ISAH RABIU

SCORE EVALUATION FOR THE CONSUMPTION OF ULTRA-PROCESSED FOODS IN CHILDREN AND ITS RELATIONSHIP WITH CARDIOMETABOLIC RISK

Dissertation submitted to the Universidade Federal de Viçosa, as part of the requirements of Graduate Program in Nutrition Science for obtaining the title of *Magister Scientiae*.

Adviser: Juliana Farias de Novaes

Co-adviser: Mariana De Santis Filgueiras

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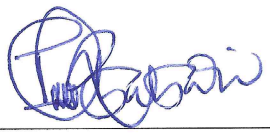

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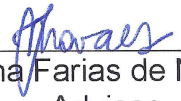

Juliana Farias de Novaes
Adviser

To my parents and brothers.

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"The only place success comes before work is in the dictionary."
(Albert Einstein)

ABSTRACT

RABIU, Isah, M.Sc., Universidade Federal de Viçosa, July 2022. **Score evaluation for the consumption of ultra-processed foods in children and its relationship with cardiometabolic risk**. Adviser: Juliana Farias de Novaes. Co-adviser: Mariana De Santis Filgueiras.

Ultra-processed foods (UPF) are industrial formulations nutritionally unbalanced and highly palatable. The high consumption of UPF is associated with development of metabolic alterations in children. However, considering that there is a diversity of UPF frequently consumed by children, it is necessary to evaluate a score specific for these foods, identifying their subgroups and their relationship with cardiometabolic risk. This study aimed to evaluate the score of ultra-processed food consumption in children and its relationship with cardiometabolic risk. Firstly, it was conducted a systematic review with the longitudinal evidence on the association between consumption of UPF and cardiometabolic risk. Data extraction of this systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Study quality and risk of bias were assessed with the Newcastle-Ottawa Scale. Scopus, Science direct, Scielo, PubMed, and Google scholar databases were searched without any restriction on publication dates. Ten longitudinal studies were selected for this review, being four conducted with children and six with adults. The findings showed a positive association between the high consumption of UPF and cardiometabolic risk a long term, independent of the age (PROSPERO registration no: CRD42022327714). For the original investigation, it was carried out a cross-sectional study with 378 children aged 8 and 9 years attending in all urban public and private schools in Viçosa, Minas Gerais Brazil. A semi-structured questionnaire was applied to obtain sociodemographic and lifestyle information. The cardiometabolic risk was evaluated according to total and android body fat, lipid profile, blood pressure, uric acid, fasting glucose, and HOMA-IR. From the application of three 24-hour recalls, a score of UPF consumption was created with 24 items. From this list, three subgroups of UPF were obtained: "sugary foods and beverages", "fatty foods" and "salty foods and processed meats". Multivariate linear regression models were used to assess the association of the UPF score and its subgroups with cardiometabolic risk markers. The “sugary foods and beverages” score was positively associated with LDL-c and uric acid. Every 1 SD

of "sugary foods and beverages” score was associated to 3.1 (95%CI: 0.8, 5.3) and 0.1 (95%CI: 0.1, 0.2) units higher in LDL-c and uric acid, respectively. The “salty foods and meat products” score was positively associated with total cholesterol and LDL-c. Every 1 SD of “salty foods and meat products” score was associated to 3.0 (95%CI: 0.2, 5.8) and 3.3 (95%CI: 1.0, 5.6) units higher in total cholesterol and LDL-c, respectively. Finally, UPF score was positively associated with LDL-c. Every 1 SD of UPF score was associated to 2.8 (95%CI: 0.6, 4.9) units higher in LDL-c. In conclusion of both investigations, it is important to implement effective strategies in the public health to prevent the excessive consumption of UPF and protect their effect in the long-term health, independent of age. In addition, the use of the score for the UPF consumption in childhood can be an easy and quick method to identify unhealthy eating habits and evaluate their associations (at whole and subgroups) with cardiometabolic risk at early age.

Keywords: Eating. Cardiometabolic risk factors. Nutritional epidemiology.

RESUMO

RABIU, Isah, M.Sc., Universidade Federal de Viçosa, julho de 2022. **Avaliação de escore para o consumo de alimentos ultraprocessados em crianças e sua relação com risco cardiometabólico**. Orientadora: Juliana Farias de Novaes. Coorientadora: Mariana De Santis Filgueiras.

Os alimentos ultraprocessados (AUP) são formulações industriais desbalanceadas nutricionalmente e de alta palatabilidade. O alto consumo de AUP está associado ao desenvolvimento de alterações metabólicas em crianças. No entanto, considerando que existe uma diversidade de AUP frequentemente consumidos por crianças, é necessário avaliar um escore específico de consumo destes alimentos, identificando seus subgrupos e suas relações com o risco cardiometabólico. Este estudo objetivou avaliar um escore de consumo de alimentos ultraprocessados em crianças e sua relação com o risco cardiometabólico. Primeiramente, foi realizada uma revisão sistemática com as evidências longitudinais sobre a associação entre o consumo de AUP e o risco cardiometabólico. A extração de dados desta revisão sistemática seguiu as diretrizes *Preferred Reporting Items for Systematic Reviews and Meta-Análises*. A qualidade dos estudos e o risco de viés foram avaliados pela Escala de Newcastle-Ottawa. As bases de dados Scopus, Science Direct, Scielo, PubMed e Google Acadêmico foram pesquisadas sem qualquer restrição de datas de publicação. Dez estudos longitudinais foram selecionados para esta revisão, sendo quatro realizados com crianças e seis com adultos. Os achados mostraram associação positiva entre o alto consumo de AUP e risco cardiometabólico a longo prazo, independente da idade (registro PROSPERO nº: CRD42022327714). Para a investigação original, foi realizado um estudo transversal com 378 crianças de 8 e 9 anos de escolas públicas e privadas de Viçosa, Minas Gerais, Brasil. Aplicou-se um questionário semiestruturado para obter informações sociodemográficas e de estilo de vida. O risco cardiometabólico foi avaliado de acordo com a gordura corporal total e androide, perfil lipídico, pressão arterial, ácido úrico, glicemia de jejum e HOMA-IR. A partir da aplicação de três recordatórios de 24 horas, um escore de consumo de AUP foi criado com 24 itens. A partir dessa lista, foram obtidos três subgrupos de AUP: "alimentos e bebidas açucarados", "alimentos gordurosos" e "alimentos salgados e embutidos". Modelos de regressão linear multivariada foram utilizados para avaliar a associação

do escore AUP e seus subgrupos com marcadores de risco cardiometabólico. O escore de alimentos e bebidas açucarados foi positivamente associado ao LDL-c e ao ácido úrico. Cada desvio-padrão do escore "alimentos e bebidas açucarados" foi associado ao aumento de 3,1 (IC 95%: 0,8, 5,3) e 0,1 (IC 95%: 0,1, 0,2) unidades no LDL-c e ácido úrico, respectivamente. O escore “alimentos salgados e embutidos” foi positivamente associada ao colesterol total e LDL-c. Cada desvio-padrão do escore “alimentos salgados e embutidos” foi associado ao aumento de 3,0 (IC 95%: 0,2, 5,8) e 3,3 (IC 95%: 1,0, 5,6) unidades no colesterol total e LDL-c, respectivamente. Por fim, o escore AUP foi positivamente associado ao LDL-c. Cada desvio-padrão de pontuação UPF foi associado ao aumento de 2,8 (IC 95%: 0,6, 4,9) unidades no LDL-c. Em conclusão de ambas as investigações, é importante implementar estratégias efetivas na saúde pública para prevenir o consumo excessivo de alimentos ultraprocessados e proteger os seus efeitos na saúde a longo prazo, independente da idade. Além disso, a utilização do escore AUP na infância pode ser um método fácil e rápido para identificar hábitos alimentares não saudáveis, e avaliar suas associações (escore total e subgrupos), com o risco cardiometabólico em idades precoces.

Palavras-chave: Consumo alimentar. Fatores de risco cardiometabólico. Epidemiologia nutricional.

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LIST OF ABBREVIATIONS AND ACRONYMS

24HR	24-hour recall
95%CI	95% confidence interval
BMI	body mass index
DBP	diastolic blood pressure
DXA	dual energy X-ray absorptiometry
HDL-c	high-density lipoprotein-cholesterol
HOMA-IR	homeostasis model assessment for insulin resistance
LDL-c	low-density lipoprotein-cholesterol
MAP	mean arterial pressure
NOS	Newcastle-Ottawa score
PASE	Pesquisa de Avaliação da Saúde do Escolar
SBP	systolic blood pressure
SD	standard deviation
T2DM	type 2 diabetes mellitus
TACO	Tabela Brasileira de Composição de Alimentos
TAG	Triglyceride
UPF	ultra-processed foods
WHO	World Health Organization

SYMBOL LIST

®	Registered mark
$	US dollar
%	Percentage
±	Plus-minus
≥	Greater than or equal to
R$	Brazilian Reais
β	Beta

SUMMARY

1 INTRODUCTION

In recent years, Brazilian schoolchildren have eaten a lot of ultra-processed foods (UPF) (IBGE, 2016). According to data from the 2015 National School Health Survey (*Pesquisa Nacional de Saúde do Escolar*, PeNSE), 41.6%, 26.7%, and 31.3% of students, ate sweets, snacks, and soft drinks, at least, five days a week, respectively (IBGE, 2016). This situation is due to the observed changes in the eating habits of the entire population, including increased consumption of highly processed products and beverages, and replacement of traditional meals by fast food or ready-made meals (ENES et al., 2010).

According to the NOVA classification, foods are divided into four different groups, which distinguish foods according to the nature, extent, and purpose of the processing (MONTEIRO et al., 2016). Food processing as identified by NOVA involves physical, biological, and chemical processes that occur after foods are separated from nature, and before they are consumed or used in the preparation of dishes and meals (MONTEIRO et al., 2016). While ultra-processed foods (UPF) are industrial formulations that are primarily processed from a combination of various ingredients and substances, such as sugar, fat, salt, and chemical additives to enhance their sensory qualities, they are often nutritionally unbalanced and highly palatable (MONTEIRO et al*.,* 2018; POTI et al., 2017; POTI et al., 2015).

UPF are often high in energy, fat, and have a good taste, which seems to be specifically related to addictive eating behavior (SCHULTE et al., 2015). They are associated with a higher blood sugar response and trigger cravings, leading to a poor response to internal food cues and a better response to external food cues (SCHULTE et al., 2015). UPF can affect the stomach and brain structures that regulate satiety, appetite, and energy balance, leading to excessive food intake and weight gain (SCHULTE et al., 2015; FARDET, 2016). The brain receives signals from the gastrointestinal tract through sensory nerves and the circulation and then it decreases satiety. Thus, the more the food is processed, the less satiating it tends to be (SCHWARTZ et al., 2000; AHIMA et al., 2008). Therefore, its effect can be through its energy content and/or its additives used in the preparations of the foods. However, there is little evidence that energy intake is a mediator between UPF and appetite characteristics (SCHULTE et al., 2015; FARDET, 2016; SMALL et al., 2019).

A study done by National Institutes of Health found that a diet filled with UPF encourages people to over-eat and gain weight compared to diets that consist of whole or minimally processed foods (HALL et al., 2019). In addition, positive associations have been identified between consumption of UPF and obesity (MONTEIRO et al., 2018, SILVER et al., 2018, MENDONCA et al., 2016) metabolic syndrome in adolescents (TAVAREZ et al., 2012), dyslipidemia in children (RAUBER et al., 2015), and adiposity in children and adolescents (COSTA et al., 2018).

The NOVA score for the consumption of UPF, obtained in a quick and practical manner using an electronic self-report questionnaire, shows a good potential in reflecting the dietary share of this food group in Brazil (COSTA et al., 2021). The UPF dietary contribution was measured in studies addressing the association between UPF consumption and nutritional quality of the diet or risk of chronic diseases using data-collection tools such as 24-hours dietary recalls, food records or food frequency questionnaires (MARCHIONI et al., 2019).

Previous studies, such as Surveillance System for Risk and Protective Factors for Chronic Diseases by Telephone Survey (VIGITEL) (VIGITEL BRASIL, 2018) and *NutriNet Brasil* (COSTA et al., 2021), developed a score with a list of UPF subgroups (answered “yes” or “no”) to assess their consumption in Brazilian adults, in a quick way with a good accuracy. However, considering that there is a diversity of UPF frequently consumed by children, it is necessary to evaluate a score specifically for this age group. In addition, it is important to know which subgroups of UPF comprise this score, as well as their relationship with cardiometabolic risk in children. Finally, to emphasize the need for quick, low-cost, and easy-to-apply methods to assess the consumption of UPF in childhood, since from an early age, this consumption may be associated to cardiometabolic risk. Despite the large number of studies on the association between consumption of UPF and cardiometabolic risk in children that are available in the literature, there is a lack of studies exploring the evaluation of the UPF score and its relationship with cardiometabolic risk in children.

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2 LITERATURE REVIEW

Consumption of UPF has increased in recent decades among children, adolescents, and adults, whereas natural or minimally processed meals has decreased (MARTINS et al., 2013). Overweight and obesity in schoolchildren have increased in recent years, leading to higher cardiometabolic risk at an early age (TODENDI et al., 2016; DROZDZ et al., 2021; BHAGAVATHULA et al., 2021). The increase in overweight and cardiometabolic risk in childhood can be assigned to a less healthy lifestyle, such as greater ultra-processed foods (UPF) consumption and sedentary behavior (DE AMICIS et al., 2022). Therefore, a healthy diet with adequate intake of nutrients can bring benefits to children´s growth and development, and good eating habit are formed at early age.

2.1 NOVA classification of foods

According to the NOVA classification, foods are divided into four different groups, which distinguish foods according to the nature, extent and purpose of the processing (MONTEIRO et al., 2016). Food processing as identified by NOVA involves physical, biological and chemical processes that occur after foods are separated from nature, and before they are consumed or used in the preparation of dishes and meals (MONTEIRO et al., 2016)

The group 1 (unprocessed or minimally processed foods) is composed of unprocessed foods mainly edible parts of plants or animals, and minimally processed foods are unprocessed foods subjected to processes such as removal of inedible or unwanted parts, drying, dehydration, crushing or grinding, fractioning, roasting, boiling, pasteurization, refrigeration or freezing, packaging, vacuum packaging, non-alcoholic fermentation and other processes that avoid the addition of substances such as salt, sugar, oils or fats. Some examples from this group are fresh, squeezed, chilled, frozen, or dried fruits and leafy and root vegetables; grains such as brown, parboiled or white rice; legumes such as beans of all types, lentils, chickpeas; starchy roots and tubers such as potatoes and cassava, in bulk or packaged; meat, poultry, fish and sea food, whole or in the form of steaks, fillets and other cuts, or chilled or frozen; eggs; milk, pasteurized or powdered; fresh or pasteurized fruit or vegetable juices without added

sugar, sweeteners or flavors; grits, flakes or flour made from corn, wheat, oats, or cassava; pasta, couscous and polenta made with flours, flakes or grits and water; tree and ground nuts and other oil seeds without added salt or sugar; herbs such as thyme and mint, fresh or dried; yoghurt with no added sugar or artificial sweeteners added; tea, coffee.

The group 2 (processed culinary ingredients) consists of cooking ingredients extracted from foods in group 1 or nature such as salt mined or from seawater; sugar and molasses obtained from cane or beet; honey extracted from combs and syrup from maple trees; vegetable oils crushed from olives or seeds; butter and lard obtained from milk and pork; and starches extracted from corn and other plants.

The group 3 (processed foods) is characterized by the addition of salt, sugar, oil, vinegar or other substances of Group 2 to Group 1 food items, composed mostly of two or three ingredients such as canned or bottled vegetables, fruits and legumes; salted or sugared nuts and seeds; salted, cured or smoked meats; canned fish; fruits in syrup; cheeses and unpackaged freshly made breads.

The group 4 (Ultra Processed Foods) is characterized by products that contain five or more ingredients of foods' group 1 and 3 containing additives that modify the color, odor, flavor or texture of the final product, for example, carbonated drinks; sweet or savory packaged snacks; ice cream, chocolate and candies (confectionery); mass produced packaged breads and buns; margarines and spreads; cookies (biscuits), pastries, cakes and cake mixes; breakfast "cereals," "cereal" and "energy" bars; "energy" drinks; milk drinks, "fruit" yoghurts and "fruit" drinks; cocoa drinks; meat and chicken extracts and "instant" sauces; ready to heat products including pre-prepared pies and pasta and pizza dishes; poultry and fish "nuggets" and "sticks", sausages, burgers, hot dogs, and other reconstituted meat products, and powdered and packaged "instant" soups, noodles and desserts (MONTEIRO et al., 2016).

2.2 UPF consumption evaluation methods

A simplified instrument addressing questions on the previous-day dietary intake of a list of 13 subgroups of ultra-processed foods (answered with "yes" or "no") was developed to monitor UPF consumption by the Brazilian adult population as part of the Surveillance System for Risk and Protective Factors for Chronic Diseases by

Telephone Survey (VIGITEL). The instrument, which has been part of the VIGITEL's annual questionnaire since 2018 (VIGITEL BRASIL 2018), allows for the calculation of a UPF consumption score ranging from zero to thirteen (COSTA et al., 2021) which is equivalent to the number of subgroups consumed by interviewees the previous day. After unfolding some of the 13 subgroups of the original instrument, another study shows the Nova screener presented a list of 23 subgroups of UPF which also allows for the calculation of a UPF consumption score ranging from zero to 23 (COSTA et al., 2021). The questions addressing the intake of each of these subgroups are presented on three categories: beverages (six subgroups); products that replace or accompany meals (ten subgroups); and products often consumed as snacks (seven subgroups) (COSTA et al., 2021).

According to large population-level studies, UPF now accounts for 30–60% of total daily energy intake in France (JULIA et al., 2017), the United Kingdom (RAUBER et al., 2018), Brazil (LOUZADA et al., 2015), Mexico (MARRON PONCE et al., 2017), and the United States (STEELE et al., 2015). According to studies in young (0–8 years old) children, UPF now accounts for 32–40 percent of total calorie consumption (BIELEMANN et al., 2018; RAUBER et al., 2014; FONSECA et al., 2018; KARNOPP et al., 2017). However, the majority of research involving children have been conducted in Brazil (BIELEMANN et al., 2018; RAUBER et al., 2014; FONSECA et al., 2018; KARNOPP et al., 2017), a middle-income nation where UPF intakes are still lower than in high-income countries as Canada and New Zealand (MONTEIRO et al., 2013). Diet records (BIELEMANN et al., 2018; RAUBER et al., 2014; FONSECA et al., 2018; KARNOPP et al., 2017) and 24-hour recalls (JULIA et al., 2017; MARRON PONCE et al., 2017; STEELE et al., 2015; RAUBER et al., 2014; KARNOPP et al., 2017) are frequently used to determine the amount of food consumed by each of the NOVA categorization groups.

2.3 Relationship between the ultra-processed foods consumption and chronic diseases in children

2.3.1. Obesity

Nationally representative dietary surveys conducted in the United States (STEELE et al., 2016), the United Kingdom (ADAMS & WHITE, 2015), Brazil (LOUZADA et al., 2015; LOUZADA, MARTINS et al., 2016) and Chile (CROVETTO, et al 2014) consistently show that ultra-processed foods are nutritionally imbalanced, and their consumption will have a negative impact on the nutritional quality of the diet. Compared with minimally processed foods, these products also provide lower satiety and increase blood sugar (FARDET, 2016). They are actively marketed, usually in large portions, and the trend to prefer snacks rather than regular meals can lead to excessive energy intake (MONTEIRO et al., 2013). In a study that assesses the cardiovascular risk, individuals who consumed higher proportions of UPF had a higher prevalence of excess body weight and abdominal obesity. When the consumption of processed and UPF was evaluated together, in addition to abdominal obesity, an association was found with hypercholesterolemia. Obesity, especially abdominal fat (subcutaneous and intra-abdominal), is one of the main factors associated with cardiovascular risk (MENEGUELLI et al., 2021). Higher consumption of ultra-processed foods was significantly associated with greater BMI and WC, and greater odds of having obesity and abdominal obesity. Trend towards positive associations of ultra-processed food consumption and obesity indicators were observed across age groups (MACHADO et al., 2020). A large prospective cohort study shows that participants consuming more UPFs tended to present higher BMI increase during follow-up and had increased risk of becoming overweight and obese, independently of their baseline BMI. These associations remained statistically significant after adjusting for a wide range of socioeconomic and lifestyle factors, and after further adjustments for several indicators of the nutritional quality of the diet (BESLAY et al., 2020). The main dietary risk factors were diets with lower portion of whole grains, fruits, nuts, seeds, vegetables, fiber, and legumes; and higher in sodium. In summary, multiple risk factors influence adiposity, T2DM, and CVD in a complex manner. Adiposity is a main risk factor for T2DM itself, and both are important risk factors for CVD. Diet is therefore a leading risk factor for all three conditions. A major component of modern diets are UPFs with nutritionally disadvantageous properties that have previously been associated with adverse cardiometabolic health (SCHULZE, 2020). Considering the high consumption of UPF increases overweigh and obesity, there is need for

development of effective nutritional policies to promote healthy eating habits since childhood and prevent obesity and cardiometabolic risk during all life.

2.3.2. Dyslipidemia

In an analysis of the United States National Health and Nutrition Examination Survey (NHANES) data from 1996 to 2006, the likelihood of adverse lipid values was higher in adolescents with greater BMI. The prevalence among youths who were normal weight, overweight (BMI 85th to 95th percentile), and obese (BMI >95th percentile) were 14%, 22%, and 43%, respectively (CDC US, 1999-2006). Lipid abnormalities in children frequently persist into adulthood and approximately half of children with high blood lipoprotein readings have high lipid levels (PEDIATRICS, 2011; HANEY et al., 2007; WEBBER et al., 1991; BAO et al., 1996). Children with high lipid levels, which are a sign of familial hyperlipidemia, have a better chance of having dyslipidemia during adulthood.

Dyslipidemia exposure throughout time appears to be linked to an increased risk of cardiovascular disease later in life. Elevated levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL-c), as well as low levels of high-density lipoprotein (HDL-c), characterize dyslipidemia. It is well established that 50% of children with dyslipidemia will develop adult dyslipidemia, a condition called as tracking, in which high cholesterol levels remain into adulthood, increasing the risk of coronary artery disease (RAMOS et al., 2011). In Brazilian studies, dyslipidemia affects children and adolescents, depending on region and criterion. Dyslipidemia was observed in 68.4% of the Pediatric population (JAF MAIA et al., 2020).

Longitudinal studies with Brazilian children, on the other hand, reinforce the potential negative effects of ultra-processed foods on children's health, such as increased total cholesterol and low-density lipoprotein (LDL) (RAUBER et al., 2015), TG (LEFFA et al., 2020), and waist circumference (COSTA et al., 2019). These alterations are linked to an increased risk of cardiometabolic disease (TORNQUIST et al., 2015; BOZZA et al., 2016). Moreover, the ultra-processed product consumption at preschool age was a significant predictor of increased total and LDL cholesterol concentrations during childhood (RAUBER et al., 2015). Thus, dietary patterns in childhood may very well mark the beginning of lipid profiles that predispose children to

early atherosclerotic changes (PEDIATRICS, 2011). Another important finding is that a 10% increase in the consumption of ultra-processed product at preschool age increase the change in total and LDL cholesterol from preschool to school age by up to 3mg/dl, even when adjusting for energy intake and BMI-for-age z-score (RAUBER et al., 2015). Therefore, a healthy diet with adequate intake of nutrients can bring benefits to children´s growth and development, as well as prevent the early diagnosis of dyslipidemia and beginning of the atherosclerosis.

2.3.3. Hypertension

Hypertension is a major risk factor for cardiovascular disease (CVD) (EZZATI et al., 2008), and is found in 37.1% of obese children (LIANG et al., 2020). This finding is worrisome and highlight the importance of blood pressure be monitored in pediatric population (PEDIATRICS, 2011).

Few studies have been conducted to examine the effects of specific types of ultra-processed food on the health of children and adolescents. A one-serving increase in sugar-sweetened beverages per day was associated with an increase in systolic blood pressure of 0.8 mmHg (95 percent CI: 0.4–1.2) and diastolic blood pressure of 0.3 (95 percent CI: 0.0–0.5) mmHg (DE BOER et al., 2016). Another study discovered that in Spanish children aged 5–16 years, diastolic hypertension was associated with a higher frequency of consumption of salty foods (700 mg of sodium/100 g), such as pizza, chips, and sausages, regardless of nutritional status (PÉREZ-GIMENO et al., 2020). In another study, the consumption of unprocessed or minimally processed foods was inversely associated with diastolic blood pressure in children; and the caloric contribution of ultra-processed foods was high in their diet. (OLIVEIRA et al., 2020). From the public health perspective, reliable estimates of the prevalence of childhood hypertension serve as the basis for adequate prevention and treatment, through the improvement of public health policy.

2.3.4. Insulin resistance

Insulin resistance (IR) in childhood plays a key role in the development of metabolic changes in adulthood, therefore, it is important to diagnose it early. The TyG

index was positively associated with other IR prediction methods and appears to be advantageous for predicting IR risk and other cardiometabolic risk factors in children and adolescents (BRITO et al. 2021). Cardiometabolic risk factors in childhood are linked to the development of obesity and IR.

Insulin resistance (IR) has become a chronic disorder and is considered a major public health issue as a result of the so-called nutritional transition (shift in eating patterns and energy expenditure) and the resulting increase in the prevalence of overweight and obesity in all population groups (GOBATA, et al, 2017, ROCHA, et al, 2017). Previous research (ANDRADE, et al, 2016, FOX, et al, 2017) has suggested that the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) be used to identify IR using validated cut-off criteria for the group examined. Despite the lack of standardized cut-off points for adolescent in Brazil (ANDRADE, et al, 2016), research show that IR prevalence ranges from 2.1 percent to 90.8 percent among adolescents at various phases of sexual maturity and nutritional status. Using the P_{75} of the distribution of the HOMA-IR index, 27% of the sample of Brazilian adolescents exhibited IR and the prevalence was higher among individuals living in the southern region of the country (35.9%) (ANDRADE, et al, 2021).

The development of insulin resistance is mostly associated with the accumulation of excessive fat in the body through high consumption of UPF (MAFFEIS et al., 2018). Fast-food consumption has strong positive associations with weight gain and insulin resistance, suggesting that fast food increases the risk of obesity and type 2 diabetes (PEREIRA et al., 2005). There are a number of specific dietary patterns that are associated with overweight and insulin resistance, including high-fat and energy-dense food intake (BAHADORAN et al., 2015). The impact of ultra-processed food consumption on non-communicable disease's global epidemic is a relevant issue. The impact of ultra-processed food consumption on non-communicable disease's global epidemic is a relevant issue.

2.3.5. Uric acid

Serum uric acid in human is the end products of purine and nucleic acid metabolism (ROUBENOFF, 1990). Hyperuricemia is a set of heterogeneous diseases caused by obstacles in purine metabolism and/or decrease in the excretion of uric acid

(XU et al., 2018). It often leads to the development of gout, which causes deposition of urate crystals and results in gouty arthritis in some individuals (CHOI et al., 2005). The prevalence of hyperuricemia doubled worldwide during the last few decades (MENESES-LEON et al., 2014). The prevalence rate of hyperuricemia in the general population of the United States is estimated at 20%, while in Brazil is 13% (SMITH et al., 2015). Serum uric acid levels vary markedly among individuals and could be influenced by several factors, including genetic, lifestyle, metabolic, environmental, and especially, dietary factors (CHOI et al., 2004; YU et al., 2008).

Exogenous fructose, an isomer of glucose from soft drinks or fruits juices may result in insulin resistance, obesity, elevated LDL-c and triglyceride leading to the metabolic syndrome (MALIK et al., 2015). Excess fructose consumption can lead to the development of metabolic syndrome and type 2 diabetes, both conditions are well-known risk factors for heart and kidney disease. Because uric acid synthesis is biochemically linked to fructose metabolism, widespread consumption of this monosaccharide has been linked to gradually increasing serum uric acid levels over the last few decades (LANASPA et al., 2011). However, because fructose is rarely consumed alone, fructose-containing sugars, sucrose, and high fructose corn syrup, which are found in sugar sweetened beverages (UPF), are the most common sources of fructose in the diet. Further to that, there is additional evidence of a link between elevated uric acid levels and the onset of cardiometabolic risk (WANG et al., 2014). These provides new insights in terms of the association between UPF consumption and human health outcomes. Nevertheless, it would be important to be evaluated in future research, mainly in pediatric population.

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3 JUSTIFICATION

Globally, the chronic diseases present high contribution to total global mortality around the world, being the diet is an important modifiable risk factor for their prevention. The cardiometabolic risk and its association with the consumption of ultra-processed foods among the populations has become the major public health concerned in early ages as well.

The increase in consumption of UPF is already related to cardiometabolic risk in childhood, and therefore there is need to propose quick and low-cost methods that have good accuracy to identify early high consumption of UPF in children.

There is a lack of investigations that studied score of UPF consumption with cardiometabolic risk among schoolchildren. In this present study, UPF score will be evaluated in children and its association with cardiometabolic risk. Therefore, the UPF score can be a good marker for assessing the current consumption of UPF, and to contribute to identify risk groups for nutritional interventions in early ages.

In addition, there is lack of systematic review of longitudinal studies that evaluate the causal effect of high intake of UPF with the cardiometabolic risk among children, adolescents, and adults. With this, we propose to review systematically the longitudinal evidence on the association between the consumption of UPF and cardiometabolic risk a long term.

This study is important to public health once it will evaluate the relation between consumption of UPF and cardiometabolic risk in schoolchildren. The investigation of the consequences of UPF intake in health conditions can improve public health policy, bringing solutions to the existing problems like obesity and comorbidities and prevention of future unfavorable health outcomes.

4 OBJECTIVES

4.1 General objective

- To evaluate the score of ultra-processed food consumption in children and its relationship with cardiometabolic risk.

4.2 Specific objectives

- To investigate the longitudinal evidence on the association between consumption of UPF and cardiometabolic risk, through systematic review;
- To evaluate a score of UPF consumption for children, based on the 24-hour recall, considering the subgroups and the whole value;
- To assess the association of subgroups' score of UPF consumption with cardiometabolic risk markers;
- To evaluate the association of the whole score of UPF consumption with cardiometabolic risk markers.

5 MATERIAL AND METHODS

5.1 Study population and design

This is a cross-sectional study of a representative sample of 8 and 9-year-old children who attended all public and private schools in the urban area of Viçosa, Minas Gerais, Brazil, from May to December 2015. According to the 2010 census, Viçosa has an area of 299 square kilometers and 72,244 inhabitants, of which 93. 2% live in urban areas. (IBGE, 2018). The study participants were from the Schoolchildren's Health Assessment Survey (*Pesquisa de Avaliação da Saúde do Escolar*, PASE, in Portuguese).

5.2 Sample calculation

Samples were calculated using the software Epi Info (version 7.2, Atlanta, Georgia, USA), considering the total number of students aged 8 and 9 in 2015 (n = 1446). Considering 5% margin of error, 95% confidence level, and a 10% of losses, a total of 378 children were included in the sample. Children were selected using a stratified random sample, and each school sample corresponded to the percentage of students enrolled according to age and gender. Children were selected by a simple random draw until the number of students required for each school was reached (FILGUEIRAS, et al, 2020).

The child's parents or guardians were contacted by phone and invited to participate in the study. The purpose of the study and its methodology were explained to the parents or guardians of the children. The first meeting was scheduled and those who have agreed to participate were signed the informed consent form (APPENDIX A) and fully informed about each step of the study (FILGUEIRAS, et al., 2020).

The non-inclusion criteria were children: 1. presenting health problems affecting their nutritional status or body composition (physical, cognitive or repeated deficiencies, thyroid disorders, etc.); 2. taking medications that interfere in glucose and/or lipid metabolism (corticosteroids, statins, hypoglycemic drugs, etc.); 3. Using vitamin or mineral supplements during the study; and 4. whose parents or guardians could not be contacted.

5.3 Sociodemographic, lifestyle and maternal characteristics

A semi-structured questionnaire was used containing sociodemographic characteristics such as age, gender, mother education, type of school (public or private), government program beneficiary and per capita income (APPENDIX B).

A lifestyle questionnaire included daily screen time (time spent sitting in front of television, video games or computers). More than 2 hours per day was classified as a sedentary behavior (AMERICAN ACADEMY OF PEDIATRICS, 2013).

Breakfast consumption was considered as the first food intake that the child consumed and/or drank in the first 2 hours after waking up (KARATZI et al., 2014). Skipping breakfast was considered when the child did not eat this meal on one of the three days evaluated in the 24HR. This instrument was also used to assess the number of daily meals, which was obtained by the average of the three days, with values lower than 4 meals a day being considered low (SILVA et al., 2017).

5.4 Anthropometry and body composition

An electronic digital balance with 150 kg capacity and 50 g sensitivity (Tanita® model Ironman BC 553; Tanita Corporation of America, Inc., Arlington Heights, IL, USA) was used to measure the weight of children. The child's height was measured using a stadiometer divided into centimeters and subdivided into millimeters (Alturexata®, Belo Horizonte, MG, Brazil) (JELLIFFE DB & WORLD HEALTH ORGANIZATION'S 1968).

The nutritional status of the child was assessed using BMI and classified according to WHO Anthro Plus software (WHO, 2009).

The body fat was estimated using dual quantification x-ray absorptiometry (Lunar Prodigy Advance; GE Medical Systems Lunar, Milwaukee, WI, USA). Children with percentage of fat higher than 20% (for boys) and higher than 25% (for girls) were classified as excess body fat (LOHMAN, 1992).

5.5 Blood pressure

Blood pressure was measured with the child in a sitting position after resting for at least 5 min at three different times, using digital blood pressure monitors (Omron, Vernon Hills, IL, USA). The median of values of systolic (SBP) and diastolic (DBP) blood pressure (mmHg) were used to estimate the mean arterial pressure (MAP), calculated [MAP = 1/3(SBP) + 2/3(DBP)].

5.6 Biochemical analysis

After 12 hours of fasting, blood was collected in the Laboratory of Clinical Analysis of the Health Division of the *Universidade Federal de Viçosa* (UFV). Intravenous aspiration was used to collect the samples, which were then centrifuged for 15 min at 3500 rpm before being separated into 1.5 ml Eppendorf tubes and stored in the freezer (80°C). The lipid profile (total cholesterol, high-density lipoprotein [HDLc], low-density lipoprotein [LDLc] and triglycerides) and serum uric acid were evaluated.

The fasting glucose was determined by enzymatic colorimetry ® and measured in an automated analyzer® (BS200 Mindray, Nanshan, China). Serum insulin was analyzed through chemiluminescence immunoassay using the Elecsys Insulin® test (Roche Diagnostics, Indianapolis, IN, USA) with a detection limit of 0·200–1000 µU/ml. Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR).

5.7 Food consumption assessment

The UPF consumption was evaluated by the average of three non-consecutive days of 24-hour recalls (24HR), including one weekend day (APPENDIX C). The children answered the food surveys accompanied by their parents or guardians, preferably being interviewed by those directly involved with the child's feeding.

To assist the participants in determining the size of the ingested portions, standard house utensils and figures of portioning of some foods in a photographic album were used (ZABOTTO, 1996). The amount of each food ingested was converted into gram, based on the food conversion table of the Food and Agriculture Organization of the United Nations (FAO) (FAO, 2012). This amount was converted into energy and the consumption of proteins, carbohydrates, lipids, cholesterol, saturated,

monounsaturated, and polyunsaturated fats, fiber, calcium, iron, sodium and vitamin D. The content of each nutrient in the diet was presented in milligrams (mg) or microgram (µg) per 1,000 kcal, as proposed by Louzada et al. (2015).

To assess the adequacy of nutrient consumption, the EAR (Estimated Average Requirement) (IOM, 2001) was used as a reference. The analysis of consumption data was carried out in Diet Pro® 5i software, version 5.8 (DIET, PRO. 1997), preferably using the Food Composition Table (TACO, 2011) and, in the absence of information, the Chemical Composition Table of Food from the United States Department of Agriculture (USDA, 2012). The foods were distributed and classified according to the degree of processing, as proposed by MONTEIRO et al. (2016). The equivalent of 10% of the volume consumed was standardized for the consumption of added sugar in juices, coffees and teas. As for the culinary preparations, the recipe for their preparation was standardized, and the ingredients were dismembered and classified according to the degree of processing. The foods were further grouped in order to verify which group would have a greater contribution to the energy intake of UPF. The groups were classified into sweets (chocolate, ice cream, and party sweets), cookies (stuffed cookies and chips), sugary drinks (industrialized juices and soda), sausages (sausage, sausage, ham, bacon) and fast food (pizza, hot dog, and hamburger). The consumption of ultra-processed foods obtained by 24h recall was therefore transformed into % of the total energy value.

5.8 Score of UPF consumption in children

Based on information from three 24HR, applied on non-consecutive days, including weekend day, all ultra-processed foods that the children consumed were identified. Some of these foods were grouped by similarity of their nutrient compositions. From this, a score consisting of 24 items was constructed, with score range from 0 to 24 points (Table 1). For the analyses, for each item consumed by the child in at least one day of the three 24HR, a value of 1 was scored (answer “yes”). If the items were not consumed on any day of the 24HR, the value 0 was scored (“no” answer).

Table 1. Score for UPF consumption in children. Viçosa, Brazil, 2015.

Item number	Items
1	Soft drink
2	Gum, candy, lollipop, and sweets
3	Sweet cookie (with or without filling)
4	Chocolate-flavored milk
5	Industrialized fruit juice
6	Margarine
7	Finger food (*coxinha, rissole, empada* etc, in Portuguese)
8	Salty cracker
9	Drink mix (powdered fruit juice)
10	Ham, mortadella, and salami
11	Industrialized loaf bread
12	Yogurt and petit suisse
13	French fries
14	Puffcorn
15	Ice cream, popsicle, milkshake, and *açaí*
16	Chocolate
17	Hamburger, hot dog, and ham and cheese sandwich
18	Sausage, beef burger, and chicken nugget
19	Ketchup, mustard, and mayonnaise
20	Instant noodles
21	Pizza
22	Breakfast cereal
23	Soft snack cake
24	Cereal bar

5.9 Statistical analysis

Exposure. "Ultra-processed food (UPF)", “sugary foods and beverages”, “fatty foods”, and “salty foods and meat products” scores were expressed in terciles.

Outcome. Total and android body fat, total cholesterol, HDL-c, LDL-c, triglycerides, MAP, uric acid, fasting glucose, and HOMA-IR as continuous variables.

Covariates. We considered as covariates the child’s sex, school type, per capita income, government program beneficiary, maternal education, and screen time.

Statistical analyses. We first compared the distributions of UPF score by categories of covariates using mean ± standard deviation (SD) for continuous variables, and frequency measurements for categorical variables. Tests for linear trend were derived from linear regression models with UPF score as the continuous outcome and a variable representing ordinal categories of each covariate introduced as a continuous predictor. Second, we compared the distributions of cardiometabolic risk

markers (outcomes) by terciles of “sugary foods and beverages”, “fatty foods”, “salty foods and meat products”, and “UPF scores” (exposures), using mean differences and 95%CI from multivariate linear regression models adjusted by sex, age, screen time, and per capita income. Finally, the multivariate model was additionally adjusted for body fat. Robust estimates of the variance were specified in all models, which are consistent with heteroscedasticity and non-normality (WHITE, 1980). The analyses were performed in the Stata® version 14 (StataCorp LP, College Station, TX, USA). The significance level was 5% for all hypothesis tests.

5.10 Ethical aspects

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Human Research Ethics Committee of the UFV (reference number 663.171/ 2014) (ANNEX A). Written informed consent was obtained from all parents or guardians of participants.

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6 RESULTS AND DISCUSSION

The results of this study are presented in the format of two articles:

1. Review article: Effect of the ultra-processed foods consumption on cardiometabolic risk among children and adults: A systematic review of longitudinal studies.
2. Original article: The score of ultra-processed foods consumption is associated with a higher cardiometabolic risk in Brazilian schoolchildren.

6.1 Review article: Effect of the Ultra-Processed Foods Consumption on Cardiometabolic Risk among Children and Adults: A Systematic Review of Longitudinal Studies.

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ABSTRACT

The systematic review demonstrated an independent causal effect of long-term high consumption of UPF in cardiometabolic risk**.** Ultra-processed foods (UPF) play a role in the development of chronic diseases and has received attention globally, among dietary factors. There is still no consensus about the magnitude of the cause-effect relationship of these consumption on cardiometabolic risk a long term. The objective of this review was to evaluate the effect of long-term high consumption of ultra-processed foods on cardiometabolic risks among children and adults. Data extraction of this systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Study quality and risk of bias were assessed with the Newcastle-Ottawa Scale. Scopus, science direct, Scielo, PubMed, and google scholar databases were searched without any restriction on publication dates. Ten (10) longitudinal studies were selected for this review. All included studies evaluated consumptions of UPF and cardiometabolic risk, being four conducted with children and six with adults. The findings showed a causal association of the high consumption of UPF with cardiometabolic risk a long term in children and adults. In conclusion, these results reinforce the importance of effective strategies to prevent the excessive consumption of UPF and protect the long-term health, independent of the age. Systematic Review Registration: PROSPERO registration no: CRD42022327714.

KEYWORDS: Adults, Child, Cardiometabolic risks, Eating, Long-term effects, Nutritional epidemiology.

INTRODUCTION

Consumption of UPF has increased in recent decades among children, adolescents, and adults, whereas natural or minimally processed meals has decreased.[1] Simultaneously, the global burden of cardiovascular disease (CVD) and death among adults is significantly increases due to poor eating habits.[2] UPF are industrial formulations primarily processed from a combination of various ingredients and substances, such as sugar, fat, salt, and chemical additives to enhance their sensory qualities. They are often nutritionally unbalanced and high palatable,[3, 4, 5] which seems to be specifically related to addictive eating behavior.[6]

In a cross-sectional study that assessed the cardiovascular risk, adults who consumed higher proportions of UPF had a higher prevalence of excess body weight and abdominal obesity.[7] When the consumption of processed and UPF was evaluated together, in addition to abdominal obesity, an association was found with hypercholesterolemia.[7] Obesity, especially abdominal fat (subcutaneous and intra-abdominal), is one of the main factors associated with cardiovascular risk.[7] Higher consumption of UPF was significantly associated with greater body mass index (BMI) and waist circumference (WC) and greater odds of having obesity and abdominal obesity in adults.[7] Trend towards positive associations of UPF consumption and obesity indicators were observed in both men and women and across age groups.[8]Another study found high consumption of UPF and positive relation with blood lipids among children and adolescents.[9]

On the other hand longitudinal studies with Brazilian children, reinforce the potential negative effects of UPF on children's health, such as increased total cholesterol and low-density lipoprotein (LDL),[10] triglycerides,[11] and waist circumference,[12]that increase the risk of cardiometabolic disease.[13, 14] A cross-sectional study showed that the higher consumption of UPF after adjusting for sociodemographic, smoking, and physical activity was associated with higher BMI and higher prevalence of overweight and obesity compared with the first quintile of people (adolescents, and adults) who consumed UPF.[15]

Despite the large number of cross-sectional studies on the association between consumption of UPF and cardiometabolic risk among children, adolescents, and adults, there is still no consensus about the magnitude of the cause-effect relationship of these consumption on cardiometabolic risk due to few longitudinal studies. The

objective of this review was to evaluate the long-term effect of the UPF consumption on cardiometabolic risk among children and adults. Our hypothesis is that UPF consumption increased the cardiometabolic risk a long-term, independent of the age.

METHODS

Identification and Selection of studies

This is a systematic review focused on the research question “what is long-term effect of the UPF consumption on cardiometabolic risks among children and adults?” This systematic review was conducted from April to June 2022, based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guideline[16] and registered in PROSPERO (registration number: CRD42022327714). Google scholar, Scopus, Science Direct, Scientific Electronic Library Online (SciELO), and PubMed databases were searched. The following combined descriptors were matched to the Medical Subject Headings (MeSH) index: “Cardiometabolic risks” or “obesity” or “body fats: or “blood lipid” or “blood glucose” or “insulin resistance” or “hypertension” or “diabetes” or “dyslipidemia” or “metabolic syndrome” AND “Ultra-processed foods” AND children or adolescent or adults.

A protocol was defined to identify and select the studies (Figure 1). The articles were independently screened and selected by two researchers. In the case of disagreements, the reviewers jointly reviewed the articles to reach consensus, and a third reviewer assisted when consensus could not be reached.

Eligibility Criteria

The following Eligibility criteria were adopted:

1. Inclusion: longitudinal studies, with children (>2-year-old) and/or adolescents, adults and elderly that evaluated UPF consumption on cardiometabolic risks.
2. Exclusion: cross-sectional studies, interventional studies, studies with pregnant women, nursing mothers; animals or cells; studies in duplicate; reviews; congress abstracts; books and book chapters; monographs, dissertations, and theses.

Data Extraction

The information extracted were from the selected articles based on:

1. Overall study information: authorship, year of publication, country, sample size, age range, length of follow-up.
2. Exposure and outcome information: main statistical method, covariates and stratification, main results, and Newcastle-Ottawa Scale (NOS) score.[17]

Quality Assessments of Studies

The included studies were analyzed by independent reviewers (I.R and M.S.F.), in duplicate, using the NOS[17] for quality assessment. This scale is a critical appraisal tool that provides three grouping items: selection, exposure and outcome, and comparability. A study can be awarded a maximum of one star for each numbered item under the patient selection (n = 4 items) and exposure (n =3 items) categories, and a maximum of two stars in the comparability of study groups (n = 2 items) category, thus, enabling a total maximum score of nine stars. Any discrepancies in the outcomes of critical appraisal were resolved through discussion.

RESULTS

Selection and description of studies included

A total of 8025 references were identified using the combined descriptors listed in the method. After exclusions of duplicate, papers were evaluated by their titles and abstracts. However, after full reading, ten original articles met the eligibility criteria and were included in this review (Figure 1).

Six studies included adults and four included children. The sample size ranged from 307 to 348,748 participants. Selected studies were performed in the Brazil (n=3), Europe (Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the United Kingdom (UK)) (n=1), France (n=1), Portugal (n=1) and Spain (n=4) and published between 2015 and 2021. The follow-up length varied from 1 to 12 years as presented in Table 1.

Ultra-processed foods

All the studies selected in this review were assessed UPF using the NOVA classification system, a four-group food classification based on the extent and purpose of food processing, including unprocessed and minimally processed foods, processed culinary ingredients, processed foods and UPF.[18]

Cardiometabolic risk

Each study investigated from one to four cardiometabolic biomarker, such as BMI (n=9), [10, 11, 12, 19, 20-22, 24 25]WC (n=3), [12, 21, 23]WHtR (n=1),[12] lipid profile (n=3)[10, 11, 24] and type 2 diabetes *mellitus* (n=1).[22]

Statistical analysis and adjustment variable

Most studies used linear regression models as their main statistical analysis (n=4), two used logistic models, two also used Cox regression, one used mixed-effect model, and one used multilevel model. Studies adjusted for a wide range of variables, with the most being sex (n=9), age (n=7), BMI (n=7), physical activity (n=6), educational level (n=4) and family income (n=3), as presented in the Table 2.

General findings

In the present review, the UPF was associated with cardiometabolic risk in both children and adults. The outcomes of the studies with children were abdominal obesity,[12] higher BMI,[20] higher blood lipids profile.[10,11] In adults were, high risk of T2DM,[22] obesity,[25] dyslipidemia incidence,[24] abdominal obesity,[23] gain in BMI and high risk of overweight and obesity,[19] and visceral fat and overall adiposity accumulation,[21] as displays in figure 2.

Association of UPF and cardiometabolic risk in children

Two studies found positive association between high UPF consumptions and serum lipids profile in children from 3 to 8 years of age.[10,11] UPF among these children were breads, savory snacks and cookies, sweets (i.e. candy, chocolate, ice cream), and other products like instant noodles, breakfast cereals, and sugary milk beverages in both age groups. Higher consumption of UPF at age 3 years was associated with higher blood lipid concentrations at age 6 years-old, from 3 to 6 age,[12] while other study observed a positive association between UPF and higher BMI in children during the follow-up of 6 years.[20]

Association of UPF and cardiometabolic risk in adults

All the six studies with adults found a long term positive association between the high UPF consumption and cardiometabolic risk such increased risk of type 2 diabetes *mellitus* during 12 years of follow-up,[22] obesity after 5 years of follow-up,[25] dyslipidemia incidence at 60 years of age ,[24] abdominal obesity during 2 years of follow-up,[23] gain in BMI and high risk of overweight and obesity at 18 years of age ,[19] and visceral fat and overall adiposity accumulation after 6 years of follow-up.[21]

The associations between UPF consumption and weight gain are driven by soft drink consumption, but other foods (or their properties) in the UPFs category also contribute. Soft drink consumption is likely also correlated with other components of UPFs and could thus be regarded as a mediator of observed associations.[25] The combination of these three major elements (free sugars, trans fatty acids, saturated fatty acids) of UPFs poor nutritional composition, additives largely added to UPFs and toxic packaging materials, together with the modification of the natural matrix of food as a result of processing could potentially explain the observed associations.[24] The food groups that contributed the most to this association were non-alcoholic beverages (including instant coffee drinks, cocoa drinks and packaged fruit juices), spirits, meat products and soft drinks.[23]

Ultra-processed beverages, dairy products, fats and sauces, and meat, fish, and egg were each associated with increased overweight and obesity risks, while ultra-processed starchy foods and breakfast cereals were associated with an increased risk of overweight but not obesity.[19]

Risk of bias

All the selected studies were evaluated according to NOS guideline. The score ranged between 8 and 9 stars, and this indicate the lower risk of bias.

DISCUSSION

To best of our knowledge this systematic review is the first to evidence the association causal of high consumption of UPF on cardiometabolic risks a long term, independent of age, according to longitudinal studies. Despite the variety of methods used to evaluate the effect of consumption of UPF, among the studies and the different associations observed, consistent results with other systematic reviews (cross-sectional studies) were found.[26-29]

All the selected longitudinal studies were conducted in South America (Brazil)[10-12] and Europe[19-25] evaluated UPF according to NOVA classification system.

The present review found a positive association between the high UPF consumption and cardiometabolic risks among children[10-13, 20] during the follow-up of 1 to 6 years; and in adults[19, 21-25] during the follow-up of 2 to 12 years. These findings confirmed our hypothesis that UPF consumption increased the cardiometabolic risk a long-term, independent of the age.

Consumption of UPF has been pointed out as a risk factor for increasing overall obesity among the children, adolescents and adults.[15, 30, 31] Higher UPF consumption at 4 years of age was positively directly associated with food responsiveness at 7 years old, which reflects the urge to eat when children see, smell or taste palatable food, such as UPF[21] These foods comprised around 42% of total energetic intake at age 4 and 48% at age 8 in a Brazilian population[12], and 33% in a Belgian children aged 3 to 9 years.[32]

The UPF consumption was associated with a higher WC,[33] which is a very sensitive measurement of abdominal obesity[34] and metabolic complications.[35] Since visceral fat in burden of pathological processes (ie. inflammation and insulin resistance), these results provide, at least partly, the link between UPF and chronic diseases observed in previous studies.[21]

There are several potential mechanisms explaining the association between UPF and high BMI, risks of overweight and obesity, and abdominal obesity. UPF have a high energy density that delays the signals of satiety,[36] and larger portions of these foods are usually consumed.[37] Another mechanisms could be their low nutritional quality, with a high content of saturated fatty acids, trans-fatty acids, refined sugars and low content of fiber, vitamins and antioxidants.[5] High purchases and household availability of UPF were associated with higher BMI and higher obesity prevalence.[36,38] All these factors are associated with overconsumption and subsequent obesity. Another important concern about the UPF is that they are loaded with artificial additive substances such as artificial sweeteners and mono sodium glutamate.[18, 57]

UPF consumption at preschool age was a significant predictor of increased total and LDL-cholesterol concentrations during childhood[10, 11]. Thus, unhealthy dietary patterns in childhood may very well mark the beginning of lipid profiles that predispose children to early atherosclerotic changes associated with cardiovascular disease

development.[40, 57] The consumption of UPF is an important factor to study as this accounted for approximately 50% of the total energy consumed by the US children,[56] almost double the average of 27% found in the overall Brazilian population.[41] The development and progression of cardiovascular disease is related to risk factors that begin in childhood, such as diet and specific blood lipid levels.[39, 40] Furthermore, it has been reported that elevated lipid concentrations track from childhood to adulthood, as lipid and lipoprotein results in childhood are predictive of future adult lipoprotein profiles.[40] Excessive consumption of energy-dense foods that are high in sugar and trans fats is associated with increased lipogenesis,[42] the secretion of very low-density lipoproteins,[43] and greater fatty acid accumulation in tissues and blood.[44]

Higher consumption of UPF at age 3 years was associated with higher blood lipid concentrations at age 6 years.[11]Among adults, high consumption of UPFs was positively associated with dyslipidemia incidence.[24] This relationship is mainly driven by overconsumption of high-fat and high-sugar foods, is associated with increased lipogenesis and increased concentrations of circulating triglycerides and cholesterol.[45] In addition to nutrient level mechanisms, an excess intake of UPF is inversely associated with a lower intake of fruits and vegetables, foods that are known to prevent CVD.[46] Furthermore, given that obesity is a significant predictor of poor cardiometabolic health,[47, 48] a high intake of UPF, which has occurred following aggressive advertising and marketing of UPF,[49,50] may promote obesity through a disruption of hunger and satiety.[51, 52] Thus, these mechanisms support the association between UPF consumption and an unhealthy lipid profile, potentially increasing the risk of CVD.

A higher consumption of UPF was associated with an increased hazard for new onset T2DM after 12 years of follow-up, even after adjustment for a wide array of potential confounding factors.[22, 53] T2DM has always been linked to poor quality diet habits and overweight. UPF is consistently associated with an overall deterioration of the nutritional quality of diets.[54] Several potential mechanisms underlying the association between UPF and T2DM is the low fiber content characteristic of UPF.[22] High-fiber foods take longer to digest so their satiating power is higher than those foods with low fiber content like UPF. In addition, high-fiber diets reduce absolute values of glycated hemoglobin and fasting plasma glucose in patients with T2DM.[55] UPF usually has a high energy density and a low nutrient density; UPF often contain high amount

of added sugars, in fact UPF contribute almost 90% of the energy obtained from added sugars[56] and these products are highly palatable, ready to consume and durable.[56] They also tend to be low-cost products.[22] These characteristics make UPF very attractive products often displacing the consumption of more nutritionally balanced foods.[22]

The strength of this review is a systematic approach based on the PRISMA guideline[16] and the quality assessment of studies was based NOS appraisal tool.[17]Second, the longitudinal time frame of the selected articles was enough to observe that the UPF consumption increased the cardiometabolic risks in follow-up studies with children and adults. The limitations of this review could be lack of study addressing the longitudinal association in adolescents which is very important stage of life because of the physiological changes of the body at this stage. Third, it was not possible to perform meta-analysis due to the different statistical methods used by selected studies. Fourth, more longitudinal studies are necessary to investigate the causal effect of UPF consumption in cardiometabolic risk a long-term, during all phases of life.

In conclusion, this review showed a causal effect of high consumption of UPF in cardiometabolic risk a long-term, such as obesity, dyslipidemia, and risk of type 2 diabetes *mellitus* in children and adults. There is need of more longitudinal studies, with emphasis in the adolescence. These results reinforce the importance of effective strategies to prevent the excessive consumption of UPF among all these age group.

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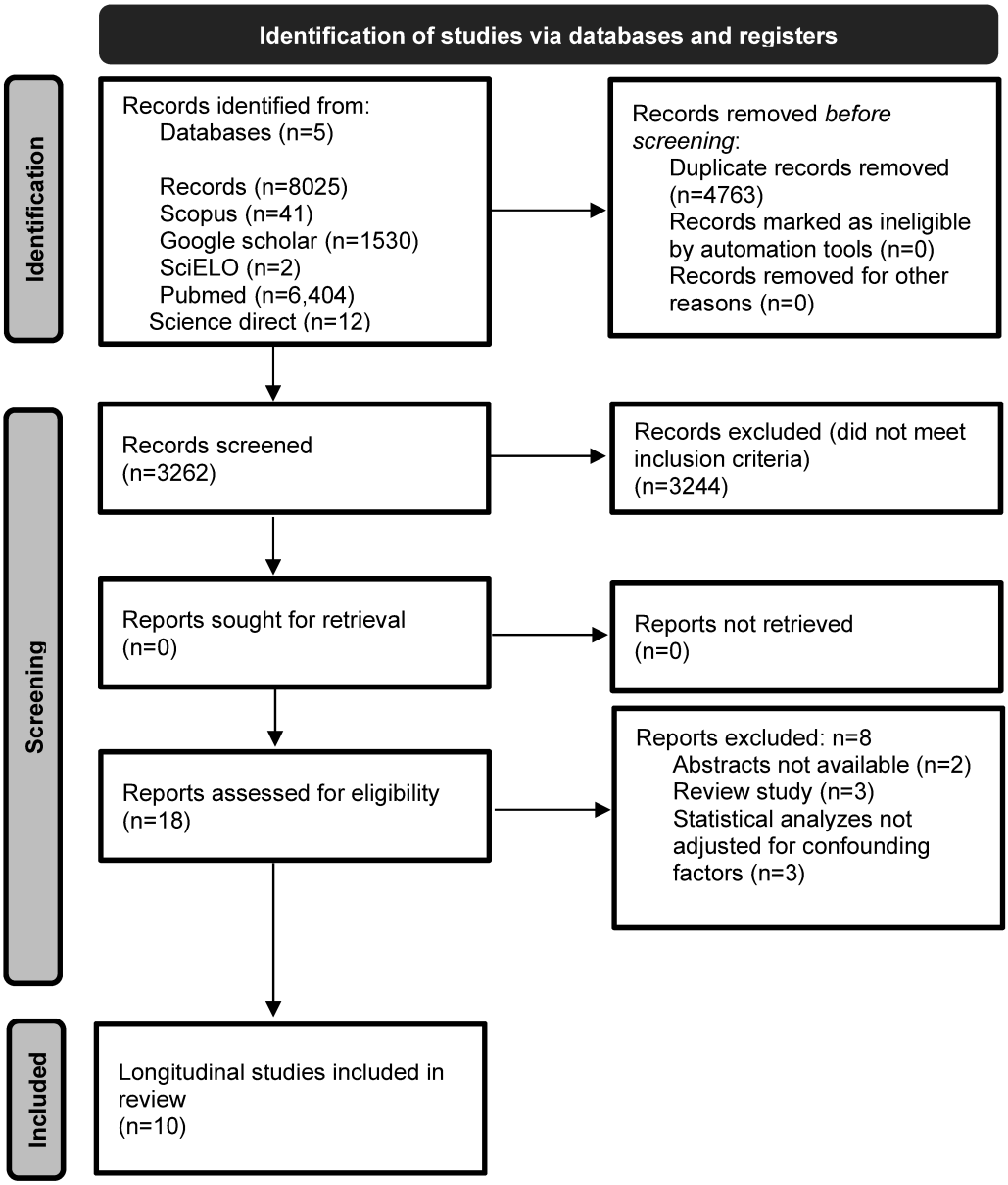

Figure 1. Protocol of identification and selection of studies eligible for the systematic review on the effect of the ultra-processed foods consumption on cardiometabolic risks among children and adults.

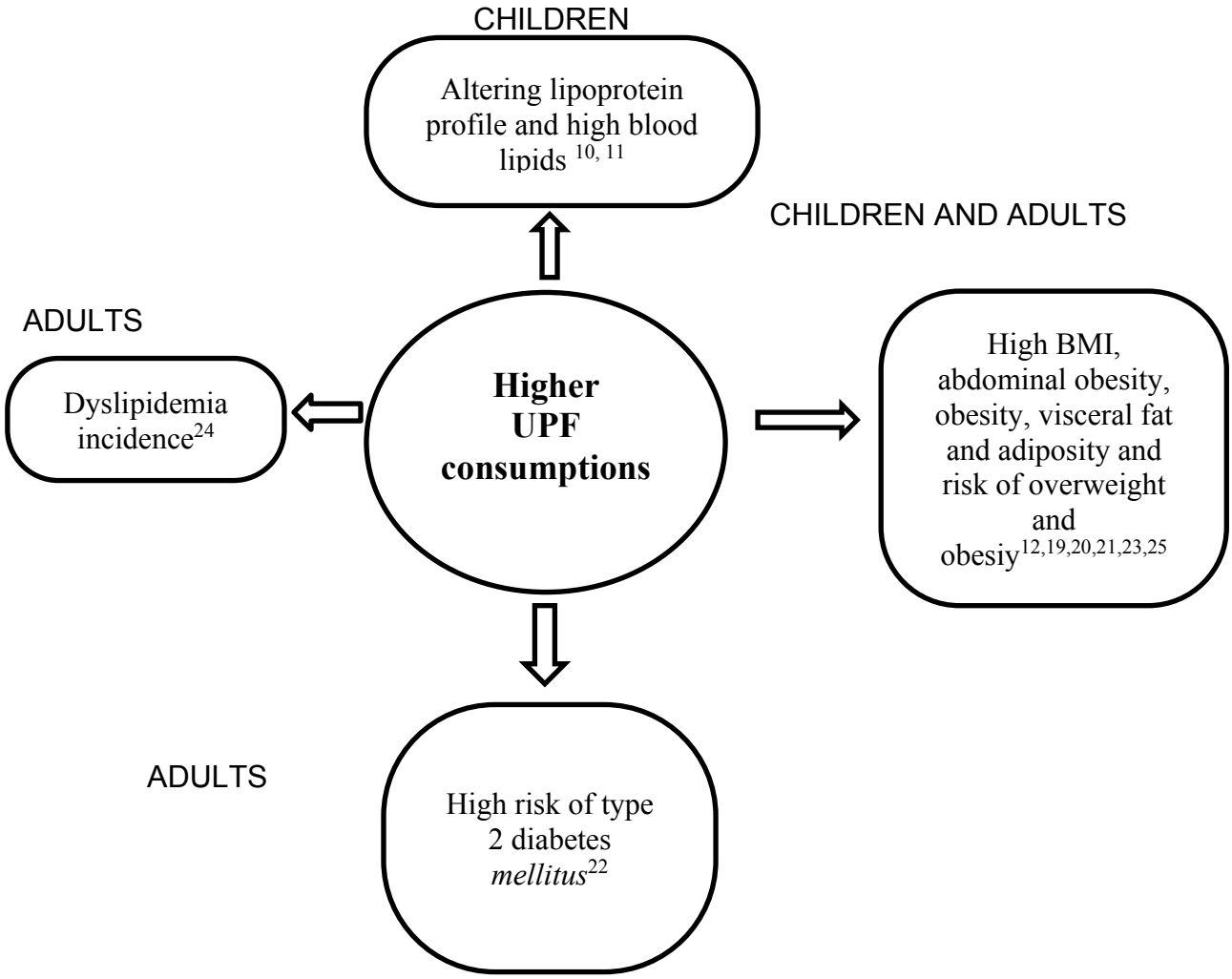

Figure 2. Cardiometabolic risks associated with higher consumptions of UPF in children and adults.

Table 1. Methodological aspects of the longitudinal studies that evaluated the association between UPF consumption and cardiometabolic risks.

Reference	Country	Age range and sample size	Length of follow-up
		Children	
Rauber et al (2015)[10]	Brazil	3 to 4 years-old and 7 to 8 years; n=345	1 year
Costa et al (2019)[11]	Brazil	4 to 8 years-old; n=307	1 year
Leffa et al (2020)[12]	Brazil	3 to 6 years-old; n=308	1 year
Vedovato et al (2021)[20]	Portugal	4 years-old; 7 to 10 years-old; n=1,175	6 years
		Adults	
Konieczna et al (2021)[21]	Spain	55 to 75 years-old; n=1,485	6 years
Llavero-Valero et al (2021)[22]	Spain	18 to 50 years-old; n=20,060	12 years
Beslay et al (2020)[19]	France	18 years-old; n=110,260	10 years
Sandoval-Insausti et al (2020)[23]	Spain	60 years-old; n=652	2 years
Donat-Vargas et al (2021)[24]	Spain	60 years-old; n=1,082	2 years
Cordova et al (2021)[25]	Europe	25 to 70 years-old; n=348,748	8 years

Table 2. Main statistical analyses and, results and quality assessments of the longitudinal studies that evaluated the association between UPF consumption and cardiometabolic risks.

Reference	Main statistical method	Adjustment variables	Main results	NOS
		Children		
Rauber et al (2015)[10]	Linear regression models	Sex, group status (intervention and control), birth weight, family income, maternal schooling, BMI z-score, and total energy intake at age 7 to 8	There was an association of total cholesterol (β= 0.430; P = 0.046), and LDL cholesterol (β= 0.369; P = 0.047) with UPF, from preschool to school age.	9
Costa et al (2019)[11]	Linear regression models	Pre-pregnancy BMI, sex, birth weight, breastfeeding, family income, maternal schooling, and total screen.	UPF consumption increased the delta of waist circumference from preschool to school age (β= 0.07; 95%CI 0.01- 0.14; P = 0.030).	9
Leffa et al (2020)[12]	Multiple linear regression models	Sex, group status in early phase (intervention or control), breastfeeding, family income, total energy intake and percentage of fat intake	UPF intakes at age 3y was associated with higher levels of TC (β 0·22 mmol/l; 95 % CI 0·04, 0·39) and TAG at age 6y (β 0·11 mmol/l, 95 % CI 0·01, 0·20). A positive dose response was observed for an absolute increment of 10 % of UPF on TC (β 0·07 mmol/l, 95 % CI 0·00, 0·14) and TAG (β 0·04 mmol/l, 95 % CI 0·01, 0·07).	9
Vedovato et al (2021)[20]	Linear regression models	Model 1: age, years of education and BMI before pregnancy Model 2: exclusive breastfeeding for the first 6 months parental concerning on eating behaviors practice of physical exercise and daily screen time at 4 years of age	UPF consumption at 4 years old was associated with BMI at 10 years old food responsiveness (β=0.019; 95%CI: 0.007; 0.037), food fussiness (β=0.007; 95% CI=0.002; 0.012), satiety responsiveness (β=0.007; 95%CI: 0.002; 0.012).	9
		Adults		
Konieczna et al (2021)[21]	Mixed-effects linear models	Sex, age, study arm (control or intervention group) follow-up time, educational level, mental status, smoking, T2D prevalence, height, physical activity, and sedentary behavior	10% daily increment in consumption of UPF was associated with greater accumulation of visceral fat (β 0.09 z-scores, 95% CI 0.05; 0.13), android-to-gynoid fat ratio (0.05, 0.00; 0.09) and total fat (0.09, 0.06; 0.13). from the 1y to 6years of follow-up.	8
Llavero-Valero et al (2021)[22]	Cox regression model	Age, sex, of body mass index (BMI), educational level, family history of diabetes, smoking status, snacking, 8-item active and sedentary lifestyle score and following a special diet at baseline.	High UPF consumption had a higher risk of T2D as compared to those in the lowest tertile (HR 1.53, 95%CI: 1.06 to 2.22) with a significant dose-response relationship (p for linear trend = 0.024). The multivariable adjusted HR using repeated measurements of UPF intake was 1.65 (95% CI 1.14-2.38) when comparing extreme tertiles at 10 years of follow-up.	8

Table 2. Main statistical analyses and, results and quality assessments of the longitudinal studies that evaluated the association between UPF consumption and cardiometabolic risks (continued).

Reference	Main statistical method	Adjustment variables	Main results	NOS
Beslay et al (2020)[19]	Cox proportional hazard models	Age, sex, educational level, smoking status, marital status, physical activity level, energy intake, alcohol intake, and number of dietary records.	Positive association between UPF intake and gain in BMI (β Time × UPF = 0.02 for an absolute increment of 10% of UPF in the diet, P< 0.001). UPF intake was associated with a higher risk of overweight (n= 7,063 overweight participants; hazard ratio (HR) for an absolute increase of 10% of UPFs in the diet = 1.11, 95% CI: 1.08–1.14; P< 0.001) and obesity (n= 3,066 incident obese participants; HR10% = 1.09 (1.05–1.13); P< 0.001) during the 10 years of follow-up.	9
Sandoval-Insausti et al (2020)[23]	Logistic regression models	Model 1: age and sex Model 2: educational level, marital status, smoking, ex-drinking status, physical activity in the household and leisure time physical activity Model 3: number of medications per day and number of chronic diseases. Model 4: fiber and very long chain omega-3 fatty acid consumption, adherence to the Mediterranean diet.	177(27.15%) developed AO during follow-up. The average consumption of UPF was 17% of total energy. The odds ratio for incident of AO risk when compared to the lowest tertile was: 1.55 (0.99–2.44) for the second tertile of UPF consumption and 1.62 (1.04–2.54) for the third tertile, at 2 years of follow-up.	9
Donat-Vargas et al (2021)[24]	Logistic regression models	Model 1: sex and age, Model 2: total energy intake, educational level marital status, smoking status, BMI, physical activity alcohol consumption, fiber intake, number of medications, and number of chronic diseases Model 3: unprocessed or minimally processed food consumption (Percentage of energy)	After a follow-up of between 5 to 7 years, 60 (out of 895) developed incident hypertriglyceridemia (≥150 mg/dL), 112 (out of 878) had low HDL cholesterol (<40 in men/<50 mg/dL in women), and 54 (out of 472) had high LDL cholesterol (>129 mg/dL). The mean percentage of UPF consumption was 19% ± 11% of total energy intake. Those in the highest versus the lowest tertile of energy intake from UPFs had more than twice the odds of incident hypertriglyceridemia (OR, 2.66; 95% CI: 1.20–5.90; P-trend, 0.011) or low HDL cholesterol (OR, 2.23; 95% CI: 1.22–4.05; P-trend, 0.012), between 5 to 7 years of follow-up.	9
Cordova et al (2021)[25]	Multilevel linear regression models	Model 1: age, sex, and BMI. Model 2: educational level, physical activity, smoking status, alcohol consumption, and an indicator for energy misreporting. Model 3: Mediterranean diet, representing healthy dietary habits, using the modified relative Medi terranean Diet Score (mrMDS).	The higher UPF consumption was positively associated with weight gain (0.12 kg/5 years, 95% CI 0.09 to 0.15). Comparing highest vs. lowest quintile of UPF consumption was associated with a 15% greater risk (95% CI 1.11, 1.19) of becoming overweight or obese in normal weight participants, and with a 16% greater risk (95% CI 1.09, 1.23) of becoming obese in participants who were overweight at baseline, when compared with the first quintile, after the 5 years of follow-up.	9

Abbreviations: UPF, ultra-processed foods; LDL, low density lipoprotein; HDL, high density lipoprotein; TC, total cholesterol; TAG, triglyceride; BMI, body mass index; T2D, type 2 diabetes mellitus; OA, abdominal obesity; NOS, Newcastle-Ottawa score; CI, 95% confidence interval.

6.2 Original article: The score of ultra-processed foods consumption is associated with a higher cardiometabolic risk in Brazilian schoolchildren.

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ABSTRACT

Ultra-processed foods (UPF) are industrial formulations nutritionally unbalanced and highly palatable that are associated with metabolic alterations in children. However, considering that there is a diversity of UPF consumed by children, it is necessary to evaluate a score specifically for this age group and its relationship with cardiometabolic risk. This study aimed to assess the association of UPF score and its subgroups with cardiometabolic risk in Brazilian schoolchildren. This is a representative cross-sectional study with 378 children aged 8 and 9 years attending in all urban public and private schools in Viçosa, Minas Gerais Brazil. A semi-structured questionnaire was applied to obtain sociodemographic and lifestyle information. The cardiometabolic risk was evaluated according to total and android body fat, lipid profile, blood pressure, uric acid, fasting glucose, and HOMA-IR. From the application of three 24-hour recalls, a score with 24 items composed of UPF was created. From this list, three subgroups of UPF were obtained: "sugary foods and beverages", "fatty foods" and "salty foods and processed meats". Multivariate linear regression models assessed the association of the UPF score and its subgroups with cardiometabolic risk markers. The “sugary foods and beverages” score was positively associated with LDL-c and uric acid. Every 1 SD of "sugary foods and beverages” score was associated to 3.1 (95%CI: 0.8, 5.3) and 0.1 (95%CI: 0.1, 0.2) units higher in LDL-c and uric acid, respectively. In addition, the “salty foods and meat products” score was positively associated with total cholesterol and LDL-c. Every 1 SD of “salty foods and meat products” score was associated to 3.0 (95%CI: 0.2, 5.8) and 3.3 (95%CI: 1.0, 5.6) units higher in total cholesterol and LDL-c, respectively. Finally, the UPF score was positively associated with LDL-c. Every 1 SD of UPF score was associated to 2.8 (95%CI: 0.6, 4.9) units higher in LDL-c. The use

of the UPF score in childhood can be an easy and quick method to identify unhealthy eating habits, as well as predict cardiometabolic risk at early age.

KEYWORDS: Children, Eating, Adiposity, Dyslipidemias, Uric acid, Nutritional epidemiology.

INTRODUCTION

Overweight and obesity in schoolchildren have increased in recent years, leading to higher cardiometabolic risk at an early age. [1-3]The increase in overweight and cardiometabolic risk in childhood can be assigned to a less healthy lifestyle, such as greater ultra-processed foods (UPF) consumption and sedentary behavior.[4]

A major component of modern diet is UPF that is associated with adverse cardiometabolic risk[5]. According to data from the 2015 National School Health Survey (*Pesquisa Nacional de Saúde do Escolar PeNSE*), 41.6%, 26.7%, and 31.3% of students ate sweets, snacks and soft drinks, five or more days a week respectively.[6]

Longitudinal studies with Brazilian children also reinforce the potential negative effects of UPF on children's health, such as increased total cholesterol and low-density lipoprotein (LDL)[7], triglycerides[8]. Moreover, the excessive intake of UPF is associated with overweight[9], uric acid[10], and insulin resistance[11], among children. Higher UPF consumption is associated with greater increases in adiposity from childhood to early adulthood. These alterations are linked to an increased risk of cardiometabolic disease.[12,13]

Previous studies, such as Surveillance System for Risk and Protective Factors for Chronic Diseases by Telephone Survey (VIGITEL)[14] and NutriNet Brasil[15], developed a score with a list of UPF subgroups (answered “yes” or “no”) to quickly assess the consumption of these foods in Brazilian adults with a good accuracy. However, considering that there is a diversity of UPF frequently consumed by children, it is necessary to propose a score specifically for this age group. In addition, it is important to know which subgroups of UPF comprise this score, as well as their relationship with cardiometabolic risk in children. In this context, the aim of this study was to assess whether the UPF score proposed for children and its subgroups were associated with cardiometabolic risk in Brazilian schoolchildren. Our hypothesis is that a higher score of UPF and its subgroup are associated with higher cardiometabolic risk in children.

METHODS

Sample and study design

This is a cross-sectional study with a representative sample of 8- and 9-year-old children who were attended in all public and private schools in the urban area of Viçosa, Minas Gerais, Brazil, carried out from May to December 2015. According to the 2010 census, Viçosa has an area of 299 km^2 and 72,244 inhabitants, of which 93.2% live in urban areas[16]. The study participants were from the Schoolchildren's Health Assessment Survey (*Pesquisa de Avaliacão da Saúde do Escolar*, PASE, in Portuguese).

The sample size calculation and the sampling process have already been described previously[17, 18]. In summary, a sample of 378 children aged 8 and 9 years were included in the study (population: 1,464 children, margin of error: 5%, confidence level: 95%, and addition for losses and confounders: 20%). Sample selection was performed randomly and stratified in the schools by sex and age.

Children with health problems affecting their nutritional status or body composition (physical, cognitive or repeated deficiencies, thyroid disorders, etc.), as well as children who were taking medications that interfere with glucose and/or lipid metabolism (corticosteroids, statins, hypoglycemic drugs, etc.) and who used vitamin or mineral supplements during the study or in the previous three months then (vitamin D and zinc supplements) were not included, as in cases where their parents or guardians could not be contacted.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Human Research Ethics Committee of the *Universidade Federal de Viçosa* (UFV) (reference number 663.171/2014). Written informed consent was obtained from all parents or guardians of participants.

Anthropometry and body composition

The weight and height of the children were measured, respectively, by an electronic digital balance with 150 kg capacity and 50 g sensitivity (Tanita® model Ironman BC 553; Tanita Corporation of America, Inc., Arlington Heights, IL, USA) and a stadiometer divided into centimeters and subdivided into millimeters (Alturexata®, Belo Horizonte, MG, Brazil). The nutritional status was evaluated by body mass index (BMI) for age and sex.[20]

Total and android body fat (%) were obtained using the dual energy X-ray absorptiometry (DXA) (Lunar Prodigy Advance, GE Medical Systems Lunar, Milwaukee, WI, USA). The android fat was measured in the region between the ribs and the pelvis, the upper demarcation was made at 20% of the distance from the iliac crest and the lower demarcation was made above the pelvis[21]. The test was performed in the Diagnostic Imaging sector of the UFV Health Center by a specialized technician. During the exam, the child was fasting, wearing light clothing with no metal adornment. Until the end of the equipment scanning, the child remained in a supine position on a stretcher. The excess body fat was classified according to the cut-off point proposed by Lohman[22] when the percentage of fat was >20% for boys and 25% for girls.

Mean arterial pressure

Blood pressure was measured with the child in a sitting position after resting for at least 5 min at three different times, using digital blood pressure monitors (Omron, Vernon Hills, IL, USA). With the median of values of systolic (SBP) and diastolic (DBP) blood pressure (mmHg), mean arterial pressure (MAP) was calculated [MAP = 1/3(SBP) + 2/3(DBP)].

Biochemical analysis

After 12 hours of fasting, blood was collected in the Clinical Analysis Laboratory of the Health Center of the UFV. Venipuncture was used to collect the samples, which were centrifuged for 15 min at 3500 rpm, separated into 1.5 ml Eppendorf tubes and stored in the freezer at -80°C.

Lipid profile (total cholesterol, high-density lipoprotein - HDLc, low-density lipoprotein - LDLc, and triglycerides), fasting glucose, and uric acid were determined by enzymatic colorimetry and measured in an automated analyzer (BS200 Mindray, Nanshan, China) at the Clinical Analytical Laboratory of the Department of Nutrition and Health of UFV. Serum insulin was analyzed through chemiluminescence immunoassay using the Elecsys Insulin® test (Roche Diagnostics, Indianapolis, IN, USA) with a detection limit of 0·200–1000 µU/ml. The homeostatic model assessment for insulin resistance (HOMA-IR) was calculated according to the equation: fasting insulin (µU/mL) x fasting blood glucose (mmol/L)/22.5.[23]

Food consumption and ultra-processed food score

Food consumption was evaluated by the average of three non-consecutive days 24-hour recalls (24hR), including one weekend day, and was completed based on information provided by the guardians and the child. To enhance the reliability of the data, the researchers received special training, and measuring kitchen tools and food photographic records were shown to the participants.[24]

The software Diet Pro® 5i, version 5.8 was used to record food consumption information. To analyze the food compositions, the *Tabela Brasileira de Composição de Alimentos* (TACO)[25] and the US Department of Agriculture's of Food Composition Database[26] were used. The measuring kitchen tools were converted into grams (g), milligrams (mg), or milliliters (mL) to access the energy intake (kcal).

Breakfast consumption was considered as the first food intake that the child consumed and/or drank in the first 2 hours after waking up[27]. Skipping breakfast was considered when the child did not eat this meal on one of the three days evaluated in the 24hR. This instrument was also used to assess the number of daily meals, which was obtained by the average of the three days, with values lower than 4 meals a day being considered low.[28]

The foods reported in 24hR were distributed and classified according to the degree of processing[29]. A list with 24 items was created from the UPF mentioned in at least one 24hR (Table 1). Each item consumed by children was scored, ranging from zero to 24 points. From these items, three subgroups were created by similarity of nutrient composition: "sugary foods and beverages", "fatty foods", and "salty foods and meat products" (Table 1).

Sociodemographic and lifestyle data

A semi-structured questionnaire was applied containing sociodemographic and lifestyle information, such as age (years), sex (female or male), school type (public or private), per capita income (USD), government program beneficiary (yes or no), maternal education (years of study), and screen time per day (hours spent watching television, playing video games, and using a cell phone or computer). Per capita income was categorized into quartiles and screen time higher than two hours per day was classified sedentary behavior.[30]

Data analyses

Exposure. "Ultra-processed food (UPF)", “sugary foods and beverages”, “fatty foods”, and “salty foods and meat products” scores were expressed in terciles.

Outcome. BMI-for-age, total and android body fat, total cholesterol, HDL-c, LDL-c, triglycerides, MAP, uric acid, fasting glucose, and HOMA-IR as continuous variables.

Covariates. We considered as covariates the child’s sex, age, school type, per capita income, government program beneficiary, maternal education, and screen time.

Statistical analyses. We first compared the distributions of UPF score by categories of covariates using mean ± standard deviation (SD) for continuous variables, and frequency measurements for categorical variables. Tests for linear trend were derived from linear regression models with UPF score as the continuous outcome and a variable representing ordinal categories of each covariate introduced as a continuous predictor. Second, we compared the distributions of cardiometabolic risk markers (outcomes) by terciles of “sugary foods and beverages”, “fatty foods”, “salty foods and meat products”, and “UPF scores” (exposures), using mean differences and 95%CI from multivariate linear regression models adjusted by sex, age, screen time, and per capita income. Finally, the multivariate model was additionally adjusted for body fat. Robust estimates of the variance were specified in all models, which are consistent with heteroscedasticity and non-normality[31]. We performed the analyses in the Stata® version 14 (StataCorp LP, College Station, TX, USA). The significance level was 5% for all hypothesis tests.

RESULTS

Our sample consisted mostly of girls (52.1%), with a mean age of 8.5 ± 0.5 years, students from public schools (70.9%) and whose family did not receive government benefits (77.0%). Most mothers had completed secondary school (34.7%) and had weight excess (57.5%). Considering the characteristics of eating habits and lifestyle, 47.6% had screen time higher than two hours per day, 90.2% had daily meals number equal to or greater than four, and 20.1% skipped breakfast.

Table 1 presents the grouping of items that composed the UPF score for children. The group “sugary foods and beverages” presented more food items than the “fatty foods” and “salty foods and meat products”. When considering each group of the UPF score, the medians (IQR) consumption of “sugary foods and beverages”, “fatty foods”, and “salty and meat products” were 5 (IQR: 4, 6), 2 (IQR: 1, 3) and 1 (IQR: 0, 2), respectively (Figure 1).

A higher mean of UPF scores was found in children studying at private schools and, whose families had higher per capita income and were not beneficiaries of government programs, who had four or more meals a day, and whose mothers had a higher level of education (Table 2).

"Sugary foods and beverages" score were positively associated with LDL-c and uric acid. After adjustment, when compared with the first, the third tercile of "sugary foods and beverages" score was related to 8.4 (95%CI: 2.0, 14.7) and 0.3 (95%CI: 0.1, 0.5) units higher in LDL-c and uric acid, respectively. Each SD of "sugary foods and beverages" score was associated to 3.1 (95%CI: 0.8, 5.3) and 0.1 (95%CI: 0.1, 0.2) units higher in LDL-c and uric acid, respectively (Table 3).

"Salty foods and meat products" score were positively associated with total cholesterol and LDL-c. When compared with the first, the third tercile of "salty foods and meat products" score was related to, respectively, 6.1 (95%CI: -0.7, 12.8) and 7.1 (95%CI: 1.4, 12.8) units higher in total cholesterol and LDL-c, after adjustment. Each SD of "salty foods and meat products" score was associated to 3.0 (95%CI: 0.2, 5.8) and 3.3 (95%CI: 1.0, 5.6) units higher in total cholesterol and LDL-c, respectively (Table 4).

UPF score was positively associated with LDL-c. The third tercile of UPF score was related to 7.4 (95%CI: 1.6, 13.1) units higher in LDL-c, when compared with the first, after adjustment. Each SD of UPF score was associated to 2.8 (95%CI: 0.6, 4.9) units higher in LDL-c (Table 5).

The "fatty foods" score was not associated with cardiometabolic risk markers after adjustment (Supplementary Material)

DISCUSSION

This study supports the hypothesis that the score for the UPF consumption and its subgroups were associated with higher cardiometabolic risk in schoolchildren. We identified direct association of "sugary foods and beverages" score with serum LDL-c and uric acid; of "salty foods and processed meats" score with serum total cholesterol and LDL-c; and between UPF scores and serum LDL-c.

Sugary foods and beverages score was positively associated with LDL-c and uric acid. Studies among China, US and Malaysian adolescents and children reveals a significant association of the sugary foods and beverages with LDL-c[32-35]. The most common source of added sugar in the diet is sugar-sweetened beverages (SSBs).

They are low in nutritional content and include carbonated and non-carbonated soft drinks and fruit drinks. There is a strong relationship between SSB intake and weight gain[36] and risk of type 2 diabetes *mellitus*[37], which is the basis of many dietary guidelines and policies targeting SSBs[38]. SSBs has a significant risk factor for cardiovascular diseases and other risk factors, such as stroke, blood lipids, inflammatory factor, and blood sugar, among adults[39-43]. The mechanism and physiology behind consumption of these foods is provide excess energy in liquid form which is not compensated by reducing food intake and altering long term taste preference toward increasing consumption of this foods.

Similarly, other studies have found an association between “sugary foods and beverages” with serum uric acid[10, 44-46]. Sugary foods provide excessive fructose with direct impact upon uric acid production, visceral fats, and the synthesis of fat in the liver[47]. The physiological mechanism is that excessive intake of exogenous fructose, an isomer of glucose from soft drinks or fruits juices may result in insulin resistance, obesity, elevated LDL-c, and triglyceride leading to the metabolic syndrome[48]. Excess fructose consumption can lead to the development of metabolic syndrome and type 2 diabetes, both conditions are well-known risk factors for heart and kidney disease. Because uric acid synthesis is biochemically linked to fructose metabolism, widespread consumption of this monosaccharide has been linked to gradually increasing serum uric acid levels over the last few decades.[49] However, because fructose is rarely consumed alone, fructose-containing sugars, sucrose, and high fructose corn syrup, which are found in sugar sweetened beverages, are the most common sources of fructose in the diet. Further to that, there is additional evidence of a link between elevated uric acid levels and the onset of cardiometabolic risk and subclinical inflamations.[50, 51]

“Salty foods and meat products” score were positively associated with serum total cholesterol and LDL-c. Higher intake of processed meats with high SFA, was associated with higher risk for abnormalities in serum total cholesterol and LDL-C levels.[52] Daily consumption of processed meat was associated with increase of LDL-c.[53] Meat products (such as ham, mortadella, and sausage etc.) are high in saturated fat and consumption of this product increases serum levels of total cholesterol and LDL-c in the bloodstream[52, 54]. The elevated level of total cholesterol and LDL-c implies that the individual increases the risk of developing cardiovascular disease.[55] While a high intake of SFAs from processed meat has been shown to increase the risks of CVD

and mortality.[56] High consumption of processed meat was associated with a 35 % increased risk of type 2 diabetes compared with the diet low in processed meat.[57]

Furthermore, UPF score were positively associated with LDL-c. Similar to our investigation, another study found high consumption of ultra-processed foods and positive relation with blood lipids among children and adolescents.[7, 58-61]

The Nova score for the consumption of ultra-processed foods, obtained in a quick and practical manner, shows a good potential in reflecting the dietary share of UPF in Brazilian adults[15]. According to the NOVA classification, foods are divided into four different groups, which distinguish foods according to the nature, extent, and purpose of the processing[29]. According to studies in young (0–8 years old) children, UPF now accounts for 32%–40% of total calorie consumption in this age range.[7, 62-64] Ultra-processed foods are often high in energy, high in fat, and have a sweet taste, which seems to be specifically related to addictive eating behavior.[65]

As the strength of this study, we can highlight that, this is a representative study with the sample composed of children, an important age group in which eating habits are formed. Second, all analyzes were adjusted for % body fat measured by DXA, a gold-standard method for assessing body composition. Third, although there are some proposals for UPF scores for Brazilian adults[14, 15], this is the first score to be applied exclusively to children, with evaluation of UPF's subgroups, allowing us to understand which are most consumed in childhood, as well as their relationship with cardiometabolic risk.

As limitations, the UPF score must be validated for epidemiological studies and outpatient application. Second, the application of the 24hR can lead memory bias; however, the interviewers were previously trained, and it was applied on three nonconsecutive days. Moreover, the cross-sectional design did not allow the establishment of cause-effect relation between UPF score and cardiometabolic risk markers, and further longitudinal studies are required.

In conclusion, UPF score and its subgroups were associated with higher cardiometabolic risk in Brazilian schoolchildren. We highlight that the UPF score is a quick and low-cost tool and may be a good predictor of cardiometabolic risk in Brazilian schoolchildren. With these findings, a collective effort should be made to educate the public about the effects of excessive UPF consumption, and there is a need to enlighten school feeding programs in both public and private schools about heathy eating habits.

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Table 1. Grouping of items that composed the ultra-processed foods (UPF) score for children according to the sugar, fat, and salt composition. Viçosa, Brazil, 2015.

Item	UPF score items	Food group	Maximum score
1	Soft drink	Sugary foods and beverages	13
2	Gum, candy, lollipop, and sweets		
3	Sweet cookie (with or without filling)		
4	Chocolate-flavored milk		
5	Industrialized fruit juice		
6	Drink mix (powdered fruit juice)		
7	Industrialized loaf bread		
8	Yogurt and petit suisse		
9	Ice cream, popsicle, milkshake, and *açaí*		
10	Chocolate		
11	Breakfast cereal		
12	Soft snack cake		
13	Cereal bar		
14	Margarine	Fatty foods	6
15	Finger food (*coxinha, rissole, empada* etc.)		
16	Salty cracker		
17	French fries		
18	Puffcorn		
19	Pizza		
20	Ham, mortadella, and salami	Salty foods and meat products	5
21	Sausage, beef burger, and chicken nugget		
22	Hamburger, hot dog, and ham and cheese sandwich		
23	Ketchup, mustard, and mayonnaise		
24	Instant noodles		

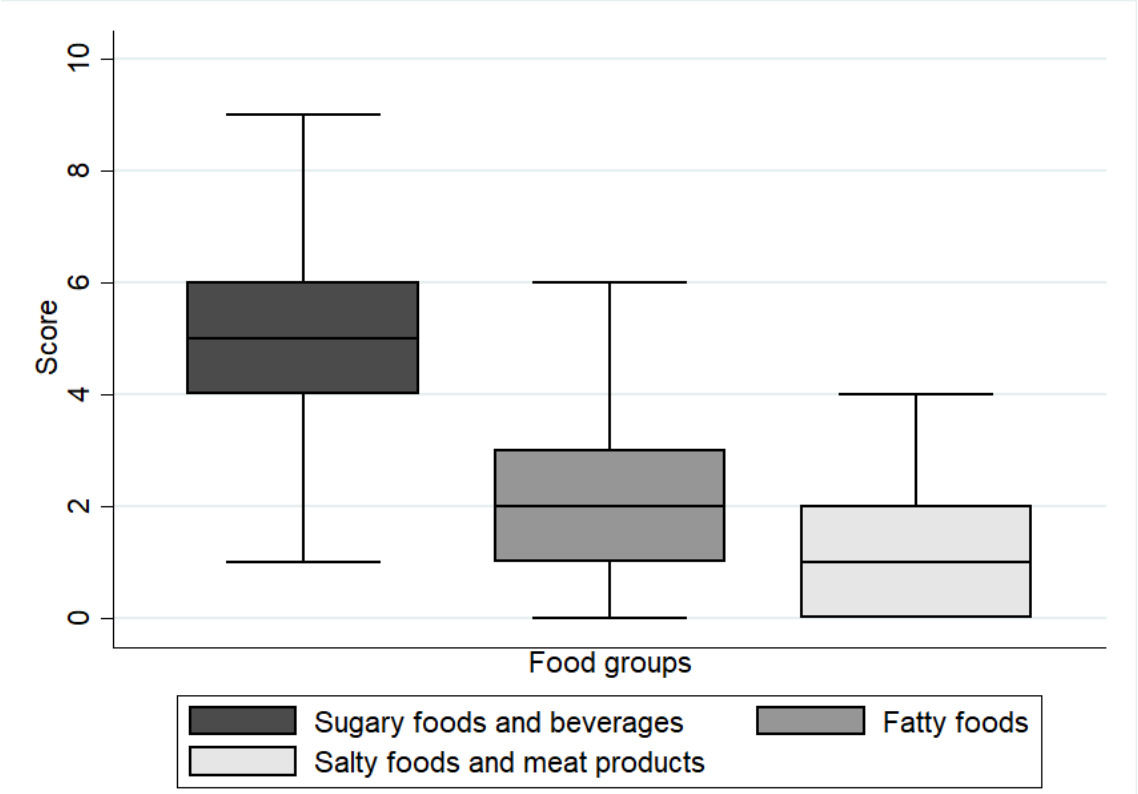

Figure 1. Scores for each group of ultra-processed foods consumed by children. Viçosa, Brazil, 2015.

Table 2. Ultra-processed food (UPF) score according to sociodemographic, lifestyle, nutritional status, body fat, and maternal characteristics. Viçosa, Brazil, 2015.

Characteristics	UPF score	
	n	Mean ± SD
Sex		
Female	197 (52.1%)	7.7 ± 2.5
Male	181 (47.9%)	8.1 ± 2.3
P-value		0.11
School type		
Public	268 (70.9%)	7.5 ± 2.3
Private	110 (29.1%)	8.8 ± 2.4
P-value		<0.001*
Per capita income (quartile)[1]		
< 79.00	93 (24.6%)	6.9 ± 2.5
79.00 – < 126.60	94 (24.9%)	7.8 ± 2.3
126.60 – 213.73	97 (25.5%)	8.4 ± 2.2
> 213.73	94 (24.9%)	8.4 ± 2.3
P, trend		0.02†
Government program beneficiary		
Yes	87 (23.0%)	7.0 ± 2.5
No	291 (77.0%)	8.1 ± 2.3
P-value		<0.001*
Nutritional status		
Overweight/Obesity	124 (32.8%)	7.9 ± 2.4
Normal	254 (67.2%)	7.8 ± 2.4
P-value		0.66
Body fat		
High	188 (49.7%)	8.1 ± 2.5
Normal	190 (50.3%)	7.6 ± 2.3
P-value		0.09
Screen time		
≤2h	198 (52.4%)	7.6 ± 2.5
>2h	180 (47.6%)	8.1 ± 2.3
P-value		0.06
Meals number		
< 4	37 (9.8%)	6.5 ± 2.1
≥4	341 (90.2%)	8.0 ± 2.4
P-value		<0.001*
Skipping breakfast		
Yes	76 (20.1%)	7.4 ± 2.3
No	302 (79.9%)	8.0 ± 2.5
P-value		0.13
Maternal education		
≤4 (primary or less)	53 (14.0%)	7.1 ± 2.6
5 to 10 (incomplete secondary)	109 (28.8%)	7.5 ± 2.3
11 (complete secondary)	131 (34.7%)	8.0 ± 2.4
P, trend		<0.001†*

Abbreviations: SD – standard deviation.
Mann-Whitney test and linear regression[†]. For variables with three or more categories, P-value was obtained from a test for linear trend representing the categories as continuous (P<0.05).
[1]Approximate exchange rates of real (R$) to dollar (USD) at the time of this study (R$1.00 = USD 3.22).

Table 3. Association between "sugary foods and beverages" score and cardiometabolic risk markers in schoolchildren from Viçosa, Brazil, 2015.

Cardiometabolic risk markers	"Sugary foods and beverages" score			P, trend[4]	Per 1 SD
	1st tercile (0 to 3) (n=85)	2nd tercile (4 to 5) (n=180)	3rd tercile (6 to 13) (n=113)		
Total fat (%)	24.0 ± 10.6	24.0 ± 9.9	24.7 ± 10.0		
Unadjusted difference (95%CI)[1]	Reference	-0.1 (-2.8, 2.6)	0.7 (-2.3, 3.6)	0.61	-0.3 (-1.3, 0.8)
Adjusted difference (95%CI)[2]	Reference	-0.2 (-2.7, 2.4)	0.2 (-2.6, 3.0)	0.47	-0.4 (-1.3, 0.6)
Android fat (%)	17.4 ± 12.7	17.4 ± 12.2	18.3 ± 12.1		
Unadjusted difference (95%CI)[1]	Reference	0.0 (-3.3, 3.2)	0.9 (-2.6, 4.4)	0.78	-0.2 (-1.4, 1.1)
Adjusted difference (95%CI)[2]	Reference	-0.1 (-3.2, 3.0)	0.3 (-3.1, 3.7)	0.61	-0.3 (-1.5, 0.9)
Total cholesterol (mg/dL)	151.0 ± 24.6	149.5 ± 26.7	157.8 ± 26.5		
Unadjusted difference (95%CI)[1]	Reference	-1.6 (-8.1, 5.0)	6.7 (-0.5, 13.9)	0.04*	2.7 (0.1, 5.3)
Adjusted difference (95%CI)[2]	Reference	-2.2 (-8.8, 4.4)	5.2 (-2.4, 12.8)	0.14	2.1 (-0.7, 4.9)
Adjusted difference (95%CI)[3]	Reference	-2.1 (-8.7, 4.5)	5.1 (-2.4, 12.7)	0.11	2.2 (-0.5, 5.0)
HDL-c (mg/dL)	50.2 ± 10.1	49.7 ± 10.3	50.6 ± 9.5		
Unadjusted difference (95%CI)[1]	Reference	-0.6 (-3.2, 2.0)	0.4 (-2.4, 3.2)	0.10	0.8 (-0.2, 1.8)
Adjusted difference (95%CI)[2]	Reference	-0.8 (-3.4, 1.8)	0.0 (-2.8, 2.8)	0.23	0.6 (-0.4, 1.6)
Adjusted difference (95%CI)[3]	Reference	-0.8 (-3.4, 1.7)	0.0 (-2.8, 2.8)	0.26	0.6 (-0.4, 1.6)
LDL-c (mg/dL)	82.8 ± 20.6	84.9 ± 24.7	93.4 ± 22.0		
Unadjusted difference (95%CI)[1]	Reference	2.2 (-3.5, 7.9)	10.7 (4.7, 16.7)	<0.001*	3.8 (1.8, 5.8)
Adjusted difference (95%CI)[2]	Reference	1.4 (-4.2, 7.0)	8.4 (2.0, 14.8)	0.01*	2.9 (0.7, 5.2)
Adjusted difference (95%CI)[3]	Reference	1.5 (-4.2, 7.1)	8.4 (2.0, 14.7)	0.008*	3.1 (0.8, 5.3)
Triglycerides (mg/dL)	76.9 ± 40.5	76.5 ± 30.6	84.1 ± 38.2		
Unadjusted difference (95%CI)[1]	Reference	-0.4 (-10.1, 9.3)	7.2 (-3.9, 18.4)	0.36	1.7 (-1.9, 5.4)
Adjusted difference (95%CI)[2]	Reference	-0.9 (-10.8, 9.0)	5.8 (-5.4, 16.9)	0.51	1.3 (-2.5, 5.0)
Adjusted difference (95%CI)[3]	Reference	-0.8 (-10.4, 8.8)	5.6 (-5.4, 16.5)	0.41	1.6 (-2.2, 5.3)
MAP (mmHg)	75.1 ± 7.2	74.1 ± 7.0	74.7 ± 6.7		
Unadjusted difference (95%CI)[1]	Reference	-0.9 (-2.8, 0.9)	-0.4 (-2.4, 1.6)	0.41	-0.3 (-1.1, 0.4)
Adjusted difference (95%CI)[2]	Reference	-0.7 (-2.5, 1.2)	0.2 (-1.8, 2.3)	0.86	-0.1 (-0.9, 0.7)
Adjusted difference (95%CI)[3]	Reference	-0.7 (-2.4, 1.0)	0.2 (-1.8, 2.1)	0.90	0.0 (-0.7, 0.8)
Uric acid (mg/dL)	3.0 ± 0.7	3.2 ± 0.8	3.3 ± 0.9		
Unadjusted difference (95%CI)[1]	Reference	0.2 (0.0, 0.4)	0.3 (0.1, 0.5)	0.06	0.1 (0.0, 0.2)
Adjusted difference (95%CI)[2]	Reference	0.2 (0.0, 0.4)	0.3 (0.1, 0.5)	0.09	0.1 (0.0, 0.2)
Adjusted difference (95%CI)[3]	Reference	0.2 (0.0, 0.4)	0.3 (0.1, 0.5)	0.04*	0.1 (0.1, 0.2)
Fasting glucose (mg/dL)	84.2 ± 8.5	85.2 ± 7.9	84.9 ± 7.7		
Unadjusted difference (95%CI)[1]	Reference	1.0 (-1.2, 3.1)	0.7 (-1.6, 3.0)	0.88	0.1 (-0.7, 0.8)
Adjusted difference (95%CI)[2]	Reference	1.0 (-1.1, 3.1)	0.8 (-1.5, 3.1)	0.93	0.0 (-0.7, 0.8)
Adjusted difference (95%CI)[3]	Reference	1.0 (-1.1, 3.1)	0.8 (-1.5, 3.1)	0.91	0.0 (-0.7, 0.8)
HOMA-IR	1.2 ± 0.9	1.2 ± 1.3	1.2 ± 0.9		
Unadjusted difference (95%CI)[1]	Reference	0.0 (-0.3, 0.3)	0.0 (-0.3, 0.3)	0.13	-0.1 (-0.2, 0.0)
Adjusted difference (95%CI)[2]	Reference	0.0 (-0.3, 0.3)	0.0 (-0.2, 0.3)	0.31	0.0 (-0.2, 0.0)
Adjusted difference (95%CI)[3]	Reference	0.0 (-0.2, 0.3)	0.0 (-0.2, 0.3)	0.48	0.0 (-0.1, 0.0)

Abbreviations: UPF - ultra-processed foods; SD - standard deviation; 95%CI - 95% confidence interval; BMI – body mass index; HDL-c – high-density lipoprotein-cholesterol; LDL-c – low-density lipoprotein-cholesterol; MAP – mean arterial pressure; HOMA-IR - homeostasis model assessment for insulin resistance.

[1]From linear regression models with cardiometabolic risk markers as continuous outcomes and sugary foods and beverages score as predictor.

[2]From linear regression adjusted by sex, age, screen time, and per capita income as the continuous outcome.

[3]From linear regression adjusted by sex, age, screen time, per capita income, and % total body fat as the continuous outcome.

[4]For a variable representing ordinal sugary foods and beverages score categories introduced into the model as a continuous predictor.

Table 4. Association between "salty foods and meat products" score and cardiometabolic risk markers in schoolchildren from Viçosa, Brazil, 2015.

Cardiometabolic risk markers	"Salty foods and meat products" score			P, trend[4]	Per 1 SD
	1st tercile (0 to 1) (n=130)	2nd tercile (2) (n=166)	3rd tercile (3 to 5) (n=82)		
Total fat (%)	23.1 ± 10.0	25.6 ± 10.2	23.7 ± 9.9		
Unadjusted difference (95%CI)[1]	Reference	2.5 (0.1, 4.9)	0.6 (-2.0, 3.2)	0.69	0.2 (-0.8, 1.2)
Adjusted difference (95%CI)[2]	Reference	1.9 (-0.4, 4.2)	0.8 (-1.7, 3.2)	0.59	0.3 (-0.7, 1.2)
Android fat (%)	16.1 ± 12.4	19.3 ± 12.2	17.4 ± 11.8		
Unadjusted difference (95%CI)[1]	Reference	3.2 (0.3, 6.1)	1.3 (-1.8, 4.4)	0.51	0.4 (-0.8, 1.6)
Adjusted difference (95%CI)[2]	Reference	2.6 (-0.3, 5.5)	1.4 (-1.6, 4.4)	0.45	0.5 (-0.7, 1.7)
Total cholesterol (mg/dL)	149.0 ± 24.4	153.5 ± 27.2	155.2 ± 27.8		
Unadjusted difference (95%CI)[1]	Reference	4.5 (-1.6, 10.6)	6.3 (-0.5, 13.0)	0.03*	3.1 (0.3, 5.9)
Adjusted difference (95%CI)[2]	Reference	3.9 (-2.1, 10.0)	6.3 (-0.5, 13.1)	0.03*	3.1 (0.3, 5.8)
Adjusted difference (95%CI)[3]	Reference	3.4 (-2.6, 9.4)	6.1 (-0.7, 12.8)	0.04*	3.0 (0.2, 5.8)
HDL-c (mg/dL)	49.5 ± 9.1	49.7 ± 10.2	51.3 ± 10.9		
Unadjusted difference (95%CI)[1]	Reference	0.1 (-2.2, 2.4)	1.8 (-0.8, 4.4)	0.18	0.7 (-0.3, 1.8)
Adjusted difference (95%CI)[2]	Reference	0.4 (-1.9, 2.7)	1.8 (-0.8, 4.4)	0.19	0.7 (-0.4, 1.8)
Adjusted difference (95%CI)[3]	Reference	0.6 (-1.6, 2.9)	1.9 (-0.7, 4.4)	0.17	0.7 (-0.3, 1.8)
LDL-c (mg/dL)	82.8 ± 22.9	88.8 ± 23.5	90.1 ± 23.3		
Unadjusted difference (95%CI)[1]	Reference	6.1 (0.6, 11.6)	7.4 (1.4, 13.3)	0.005*	3.4 (1.0, 5.8)
Adjusted difference (95%CI)[2]	Reference	5.0 (-0.4, 10.4)	7.4 (1.6, 13.2)	0.004*	3.4 (1.1, 5.8)
Adjusted difference (95%CI)[3]	Reference	4.3 (-1.1, 9.6)	7.1 (1.4, 12.8)	0.005*	3.3 (1.0, 5.6)
Triglycerides (mg/dL)	76.6 ± 31.0	80.4 ± 34.0	79.7 ± 42.5		
Unadjusted difference (95%CI)[1]	Reference	3.9 (-3.8, 11.6)	3.2 (-6.6, 13.0)	0.71	0.7 (-3.1, 4.5)
Adjusted difference (95%CI)[2]	Reference	2.9 (-4.8, 10.6)	3.4 (-6.2, 13.1)	0.68	0.8 (-2.9, 4.5)
Adjusted difference (95%CI)[3]	Reference	1.3 (-6.4, 9.1)	2.8 (-6.4, 12.1)	0.76	0.6 (-3.0, 4.1)
MAP (mmHg)	73.7 ± 6.5	74.8 ± 6.9	75.1 ± 7.4		
Unadjusted difference (95%CI)[1]	Reference	1.1 (-0.5, 2.7)	1.4 (-0.4, 3.2)	0.12	0.6 (-0.1, 1.3)
Adjusted difference (95%CI)[2]	Reference	1.1 (-0.5, 2.7)	1.4 (-0.4, 3.2)	0.11	0.6 (-0.1, 1.3)
Adjusted difference (95%CI)[3]	Reference	0.5 (-0.9, 2.0)	1.1 (-0.5, 2.8)	0.15	0.5 (-0.2, 1.1)
Uric acid (mg/dL)	3.2 ± 0.8	3.2 ± 0.9	3.2 ± 0.7		
Unadjusted difference (95%CI)[1]	Reference	0.0 (-0.2, 0.2)	0.0 (-0.2, 0.2)	0.75	0.0 (-0.1, 0.1)
Adjusted difference (95%CI)[2]	Reference	0.0 (-0.2, 0.2)	0.0 (-0.2, 0.2)	0.72	0.0 (-0.1, 0.1)
Adjusted difference (95%CI)[3]	Reference	-0.1 (-0.3, 0.1)	0.0 (-0.2, 0.2)	0.87	0.0 (-0.1, 0.1)
Fasting glucose (mg/dL)	85.0 ± 7.8	84.5 ± 8.1	85.1 ± 8.0		
Unadjusted difference (95%CI)[1]	Reference	-0.5 (-2.4, 1.4)	0.1 (-2.0, 2.1)	0.83	-0.1 (-0.9, 0.7)
Adjusted difference (95%CI)[2]	Reference	-0.4 (-2.3, 1.5)	-0.1 (-2.1, 1.9)	0.73	-0.1 (-0.9, 0.6)
Adjusted difference (95%CI)[3]	Reference	-0.4 (-2.4, 1.5)	-0.1 (-2.1, 1.9)	0.72	-0.1 (-0.9, 0.6)
HOMA-IR	1.3 ± 1.6	1.2 ± 0.7	1.1 ± 0.7		
Unadjusted difference (95%CI)[1]	Reference	-0.1 (-0.4, 0.2)	-0.2 (-0.5, 0.1)	0.19	-0.1 (-0.2, 0.0)
Adjusted difference (95%CI)[2]	Reference	-0.1 (-0.4, 0.2)	-0.2 (-0.5, 0.1)	0.20	-0.1 (-0.2, 0.0)
Adjusted difference (95%CI)[3]	Reference	-0.2 (-0.5, 0.1)	-0.2 (-0.5, 0.1)	0.12	-0.1 (-0.2, 0.0)

Abbreviations: UPF - ultra-processed foods; SD - standard deviation; 95%CI - 95% confidence interval; BMI – body mass index; HDL-c – high-density lipoprotein-cholesterol; LDL-c – low-density lipoprotein-cholesterol; MAP – mean arterial pressure; HOMA-IR - homeostasis model assessment for insulin resistance.

[1]From linear regression models with cardiometabolic risk markers as continuous outcomes and salty foods and meat products score as predictor.

[2]From linear regression adjusted by sex, age, screen time, and per capita income as the continuous outcome.

[3]From linear regression adjusted by sex, age, screen time, per capita income, and % total body fat as the continuous outcome.

[4]For a variable representing ordinal salty foods and meat products score categories introduced into the model as a continuous predictor.

Table 5. Association between ultra-processed foods (UPF) score and cardiometabolic risk markers in schoolchildren from Viçosa, Brazil, 2015.

Cardiometabolic risk markers	UPF score			P, trend[4]	Per 1 SD
	1st tercile (<7) (n=111)	2nd tercile (7 to 8) (n=125)	3rd tercile (>8) (n=142)		
Total fat (%)	24.6 ± 10.7	23.9 ± 10.0	24.2 ± 9.8		
Unadjusted difference (95%CI)[1]	Reference	-0.7 (-3.3, 2.0)	-0.4 (-3.0, 2.2)	0.85	0.1 (-0.9, 1.1)
Adjusted difference (95%CI)[2]	Reference	-0.2 (-2.8, 2.4)	-0.2 (-2.7, 2.3)	0.78	0.1 (-0.8, 1.1)
Android fat (%)	18.1 ± 13.4	17.2 ± 12.0	17.7 ± 11.6		
Unadjusted difference (95%CI)[1]	Reference	-0.8 (-4.1, 2.5)	-0.3 (-3.5, 2.9)	0.74	0.2 (-1.0, 1.4)
Adjusted difference (95%CI)[2]	Reference	-0.4 (-3.6, 2.9)	-0.2 (-3.3, 2.9)	0.75	0.2 (-1.0, 1.4)
Total cholesterol (mg/dL)	150.1 ± 24.8	150.8 ± 26.1	155.3 ± 27.8		
Unadjusted difference (95%CI)[1]	Reference	0.7 (-5.8, 7.3)	5.2 (-1.4, 11.8)	0.07	2.3 (-0.2, 4.8)
Adjusted difference (95%CI)[2]	Reference	0.4 (-6.2, 7.1)	4.4 (-2.3, 11.2)	0.14	1.9 (-0.6, 4.4)
Adjusted difference (95%CI)[3]	Reference	0.5 (-6.2, 7.1)	4.5 (-2.2, 11.2)	0.14	1.9 (-0.6, 4.4)
HDL-c (mg/dL)	49.8 ± 10.0	50.1 ± 10.1	50.2 ± 9.9		
Unadjusted difference (95%CI)[1]	Reference	-0.3 (-2.3, 2.9)	0.4 (-2.2, 2.9)	0.39	0.4 (-0.5, 1.3)
Adjusted difference (95%CI)[2]	Reference	-0.1 (-2.5, 2.7)	0.0 (-2.5, 2.5)	0.55	0.3 (-0.6, 1.2)
Adjusted difference (95%CI)[3]	Reference	-0.1 (-2.4, 2.6)	0.0 (-2.5, 2.5)	0.53	0.3 (-0.6, 1.2)
LDL-c (mg/dL)	83.2 ± 22.4	85.1 ± 23.0	91.4 ± 23.9		
Unadjusted difference (95%CI)[1]	Reference	1.9 (-4.0, 7.8)	8.1 (2.3, 14.0)	0.002*	3.3 (1.2, 5.4)
Adjusted difference (95%CI)[2]	Reference	2.1 (-3.6, 7.8)	7.3 (1.5, 13.1)	0.01*	2.8 (0.7, 5.0)
Adjusted difference (95%CI)[3]	Reference	2.2 (-3.5, 7.9)	7.4 (1.6, 13.1)	0.01*	2.8 (0.6, 4.9)
Triglycerides (mg/dL)	80.4 ± 39.1	75.2 ± 31.0	81.0 ± 36.3		
Unadjusted difference (95%CI)[1]	Reference	-5.2 (-14.5, 4.0)	0.6 (-9.0, 10.2)	0.47	1.5 (-2.5, 5.5)
Adjusted difference (95%CI)[2]	Reference	-5.4 (-14.8, 4.1)	0.2 (-9.2, 9.6)	0.51	1.3 (-2.6, 5.2)
Adjusted difference (95%CI)[3]	Reference	-5.2 (-14.3, 3.9)	0.3 (-8.9, 9.6)	0.55	1.2 (-2.7, 5.1)
MAP (mmHg)	75.0 ± 7.0	74.6 ± 7.0	74.1 ± 6.8		
Unadjusted difference (95%CI)[1]	Reference	-0.4 (-2.2, 1.4)	-0.9 (-2.7, 0.8)	0.77	-0.1 (-0.8, 0.6)
Adjusted difference (95%CI)[2]	Reference	-0.3 (-2.2, 1.6)	-0.7 (-2.5, 1.1)	0.95	0.0 (-0.7, 0.7)
Adjusted difference (95%CI)[3]	Reference	-0.3 (-1.9, 1.4)	-0.7 (-2.3, 1.0)	0.82	0.0 (-0.7, 0.6)
Uric acid (mg/dL)	3.1 ± 0.7	3.2 ± 0.8	3.3 ± 0.9		
Unadjusted difference (95%CI)[1]	Reference	0.1 (-0.1, 0.3)	0.2 (0.0, 0.4)	0.07	0.1 (0.0, 0.2)
Adjusted difference (95%CI)[2]	Reference	0.2 (0.0, 0.4)	0.2 (0.0, 0.4)	0.08	0.1 (0.0, 0.2)
Adjusted difference (95%CI)[3]	Reference	0.2 (0.0, 0.3)	0.2 (0.0, 0.4)	0.08	0.1 (0.0, 0.2)
Fasting glucose (mg/dL)	85.2 ± 8.1	84.8 ± 8.0	84.7 ± 7.9		
Unadjusted difference (95%CI)[1]	Reference	-0.4 (-2.5, 1.7)	-0.5 (-2.5, 1.6)	0.98	0.0 (-0.8, 0.8)
Adjusted difference (95%CI)[2]	Reference	-0.7 (-2.8, 1.4)	-0.8 (-2.8, 1.3)	0.82	-0.1 (-0.9, 0.7)
Adjusted difference (95%CI)[3]	Reference	-0.7 (-2.8, 1.4)	-0.8 (-2.8, 1.3)	0.81	-0.1 (-0.9, 0.7)
HOMA-IR	1.4 ± 1.7	1.2 ± 1.0	1.1 ± 0.6		
Unadjusted difference (95%CI)[1]	Reference	-0.2 (-0.6, 0.2)	-0.2 (-0.6, 0.1)	0.13	-0.1 (-0.2, 0.0)
Adjusted difference (95%CI)[2]	Reference	-0.2 (-0.5, 0.2)	-0.2 (-0.5, 0.1)	0.19	-0.1 (-0.1, 0.0)
Adjusted difference (95%CI)[3]	Reference	-0.2 (-0.5, 0.1)	-0.2 (-0.5, 0.1)	0.13	-0.1 (-0.1, 0.0)

Abbreviations: UPF - ultra-processed foods; SD - standard deviation; 95%CI - 95% confidence interval; BMI – body mass index; HDL-c – high-density lipoprotein-cholesterol; LDL-c – low-density lipoprotein-cholesterol; MAP – mean arterial pressure; HOMA-IR - homeostasis model assessment for insulin resistance.

[1]From linear regression models with cardiometabolic risk markers as continuous outcomes and ultra-processed foods score as predictor.

[2]From linear regression adjusted by sex, age, screen time, and per capita income as the continuous outcome.

[3]From linear regression adjusted by sex, age, screen time, per capita income, and % total body fat as the continuous outcome.

[4]For a variable representing ordinal ultra-processed foods score categories introduced into the model as a continuous predictor.

Supplementary Material. Association between "fatty foods" score and cardiometabolic risk markers in schoolchildren from Viçosa, Brazil, 2015.

Cardiometabolic risk markers	"Fatty foods" score			P, trend[4]	Per 1 SD
	1st tercile (0 to 1) (n=154)	2nd tercile (2) (n=124)	3rd tercile (3 to 6) (n=100)		
Total fat (%)	24.1 ± 9.8	24.0 ± 10.5	24.6 ± 10.1		
Unadjusted difference (95%CI)[1]	Reference	-0.1 (-2.5, 2.3)	0.5 (-2.0, 3.0)	0.41	0.4 (-0.6, 1.4)
Adjusted difference (95%CI)[2]	Reference	0.2 (-2.2, 2.6)	0.8 (-1.6, 3.2)	0.29	0.5 (-0.4, 1.5)
Android fat (%)	17.2 ± 12.1	18.0 ± 13.3	17.9 ± 11.1		
Unadjusted difference (95%CI)[1]	Reference	0.8 (-2.3, 3.8)	0.7 (-2.2, 3.6)	0.46	0.4 (-0.7, 1.6)
Adjusted difference (95%CI)[2]	Reference	1.0 (-2.0, 4.0)	1.0 (-1.8, 3.8)	0.40	0.5 (-0,6, 1.6)
Total cholesterol (mg/dL)	154.9 ± 27.8	149.4 ± 26.3	151.9 ± 24.0		
Unadjusted difference (95%CI)[1]	Reference	-5.6 (-12.0, 0.8)	-3.0 (-9.5, 3.4)	0.41	-1.1 (-3.6, 1.4)
Adjusted difference (95%CI)[2]	Reference	-5.7 (-12.2, 0.9)	-3.1 (-9.7, 3.4)	0.40	-1.1 (-3.7, 1.4)
Adjusted difference (95%CI)[3]	Reference	-5.7 (-12.3, 0.8)	-3.4 (-10.0, 3.2)	0.33	-1.3 (-3.9, 1.3)
HDL-c (mg/dL)	51.5 ± 10.4	48.3 ± 9.7	50.0 ± 9.4		
Unadjusted difference (95%CI)[1]	Reference	-3.2 (-5.6, -0.8)	-1.5 (-4.0, 0.9)	0.21	-0.6 (-1.6, 0.4)
Adjusted difference (95%CI)[2]	Reference	-3.1 (-5.5, -0.8)	-1.6 (-4.1, 0.8)	0.21	-0.6 (-1.6, 0.4)
Adjusted difference (95%CI)[3]	Reference	-3.1 (-5.5, -0.7)	-1.5 (-4.0, 0.9)	0.25	-0.6 (-1.6, 0.4)
LDL-c (mg/dL)	88.3 ± 24.7	86.2 ± 23.2	85.9 ± 21.5		
Unadjusted difference (95%CI)[1]	Reference	-2.1 (-7.8, 3.6)	-2.3 (-8.1, 3.5)	0.42	-0.9 (-3.0, 1.2)
Adjusted difference (95%CI)[2]	Reference	-1.9 (-7.4, 3.6)	-2.2 (-7.9, 3.4)	0.40	-0.9 (-3.0, 1.2)
Adjusted difference (95%CI)[3]	Reference	-2.0 (-7.5, 3.5)	-2.6 (-8.2, 3.0)	0.29	-1.1 (-3.2, 0.9)
Triglycerides (mg/dL)	80.3 ± 39.2	77.0 ± 30.9	78.8 ± 34.7		
Unadjusted difference (95%CI)[1]	Reference	-3.3 (-11.5, 5.0)	-1.5 (-10.7, 7.8)	0.86	-0.3 (-4.1, 3.4)
Adjusted difference (95%CI)[2]	Reference	-3.0 (-11.2, 5.2)	-0.9 (-10.3, 8.5)	0.93	-0.2 (-4.0, 3.7)
Adjusted difference (95%CI)[3]	Reference	-3.1 (-11.1, 4.9)	-1.6 (-10.8, 7.6)	0.74	-0.6 (-4.4, 3.1)
MAP (mmHg)	74.7 ± 7.0	74.5 ± 7.2	74.1 ± 6.4		
Unadjusted difference (95%CI)[1]	Reference	-0.2 (-1.9, 1.5)	-0.6 (-2.3, 1.1)	0.79	-0.1 (-0.7, 0.5)
Adjusted difference (95%CI)[2]	Reference	-0.4 (-2.1, 1.3)	-0.8 (-2.5, 0.9)	0.70	-0.1 (-0.7, 0.5)
Adjusted difference (95%CI)[3]	Reference	-0.5 (-2.0, 1.0)	-1.1 (-2.6, 0.5)	0.31	-0.3 (-0.9, 0.3)
Uric acid (mg/dL)	3.2 ± 0.8	3.2 ± 0.8	3.2 ± 0.8		
Unadjusted difference (95%CI)[1]	Reference	0.0 (-0.2, 0.2)	0.0 (-0.2, 0.2)	0.35	0.0 (0.0, 0.1)
Adjusted difference (95%CI)[2]	Reference	0.0 (-0.1, 0.2)	0.0 (-0.2, 0.2)	0.33	0.0 (0.0, 0.13)
Adjusted difference (95%CI)[3]	Reference	0.0 (-0.1, 0.2)	0.0 (-0.2, 0.2)	0.52	0.0 (-0.1, 0.1)
Fasting glucose (mg/dL)	85.3 ± 7.9	83.8 ± 8.2	85.4 ± 7.8		
Unadjusted difference (95%CI)[1]	Reference	-1.5 (-3.4, 0.4)	0.0 (-2.0, 2.0)	0.62	0.2 (-0.6, 1.0)
Adjusted difference (95%CI)[2]	Reference	-1.9 (-3.8, 0.1)	-0.4 (-2.4, 1.6)	0.86	0.1 (-0.8, 0.9)
Adjusted difference (95%CI)[3]	Reference	-1.9 (-3.8, 0.1)	-0.4 (-2.4, 1.6)	0.89	0.1 (-0.8, 0.9)
HOMA-IR	1.3 ± 1.5	1.2 ± 0.9	1.1 ± 0.7		
Unadjusted difference (95%CI)[1]	Reference	-0.1 (-0.4, 0.2)	-0.1 (-0.4, 0.1)	0.51	0.0 (-0.1, 0.1)
Adjusted difference (95%CI)[2]	Reference	-0.1 (-0.4, 0.2)	-0.1 (-0.4, 0.1)	0.51	0.0 (-0.1, 0.1)
Adjusted difference (95%CI)[3]	Reference	-0.1 (-0.4, 0.1)	-0.2 (-0.4, 0.1)	0.27	0.0 (-0.1, 0.0)

Abbreviations: UPF - ultra-processed foods; SD - standard deviation; 95%CI - 95% confidence interval; BMI – body mass index; HDL-c – high-density lipoprotein-cholesterol; LDL-c – low-density lipoprotein-cholesterol; MAP – mean arterial pressure; HOMA-IR - homeostasis model assessment for insulin resistance.

[1]From linear regression models with cardiometabolic risk markers as continuous outcomes and fatty foods score as predictor.

[2]From linear regression adjusted by sex, age, screen time, and per capita income as the continuous outcome.

[3]From linear regression adjusted by sex, age, screen time, per capita income, and % total body fat as the continuous outcome.
[4]For a variable representing ordinal fatty foods score categories introduced into the model as a continuous predictor.

7 FINAL CONSIDERATIONS

The systematic review demonstrated an independent causal effect of long-term high consumption of UPF in cardiometabolic risk, such as obesity, dyslipidemia, and high risk of type 2 diabetes *mellitus* in children and adults. These results reinforce the importance of effective strategies to prevent the excessive consumption of UPF and protect the long-term health, independent of the age.

Moreover, this study evaluated the score of the UPF consumption (subgroups and at whole) in children and its relationship with cardiometabolic risks. We identified direct association of “sugary foods and beverages” score with serum LDL-c and uric acid; of “salty foods and processed meats” score with serum total cholesterol and LDL-c; and for UPF scores and serum LDL-c.

In addition, for the first time, UPF score was created and applied exclusively in children, with evaluation of UPF’s subgroups, allowing us to understand which are most consumed in childhood, as well as their relationship with cardiometabolic risk. The UPF score is a quick and low-cost tool and may be a good predictor of cardiometabolic risk in Brazilian schoolchildren. However, the UPF score evaluated in our sample must be validated for epidemiological studies and for clinical area. In addition, more longitudinal studies are necessary to investigate a long-term causal effect of UPF consumption in cardiometabolic risk in different phases of life, mainly in children and adolescents.

A collective effort should be made to educate the children about the health negative effects of excessive UPF consumption. There is a need to improve the school feeding programs in both public and private schools to stimulate the consumption of natural and healthy foods by the pediatric public and their families.

Finally, there is an urgent need to improve the public health policies reinforcing the importance of effective strategies to prevent the excessive consumption of UPF among all the age group, and to increase the accessibility of healthy foods by different segments of the population, once social inequalities can contribute to unhealthy food habits.

APPENDICES

Appendix A - Informed Consent Term (ICF)

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Seu filho(a) está sendo convidado(a) a participar dos projetos "Vitamina D na infância: ingestão, níveis séricos e associação com fatores cardiovasculares e Relação entre insegurança alimentar e fatores de risco cardiometabólicos em crianças do Município de Viçosa-MG" cujo os objetivos são avaliar a ingestão e níveis séricos de vitamina D e suas associações com fatores de risco cardiovasculares na infância e avaliar se a insegurança alimentar é maior nas crianças com excesso de peso e contribui para a ocorrência de fatores de risco cardiometabólicos. A avaliação nutricional das crianças será realizada por meio das medidas de peso, altura, pregas cutâneas e circunferências da cintura e do quadril, bem como análise da composição corporal e da pressão arterial. Será realizada coleta de sangue para análise dos níveis de colesterol total e frações, triglicerídeos, glicose, insulina, vitamina D, paratormônio e marcadores inflamatórios. Todos os dados serão utilizados com a finalidade de pesquisa e, se necessário, para projetos a ela vinculados, mantendo total segredo sobre a identidade do seu filho(a). Seus dados serão mantidos em lugar seguro e só os pesquisadores terão acesso.

Como benefício da pesquisa, todos os participantes terão direito a orientações nutricionais individuais para melhoria dos hábitos alimentares e do estado nutricional. A participação das crianças não envolve nenhum risco potencial à saúde. Entretanto poderá ocorrer desconforto ou incômodo na coleta de sangue e na aferição das medidas antropométricas durante avaliação nutricional na escola. Como medida preventiva, a coleta de sangue será realizada por enfermeiros devidamente treinados com materiais descartáveis, sem risco de contaminação. A avaliação nutricional será realizada em salas agradáveis e com privacidade para minimização de possíveis constrangimentos, sendo todas as medidas antropométricas indolores.

Se você não concordar com a participação do seu filho(a), não haverá nenhum problema e não afetará a realização do estudo. Todos os procedimentos serão gratuitos e realizados segundo a Resolução CNS 466/2012. Se você tiver alguma dúvida ou consideração a fazer quanto aos aspectos éticos da pesquisa, procure a pesquisadora responsável: Profª. Juliana Farias de Novaes. Departamento de Nutrição e Saúde (DNS)/UFV. Tel: 3899-3735. Email: jnovaes@ufv.br

Profª. Juliana Farias de Novaes Coordenadora do projeto – DNS/UFV	Ana Paula Pereira Castro Doutoranda	Luana Cupertino Milagres Mestranda
Fernanda M. de Albuquerque Mestranda	Mariana De Santis Filgueiras Mestranda	Naruna Pereira Rocha Mestranda

Para conhecimento: Endereço e contato do **Comitê de Ética em Pesquisa com Seres Humanos da Universidade Federal de Viçosa – CEP/UFV:** Prédio Arthur Bernardes, piso inferior, campus UFV. Telefone: (31)3899-2492. email: cep@ufv.br site: www.cep.ufv.br

Eu, _____declaro que fui informado (a) dos objetivos do estudo acima descrito, de maneira clara e detalhada e esclareci as minhas dúvidas. Declaro também que autorizo de livre e espontânea vontade, a participação do meu filho(a)_____ e que recebi uma cópia do Termo de Consentimento Livre e Esclarecido.
Viçosa, _____de _____de 2015
Assinatura:_____

Appendix B - Semi-structured questionnaire to collect socioeconomic, demographic and lifestyle information

PASE

PESQUISA DE AVALIAÇÃO DA SAÚDE DO ESCOLAR – VIÇOSA (MG)

Pesquisador:		**NQUES**			
Nome da Escola:		**ESCOLA**			
Nome do Responsável:		**ANO**		**TURM**	
Nome Criança:		**TURN**			
Ano que a criança se encontra: _____ (Ano) Turma: _____ Turno: (1) M (2) T		**DATNASC**			
Data de Nascimento: _____/_____/_____ Idade da criança: _____(anos)		**IDADE**			
Sexo (1) M (2) F		**SEXCRI**			
Data entrevista: _____/_____/_____		**DATENTR**			
Telefone:	**Cel:**	**TEL:**			
Endereço do responsável:		**CEL:**			

ESTAÇÃO DO ANO		
01. Estação do ano na data da entrevista: (1) Inverno (2) Primavera (3) Verão (4) Outono	**EST**	
DADOS EDUCAÇÃO FÍSICA NA ESCOLA (DIRETORA)		
02. A escola oferece Educação Física regularmente aos alunos? (0) Sim (1) Não	**EFI**	
03. Duração da atividade física TOTAL na escola/SEMANA:_____minutos (8888) NSA	**DUREFI**	
04. O local que o _____ **ANO** faz educação física na escola é coberto? (0) Sim (1) Não	**COBEFI**	
DADOS DA CRIANÇA		
05. Como você vem para a escola? (1) Caminhando (2) Transporte/carro (3) Bicicleta/moto	**TRANS**	
06. Você faz educação física na escola? (0) Sim (1) Não	**EDFI**	
07. Com que frequência você consome por semana a alimentação da escola? (0) Nenhuma vez (1) 1 vez (2) 2 vezes (3) 3 vezes (4) 4 vezes (5) Diariamente	**FRECO**	
Caso a resposta da questão 07 seja o código ZERO (0) colocar o código 8888 (NSA) nas questões 08 a 11.		
08. Você tem o hábito de repetir o prato? (0) Sim (1) Não (77) NI (8888) NSA	**REPR**	
09. A alimentação que é servida na escola é? (0) Muito Boa (1) Boa (2) Regular (3) Ruim (77) NI (8888) NSA	**ALISER**	
10. A quantidade de comida servida na escola deixa você satisfeito/a: (0) Sim (1) Não (77) NI (8888) NSA	**QUAN**	
11. A alimentação servida é variada? (0) Sim, sempre tem comidas diferentes (1) Não, quase todo dia é a mesma preparação (8888) NSA	**VARI**	
12. Existe algum alimento servido na escola que você não gosta? (0) Sim* (1) Não (77) NI *Quais:_____	**ALNA**	
13. Tem dias que a merenda escolar não é servida? (0) Sim (1) Não (77) NI	**FALT**	
14. A merenda escolar é importante para você? (0) Sim (1) Não **(JUSTIFICAR A RESPOSTA SIM OU NÃO)** Porque?_____	**IMPO**	
15. Você costuma trazer/comprar lanche para comer na escola? (0) Nunca (1) Às vezes (2) Sempre	**LANC**	
16. Em qual local você realiza as refeições em casa? (0) Na mesa (1) Em frente a TV/computador (4) Outros:_____	**REFEI**	
DADOS COM OS PAIS DA CRIANÇA CARACTERÍSTICAS SOCIOECONÔMICAS, DEMOGRÁFICAS E SANITÁRIAS		
17. Qual a cor da criança? (1) Branca (2) Parda/mulata/morena (3) Negra (4) Amarela/oriental (japonesa, chinesa, coreana) (5) Indígena (77) NI	**COR**	
18. Qual o seu grau de parentesco com a criança: (1) Mãe (2) Pai (3) Irmão/ã (4) Avó/ô (5) Outro:_____	**GPAREN**	
19. A criança mora: (1) Com a mãe e o pai (2) Só com a mãe (3) Só com o pai (4) Nenhum dos dois	**CMORA**	
20. Quantos irmãos a criança tem e convive junto? (0) Nenhum (1) Um (2) Dois (3) Três (4) Quatro (5) Mais de quatro	**NIRM**	
21. Quantos anos a mãe/responsável pela criança estudou com aprovação: _____ (anos)	**ANOSM**	
(0) Analfabeto (1) Ensino Fundamental completo (2) Ensino Fundamental incompleto (3) Ensino Médio completo (4) Ensino Médio incompleto (5) Ensino Técnico completo (6) Ensino superior completo (77) NI (8888)NSA	**ESCM**	
22. Quantos anos o pai/responsável pela criança estudou com aprovação: _____ (anos)	**ANOSP**	

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PESQUISA DE AVALIAÇÃO DA SAÚDE DO ESCOLAR – VIÇOSA (MG)

(0) Analfabeto (1) Ensino Fundamental completo (2) Ensino Fundamental incompleto (3) Ensino Médio completo (4) Ensino Médio incompleto (5) Ensino Técnico completo (6) Ensino superior completo (77) NI (8888)NSA	ESCP	
23. Qual a região que o/a senhor(a) reside? (1) Urbana (2) Rural	REGI	
24. A mãe/responsável trabalha fora? (1) Sim, com carteira assinada (2) Sim, sem carteira assinada (3) Não (4) Aposentada/Pensionista (77) NI	TRABM	
25. O pai/responsável trabalha fora? (1) Sim, com carteira assinada (2) Sim, sem carteira assinada (3) Não (4) Aposentado/Pensionista (77) NI	TRABP	
26. Algum morador está **CADASTRADO** e **RECEBE** benefício de algum programa do governo? (1) Sim (1) Não **(*Caso a resposta seja NÃO, colocar o código (8888) NSA nas questões 27 a 34)**	PROG	
27. Bolsa Família: (0) Sim (1) Não (8888) NSA Valor:_____	PROGA	
	VALORA	
28. Cesta de Alimentos: (0) Sim (1) Não (8888) NSA Valor:_____	PROGB	
	VALORB	
29. Programa de Erradicação do Trabalho Infantil (PETI): (0) Sim (1) Não (8888) NSA Valor:_____	PROGC	
	VALORC	
30. Assistência a Pessoas Idosas e Deficientes (BPC): (0) Sim (1) Não (8888) NSA Valor:_____	PROGD	
	VALORD	
31. Programa Nacional de Fortalecimento da Agricultura Familiar (PRONAF): (0) Sim (1) Não (8888) NSA Valor:_____	PROGE	
	VALORE	
32. Auxílio Desemprego: (0) Sim (1) Não (8888) NSA Valor:_____	PROGF	
	VALORF	
33. Auxílio Maternidade: (0) Sim (1) Não (8888) NSA Valor:_____	PROGG	
	VALORG	
34. Outro: _____ (0) Sim (1) Não (8888) NSA Valor:_____	PROGH	
	VALORH	
35. Qual a renda **TOTAL** da família que contribui com as despesas domésticas (Incluindo o valor do benefício recebido)? R$:_____ (77) NI	REN	
36. Quantas pessoas moram no domicílio que dependem da renda TOTAL? _____	NPESS	
37. Renda per capita: R$ _____	RENP	
38. Condição de moradia: (1) Própria (2) Alugada (3) Emprestada (4) Outras:_____	MORA	
39. Sua casa possui energia elétrica? (0) Sim (1) Não	ENER	
40. Sua casa possui banheiro com vaso sanitário? (0) Sim (1) Não	BANH	
41. Qual o tipo de esgoto sanitário da sua casa? (1) Rede pública (2) Fossa séptica (3) Fossa rudimentar (4) Vala/ Céu aberto	ESGOT	
42. De onde vem a água que a família utiliza? (1) Rede pública (2) Poço/Barreiro (3) Cisterna ou água da chuva (4) Outro: _____	AGBEB	
43. Qual o tratamento da água de beber? (1) Filtrada (2) Fervida (3) Clorada (4) Coada ou sem tratamento (5) Mineral (6) outro:_____	TRAT	
44. Sua casa possui coleta de lixo? (0) Sim (1) Não* * Se não, o que a família faz com o lixo?_____	LIXO	
HISTÓRIA FAMILIAR E DE SAÚDE		
45. O pai/responsável da criança tem ou teve alguma destas doenças?	INFP	
Infarto (0) Não (1) Sim (77) NI/NSA	DIAP	
Diabetes (0) Não (1) Sim (77) NI/NSA	HASP	
HAS (0) Não (1) Sim (77) NI/NSA	AVCP	
Câncer (0) Não (1) Sim (77) NI/NSA	CAP	
Derrame/AVC (0) Não (1) Sim (77) NI/NSA	DISP	
Dislipidemia (0) Não (1) Sim (77) NI/NSA		
46. A mãe/responsável da criança tem ou teve alguma destas doenças?	INFM	
Infarto (0) Não (1) Sim (77) NI/NSA	DIAM	
Diabetes (0) Não (1) Sim (77) NI/NSA	HASM	
HAS (0) Não (1) Sim (77) NI/NSA	CAM	

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PESQUISA DE AVALIAÇÃO DA SAÚDE DO ESCOLAR – VIÇOSA (MG)

	Câncer	(0) Não (1) Sim (77) NI/NSA	**AVCM**	
	Derrame/AVC	(0) Não (1) Sim (77) NI/NSA	**DISM**	
	Dislipidemia	(0) Não (1) Sim (77) NI/NSA		
47. A mãe/responsável fuma? (0) Não (1) Sim (77) NI Quantidade (n° cigarros/dia):_____			**MFUMA**	
CASO A RESPOSTA SEJA NÃO →COLOCAR O CÓDIGO (8888) NSA NA BARRA QUACM			**QUACM**	
48. O pai/responsável fuma? (0) Não (1) Sim (77) NI Quantidade (n° cigarros/dia):_____			**PFUMA**	
CASO A RESPOSTA SEJA NÃO →COLOCAR O CÓDIGO (8888) NSA NA BARRA QUACP			**QUACP**	
49. A mãe consome bebida alcoólica? (0) Não (1) Sim (77) NI Quantidade/sema (L):_____			**MBEBE**	
CASO A RESPOSTA SEJA NÃO →COLOCAR O CÓDIGO (8888) NSA NA BARRA QBEM			**QBEM**	
50. O pai consome bebida alcoólica? (0) Não (1) Sim (77) NI Quantidade/sema (L): _____			**PBEBE**	
CASO A RESPOSTA SEJA NÃO →COLOCAR O CÓDIGO (8888) NSA NA BARRA QBEP			**QBEP**	
51. A criança possui algum problema crônico de saúde (ASMA, DM, DISLIPIDEMIA, HAS, CÂNCER)? (0) Não (1) Sim (77) NI Qual? _____			**PRSAU**	
52. A criança possui algum tipo de restrição alimentar (alergia/intolerância alimentar)? (0) Não (1) Sim (77) NI Qual restrição? _____			**RESAL**	
53. A criança usa alguma medicação? (0) Não (1) Sim (77) NI Qual? _____			**MED**	
54. A criança foi amamentada? (0) Sim (1) Não (77) NI			**AMAM**	
55. Qual foi a duração do aleitamento materno exclusivo? _____( )dias ( ) meses (77) NI			**AME (DIAS)**	
56. Qual foi a duração do aleitamento materno TOTAL? _____ ( )dias ( ) meses (77) NI			**AMC (DIAS)**	
57. A criança utilizou fórmula infantil/leite em pó/leite de vaca antes de completar 6 meses de nascimento? (0) Não (1) Sim (77) NI			**FORM**	
58. Qual o peso da criança ao nascer? _____g (77) NI			**PN**	
PERCEPÇÃO ATIVIDADE FÍSICA SEGUNDO OS PAIS				
59. Quanto tempo diariamente a criança passa em frente à TV, *vídeo game*, computador? (0) Zero (1) 30 minutos (2) 1 hora (3) 2 horas (4) 3 horas (5) 4 horas (6) Mais de 4 horas			**TEMDI**	
60. A criança pratica alguma atividade física fora da escola? (0) Sim (1) Não			**ESPOR**	
***CASO A RESPOSTA SEJA (1) NÃO, COLOCAR O CÓDIGO (8888) NSA EM DURAÇÃO.** Qual:_____ Duração: _____Hora/semana			**DURA**	
61. Quanto tempo a criança passa sentada brincando (boneca, casinha, carrinho) e se dedicando às atividades escolares? (0) Zero (1) 30 minutos (2) 1 hora (3) 2 horas (4) 3 horas (5) 4 horas (6) Mais de 4 horas			**CRISEN**	
62. Quanto tempo a criança realiza atividades mais intensas (bola, bicicleta, brincando na rua)? (0) Zero (1) 30 minutos (2) 1 hora (3) 2 horas (4) 3 horas (5) 4 horas (6) Mais de 4 horas			**CRIBRI**	
63. Quanto tempo ao longo do dia a criança se expõe ao sol (ir a pé para a escola, brincar rua/quintal)? (0) Zero (1) 30 minutos (2) 1 hora (3) 2 horas (4) 3 horas (5) 4 horas (6) Mais de 4 horas			**EXPSO**	
64. Você tem o hábito de passar filtro solar na criança? (1) Todos os dias (2) As vezes (3) Nunca			**HFS**	
PERCEPÇÃO DA ALIMENTAÇÃO DA CRIANÇA PELOS PAIS				
65. Você tem o conhecimento da alimentação que é servida na escola do para a criança? (0) Sim (1) Não (77) NI **(*Caso a resposta seja NÃO, colocar o código (8888) NSA nas questões 66 e 67)**			**CONH**	
66. Você gosta da merenda que é servida para a criança na escola? (0) Sim (1) Não (77) NI (8888)NSA			**GOALI**	
67. Em sua opinião, a quantidade servida é satisfatória? (0) Sim (1) Não (77) NI (8888)NSA			**QUAS**	
68. Caso a escola não forneça mais a merenda, você teria condições financeiras de mandar lanche todos os dias para a criança? (0) Sim (1) Não (77) NI			**COND**	
69. Você costuma mandar algum lanche para a criança na escola quando ele/a está na escola? (0) Sim (1) Não Qual?_____			**LANC**	

PASE

POR QUÊ MANDA LANCHE?_____		
70. A merenda escolar é servida regularmente na escola do seu filho? (0) Sim (1) Não (77) NI	**FMER**	
71. Você tem conhecimento de atrasos do repasse dos recursos e/ou entrega dos alimentos na escola? (1) Sim (2) Não (77) NI	**ATRA**	
72. As aulas já foram suspensas devido a falta da merenda escolar? (0) Sim (1) Não (77) NI	**SUSP**	
73. Você já ouviu falar do Conselho de Alimentação Escolar? (0) Sim (1) Não **(*Caso a resposta seja NÃO, colocar o código (8888) NSA na questão 74.**	**CAE**	
74. Você participa do CAE? (0) Sim (1) Não (3) Pertence ao CAE, mas não desenvolve atividades.	**PARTI**	

Appendix C - 24-hour recall sheet

PESQUISA DE AVALIAÇÃO DA SAÚDE DO ESCOLAR – VIÇOSA (MG)

1º RECORDATÓRIO 24 HORAS			NQUES			
PESQUISADOR:			Dat. Entre:			
NOME DA CRIANÇA:			Dia semana:			
NOME DA ESCOLA			Ano:			
REFEIÇÃO	**ALIMENTOS**	**MEDIDA CASEIRA**				**GRAMA/ML**
REFEIÇÃO: HORA: LOCAL:						
REFEIÇÃO: HORA: LOCAL:						
REFEIÇÃO: HORA: LOCAL:						
REFEIÇÃO: HORA: LOCAL:						
REFEIÇÃO: HORA: LOCAL:						
REFEIÇÃO: HORA: LOCAL:						

A criança consumiu: ( ) Bala/chiclete ( ) Doce ( ) Chocolate ( ) Refrigerante ( ) Salgadinho ( ) Ketchup/Mostarda

Consumo de água: _____ ml

OBSERVAÇÕES:

ANNEX

Annex A - Approval by the UFV Research Ethics Committee with Human Beings

UNIVERSIDADE FEDERAL DE VIÇOSA - UFV

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Titulo da Pesquisa: VITAMINA D NA INFÂNCIA: INGESTÃO, NÍVEL SÉRICO E ASSOCIAÇÃO COM FATORES DE RISCO CARDIOVASCULARES

Pesquisador: Juliana Farias de Novaes

Área Temática:

Versão: 3

CAAE: 19532414.9.0000.5153

Instituição Proponente: Departamento de Nutrição e Saúde

Patrocinador Principal: MINISTERIO DA CIENCIA, TECNOLOGIA E INOVACAO

DADOS DO PARECER

Número do Parecer: 663.171

Data da Relatoria: 03/06/2014

Apresentação do Projeto:

O presente protocolo foi enquadrado como pertencente à(s) seguinte(s) Área(s) Temática(s): "Ciências da Saúde e Saúde Coletiva / Saúde Pública".

No documento intitulado "PB_PROJETO_DE_ PESQUISA_195324%20(1).pdf", item introdução, lê-se: "A 1,25(OH)2 D3 (vitamina D) é um hormônio que regula o metabolismo do cálcio e do fósforo. Sua principal função é manter os níveis de cálcio e fósforo em um estado normal capaz de propiciar condições à maioria das funções metabólicas, entre elas a mineralização óssea (HOLICK,2006). A vitamina D é essencial durante a infância porque está envolvida no crescimento. Os níveisséricos normais de vitamina D determinam a absorção de 30% de cálcio da dieta e a sua deficiênciapode causar atraso no crescimento, anormalidades ósseas e aumento do risco de fraturas (BUENO&CZEPIELEWSKI, 2008). A síntese cutânea da vitamina D, a partir da exposição solar, é a principal fonte para osindivíduos, além desta vitamina também ser obtida pela alimentação e uso de suplementos.Entretanto, a síntese cutânea pode variar de acordo com a época do ano,pigmentação da pele, idade e uso de filtros solares (HOLICK, 2007)Supõe-se que uma alimentação saudável seja suficiente para fornecer níveis adequados devitamina D, entretanto, nem sempre isto ocorre. Existem alguns alimentos fontes de vitamina D tais como gema de ovo, fígado, manteiga e leite que podem ser menos consumidos em

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função do teor aumentado de colesterol. Óleos de peixe também são excelentes fontes de vitamina D apesar de,muitas vezes, não serem consumidos em quantidades necessárias por populações (CALVO &WHITING,2006).A deficiência/insuficiência de vitamina D tem sido considerada um problema de saúde pública no mundo (BINKLEY et al., 2010). Apesar do Brasil ser um país de clima tropical, níveis subclínicos de vitamina

D tem sido encontrados na população (PETERS et al., 2009; FOSS, 2009). Em estudos brasileiros,realizados com adolescentes, foram encontradas prevalências de 60 e 70,6%de níveis séricos insuficientes de vitamina D nos municípios de São Paulo (SP) e Juiz de Fora(MG), respectivamente (PETERS et al.,2009; OLIVEIRA et al., 2013).3Um adequado nível de vitamina D é essencial em todos os estágios de vida e há um consenso de que a concentração sérica de calciciol [25(OH)D] é o melhor indicador desta vitamina(BINKLEY et al., 2010). Baixos níveis de calcidiol afetam diretamente a absorção de cálcio e

a mineralização óssea. Além disso, estudos têm mostrado que a deficiência desta vitamina é um fator associado ao desenvolvimento de doenças metabólicas e endócrinas (FOSS, 2009; BORGES et al.,2011). A vitamina D pode estar envolvida em vários processos tais como diferenciação e proliferação celular, secreção hormonal (ex: insulina), sistema imune e diversas doenças crônicas não-transmissíveis tais como obesidade, intolerância a glicose, aumento da pressão arterial e dislipidemias (KELLY et al.,2011).Estudos epidemiológicos recentes têm demonstrado que altos níveis séricos da 25-hidroxivitamina D (25OHD)estão associados com menor pressão arterial média e com redução da prevalência de hipertensão (PARIKH et al., 2005; SCRAGG et al., 2007). Por outro lado, a elevação na pressão arterial está associada com a gordura visceral, assim como níveis séricos de vitamina D também se apresentam reduzidos em indivíduos com maior quantidade de gordura corporal (SYME et al., 2008).A vitamina D pode afetar a resposta insulínica ao estímulo da glicose direta ouindiretamente (ZEITZ et al., 2003). O efeito direto parece ser mediado pela ligação da 1,25(OH)2D3 ao receptor da vitamina D da célula-. Além disso, a ativação da vitamina D pode ocorrerdentro das células- pela enzima 1-hidroxilase, expressa nessas células (BLAND et al.,2004). O efeito indireto é mediado pelo fluxo de cálcio intra e extracelular nas células-. O aumento na 1,25(OH)2D3 e no PTH induz maior influxo de cálcio para o interior das células. Como a secreção de insulina é um processo cálcio-dependente mediado pela 1,25(OH2)D3 e pelo PTH, o aumento nas concentrações destes, devido à insuficiência de 25(OH)D, pode reduzir a capacidade secretora dessas células (ZEITZ et al., 2003;). Além disso, a deficiência de 25(OH)D parece dificultar acapacidade das células- na conversão da pró-insulina à insulina (AYESHA et al., 2001). Em resumo, os efeitos da vitamina D no diabetes

evidenciam que a deficiência de 25(OH)D altera asíntese e secreção de insulina, tanto em modelos animais como em humanos (SCHUCH et al.,2009).O marcante número de publicações que identificam uma inadequação na concentração sérica de vitamina D em todo o mundo tem despertado o interesse de pesquisadores de avaliar a relação desta vitamina com doenças metabólicas (PETERLICK & CROSS,2005). Entretanto, esses estudos foram realizados principalmente com adultos e idosos e, até o momento, não há pesquisas avaliando vitaminaD sérica em crianças no Brasil. Como estudos epidemiológicos têm constatado aumento da prevalência de obesidade e de comorbidades associadas na infância (WANG et al., 2002; CÂNDIDO et al., 2009),o objetivo deste estudo é avaliar a ingestão e nível sérico de vitamina D entre crianças, e suas associações com fatores de risco cardiovasculares.

Objetivo da Pesquisa:

De acordo com o documento intitulado "PB_PROJETO_DE_ PESQUISA_195324%20(1).pdf", o objetivo do projeto é: "Avaliar a ingestão e nível sérico de vitamina D e suas associações com fatores de risco cardiovasculares na infância."

Avaliação dos Riscos e Benefícios:

Os pesquisadores indicam no documento intitulado "PB_PROJETO_DE_PESQUISA_195324%20(1).pdf", os seguintes Riscos: "A participação das crianças não envolve nenhum risco potencial à saúde. Entretanto poderá ocorrer desconforto ou incômodo na coleta de sangue e na aferição das medidas antropométricas durante avaliação nutricional. Como medida preventiva, a coleta de sangue será realizada por enfermeiros devidamente treinados com materiais descartáveis, sem risco de contaminação. A avaliação nutricional será realizada em salas agradáveis e com privacidade para minimização de possíveis constrangimentos, sendo todas as medidas antropométricas indolores." e os seguintes benefícios: "Os resultados de ingestão e níveis séricos de vitamina D e suas associações com fatores de risco cardiovasculares na infância serão apresentados para a Prefeitura Municipal de Viçosa com o objetivo de subsidiar as políticas públicas de saúde, bem como os programas de atenção à saúde de crianças, de forma a aprimorar a prática dos profissionais envolvidos na área de saúde pública,especialmente aqueles do município de Viçosa e microrregião. O objetivo é estabelecer uma relação de diálogo entre pesquisadores e sociedade, fortalecendo a integração ensino-pesquisa
-serviço,fundamentados nas propostas do SUS através da qualificação dos profissionais e dos serviços prestados, com benefício direto à população e com alcance social local e regional.Este projeto proporcionará atendimentos nutricionais individuais com as crianças visando à reeducação alimentar e alteração do estilo de vida, quando necessário. Esta orientação nutricional será

importante para promoção da alimentação saudável e do
estilo de vida ativo, prevenindo assim,os fatores de risco cardiovasculares na vida atual e futura.".
Os benefícios apresentados pelos pesquisadores sobrepõem os riscos informados, sendo estes considerados mínimos.

Comentários e Considerações sobre a Pesquisa:
O projeto apresentado atendeu às exigências referentes aos aspectos éticos que envolvem as pesquisas com seres humanos.

Considerações sobre os Termos de apresentação obrigatória:
Os termos de apresentação obrigatória foram apresentados.

Recomendações:

Conclusões ou Pendências e Lista de Inadequações:
Projeto aprovado.

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

Considerações Finais a critério do CEP:
Ao término da pesquisa é necessária a apresentação do Relatório Final e após a aprovação desse, deve ser encaminhado o Comunicado de Término dos Estudos.
Projeto analisado durante a 3ª reunião de 2014.

VICOSA, 27 de Maio de 2014

Assinado por:
Patrícia Aurélia Del Nero
(Coordenador)