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SAÚDE DA CRIANÇA E DO ADOLESCENTE

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**Avaliação do consumo de alimentos  
ultraprocessados e seu impacto na  
pressão arterial de crianças e fatores  
associados à preferência ao sabor  
salgado entre adolescentes.**

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**Avaliação do consumo de alimentos ultraprocessados e seu impacto na pressão arterial de crianças e fatores associados à preferência ao sabor salgado entre adolescentes.**

Tese submetida ao Programa de Pós-Graduação Pediatria: Atenção à Saúde da Criança e do Adolescente da Fundação Universidade Federal de Ciências da Saúde de Porto Alegre como requisito para a obtenção do grau de Doutor

Orientador: Dr. Márcia Regina Vítolo

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## RESUMO

Objetivos: Os objetivos gerais desta tese foram 1) avaliar o efeito do consumo de alimentos ultraprocessados aos 3 anos de idade na pressão arterial de crianças aos 6 anos e 2) identificar os fatores associados à preferência ao sabor salgado entre adolescentes de 12 anos de idade. Assim, desenvolveram-se dois artigos científicos em que foram utilizados dados de ensaios de campo randomizados conduzidos pelo Núcleo de Pesquisa em Nutrição da Universidade Federal de Ciências da Saúde de Porto Alegre.

Metodologia: Os artigos científicos apresentados nesta tese utilizam dados secundários de dois ensaios de campo randomizados, realizados com objetivo de avaliar o impacto da implementação de orientações sobre aleitamento materno e alimentação infantil para crianças menores de dois anos, preconizadas pelo Ministério da Saúde por meio do guia alimentar “10 passos para a alimentação saudável para crianças menores de dois anos” e oferecidas às mães por meio de duas estratégias. A primeira estratégia empregada foi a orientação direta das mães por meio de visitas domiciliares mensais até as crianças completarem 6 meses, depois trimestrais até 1 ano de idade. Os participantes deste estudo foram recrutados na maternidade de um hospital geral do município de São Leopoldo/RS e receberam visitas domiciliares para coleta de dados aos 6 meses, 12 meses, 4 anos, 8 anos e 12 anos de idade. A segunda estratégia foi a de randomizar unidades de saúde de Porto Alegre para atualizar os profissionais de saúde que atuavam na atenção primária para que eles implementassem as orientações do guia alimentar nas consultas de puericultura. As participantes do estudo foram recrutadas nas unidades de saúde, enquanto aguardavam consulta de pré-natal e receberam visitas domiciliares para coleta de dados aos 6 meses, 12 meses, 3 anos e 6 anos de idade das crianças. Em ambos os estudos foram coletados dados sociodemográficos, por meio de questionários estruturados; dados antropométricos, como peso, estatura, circunferência da cintura e dobras cutâneas, seguindo normas da Organização Mundial da Saúde; e dados dietéticos por meio de Inquéritos Recordatórios de 24-horas. Os adolescentes de 12 anos reportaram seu estágio puberal, de acordo com a classificação de Tanner. Para ambos os artigos apresentados nesta Tese, os dados dietéticos foram classificados conforme a classificação NOVA que avalia os alimentos conforme seu grau de processamento.

Resultados: Foram produzidos dois artigos científicos, o primeiro denominado “Early consumption of ultra-processed foods is associated with higher blood pressure at 6 years of age” que identificou que o consumo de alimentos ultraprocessados entre crianças aos 3 anos de idade representou mais de 40% das calorias diárias consumidas e que este consumo está associado a níveis mais elevados da pressão arterial diastólica de crianças aos 6 anos ( $p=0,025$ ). O segundo artigo apresentado é denominado “Sodium intake tracking from infancy to salt preference during adolescence: A randomized trial” em que foi identificado que o consumo excessivo de sódio se mostrou associado a preferência por concentrações mais elevadas de sal ( $p=0.020$ ) e que adolescentes nos estágios mais iniciais de puberdade apresentaram preferências por maiores concentrações de sódio ( $p=0,027$ ).

Conclusões: Os dados apresentados nesta tese somam ao corpo de evidências de que alterações metabólicas importantes, como a de pressão arterial, têm início ainda na infância e que a alimentação desempenha papel relevante neste processo desde muito cedo. Além disso, a avaliação da preferência pelo sabor salgado reforça que crianças em períodos de crescimento acelerado são particularmente suscetíveis ao consumo excessivo de sódio por terem suas preferências por esse sabor aumentadas nestes períodos. Esses dados em conjunto demonstram a importância de intervenções focadas na qualidade da alimentação infantil e que estas precisam acompanhar o desenvolvimento das crianças para garantir hábitos alimentares saudáveis ao longo da vida e, conseqüentemente, melhores condições de saúde a longo-prazo.

## ABSTRACT

**Objectives:** The general objectives of this thesis were 1) to evaluate the effect of ultra-processed foods consumption at 3 years of age on the blood pressure of children at 6 years of age and 2) to identify factors associated with the preference for salty flavor among 12-year-old adolescents. Thus, two scientific manuscripts were produced in which data from randomized field trials led by the *Núcleo de Pesquisa em Nutrição* of the *Universidade Federal de Ciências da Saúde de Porto Alegre Federal* were used.

**Methodology:** The scientific manuscripts presented in this thesis use secondary data from two randomized field trials, carried out with the aim of evaluating the impact of the implementation of guidelines on breastfeeding and infant feeding for children under two years old, recommended by the Ministry of Health through the food guide “10 steps to healthy eating for children under two years old” and offered to mothers through two strategies. The first strategy used was the direct guidance of mothers through monthly home visits until the children were 6 months old, then quarterly until 1 year of age. Participants in this study were recruited from the maternity hospital of a general hospital in the city of São Leopoldo/RS and received home visits for data collection at 6 months, 12 months, 4 years, 8 years, and 12 years of age. The second strategy was to randomize health units in Porto Alegre to update health professionals working in primary care so that they could implement the guidelines in the food guide in childcare consultations. Study participants were recruited from health facilities while awaiting prenatal consultations and received home visits for data collection at 6 months, 12 months, 3 years, and 6 years of age. In both studies, sociodemographic data were collected through structured questionnaires; anthropometric data, such as weight, height, waist circumference and skinfolds, following the norms of the World Health Organization; and dietary data through 24-hour Recall Surveys. The 12-year-olds reported their pubertal stage, according to the Tanner classification. For both articles presented in this Thesis, dietary data were classified according to the NOVA classification, which evaluates foods according to their degree of processing.

**Results:** Two scientific manuscripts were produced, the first, entitled "Early consumption of ultra-processed foods is associated with higher blood pressure at 6 years of age", which identified that the consumption of ultra-processed foods among children aged 3

years represented more than 40 % of daily calories consumed and that this consumption is associated with higher levels of diastolic blood pressure in children aged 6 years ( $p=0.025$ ). The second manuscript presented is entitled “Sodium intake tracked from infancy and salt taste preference during adolescence: Follow-up of a randomized controlled field trial in Brazil” in which it was identified that high sodium intake was associated with a preference for higher salt concentrations ( $p=0.01$ ) and that adolescents in the earlier stages of puberty showed preferences for higher sodium concentrations ( $p=0.02$ ).

Conclusions: The data presented in this thesis add to the body of evidence that important metabolic changes, such as blood pressure, start in childhood and that nutrition plays a relevant role in this process from a very early age. In addition, the assessment of preference for salty flavor reinforces that, children in periods of accelerated growth are particularly susceptible to excessive sodium intake, as their preferences for this flavor are increased during these periods. These data together demonstrate the importance of interventions focused on the quality of infant feeding and that these need to monitor the development of children to ensure healthy eating habits throughout life and, consequently, better health conditions in the long term.

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## 1. INTRODUÇÃO

O Núcleo de Pesquisa em Nutrição (NUPEN) da Universidade Federal de Ciências da Saúde de Porto Alegre conduziu dois estudos desenvolvidos com o objetivo de investigar o impacto de estratégias de implementação das orientações dietéticas baseadas no guia alimentar “Dez passos para uma alimentação saudável para crianças brasileiras menores de dois anos” em desfechos dietéticos, antropométricos e de saúde de crianças de baixo nível socioeconômicos. Primeiramente foram fornecidas orientações diretamente às mães e demais cuidadores por meio de visitas domiciliares durante o primeiro ano de vida e posterior acompanhamento longitudinal das crianças, posteriormente, foi desenvolvido estudo semelhante com estratégia de orientação por meio da capacitação de profissionais de saúde que atuavam na atenção primária de Porto Alegre [1,2].

Os resultados dessas duas abordagens, publicados desde 2005, mostraram que ambas estratégias de intervenção foram efetivas em aumentar o tempo de aleitamento materno exclusivo, reduzir a prevalência de diarreia, doenças respiratórias e cáries, melhorar as práticas alimentares no primeiro ano de vida e promover melhoras nos níveis de lipídeos séricos na idade escolar [1,3–11]. Entretanto, foi observado que o comportamento de introdução e oferta de alimentos não recomendados para as crianças acompanhadas ocorria de forma bastante precoce e prevalente, apesar do passo 8 do guia alimentar para crianças brasileiras menores de dois anos trazer uma lista de alimentos não recomendados e preconizar que esses alimentos não fossem ofertados antes dos dois anos de idade.

Além disso, observa-se que o Brasil vem enfrentando aumento expressivo do sobrepeso e da obesidade em todas as faixas etárias, e as doenças crônicas são atualmente a principal causa de morte entre adultos [12]. Apesar das doenças crônicas repercutirem mais fortemente como problemas de saúde pública entre adultos, os fatores de risco mais comuns para seus desenvolvimentos estabelecem-se na infância e estão associados à práticas alimentares inadequadas [13,14].

Mais recentemente, após o desenvolvimento da estratégia NOVA que classifica os alimentos em quatro grupos distintos conforme seu grau de processamento, associações

entre o consumo de alimentos Ultraprocessados e o desenvolvimento de diversas doenças, em especial as cardiovasculares estão sendo observadas [15]. Dessa forma, para o estabelecimento de estratégias de prevenção e tratamento da obesidade e de doenças crônicas, como as cardiovasculares, é de extrema importância o entendimento de como as práticas alimentares se estabelecem no início da vida e como elas impactam no processo saúde-doença a longo-prazo.

Sendo assim, a presente Tese de doutorado teve o objetivo de verificar se o consumo precoce de alimentos Ultraprocessados entre crianças aos 3 anos de idade estava associado aos níveis de pressão arterial de crianças aos 6 anos de idade e de investigar o impacto da intervenção baseada no guia alimentar para crianças menores de dois anos no consumo de sódio e fatores associados à preferência ao sabor salgado entre adolescentes de 12 anos de idade, trazendo informações relevantes sobre o tema e aumentando o corpo de evidências que demonstram a importância de priorizar intervenções e desenvolver políticas públicas focadas em práticas alimentares no início da vida.

## 2. REVISÃO DA LITERATURA

### 2.1 Grau de processamento de alimentos a Classificação NOVA

#### 2.1.1 A origem da classificação NOVA

As classificações convencionais de alimentos apresentam limitações importantes frente à realidade da alimentação humana atual. Esse tipo de classificação geralmente agrupa alimentos e gêneros alimentícios de acordo com sua origem botânica ou espécie animal e com os nutrientes que contêm. Porém, ao classificar os alimentos conforme estes critérios, o agrupamento de alimentos que têm origens semelhantes, porém ingredientes e efeitos diferentes sobre a saúde, é frequente. Dessa forma, produtos em sua forma natural e derivados desses produtos, que, no entanto, não preservam características básicas essenciais acabam classificados nas mesmas categorias. Um exemplo disso é o que ocorre com as carnes e produtos à base de carnes, em que o frango fresco e os “nuggets” (produtos à base de carne de frango acrescido de gordura, sal e diversos aditivos), são normalmente incluídos no mesmo grupo [16].

Nas últimas décadas, evidências de que ingredientes comumente utilizados pela indústria alimentícia exercem efeitos deletérios na saúde estão se acumulando. Um exemplo clássico é o das gorduras trans, que são produzidas pela hidrogenação de óleos vegetais, um processo extremamente comum, utilizado para alterar características como a textura dos óleos e um ingrediente frequente em produtos como margarinas e biscoitos [17]. Entretanto, o consumo de gorduras trans é um conhecido fator de risco para o desenvolvimento de doenças cardiovasculares e diabetes do tipo 2 [18]. Conforme evidências de que certas características e/ou ingredientes presentes nos alimentos estavam associadas a desfechos de saúde desfavoráveis, recomendações para evitar certos ingredientes ou tipos de alimentos (como “alimentos ricos em açúcar” ou “alimentos de alta densidade energética”) foram sendo desenvolvidas [19,20], no entanto, observou-se a necessidade de se desenvolver uma forma prática de agrupar esses alimentos, com o objetivo de facilitar a identificação e orientar a população [16].

Dessa forma, o conceito de classificação dos alimentos conforme seu grau de processamento, denominado NOVA, foi desenvolvido por um grupo de pesquisadores da Universidade de São Paulo considerando que a natureza, a extensão e a finalidade do processamento dos alimentos afetam a relação entre alimentação, nutrição, saúde e doença [15].

### 2.1.2 Como classificar os alimentos segundo a NOVA

O processamento de alimentos conforme identificado pela NOVA engloba os processos físicos, químicos e biológicos utilizados após os alimentos serem retirados da natureza e antes de serem consumidos ou preparados. De modo geral, os alimentos podem ser consumidos sozinhos e sem grandes diferenças em relação à forma em que são encontrados na natureza, como frutas, grãos, ovos e leite; ou como ingredientes utilizados na preparação de pratos, como sal, açúcar e óleos; ou ainda podem ser encontrados em forma modificada ao seu estado natural, porém sem a necessidade do consumidor final realizar as etapas de preparo, prontos para consumir ou aquecer (ou hidratar e aquecer), como queijos, *snacks* embalados, refrigerantes, sucos e pratos congelados pré-confeccionados. Sendo assim, a NOVA classifica os alimentos e produtos alimentícios em quatro grupos distintos, descritos a seguir: 1) *In Natura* ou Minimamente processados; 2) Ingredientes Culinários; 3) Alimentos Processados; 4) Alimentos Ultraprocessados. [16,21].

#### Grupo 1: Alimentos *In Natura* ou Minimamente processados:

Os alimentos *In Natura* são as partes comestíveis de plantas (sementes, frutas, folhas, caules, raízes) ou de animais (carnes, ovos, leite), fungos, algas e água, após a sua retirada da natureza. Os alimentos minimamente processados são alimentos naturais alterados por processos que incluem a remoção de partes não comestíveis ou indesejadas, secagem, trituração, moagem, fracionamento, filtração, torrefação, fervura, fermentação não alcoólica, pasteurização, refrigeração, resfriamento, congelamento, colocação em recipientes e embalagem a vácuo. Esses processos conservam os

alimentos naturais, tornando-os adequados para armazenamento, ou os deixam mais agradáveis de consumir. Estes alimentos são consumidos crus ou são preparados e cozidos em casa ou em cozinhas de restaurantes em combinação com ingredientes culinários como pratos ou refeições.

#### Grupo 2: Ingredientes culinários:

São substâncias como sal, açúcar, manteiga e óleos, que são derivados de alimentos do Grupo 1 ou adquiridos da natureza por processos que incluem prensagem, refino, moagem e secagem. O objetivo de tais processos é fazer produtos duráveis que sejam adequados para uso em cozinhas domésticas e de restaurantes para preparar, temperar e cozinhar alimentos do Grupo 1 e fazer com eles pratos e refeições variados e agradáveis feitos à mão. Eles não são consumidos por si próprios, mas são normalmente usados em combinação com alimentos do Grupo 1 para fazer bebidas, pratos e refeições.

#### Grupo 3: Alimentos processados:

Os alimentos processados, como vegetais enlatados, conservas, frutas em calda, queijos e alguns pães, são feitos essencialmente pela adição de sal, óleo, açúcar ou outras substâncias do Grupo 2 aos alimentos do Grupo 1. Os processos incluem métodos de conservação ou cozimento e, no caso de pães e queijo, fermentação não alcoólica. A maioria dos alimentos processados tem dois ou três ingredientes no total e são facilmente reconhecíveis como versões modificadas dos alimentos do Grupo 1. Eles são comestíveis sozinhos ou, mais comumente, em combinação com outros alimentos. O objetivo do processamento neste caso é aumentar a durabilidade dos alimentos do Grupo 1 e/ou modificar suas qualidades sensoriais.

#### Grupo 4: Alimentos Ultraprocessados:

Os alimentos ultraprocessados são tipicamente produtos alimentícios fabricados a partir de formulações de ingredientes, sendo que muitos deles são de uso exclusivo da indústria alimentícia e que resultam de uma série de processos industriais [17]. O processo para fabricar os alimentos ultraprocessados normalmente envolve várias

etapas, iniciando com o fracionamento dos alimentos em sua forma integral ou minimamente processada para extrair seus componentes básicos como açúcares, óleos e gorduras, proteínas, amidos e fibras. Posteriormente, muitas dessas substâncias são submetidas à hidrólise, hidrogenação ou outra modificação química. Os processos subsequentes envolvem a combinação dessas substâncias com pouca ou nenhuma quantidade do alimento em sua forma original, além disso, a adição de corantes, saborizantes, emulsificantes e outros aditivos é comum. O processo termina com a adoção de embalagens sofisticadas, usualmente com materiais sintéticos e imagens atrativas [17].

É característica de alimentos ultraprocessados a presença de ingredientes que podem ser divididos em substâncias alimentares que raramente são utilizadas na culinária e classes de aditivos cuja função é tornar o produto final extremamente saboroso, os denominados "aditivos cosméticos". As substâncias alimentares de uso culinário raro, e que são utilizadas apenas na fabricação de alimentos ultraprocessados, incluem diversos tipos de açúcares, como frutose, xarope de milho rico em frutose, açúcar invertido, maltodextrina, dextrose, lactose; óleos modificados como os hidrogenados ou interesterificados e fontes de proteína, como proteínas hidrolisadas, isolado de proteína de soja, glúten, caseína, proteína de soro de leite e carne mecanicamente separada. Os aditivos cosméticos, também usados apenas na fabricação de alimentos ultraprocessados, são aromas, intensificadores de sabor, corantes, emulsificantes, adoçantes e espessantes, entre outros. Essas classes de aditivos tem como sua principal função disfarçar propriedades sensoriais indesejáveis, comumente criadas por ingredientes ou processos usados na fabricação dos alimentos ultraprocessados, ou então conferem ao produto final propriedades sensoriais especialmente atraentes de textura, sabor, odor ou aparência visual.[16,17].

### 2.1.3 Consumo de Ultraprocessados na Infância

Estudos populacionais têm utilizado a classificação NOVA para avaliar a disponibilidade e o consumo de alimentos de acordo com os diferentes níveis de

processamento. Recentemente, um grupo de pesquisadores mostrou que a disponibilidade destes produtos nas residências varia de 10,2% dos produtos alimentícios em Portugal, a mais de 50% no Reino Unido. O estudo conclui que entre os dezenove países avaliados na Europa, alimentos ultraprocessados representam em média 26,4% do total dos alimentos adquiridos [22]. Outros estudos corroboram estes dados e observam também que a presença de Ultraprocessados na alimentação independe da condição socioeconômica das famílias [23].

O percentual de alimentos ultraprocessados na dieta infantil também atinge valores altos, porém, os dados referentes à esta população ainda se encontram em menor quantidade na literatura. No Brasil, estudos observaram que a introdução de alimentos ultraprocessados frequentemente ocorre entre o terceiro e o sexto mês [24], juntamente com a introdução alimentar, chegando a representar 43% das calorias consumidas no final do primeiro ano de vida [25]. Esses valores tendem a piorar conforme a idade aumenta, pois, a partir dos dois anos, a escolha dos alimentos consumidos passa a envolver a autonomia da criança e os hábitos alimentares já adquiridos nos primeiros anos de vida. Por esse motivo, os resultados encontrados nessa faixa etária espelham a preferência alimentar da criança, que é aprendida conforme suas experiências [26].

Estudos de análise transversal e de coorte realizados no México, Chile e Brasil mostraram que o consumo de ultraprocessados colabora com 30%, 38,6% e 49,2% da energia total consumida em um dia, respectivamente [27–29], com consumo acentuado especialmente a partir da idade pré-escolar [28].

#### 2.1.4 Efeitos dos Ultraprocessados na saúde

Os ingredientes adicionados aos produtos ultraprocessados os tornam, ricos em açúcar e/ou sal, gorduras totais, saturadas e/ou trans e com teores reduzidos de fibras dietéticas e outros compostos bioativos. Conseqüentemente, o maior consumo desses produtos vem se mostrando associado a perfis nutricionais não saudáveis e várias doenças não transmissíveis relacionadas à dieta [16]. Além de terem altos teores de

açúcar, a combinação de sua composição nutricional faz com que muitos dos ultraprocessados apresentem altas cargas glicêmicas, o que os torna potencialmente capazes de desorganizar processos endógenos do sistema nervoso que sinalizam saciedade e controle do apetite, aumentando assim o risco de consumo excessivo, obesidade e diabetes [30].

Entre adultos, estudos com amostras representativas de populações de diferentes países demonstraram associação positiva e independente entre o consumo de alimentos ultraprocessados e obesidade [31–34]. Além disso, estudo randomizado recente que investigou os efeitos de dieta rica em alimentos ultraprocessados em comparação a dieta a base de alimentos minimamente processados ou in natura, demonstrou que com a dieta a base de ultraprocessados, os participantes do estudo ingeriram em média 500 calorias a mais por dia e ganharam 900 gramas de peso corporal em duas semanas. Também foram observadas alterações significativas em perfil hormonal envolvido na regulação da ingestão de alimentos [35].

Na França, estudo de coorte populacional avaliou longitudinalmente o efeito do consumo de alimentos ultraprocessados na saúde. Os resultados mostram que o aumento de 10% na proporção de consumo de alimentos ultraprocessados na dieta foi associado a um aumento significativo no risco de doenças cardiovasculares, câncer, diabetes tipo 2, além de maior risco de morte por todas as causas [36–38].

Embora a literatura venha demonstrando que a associação entre o consumo de ultraprocessados na saúde de adultos seja rica e em expansão, até o momento poucos estudos avaliaram essa relação na população infantil. Estudos longitudinais com crianças de baixa condição socioeconômica no sul do Brasil realizados por pesquisadores do Núcleo de Pesquisa em Nutrição (NUPEN) evidenciaram que o consumo de alimentos ultraprocessados na idade pré-escolar foi associado ao aumento das concentrações de lipídios séricos aos 6 e 8 anos de idade [29,39]. Outro estudo realizado com esta mesma população mostrou associação positiva entre o consumo de alimentos ultraprocessados e adiposidade abdominal aos 8 anos de idade [40].

O foco nos alimentos e na qualidade geral da dieta em detrimento dos nutrientes isolados, conforme proposto pelo sistema NOVA, auxilia na compreensão global da

prevenção e desenvolvimento das doenças crônicas não transmissíveis, além de facilitar a avaliação e acompanhamento das características alimentares da população [17].

## 2.2 Formação dos hábitos e preferências alimentares

Exposições aos diversos fatores biológicos e sociais na infância estão relacionados às trajetórias da saúde ao longo da vida, e as experiências vivenciadas nos primeiros anos têm efeitos de longo prazo no comportamento dos indivíduos. [41]. A ingestão dietética e, mais particularmente, a ingestão excessiva de alimentos ricos em sal e açúcares refinados no início da vida está relacionada uma série condições de saúde, como obesidade, síndrome metabólica e doenças cardiovasculares na idade adulta [42,43].

Pesquisas recentes demonstraram a existência de períodos em que o cérebro em desenvolvimento apresenta sensibilidade aumentada às influências externas [44]. Períodos estes em que existe maior plasticidade cerebral, em que os fatores externos podem influenciar circuitos neurais e, conseqüentemente, o comportamento humano. Dessa forma, as experiências sensoriais vividas no início da vida têm o potencial de moldar e modificar as nossas respostas aos diferentes sabores e preferências alimentares [26,45,46]. Assim, experiências positivas precoces com alimentos nutritivos e maior variedade de sabores podem maximizar a probabilidade de que, à medida que as crianças crescem, elas escolham dietas mais saudáveis por gostarem dos sabores e de maior variedade de alimentos.

Estudos longitudinais demonstraram que padrões alimentares que começam a ser identificados na infância são determinantes significativos da qualidade da dieta do adulto [47,48]. O período mais aparente de mudança nos padrões alimentares foi evidente durante os primeiros anos de vida, com novos alimentos mais propensos a serem aceitos quando as crianças têm até 3 anos de idade em comparação com as idades mais avançadas [49,50].

### 2.2.1 Determinantes das práticas e preferências alimentares na infância

Embora o ser humano sofra influências de diversos fatores para o estabelecimento de suas práticas alimentares, dentre as crianças os indicadores mais fortes de suas escolhas alimentares são 1) se gostam do sabor dos alimentos, 2) por quanto tempo foram amamentadas e os alimentos consumidos por elas durante o período de lactação, e 3) os alimentos aos quais elas foram expostas em idade precoce [49–52].

Evidências científicas demonstram também que existe uma concordância entre as preferências alimentares na infância por todo o mundo, independentemente da cultura em que a criança esteja inserida, em que os alimentos com alto teor de gordura, sal e açúcar ganham a preferência, e os vegetais, com sabor amargo e azedo, tentem a serem rejeitados [50,53]. Todavia, as preferências inatas podem ser modificadas e a interação entre as diferentes predisposições genéticas e os fatores ambientais é o que realmente será responsável pela formação das preferências e hábitos alimentares dos indivíduos [54–56].

Por meio das experiências e familiarização, as crianças desenvolvem a percepção do sabor que os alimentos e bebidas devem ter [57–59]. Crianças alimentadas frequentemente com água adoçada durante a infância tendem a preferir líquidos mais doces do que as crianças que não eram expostas ao açúcar [60] e em experimento realizado com crianças que foram expostas repetidamente a uma bebida adoçada com sabor de laranja por 8 dias consecutivos, observou-se que elas não apenas apontaram preferência maior para a bebida adoçada, mas também beberam mais no final do período de exposição [61].

Ao nascer, a capacidade de detectar sabores doces já existe e interage com o sistema límbico [62–64]. Poucas horas após o nascimento, os recém-nascidos diferenciam vários graus de doçura e já apresentam preferência por consumir em maior quantidade soluções adoçadas do que água pura [65] e é possível observar que quando uma solução doce é colocada na cavidade oral, os bebês relaxam o rosto e muitas vezes sorriem [62–64]. Sua capacidade de atuar como analgésico foi investigada extensivamente em bebês e em crianças [60,66,67]. O sabor doce é eficaz na redução

do choro espontâneo e da dor em bebês prematuros e a termo durante uma série de procedimentos dolorosos, como punção venosa ou injeções intramusculares [66].

Estudos transversais e longitudinais mostraram que as preferências por doces permanecem intensificadas durante a infância e no início da adolescência, diminuindo para níveis semelhantes ao de adultos no final da adolescência [60,68,69]. As crianças também preferem concentrações substancialmente mais altas de sal do que os adultos, e adicionar sal aos alimentos pode aumentar o seu consumo [59,70,71]. No entanto, os recém-nascidos geralmente não reagem fortemente a concentrações moderadas de sal, a detecção do sabor salgado parece se desenvolver mais tarde, entre os 2 e 6 meses. Em comparação com as preferências doces entre crianças, a avidez ao sal é mais complexa e menos compreendida. [63,70].

A preferência pelo sal é afetada por experiências pré-natais e é aparentemente mais plástica do que a preferência pelo doce [72–74]. É referido que bebês nascidos de mulheres com enjoo matinal moderado a grave apresentam ingestão significativamente maior de soluções com sal aos 4 meses de idade do que aqueles cujas mães relataram não ter mais do que enjoo matinal leve [73]. Adolescentes e adultos jovens preferiram concentrações mais altas de sal em uma base de sopa no laboratório e relataram um consumo diário significativamente maior de sal se eles próprios sofreram de vômito infantil ou diarreia ou se suas mães tiveram enjoos matinais durante a gravidez [72].

A maioria dos alimentos e bebidas vendidos com foco em populações pediátricas são muito ricos em açúcares refinados ou sal ou ambos e a grande maioria do consumo vem de alimentos ultraprocessados [17,75–77], assim, os consumidores têm relativamente pouco controle e conhecimento sobre a quantidade de sal e açúcar que consomem. Pesquisas mostraram que adicionar açúcar às bebidas e a alimentos sólidos aumenta sua aceitação entre crianças pequenas [59] e, assim como as experiências com o sabor doce, as preferências pelo sabor salgado são moldadas por suas experiências durante os primeiros anos de vida. O consumo de soluções com concentrações moderadas e altas de sal por crianças com menos de 6 meses de idade pode modificar seus padrões alimentares, uma vez que começam a comer alimentos sólidos [78].

Em um estudo longitudinal com bebês, aqueles expostos a alimentos ricos em amido, uma fonte significativa de sódio na dieta de bebês, eram significativamente mais

propensos a preferir soluções mais salgada durante a infância e tinham uma maior afinidade para alimentos salgados em idade pré-escolar, em comparação com crianças alimentadas com menores quantidades de sódio [78]. Assim, é possível afirmar que as primeiras experiências têm alto potencial de modular as respostas hedônicas a esses estímulos básicos.

A maior parte das doenças crônicas que assolam a sociedade atualmente, como obesidade, diabetes e hipertensão, derivam em grande parte de escolhas alimentares inadequadas, que se relacionam com experiências alimentares no início da vida. Embora a maioria das pessoas veja a escolha dos alimentos como um traço cultural, não diretamente relacionado à nossa biologia [79], evidências esmagadoras sugerem que a biologia das crianças as torna especialmente vulneráveis ao ambiente atual de alimentos com alto teor de sal e açúcares refinados. Em relatório do Institute of Medicine enfatizou-se a importância de se compreender melhor os sabores do sal e do açúcar, as preferências por estes sabores entre as crianças, e como as experiências precoces modulam essas respostas sensoriais, já que modificações destes componentes no ambiente alimentar de bebês e crianças - e quaisquer mudanças na redução das quantidades gerais - podem ter efeitos profundos a longo prazo [43].

### 3. OBJETIVOS

#### Objetivos Principais

Avaliar se o consumo de alimentos Ultraprocessados aos 3 anos interfere nos níveis de pressão arterial Sistólica e Diastólica de crianças aos 6 anos.

Avaliar longitudinalmente se o consumo de alimentos ultraprocessados interfere na preferência ao sabor salgado entre adolescentes aos 12 anos de idade.

Verificar se o consumo de sódio e alimentos ultraprocessados estão associados à preferência pelo sabor salgado entre adolescentes aos 12 anos de idade.

Verificar se a puberdade interfere na preferência pelo sabor salgado entre adolescentes aos 12 anos de idade.

#### Objetivos Secundários

Identificar o percentual de contribuição de energia oriunda de alimentos Ultraprocessados nas dietas das crianças aos 3 anos.

Identificar os valores médios de pressão arterial sistólica e diastólica de crianças aos 6 anos de idade.

Verificar associação transversal de medidas antropométricas e níveis de pressão arterial de crianças aos 6 anos de idade.

Verificar a associação da prática de atividade física e níveis de pressão arterial de crianças aos 6 anos de idade.

Identificar o percentual de contribuição de sódio oriundo de alimentos processados e Ultraprocessados nas dietas de crianças com 1, 4, 8 e 12 anos de idade.

Identificar demais fatores que interferem na preferência pelo sabor salgado entre adolescentes aos 12 anos de idade.

#### 4. HIPOTESES

O consumo de alimentos Ultraprocessados aos 3 anos está associado a valores mais elevados das pressões arterial Sistólica e Diastólica de crianças aos 6 anos.

Variáveis antropométricas como IMC/Idade e circunferência da cintura estão associadas a valores de pressão arterial Sistólica e Diastólica.

Os alimentos Ultraprocessados são a principal fonte de sódio na alimentação de crianças aos 4, 8 e 12 anos de idade.

O consumo de sódio e alimentos ultraprocessados está associado à preferência por níveis mais elevados de sal aos 12 anos.

Crianças antes da puberdade preferem menores concentrações de sal no caldo do teste de preferência pelo sabor salgado entre adolescentes aos 12 anos de idade.

## 5. CONCLUSÕES

Os artigos apresentados nesta tese adicionam evidências de que o consumo alimentar de crianças se apresenta como fator de risco para o desenvolvimento de doenças crônicas não transmissíveis, e que o início deste processo pode iniciar ainda na infância, já que o consumo de alimentos ultraprocessados mostra-se como importante fonte de energia e sódio na dieta das crianças avaliadas.

Os dados apresentados demonstram que a alimentação das crianças aos 3 anos de idade está associada aos níveis de pressão arterial aos 6 anos e que, quanto maior o consumo de ultraprocessados, mais elevada a pressão arterial diastólica. Além disso, no estudo que avaliou a preferência pelo sabor salgado entre adolescentes, observou-se que em períodos de crescimento mais acelerado, como antes e durante a puberdade, as preferências pelo sabor salgado estão mais pronunciadas, o que as torna ainda mais suscetíveis ao consumo excessivo de sódio, um componente muito utilizado pela indústria de alimentos e presente em abundância nos alimentos ultraprocessados.

Esses dados em conjunto apoiam a importância de se realizar intervenções dietéticas focadas na prevenção da introdução precoce de alimentos ultraprocessados com foco na qualidade da alimentação infantil, uma vez que um ambiente alimentar rico em alimentos com alto teor de sódio, açúcares e gorduras reforça o papel das exposições repetidas a alimentos altamente palatáveis e se soma às preferências alimentares biologicamente inerentes ao ser humano, tornando a promoção da alimentação saudável um grande desafio.

As evidências trazidas nos estudos apresentados nesta tese, juntamente com dados presentes na literatura, demonstram que estratégias para promoção da alimentação saudável devem ser prioridades para a saúde pública, iniciando ainda na gestação e que, para terem efeito a longo prazo, estas precisam acompanhar o crescimento e desenvolvimento das crianças, abordando as características e necessidades de todas as fases evolutivas para garantir hábitos alimentares saudáveis ao longo da vida e, conseqüentemente, melhores condições de saúde na vida adulta.

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ANEXO 1 – Artigo a ser submetido no periódico Nutrition, Metabolism and Cardiovascular Diseases

Title page

Title: Early consumption of ultra-processed foods is associated with higher blood pressure at 6 years of age

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## Highlights

- The NOVA System classifies foods according to their degree of processing
- Ultra-processed foods represent more than 40% of the energy consumed by children
- Early consumption of ultra-processed foods is associated with blood pressure levels
- BMI and waist circumference are associated with blood pressure among children

## ABSTRACT

**Background and Aims:** Emerging evidence suggest that the consumption of ultra-processed foods (UPF) plays a critical role in the development of chronic diseases, but evidence of their influence in children's health is still limited. The objective of the present study was to verify whether the consumption ultra-processed foods at 3 years of age is associated with systolic (SBP) and diastolic blood pressure (DBP) levels in 6-year-old children.

**Methods and Results:** The present study was a follow-up of a randomized field trial of children (n=305) from Porto Alegre, Brazil. Dietary intake was collected using two 24-h recalls at 3 years of age, and food consumption was classified according to the NOVA system to identify the percentual of calories from UPF. At age 6 years, anthropometric measures were collected, and SBP and DBP were evaluated. Linear regression analysis was used to assess the relationship between PF and UPF consumption and the blood pressure. The percentage of daily energy provided by UPF was 40,85 % (IQR: 34,15–48,48). The adjusted linear regression analyses showed that the UPF consumption at 3 years old was associated with higher levels of DBP at the age 6 years ( $\beta=0,109$ ; 95%IC= 0,014-0,204;  $p=0,025$ ).

**Conclusions:** Our data suggest that early ultra-processed food consumption played a role in increasing DBP. These results reinforce the importance of effective strategies to prevent the excessive consumption of ultra-processed foods, especially in early ages.

Registration number for clinical trials: NCT00635453

**Keywords:** Arterial Pressure; Eating; Nutrition Survey; Child Nutrition

## INTRODUCTION

The NOVA system classifies foods according to the degree and extent of their processing. According to this system, foods are classified into four categories: 1) unprocessed or minimally processed, 2) processed culinary ingredients, 3) processed foods and 4) ultra-processed foods (UPF). Ultra-processed foods are composed by formulations of ingredients derived from a series of industrial processes, which result in ready-to-eat, high energy-dense products, high in sugar, fats and sodium, low in dietary fiber, and micronutrients [1–4]. Cosmetic additives, such as flavor enhancers, artificial colors, and sweeteners are also often used in the manufacture of UPF to disguise undesirable sensory properties created in the manufacture of UPF or to enhance the final product sensory properties [1]. Since this concept of food classification is new, the impacts of the food processing on human health are an area of great interest and are being intensively investigated.

UPF consumption already represent more than 50% of the total dietary energy consumed in high-income countries [2,3,5] and between 20% and 30% percent of the total dietary energy intake in middle-income countries [6,7]. In Brazil, studies showed that, among children from urban areas, the UPF consumption pattern is similar to the observed in high income countries, reaching to almost half of the calories ingested [8–10]. In adults, positive associations between UPF consumption and excessive weight gain [11], obesity [12–14], dyslipidemia,, metabolic syndrome [15], hypertension [16], and cancer [17] were already documented.

Although studies with children observed association between UPF consumption and increased total cholesterol and low-density lipoprotein [8,9], triglycerides [9], and

anthropometric measures, such as waist circumference [11], the effect of food consumption in its different degrees of processing on children's health is still scarce, and its relation to the blood pressure levels in children is still barely described [15,18]. Therefore, the aim of the present study was to use a longitudinal study design to verify whether the consumption of ultra-processed foods at 3 years of age is associated with systolic and diastolic blood pressure levels in 6-year-old children.

## METHODS

### *Study Design and participants*

Longitudinal study carried out with data from children who participated in a randomized intervention study aiming to improve breastfeeding rates and children's dietary practices [19] (NCT00635453). The intervention trial was conducted in primary health care centers who mainly served low-income families in Porto Alegre, Brazil, and the outcomes were evaluated in children who attended these centers for routine childcare consultations.

Briefly, all health workers and administrative staff of the intervention allocated health centers participated in a training based on "Ten steps for healthy feeding for Brazilian children from birth to two years of age" guideline. From April to December 2008, pregnant women in the third trimester of pregnancy attending at the participating health centers were invited to sign up for outcome tracking. All children enrolled in the study were born between May 2008 and February 2009.

The sample size determined for the trial was based on the goal to detect a difference in the prevalence of exclusive breastfeeding at 4 months [20]. A power of 90 %,  $\alpha$  of 0.5, design effect of 1.5 and a loss prediction of 20 % were used to calculate the sample size, resulting in the inclusion of 360 mother–baby pairs in the intervention group and another

355 in the control group. Seven hundred and fifteen pregnant women were registered for the study, of which, 635 children were enrolled at the study at 6 months of age. A total of 476 and 387 children underwent assessment in the follow-up studies, at 3 and 6 years of age, respectively.

This study was conducted according to the Declaration of Helsinki guidelines, and all procedures involving human subjects were approved by the *Universidade Federal de Ciências da Saúde de Porto Alegre* Ethics Committee. Informed consent was obtained from mothers on behalf of their children at each stage of data collection.

#### *Data Collection*

Interviews were conducted with the mothers and/or main caregivers at home visits by trained interviewers when their children were at 6 months, 3 years and 6 years of age. Socio-economic and family characteristics were obtained from the pregnant women at recruitment. Birth weight and length, and sex were collected from the children's health records at the first home visit, at 6 months. Weight and height data of all children at 6 years were obtained using a digital scale to the nearest 0.1 kg and a stadiometer to the nearest 0.1 cm. BMI for age z-score was calculated based on the WHO standards and obesity was defined as BMI z-score  $>2$  SD [REF]. Waist circumference (WC) was measured at minimum circumference between the iliac crest and the rib cage site by using a non-stretchable fiberglass insertion tape to the closest 0.1 cm.

#### *Dietary Assessment*

Two multiple-pass 24-h dietary recalls were collected during the home visits, on two non-consecutive days, randomly determined within 2 weeks to 1 month [21] for each child at age 3. The recalls were provided by mothers or other caregivers, which reported all the foods and beverages consumed the day before the interview. For children who spent time with a caregiver other than the parent (e.g. during school hours), we contacted the caregiver to record all items the children consumed with them during the previous day. Details about amounts, food types, and preparation methods were asked. Common household measures (e.g. tablespoons, cups and serving sizes) were used to help to report the food amounts given to their children and to standardize portion sizes. The Interviews were conducted by dietitians/nutritionists and undergraduate students in nutritional sciences, trained and supported in the 24-h recall method with standardized procedures, and the research supervisor reviewed all the dietary recalls. Dietary energy intake was estimated using the Dietwin® software program (version 2008 professional Dietwin®), and the Brazilian Food Composition Table (TACO, 2006) was preferentially used as a reference, followed by the United States Department of Agriculture chemical composition tables (Agricultural Research Service, 1998). For commercial products, we individually added all nutritional composition provided by the manufacturer to the software.

#### *Ultra-processed food consumption*

UPF consumption was assessed using the NOVA classification system [1,22], a classification based on the extent and purpose of food processing, including unprocessed and minimally processed foods, processed culinary ingredients, Processed foods, and

Ultra-processed Foods. This study focused on the NOVA groups of UPF. Briefly, UPF are composed of formulations of ingredients, most of exclusive industrial use, that result from a series of industrial processes and typically including little or no fresh food, mostly presented as ready to eat, drink, or heat foods

All food and drink items assessed in the dietary survey were categorized based on the food classification previously reported. This categorization was performed by a team of dietitians trained, supervised by researchers. Home-made recipes were identified and decomposed using standardized recipes, and the classification was applied to their ingredients. For a small number of specific food items such as pizza, there was insufficient information for classification purposes. In those cases, we used a conservative approach, such that the lower level of processing was chosen. The UPF subcategories analyzed in the present study included (a) savoury and biscuits (crackers, chips, salty snacks, cookies), (b) soft drinks (soda, sweetened juice), (c) sweets (candies, chocolate and ice cream), (d) powdered chocolate, (e) sugary milk beverages, (f) processed meats, (g) bread, (h) baby cereal, (i) margarine, mayonnaise and dressing and (j) ready-made soup/noodle (instant noodle and dehydrated soup).

#### *Blood pressure measurement*

Systolic and diastolic blood pressures were measured in the right arm, with the child seated and calm after 5 minutes of rest. Two blood pressure measurements were taken, and the second reading was used to assess blood pressure status. The measurements were taken with a calibrated aneroid sphygmomanometer (Brazilian Institute of Metrology, Standardization and Industrial Quality - INMTERO) which was used only in the

participants of the present study. We selected the appropriate cuff for the arm circumference based on the Fourth Report on the Diagnosis, Assessment and Treatment of Arterial Hypertension in Children and Adolescents [23].

Systolic and diastolic blood pressures were considered altered when observed values were above the 90th percentile for age, sex, and height, according to the population-based percentiles provided by the American Academy of Pediatrics in the “Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents” [24]. Specifically for the classification of blood pressure, the children's height was classified according to the CDC reference [25].

### *Data Analysis*

The usual dietary energy intake and energy from PF and UPF were estimated by the Multiple Source Method (<https://msm.dife.de>) [26] that calculates dietary intake for individuals and then constructs the population distribution based on these data [27]. All participants were considered consumers of total energy intake and for PF and UPF groups; a probability value of 0.5 (50 %) was used to assign the status of habitual consumer. The contribution of each subgroup of UPF to the total energy intake was calculated as a percentage of total energy. Differences between intervention and control groups with respect to energy, PF, and UPF consumption were analyzed, and no differences were observed (data not shown).

Continuous variables were expressed as mean and standard deviation or median and interquartile range and percentage frequency. Multivariable linear regression models were used to determine the relationship between the consumption of UPF at age 3 years

and other potential factors associated with the systolic and diastolic blood pressures at age 6 years (birth weight, exercise practice, maternal pre-gestational BMI, BMI z-scores, and waist circumference at 6 years). The models were also adjusted for group status in early phase (intervention or control). All statistical analyses were conducted using SPSS version 21.0 (IBM Statistics Inc.), and statistical significance was set at  $P < 0.05$ .

## RESULTS

From the 633 infants initially enrolled at the study at 6 months of age, 476 and 387 children underwent assessment at the ages of 3 and 6 years, respectively. The main reasons for loss were refusal to participate in the study and change of address (Fig. 1). No differences were found for sex, birth weight, maternal age at child's birth and family income between the children who were lost to follow-up and those who remained at 6 years of age ( $P > 0.05$ ; data not shown). The outcome analysis included 305 children with both complete dietary at age 3 years and blood pressure data at age 6 years.

Study participants' characteristics are presented in Table 1. Briefly, 19 % of the mothers were under age 20 years at the child's birth and 44,6 % had 8 years of schooling or less. More than half of the children were male (51,5 %), and the obesity prevalence was 17,5 % at 3 years and 18,4 % at 6 years of age. The mean value of systolic blood pressure observed was 96.6 mmHg (SD=10.4 mmHg) and the mean value of diastolic blood pressure observed was 58.9 mmHg (SD=10.3 mmHg).

The median consumption of UPF at the age 3 years represented 40,9% of the total energy intake at 3 years of age (Table 2). Within the UPF food groups, the main energy contributors were savory and biscuits, sweets, soft drinks, and powdered chocolate,

providing 28,2% of the total energy intake when taken together. Longitudinal associations between UPF consumption at 3 years old and blood pressures at 6 years old are shown in Table 3. There was significant association between PF and UPF consumption and the diastolic blood pressure ( $p=0,025$ ), but not with systolic blood pressure ( $p=0,688$ ). There was observed also positive association between low birth weight and waist circumference at 6 years old with both the systolic ( $p=0,010$  and  $p=0,032$ , respectively) and diastolic blood pressure levels ( $p=0,034$  and  $p=0,001$ , respectively). BMI z-score at 6 years old was associated with diastolic blood pressure ( $p=0,042$ ), but not with systolic blood pressure ( $p=0,378$ ). We also observed that children who exercised regularly at least once a week at 6 years old had lower levels of systolic blood pressure ( $p=0,046$ ).

## DISCUSSION

In this longitudinal study, it was observed that the UPF consumption accounted for more than 40% of the total calories' intake among the children at 3 years of age. Our study showed that the UPF consumption at 3 years old was associated with higher levels of DBP at age 6 years. Association between low birth weight and waist circumference at age 6 years with both SBP and DBP, BMI z-score at 6 years old children with DBP, and regular exercise practice with SBP was also observed.

The investigation into the consumption of ultra-processed foods is of great importance due to its growing consumption and unbalanced nutritional characteristics, such as high energy density and high content of sugar, salt and total, saturated, and trans fats [1]. In the present study, the percentage of energy intake from UPF was much higher

than the data observed in national surveys in Brazil, which were lower than 30% [4,28]. The food groups with greatest impact on the 3-years-old children's diet were: savory and biscuits, sweets and candies, soft drink, powdered chocolates and breads, similar to observed in other studies, both in Brazil and in other countries [8,28,29]. Such products are highly palatable, soft and easy to chew and swallow [1] and can lead to the physiological disruption of hunger and satiety signals, thus leading to overeating [30]. They are also fast, ready-to-eat and easily available to purchase, which makes them convenient and attractive. All these factors explain excessive ultra-processed product consumption by children [31].

The Consumption of UPF by children at 3 years of age was associated to higher levels of DBP when they were 6 years old. The findings of the present study showed that a 10% increase in energy intake from PF and UPF was associated with a 1.09 mmHg increase in the DBP. We believe that this associations could be explained by the nutritional profile of the UPF - rich in sodium [1,29] – which is highly associated to changes in the cardiovascular metabolism [23].

The self-regulation mechanism is the primary physiological process associated to the human response to sodium consumption and blood pressure. It occurs mainly in small-caliber arteries in response to changes in plasma volume, often prompted by the need for the kidneys to excrete excess sodium. The expansion of blood volume increases cardiac preload, which leads to increased perfusion of peripheral tissues. This excessive perfusion triggers an process of arterial constriction and, consequently increases vascular resistance and, blood pressure. This resulting increase in cardiac afterload causes cardiac output to return to its normal level, normalizing the SBP, but keeping the DBP

higher, as the vascular resistance remains. Over time, events like this may cause permanent remodeling of blood vessels, which can trigger metabolic changes that will also affect SBP and perpetuate Systemic Arterial Hypertension [32].

The association between the consumption of UPF observed with DBP was not observed in the SBP. It is possible that, in the present study, no association was observed between UPF consumption and SBP because of the age of the participants, since SBP is primarily associated with cardiac output, while DBP is associated with vascular resistance and heart rate; the physiology of the self-regulation mechanism may explain why in younger individuals, it is more frequent to see alterations only in diastolic blood pressure.

Although it is highly likely that the findings of the present study are related to the self-regulation mechanism, due to the high sodium content of UPF, the mechanisms behind the effects of consumption of these products on blood pressure in humans are not yet fully understood and recent evidence suggests that there are other mechanisms also related to these effects [33,34]. The processing of the *in natura* ingredients by the food industry to produce ready-to-eat, with long shelf-life and highly palatable UPF, causes profound changes in the original characteristics of the food, leading the nutrients to exhibit different properties and functions, due to interactions with artificially inserted substances that would not be naturally present in the food [35,36]. Animal model studies shows that artificial sweeteners and emulsifiers can negatively alter the gut microbiota composition [37], which may influence the host cardiovascular metabolism [37,38]. Also, there is evidence from animal models and studies in humans, showing that molecules such as acrolein, acrylamide, bisphenol A, and other additives commonly found in UPF may show deleterious health effects in the cardiovascular metabolism [36,39,40].

Waist circumference at 6 years of age was associated with higher levels of both SBP and DBP, corroborating data already well established in the literature, based on studies carried out in adults [41], which observed that fat mass might cause an elevated blood pressure by raising cardiac output with increased peripheral vascular resistance [42]. A previous study, carried out by our group, observed positive association between the waist-to-height ratio of children and their SBP levels, reinforcing the association between abdominal obesity and a higher risk of cardiovascular disease since childhood [43]. BMI z-score was only significantly associated with DBP, however, studies that evaluated factors associated with isolated changes in systolic and diastolic blood pressure found a stronger association between BMI and DBP when compared to SBP [44]. Thus, at least among children, measures of abdominal adiposity appear to be better indicators of cardiovascular risk than BMI.

The association between low birth weight and higher blood pressure was also observed in our study, adding evidence to the hypothesis that fetal malnutrition might affect the plasticity of the fetus development, reduce nephron number and lead to hypertension [45]. An inverse association was between the practice of physical exercise and SBP levels was observed, in which a reduction of approximately 3mmHg was observed among those who performed physical exercises at least once a week. A review of nine interventional studies with obese children and adolescents suggested that 40 minutes of moderate to vigorous, aerobic physical activity at least 3 days per week lowered approximately 6,6mmHg the SBP and prevented vascular dysfunction [46].

Our study has some potential limitations that should be discussed for a proper appreciation of our results. First, several participants discontinued follow-up, but we did

not observe significant differences between the characteristics of children who remained in the study and those lost to follow-up. Second, most of our sample has low family income, which may limit the applicability of our findings to more privileged populations. Third, the mean of the two dietary recalls may not represent the entire distribution of usual intake due to the intra-individual variance. Despite the limitations presented, our study has strengths that deserve attention. The prospective design of this study allowed us to assess the longitudinal association between UPF intake and blood pressure levels. In addition, the dietary data collected was extremely detailed, including food preparation methods, ingredients used and the brand name of commercial products, which allowed us to accurately classify foods according to the NOVA system.

## CONCLUSIONS

In conclusion, we observed a high consumption ultra-processed foods among 3-year-old children, far exceeding the values observed by the Brazilian population in general. We observed that the consumption of UPF was positively associated with higher DBP, confirming the study's main hypothesis. Secondary findings showed association of anthropometric measures and physical exercise practice with levels of DBP and SBP.

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## TABLES

Table 1: Characteristics of children and their families (n 305)\* (Percentages and numbers; median values and Interquartile Range (IQR))

	%	n	Median	IQR
Maternal and family				
Maternal age <20 years at birth	19,0	58	-	-
Maternal pre-gestational BMI >25 kg/m <sup>2</sup>	37,0	111	-	-
Maternal education ≤ 8 years	44,6	136	-	-
Annual household income > US\$3000	18,0	55	-	-
Child at birth				
Sex (boys)	51,5	157	-	-
Birth weight < 2500g	6	18	-	-
Child at 3 years				
BMI-for-age (z-score)	-	-	0,82	0,04 ; 1,59
Waist circumference (cm)	-	-	51,5	49,0 ; 54,1
Obesity	17,5	48	-	-
Child at 6 years				
Systolic Blood Pressure (mmHg) <sup>a</sup>	-	-	96,6	10,4
Diastolic Blood pressure (mmHg) <sup>a</sup>	-	-	58,9	10,3
BMI-for-age (z-score)	-	-	0,47	-0,25 ; 1,36
Waist circumference (cm)	-	-	54,6	51,7 ; 58,5
Obesity	18,4	56	-	-
Regular exercise practice	17,3	52	-	-

\*Values may not equal to total number of subjects in each group because of missing data

<sup>a</sup> Values presented as mean and standard deviation

Table 2: Energy intake, Processed Foods (PF) and Ultra-processed Food (UPF) consumption at 3 years old (median values and Interquartile ranges (IQR)).

	median	IQR
Total Energy intake (Kcal/day)	1467	1270 – 1686
UPF Groups (% of total energy intake)		
Savory and biscuits	9,96	5,44 – 14,47
Soft drinks	6,55	4,68 – 8,78
Sweets	8,11	4,67 – 11,44
Powdered chocolate	3,48	0,97 – 6,44
Sugary milk beverages	2,44	0,11 – 6,20
Processed meat	2,39	0,72 – 4,59
Bread	2,86	0,00 – 3,22
Baby cereal	0,23	0,00 – 0,80
Margarine, Mayonnaise and dressings	0,14	0,00 – 0,35
Ready-made soups and noodles	0,14	0,00 – 0,36
Total UPF (% of total energy intake)	40,85	34,15 – 48,48

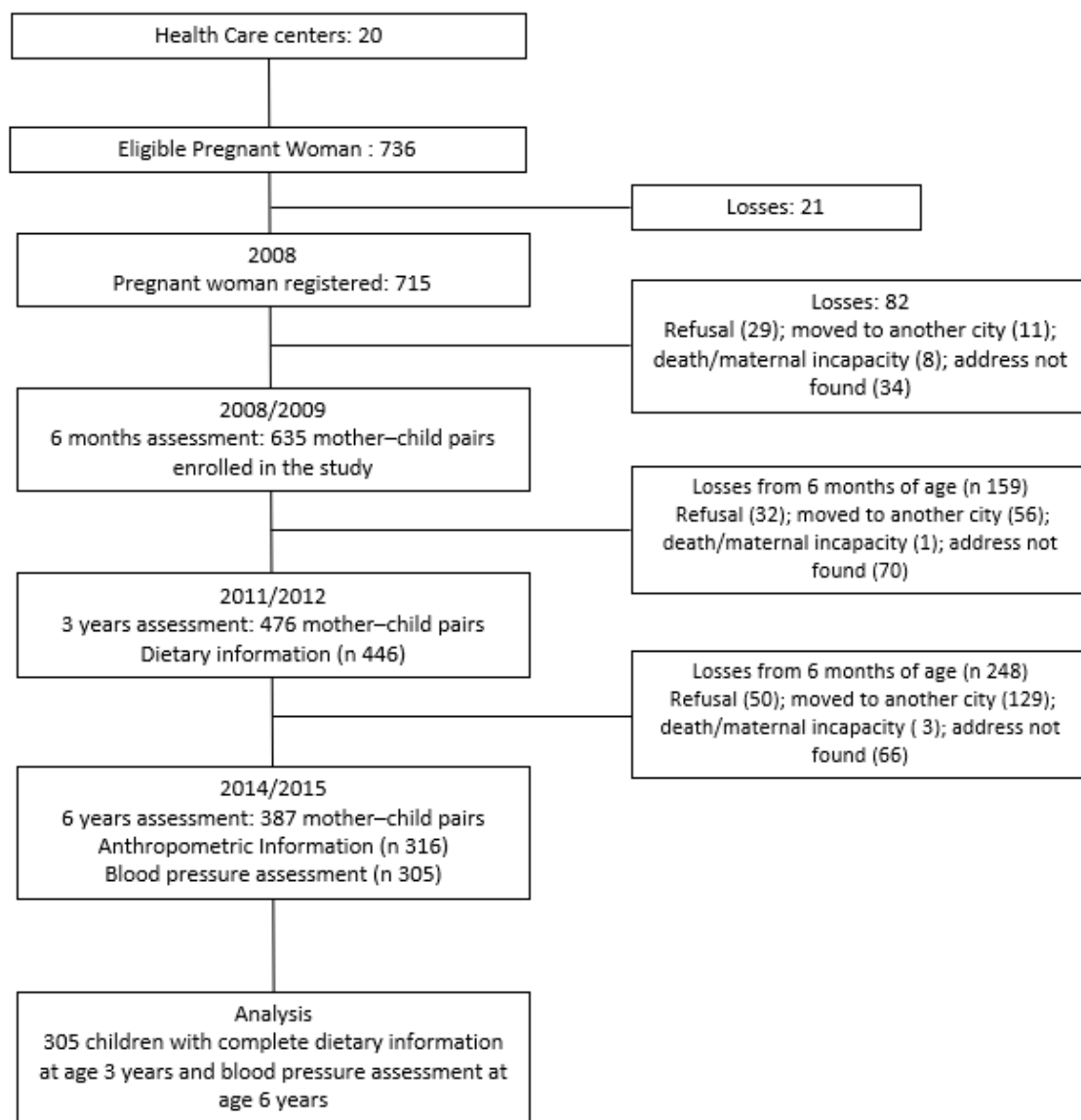
Table 3: Linear regression analysis of the association between PF and UPF consumption and other independent variables with systolic and diastolic blood pressure at 6 years old ( $\beta$  Values and 95 % confidence intervals)

	Systolic Blood pressure			Diastolic blood pressure		
	$\beta$	95% IC	P	B	95% IC	P
UPF Consumption at age 3 years (% of total energy intake)	0,021	-0,082;0,123	0,688	0,109	0,014;0,204	0,025
Low Birth Weight (< 2500g)	6,057	1,431;10,682	0,010	4,641	0,344;8,937	0,034
Waist Circumference at age 6 years(cm)	0,457	0,041;0,873	0,032	0,676	0,289;1,063	0,001
BMI-for-age at age 6 years (z-score)	0,789	-0,969;2,546	0,378	1,696	0,064;3,329	0,042
Regular Exercise practice at age 6 years	-3,002	-5,953;-0,052	0,046	-0,917	-3,657;1,824	0,511
Maternal pre-gestational BMI (kg/m <sup>2</sup> )	0,155	-0,097;0,407	0,227	0,096	-0,138;0,330	0,421
Randomized group (Control group)	-1,154	-3,424;1,116	0,318	-1,,199	-3,308;0,910	0,264

\*p < 0,05

## FIGURES

Figure 1. Flow diagram of the study



ANEXO 2 – Artigo submetido no periódico *Current developments in Nutrition*

## **TITLE PAGE**

**Title:** Sodium intake tracked from infancy and salt taste preference during adolescence: Follow-up of a randomized controlled field trial in Brazil

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**Short Running Head:** Diet and salt taste preference in adolescence

**Abbreviations:** year (y); day (d); month (m); randomized controlled trial (RCT)

## 1 ABSTRACT

2 **Background:** Effective interventions to promote healthy sodium intakes require understanding  
3 factors driving liking for salt taste.

4 **Objective:** To identify age-related changes in sources of sodium in diet and determine the effect  
5 of an early feeding intervention delivered to low-income mothers in Brazil during the first year  
6 postpartum on energy and sodium intake from unprocessed, processed or ultra-processed foods  
7 post-intervention and salt taste preferences at 12 y.

8 **Methods:** Using secondary data from a randomized controlled trial in which mothers received  
9 dietary counseling during first year postpartum, foods in 2-day dietary recalls at the end of the  
10 trial (1 y) and at 4-, 8-, and 12-y follow-up visits were analyzed and categorized as unprocessed,  
11 processed, or ultra-processed. At the 12-y visit, children self-assessed their pubertal stage and  
12 determined their most preferred concentration of salt using Monell's two-series, forced-choice,  
13 paired-comparison tracking method.

14 **Results:** The early intervention reduced energy intake from all food categories at 1 y ( $p = 0.04$ )  
15 but had no effect at 4, 8, or 12 y. Sodium intake increased from processed foods ( $p < 0.01$ ) from 4  
16 to 12 y and from ultra-processed foods ( $p < 0.01$ ) from 1 to 4 y and decreased from unprocessed  
17 foods from 1 to 8 y ( $p < 0.01$ ). At 12 y, children at early pubertal Tanner stages 1–3 ( $p = 0.04$ ) or  
18 in the  $\geq 75^{\text{th}}$  percentile of sodium intake ( $p < 0.01$ ) preferred higher concentrations of salt.

19 **Conclusions:** While the dietary intervention reduced energy intake at 1 y, it had no effect on  
20 energy or sodium intake from 4 to 12 y. At 12 y, children in early puberty or with greater sodium  
21 intake preferred higher concentrations of salt. Childhood and adolescence are important periods  
22 for understanding how factors underlying salt taste sensations shape our diet—the most  
23 important influence on health in modern societies.

24

25 **Clinical Trial Registration:** This manuscript reports on secondary data analysis of data

26 collected in trial NCT00629629 (2001–3) and followup visits;

27 <https://clinicaltrials.gov/ct2/show/NCT00629629?term=NCT00629629&draw=2&rank=1>

28

29 **KEY WORDS:** diet, sodium, salt taste preference, child, adolescence, processed and ultra-

30 processed foods, randomized controlled trial, Brazil

31

32 **Teaser Text:** This RCT evaluated the effect of an early life intervention on energy and sodium

33 intake and assessed salt taste preferences at 12 y.

## 34 INTRODUCTION

35 Sodium plays a critical role in maintaining homeostasis, and proper functioning of the  
36 human body (1). However, people of all ages and from many nations are eating more sodium  
37 than is required (2, 3), due in part, to the powerful hedonic appeal of the taste of salt (4, 5), one  
38 of the main sources of dietary sodium (6). When in excess, dietary sodium intake can be  
39 associated with increased health risks for cardiovascular diseases, especially those deemed ‘salt-  
40 sensitive’ (7). Although the health conditions related to excessive sodium intake typically  
41 manifest during adulthood, their origins commonly begin in childhood (8), a period in life when  
42 salt taste preferences are heightened and when greater sodium intake associated with heightened  
43 preferences for salty tasting foods (5, 9).

44 During the past few decades, research in several countries, including Brazil, have  
45 reported excessive sodium intake among children and adolescents, with intakes rapidly  
46 increasing once complementary foods are introduced to the diet (10-13). To understand the  
47 important role of early life feeding practices on setting the stage for life-long health, in 2001 we  
48 initiated a randomized controlled trial (RCT) in the city of São Leopoldo, Brazil to low-income  
49 mothers during the first year postpartum. We found that the intervention that promoted healthy  
50 feeding practices had positive effects on the health and nutrition outcomes of their children; it  
51 improved breastfeeding rates at 6 and 12 months and reduced the consumption of sugar-dense  
52 and lipid-dense foods at one y, and improving overall diet quality at 4 y and overall lipid profile  
53 at 8 y (13-16).

54 Considering the alarming overconsumption of sodium and that the antecedents of  
55 elevated blood pressure (17), as well as food preferences (18), begin in childhood, the goal of the  
56 present secondary analysis was twofold. First, we determined whether the randomized

57 intervention impacted sodium and energy intake at the end of the trial (1 y) and then at the 4-, 8-,  
58 and 12-y follow-up visits. We focused in particular on unprocessed, processed and ultra-  
59 processed foods, as defined by the NOVA classification system (19), because these foods are  
60 typically high in sodium (20) and associated with unhealthy diets (21). Second, we used a  
61 validated, forced-choice, paired-comparison method (22) to determine children's most preferred  
62 concentration of salt at the 12-y follow-up visit. Because preference for salt is heightened during  
63 childhood (5), with the adult pattern emerging during adolescence (23), we determined the  
64 Tanner stage of puberty for each child, hypothesizing that salt taste preferences would be  
65 heightened among those who were in the earlier stages of puberty compared to those in the  
66 culminating stages. Because dietary patterns are established early (18), childhood is an important  
67 period for understanding how the biological and experiential factors underlying salt taste  
68 sensations shape what we eat—the most important influence on health in modern societies.

## 69 **SUBJECTS AND METHODS**

### 70 **Design of the Parent RCT**

71 The parent RCT was conducted from 2001 to 2003 in the field through home visits to  
72 low-income mothers during the first year postpartum, with follow-up visits at 4, 8, and 12 y. The  
73 RCT study design, inclusion and exclusion criteria, and CONSORT table have been published  
74 (14, 15).

75 In brief, 500 mother-child pairs were randomly assigned, in a 2:3 ratio, to either the  
76 intervention or control group. Mothers in the intervention group received dietary advice based on  
77 Brazilian guidelines ["Ten steps for the healthy eating: Feeding guidelines for Brazilian children  
78 from birth to two years" (13)] during monthly home visits from 2 weeks to 6 months postpartum  
79 and then every 2 months thereafter until 1 y postpartum. The study did not interfere in the

80 routines of pediatric health care. Mothers in both groups received home visits by trained  
81 fieldworkers, blind to the hypothesis, who carried out face-to-face interviews on breastfeeding  
82 practices and collected family demographics at 6–9 months and information on children’s health  
83 history, breastfeeding practices, and complementary feeding at the end of the trial (1 y).  
84 Fieldworkers also collected 24-hour dietary recalls at 1 y.

85         The parent trial was approved by the ethics committee of the Federal University of Health  
86 Sciences of Porto Alegre and by the Office of Regulatory Affairs of the Unisinos University and  
87 was conducted according to the guidelines laid down in the Declaration of Helsinki. It was  
88 registered online at [clinicaltrials.gov](https://clinicaltrials.gov) prior to the start of the trial (NCT00629629).

#### 89 **Follow-up Study: 4, 8, and 12 y**

90         All children whose mothers participated in the parent trial were eligible to participate in  
91 the 4-, 8-, and 12-y follow-up visits, which aimed to determine if the early-life intervention had  
92 independent effects on nutritional outcomes. Through home visits, we contacted mothers or, in  
93 rare cases, other legal caregivers (hereafter referred to as mothers) to invite them to participate in  
94 the follow-up study; if they were interested, we provided procedural details, after which we  
95 obtained informed consent from the mothers. Written assent was also obtained from the children  
96 at the 12-y follow-up visit. Mothers and children were not informed of the study hypothesis, and  
97 study personnel were blind to children’s assignment group. The follow-up studies were approved  
98 by the ethics committee of the Federal University of Health Sciences of Porto Alegre and by the  
99 Office of Regulatory Affairs of the University of Vale dos Sinos and were conducted according  
100 to the guidelines laid down in the Declaration of Helsinki

101         At each follow-up visit, trained fieldworkers conducted face-to-face interviews with the  
102 dyads. Anthropometric measures and the 2-day, 24-hour dietary recalls were taken in the home at

103 the 4- and 8-y visits; for the 12-y visit the first day of dietary recall was conducted with the child  
104 at the home, and the second day of dietary recall, along with psychophysical taste testing,  
105 pubertal stage evaluation, and anthropometry measurements, was conducted in the Laboratory of  
106 Gastronomy, Technology, and Innovation at the Technological Institute in Food for Health,  
107 University of Vale dos Sinos.

## 108 **Primary Outcomes**

### 109 *Dietary Intake: 1, 4, 8, 12 y*

110 Dietary intake was assessed using two multiple-pass 24-hour dietary recalls, which  
111 occurred on nonconsecutive days chosen randomly within a 2-week to 1-month period, except  
112 when children were 1 y, when only one dietary recall was collected. Recalls were provided by  
113 mothers or main caregivers when children were 1, 4, and 8 y and by the children themselves  
114 when they were 12 y. For children who spent time with a caregiver other than the mother (e.g.,  
115 during school hours), we interviewed the caregiver and recorded all items the children consumed  
116 during the previous day.

117 Mothers of children at 1, 4, and 8 y and the children themselves at 12 y were asked to  
118 report all the foods and beverages the child ingested the day before the interview, with guidance  
119 from trained staff. Common household measures were used to standardize portion sizes. From  
120 these dietary recalls, energy and sodium intake were estimated using Dietwin® nutrition  
121 software (Porto Alegre, RS, Brazil) which is available in Portuguese and which is based on the  
122 Brazilian Food Composition Table. The amount of salt added to culinary preparations or at the  
123 table was not included in the recall.

124 We focused on dietary intake of sodium from unprocessed, processed, and ultra-  
125 processed foods. When applicable, foods were categorized into either unprocessed, processed or

126 ultra-processed food according to the NOVA classification system (19, 20), as defined at **Table**  
127 **1**. From these data, we determined sodium (mg/d) and energy (kcal/d, kcal/kg/d) intake from  
128 unprocessed, processed, and ultra-processed foods for each of the four time points (1, 4, 8, 12 y).  
129 To allow comparison between ages, sodium was adjusted according to energy intake (mg  
130 Na/1000kcal/d). We also identified the top 5 foods, based on intake, of each of the three  
131 categories and for each age.

### 132 *Most Preferred Concentration of Salt, 12 y*

133 The Monell two-series, forced-choice, paired-comparison tracking method was used to  
134 determine each child's most preferred concentration of salt in broth (22). Five different taste  
135 stimuli (0.34%, 0.80%, 1.61%, 3.00%, 5.56% wt/vol NaCl, equivalent to 0.06, 0.14, 0.28, 0.51,  
136 and 0.95 mM/L) were made by adding varying concentrations of salt (without iodine) to a  
137 homemade NaCl-free vegetable broth made from turnips, carrots, onions, celery, black pepper,  
138 garlic, bay leaves, thyme, and parsley. Solutions were stored refrigerated for no longer than 1  
139 week, or frozen for no longer than 3 weeks. Prior to testing, broths were placed in a 32°C water  
140 bath, and the temperature of each solution was verified immediately prior to testing.

141 Participants were tested individually in a facility specially designed for gastronomic and  
142 sensory testing (with airflow control, but no red lights). They were presented with pairs of broth  
143 samples (30 ml each) in a disposable cup, following abstinence from eating for at least 1 hour.  
144 The first pair presented was from the middle range of concentrations (0.8% and 3.0% wt/vol  
145 NaCl). Participants tasted each sample of the pair for 5 s and then pointed to which of the pair  
146 they liked better, without instruction on how the stimuli differed. Each subsequent pair contained  
147 the selected concentration paired with an adjacent stimulus concentration. This pattern continued  
148 until the participant chose two consecutive times the same concentration paired with both a

149 higher and a lower concentration or chose the highest or lowest concentration in the series.  
150 Participants rinsed their mouth once with water after tasting each sample and twice between each  
151 pair of solutions; a 1-minute interval separated each pair presentation.

152 The entire task was repeated after a 3-minute break, with stimulus pairs presented in  
153 reverse order (i.e., weaker stimulus presented first in the first series, stronger stimulus first in the  
154 second series). This method controls for position bias and enables researchers to determine  
155 objectively whether the child understands the task or is responding by pointing to whatever is  
156 presented to the right or left. The geometric mean of the two concentrations chosen in series 1  
157 and 2 provided the estimate of the participant's most preferred concentration of salt.

#### 158 *Pubertal Stage, 12 y*

159 In a private room, with the help of a trained field worker and a photo album, each  
160 participant self-assessed their pubertal development using the Tanner staging (24), which assigns  
161 pubic hair and breast development in girls (25) and pubic hair and testicular development in boys  
162 (26). Girls were asked whether they had reached menarche. Each adolescent was assigned a  
163 Tanner stage, which ranged from 1 (absence of pubertal signs) to 5 (final pubertal stage). If pubic  
164 hair stage differed from mammary or testicular stage, the latter was chosen. Based on Tanner  
165 stage, children were categorized as in either early puberty (Tanner stages 1–3) or late puberty  
166 (Tanner stages 4–5).

#### 167 **Secondary Outcomes**

##### 168 *Anthropometric Measures*

169 At 1 y, children were weighed without clothes and diapers, while on their mother's lap, to  
170 the nearest 0.1 kg on a digital scale (Techline®, São Paulo, SP, Brazil), and length was measured  
171 to the nearest 0.1 cm using a pediatric stadiometer (Altorexata®). At 12 y, children were

172 weighted with light clothes and no shoes to the nearest 0.1 kg on a digital scale (Techline®), and  
173 standing height was measured to the nearest 0.1 cm with a stadiometer (SECA®). Height-to-age  
174 and BMI-to-age Z scores were computed for all ages using WHO pediatric growth charts (27).

#### 175 *Demographics and Confounders*

176 Confounders that could impact salt taste preference, determined *a priori*, were birth  
177 weight, sex, maternal-reported race, and BMI-to-age Z scores (5, 9, 28). Birth weight was  
178 collected from birth records at trial enrollment, and mothers reported their child's race, which  
179 was categorized as either white or nonwhite.

#### 180 **Statistical Analysis**

181 All data were double entered by different staff members and validated in EPI INFO 6.4  
182 (CDC). Data were analyzed using SPSS version 21.0 (IBM Statistics Inc., Chicago, IL, USA),  
183 and results were considered significant at  $p < 0.05$ . All continuous variables are presented as  
184 mean  $\pm$  SEM, and categorical variables as percentages (% ,  $n$ ), unless otherwise stated.

185 We used unpaired  $t$ -tests (or the Mann-Whitney  $U$ -tests if not normally distributed) for  
186 continuous variables and chi-square tests for categorical variables to examine differences  
187 between randomized groups at the start (enrollment), at the last visit (1 y) of the RCT and at the  
188 last follow-up visit (12 y). To determine whether the RCT intervention had an impact on the  
189 primary and secondary outcomes, we conducted an intention-to-treat analysis (29), using data  
190 from all children regardless of study withdrawal and according to their original group  
191 assignment. We used unpaired  $t$ -tests (or the Mann-Whitney  $U$ -tests if not normally distributed)  
192 for continuous variables and chi-square tests for categorical variables. We used repeated-  
193 measures Friedman tests to examine independent or interactive effects of randomized group by  
194 age on sodium intake, adjusted for energy (mg Na/1000kcal/d), from unprocessed, processed,

195 and ultra-processed foods. Significant effects were further examined with post hoc paired t-tests  
196 with Bonferroni correction.

197 To determine whether early nutritional intervention (randomized group), current or past  
198 dietary intake, and pubertal stage of development had interactive or independent effects on  
199 concentration of salt taste most preferred, we carried out a gradual progression from exploratory  
200 data analysis for identifying covariates to modeling, in a highly procedural manner. Significant  
201 effects were followed by splitting continuous variables into meaningful groups to illustrate  
202 findings and conduct further analyses.

203 First, we used bivariate analysis to examine statistically significant associations between  
204 the concentration of salt most preferred and randomized group, Tanner stage group, and dietary  
205 and sodium intake variables at 1, 4, 8, and 12 y (Mann Whitney *U*-tests, chi-square tests, or  
206 linear regression, depending on variable characteristics). Second, we performed multivariate  
207 linear regression to explore multiple factors associated with most preferred salt concentration at  
208 12 y. Model 1 included confounders identified a priori plus all statistically significant variables  
209 from the bivariate analysis that were associated with most preferred salt concentration. Model 2  
210 then included the statistically significant predictors identified in Model 1, to determine if the  
211 associations remained significant. To determine if the predictors were independent or correlated,  
212 we used Pearson correlations generated in the multivariate linear regression models.

## 213 **RESULTS**

### 214 **Participants**

215 Among the 500 mother-child dyads initially enrolled in 2001 and 2002, 79.4% were  
216 evaluated at 1 y, 70.8% at 4 y, 63.0% at 8 y, and 42.4% at 12 y (**Figure 1**). Of the 212 children at

217 12 y, 187 (80 girls, 107 boys) participated in the psychophysical taste task and were evaluated  
218 for pubertal stage.

219       There were no significant differences between children who were lost to follow-up and  
220 those who participated in the 12-y follow-up visit regarding randomized group assignment ( $p =$   
221 0.89), child sex ( $p = 0.73$ ), infant delivery mode ( $p = 0.15$ ), gestational age at birth ( $p = 0.32$ ),  
222 birth weight ( $p = 0.81$ ), birth length ( $p = 0.81$ ), mother's age ( $p = 0.24$ ), mother's employment ( $p =$   
223 0.40), or family income ( $p = 0.44$ ). Except for maternal education, which was higher among  
224 those who remained in the trial ( $7.2 \pm 2.7$ ) than among those lost to follow-up ( $6.4 \pm 2.7$  y;  $p =$   
225 0.02), there were no differences between the randomized groups in demographic and  
226 socioeconomic characteristics at enrollment and at the 12-y visit (**Table 2**). The groups also did  
227 not differ in children's height-for-age or BMI-for-age Z scores at 1, or 12 y (**Table 2**).

## 228 **Dietary Intake**

229       At 1 y, children in the intervention group ate significantly less unprocessed, processed,  
230 and ultra-processed foods (kcal/d; kcal/kg/d) than those in the control group. No group  
231 differences were observed in sodium intake (mg/d; mg/1000 kcal/d) at 1, 4, 8, or 12 y (**Table 3**).

232       To determine how sodium intake from these foods changed over time, we focused on the  
233 164 children for whom we had dietary data at all ages. Daily sodium intake from unprocessed,  
234 processed, and ultra-processed foods (mg/1000kcal/d) changed with age (**Figure 2**). Sodium  
235 intake from unprocessed foods decreased from 1 to 4 y ( $p = 0.02$ ) and from 4 to 8 y ( $p < 0.01$ )  
236 but not from 8 to 12 y ( $p = 0.80$ ). There was no difference in sodium intake from processed foods  
237 from 1 to 4 y ( $p = 0.47$ ) but a significant increase from 4 to 8 y ( $p < 0.01$ ) and then from 8 to 12  
238 y ( $p < 0.01$ ). Sodium intake from ultra-processed foods increased from 1 to 4 y ( $p < 0.01$ ) but did

239 not change from 4 to 8 y ( $p = 0.08$ ) or from 8 to 12 y ( $p = 1.00$ ). The most consumed foods from  
240 each food group also differed according to age of the children at assessment (**Table 3**).

241 At each age, we found wide variation in sodium intake from unprocessed, processed, and  
242 ultra-processed foods. Thus, for further analysis we combined sodium intake (mg/d) from  
243 unprocessed, processed, and ultra-processed foods and split children into two groups using the  
244 75th percentile of intake as a cutoff point: 896 mg/d at 1 y, 1611 mg/d at 4 y, 1800 mg/d at 8 y,  
245 and 2238 mg/d at 12 y.

### 246 **Pubertal Stage**

247 Of the 187 children who had their pubertal stage assessed, 62% ( $n = 116$ ) were classified  
248 in early puberty (Tanner stages 1–3). Intervention and control groups did not significantly differ  
249 in the proportion of children in early versus late puberty ( $p = 0.73$ ). As expected, a higher  
250 percentage of girls than boys at 12 y were in Tanner stages 4–5 ( $p < 0.01$ ). Because Tanner stage  
251 was highly associated with biological sex ( $p < 0.01$ ), we included only Tanner stage in analyses,  
252 to avoid multicollinearity in subsequent analyses. Sodium intake (mg/d) did not significantly  
253 differ between Tanner stages 1–3 ( $1882 \pm 112$  mg/d) and stages 4–5 ( $1816 \pm 101$ ;  $p = 0.12$ ).

### 254 **Concentration of Salt Taste Most Preferred**

255 Of the 187 children who participated in this task, 9 (5%) responded at random, 5 (3%)  
256 asked to stop before completion, and 2 (1%) were stopped by the interviewer for noncompliance  
257 with the protocol. Thus, subsequent analyses focused on the 171 adolescents for whom we have  
258 valid psychophysical data. Their most preferred concentration of salt ranged from 0.34 to 5.56%  
259 wt/vol, averaging  $1.25 \pm 0.08\%$  wt/vol.

### 260 **Statistical Models: Effects of Randomized Intervention Group, Dietary Intake, and** 261 **Pubertal Development Effects on Salt Taste Preferences**

262           Although there was no significant association between randomized group and most  
263 preferred concentration of salt ( $p = 0.75$ ), we found independent effects of pubertal development  
264 and dietary intake on salt taste preferences at 12 y. Children in Tanner stages 1–3 preferred  
265 significantly higher concentrations of salty taste ( $1.40 \pm 0.11\%$  wt/vol) than those in stages 4–5  
266 ( $1.02 \pm 0.10\%$  wt/vol;  $p = 0.04$ ). At 1 y, children in the  $<75^{\text{th}}$  percentile for sodium intake  
267 preferred significantly higher concentrations of salt at 12 y ( $1.36 \pm 0.10\%$  wt/vol) compared to  
268 those in the  $\geq 75^{\text{th}}$  percentile group ( $0.89 \pm 0.13\%$  wt/vol;  $p = 0.01$ ). In contrast, at 12 y, children  
269 in the  $\geq 75^{\text{th}}$  percentile preferred significantly higher concentrations of salt ( $1.69 \pm 0.20\%$  wt/vol)  
270 than those in the  $<75^{\text{th}}$  percentile ( $1.15 \pm 0.08\%$  wt/vol;  $p < 0.01$ ). There were no associations  
271 between sodium intake at 4 or at 8 y and the most preferred concentration of salt at 12 y ( $p =$   
272  $0.60$  and  $0.97$ , respectively).

273           Multivariate linear regression models were conducted to examine multiple factors related  
274 to the most preferred concentration of salt (**Table 4**). Model 1 included the following  
275 confounders: sodium intake percentile group ( $<75^{\text{th}}$  vs.  $>75^{\text{th}}$ ) at 1 y and 12 y and Tanner stage  
276 group (1–3 vs. 4–5). Because Tanner stage was highly associated with biological sex ( $p < 0.01$ ),  
277 we included only Tanner stage to avoid multicollinearity in the model.

278           As a result of Model 1, children in Tanner stage group 1–3 ( $p = 0.04$ ) or in the  $\geq 75^{\text{th}}$   
279 percentile sodium intake group at 12 y ( $p = 0.03$ ) preferred significantly higher concentrations of  
280 salt than those in Tanner stages 4–5 or in the  $<75^{\text{th}}$  percentile, respectively. Neither the  
281 confounders nor sodium intake group at 1 y ( $p = 0.12$ ) was statistically associated with the most  
282 preferred concentration of salt.

283           In a second multivariate linear regression, Model 2 included Tanner stage and sodium  
284 intake groupings at 12 y as predictors of the most preferred concentration of salt (**Table 4**).

285 Children in the early Tanner stages (1–3) preferred significantly higher salt concentrations than  
286 those in the later stages ( $p = 0.02$ ; **Figure 3A**). Likewise, children in the  $\geq 75^{\text{th}}$  percentile for  
287 sodium intake at 12 y preferred higher salt concentrations than those in the  $< 75^{\text{th}}$  percentile ( $p =$   
288  $0.01$ ; **Figure 3B**). Tanner stage group and 12-y sodium intake group were not associated with  
289 each other as predictors of the most preferred concentration of salt ( $p = 0.42$ ).

## 290 **DISCUSSION**

291 The field-based intervention, which counseled low-income mothers on exclusive  
292 breastfeeding for first 6 months and healthy complementary feeding, had a modest yet significant  
293 effect on lowering the intake of unprocessed, processed, and ultra-processed foods, compared to  
294 the control group, when children were 1 y but not when they were 4, 8, or 12 y. Regardless of  
295 randomized group assignment, children's energy and sodium intake from unprocessed foods  
296 decreased and their sodium intake from processed and ultra-processed foods increased, with  
297 much of these dietary changes occurring between 4 y and 8 y. Modeling of these data revealed  
298 that sodium intake at 12 y and stage of puberty predicted preferences for salty taste at 12 y: the  
299 higher the dietary sodium intake and the lower the Tanner puberty stage, the higher the  
300 concentration of salt preferred. The associations of preferred salt concentration with sodium  
301 intake at 12 y and with pubertal stage were independent of each other and remained after  
302 adjustment for potential confounders.

303 Several explanations are posited for the intervention's lack of impact as the children grew  
304 and the age-related changes observed in their diet, particularly as they relate to sodium intake.  
305 We found that maternal counseling on what foods to avoid feeding their child (e.g., canned  
306 goods, fried foods, soft drinks, candies, salty snacks) and what foods to use in moderation (e.g.,  
307 salty foods) resulted in decreased intake of unprocessed and processed foods at 1 y, findings

308 consistent with prior reports on this cohort that maternal counseling increased breastfeeding rates  
309 and quality of the child's complementary diet at 1 y (13, 14) and increased intake of vegetables,  
310 fruits, and diet variety at 4 y (15). While the early intervention had no effect on diet quality at the  
311 8-y follow-up visit, children in the intervention group had healthier lipid profiles, suggesting an  
312 effect on metabolism from previous healthier diets (16). An important area for future research is  
313 whether an intervention that provides guidance for mothers on how to identify high-sodium  
314 foods and educates them on the effects of food processing would be more effective in the long  
315 term. Furthermore, even for those mothers who were able to implement the guidelines, the  
316 intervention did not provide subsidies for these low-income mothers to maintain healthy eating  
317 habits or guidelines for how to handle challenges that arise as children grow older (18, 30).

318         What toddlers eat reflects what caregivers choose to feed them and the types of foods  
319 available in the home. In our study, regardless of the intervention effect, at 1 y children from  
320 both groups consumed mostly unprocessed foods, such as beans, milk, fresh meats, grains, and  
321 vegetables, and ultra-processed foods such as cookies without filling, baby cereals, and flavored  
322 sweetened yogurts—foods made and marketed for children (31, 32). Mothers can influence what  
323 their children eat through purchasing and preparing food, setting rules about food and eating,  
324 acting as role models, and speaking about food with their children (33). However, as children  
325 grow, their experiences with food extend beyond the home environment, decreasing maternal  
326 influences (30), as evidenced herein by the significant changes in children's diets between 4 y  
327 and 8 y, when unprocessed foods began to be replaced by processed and ultra-processed foods,  
328 such as sweets and desserts, cookies, and sugar-sweetened beverages.

329         One of the primary outcomes of the present study was the independent effects of dietary  
330 sodium and stage of puberty on salt taste preference—a primary driver for intake (34). What

331 children were eating at 12 y and their pubertal stage of development together explained the  
332 variance in salt taste preference yet were independent of each other, and significance remained  
333 after adjustment for potential confounders, including birth weight, sex, maternal-reported race,  
334 and BMI-to-age Z scores. Overall, the higher the sodium intake or the earlier the puberty stage at  
335 12 y, the higher the concentration of saltiness most preferred. To our knowledge, this is the first  
336 study to measure the concentration of salt taste most preferred in Brazilian children. However,  
337 these findings are consistent with a body of research that revealed US children preferred  
338 solutions with higher salt content than did adults, with the adult-like preference patterns  
339 emerging during mid-adolescence and associated with biomarkers of growth (5, 23).

340         Although the causal mechanisms between dietary intake and taste preferences are not  
341 well understood, it is known that the most effective strategy to reduce the preference for sodium-  
342 rich foods is repeated exposure to foods with little or no added salt (35, 36). Conversely,  
343 increasing dietary salt intake increased the most preferred concentration of salt but only in  
344 individuals who had the salt added in meals; individuals who received supplemental salt in  
345 capsules showed no changes in their preferences (37). In our study, children whose sodium  
346 intake was in the  $\geq 75^{\text{th}}$  percentile at 12 y preferred significantly higher concentrations of salt, as  
347 did those in early puberty stages. Taken together, the data suggest that a shift in preference  
348 probably relates not only to biological underpinnings of puberty but also to children's current  
349 diet and thus current taste experiences with saltiness.

350         Several studies show similar dietary patterns in Brazilian children and adolescents,  
351 characterized by consumption of traditional foods, combined with a high prevalence of ultra-  
352 processed foods (12, 31, 38, 39) that are extremely attractive and relatively inexpensive and  
353 accessible (40). These taste experiences consolidate children's vulnerability to excess intakes as

354 they become more independent from the family and start purchasing and eating food outside the  
355 home and being influenced by people outside the family circle, such as their peers and media, as  
356 is quite common among schoolchildren and adolescents (41). This dietary pattern results in a  
357 nutritional profile rich in sodium, as well as energy, trans and saturated fats, and free sugars (39,  
358 42). The addition of salt to a food reduces bitterness and increases palatability (43) which  
359 contributes in part to excessive consumption and increased the risk of cardiovascular diseases,  
360 obesity, and other diet-related diseases (44). Thus, interventions to promote children's healthy  
361 eating should include community-level actions, such as nutritional education in schools and food  
362 marketing regulations, to soften the impact of the food environment, full of salt-rich processed  
363 and ultra-processed foods, as observed in Brazil (39), on children's natural preferences.

364         There were limitations in the present study. First, we did not measure biomarkers of  
365 growth rates, and pubertal development was self-assessed. However, a recent systematic review  
366 revealed that "self-assessment of puberty is most accurate when development is categorized as  
367 into prepubertal and completing puberty phases (45), as was done in the present study. Second,  
368 we did not obtain information from the mothers or children on the amount of salt added during  
369 food preparation or at the table. This information is relevant because, although the Brazilian  
370 population is gradually replacing unprocessed foods with ready-to- eat processed and ultra-  
371 processed foods (46), there is evidence that table salt remains the greatest contributor to dietary  
372 sodium intake (47). However, we should consider this evidence carefully, as the data were  
373 published more than a decade ago.

## 374 **Conclusions**

375         While there is unanimous agreement that increasing healthy dietary behaviors is the  
376 single most important aspect of reducing risks for preventable diseases, there is a paucity of

377 research on how to achieve this, especially as it relates to learning to like foods lower in  
378 saltiness. The present analysis, which focused on data from children whose mothers were  
379 enrolled in an infant feeding intervention study during the first year of postnatal life, indicates  
380 that to maintain effectiveness in the long-term, interventions to promote children's healthy eating  
381 must continue to be reinforced in and outside the home and combined with community-level  
382 actions, such as nutritional education in schools and food marketing regulations. In addition, our  
383 study results point to a relationship between physiological needs and the preference for saltier  
384 tastes in periods of greater growth, such as during puberty, which suggests that children and  
385 adolescents are highly vulnerable to excessive sodium consumption at this time. This, combined  
386 with the current food environment, rich in high-sodium processed and ultra-processed foods, plus  
387 the role of repeated exposures as children learn about and establish their food preferences (18),  
388 makes the development of strategies that effectively reduce sodium consumption in the long term  
389 a great challenge (6, 36). Thus, developing evidence-based strategies that promote healthy eating  
390 during the vulnerable periods of childhood and adolescence, when preferences are set, should be  
391 a public health investment priority.

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401 the manuscript. JAM supervised statistical analyses and co-drafted and revised the manuscript.  
402 MRV conceptualized and designed the trial, coordinated and supervised data collection, co-  
403 drafted and revised the manuscript and had primary responsibility for final content. All authors  
404 approved the final manuscript as submitted and agree to be accountable for all aspects of the  
405 work.

406 **Data Sharing:** Data described in the manuscript, code book, and analytic code will be made  
407 available upon request pending application and approval.

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<b>Table 1:</b> NOVA Food Classification System: Definition for unprocessed, processed and ultra-processed foods <sup>1</sup>	
Food Category	Definition
Unprocessed or minimally processed food	Natural foods or foods altered by processes such as drying, freezing, and pasteurization that do not add substances such as salt, sugar, oil, or fats to the original product.
Processed foods	Products made by adding sugars, oil, or salt to unprocessed or minimally processed foods, with the main purpose of increasing the durability of foods or to modify their sensory qualities (e.g., fresh unpacked breads; cheese; vegetables, fruits, and other plant foods preserved in brine or syrup).
Ultra-processed foods	Industrial formulations of substances not commonly used in culinary preparations and additives whose purpose is to imitate the sensory qualities of unprocessed or minimally processed foods or to disguise the undesirable sensory qualities of the final products (e.g., ready-to-drink milk-based beverages, ready-to-eat cakes, cookies, “instant” soups and noodles, ham, and sausages).
<sup>1</sup> Information from Monteiro et al., (19)	

1

<b>Table 2.</b> Subject characteristics at enrollment, end of trial (1y) and last visit (12 y) <sup>2</sup>			
Characteristic	Randomized Group		<i>p</i> -Value <sup>1</sup>
	Intervention	Control	
<i>Mothers</i> <sup>2</sup>	<i>n</i> = 176	<i>n</i> = 244	
Age at childbirth (y)	25.9 ± 0.5	25.7 ± 0.4	0.81
Education (y) <sup>3</sup>	6.6 ± 0.2	6.8 ± 0.2	0.41
Employment (paid) <sup>4</sup>	35.8% (58)	33.2% (76)	0.59
Family income < US\$300 <sup>5</sup>	75.6% (96)	67.1% (116)	0.11
Delivery by C-section <sup>6</sup>	35.1% (52)	41.6% (94)	0.23
<i>Children, at birth</i> <sup>2</sup>	<i>n</i> = 176	<i>n</i> = 244	
Sex (% girls)	44.3% (78)	44.3% (108)	0.99
Race (% white) <sup>7</sup>	40.7% (59)	45.0% (86)	0.43
Birth weight (kg) <sup>8</sup>	3.4 ± 0.1	3.3 ± 0.1	0.55
Birth length (cm) <sup>8</sup>	48.7 ± 0.1	48.8 ± 0.1	0.59
Gestational age at birth (weeks) <sup>9</sup>	39.4 ± 0.1	39.4 ± 0.1	0.98
<i>Children, 1 y</i>	<i>n</i> = 163	<i>n</i> = 234	
Sex (% girls)	42.9% (70)	43.8% (102)	0.87
Race (% white) <sup>10</sup>	41.1% (58)	45.0% (85)	0.47
Age (months)	12.6 ± 0.1	13.1 ± 0.1	0.42
Height-for-age Z score	-0.29 ± 0.08	-0.34 ± 0.07	0.64
BMI-for-age Z score	0.68 ± 0.08	0.58 ± 0.07	0.53
% with obesity <sup>11</sup>	3.1% (5)	2.1% (5)	0.56
<i>Children, 12 y</i>	<i>n</i> = 92	<i>n</i> = 121	
Sex (% girls)	42.4% (39)	39.7% (48)	0.69
Race (% white) <sup>12</sup>	39.1% (34)	45.0% (49)	0.41
Age (y)	12.4 ± 0.1	12.4 ± 0.1	0.82
Height-for-age Z score	0.19 ± 0.11	0.33 ± 0.08	0.38
BMI-for-age Z score	0.73 ± 0.14	0.62 ± 0.11	0.41
With obesity <sup>11</sup>	22.8% (21)	16.7% (20)	0.26
Values are % ( <i>n</i> ) or mean ± SEM.			
<sup>1</sup> Significant difference between groups (two-sample <i>t</i> -tests for continuous variables; chi-square tests for categorical variables).			
<sup>2</sup> Data collected at the 6-month visit.			
<sup>3</sup> Intervention group <i>n</i> = 175, due to missing data.			
<sup>4</sup> Intervention group <i>n</i> = 162, control group <i>n</i> = 229, due to missing data.			
<sup>5</sup> Intervention group <i>n</i> = 127, control group <i>n</i> = 173, due to missing data.			
<sup>6</sup> Intervention group <i>n</i> = 148, control group <i>n</i> = 226, due to missing data.			
<sup>7</sup> Intervention group <i>n</i> = 145, control group <i>n</i> = 191, due to missing data.			
<sup>8</sup> Control group <i>n</i> = 237, due to missing data.			
<sup>9</sup> Intervention group <i>n</i> = 167, control group <i>n</i> = 230, due to missing data.			
<sup>10</sup> Intervention group <i>n</i> = 141, control group <i>n</i> = 189, due to missing data.			
<sup>11</sup> BMI-for-age Z score >3 at 1 y and >2 at 12 y [BMI Categories from the World Health Organization (27)].			
<sup>12</sup> Intervention group <i>n</i> = 87, control group <i>n</i> = 109, due to missing data.			

**Table 3.** Intervention effect on dietary intake of unprocessed, processed, and ultra-processed foods by randomized group assignment at 1, 4, 8, and 12 y.

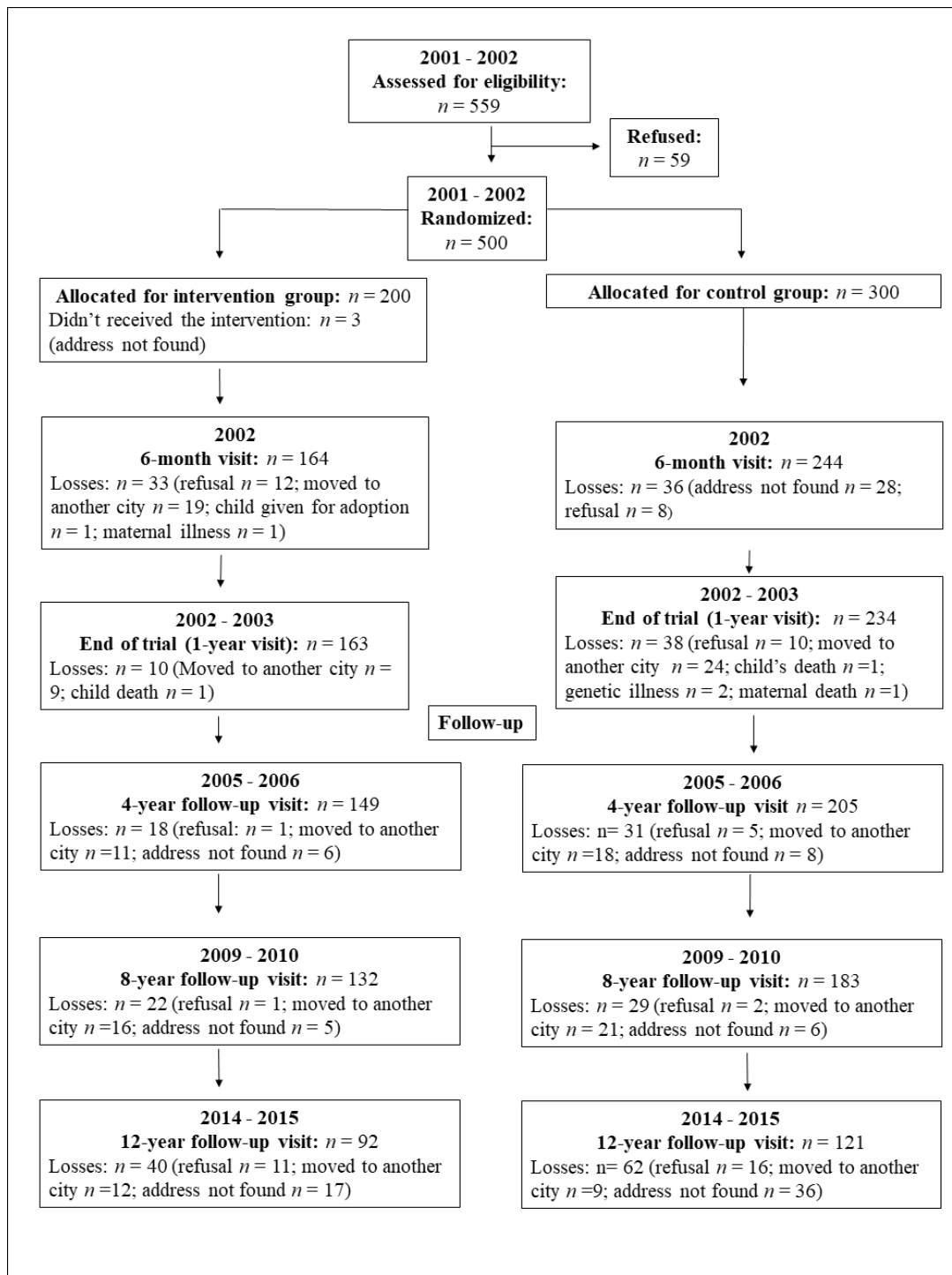
	<b>Unprocessed foods</b>			<b>Processed foods</b>			<b>Ultra-processed foods</b>		
Intake	Intervention	Control	<i>p</i> -Value <sup>1</sup>	Intervention	Control	<i>p</i> -Value <sup>1</sup>	Intervention	Control	<i>p</i> -Value <sup>1</sup>
<b>Age 1 y</b>	<i>n</i> = 154	<i>n</i> = 216		<i>n</i> = 154	<i>n</i> = 216		<i>n</i> = 154	<i>n</i> = 216	
Energy (kcal/d)	651 ± 26	724 ± 23	0.04	43 ± 511	54 ± 4	0.02	166 ± 12	205 ± 13	0.04
Energy (kcal/kg/d)	66 ± 3	73 ± 2	0.03	4 ± 1	5 ± 1	0.03	17 ± 1	21 ± 1	0.04
Sodium (mg/d) <sup>2</sup>	338 ± 17	374 ± 16	0.19	72 ± 8	79 ± 7	0.08	233 ± 26	300 ± 29	0.08
Sodium (mg/1000kcal/d) <sup>2</sup>	390 ± 17	368 ± 12	0.49	94 ± 12	84 ± 7	0.57	270 ± 31	306 ± 30	0.32
Top 5 foods	Beans			Bread <sup>3</sup>			Cookies <sup>5</sup>		
	Cow milk			Canned fruit and jam			Baby cereal <sup>6</sup>		
	Fresh meats			Cheese			Flavored sweetened yogurt		
	Grains and tubers			Salty canned foods <sup>4</sup>			Instant flavored powder drink		
	Vegetables			Died meat			Chocolate powder		
<b>Age 4 y</b>	<i>n</i> = 135	<i>n</i> = 187		<i>n</i> = 135	<i>n</i> = 187		<i>n</i> = 135	<i>n</i> = 187	
Energy (kcal/d)	861 ± 25	858 ± 22	0.87	110 ± 9	103 ± 7	0.42	516 ± 23	566 ± 21	0.14
Energy (kcal/kg/d)	51 ± 2	52 ± 1	0.60	7 ± 1	6 ± 1	0.67	30 ± 1	34 ± 1	0.14
Sodium (mg/d) <sup>2</sup>	486 ± 21	502 ± 19	0.42	175 ± 16	199 ± 16	0.76	571 ± 52	614 ± 44	0.29
Sodium (mg/1000kcal/d) <sup>2</sup>	326 ± 12	332 ± 11	0.93	118 ± 11	131 ± 11	0.89	375 ± 35	411 ± 32	0.29
Top 5 foods	Cow milk			Bread <sup>3</sup>			Sweets and desserts <sup>7</sup>		
	Fresh meats			Cheese			Chocolate powder		
	Grains and tubers			Canned fruit and jam			Instant flavored powder drink		
	Beans			Salty canned foods <sup>4</sup>			Cookies <sup>5</sup>		

	Vegetables			Dried meat			Carbonated soft drinks		
<b>Age 8 y</b>	<i>n</i> = 129	<i>n</i> = 176		<i>n</i> = 129	<i>n</i> = 176		<i>n</i> = 129	<i>n</i> = 176	
Energy (kcal/d)	779 ± 25	772 ± 22	0.84	110 ± 8	111 ± 7	0.77	672 ± 29	675 ± 22	0.49
Energy (kcal/kg/d)	29 ± 1	30 ± 1	0.41	4 ± 1	5 ± 1	0.48	25 ± 1	26 ± 1	0.33
Sodium (mg/d) <sup>2</sup>	390 ± 16	395 ± 13	0.65	546 ± 20	394 ± 16	0.16	711 ± 46	680 ± 37	0.97
Sodium (mg/1000kcal/d) <sup>2</sup>	256 ± 10	261 ± 8	0.78	295 ± 12	258 ± 10	0.17	443 ± 26	428 ± 19	0.89
Top 5 foods	Cow milk			Bread <sup>3</sup>			Sweets and desserts <sup>7</sup>		
	Fresh meats			Cheese			Ultra-processed meats <sup>8</sup>		
	Grains and tubers			Salty canned foods <sup>4</sup>			Cookies <sup>5</sup>		
	Beans			Canned fruit and jam			Carbonated soft drinks		
	Vegetables			Dried meat			Instant flavored powder drink		
<b>Age 12 y</b>	<i>n</i> = 89	<i>n</i> = 111		<i>n</i> = 89	<i>n</i> = 111		<i>n</i> = 89	<i>n</i> = 111	
Energy (kcal/d)	857 ± 38	858 ± 33	0.28	201 ± 14	236 ± 17	0.28	675 ± 41	682 ± 38	0.69
Energy (kcal/kg/d)	19 ± 1	17 ± 1	0.38	4 ± 1	5 ± 1	0.29	15 ± 1	15 ± 1	0.77
Sodium (mg/d) <sup>2</sup>	391 ± 19	390 ± 21	0.46	622 ± 37	675 ± 38	0.41	727 ± 49	831 ± 63	0.49
Sodium (mg/1000kcal/d) <sup>2</sup>	239 ± 11	237 ± 11	0.59	362 ± 17	388 ± 19	0.58	412 ± 24	474 ± 36	0.60
Top 5 foods	Fresh meats			Bread <sup>3</sup>			Ultra-processed meats <sup>8</sup>		
	Grains and tubers			Cheese			Instant flavored powder drink		
	Cow milk			Canned fruit and jam			Carbonated soft drinks		
	Beans			Salty canned foods <sup>4</sup>			Sweets and desserts <sup>7</sup>		
	Vegetables			Dried meat			Mayonnaise, margarine, and sauces		
Values are mean ± SEM. Dietary intake was assessed by the 24-hour diet recall method									

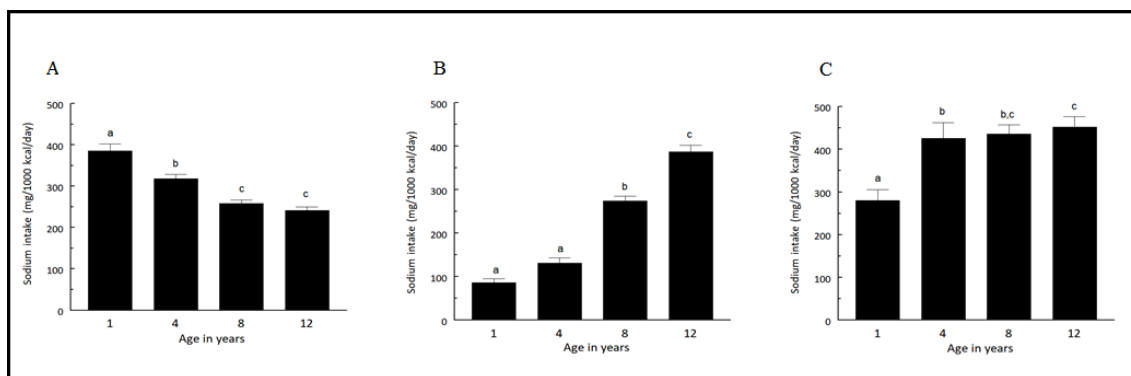
- <sup>1</sup> Significant difference between age (Mann-Whitney *U*-test).
- <sup>2</sup> Total sodium does not include salt added to food during cooking or at the table.
- <sup>3</sup> Bread includes breads made with only flour, water, salt and yeast, bought ready to eat
- <sup>4</sup> Salty canned foods include canned corn, peas, pickles, tuna, and sardines.
- <sup>5</sup> Cookies include any kind of industrially produced sweet, savory, or filled biscuit.
- <sup>6</sup> Baby cereal includes industrially produced cereal-based powder products usually added to milk.
- <sup>7</sup> Sweets and desserts include chocolate, candy, gum, ice cream, popsicles, and other sweet treats.
- <sup>8</sup> Ultra-processed meats include sausages, ham, bologna, chicken nuggets, and other processed meats.

<b>Table 4.</b> Multivariate models			
Predictor	$\beta \pm \text{SEM}$	95% CI	<i>p</i> -Value
<b>Model 1:</b> All confounders defined a priori, plus statistically significant variables from the bivariate analysis associated with the most preferred concentration of salt.			
Birth weight (kg)	0.67 $\pm$ 0.23	-0.39, 0.54	0.75
Skin color (white vs. not white)	0.04 $\pm$ 0.19	-0.35, 0.43	0.83
BMI-for-age Z score at 12 y	-0.03 $\pm$ 0.08	-0.18, 0.12	0.79
Tanner stage (1–3 vs. 4-5) <sup>1</sup>	0.41 $\pm$ 0.19	0.03, 0.79	<b>0.04</b>
Sodium intake from unprocessed, processed, and ultra-processed foods ( $\geq 75^{\text{th}}$ percentile vs. $< 75^{\text{th}}$ percentile)			
At 1 y	-0.36 $\pm$ 0.23	-0.82, 0.10	0.12
At 12 y <sup>1</sup>	0.50 $\pm$ 0.23	0.05, 0.95	<b>0.03</b>
<b>Model 2:</b> Only the statistically significant variables from Model 1			
Tanner stage (1–3 vs. 4-5) <sup>2</sup>	0.44 $\pm$ 0.19	0.06, 0.82	<b>0.02</b>
Sodium intake from unprocessed, processed, and ultra-processed at 12 y ( $\geq 75^{\text{th}}$ percentile vs. $< 75^{\text{th}}$ percentile) <sup>2</sup>	0.54 $\pm$ 0.21	0.13, 0.95	<b>0.01</b>
<p><math>\beta</math>: regression coefficient represents the mean difference (<math>\pm</math> SEM) of the most preferred concentration of salt according to variation of the independent predictor variable.</p> <p><sup>1</sup>Pearson correlation between sodium intake groups and Tanner stage groups = -0.07, <i>p</i> = 0.21</p> <p><sup>2</sup>Pearson correlation between sodium intake groups and Tanner stage groups = -0.01, <i>p</i> = 0.42.</p>			

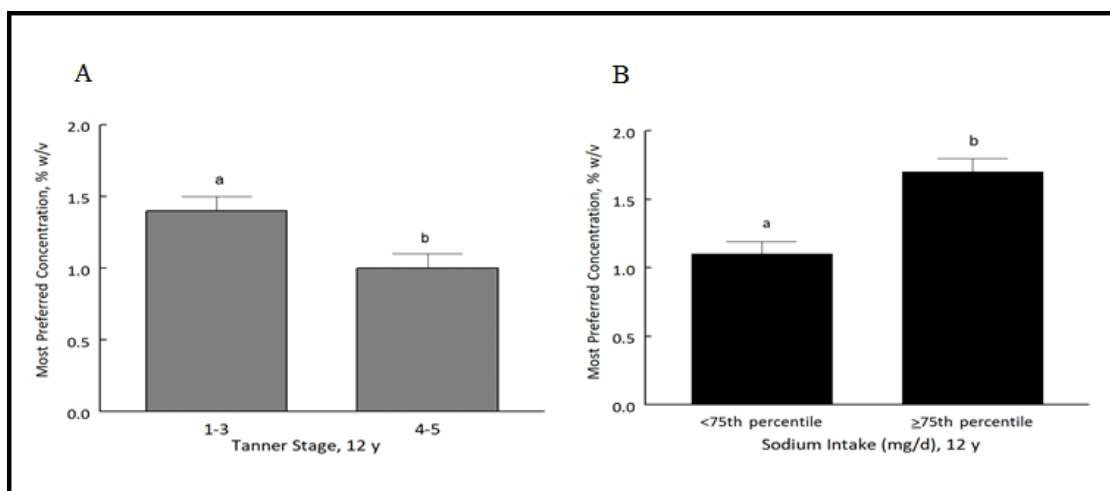
**Figure 1.** Profile of the randomized controlled trial from recruitment of mother–child pairs (2001–2) during the early postnatal period through assessment at the 12-y follow-up visit.



**Figure 2.** Age-related changes in sodium intake (mg/1000 kcal/d) from unprocessed foods (A), processed foods (B), and ultra-processed foods (C). Different letters represent significant differences at  $p < 0.05$ . Mean  $\pm$  SEM, repeated measures Friedman tests; significant effects were further examined with post-hoc paired t-tests with Bonferroni correction.



**Figure 3.** Main effects of pubertal development (A; Tanner stages 1–3 vs. 4–5;  $p = 0.04$ ) and sodium intake from unprocessed, processed, and ultra-processed foods combined (B;  $<75^{\text{th}}$  percentile vs.  $\geq 75^{\text{th}}$  percentile;  $p = 0.03$ ) on most preferred salt concentration. Mean  $\pm$  SEM; multivariate linear regression, Model 2. Different letters indicate significant differences at  $p < 0.05$ .



## Anexo 3 – Aprovações pelos Comitês de Ética em Pesquisa





## COMISSÃO CIENTÍFICA E COMISSÃO DE PESQUISA E ÉTICA EM SAÚDE

COMITÊ DE ÉTICA EM PESQUISA - CEP  
UFCSPA

O Comitê de Ética em Pesquisa da UFCSPA, registrado na Comissão Nacional de Ética em Pesquisa (CONEP) sob o nº 075/05 em 23/07/04, analisou o Projeto:

**Projeto:** 11-748

**Versão do Projeto:**

**Versão do TCLE:**

**Pesquisadores:**

MÁRCIA REGINA VITOLO

CARLOS ALBERTO FELDENS

**Título:** IMPACTO DE INTERVENÇÃO NA ATENÇÃO PRIMÁRIA À SAÚDE NAS CONDIÇÕES NUTRICIONAIS DE CRIANÇAS EM IDADE PRÉ-ESCOLAR: SEGUNDA FASE DE AVALIAÇÃO DE ENSAIO DE CAMPO RANDOMIZADO POR CONGLOMERADOS

Esse projeto foi aprovado em seus aspectos éticos e metodológicos conforme as Resoluções 196/09 e demais Resoluções complementares. Toda e qualquer alteração do projeto, assim como eventos adversos graves, deverão ser comunicados a este CEP. Os TCLE, quando necessários, somente poderão ser utilizados após prévia e explícita aprovação (carimbo) de sua redação por este CEP\*.

Porto Alegre, 06 de maio de 2011.



José Geraldo Vernal Fabris  
Coordenador do CEP/UFCSPA

UNIVERSIDADE FEDERAL DE  
CIÊNCIAS DA SAÚDE DE  
PORTO ALEGRE



**PARECER CONSUBSTANCIADO DO CEP**

**DADOS DO PROJETO DE PESQUISA**

**Título da Pesquisa:** Impacto nas condições nutricionais e de saúde de crianças na idade de 6 e 7 anos que participaram de um ensaio de campo randomizado por conglomerados no primeiro ano de vida

**Pesquisador:** Marcia Regina Vitolo

**Área Temática:**

**Versão:** 1

**CAAE:** 30741714.7.0000.5345

**Instituição Proponente:** Universidade Federal de Ciências da Saúde de Porto Alegre

**Patrocinador Principal:** Conselho Nacional de Desenvolvimento Científico e Tecnológico

**DADOS DO PARECER**

**Número do Parecer:** 689.696

**Data da Relatoria:** 12/06/2014

**Apresentação do Projeto:**

O presente estudo é continuidade de um projeto (471-07 e nº 748/11 Comitê de Ética e Pesquisa da UFCSPA) desenvolvido para avaliar o impacto de atualização de profissionais da atenção primária à saúde em relação ao guia alimentar "Dez passos para uma alimentação saudável para crianças brasileiras menores de dois anos" nas condições nutricionais e de saúde de crianças avaliadas por unidades de saúde da cidade de Porto Alegre.

O mesmo visa estudar se existe impacto da atualização para profissionais da atenção primária em relação às práticas alimentares no primeiro ano de vida (realizado no estudo anterior) nas condições de nutrição e saúde de crianças na idade escolar e os fatores de risco para obesidade, anemia, dislipidemias e alterações metabólicas.

Para isso, crianças na idade de 6-7 anos receberão visitas domiciliares. Os dados antropométricos e dietéticos serão coletados por estudantes de graduação e pós-graduação da Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA) por meio de questionário abordando fatores familiares, antropométricos e dietéticos. Os entrevistadores não terão conhecimento do grupo no qual as crianças pertenceram (intervenção ou controle) e serão previamente treinados para coleta de dados. Será realizada confirmação dos dados coletados em 5% da amostra por telefone. Será realizada análise de amostras de sangue na Universidade Federal de Ciências da

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Continuação do Parecer: 808.599

Saúde de Porto Alegre (UFCSPA). O deslocamento das mães e crianças, em grupos, será realizado por meio de serviço terceirizado de transporte.

**Objetivo da Pesquisa:**

Avaliar o impacto de uma atualização para profissionais de atenção primária em relação às práticas alimentares no primeiro ano de vida nas condições de nutrição e saúde de crianças na idade escolar e os fatores de risco para obesidade, anemia, dislipidemias e alterações metabólicas.

**Avaliação dos Riscos e Benefícios:**

A nível individual, as crianças terão os resultados de todos os exames e serão encaminhadas ao posto de saúde se necessário. Os resultados dessa pesquisa poderão subsidiar políticas públicas de alimentação e nutrição, sobretudo da população infantil de baixa renda.

Os riscos são pequenos e envolvem a realização de punção venosa na fossa cúbica. Os autores não descrevem os potenciais riscos de equimoses, dor local etc.

**Comentários e Considerações sobre a Pesquisa:**

É um estudo relevante que poderá auxiliar em políticas públicas de alimentação e nutrição na população infantil. O mesmo apresenta objetivos e metodologia claros. O mesmo foi contemplado com o Edital do Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ) N° 14/2013-47731/2013-8.

**Considerações sobre os Termos de apresentação obrigatória:**

As mudanças solicitadas no termo de consentimento livre e esclarecido foram atendidas.

Os pesquisadores justificaram a falta de anuência da Secretaria Municipal de Saúde uma vez que o projeto não será realizado nas Unidades Básicas de Saúde e sim por visitas domiciliares.

**Recomendações:**

As sugestões foram atendidas.

**Conclusões ou Pendências e Lista de Inadequações:**

Parecer favorável a aprovação.

**Situação do Parecer:**

Aprovado

**Necessita Apreciação da CONEP:**

Não

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Bairro:

CEP: 91.503-170

UF: RS

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Contribuição do Paciente: 600,000

**Considerações Finais a critério do CEP:**

Término do projeto 05/2015.

De acordo com o parecer do Relator.

PORTO ALEGRE, 17 de Junho de 2014

Assinado por:  
José Geraldo Vernet Taborda  
(Coordenador)

Júlia S. Pereira Lima  
Vice-Coordenadora CEP/UFSCPA.

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PRÓ-REITORIA DE PESQUISA **PROPESQ**

**COMITÊ DE ÉTICA EM PESQUISA**

### **RESOLUÇÃO**

O Comitê de Ética em Pesquisa da Universidade Federal do Rio Grande do Sul analisou o projeto:

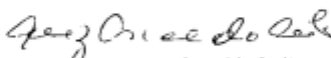
**Número:**200245

**Título:** Implementação e Avaliação do Impacto do Programa de Promoção para a Alimentação Saudável para crianças menores de dois anos

**Investigador principal:** Márcia Regina Vitolo(UNISINOS)

- O mesmo foi aprovado em reunião realizada dia 11.04.2002, por estar adequado ética e metodologicamente e de acordo com a Resolução 196/96 do Conselho Nacional de Saúde. **O investigador deverá encaminhar relatórios semestrais sobre o andamento do Projeto.**

Porto Alegre, 12 de abril de 2002.

  
Prof. Luiz Osvaldo Leite  
Coordenador CEP/UFRGS



MINISTÉRIO DA EDUCAÇÃO  
FUNDAÇÃO FACULDADE FEDERAL DE CIÊNCIAS MÉDICAS DE PORTO ALEGRE  
COMITÊ DE ÉTICA EM PESQUISA  
APROVADO PELA CARTA Nº 880/2004-CONEP/CNS/MS  
RUA SARMENTO LUIZ, 243 – FONE: (51) 3224.8822  
CEP 90050-170 – PORTO ALEGRE – RS - cep@fffcempa.ufrpe.br

Of. 160/06-CEP

Porto Alegre, 12 de janeiro de 2006.

Ilma. Sra.

Profa. Márcia Regina Vitolo

Nesta Faculdade

Prezada Senhora

Informamos que seu projeto "Investigação dos fatores de risco para obesidade precoce e anemia em uma coorte de crianças submetidas a um programa de intervenção nutricional no primeiro ano de vida.", Processo nº 061/05, foi avaliado pelo Comitê de Ética em Pesquisa, na reunião de 12 de janeiro de 2006, sendo o projeto aprovado, conforme parecer consubstanciado nº 122-06, em anexo.

Outrossim informamos que de acordo com o Art. 4º, letra c, do Regulamento do CEP, V. Sa. deverá nos encaminhar relatórios semestrais do desenvolvimento do projeto.

Atenciosamente,

  
Prof. José Geraldo Vernet Faborda  
Coordenador do CEP/FFFCMPA

Katya Vianna Rigatto  
Membro do Depto. de Ciências  
Médicas - FFCMPA



## COMISSÃO CIENTÍFICA E COMISSÃO DE PESQUISA E ÉTICA EM SAÚDE

COMITÊ DE ÉTICA EM PESQUISA - CEP  
UFCSPA

O Comitê de Ética em Pesquisa da UFCSPA, registrado na Comissão Nacional de Ética em Pesquisa (CONEP) sob o nº 075/05 em 23/07/04, analisou o Projeto:

**Projeto:** 09-479

**Versão do Projeto:**

**Versão do TCLE:**

**Pesquisadores:**

MÁRCIA REGINA VITOLO

CÍNTIA MENDES GAMA

PAULA DAL BÔ CAMPAGNOLO

**Título:** IMPACTO DE UM PROGRAMA DE INTERVENÇÃO  
NUTRICIONAL NO PRIMEIRO ANO DE VIDA EM CRIANÇAS  
COM IDADE ESCOLAR.

Esse projeto foi aprovado em seus aspectos éticos e metodológicos conforme as Resoluções 196/09 e demais Resoluções complementares. Toda e qualquer alteração do projeto, assim como eventos adversos graves, deverão ser comunicados a este CEP. Os TCLE, quando necessários, somente poderão ser utilizados após prévia e explícita aprovação (carimbo) de sua redação por este CEP.

Porto Alegre, 19 de junho de 2009.



José Geraldo Vermet Taborda  
Coordenador