumption of high-fat diets and high levels of plasma lipids, factors that generally begin in childhood (8, 9). As reported by Berenson et al. (10), the level of cholesterol in infancy is a predictive factor of the cholesterol level in adulthood. Atherosclerosis begins in infancy by the increase of plasma cholesterol and can be accelerated by obesity through a number of factors, such as family history, physical inactivity, and hypertension (11). Therefore, it is important to intervene as soon as possible to prevent risk factors from becoming more severe or numerous. Yet, it is unclear what anthropometric variable are most associated with abnormal lipid profiles, making the criteria for intervention difficult to determine.

Overweight in infancy is a risk factor for adult obesity and many obese children continue to remain obese as adolescents and adults (12). The assessment of excess body weight and its relationship to other biological risk factors can be accomplished with relatively simple anthropometric markers. Two of the most common anthropometric assessments of overweight are Body Mass Index (BMI) and waist circumference (WC) which may explain part, but not all, of the potential risk for CVD in children.

These two anthropometric tools have presented strong association with fat mass for children and adults (13). BMI is expressed as kg/m² and is not able to differentiate whole body adiposity from central adiposity, a strong predictor for the development of non noncommunicable diseases (14). WC, in other hand, is positively associated with longitudinal growth and requires specific cut-off values for evaluation, according to sex and age. Thus, there's no single universal value to measure possible outcomes due alterations in this parameter (15).

Waist-to-Height Ratio has been proposed as an alternative measure that concerns both longitudinal growth and central adiposity (16). As a simple message to "keep your waist circumference to less than half your height", this tool can be used to screen relevant changes in body composition and have already been used to identify risk for chronic diseases in adults and children (17, 18). However, how well these three anthropometric tools are able to identify CVD risk in children of different ages and sex have not been well established. Therefore, the aim of this study was to evaluate the accuracy of BMI, WC and WHtR to identify lipid profile alterations in school age children.

6.4 METHODS:

Population:

This study was based on a population of 618 children of school age (6-17 years) from 11 municipal schools from Sapucaia do Sul city, Rio Grande do Sul. This is derivative from the project called Investigation of Dyslipidemia of a scholar population from Sapucaia do Sul, conducted in 2008. After application of extreme studentized deviate for outliers, according to distribution of anthropometric and lipid variables, 592 children were used for the final analysis.

Logistic

The staff that conducted the data collection was previously trained and informed according to the project's ethical aspects. To insure tool's precision, pre-test was applied. Children at school age and regularly matriculated at the selected schools were invited to initiate in the study. Familiar responsible signed the Informed Consent with the supervision of previously trained member of the research's staff.

Groups were distributed according to age and sex. Children were stratified into four groups: boys from 6 to 11.99 years; boys from 12 to 17.99 years; girls from 6 to 11.99 years; girls from 12 to 17.99 years.

Anthropometry:

Body composition variables were collected by the same trained measurer. Subject's weight was measured with no shoes and light clothes on by digital weighing-machine (Techline®, Brazil) with precision of 100g; Standing height was measured with a stadiometer (Seca®, Germany) fixated on a straight wall. Subject was positioned with both heels touching the wall; Waist Circumference (WC) was obtained from the narrowest point of the subject's chest with a non-extensive tape-measure; Waist-to-height Ratio (WHtR) value was obtained from the equation: Waist (cm)/Height (cm); Body-mass-Index (BMI) value was obtained from the equation: weight (kg)/ height(m)^2.The definition of overweight and obesity was according to BMI-per-age. Children who presented ≥1 z-score alteration were classified as overweight, and ≥ 2 z-scores alteration were classified as obese.

Blood analysis:

Blood samples were obtained from 12 hour fasting subjects, with a vacuum system from the brachial vein. The material was collected in tubes with sodium fluoride (EDTA conjugated) for plasma and in tubes with no anti-coagulant for serum. The material was centrifuged at 3,500/10 minutes and analyzed immediately afterwards. Analysis were obtained with automation apparatus Labmax (Labtest, Brazil), after quality control procedures and control and pathologic serum, at Laboratory of Clinics Analysis from Cruzeiro do Sul's Health Unity – Porto Alegre. Total Cholesterol (calorimeter enzymatic test), Triglycerides, HDL-cholesterol (precipitation method) and LDL-cholesterol (Friedwald equation) specific doses were measured with Labtest kits.

Statistical Analysis:

Data was analyzed with the software Statistical Package for the Social Sciences (SPSS) version 21.0. In order to evaluate homogeneous distribution, Kolmogorov-Smirnov test was applied. Normal distribution variables were presented as mean and standard deviation, while non-parametric variables as median and interquartile intervals. Qualitative variables were presented as absolute and relative frequencies. One-way Analysis of Variance (ANOVA) was applied to compare the groups according to anthropometric and biochemistry data. Tukey's post-hoc test was applied to express significant differences among groups, defined as < 5%. Outliers were handled with the use of extreme studentized deviate, by maximum deviation from the mean.

Receiver operating characteristic (ROC) analysis was used to determine the performance of anthropometric indices to identify cardiovascular risk. The accuracy of the anthropometric measures in predicting cardiovascular risk were assessed by the area under the operating characteristic curve (AUC); a 95% confidence interval was used (95% CI), based on two or more alterations in the lipid profile. In order to calculate the optimal cut-off point, Youden index (sum of sensitivity and specificity - 1) was used (19).

Ethical aspects:

The current study was submitted and approved by the Ethical and Scientific Committee of UFCSPA (716/08).

6.5 RESULTS:

This study utilized a cross-sectional analysis of 592 low income children and adolescents from 6-17 years old. Among those, 220 boys were evaluated, 141 from 6 to 11 years and 79 from 12 to 17 years; while 372 girls were evaluated, 224 from 6 to 11 years and 148 from 12 to 17 years. A significant number of families were of low-income, as 44.3% had an annual income of under US$3.141.52, which represents a monthly income equal to or lower than the national minimum wage (approximately US$261.79 per month). Mothers spent an average of 6.79 ±2.8 years in school, while fathers spent 7.01 ±2.8 years in school.

The anthropometric and lipid profile stratified by sex and age group are presented in Tables I and II. The prevalence of overweight was 40.5% for the boys and 34.4% for the girls, while 20% of the boys and 12.9% of the girls were classified as obese, according to BMI-for-age (≥ 1 Z-score and ≥2 Z-score, respectively). High Waist/Height ratio (≥0.5) was identified in 28.2% of the boys and 29.6% of the girls. Central obesity was identified in 22.2% of the boys and in 25.4% of the girls, according to WC for age (≥90th percentile). Boys showed lower levels of HDL-cholesterol at 12-17 years when compared to 6-11 years (48.7 ±12 vs. 43.9 ±9.4) and when compared to girls at 12-17 years (48.7 ±10.9 vs. 43.9 ±9.4). Boys presented higher Triglycerides alterations at both age groups, when compared to girls (8.5% vs. 5.8% at 6-11 and 11.4% vs 6.1% at 12-17) At least one lipid profile alteration was detected in 42.7% of the boys and in 41.4% of the girls. Risk for cardiovascular diseases was identified in 11.8% of the boys and 10.5% of the girls (which presented two or more alterations in the lipid profile).

The AUC for BMI, WC and WHtR are presented in Table III, according to sex and age group. AUC was higher for all anthropometric indices in boys when compared to girls, stratified by age group (Table III; Figure 1).

The optimal cut-off values of the anthropometric indices found to predict children and adolescents with two or more cardiovascular risk factors using the ROC curve analysis are summarized in Table IV.

6.6 DISCUSSION:

As the prevalence of overweight and obesity increases around the globe, especially in children, effective tools are needed for screening early stages of possible outcomes from this condition (5). Anthropometric variables are simple and low cost tools that are able to identify relevant changes in body composition that can be considered of risk for chronic diseases in children and adults (20). Briefly, in our cross-sectional study, we found that WHtR was the most accurate anthropometric marker for increased cholesterol and triglycerides, HDL, and LDL in children of 6-17 years of age. Thus, it may be proposed that using an index that incorporates both central body size and growth may be better markers for CVD risk than traditional markers, such as BMI or WC.

In a meta-analysis conducted by (21), twenty-four cross-sectional studies and ten prospective studies with a total number of 512.809 adult participants were identified. WHtR was found to have a stronger association than BMI with diabetes mellitus (rRR: 0.71, 95% CI: 0.59-0.84) and metabolic syndrome (rRR: 0.92, 95% CI: 0.89-0.96) in cross-sectional studies. In prospective studies, WHtR was superior to BMI in detecting several outcomes, including CVD incidence and mortality, as well as all-cause mortality. BMI did not perform better for any outcome.

Previous studies of anthropometric markers for CVD in children have being focused in alteration of central adiposity as a risk for cardiovascular disease (22, 23). WC and WHtR showed better performance than BMI as predictors for cardiovascular disease in children populations (17, 20). A systematic review from cross sectional analyses, forty-four in adults, thirteen in children, supported these predictions. Analysis revealed mean areas under ROC values of 0.704, 0.693 and 0.671 for WHtR, WC and BMI, respectively. The AUC for ROC analyses indicate that WHtR may be a more useful global clinical screening tool than WC, with a weighted mean boundary value of 0.5 (24).

The results presented in our study are consistent with most, but not all, studies looking at the relationship between various anthropometric measures in childhood and risk of developing chronic diseases. Freedman et al. (25), evaluated 2498 children (Bogalusa Heart Study), from 5 to 17 years, and found that the AUC for BMI and WHtR were similar to cardiometabolic risk and ranged from 0.85–0.86 for risk factor sum (Total-to-HDL cholesterol ratio, Triglycerides, LDL-cholesterol, HDL-cholesterol, Fasting insulin, Systolic blood pressure and Diastolic blood pressure). However, waist-to-height ratio was slightly better in predicting concentrations of total-to-HDL cholesterol ratio and LDL cholesterol, similar to our study. Although WHtR may be preferred because of its simplicity, additional longitudinal data are needed to examine its relation to disease outcomes. It is important to note that there is no gold standard for cardiovascular risk diagnostic measures in childhood, which is largely the result of instability during this period of growth.

Our results suggest optimal cut-off points of 0.74 and 0.845 of BMI, for boys from 6-11 years and girls from 12-17 years, respectively. These findings may provide evidence for the early development of risk factors, even in children with lower BMI values than 1 z-score, likely due consequences of unhealthy eating and physical activity habits (26). Widespread change in children's lifestyles may be affecting their body composition, which results in higher fat mass and lower fat-free mass, even when BMI falls in the normal range.

It's important to notice the differences for that there is no universal cut-off point that can be used to identify alterations in WC for children of all ages (15). Contrary to WC, WHtR has the advantage of not requiring population specific reference tables as well as age and sex specific cutoffs.

Sensibility and specificity of each cut-off point among are different for sex and for age groups. For boys at the age of 6-11 years, BMI and WC were strongly sensible markers. This indicates that these cut-offs were adequate to screen true positives alterations in lipid profile. For boys at 12-17 years, WHtR showed maximum sensibility, with a strong specificity. This demonstrates how accurate the value of 0.5 is to identify risk of cardiovascular disease, as suggested in other studies (17, 24, 27). For girls of 6-11 years, BMI and WHtR showed high specificity. Both cut-off points were adequate to identify false negatives alterations in lipid profiles. For girls of 12-17 years, WC and WHtR showed very high sensibility, with a great screening capacity of true positives alterations in lipid markers.

Optimal cut-off values for WHtR ratio were similar to 0.5, except for girls at 12 to 17 years. They have all showed high sensibility, however, the latter had presented low specificity. When comparing the optimum cut-off point of this anthropometric tool for boys for 12-17 with girls for 12-17, they've presented significant different values according to the Youden Index (1.757 vs. 1.404, respectively). This result shows that, even though they are the best performances for their specific gender and age group, 0.5 is a more reliable universal value (28), being able to distinguish the true positive and the false negative individuals more clearly. However, the 0.45 value shows that even a lower presence central obesity could identify alterations in the lipid profile. Nevertheless, there were no statistical difference between the cutoff points of 0.45 and 0.50 for girls at this age according to the Youden Index (1.349 vs. 1.346, respectively). Solorzano et al. (29) alert that most of these girls should already be in post-pubertal stage, suggesting a consequence of more stable group height. It demonstrates that the value of 0.5 could misclassify girls with adequate WC for height, which have in fact compromised lipid status. Finally, these girls have been shown to be more vulnerable to CVD risk and require further attention for diagnosis.

While the results presented are robust, it is necessary and important to discuss potential limitations that may limit broader conclusions when interpreting the data. Even though our study showed higher absolute number of girls than boys in both age groups, the proportions between the two groups were the same. Nevertheless, our study haven't analyzed the biological state of maturation for this population. The literature demonstrates that 50% of girls would have menstruated at the mean age of 12.5 years, as our cut-off point for age groups was defined at 12 years old. Recent data suggests that excess adiposity during childhood may advance puberty in girls and delay puberty in boys. However, how obesity influences hormone aspects of pubertal development remains unclear (29).

In conclusion, based on our data, we've found that BMI, WC and WHtR were adequate to identify cardiovascular risk for children from 6-17 years. WHtR showed equivalent or better performance as the highest tools' accuracy values, except for boys from 6 to 11 years (BMI and WC). By using WHtR the diagnostic process is facilitated, so it's not necessary to be expressed by using Z-scores and a single cut-off point (0,5) is possible to be used with the simple message of "keep your waist circumference to than half of your height". Overall, the application of this tool as an indicator of cardiovascular risk in public health screening has not only statistical advantages but is simpler.

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6.9 Appendices:

Table I

	Boys (M ± SD)			Girls (M ± SD)		
	6-11	12-17	Total boys	6-11	12-17	Total girls
Age, years.	9.5 ±1.6	13.6 ±1.2	11.0 ±2.5	9.8 ±1.3	13.7 ±1.2	11.4 ±2.2
Weight, kg.	35.5 ±11.4	53 ±14	41.9 ± 15	36.8 ±10.6	51.6 ±12.8	42.7 ± 13.6
Height, cm.	136.9±10.7	158.5±11.7	144.8±15.2	138.8±10.4	156 ±7	145.7±12.5
BMI-for-age, Z-score; mediana ± IR	0.83 ±1.44	0.5 ±1.4	0.7 ± 1.42	0.68 ±1.2	0.38 ±1.1	0.56 ±1.2
WC, cm.	65.6 ±11.2	74.3 ±11.2	68.8 ± 12	66.8 ±10.7	74.4 ±11	69.8 ±11.4
WHtR;	0.48 ±0.06	0.47 ±0.06	0.47 ±0.06	0.48 ±0.06	0.48 ±0.06	0.48 ±0.06

M: mean; SD: standard deviation; IR:Interquartile range; BMI: Body-mass-index; kg: kilograms; cm: centimeters; WC: Waist circumference; WHtR: Waist-to-height ratio.

Table II

	Boys (M ± SD)			Girls (M ± SD)		
	6-11	12-17	Total Boys	6-11	12-17	Total girls
TC, mg/Dl.	158.4 ±27.2	148.8 ±25.8	155 ±27	158.9 ±26.3	154.3 ±27.3	157 ±26.8
Tg, mg/dL.	69.3 ±31.2	78 ± 42.5	72.4 ±35.8	74.8 ±34	74 ±30.7	74.5 ±30.7

HDL-c, mg/dL.	48.7 ±12	43.9 ±9.4*	47 ±11.4	46.8 ±11.5	48.7 ±10.9†	47.6 ±11.3
LDL-c, mg/dL.	95.8 ±23.9	89.3 ±22.3	93.5 ±23.5	97.1 ±23	90.8 ±22	94,6 ±22.8

TC: Total cholesterol; Tg: Triglycerides; HDL-c: High density lipoprotein cholesterol; LDL-c: Low density lipoprotein cholesterol; M: mean; SD: Standard deviation; mg/dL: miligrams/deciliters. * p=0.03 vs 6-12 years; † p=0,001 vs boys 12-18 years.

Table III:

	6-11		12-17	
	AUC ±SD	min/max	AUC ±SD	min/max
Boys				
BMI (Z-score)	0.735 ±0.05	0.62/0.84	0.855 ±0.05	0.75/0.96
WC (cm)	0.728 ±0.06	0.6/0.85	0.872 ±0.04	0.79/0.95
WHtR	0.719 ±0.06	0.60/0.84	0.902 ±0.04	0.82/0.98
Girls				
BMI (Z-score)	0.704 ±0.06	0.58/0.82	0.635 ±0.08	0.47/0.8
WC (cm)	0.661 ±0.06	0.54/0.78	0.712 ±0.06	0.59/0.83
WHtR	0.696 ±0.05	0.58/0.80	0.702 ±0.06	0.58/0.82

BMI: Body-mass-index per age; cm: centimeters; WC: Waist circumference; WHtR: Waist-to-height ratio; AUC: Area under the curve; SD: Standard deviation; min: minimum; max: maximum

Figure 1:

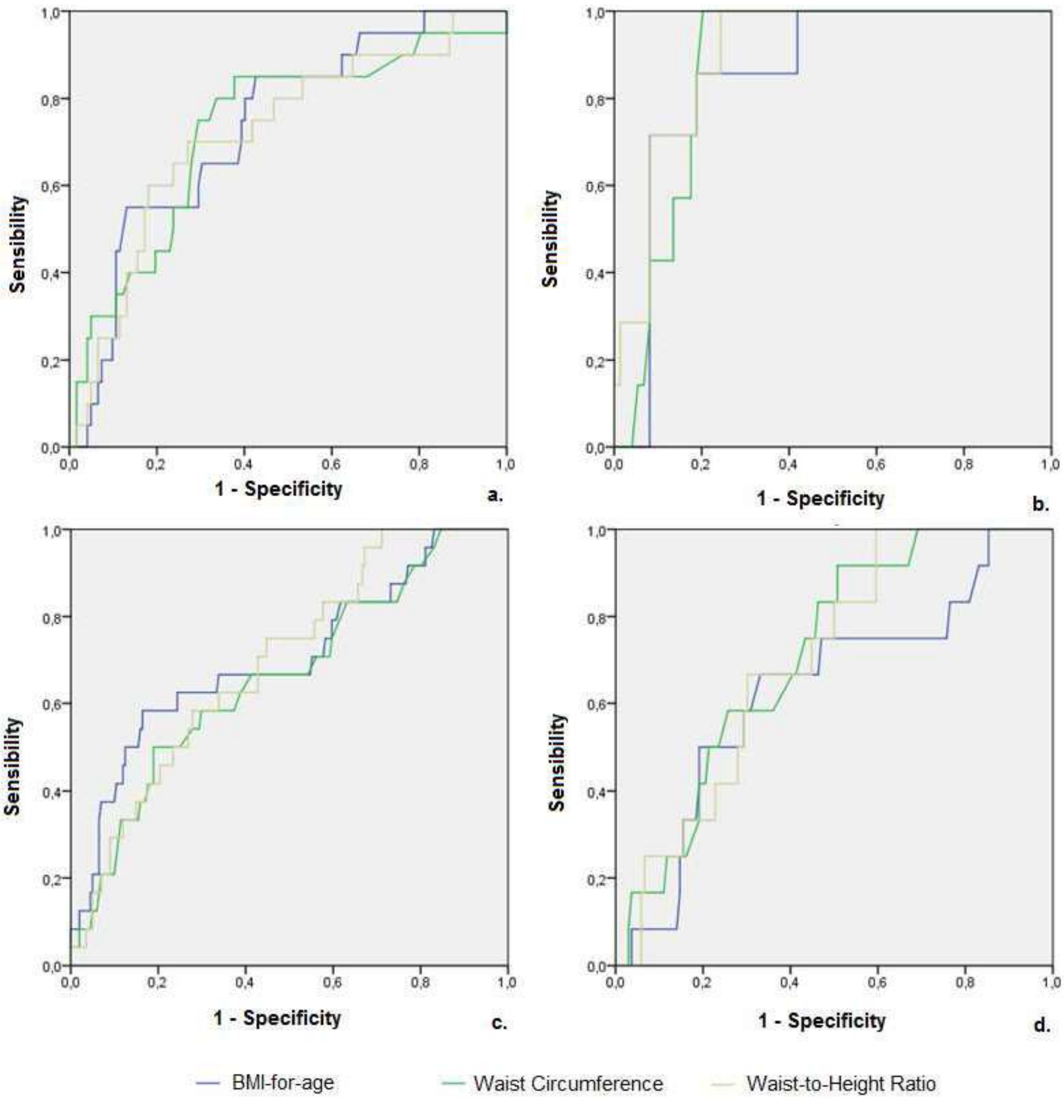

Table IV:

	BMI-for-age (Z-score)		Waist circumference (cm)		Waist/height ratio	
	6-11	12-17	6-11	12-17	6-11	12-17
Boys						
Cut-off	0.74	1.455	63.25	81.25	0.485	0.50
Sensibility	0.850	0.857	0.850	1	0.7	1
Specificity	0.574	0.811	0.623	0.797	0.73	0.757
Girls						
Cut-off	1.715	0.845	73.75	71.25	0.499	0.445
Sensibility	0.583	0.667	0.5	0.917	0.583	1.0
Specificity	0.836	0.669	0.811	0.493	0.721	0.404

BMI: Body mass index; cm: centimeters.

6.10 Tables, Figure legends

Table I: Anthropometric indices for boys and girls by age group.

Table II: Lipid profile for boys and girls by age group.

Table III: Area under ROC curve of body mass index, waist circumference and waist-to-height ratio as identifiers of cardiovascular risk factors in boys and girls by age group.

Figure 1: Area under the receiver operating characteristic curve according to anthropometric indices as identifiers of cardiovascular risk in: **a.**: boys at 6-11 years; **b.**: boys at 12-17 years; **c.**: girls at 6-11 years; **d.**: girls at 12-17 years.

Table IV: Optimal cut-off points for anthropometric indices as identifiers of cardiovascular risk in boys and girls by age group.

7.CONCLUSÃO

Com base em nossos dados, foi demonstrado que o IMC, a CC e a RCE apresentaram associação com a alteração de marcadores lipídicos e acurácias adequadas para identificar risco cardiovascular em uma população de idade escolar do Município de Sapucaia do Sul. A RCE apresentou desempenho melhor ou equivalente aos maiores valores de acurácia das demais ferramentas antropométricas, exceto para os meninos dos 6 aos 11 anos (IMC e CC). Ao utilizar RCE o processo de diagnóstico é facilitado, pois não é necessário ser expresso em escores-Z e um único ponto de corte (0,5) é possível de ser usado. Assim, é importante a divulgação da simples mensagem de "mantenha sua circunferência da cintura menor que metade da sua estatura". No geral, a aplicação desta ferramenta como um indicador de risco cardiovascular em saúde pública não apresenta somente vantagens estatísticas, como é mais simples.

8.ANEXOS

8.1 Aceite do Comitê de Ética em Pesquisa:

Parecer Consubstanciado de Projeto de Pesquisa

Título do Projeto: Investigação de Dislipidemia na População Infantil Atendida pelo SUS, em Laboratório da Rede Municipal de Porto Alegre
alterado para:
INVESTIGAÇÃO DE DILIPIDEMIAS NA POPULAÇÃO DE ESCOLARES DA REDE MUNICIPAL DE ENSINO DE SAPUCAIA DO SUL/RS.

Pesquisador Responsável Liane Nanci Rotta — PARECER Nº 716/08

Data da Versão 25/09/2008 — Cadastro 163/06 — Data do Parecer 19/10/2008

Grupo e Area Temática — III - Projeto fora das áreas temáticas especiais

Objetivos do Projeto
Geral: Avaliar a prevalência de dislipidemias em crianças atendidas no Laboratório Municipal de Análises Clínicas, da cidade de Porto Alegre/RS avaliando a associação com fatores genéticos (causas primárias) ou fatores associados (causas secundárias), assim como, a interação destes dois fatores, visando a implementação de medidas preventivas ainda na infância, a fim de evitar o processo arterosclerótico e a incidência de doenças arteriocoronarianas.

Específicos:
(1) Avaliar a prevalência de dislipidemias em crianças atendidas no Laboratório de Análises Clínicas do Posto de Atendimento da Vila Cruzeiro do Sul, da cidade de Porto Alegre/RS;
(2) Identificar parâmetros nutricionais como: IMC, pregas cutâneas etc. em indivíduos crinças atendidas no Laboratório supra-citado;
(3) Avaliar a associação entre o perfil lipídico, diabetes e obesidade;
(4) Avaliar a prevalência de crianças dislipidêmicas causada por alteraçãoes primárias (genética) e secundárias;
(5) Avaliar a variabilidade dos genes que codificam enzimas envolvidas no metabolismo de lipídios (Apo-lipoproteína E, C1, C2 e C4) envolvidas na causa das dislipidemias na infância;
(6) Analisar a interção entre variabilidade genética e os fatores ambientais;
(7) Adotar medidas de atenção primária (preventivas) aos indivíduos dislipidêmicos: adequação nutricional, adoção de atividades físicas, etc.;
(8) Avaliar o impacto da adoção das medidas primárias sobre os lipídios séricos.

Sumário do Projeto
Delineamento: Estudo transversal

Critérios de inclusão: crinças com idade inferior a 12 anos, acompanhadas do responsável, atendidas no Posto de Posto de Atendimento da Vila Cruzeiro do Sul.

Operacionalização:
- Será coletada uma amostra de sangue de 5mL, após 12h de jejum , por venopunção.
- Serão dosados: glicose, TAG, colesterol total, HDL, proteína C reativa, LDL, uréia, creatinina, TSH, T3, T4, TGO, TGP, fosfatase alcalina, GGT. As crinças dislipidêmicas terão as dosagens repetidas após 4 meses da adoção das medidas preventivas.
- Serão avaliadas as seguintes variáveis antropométricas: peso (com crianças descalça e com roupas leves); estatura, classificação do estado nutricional (IMC), circunferência da cintura, dobras cutâneas. Serão realizados o inquérito dietético recordatório de 24h em dias alternados e o cálculo nutricional da ingestão alimentar
- Será feita a avaliação dos polimorfismos nos genes da Apo-E, C1, C2 e C4 pela técnica de Lahiri & Nurnberger (1991) e PCR.
-Os dados serão analisados em SPSS 10.0.

Itens Metodológicos e Eticos	Situação

Título	Adequado
Autores	Comentário
Local de Origem na Instituição	Adequado
Projeto elaborado por patrocinador	Não
Aprovação no país de origem	Não necessita
Local de Realização	Outro (citar no comentário)
Outras instituições envolvidas	Sim
Condições para realização	Comentário

Comentários sobre os itens de Identificação

- O título foi alterado para: INVESTIGAÇÃO DE DILIPIDEMIAS NA POPULAÇÃO DE ESCOLARES DA REDE MUNICIPAL DE ENSINO DE SAPUCAIA DO SUL/RS.
- Foi incluído mais um colaborador: MARÍLIA REMUZZI ZANDONÁ.

Introdução	Adequada

Comentários sobre a Introdução

Objetivos	Adequados

Comentários sobre os Objetivos

Pacientes e Métodos	
Delineamento	Adequado
Tamanho de amostra	Total 460 Local
Cálculo do tamanho da amostra	Adequado
Participantes pertencentes a grupos especiais	Menores de 18 anos
Seleção eqüitativa dos indivíduos participantes	Não se aplica
Critérios de inclusão e exclusão	Adequados
Relação risco-benefício	Adequada
Uso de placebo	Não utiliza
Período de suspensão de uso de drogas (wash out)	Não utiliza
Monitoramento da segurança e dados	Não se aplica
Avaliação dos dados	Adequada - quantitativa
Privacidade e confidencialidade	Adequada
Termo de Consentimento	Comentário
Adequação às Normas e Diretrizes	Sim

Comentários sobre os itens de Pacientes e Métodos

- O número de sujeitos foi calculado em 460.
- As coletas serão feitas nas escolas da rede municipal de Sapucaia do Sul-RS.
- As amostras serão processadas no Laboratório UNILAB de Porto Alegre-RS, CGC 87.381.869/001-01.

Cronograma	Adequado
Data de início prevista	assim que aprovado
Data de término prevista	dez/08
Orçamento	Comentário
Fonte de financiamento externa	Agência de fomento

Comentários sobre o Cronograma e o Orçamento

Referências Bibliográficas	Adequadas

Comentários sobre as Referências Bibliográficas

Recomendação

Aprovar

Comentários Gerais sobre o Projeto

Em carta de 25/09/2008, a pesquisadora responsável informa que o Município de Sapucaia do Sul não possui CEP e que o projeto foi apresentado às Secretarias Municipais de Saúde e de Educação, sendo aprovado por ambas. Salienta, ainda, que o projeto foi apresentado em reunião com a presença dos diretos das escolas municipais, onde foram esclarecidas as etapas de seu desenvolvimento e informado que o projeto havia sido aprovado pelo CEP da UFCSPA. Em anexo a carta-resposta, foram encaminhados uma cópia da nova versão do projeto, bem o formulário de encaminhamento de projeto e a folha de rosto.

8.2 Normas de submissão à Revista: Nutrition, Metabolism & Cardiovascular Diseases.

GUIDE FOR AUTHORS.

INTRODUCTION

COVER LETTER, ARTICLE TYPES

COVER LETTER

Cover letters must state that all authors have seen and approved the study submitted. Provide a statement that no part of the submitted work has been published or is under consideration for publication elsewhere (except in the form of abstract). Provide a statement of financial or other relationships that might lead to a conflict of interest. In case of clinical trials, starting July 1st 2009, provide registration number and date.

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Electronic artwork

General points

• Make sure you use uniform lettering and sizing of your original artwork.

• Embed the used fonts if the application provides that option.

• Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.

• Number the illustrations according to their sequence in the text.

• Use a logical naming convention for your artwork files.

• Provide captions to illustrations separately.

• Size the illustrations close to the desired dimensions of the published version.

• Submit each illustration as a separate file.

A detailed guide on electronic artwork is available on our website: http://www.elsevier.com/artworkinstructions .

You are urged to visit this site; some excerpts from the detailed information are given here.

Formats

If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format.

Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings, embed all used fonts.

TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.

TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.

TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.

Please do not:

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;

• Supply files that are too low in resolution;

• Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear

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Please note: Because of technical complications that can arise by converting color figures to 'gray scale' (for the printed version should you not opt for color in print) please submit in addition usable black and white versions of all the color illustrations.

Figure captions

Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (not on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

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Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules.

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