Universidade de São Paulo

Faculdade de Saúde Pública

Dieta, excesso de peso e puberdade em adolescentes chilenos

Ángela Martínez Arroyo

Tese apresentada ao Programa de Pós-graduação em Nutrição em Saúde Pública para obtenção do título de Doutor em Ciências.

Área de concentração: Nutrição em Saúde Pública

Orientador: Profa. Assoc. Regina Mara Fisberg

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“O correr da vida embrulha tudo.

A vida é assim: esquenta e esfria,

aperta e daí afrouxa,

sossega e depois desinquieta.

O que ela quer da gente é coragem”.

“Vivendo, se aprende;

mas o que se aprende, mais,

é só a fazer outras maiores perguntas”.

Grande Sertão: Veredas

Guimarães Rosa

RESUMO

Introdução: A obesidade é um problema de saúde pública e tem sido associada ao início da puberdade, no entanto, há controvérsia sobre a consistência e plausibilidade biológica dessa associação. Alguns nutrientes e grupos de alimentos tais como proteínas de origem animal, laticínios e bebidas adoçadas têm sido associados à puberdade precoce, enquanto proteínas origem vegetal, com puberdade tardia. Entretanto, a dieta é fenômeno complexo porque alimentos não são consumidos isoladamente; sendo importante avaliar a dieta de forma global. **Objetivo:** Investigar a relação entre dieta, estado nutricional e início da puberdade em adolescentes chilenos. **Metodologia:** Foram utilizados dados secundários de adolescentes de ambos sexos (idade média: 12.5 anos) do *Growth and Obesity Cohort Study*, de Santiago, Chile, avaliados durante os anos 2014-2015. Dados sociodemográficos, aferições antropométricas (peso, estatura), avaliação puberal (estágio de Tanner, idade do início da menarca) e recordatório alimentar de 24 horas (R24h); foram utilizados para o presente estudo. Do total de 1196 participantes da coorte, 882 adolescentes tinham dados de consumo alimentar e medidas antropométricas; desses, 270 meninas apresentaram dados prospectivos de dieta antes do início da menarca. Alimentos provenientes do R24h, foram classificados em grupos de alimentos segundo suas características nutricionais, cultura alimentar e corrigidos pela variância intrapessoal da ingestão por procedimentos estatísticos da plataforma online *Multiple Source Method*. Os padrões da dieta foram identificados por análise fatorial exploratória. O relato implausível de energia foi categorizado como sub-relatores, plausível e super-relatores, e como porcentagem para o ajuste dos modelos de regressão múltipla. Regressão logística múltipla foi usada para identificar fatores associados e impacto do subrelato em nutrientes e grupos de alimentos (manuscrito 1) e associação entre padrões da dieta e excesso de peso (manuscrito 2). A associação longitudinal entre padrões de dieta e tempo até início

da menarca foi verificada por meio da análise de regressão de Cox (manuscrito 3). Todas as análises foram realizadas com um nível de confiança do 95%. **Resultados:** A frequência de adolescentes sub-relatores, plausíveis e super-relatores foi 50.7%, 40.5% e 8.8%, respectivamente; sendo maior em adolescentes com excesso de peso e meninos. A prevalência de excesso de peso do GOCS foi 51.6%. Quatro padrões foram identificados explicando 24.9% da variabilidade da dieta. *"Breakfast/Once"* e *"Meats and Vegetables"* foram associados com maior ingesta de sódio, *"Western"* com gordura saturada e *"Sweet Snack"* com açúcar de adição ($p<0.05$). Adolescentes com maior aderência (terceiro tercil) aos padrões *"Western"* e *"Sweet Snack"* apresentaram maior chance de ter excesso de peso (OR=1.67; IC95%:1.103-2.522 e OR=1.86; IC95%:1.235-2.792; respectivamente) quando comparado aqueles com menor aderência (primeiro tercil); o padrão *"Meats & Vegetables"* também foi associado positivamente ao excesso de peso (OR=1.83; IC 95%: 1.219-2.754). Em adolescentes do sexo feminino foram identificados três *padrões "Breakfast/Once, "Prudent*" e *"Western";* explicando 19.4% da variabilidade da dieta. Meninas com excesso de peso e que aderiram mais ao padrão *"Prudent"* (terceiro tercil) tinham 55% menor risco de apresentar uma idade de menarca precoce (HR=0.51; IC95%:0.31-0.85) quando comparado àquelas com menor aderência (primeiro tercil). **Conclusões:** Padrões de dieta identificados revelaram uma baixa qualidade da dieta e foram associados ao excesso de peso, nas análises transversais. Nas análises longitudinais, o padrão *"Prudent"* associou-se com um menor risco de idade da menarca precoce, em meninas com excesso de peso. Esperamos que esses achados fomentem futuras pesquisas e auxiliem as atuais políticas de saúde publica no Chile.

Palavras-chaves: excesso de peso, menarca, adolescentes, padrões de dieta.

ABSTRACT

Introduction: Obesity, a public health problem, has been associated with the early onset of puberty; however, there is controversy about the consistency and biological plausibility of this association. Some specific nutrients and food groups have been associated with puberty such as vegetable proteins, milk, sugar-sweetened beverages have been associated with an early onset puberty and animal proteins with late onset puberty. However, foods or nutrients are not consumed in isolation, and it is important to evaluate the overall diet. **Objective:** To investigate the relationship between diet, nutritional status and onset of puberty in Chilean adolescents. **Methodology:** Secondary data were used of adolescents of both sexes (mean age: 12.5 years) from the Growth and Obesity Cohort Study (GOCS) of Santiago, Chile, evaluated between 2014-2015. Sociodemographic data, anthropometric measurements (weight, height), pubertal evaluation (tanner stage, age at menarche) and 24-hour dietary recall (24HR) were used to the present study. From a total of 1.196 adolescents of the cohort, 882 adolescents had food consumption data and anthropometric measurements, from this number, 270 girls have prospective dietary data before onset of menarche. Foods from 24HR were classified into food groups according to their nutritional characteristics, feeding culture and corrected by intrapersonal variance intake by statistical procedures of Multiple Source Method´s online platform. Dietary patterns were identified by exploratory factor analysis. Misreporting was categorized as under-reporting, plausible and over-reporting estimated and as percentage to models adjustment. Multiple logistic regression was used to relate under-reporting and their associated factors (manuscript 1). The association between dietary patterns and overweight was verified by logistic regression models (manuscript 2). The longitudinal association between dietary patterns and time to age at menarche was verified by Cox regression analysis (manuscript 3). All analyzes were performed with a 95% confidence

level. **Results:** The frequencies of under-reporting, plausible and over-reporting adolescents were 50.7%, 40.5% and 8.8%; respectively, being higher in overweight and boys. The prevalence of overweight on GOCS was 51.6%. Four patterns were identified, explaining 24.9% of dietary variability. "Breakfast/*Once*" and "Meats and Vegetables" were associated with higher sodium intake, "Western" with saturated fat and "Sweet Snack" with added sugar ($p<0.05$). Adolescents with higher (third tertile) adherence to "Western" and "Sweet Snack" patterns had higher odds of being classified as overweight (OR=1.67; 95% CI:1.103-2.522 and OR=1.86; 95% CI:1.235-2.792 respectively) when compared to those of lower adherence (first tertile); "Meats and Vegetables" pattern was also associated with overweight (OR=1.83; 95% CI:1.219-2.754). In girls, three patterns were identified: "Breakfast/*Once*", "Prudent" and "Western"; explaining 19.4% of dietary variability. Girls with excess weight had a higher adherence to "Prudent" pattern had a later age at menarche compared to those with lower adherence (HR=0.51; IC95%: 0.31-0.85). **Conclusions:** Identified dietary patterns showed poor diet quality that were associated to excess weight on cross-sectional analyzes. Longitudinal analyze of the "Prudent" pattern was associated with a later age at menarche on girls with excess weight. Hopefully, these findings may incentive future researches and help current public health policies in Chile.

Key words: excess weight, menarche, adolescents, dietary patterns.

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LISTA DE ABREVIATURAS

AC, Analise Clusters

ACP, Analise componentes principais

AFE, Analise fatorial exploratoria

AMPM, Automated Multiple Source Method

CC, Circunferência cintura

DCNT, doenças crônicas não transmissíveis

DP desvio padrão

ENCA, *Encuesta Nacional de Consumo Alimentario*

GnRH hormônio liberador de gonadotrofina

GOCS Growth and obesity cohort study

HHG, hipotálamo hipófise gonadal

HR, Hazard Ratio

IC , Intervalo de confiança

IE, Ingesta Energetica

IGF-1, Insulin growth factor

IMC, Indice de massa corporal

INTA, *Instituto Nacional de Tecnologia de los Alimentos*

IOM, *Institute of medicine*

JUNAEB, *Junta Nacional de Auxilio Escolar y Becas*

MSM, *Multiple Source Method*

NDSR, *Nutrition Data Sistem Research*

NEE, Necessidade energética estimada

NHANES, *National Health and Nutrition Examination Survey*

OMS, Organização Mundial da Saúde

OR, Odds ratio

R24h, Recordatório 24 horas

RR, Risco relativo

RRR, Reduction Rank Regression

SHBG, Sex hormone binding globulin

USDA, *United State department agriculture*

APRESENTAÇÃO

A tese está estruturada em formato de artigo científico, conforme as diretrizes aprovadas na 9a. Sessão da Comissão da Pós-graduação da Faculdade de Saúde Pública, em 05 de junho de 2008, e segue as normas estabelecidas pela Guia de Apresentação de Teses elaborada pela Instituição.

A tese está organizada nas seguintes seções: (1) *Introdução*, que aborda o referencial teórico do presente trabalho; (2) *Justificativa,* que discorre sobre a relevância do trabalho e as possíveis contribuições para o conhecimento científico; (3) *Objetivos*, no qual são expostos os propósitos do estudo; (4) *Metodologia*, que comtempla os procedimentos, técnicas e instrumentos utilizados na coleta, bem como o processamento e análise dos dados; (5) *Resultados e Discussão*, que incluem os manuscritos elaborados; (6) *Considerações finais*, que apresenta a síntese dos principais resultados do estudo.

O primeiro manuscrito intitulado "*Misreporting of energy intake and factors associated among adolescents from the Growth and Obesity Chilean Cohort Study (GOCS)"* foi submetido no periódico *Journal of Adolescents Health*. O segundo manuscrito intitulado *"Dietary patterns among Chilean adolescents from the Growth and Obesity Cohort Study indicate poor dietary quality"* foi submetido ao *periódico Jornal Nutrition Research.* Já o terceiro manuscrito intitulado *"Prudent pattern is associated to age at menarche in adolescents with excess weight from Growth and Obesity Cohort Study"* será submetido*,* após da avaliação da banca examinador.

1 INTRODUÇÃO

A Organização Mundial da Saúde (OMS) define a adolescência como a idade entre 10 e 19 anos, sendo uma das etapas mais importantes de transição na vida do ser humano. Esta é caracterizada por uma taxa acelerada de crescimento, mudanças biológicas, psicológicas e sociais (PATTON et al., 2016; WHO, 2019). Determinantes biológicos da adolescência são praticamente universais, no entanto, a duração e as características desse período podem variar ao longo do tempo, dependendo do contexto socioeconômico e cultural (WHO, 2019).

A primeira etapa da adolescência se inicia com uma fase de crescimento e maturação dos sistemas reprodutivo, músculo esquelético, neurológico, endócrino, imunológico e cardiometabólico, e se estende até a terceira década de vida (PATTON e VINER, 2007). Por essa razão, a adolescência pode ser considerada uma fase sensível, durante a qual fatores físicos, nutricionais e sociais podem alterar as condições de saúde e desenvolvimento para a vida adulta e descendência (PATTON et al., 2018; PATTON et al., 2016; PRENTICE et al., 2013).

1.1 EPIDEMIOLOGIA DO EXCESSO DE PESO NA ADOLESCÊNCIA

Uma nutrição adequada é um fator determinante para alcançar o pleno potencial de crescimento. Apesar das taxas de baixo peso ainda serem preocupantes em alguns países do mundo, o incremento das prevalências de sobrepeso e obesidade na infância e adolescência se tornaram um problema de saúde pública (PATTON et al., 2018). Estima-se que, entre 42,5 e 51,8 milhões de crianças e adolescentes (0-18 anos) na América Latina apresentem sobrepeso ou obesidade, o que representa 20 a 25% da população total desse grupo etário na região (RIVERA et al., 2014).

No Chile, a situação é ainda mais grave. Segundo o último *Encuesta Nacional de Salud* (ENS) a prevalência de excesso de peso dos adolescentes entre 15 e 19 anos é 40,8% (ENS, 2017). Entre os anos 2009 e 2018, a prevalência de obesidade em adolescentes do primeiro ano do ensino fundamental de escolas públicas aumentou de 8,7% para 14,7%, e a prevalência de sobrepeso, de 26,6% para 31,7 %, respectivamente (JUNAEB, 2013).

Esse cenário é preocupante, tendo em vista que a obesidade pode gerar efeitos adversos à saúde, inclusive anular o aumento da expectativa de vida gerada por muitos avanços em saúde (WHO, 2016). A curto prazo, adolescentes obesos apresentam problemas comportamentais, emocionais, além de dificuldades na socialização com seus colegas, o que pode reduzir seu desempenho escolar (REILLY et al., 2003; HAN et al., 2010). Além disso, há evidências suficientes de que o excesso de peso está associado ao maior risco de desenvolver alterações cardiometabólicas, tais como dislipidemia, pressão arterial elevada, hiperglicemia e hiperinsulinemia (HAN et al., 2010; BERENSON, 2012; FRIEDEMANN et al., 2012) . A presença de fatores de risco cardiovascular na infância e adolescência pode gerar complicações médicas tanto nessa fase da vida, como também durante a vida adulta como diabetes *mellitus* tipo 2, hipertensão arterial, dislipidemia e acidente vascular cerebral (JUONALA et al., 2011; BERENSON, 2012; FRIEDEMANN et al., 2012; HEROUVI et al., 2013), que são as principais causas mundiais de mortalidade e de anos de vida perdidos ou vividos com incapacidade (WANG et al., 2016).

1.2 PADRÕES DE DIETA E EXCESSO DE PESO

Frequentemente, os estudos que avaliam dieta têm associado a ingestão de nutrientes ou determinados grupos de alimentos com alguns fatores de risco para doenças crônicas não transmissíveis (DCNT). No entanto, essa abordagem é considerada reducionista, pois não leva em

consideração o efeito global da dieta e seu impacto na carga atual dessas doenças (HU, 2002; FISBERG, 2015). A análise de padrões de dieta tornou-se uma abordagem alternativa e complementar para o estudo da relação entre desfechos de saúde-doença (KANT, 2004; MICHELS e SCHULZE, 2005; USDA, 2014; GLEASON et al., 2015). Conceitualmente, padrões de dieta representam uma visão global do consumo de alimentos e nutrientes e, portanto, podem ser mais preditivos do risco de doenças quando comparados à avaliação individual de alimentos ou nutrientes (KANT, 2004; MICHELS e SCHULZE, 2005). Essa abordagem é importante pois considera a alimentação como um fenômeno complexo, representando preferências individuais que podem ser moduladas por fatores genéticos, socioculturais, de saúde, estilo de vida, meio ambiente e determinantes econômicos (KRONDL e COLEMAN, 1986; VAN DEN BREE et al., 1999; CESPEDES e HU, 2015).

A epidemiologia nutricional tem definido três abordagens para estimar padrões alimentares. Os métodos teóricos baseados em hipóteses (*hypotesis driven methods*), no qual escores ou índices são definidos para avaliar a qualidade global da dieta, fundamentados principalmente em orientações dietéticas populacionais. Os métodos empíricos baseados em dados (*data driven methods*), como o Análise Fatorial Exploratória (AFE), Análise de Componentes Principais (ACP) e Análise de Cluster (AC); no qual os padrões de dieta são derivados por procedimentos estatísticos exploratórios dos dados de consumo alimentar. E finalmente, os métodos teórico-empírico, também denominados híbridos (*hybrid methods*) como o *Reduced Rank Regression* (RRR), que combina técnicas de derivação teórica com análise exploratória de dados (HU, 2002; KANT, 2004).

Padrões de dieta tem sido amplamente utilizados na epidemiologia nutricional para associar variáveis dietéticas, características sociodemográficas e desfechos em saúde. Uma revisão sistemática de países de alto, médio e baixo desenvolvimento humano avaliou associações entre educação, renda e padrões de dieta em crianças e adolescentes. Os autores observaram que em países de alto desenvolvimento humano houve uma associação inversa entre educação parental e padrões de dieta "não saudáveis" (caracterizados por alimentos de alta densidade energética, carnes processadas, cereais refinados, açúcares e doces) e associação direta com padrões "saudáveis" (compostos por

vegetais, frutas, hortaliças, peixes, frango e grãos integrais). Nos países com nível médio de desenvolvimento humano, embora um padrão de dieta “não saudável” seja encontrado entre a população de alta renda e escolaridade, as associações não são claras. Pesquisas adicionais são necessárias para esclarecer as associações entre renda e educação com padrões de dieta "não saudáveis" e "saudáveis" nos países de médio e baixo desenvolvimento humano (HINNIG et al., 2018).

No geral, evidências sobre associação entre padrões de dieta e estado nutricional nos adolescentes sugerem que padrões alimentares compostos por alimentos com alto teor de energia, gorduras e baixo em fibras, predispõem os jovens à excesso de peso e obesidade (ABURTO et al., 2015; AMBROSINI, 2014). Os achados no *Avon Longitudinal Study of Parents and Children* (ALSPAC), que acompanhou prospectivamente 6772 crianças entre 7 e 15 anos, encontrou que cada unidade de aumento do Z-escore do padrão alto em densidade energética, gordura e baixo em fibras (composto principalmente por doces, bolos, leite integral, pão, carnes processadas, entre outros alimentos) foi associado com um incremento médio de 0,04 unidades do Z-escore de IMC (Coef : 0.04; IC95%=0.01-0.07) (AMBROSINI et al., 2012). Ratificando os resultados anteriores, uma revisão sistemática e meta-análise de estudos observacionais realizadas em adolescentes de 14-19 anos, observou que adolescentes que aderiram mais (últimos tercis, quartis e quintis) a padrões de dieta não saudáveis (compostos por refrigerantes, bolos, salgadinhos, bolachas, sorvetes e carnes processadas) tinham em média 0,58 kg/m2 a mais de IMC (95%IC 0.52; 0.64) que aqueles com menor adesão. Ao contrário do esperado, adolescentes que aderiram menos (primeiro tercil, quartil e quintil) a padrões saudáveis (compostos principalmente por frutas, vegetais, leguminosas, carnes magras, óleos, laticínios, sementes, suco natural de fruta e grãos integrais) tinham em média 0,41 Kg/m2 a menos de IMC (IC95% -0,46; -0,36) que aqueles com maior adesão (CUNHA et al., 2018). Esses achados que relacionam uma menor aderência a padrões de dieta saudáveis e menor IMC são controversos, considerando o efeito protetor dos grupos de alimentos que compor esses padrões denominados saudáveis, tais como legumes, frutas e verduras. Os autores justificam esses achados

expondo que a maioria dos estudos incluídos são de desenho transversal, o que dificulta estabelecer causalidade, além da elevada heterogeneidade que existe entre os estudos de padrões de dieta como a categorização da variável de exposição (CUNHA et al., 2018). Destacam ainda que, a adolescência traz alterações hormonais durante a puberdade e estado de maturação sexual que podem influenciar a associação entre dieta e IMC (VILLAMOR e JANSEN, 2016).

Considerando o escopo de nosso conhecimento, não há estudos no Chile que investigaram padrões da dieta baseados em dados de adolescentes. Os dados de consumo alimentar de crianças e adolescentes (n=673 de 6 a 13 anos) em nível populacional, no Chile, são provenientes da *"Encuesta Nacional de Consumo Alimentario"* (ENCA), realizada em 2010. Nesta faixa etária, 89% reportaram tomar café da manhã, 97% almoço e apenas 29% relataram realizar o jantar. No tocante à realização de lanches intermediários, entre 30% e 50% reportaram consumir alimentos entre as principais refeições. Em relação às recomendações expostas no guia alimentar chileno sobre o consumo de alimentos, apenas 42% atenderam a recomendação de frutas e verduras, 32% a recomendação de leite e derivados, 28% a recomendação de leguminosas e 16% a recomendação de peixes. Observou-se ainda que, quanto maior o nível socioeconômico das familias melhor era o consumo de frutas e verduras, leguminosas e peixes. Neste inquérito populacional foi determinada, ainda, a qualidade da dieta dos indivíduos por meio do "*Healthy Eating Index",* no qual foi verificado que 90% das crianças e adolescentes necessitam de mudanças em sua alimentação (ENCA, 2010).

Jensen et al. (2019) examinaram transversalmente o consumo, fontes de alimentos e perfis nutricionais de lanches de crianças e adolescentes chilenas de baixa e média renda, participantes dos estudos *"Food Environment Chilean Cohort"* (n=958, 4-6 anos) e *"Growth and Obesity Cohort Study"* (n=752, 12-14 anos). Eles constataram uma média de consumo diária de 2,3 porções de lanches, que contribuíram em média com 530 kcal/dia (27,4% da contribuição diária de energia) em adolescentes. Alimentos tais como pães, doces, bolos, salgadinhos, balas, sorvetes, bebidas lácteas, foram os principais contribuintes de energia, gordura saturada, sódio e/ou açúcares totais (JENSEN et al., 2019).

Associações dos padrões de dieta com desfechos em saúde, entre eles o excesso de peso, são análisadas a partir de dados de consumo alimentar auto relatados. Nesse caso, é importante considerar a magnitude e prevalência do relato implausível de energia, já que este pode atenuar ou reverter a direcionalidade das associações (MACDIARMID e BLUNDELL, 1998; NHI, 2019).

1.3 RELATO IMPLAUSÍVEL DA INGESTÃO DE ENERGIA NA ADOLESCÊNCIA

A maioria dos instrumentos para avaliar o consumo alimentar dependem de auto relato dos indivíduos, sendo portanto, susceptíveis à erros (FISBERG, 2015). Um desses principais viéses é o relato implausível da ingestão de energia, caracterizado por valores de ingestão energética (IE) implausivelmente baixos (sub-relato) ou altos (super-relato), quando comparados às necessidades energéticas estimadas por meio de métodos objetivos de gasto de energia, como a técnica de água duplamente marcada (LIVINGSTONE e BLACK, 2003). O relato implausível pode ocorrer por lapsos de memória, dificuldade do entrevistado em quantificar as porções, incompreensão das questões feitas pelo entrevistador e até mesmo por constrangimento ao relatar o consumo de alguns alimentos (LIVINGSTONE et al., 2004; FORRESTAL, 2011).

O sub-relato da ingestão energética é mais frequente que o super-relato (NHI, 2019). Estudos que investigaram essa temática apontaram várias características associadas ao sub-relato, Mulheres, idosos e pessoas com excesso de peso tendem a sub-relatar mais. Ainda, menor nível socioeconômico, escolaridade ou imagem corporal também estão associados ao sub-relato (LIVINGSTONE et al., 2004; FORRESTAL, 2011). Embora o relato implausível nos adultos seja uma temática bem

documentada, relativamente pouco se sabe sobre a natureza e a extensão desse fenômeno entre adolescentes (FORRESTAL, 2011).

É provável que em adolescentes, os padrões de resposta do consumo de alimentos diferem com base nas habilidades cognitivas e hábitos alimentares (LIVINGSTONE e ROBSON, 2000). Dependendo da idade e do seu desenvolvimento cognitivo, crianças e adolescentes podem ter maior dificuldade em lembrar os alimentos consumidos, estimar o tamanho das porções e/ou conhecer os métodos culinários de preparação dos alimentos. Além disso, o padrão alimentar dos adolescentes é menos estruturado quando comparado ao das crianças. Fazer refeições em horários incomuns ou fora de casa, pular refeições principais ou substituí-las por refeições não tradicionais são atos corriqueiros nessa faixa etária (FORRESTAL, 2011; LIVINGSTONE et al., 2004). Em adição, a literatura tem sugerido que o relato implausível pode ser seletivo para alguns tipos de alimentos. Refrigerantes, bolachas e salgadinhos, por exemplo, têm maior probabilidade de serem subnotificados, enquanto aqueles considerados saudáveis, como vegetais, frutas e grãos integrais, são mais propensos a serem super-relatados (MACDIARMID e BLUNDELL, 1998; RANGAN et al., 2014).

1.4 ADOLESCÊNCIA E PUBERDADE

A puberdade é iniciada no final da infância e pode ser definida como um processo biológico de maturidade do eixo hipotálamo-hipófise gonadal (HHG), e é influenciada por fatores ambientais, nutricionais e sociais (GLUCKMAN e HANSON, 2006; VILLAMOR e JANSEN, 2016). Isso resulta em crescimento e desenvolvimento dos órgãos genitais e, concomitantemente, em mudanças físicas

e psicológicas que preparam para a vida adulta, levando à capacidade de reprodução (PATTON e VINER, 2007).

Essa fase da vida é caracterizada por mudanças biológicas e começa com a maturação sexual ou gonadarca, que é iniciada pelo desencadeamento dos estímulos hormonais do HHG. O crescimento gonadal (testículos e ovários) resultante e a produção de esteróides sexuais gonadais promovem o desenvolvimento de características sexuais secundárias (DELEMARRE-VAN DE WAAL, 2002). Precedendo e independente do eixo HHG, a produção de andrógenos adrenais, que desempenham um papel no desenvolvimento dos pelos axilares e pubianos, aumenta entre os 6 a 8 anos em um processo conhecido como adrenarca (DELEMARRE-VAN DE WAAL, 2002).

Um sistema confiável para avaliar as características sexuais secundárias (desenvolvimento mamário, genital e pelos pubianos) foi desenvolvido por Marshall e Tanner na década de 1960 (TANNER, 1962). O estagiamento de Tanner é baseado em uma escala de cinco estágios progressivos descritos e retratados em fotografias, em que o estágio um corresponde a uma etapa pré-puberal, o estágio dois ao início da puberdade e o último estágio, à finalização do processo de maturação sexual **(Quadro 1).**

Quadro 1 – Características do adolescente de acordo com o sexo e o estágio de maturação sexual de Tanner.

MENINAS		**MENINOS**	
M1 - mama infantil.	P1 - ausentes	G1 - caraterísticas infantis	P1 - ausentes
M2 - Broto mamário	P2 - pequenas quantidades, longos, finos e lisos, distribuídos aos longos dos lábios externos	G2 - aumento do pênis pequeno ou ausente. Aumento inicial do volume testicular	P2 - presença de pelos finos e claros
M3 - maior aumento da mama, sem separação dos contornos.	P3 - aumento de quantidade e espessura, mais escuros e encaracolados.	G3 - crescimento peniano em comprimento, maior crescimento dos testículos e escroto	P3 - púbis coberto

M4 - maior crescimento da mama e da aréola, sem separação de contornos	P4 - pelos de tipo adulto: cobrindo densamente a região púbica	G4 - crescimento peniano principalmente no diâmetro	P4 - tipo adulto, sem extensão para costas
M5 - mamas com aspecto adulto	P5 - pilosidade pubiana igual que a do adulto	G5 - desenvolvimento completo genitália	P5 - tipo adulto com expansão para as costas

Adaptado de: Nutrição da Gestação ao envelhecimento. (VITOLO, 2008)

As mudanças externas mais precoces são aparição do broto mamário nas meninas e aumento do volume testicular para mais de 4 mL nos meninos (TANNER, 1962). A menarca, frequentemente vista como o elemento definidor da puberdade feminina, ocorre no final da puberdade, cerca de 2 a 2,5 anos após o brotamento mamário. Nos meninos é mais difícil de identificar o final da puberdade, embora a espermatúria e a primeira ejaculação ocorram entre os 13 e 14 anos de idade (PATTON e VINER, 2007).

Puberdade precoce é geralmente definida pelo aparecimento de características sexuais secundárias em mulheres antes dos oito anos de idade e em homens antes dos nove anos de idade (GLUCKMAN e HANSON, 2006). A puberdade precoce é mais frequente em meninas que em meninos (PARENT et al., 2003). A telarca precoce refere-se ao desenvolvimento mamário de início precoce isolado que é geralmente benigna, embora tenha sido relatada a associação com a exposição de poluentes ambientais estrogênicos (GLUCKMAN e HANSON, 2006; PARENT et al., 2003). A adrenarca prematura em meninas pode ser um precursor da síndrome dos ovários policísticos e alterações metabólicas (STAFFORD e GORDON, 2002). Já o atraso da puberdade é frequentemente associado às doenças crônicas, stress e desnutrição (PARENT et al., 2003).

Desde o final do século XIX, há uma tendência secular do início precoce da puberdade na maioria dos países desenvolvidos, e nos últimos anos, também nos países em desenvolvimento por melhoras em saúde, nutrição e higiene. No entanto, nos últimos quarenta anos, pesquisadores notaram estagnação ou mesmo uma reversão nessa tendência em países onde níveis gerais de saúde e nutrição são ótimos (ONG, 2006; AHMED e DUNGER, 2006; EULING et al., 2008; WALVOORD, 2010).

A avaliação de tendências é dificultada pela heterogeneidade dos estudos, como por exemplo, desenhos epidemiológicos (transversais e longitudinais), características da população (idade, raça e nível socioeconômico) e marcadores de puberdade utilizados como desfecho (marcadores de inicio da puberdade, como broto mamário ou tardios, como a menarca) (EULING et al., 2008).

Estimativas do início da puberdade em estudos observacionais têm foco em meninas pela simplicidade de avaliar os marcadores como broto mamário e menarca. O broto mamário pode ser auto relatado mediante a observação das imagens do estagiamento de Tanner ou examinadas por um especialista treinado. Todavia, tendo em vista que marcadores de puberdade podem diferir ou indicar diferentes mecanismos, é importante comparar dados para o mesmo marcador (EULING et al., 2008). Por isso, a idade de menarca é frequentemente utilizada para medir o estado de saúde populacional, por ser uma medida mais fácil de coletar, tanto retrospectivamente como prospectivamente (PARENT et al., 2003).

Entre os principais fatores identificados que afetam o momento da puberdade, podemos destacar fatores genéticos, ambientais, incluindo obesidade, raça e disruptores endócrinos, particularmente os imitadores de estrogênio e antiandrogênicos que interferem com hormônios esteroidais (EULING et al., 2008; EULING e SELEVAN, 2008).

Pesquisas em diferentes países do mundo indicam uma idade média da aparição do broto mamário entre 8-9 anos e da menarca entre 12-13 anos **(Figura 1)** (PARENT et al., 2003). Uma publicação da *Pediatric Research in Office Settings* (PROS) com uma amostra não representativa de mais de 17.000 meninas residentes nos Estados Unidos da América reportou uma tendência de início mais precoce do desenvolvimento mamário (10 anos para meninas de raça branca e 8,9 anos para afrodescentes) e menarca (12,6 anos para meninas de raça branca e 12,1 anos para afro-americanas). No entanto, essa tendência não foi observada para outros marcadores do desenvolvimento puberal feminino (HERMAN-GIDDENS, 2006).

Em contraste com o desenvolvimento mamário, a idade de menarca tem menores mudanças. Dados do NHANES III (1984-1994) mostraram uma idade de início da puberdade similar. 10,36 anos

para meninas de raça branca e 9,48 anos para afrodescendentes; uma média de idade de menarca de 12,43 anos; 12,06 anos para raça branca e 12,55 anos para afrodescendentes (SUN et al., 2002). O estudo longitudinal *Bogalusa* encontrou queda da idade da menarca de 9,5 meses para meninas de raça branca e 2 meses para afrodescendentes (FREEDMAN et al., 2002). Em meninos, os dados de marcadores de puberdade atuais são insuficientes para avaliar as tendências seculares no desenvolvimento puberal masculino (EULING et al., 2008; HERMAN-GIDDENS, 2006).

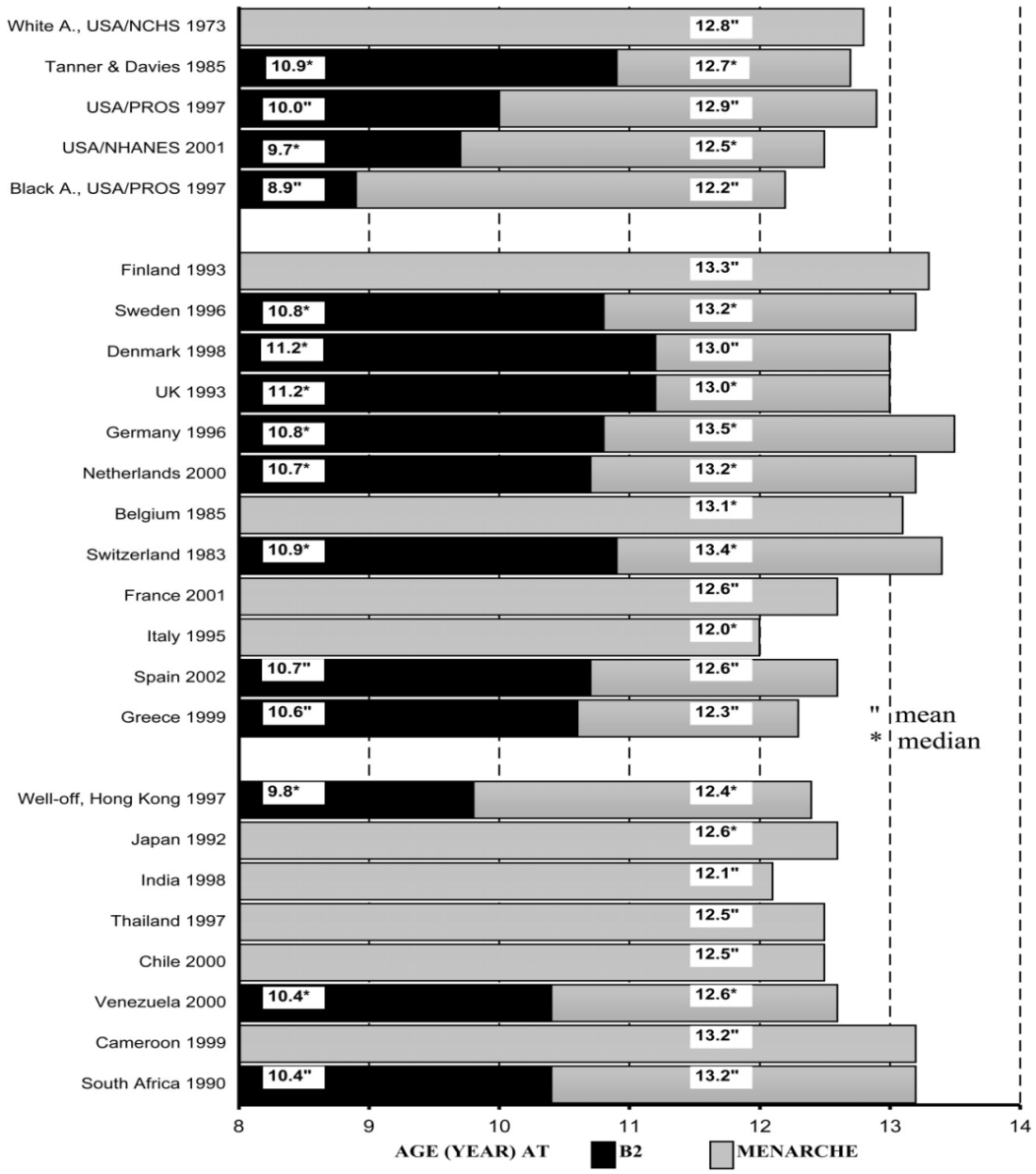


Figura 1- Média ou mediana de idades do início no desenvolvimento das mamas (B2) ou menarca em diferentes populações do mundo. Extraída de (PARENT et al., 2003)

No Chile, estudos transversais tem evidenciado que, meninas de ensino fundamental da cidade de Santiago (n=1302) têm idade média de menarca de 12,7 anos (DP± 0,04), sendo que as oriundas de escolas públicas apresentaram média de idade da menarca de 12,5 (DP± 0,1) e as de escolas privadas de 13,05 (DP± 0,05) (HERNÁNDEZ et al., 2007). Amigo et al. (2012) relacionaram nível socioeconômico e idade da menarca em 8495 adolescentes indígenas e não indígenas da região da Araucanía (Sul do Chile), e estimaram que a idade da menarca ocorreu em 12,5 (DP± 0,89) anos em indígenas e 12.2 (DP± 0.09) anos em não indígenas. No grupo indígena, a idade da menarca no nível socioeconômico menor foi 5,4 meses mais tardia do que no nível socioeconômico mais elevado (AMIGO et al., 2012).

1.5 INFLUÊNCIA DO EXCESSO DE PESO E INÍCIO DA PUBERDADE

Fatores relacionados à nutrição têm sido associados ao início e duração da puberdade (VILLAMOR e JANSEN, 2016). A obesidade tem sido relacionada a um início precoce da puberdade, no entanto, a consistência e plausibilidade biológica dessa associação ainda é controversa (AHMED et al., 2009; BIRO e KIESS, 2016).

A relação entre obesidade e puberdade foi corroborada pela observação da tendência de início precoce do desenvolvimento puberal, concomitante ao aumento da prevalência da obesidade durante as últimas décadas (BURT et al., 2010; WAGNER et al., 2012; BIRO e KIESS, 2016). Wattigney et al. (1999) compararam duas coortes de meninas do estudo de saúde *Bogalusa* e constataram que meninas da segunda coorte (1992-1994) com excesso de peso tinham duas vezes mais risco de alcançar a menarca antes dos 12 anos quando comparadas as meninas da mesma idade da primeira coorte (1978-1979) (WATTIGNEY et al., 1999). Outros estudos observacionais têm evidenciado que

um maior peso corporal durante a infância prediz um início precoce da puberdade, observado por meio do broto mamário (BIRO et al., 2013; DAVISON et al., 2003; DE LEONIBUS et al., 2014; ROSENFIELD et al., 2009) e menarca precoce (AKSGLAEDE et al., 2009; DE LEONIBUS et al., 2014; ROSENFIELD et al., 2009; YERMACHENKO e DVORNYK, 2014). Entretanto, outros estudos sugeriram que o fator peso corporal pré-puberal seja mais influente na progressão ou duração da puberdade do que o momento de seu início (BUYKEN et al., 2009).

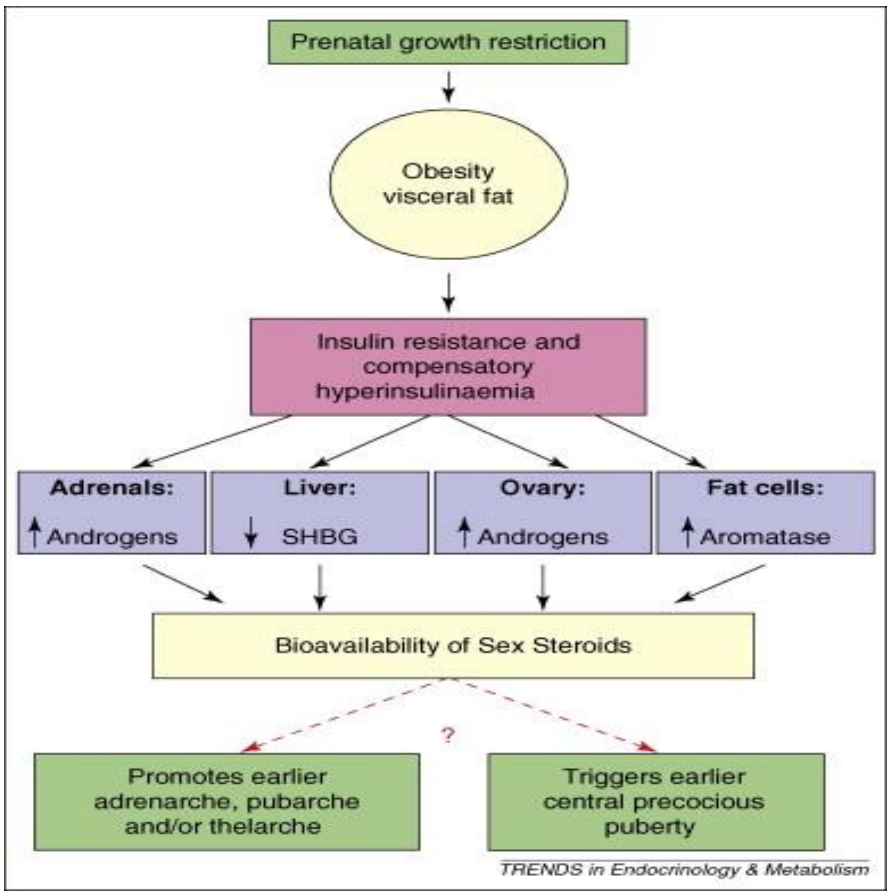
Corroborando com essa tendência, uma revisão sistemática e meta-análise de estudos longitudinais evidenciou possível contribuição da obesidade no início precoce da puberdade em meninas. Comparado com o grupo de meninas com peso normal, o grupo obeso teve mais meninas com menarca (RR: 1,87, IC 95%: 1,59-2,19, 2 estudos) e puberdade precoce (RR: 2,44, IC 95%: 1,32-4,52, 5 estudos). No entanto, não foram detectadas diferenças entre as meninas obesas ou com peso normal na idade da menarca (diferença média: −0,53 anos, IC 95%: −1,24–0,19, 2 estudos) (LI et al., 2017),

O excesso de adiposidade durante a infância pode influenciar os padrões de crescimento e desenvolvimento puberal. Durante a pré-puberdade, crianças obesas têm maior velocidade de crescimento e idade óssea acelerada em comparação com as de peso normal. No entanto, essa vantagem pré-púbere no crescimento tende a diminuir gradualmente durante a puberdade, quando crianças obesas apresentam uma queda do crescimento em comparação com de peso normal (BOYNE et al., 2010; DE LEONIBUS et al., 2014; MARCOVECCHIO e CHIARELLI, 2013).

A relação entre obesidade infantil e puberdade precoce em meninas pode ser explicada por mecanismos como a resistência à insulina / hiperinsulinemia associada à obesidade (AHMED et al., 2009; DUNGER, 2009; BURT et al., 2010). Em particular, o aumento dos níveis de insulina pode estimular a produção de esteróides sexuais, agindo sobre as glândulas supra-renais, ovário, figado e células adiposas (DELEMARRE-VAN DE WAAL, 2002). O aumento dos níveis de androgênio pode, por sua vez, promover o desenvolvimento puberal, agindo periférico ou centralmente no eixo HHG. Outro fator importante que explica a associação entre obesidade e puberdade é a leptina, que pode

exercer efeitos diretos sobre a secreção de gonadotrofinas (AHMED et al., 2009; BIRO et al., 2006; BURT et al., 2010; EULING et al., 2008).

Figura 2 - Representação esquemática do papel da obesidade no momento da puberdade



Fonte: Extraído de AHMED (2009)

Peso e estatura podem fazer parte do mecanismo subjacente da relação entre idade da menarca precoce e DCNT na vida adulta, tais como câncer de mama, síndrome metabólica, maiores taxas de depressão e estresse (AHMED et al., 2009; WALVOORD, 2010; LUIJKEN et al., 2017;). O inquérito nacional de saúde do México observou tendência para idade mais jovem na menarca e risco de doenças não transmissíveis relacionadas, entre as décadas de 1920 e 1980. Mais especificamente, a idade precoce de menarca se relacionou com menor estatura do adulto, maior IMC e risco de diabetes e hiperlipidemia (PETERSOHN et al., 2019).

1.6 PADRÕES DE DIETA E INÍCIO DA PUBERDADE

As primeiras evidências que associaram nutrientes e idade da menarca foram observadas em relação à ingestão de proteínas de origem animal com o desenvolvimento sexual precoce e a ingestão de proteínas vegetais com a maturação sexual tardia (BERKEY et al., 2000; GÜNTHER et al., 2010; ROGERS et al., 2010). Dentre as fontes alimentares de proteínas animais, os leites foram associados à maior probabilidade de menarca precoce (RAMEZANI et al., 2013; WILEY, 2011). Os efeitos potenciais de alimentos de origem animal, especialmente produtos lácteos durante a puberdade, foram atribuídos a uma possível estimulação mediada pela proteína da secreção de IGF-1 (KERVER et al., 2010). No entanto, alimentos de origem animal também são fontes de outros nutrientes, especialmente alguns micronutrientes como zinco e ferro, e ácidos graxos, que também podem desempenhar um papel no momento da maturação sexual (KERVER et al., 2003; VILLAMOR e JANSEN, 2016). Jansen *at el.* (2016) encontraram associação entre maior frequência de consumo de carnes vermelhas (2 vezes por dia) e menor idade de menarca (HR: 1.64; IC95%: 1.11, 2.41; P-*trend*= 0.009), quando comparadas àquelas de menor frequência (<4 vezes por semana). Por outro lado, o consumo frequente de peixes (>1 vez por semana) se associou com uma idade tardia (HR: 0.62; IC95%: 0.42, 0.90; P - *trend*= 0.01), quando comparadas àquelas de menor frequência (<1 vez por mês) (JANSEN et al., 2016).

Atualmente, existem evidências associando o consumo frequente de bebidas açucaradas ao início precoce da puberdade em adolescentes. Um estudo prospectivo nos Estados Unidos com 5.583 meninas observou que a ingestão de bebidas açuraradas foi associada ao desenvolvimento sexual precoce (CARWILE et al., 2015). Uma possível explicação para essa associação seria o alto índice glicêmico desses alimentos, aumentando, portanto, os níveis de insulina circulante, que por sua vez, regula a proteína de ligação ao hormônio sexual (SHBG) e IGF-1 (CARWILE et al., 2015). No entanto, esta associação não pode ser atribuída unicamente ao açúcar das bebidas. Outro estudo

prospectivo realizado em meninas de 9-10 anos afro-americanas e caucasianas nos Estados Unidos, observou que o maior consumo de bebidas com cafeína e artificialmente adoçadas foi associado ao risco aumentado de menarca precoce, independentemente da adiposidade, mas não foi observada associação entre o consumo de bebidas sem cafeína e menarca precoce (MUELLER et al., 2015). Curiosamente, esses estudos não consideraram outros grupos de bebidas fontes de cafeína e açúcar, como café e chá, o que se faz necessário para esclarecer as associações observadas.

Evidências de indicadores globais de dieta com técnicas multivariadas, como padrões de dieta *a posteriori,* e maturação sexual em adolescentes são escassas. Apenas dois estudos transversais abordam essa temática. O primeiro foi realizado em adolescentes Coreanos (n=365 meninas, faixa etária 6-12 anos), no qual foi observada associação direta entre o padrão alimentar definido como "*Shellfish and Processed Meats*" (composto por carnes processadas, pão e frutos de mar) e estágio dois de Tanner (OR=1.88, IC95%: 1.08-3.26) (LI et al., 2006). Outro estudo conduzido em adolescentes de Shangai, China (n=469, faixa etária 6-8 anos) encontrou associação direta entre o padrão "*Unhealthy*" (composto por alimentos fritos, refrigerantes, bolachas e doces) e início da puberdade em meninas (estágio dois de Tanner), ajustando por IMC (OR= 1.25, IC95%: 1.04–1.49), mas o resultado perdeu significância estatística após ajuste por variáveis sociodemográficas (CHEN et al., 2018). De nosso conhecimento, só há um estudo longitudinal realizado em 268 adolescentes mexicanas investigando a relação entre padrões alimentares e marcadores de puberdade. Esse estudo observou que meninas com maior aderência ao padrão "*Vegetables and lean proteins-based"* (caracterizado por vegetais, hortaliças, batatas, legumes e frango) tinham 35% a menos de probabilidade de alcançar o estágio quatro de desenvolvimento mamário (HR=0.35; IC 95%: 3%-67%) quando comparadas àquelas com menor aderência. Entretanto, não foi observada associação entre padrões alimentares e idade da menarca (JANSEN et al., 2018).

2 JUSTIFICATIVA

Os adolescentes são um grupo pouco estudado e altamente influenciável socialmente, além de biologicamente vulneráveis, já que a puberdade é o segundo período da vida extrauterina de maior crescimento. Nesse contexto, o excesso de peso pode alterar as trajetórias de saúde e desenvolvimento para a vida adulta e descendência. Tendo em vista que o excesso de peso é um problema de saúde pública no Chile, a dieta é um dos principais determinantes ambientais possíveis de modificação para o enfrentamento desse problema. Neste sentido, um ponto relevante do presente trabalho é identificar em adolescentes padrões de dieta e grupos de alimentos com alto teor de energia, sódio, açúcares e gordura saturadas, que são alvos das principais políticas de saúde no Chile. Essas informações são essenciais para auxiliar tomadores de decisão e pesquisadores, a fim de reorientar as atuais políticas e programas de prevenção da obesidade e promoção de saúde no país.

O relato implausível, tanto sub ou super-relato da ingestão energética, é esperado em todo estudo de avaliação de consumo alimentar que utilize instrumentos que dependem do auto relato, como o recordatório alimentar de 24 horas. Esse tema não tem sido estudado no Chile e ainda existe pouca evidência dos fatores associados ao relato implausível, especialmente em adolescentes. Estimar a prevalência, identificar características associadas e seu impacto em nutrientes e alguns grupos de alimentos frequentemente consumidos nessa faixa etária é relevante, porque o relato implausível pode comprometer a interpretação dos dados dos estudos que avaliam a interação entre dieta e desfechos de saúde.

O *Growth and Obesity Cohort Study* é único no Chile, com seguimento longitudinal de 12 anos, aferições antropométricas e de desenvolvimento puberal, mesmo que a coleta de dados dietéticos tenha começado em 2013, período em que alguns dos participantes da coorte já haviam iniciado sua puberdade. Sendo a menarca um marcador tardio do início da puberdade e considerando que pesquisas epidemiológicas têm usado esse marcador para associar nutrientes e alguns grupos de

alimentos, tais estudos apresentam resultados controversos. Espera-se com esse estudo, avançar no estado da arte da relação entre alimentação, utilizando indicadores globais como os padrões de dieta, idade de menarca e sua relação com excesso de peso, a fim de contribuir no desenvolvimento de recomendações e políticas nutricionais neste estágio crítico da vida.

3 OBJETIVOS

3.1 OBJETIVO GERAL

- Investigar a associação entre dieta, excesso de peso e puberdade em adolescentes chilenos.

3.2 OBJETIVOS ESPECÍFICOS

- Avaliar relato implausível da ingestão energética e identificar fatores associados em adolescentes chilenos do GOCS (manuscrito 1)
- Identificar padrões da dieta e sua associação com excesso de peso de adolescentes chilenos do GOCS (manuscrito 2)
- Investigar a associação entre padrões de dieta, idade da menarca e excesso de peso (manuscrito 3).

4 METODOLOGIA

4.1 ANTECEDENTES

O presente estudo utilizou dados provenientes da pesquisa *Growth and Obesity Cohort Study* (GOCS), no qual investigador responsável é a Professora Doutora Camila Corvalán Aguilar, Diretora do *Centro de Investigación em Ambientes Alimentarios y Prevención de Enfermedades Crónicas Asociadas a la Nutrición,* do *Instituto de Nutrición y Tecnología de los Alimentos, Fernando Monckeberg,* da *Universidad de Chile*.

GOCS é um estudo longitudinal ambispectivo, que coletou dados retrospectivos dos participantes desde o nascimento; e os seguiu prospectivamente desde o ano 2006 até o presente. A taxa de perda por seguimento da coorte é de aproximadamente 10-15%. Os objetivos gerais de cada seguimento da coorte foram os seguintes:

- GOCS I: Avaliar a associação entre ganho ponderal de peso precoce, crescimento linear e trajetórias do IMC em crianças.
- GOCS II: Avaliar o impacto do IMC e do crescimento linear em desfechos como obesidade, grau de maturação sexual e níveis de biomarcadores precoces de doenças crônicas não transmissível em escolares em fase pré-puberal no Chile.
- GOCS III:
    - Avaliar interações do crescimento precoce, adiposidade, taxa de maturação esquelética na determinação: do tempo e progresso de puberdade e estado metabólico adolescentes chilenos (ANEXO 1).
    - Crescimento inicial, final e composição do tecido mamário: Compreender os mecanismos do risco de câncer de mama em adolescentes chilenos.

- Adrenarca prematura e seus efeitos na função ovariana, tempo puberal e risco metabólico.

- GOCS IV:
  - Avaliar compostos químicos do meio ambiente e composição da mama pós-puberal em uma coorte latina (ANEXO 2).
  - Avaliar a nova regulamentação alimentar chilena
  - Esteatose hepática e sua relação com a síndrome metabólica, genética e microbiota intestino em chilenas em idade escolar.
  - Facetas de consumo de impulsividade de álcool e outras drogas.
  - Exposição ao estrogênio no final da puberdade e sua influência na composição da mama aos 4 anos após a menarca em adolescentes.
  - Variações microbianas e metabólicas como mediadores dos disruptores endócrinos e oligoelementos, na infância e adolescência, na densidade mamária.

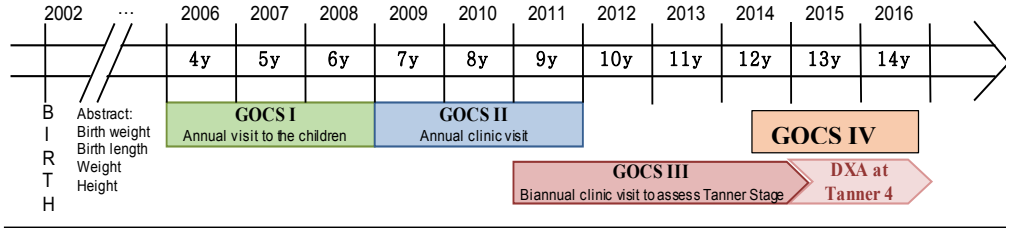


Figura 3: Seguimento longitudinal da coorte GOCS

Fontes de financiamento do GOCS 2014-2015 :

- FONDECYT 1140447. "*Premature adrenarche and effects on ovarian function, pubertal tempo and metabolic risk*". Años 2014-2018. PI: Verónica Mericq
- WCRF 2010/245. "*Role of early growth and adiposity rebound on Pubertal onset & progression Pubertal Obesity & Metabolic Stat Breast Composition at B4*". Años 2011-2014. PI: Ricardo Uauy.

- FONDECYT 1120326. "*Interactions of early growth, adiposity and rate skeletal maturation in determining timing and progression of puberty and metabolic status of chilean children*". Anos 2012-2016. PI: Camila Corvalán.

O presente estudo utilizou dados entre os seguimentos GOCSIII e GOCS IV (2014-2015), momento que começaram a ser avaliados sistematicamente dados de consumo alimentar em cada visita clínica (bianual) (ANEXO 1 e 2).

4.2 DELINAMENTO E POPULAÇÃO DO ESTUDO

O primeiro e segundo manuscritos possuem delineamento transversal e o terceiro manuscrito, delineamento longitudinal prospectivo.

4.3 AMOSTRAGEM

Foram convidados a participar do estudo GOCS todas as mães de crianças que estavam frequentando creches da *"Junta Nacional de Jardines Infantiles"* (JUNJI) da área Sudeste da cidade de Santiago no ano 2006 e cumpriram os seguintes critérios de inclusão: 1) gravidez simples, 2) idade gestacional superior a 37 semanas, 3) peso ao nascer normal (entre 2.500 e 4.500 gramas), 4) ausência de doença física ou psicológica que poderia afetar seriamente o crescimento. Do total de 1953 mães convidadas e 1498 foram elegíveis, 1190 concordaram em participar desse estudo. Essas crianças não diferiam das que se recusaram a participar e da totalidadde de crianças de creches JUNJI no país em

termos de idade, nível socioeconômico e estado nutricional; por isso esse estudo é considerado uma coorte representativa de crianças chilenas de nível socioeconômico médio e médio-baixo.

4.4 TAMANHO DA AMOSTRA

Os principais critérios de inclusão adotados para este estudo foram: adolescentes com, pelo menos, um recordatório alimentar de 24 horas (R24h) entre os anos 2014-2015 de seguimento da coorte e medidas antropométricas.

GOCS começou a coleta de dados dietéticos em 2013, com a aplicação opcional dos R24h para os participantes. A partir de 2014, no entanto, a aplicação dos R24h foi realizada sistematicamente, em cada visita clínica a todos os participantes, como parte do protocolo do estudo. As visitas clínicas foram programadas segundo o estágio de Tanner de cada adolescente. Considerando que as características de maturação sexual acontecem primeiro em mulheres do que em homens, a distribuição de visitas no ano de 2014 considerou predominantemente adolescentes mulheres, enquanto que em 2015, as visitas incluíram, principalmente, os meninos. De modo a dar cobertura semelhante a todos os participantes do estudo, optou-se por considerar, portanto, os R24h dos anos 2014 e 2015 (n=913),

Para os participantes que tiveram a coleta de um segundo R24h (64,3% da amostra), a média de tempo entra a primeira e segunda coleta foi de 6 meses.

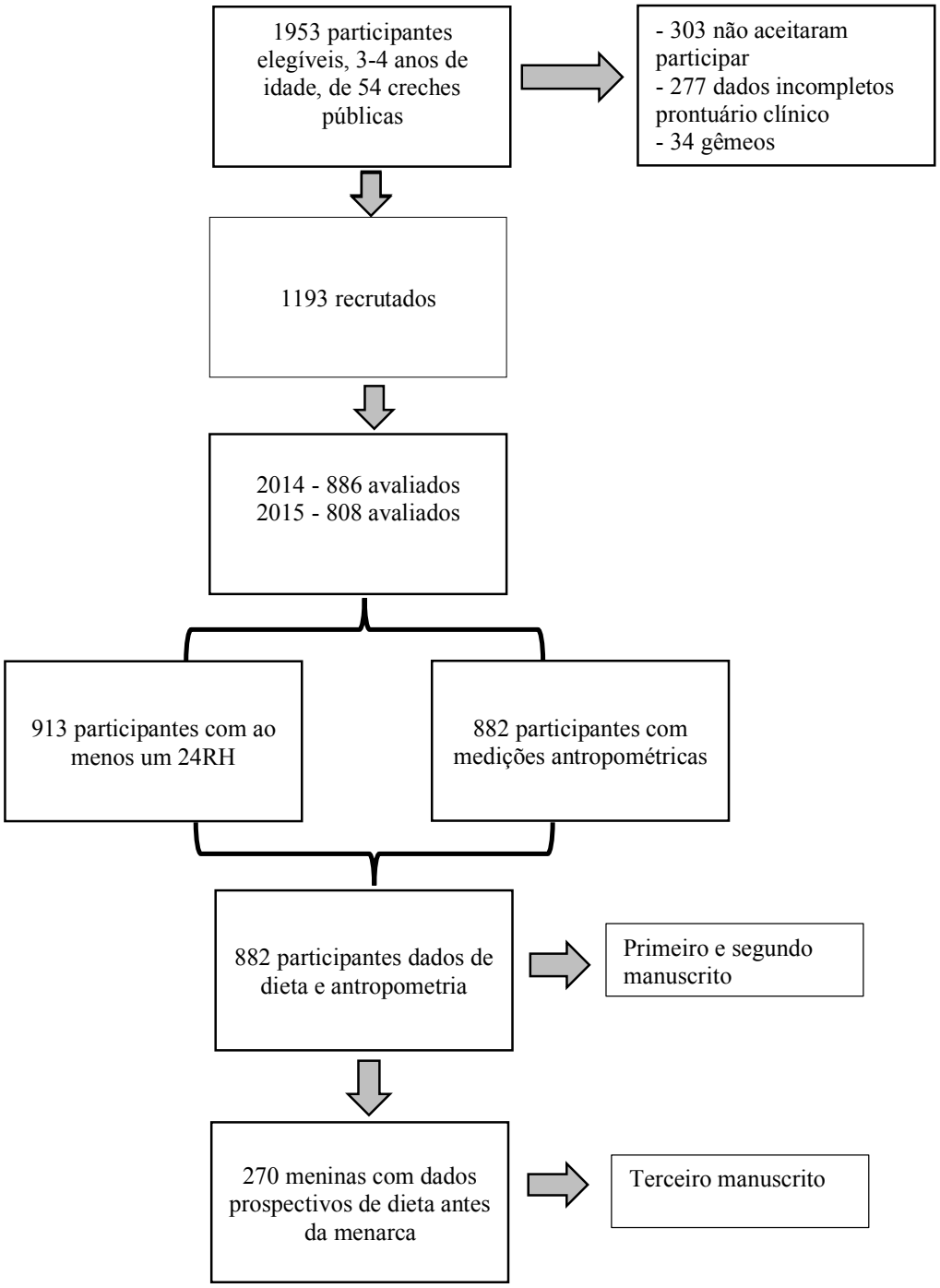
Dos 913 adolescentes com dados de consumo alimentar, 882 tiveram medidas antropométricas aferidas no dia da coleta do R24h, sendo, portanto, essa a amostra considerada para o primeiro e segundo manuscrito (n=882).

Para o terceiro manuscrito, que tem objetivou associar longitudinalmente padrões de dieta e idade de menarca; apenas as participantes do sexo feminino foram incluídas. Assim, dos 882 adolescentes,

458 eram meninas que apresentavam dados de consumo alimentar e antropometria (52%). Destas, 270 (59%) tinham dados de dieta coletados antes do desfecho (menarca), amostra considerada para o terceiro manuscrito.

O fluxograma da distribuição das amostras elegíveis para o presente estudo está apresentado na **Figura 4.**

Figura 4: Fluxograma de distribuição da amostra participantes GOCS



4.4.1 Primeiro Manuscrito

Para o primeiro manuscrito, cujo objetivo foi avaliar o relato implausível da ingestão energética e identificar fatores associados em adolescentes chilenos do GOCS, foram utilizados dados de 913 adolescentes submetidos à primeira avaliação do consumo alimentar. Desses, 31 foram excluídos por apresentarem dados faltantes em uma ou mais variáveis. Dessa forma, a amostra final totalizou 882 indivíduos com dados completos.

4.4.2 Segundo Manuscrito

A amostra selecionada para o segundo manuscrito, cujo objetivo foi identificar padrões da dieta e sua associação com excesso de peso em adolescentes chilenos do GOCS, foi composta por 882 indivíduos com dados completos.

4.4.3 Terceiro Manuscrito

Para o terceiro manuscrito, cujo objetivo foi identificar a associação entre padrões de dieta, idade da menarca e excesso de peso, a amostra foi composta por 270 meninas possuíam dados de consumo alimentar antes da idade da menarca.

4.5 COLETA E PROCESSAMENTO DE DADOS

Para o presente estudo foram utilizados os bancos de dados secundários das coletas de dados dos seguimentos de GOCS III e GOCS IV.

4.5.1 Dados sociodemográficos

As informações referentes a idade, escolaridade materna, ocupação materna, tipo de familia (nuclear, monoparental, extendida), chefe de família, participação no programa de alimentação escolar, horas de sonho, horas de televisão, hábitos de alimentação, foram obtidos por entrevistadores treinados, por meio de questionários estruturados realizados com os pais ou responsáveis durante as visitas ao Centro Diagnóstico do INTA.

4.5.2 Avaliação puberal

A avaliação puberal foi realizada em cada visita clinica por dois nutricionistas de sexos diferentes, treinados por médico endocrinologista pediátrico como padrão ouro. Realizou-se uma avaliação clínica do desenvolvimento mamário (meninas) e testicular (meninos), segundo estágios do desenvolvimento puberal de Tanner (TANNER, 1962). Em caso de duvidas do estagio de Tanner, o medico endocrinologista fazia a confirmação. Em cada avaliação de maturação sexual, as meninas acompanhadas por um adulto responsável foram solicitadas a informar a data (dia e mês) da primeira menstruação. Quando foi informada a data da primeira menstruação, foi solicitada uma visita clínica para confirmar as informações e avaliar o estágio de Tanner (ANEXO 5).

4.5.3 Dados antropométricos

Foram coletados dados de peso, estatura dos adolescentes. As mensurações foram realizadas em duplicata por dois nutricionistas (um para cada sexo) treinados e padronizados, com correlação intra e interindividual > 0,9 utilizando técnicas validadas (WHO, 1995) (ANEXO 3 e 4). O peso corporal foi mensurado utilizando o analisador de composição corporal, balança *Body Composition Analyser* TANITA BC-418, com precisão de 0,1 kg. A estatura foi aferida por meio do estadiômetro longitudinal Seca modelo 222, com uma capacidade de 0-230 cm e 0,1 cm de precisão. A partir da média dessas variáveis foi calculado o IMC (peso (kg)/altura $(m)^2$) e estimado o escore z do IMC/idade de acordo com as curvas da OMS de 2007 (WHO, 2007). O IMC foi categorizado segundo OMS usando a classificação de estado nutricional para adolescentes como baixo peso (≤ -1 DP), normal (< -1 DP e < +1 DP), sobrepeso (≥+1 DP e< +2DP), e obesidade (≥ +2 DP) (ONIS et al., 2007).

4.5.4 Dados de consumo alimentar

As informações do consumo de alimentar foram coletadas por meio do recordatório de 24h (R24h) aplicados por nutricionistas treinados. As entrevistas foram realizadas pessoalmente e com a presença do responsável pela alimentação dos adolescentes, a fim de evitar omissões da quantidade e tipo de alimento. A coleta seguiu a metodologia do *Automated Multiple-Pass Method* (AMPM), cujo objetivo era auxiliar adolescente e/ou seus responsáveis a lembrarem dos alimentos e bebidas consumidos, relatando-os em detalhes e minimizando os erros da medida dietética. Esse método propõe a coleta de dados dietéticos em cinco “passos” ou etapas sucessivas (MOSHFEGH et al., 2008).

Passo 1- Preenchimento da listagem rápida de alimentos.

Passo 2- Listagem dos alimentos consumidos esquecidos.

Passo 3- Definição do horário e local da refeição.

Passo 4- Ciclo de detalhamento e revisão

Passo 5- Revisão final do recordatório.

Os adolescentes e seus responsáveis foram orientados a informar as quantidades dos alimentos em medidas caseiras com a ajuda do atlas fotográfico da Pesquisa Nacional de Consumo de Alimentos do Chile e descrever em detalhe as porções, formas de preparo, nome e horário das refeições, marcas dos alimentos consumidos, entre outros (CERDA, 2010). A padronização na coleta de dados foi realizada através do uso de um formulário padrão, no formato Excel e um manual explicativo para seu registro. Em subamostra (n=458) foi coletado o segundo R24h.

Para o processamento dos R24h foi utilizado o programa *Nutrition Data System for Research* (NDSR) (versão de 20014, NCC, da Universidade de Minnesota, Minneapolis) cuja base de dados é originada da tabela de composição do *United States Department of Agriculture* (USDA). O software tem uma série de recursos que ajudam a entrada de dados, além das vantagens de ter mais de 18.000 alimentos e exportar mais de nove tipos de arquivos que permitem a análise de nutrientes, alimentos e refeições individualmente.

Como o NDSR utiliza banco de dados norte-americano, foi feita uma listagem com a tradução de alimentos, bebidas, preparações e formas de preparo utilizadas pela população chilena, com o intuito de padronizar a entrada dos alimentos no programa. Além disso, o valor nutritivo dos alimentos do programa foi comparado com os valores disponíveis nas tabelas de composição de alimentos do Chile e as informações nutricionais dos rótulos de alimentos declarados pelo fabricante. Foram utilizados alimentos e receitas que obtiverem a adequação entre 80% a 120% dos valores de energia e macronutrientes. Refeições ou alimentos típicos chilenos que não estão disponíveis no programa, foram incluídos usando receitas padronizadas desenvolvidas por nutricionistas.

Os alimentos foram agrupados segundo o valor nutritivo, cultura alimentar do Chile, correlação entre alimentos; atendendo os objetivos de cada manuscrito. No primeiro manuscrito os alimentos foram agrupados em 26 grupos, segundo manuscrito em 29 grupos e terceiro manuscrito em 30 grupos. A descrição de cada agrupamento é descrita no material suplementar de cada manuscrito.

4.5.5 Estimação do relato implausível

No primeiro manuscrito, o relato implausível da IE foi calculado com base na metodologia proposta Goldberg e col (1991) (GOLDBERG et al., 1991), atualizada por Huang e col (2012) para crianças (HUANG et al., 2012). Essa metodologia leva em consideração o número de R24h, coeficiente de variação intrapessoal da ingestão energética, coeficiente de variação das equações que estimam a necessidade energética e o coeficiente do nível de atividade física para identificar os relatores plausíveis, bem como sub e super-relatores de IE.

Para o segundo e terceiro manuscritos, foi estimado o percentual de relato implausível de energia por meio da equação utilizada por Kelly *et al*. (KELLY et al., 2009) (IE– NEE (necessidade energética estimada) / NEE *100), sendo as necessidades energéticas individuais determinadas a partir das equações do *Institute of Medicine of the National Academics* (IOM, 2002). Essa variável foi utilizada para ajustar os modelos de regressão múltipla.

5 VARIÁVEIS DO ESTUDO

Diferentes variáveis de estudo foram investigadas em atendimento às análises estatísticas e os objetivos de cada manuscrito, sendo sumarizadas no **Quadro 2-4.**

Quadro 2- Relação das variáveismanuscrito 1

		Descrição	Tipo de variável
Manuscrito 1	**VARIÁVEIS DEPENDENTE**		
	Relato implausível energia	(IE-/necessidade energética . Categorizado como: plausível, sub-relato, super-relato	-Qualitativa nominal
	VARIÁVEIS INDEPENDENTES		
	Estado Nutricional do adolescente	Obesidade, não=0 /sim =1	-Qualitativa nominal dicotômica
	Energia total	Quilocalorias/dia	Quantitativa contínua
	% Açúcar de adição IE	(Gramas/dia*4 kcal/IE)*100	Quantitativa contínua
	Sódio	Gramas/dia/1000 kcal	Quantitativa contínua
	% Gordura Saturada IE	(Gramas/dia*9/IE)*100	Quantitativa contínua
	Grupos de alimentos	Segundo objetivo do manuscrito	Qualitativo nominal
	Idade	Calculada a partir da diferença entre a data de nascimento e entrevista (anos)	Quantitativa contínua
	Sexo	Masculino/feminino	Qualitativa dicotômica
	Estágios de Tanner	Estágio puberal (Tanner 1-3, tanner 4-5)	Qualitativa nominal
	Alimentação escolar	Beneficiário do programa de alimentação escolar (não=0 / sim=1)	Qualitativa nominal
	Horas de sono	≥ 9 horas / < 9 horas	Qualitativa dicotômica
	Horas de tela	< 2 horas, ≥2 horas	Qualitativa nominal
	Escolaridade materna	Anos completos de escolaridade (≥ 12 anos / <12 anos)	Qualitativa dicotômica
	Estado nutricional materno	IMC (≥30 kg/m2/<30 kg/m2)	Qualitativa dicotômica
	Ocupação da mãe	Trabalho (sim/não)	Qualitativa dicotômica
	Chefe de família	Mãe, pai, outro	Qualitativa nominal
	Renda	Em pesos chilenos (0-300.000, 300.001-600.000, 600.001-2.000.000)	Qualitativa nominal
	Aleitamento materno	Aleitamento (meses)	Quantitativa continua
	Introdução de refrigerantes	Mês de vida em que iniciou consumo de refrigerantes (meses)	Quantitativa continua
	Introdução de doces	Mês de vida em que iniciou consumo de doces (meses)	Quantitativa continua
	Introdução de alimentação complementar	Mês de vida em que iniciou alimentação complementar (meses)	Quantitativa continua

Quadro 3- Relação das variáveis manuscrito 2

		Descrição	Tipo de variável
Manuscrito 2	**VARIÁVEIS DEPENDENTE**		
	Estado Nutricional do adolescente	excesso de peso, não=0 /sim =1	-Qualitativa nominal dicotômica
	VARIÁVEIS INDEPENDENTES		
	Padrões de dieta	Escore fatorial, categorizado em tercil	Qualitativa ordinal
	Energia total	Quilocalorias/dia	Quantitativa contínua
	% Açúcar de adição IE	(Gramas/dia*4 kcal/IE)*100	Quantitativa contínua
	Sódio	Gramas/dia/1000 kcal	Quantitativa contínua
	% Gordura Saturada IE	(Gramas/dia*9/IE)*100	Quantitativa contínua
	Idade	Calculada a partir da diferença entre a data de nascimento e entrevista (anos)	Quantitativa contínua
	Estágios de Tanner	Estágio puberal (Tanner 1-3, Tanner 4-5)	Qualitativa ordinal
	Alimentação escolar	Beneficiário do programa de alimentação escolar (não=0 / sim=1)	Qualitativa nominal
	Sono	Horas de sono (≥ 9 horas / < 9 horas)	Qualitativa dicotômica
	Escolaridade materna	Anos completos de escolaridade (≥ 12 anos / <12 anos)	Qualitativa dicotômica
	Estado nutricional materno	IMC (≥ 30 kg/m2/<30 não kg/m2)	Qualitativa dicotômica
	Estatura materna	Estatura materna (centímetros)	Quantitativa contínua
	Relato implausível energia	(IE– NEE / NEE *100)	Quantitativa continua

Quadro 4- Relação da variável manuscrito 3

		Descrição	Tipo de variável
Manuscrito 3	**VARIÁVEIS DEPENDENTE**		
	Idade de menarca	Calculada a partir da diferença entre a data de nascimento e relato de menarca (meses)	Quantitativa contínua
	VARIÁVEIS INDEPENDENTES		
	Estado Nutricional do adolescente	escore z do IMC/idade escore z do IMC/idade≥1DP: excesso de peso, não=0 /sim =1	-Qualitativa nominal dicotômica
	Peso corporal	Quilogramas de peso em Tanner 4	Quantitativa continua
	Altura corporal	Metros de altura em Tanner 4	Quantitativa continua
	Idade	Calculada a partir da diferença entre a data de nascimento e entrevista (anos)	Quantitativa contínua
	Estágios de Tanner	Estágio puberal (Tanner 1-3, Tanner 4-5)	Qualitativa ordinal
	Energia total	Quilocalorias/dia	Quantitativa contínua
	% Açúcar de adição IE	(Gramas/dia*4 kcal/IE)*100	Quantitativa contínua
	Sódio	Gramas/dia/1000 kcal	Quantitativa contínua
	% Gordura Saturada IE	(Gramas/dia*9/IE)*100	Quantitativa contínua
	Grupos de alimentos	Segundo objetivo do manuscrito	Qualitativo nominal
	Alimentação escolar	Beneficiário do programa de alimentação escolar (não=0 / sim=1)	Qualitativa nominal
	Hora de Sono	9 horas / < 9 horas	Qualitativa dicotômica
	Horas de tela	< 2 horas, ≥ 2 horas	Qualitativa nominal
	Escolaridade materna	Anos completos de escolaridade, categorizada: (≥ 12 anos / <12 anos)	Qualitativa dicotômica
	Estado nutricional materno	IMC (≥30 kg/m2/<30 não kg/m2)	Qualitativa dicotômica
	Idade menarca mãe	Idade em anos	Qualitativa continua
	Relato implausível energia	(IE– NEE / NEE *100)	Quantitativa continua

6 ANÁLISE ESTATISTICA

Normalidade das variáveis quantitativas foi testada usando teste de Kolmogorov-Smirnov. Medidas de tendência central (média ou mediana) e de dispersão (desvio-padrão ou intervalo interquartil) para as variáveis contínuas e frequências relativas para variáveis qualitativas foram usadas para as analises descritiva dos dados.

O primeiro manuscrito faz uso de modelos de regressão logística múltipla para identificar fatores associados ao subrelato e super-relato de energia. O teste de Hosmer–Lemeshow foi usada para avaliar a qualidade do modelo final. Modelos de regressão linear múltipla foram utilizados para avaliar o impacto do subrelato de energia em alguns nutrientes e grupos de alimentos de interesse.

O segundo manuscrito, faz uso de métodos estatísticos de análise multivariada de dados. O manuscrito emprega a análise fatorial exploratória (AFE) com o propósito de derivar os padrões de dieta. Para investigar associação entre excesso de peso e aderência aos padrões de dieta foi utilizado modelos de regressão logística múltipla.

Já o terceiro manuscrito aplica AFE com o propósito de derivar padrões de dieta em adolescentes do sexo feminino. A análise de sobrevida foi utilizada para observar o tempo até início de menarca. Finalmente com o propósito de investigar a relação entre padrões de dieta e idade da menarca foi utilizado modelo semi-paramétrico de Regresso de Cox.

A análise estatística foi descrita detalhadamente em cada manuscrito e realizada no programa

STATA versão 15.0. Em todos os testes, adotou-se nível de confiança do 95% e um nível significância estatística de 5%.

7 ASPECTOS ÉTICOS

O presente trabalho foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Saude Publica da Universidade de São Paulo (CAAE n: 04256118.1.0000.5421**) (ANEXO 6)**. Alem, do Comitê de Ética do Instituto de Nutrição e Tecnologia dos Alimentos (INTA), Doutor Fernando Monckeberg Barros; atas de aprovação 12.14 e 18 **(ANEXO 7)**

8 RESULTADOS E DISCUSÃO

Devido à apresentação de tese em formato de artigo científico, os resultados e a discussão da tese estão descritos em três manuscritos, dos quais dois estão formatados segundo as normas das revistas as quais foram submetidos.

- Manuscrito 1: "*Misreporting of energy intake and factors associated among adolescents from the Growth and Obesity Chilean Cohort Study (GOCS)"* - a submissão no periódico *Journal of Adolescents Health*.

- Manuscrito 2: "Dietary patterns among Chilean adolescents from the Growth and Obesity Cohort Study indicate poor dietary quality". -a submissão no *periódico Nutrition Research.*

-Manuscrito 3: *"Prudent pattern is associated to age at menarche in adolescents with excess weight from Growth and Obesity Cohort Study"* sera submetido ao periódico após da avaliação da banca examinadora.

8.1 PRIMEIRO MANUSCRITO

MISREPORTING OF ENERGY INTAKE AND FACTORS ASSOCIATED AMONG ADOLESCENTS FROM THE GROWTH AND OBESITY CHILEAN COHORT STUDY (GOCS)

Abstract

Purpose

Misreporting of energy can affect the validity of studies exploring diet and health outcomes. In adolescents little is known about determinants of misreporting. The present study aimed to evaluate the prevalence, factors associated and the impact misreporting status of intake energy of some nutrients and foods, in a cohort of Chilean adolescents.

Methods: A total of 882 adolescents participated in this cross-sectional study. Dietary intake was assessed through 24-h recalls. Anthropometrics measurements, socio-demographics and maternal characteristics were obtained during clinical visit. The ratio of energy intake to total energy expenditure requirements (EI:TEE) was used to categorize as under-reporters (UnR) (EI:TEE<0.78), over-reporters (OvR) (EI:TEE>1.22) or plausible reporters (PR) (EI:TEE=0.78-1.22). Associations between misreporting and characteristics associated were examined by logistic regression analyses. Linear regression was used to evaluate impact misreporting status.

Results: Less than half of adolescents were classified as PR of energy intake, while about 51% were UnR and 9% were OvR. UnR girls and boys had a higher average of protein energy and sodium intake and lower energy share from total fat, and from saturated fat. OvR girls had a higher contribution of added sugar to EI. Food items such as: junk food, crackers, salty snack, chocolate and confectionary were frequently UnR and Vegetables OvR. Adolescents men, obesity status were factors associated to UnR.

Conclusions: The frequency of misreporting was high, particularly UnR among adolescents with excess weight and boys. Besides, we show that misreporting was selective to some food groups and it can change the directionality of associations between some nutrients or food groups and body mass index.

Key words: misreporting, energy intake, food consumption, adolescents.

Abbreviations

EI, Energy intake

TEE, Total energy expenditure

BMI, Body mass index

SES, Socioeconomic status

24HR, 24 hours recalls

UnR, Under-reporters

OvR, Over-reporters

PR, Plausible reporters

pER, Predicted energy requirements

rEI, Report energy intake

DRI, Dietary Reference Intakes

CV, Coefficient of variation

GOCS, Growth and Obesity Cohort Study

WHO, World Health Organization

EER, estimated energy requirements

OR, Odds ratios

CI, Confidence interval

Implications and Contribution

Latino-American adolescents is little is known about determinants of misreporting of energy. We evidenced a high frequency of under-reporting among boys, and obesity was the main predictor. Misreporting was selective to some food groups and it can change the directionality of associations between some nutrients or food groups and body mass index.

Introduction

It is widely accepted that one of the main problems in self-reported dietary surveys is the misreporting of energy intake (EI) which encompasses both under- and over reporting [1]. Under- and over reporting of EI are measurement errors that can lead to spurious relationships between dietary variables and health outcomes [2, 3]. Thus, it is essential to identify characteristics associated with misreporting of dietary intake to improve the quality and accuracy of dietary data.

Energy misreporting and its associated factors have been mainly studied in adults, but in the case of children and adolescents there is less evidence of its magnitude and poorer agreement on the determinant factors [4]. It is likely that in children response patterns of consumption of food differ based on cognitive abilities as well as dietary habits [5]. Depending on age and their cognitive development, children may have greater difficulty to remember the foods consumed and to estimate the portion sizes; knowledge of some types of foods or cooking methods may also vary with age. In addition, adolescent's dietary patterns are less structured than dietary patterns of adults; they can have meals at unusual times or outside home, skip main meals and replace them by non-traditional eating occasions, which can particularly affect the quality of the dietary data collected [1, 6].

Some studies in Europe and North America showed that misreporting in adolescents is frequent and varies considerably between studies, ranging from 2% to 85% classified as under-reporters and from 3% to 46% classified as over-reporters [6]. In general, under-reporting tends to be more common than over-reporting, and has been associated with older age, female sex, higher Body Mass Index (BMI), low Socio-economic Status (SES) and health consciousness [7-10].

Moreover, it has been suggested that misreporting can be selective for some types of foods: unhealthy food items such as cakes, sweets, confectionery are more likely to be under-reported, whereas those considered healthy such as fruits and vegetables are more likely to be over-reported [2, 6, 11]. Considering that adolescence as a critical life stage in which multiple physical and social changes take place [12] and the relevance of diet during this period, that affects adolescent's nutritional status and their future feeding behaviors and health conditions [13-15], the present study aimed to evaluate the prevalence and characteristics associated with misreporting of EI in a cohort of low to low-middle income Chilean adolescents; we focus particularly in under-reporting because it is more frequent and there are few studies in adolescents of countries middle income.

Materials and methods

Study population

The sample was drawn from children enrolled in the Growth and Obesity Chilean Cohort (GOCS) study. GOCS was initiated in 2006 and included 1195 children born in 2002-2003 in families of middle-low to low-income counties from the Southeast area of Santiago. The inclusion criteria of GOCS were singleton who were born at term (37–42 week), had a birth weight ≥2500 and <4500 g, and were free from conditions that could affect their adequate growth. Details of the design, objectives and recruitment strategies of GOCS have been described elsewhere [16, 17].

For this cross-sectional study, we included all adolescents evaluated between 2014 and 2015, who had at least one 24 hours recall (24HR) (n=913) with a concomitant anthropometric measurement (n=882). We excluded 31 adolescents (n=21 boys and n=11 girls) because no anthropometric measurements were available. The final sample of this study was n=882 adolescents.

The study protocol was approved by the Ethics Committee of the Institute of Nutrition and Food Technology (INTA), University of Chile. Informed consent was obtained from all parents or guardians of adolescents and adolescents provided their assents before beginning data collection.

Dietary data collection

Dietary intakes data were collected by trained dietitians following the "Multiple Pass Method" to help them remember and describe foods that they had consumed over the past 24 hours [10]**.** Sixty percent (60%) of the adolescents had a second 24HR (6 months after the first collection (median)).

24HR were conducted in-person including the individual responsible for the adolescents' feeding, in order to avoid omissions in foods consumed. Data collection included meal times, preparation names and methods, food brands and portions which were described in homemade measurements, e.g, beverages in glasses, mugs, bowls, and plates; with the aid of the photographic atlas of the National Survey of Food Consumption of Chile [18].

Foods and beverages reported on the 24HR interviews were matched in the Nutrition Data System for Research (NDS-R) program (version of 20014, NCC, of the University of Minnesota, Minneapolis) that uses the United States Department of Agriculture (USDA) database as the main food composition table. Energy and macronutrient values available in Chilean food composition tables (TCA), local food industry composition tables and/or nutrition labels were compared to values described in the software. A concordance rate between 80 and 120% for each parameter analyzed was required to accept food harmonization. Typical Chilean recipes such as: *charquican, cazuela, sopaipillas, porotos con riendas, chilean hot dog*, among others; were added in the software database in the case of commonly consumed foods.

In the two 24HR, a total of 1053 different foods were reported, of which 993 were consumed by at least 5% of the sample. These food items were grouped in 26 food categories based on their nutritional value, culinary usage, and dietary behaviors of the Chilean population **(Supplemental files 1)**.

Misreporting of Energy Intake

To determine adolescents who misreported EI, we first calculated the predicted energy requirements (pER) using the equations of the Dietary Reference Intakes (DRI) based on age, sex, weight, height and physical activity level [19]. The low physical activity level was adopted for this sample of adolescents because the last Chilean report of physical activity indicates high sedentarism levels among this age-group [20]. We classified adolescents as under-reporters (UnR), plausible reporters

(PR) or over-reporters (OvR) of EI, if the reported energy intake (rEI) was <1 , ± 1, or >1 standard deviation (SD) of the predicted energy requirements, respectively (pERs: rEI /pER * 100) based on the proposal by McCrory et al. [21] reviewed by Huang et al. [22, 23].

The equation to establish the cut-off ±1 SD includes error variances from intra-individual variation in rEI over the number of days of intake, the error in equations for pER, and measurement error and day-to-day biological variation in the total energy expenditure estimated by doubly-labeled water-method [21, 22, 24]. Therefore, the ±1 SD cut-offs for rEI as a percentage of pER were calculated as follows**:**

$$\pm 1\ SD = \sqrt{CV^2_{rEI}/d + CV^2_{pER} + CV^2_{mTEE}}$$

Where CV= coefficient of variation; rEI= report energy intake of 24HR; d= number 24HR; pER= predicted energy requirement; mTEE= measured total energy expenditure **(Supplemental files 2)**.

Covariates

Anthropometric measurements were obtained using validated techniques, and they were duplicated by two trained dietitians under standard procedure (one for each sex; intra and inter class correlation >0.9)[25]. BMI was calculated dividing weight in kilograms by height in squared meters. We estimated BMI-for-age *z* scores based on the WHO 2007 Growth References [26]. Besides, breast and genitalia development were checked in girls and boys, respectively to classified them according to Tanner stages [27], inconsistent cases were confirmed by a pediatric endocrinologist. Weight and height of the mother was also measured and used to calculate BMI.

Participants' mothers self-reported information on educational level (≥ 12 years/<12 years), type of work (yes, no, sometimes), type of school of the adolescent (public/ private), hours of sleep (≥ 9 hours/<9 hours), recommended to children 12 years [28] and consumption of school meals (yes/no) of adolescents. Perinatal and infant information such as breastfeeding (in months) and age (in months) of the introduction of soft drinks and juices, confectionary, complementary foods were collected at

recruitment in 2006-2007. Proxy variables of sedentary behavior (hours of sleep and television) were collected by structured questionnaires in 2015.

Statistical analysis

Normal distribution of the variables was tested using the Kolmogorov-Smirnov test. A descriptive analysis of the data was performed using measures of central tendency (mean or median) and dispersion (standard deviation or interquartile range) for continuous variables and relative frequencies for qualitative variables. Differences between groups were tested by ANOVA with Bonferroni's multiple comparison test or Kruskal-Wallis test with Dunn's multiple comparison. Qualitative variables were evaluated by Pearson's Chi-square test.

Energy intake, macronutrients and specific nutrients of interest (saturated fat, sodium and added sugars) was estimated with the individual means of two 24HR. To identify the contribution of the food groups to the total EI, the methodology proposed by Block et al was used [29].

Factors associated with underreporting were evaluated using multiple logistic regression models; adjusted Odds Ratios (OR) with 95% Confidence Intervals (CI) were estimated. Variables that presented a $p < 0.20$ in the univariate models were retained for the final model. The Hosmer-Lemeshow test was used to test the Goodness-of fit of the final model.

To evaluate the impact of misreporting classification on the relation between Z score BMI and some nutrients or foods group, 4 multiples linear regression models were developed: in model 1 (univariate), model 2 adjusted by covariables, model 3 adjusted by covariables and misreporting status and models 4 only in PR. The analyzes were performed with the software STATA 15.0 (Stata Corp, Texas, USA).

Results

Participants were 434 boys (49%) and 448 girls (51%), with an average age of 12 years (SD 0.7). Percentages of UnR, PR and OvR of EI were 51%, 40% and 9%, respectively. The percentage of UnR was higher among boys (58.5%) than girls (43.1%, $p<0.05$) and OvR in girls were higher (10.5%) than in boys (7.1%, $p<0.05$). About four out of five adolescents with obesity were UnR

(81.7%) and adolescents without obesity had a higher prevalence of PR (46.6%). Adolescents with obese mothers had higher UnR (58.3%) and lower OvR (6.8%) than those adolescents with mothers, which had normal weight (UnR=46.2% and OvR=10.2%, $p<0.05$). A complete description of the anthropometric, sociodemographic and maternal characteristics and eating and sedentary behaviors of the study population is shown in **Table 1**.

Comparing energy requirements with energy intake by misreporting group and sex **(Table 2)**, UnR girls consumed on average about 63% less and OvR girls consumed about 48% more of their daily energy requirements while, boys UnR consumed about 60% less and OvR boys consumed about 38% more of their energy requirements. In the case of macronutrients, we evidenced that UnR girls and boys had a higher average of protein energy share ($p<0.001$) and sodium intake ($p<0.002$ and $p<0.07$ respectively) than PR girls and boys. On the other hand, UnR adolescents had a lower energy share from total fat ($p<0.001$ girls and $p<0.001$ boys), and from saturated fat ($p<0.003$ and $p<0.016$ for girls and boys respectively) than PR and OvR adolescents. OvR girls had a higher contribution of added sugar to EI than girls PR and UnR ($p<0.014$).

Table 3 shows the energy contribution (%) of some food groups among PR, UnR, OvR by sex. The 21 selected food groups represent about 95% of the total EI of the study sample. The food group that contributed most to EI was bread (13-19% of the total EI) and its contribution was lower among adolescents OvR (13.88 % for girls and 14.09% boys) in comparison to PR (16.88% and 18.36% respectively) and UnR (17.563% and 19.55% respectively). Girls UnR were more likely to refer higher consumption of vegetables ($p<0.025$) and lower consumption of cookies and cake ($p<0.001$), confectionary and chocolate ($p<0.017$) groups than PR and OvR. Similarly, boys UnR refer high consumption of vegetables ($p<0.006$), but they reported a lower consumption of junk foods ($p<0.003$), crackers and salty snacks ($p<0.001$) and mayonnaise, ketchup and mustard ($p<0.044$) groups than those PR and OvR.

In **Table 4**, when we observed associated factors the UnR, obesity adolescents had five times more odds of being classified as UnR than no obesity adolescents (OR=5.10; 95% CI=3.24, 8.04). Girls

presented 51% lower odds of being classified as UnR (OR=0.51, CI=0.33, 0.80) than boys. Non-attendance of school feeding program and Tanner stage of 4 to 5 were borderline of the statistical significance. Maternal obesity and age were not associated with UnR. We no found associated factors to OvR.

Multiple linear regression models were used to study the misreporting impact in the association between Z score BMI and macronutrients or food group **(Table 5)**. We observed that in the first and second model, in which the misreporting status was not considered; higher intake from proteins, sodium, vegetables (expressed as % EI) were associated positively with Z score de BMI and added sugar negatively ($p<0.05$). When misreporting status was included as ajusted, processed meat, sodium and total fat were positively associated with Z score BMI and carbohydrates and yogurt negatively ($p<0.005$). For last, in model 4 (only PR) total fat, processed meats, juice and soft drinks were positively associated with Z score BMI ($p<0.05$).

Discussion

To our knowledge, this is the first study conducted in Latin America that has evaluated the prevalence and factors associated to misreporting in a sample of adolescents using a rigorous methodology. The main findings of the GOCS study were that less than half of young adolescents were classified as accurate self-reporters of energy intake, while about 51% were UnR and 9% were OvR. These findings agree with those found in international literature, where it has been showed that the UnR prevalence range from 2 to 85% and the OvR prevalence range from 3 to 46% [6]. Previdelli et al. [30] found in Chile a prevalence of 13.08% to UnR and 13.77% to OvR mainly in adults. Differences between studies could be explained by the use of different methodologies to assess dietary intake, equations used for predicting energy requirements or by the criteria used to estimate cutoff values to evaluate misreporting, besides the inner characteristics of the population under study [2, 6, 31].

Evidence suggests that under-reporting is not random, instead it is likely to be more prevalent in particular subgroups, mainly in women. However, this it is not conclusive among children and adolescents [2, 6]. Sociocultural factors have been associated to the UnR in female sex, such as the

social pressure of the ideal body image or social desirability [2, 4, 6]. An interesting finding in the current study was the finding of a higher prevalence of UnR in boys than in girls (58.5% and 43.1% respectively). This can be explained by the fact that adolescent boys could have less interest reporting their food intake than girls. They tend not to remember the portion size of the foods consumed and are less likely to remember the recipes, even if they could have an extensive knowledge of food. However, we found also that boys have lower prevalence of OvR and this can be controversial, because we would expect the same tend. A reason may be that our boys reported a lower consumption of junk food (high energy density foods), which could affect our estimates of OvR. For these reasons, the 24HR were conducted in the presence of the person responsible for adolescents' feeding. Besides, it should be stressed that GOCS sample was representative of adolescents of middle-low to low-income families, therefore, the social pressure of an adequate body image in this group (boys) could be lower than in those adolescents with high income families [4, 32].

Under-reporting was positively associated with obesity; similar associations have been already reported in some studies [6-9]. We showed that obesity adolescents (z score BMI $\geq$ 2) had higher UnR than those without obesity (82% and 43% respectively). The reasons why UnR of energy intake were higher among obese adolescents remain unclear, but probably share similarities with those that have been identified among obese adults who UnR energy intake. Features such as willful failure to report due to a conscious desire to misrepresent a lower energy intake, reporting of more dietary items considered healthy than unhealthy, omission of meals consumed outside home and at unusual times, high concerns with body weight and image, and social desirability may contribute to the UnR of energy intake among adolescents [1, 4, 5]. Additionally, considering that most of 24HR were made in the presence of the adolescents' mothers, we evaluated if maternal obesity (highly frequent in GOCS 38%) was associated with increased frequency of misreporting in univariate models. We observed a higher prevalence of UnR among adolescents whose mothers were obese than among their counterparts, i.e., among adolescents whose mothers were normal weight (58.3% UnR versus 46.2% UnR, respectively). This could be explained by the relationship between parents and childhood

obesity [33], since that parents and children can feel judged by the interviewers of GOCS because they are nutritionists.

Few studies have reported if specific macronutrients or food groups are affected by misreporting of energy intake and overall, results have been inconclusive [2, 9, 11, 34]. We found that UnR reported lower contributions of total and saturated fats and higher contribution of protein (expressed as a percentage of energy) independent of gender. However, we did not find associations with carbohydrate consumption, although UnR girls reported lower contributions of added sugars. Besides, we showed that UnR had higher intakes of sodium (expressed as mg/1000 kcal) than their counterparts. Our finding were consistent with a recent study realized in 630 Caucasian children aged 8-10 aged, where the authors observed a lower report of fat, saturated fat and a higher report of protein and sodium [35]. Care should be taken in interpreting these data, because macronutrient tend to be related, for example carbohydrates (sugar) and fat; besides the people under or over report foods mainly to a reasons socially desirable [2]. The under report de fat in our study was consistent with under report of unhealthy food (cookies, chocolate, salty snack), high in fat total and saturated fat but also high in added sugar and sodium. Adolescents are susceptible to foods advertising, for this reason warning front labeling, advertising control and prohibition of food sales within schools are measures of current Chilean public health policies to prevent obesity aimed to children and adolescents under 14 years old [36].

Bread was the food groups that contributed most to EI and also were those that likely contributed most to sodium intake (500 mg/100 g of bread). In Chile, bread consumption is one of the highest worldwide (86.5 kilograms per person/year), mainly among low-income families [18]. Nevertheless, it is interesting that UnR among adolescents of both sexes had higher consumption than those PR or OvR. This could be due to the fact is a very well accepted food in the Chilean population and people may believe that its consumption or higher intake is healthier. Conversely, selective misreporting was observed for the vegetable group, which is considered socially desirable and commonly perceived as healthy by population. UnR adolescents (boys and girls) reported a higher intake (expressed as a

percentage of total energy) of vegetables that those PR, these findings are similar to those found in international literature [2, 10]. In our study we found that UnR girls reported less unhealthy foods whit high sugar content such as cakes, cookies, candies, chocolate; than those PR or OvR [1]. On the other hand, UnR boys reported less unhealthy foods with high sodium and fat such as junk food (*sopaipillas, Chilean hot dog, sandwiches, empanadas*), salty snack, crackers, mayonnaise, ketchup among others. We did not find previous studies about selective misreporting of foods and/or nutrients, but this kind of misreporting would seriously mislead the results of a study, such as overestimation in the number of subjects with inadequate nutrient intakes and attenuation or biased associations between diet and diseases. We observed spurious associations between some nutrients or food groups intake with the Z score BMI in the models that were not adjusted by misreporting status. The adjust by misreporting or the associations only in PR were consistent with previous studies that link some nutrients with obesity [14, 37-39]. For this reason, it is important to considerate misreporting status, because associations between dietary exposures and health outcomes are strongly affected or even masked by measurement errors [1, 31].

Regarding the factors associated to UnR, as already acknowledged by previous studies, obesity was the main predictor of UnR [6-10]. The associations between pubertal development and UnR of energy intake has not been previously reported in the literature. We found that adolescents in advanced stages pubertal had higher odds of being classified as UnR but with borderline significance statistical. The development of the sexual secondary characteristics, could affect the body image in adolescents [40], and this could influence the UnR (1) of some high energy density foods such as junk food, crackers, salty snack, chocolates and confectionary as was saw in our study, but we need more studies to corroborate this association.We no found associated factors to OvR in adolescents, likely for lack statistical power. OvR has been few studied.

Adolescents that did not attend school feeding program had higher odds of being classified as UnR, but with borderline significance statistical. It is likely that children who participate in the school

feeding program have more structured eating behaviors and healthier nutrition and therefore, are less inclined to change the report of their dietary intake [41].

As a limitation of the present study, we could mention that the sample does not have national representativeness, since the sample is comprised only of adolescents from lower and middle-income class neighborhoods in Santiago. However, GOCS sample is representative of Chilean adolescents from public schools (16, 17), a population group not frequently evaluated in longitudinal studies. In addition, we decided to assume that all adolescents had a low physical activity level for the energy requirements estimation (20) what might be a conservative estimation; although unlikely given the extend of sedentarism in the population. Strengths of this study include the anthropometric measurements and the 24HR that were collected by trained nutritionists following standard and validated protocols, in order to reduce measurement errors or response bias. In addition, our study was the first to assess pubertal development and to analyze its association with misreporting of energy intake.

Conclusion

In a sample of Chilean adolescents, the frequency of misreporting was high, particularly UnR among boys, likely reflecting the fact that in this population boys tend to be less on control of their dietary behaviors compared to girls. Obesity was the main predictor of under-reporting and pubertal development should also be taken into account when analyzing dietary behaviors. Besides, we show that misreporting was selective to some food groups and it can change the directionality of associations between some nutrients or food groups and body mass index.

Table 1: Anthropometric, sociodemographic, maternal characteristics, sedentary and eating behaviors of Chilean adolescents, according categories of misreporting, GOCS Study 2014-2015.

	Total		PR (n=357)		UnR (n=447)		OvR (n=78)		
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**p Value***
	882	100	357	40.5	447	50.7	78	8.8	
Sociodemographic									
Age, years‡	12.18	0.07	12.10	0.69	12.24	0.69	12.19	0.80	0.163
Sex									
Boys	434	49.2	149	34.3	254	58.5	31	7.1	**<0.001**
Girls	448	50.8	208	46.4	193	43.1	47	10.5	
Type of family									
Nuclear	481	54.5	191	39.7	252	52.4	38	7.9	0.193
Single-Parent	169	19.2	78	46.2	72	42.6	19	11.2	
Extended	232	26.3	88	37.9	123	53.0	21	9.1	
Family income (CLP)									
0-300.000	221	29.1	98	44.3	104	47.1	19	8.6	0.730
300.001-600.000	401	45.5	154	38.4	209	52.1	38	9.5	
600.001-2.000.000	138	15.6	60	43.5	68	49.3	10	7.3	
missing	122	13.8	45	36.9	66	54.1	11	9.0	
Head of household									
mother	256	29.0	108	42.2	126	49.2	22	8.6	
father	410	46.5	167	40.7	210	51.2	33	8.1	0.918
another	193	21.9	74	38.3	99	51.3	20	10.4	
missing	23	2.6	8	34.8	12	52.2	3	13.0	
Nutritional status									
Obesity (BAZ≥2)§									
yes	702	79.6	30	16.7	147	81.7	3	1.7	**<0.001**†
no	180	21.4	327	46.6	300	42.7	75	10.7	
Tanner (stage)									
1-3	420	47.6	162	38.6	219	52.1	39	9.3	0.131
4-5	439	49.8	185	42.1	220	50.1	34	7.7	
undefined	23	2.6	10	43.5	8	34.8	5	21.7	
Sedentary behavior									
Sleep time (h/d)									
≥ 9	236	26.8	99	41.9	122	51.7	15	6.4	0.291
< 9	532	60.3	211	39.7	273	51.3	48	9.0	
missing	114	12.9	47	41.2	52	45.6	15	13.2	
Screen time (h/d)									
≥ 2	205	23.2	84	40.9	107	52.2	14	6.8	0.720
< 2	496	56.2	196	39.5	254	51.2	46	9.3	
missing	181	20.5	77	42.5	86	47.5	18	9.9	
Maternal characteristics									
Maternal education (years)									
≥ 12	578	65.5	237	41.0	298	51.6	43	7.4	0.335

< 12	280	31.7	111	39.6	136	48.6	33	11.8	
missing	24	2.7	9	37.5	13	54.2	2	8.3	
Maternal obesity (BMI≥30 k/m2)									
No	520	58.9	227	43.7	240	46.2	53	10.2	**0.009**
Yes	338	38.3	118	34.9	197	58.3	23	6.8	
missing	24	2.7	12	50	10	41.7	2	8.3	
Mother works outside home									
yes	562	63.7	238	42.4	278	49.5	46	8.2	0.536
no/sometimes	282	31.9	106	37.6	149	52.8	27	9.6	
missing	38	4.3	13	34.2	20	52.6	5	13.2	
Eating behaviour									
Exclusive breastfeeding (days)									
≥ 120	300	34.0	118	39.3	162	54.0	20	6.7	0.246
<120	524	59.4	219	41.8	255	48.7	50	9.5	
missing	58	6.6	20	34.5	30	51.7	8	13.8	
Breastfeeding (months)									
≥ 12	283	32.1	105	37.1	155	54.8	23	8.1	0.236
< 12	525	59.5	227	43.2	252	48.0	46	8.8	
missing	74	8.4	25	33.8	40	54.1	9	12.2	
Introduction of soft drink (months)									
≤ 12	613	69.5	293	47.8	292	47.6	28	4.6	0.735
> 12	206	23.4	97	47.1	98	47.6	11	5.3	
	32	3.6	26	50.8	5	41.3	63	7.9	
Introduction of confectionary (months)									
<12	275	31.2	103	37.5	146	53.1	26	9.5	0.171
≥ 12	549	6.2	235	42.8	271	49.4	43	7.8	
missing	58	6.6	19	32.8	30	51.7	9	15.5	
Introduction of complementary feeding (months)									
< 6	202	22.9	83	41.1	103	51.0	16	7.9	0.458
≥ 6	629	71.3	257	40.9	318	50.6	54	8.6	
missing	51	5.8	17	33.3	26	51.0	8	15.7	
Consumption of school meals									
yes	279	31.6	122	43.7	126	45.2	31	11.1	0.053
no	603	68.4	235	39.0	321	53.2	47	7.8	

PR, plausible reporters; UnR, under-reporters; OvR, over-reporters.
* p value: Chi2 test
‡ T- test
† p value: Fisher test
§ BMI-for-age *z* scores ≥ 2 [26]

Table 2: Energy, macronutrients and key nutrients intake of Chilean adolescents (n=882) according categories of misreporting; GOCS Study 2014-2015.

	TOTAL							GIRLS							BOYS						
	PR (n:357)		UnR (n:447)		OvR (n:78)			PR (n:208)		UnR(n:193)		OvR (47)			PR(n:149)		UnR(n:254)		OvR(n:31)		
	mean	sd	mean	sd	mean	sd	p value	mean	sd	mean	sd	mean	sd	p value	mean	sd	mean	sd	mean	sd	p value
Energy requeriment (Kcal)	2105	*305*	2441	414	2019	254	<0.001$_{a,b,c}$	1974	186	2128	199	1942	181	<0.001$_{a,c}$	2289	343	2680	373	2136	302	<0.001$_{a,c}$
Energy Intake (Kcal)	2012	322	1487	310	2902	497	<0.001$_{a,b,c}$	1907	262	1343	219	2871	516	<0.001$_{a,b,c}$	2158	340	1595	325	2948	472	<0.001$_{a,b,c}$
Fat (% of total EI)	29.99	6.05	28.22	6.39	32.41	6.24	<0.001$_{a,b,c}$	30.19	6.17	28.35	6.55	32.54	6.95	<0.001$_{a,b,c}$	29.72	5.89	28.11	6.26	32.22	5.08	<0.001$_{a,b,c}$
Carbohydrates (% of total EI)	57.20	6.58	58.36	7.68	56.29	7.04	0.007$_{a,c}$	57.00	6.65	58.17	8.20	56.24	7.88	0.099$_{a,c}$	57.48	6.50	58.51	7.27	56.38	5.64	0.100$_{c}$
Proteins (% of total EI)	13.88	2.92	14.66	3.13	12.43	2.63	<0.001$_{a,b,c}$	13.92	3.05	14.81	3.44	12.45	2.64	<0.001$_{a,b,c}$	13.83	2.75	14.56	2.88	12.41	2.67	<0.001$_{a,b,c}$
Saturated fat (% of total EI)	10.09	2.95	9.26	2.72	10.42	2.85	<0.001$_{a,c}$	10.23	3.17	9.27	2.75	10.63	3.31	0.003$_{a,c}$	9.89	2.61	9.24	2.71	10.10	1.97	0.016$_{a,c}$
Sodium (mg/1000 kcal)	1553	321	1658	399	1485	296	<0.001$_{a,c}$	1538	339	1669	434	1459	314	0.002 $_{a,c}$	1574	295	1650	371	1524	268	0.077$_{a}$
Added sugars (% of total EI)	17.48	6.42	17.01	7.29	20.15	7.41	0.003$_{b,c}$	17.17	6.36	16.79	7.71	20.62	8.19	0.014$_{c,b}$	17.92	6.50	17.18	6.95	19.44	6.09	0.125$_{a}$

PR, plausible reporters; UnR, under-reporters; OvR, over-reporters.
P value: ANOVA with Bonferroni's multiple comparison test
a Significant difference between plausible reporters & under-reporters
b Significant difference between plausible reporters & over-reporters
c Significant difference between under-reporters &-over-reporters

Table 3: Food groups (% energy intake) consumption among Chilean adolescents according categories of misreporting of energy intake, GOCS Study 2014-2015.

	TOTAL							GIRLS							BOYS						
	PR (n:357)		UnR (n:447)		OvR (n:78)			PR (n:208)		UnR (n:193)		OvR (n:47)			PR (n:149)		UnR (n:254)		OvR (n:31)		
	mean	SD	mean	SD	mean	SD	P value	mean	SD	mean	SD	mean	SD	P value	mean	SD	mean	SD	mean	SD	P value
Yogurts	2.59	3.82	2.99	4.46	1.77	2.73	0.202c	2.59	3.81	3.38	4.82	1.94	2.88	0.214	2.60	3.84	2.69	4.15	1.52	2.60	0.434
Cheese	2.17	3.24	1.93	3.57	2.08	3.25	0.059a	2.25	3.42	1.81	3.32	2.15	3.24	0.080a	2.06	2.97	2.03	3.76	1.99	2.06	0.496
Milk	6.18	6.53	5.89	6.58	4.53	4.12	0.348	6.13	6.56	5.80	6.15	4.21	4.51	0.289	6.25	6.50	5.96	6.89	5.01	6.25	0.646
Meat	4.76	6.12	5.67	7.01	3.78	4.94	0.129c	4.96	6.45	5.83	7.78	4.04	4.88	0.879	4.47	5.62	5.55	6.38	3.38	4.47	0.067
Eggs	1.46	2.49	2.32	3.84	1.30	2.39	0.143a	1.46	2.38	2.26	3.60	1.04	2.32	0.088c	1.45	2.64	2.36	4.02	1.70	1.45	0.460
Bread	17.49	9.35	18.69	11.05	13.96	9.24	0.001b,c	16.88	8.67	17.56	11.30	13.88	9.07	0.051b,c	18.36	10.19	19.55	10.81	14.09	18.36	0.036b,c
Rice, potato and pasta	13.80	10.93	14.58	11.13	12.65	9.59	0.318	14.15	11.05	14.07	11.83	11.63	10.10	0.364	13.31	10.78	14.97	10.58	14.21	13.31	0.241a
Vegetables	1.67	2.24	2.42	3.05	1.57	2.66	0.001a,c	1.85	2.47	2.58	2.98	2.03	3.24	0.025a	1.42	1.87	2.29	3.11	0.88	1.43	0.006a,c
Fruit	2.37	3.35	2.79	4.08	1.57	2.65	0.079b,c	2.51	3.75	3.03	4.34	1.81	3.11	0.235c	2.18	2.69	2.61	3.86	1.21	2.18	0.276
Homemade dishes	5.11	8.35	5.84	8.71	4.50	6.58	0.653	5.29	9.05	6.56	8.93	4.32	6.71	0.218	4.87	7.29	5.29	8.52	4.77	4.87	0.824
Junk food	7.08	11.74	5.19	10.26	9.15	13.07	0.001a,c	5.78	10.22	4.61	9.63	8.90	13.68	0.060c	8.89	13.41	5.62	10.71	9.54	8.89	0.003a,c
Processed meats	3.71	5.31	3.23	5.23	4.05	6.34	0.201	3.27	4.90	3.13	5.54	4.07	7.52	0.413	4.31	5.80	3.31	5.0	4.02	4.31	0.112c
Juice and soft drink	7.46	5.59	7.77	6.56	8.22	6.79	0.845	7.12	5.29	7.16	6.19	8.37	7.48	0.708	7.95	5.98	8.23	6.79	8.00	7.95	0.977
Ready-to-eat cereal	1.62	3.15	1.87	3.46	1.23	3.34	0.259	1.55	3.22	1.73	3.12	0.76	1.47	0.285	1.71	3.06	1.98	3.71	1.94	1.71	0.791
Crackers and salty snack	3.06	5.61	2.05	4.79	4.42	7.64	<0.001a,c	3.48	5.92	2.80	6.02	3.56	7.01	0.110a	2.49	5.12	1.48	3.49	5.72	2.49	<0.001a,b,c
Chocolate and confectionary	3.02	6.19	2.08	4.09	6.16	9.30	<0.001a,b,c	3.34	7.13	1.63	3.58	7.19	9.85	<0.001a,b,c	2.58	4.54	2.42	4.42	4.59	2.58	0.171c
Cookies and cake	8.74	9.72	6.85	8.94	11.04	12.33	<0.001a,c	9.88	10.59	7.67	9.77	12.27	13.83	0.017a,c	7.15	8.14	6.22	8.22	9.17	7.15	0.088c
Dessert and ice cream	1.92	3.54	2.05	4.00	2.23	3.82	0.216c	1.78	3.41	2.54	4.68	2.05	3.01	0.419	2.13	3.72	1.68	3.35	2.51	2.13	0.087a
Sugar	2.19	2.61	2.12	2.91	1.57	1.88	0.118b	2.09	2.40	2.26	3.04	1.33	1.43	0.220b	2.32	2.89	2.02	2.81	1.93	2.32	0.216a
Butter & margarine	1.32	2.22	1.06	1.73	1.25	1.79	0.083a	1.31	2.48	0.93	1.51	1.32	2.01	0.199	1.33	1.80	1.17	1.87	1.14	1.33	0.253
Mayonnaise, ketchup, mustard	0.20	0.89	0.41	1.85	0.32	1.43	0.006a,b,c	0.23	0.85	0.21	0.97	0.41	1.68	0.099b,c	0.58	0.71	0.88	1.06	0.68	0.58	0.044a,c

PR, plausible reporters; UnR, under-reporters; OvR, over-reporters.

p value: Kruskall Wallis test, Dunn test pos hoc

a Significant difference between plausibles & under-reporting, b Significant difference between plausibles & over-reporting, c Significant difference between under-reporting &-over-reporting

Table 4: Multiple logistic regression models of factors associated to misreporting GOCS Study 2014-2015.

	Model UnR (n:764)				Model OvR (n:406)			
	Odds ratio	**95% Conf. Interval**		**P value**	**Odds ratio**	**95% Conf. Interval**		**P value**
Sex (girls)	0.51	0.33	0.80	**0.003**	1.35	0.63	2.88	0.438
Adolescent Obesity (yes)	5.10	3.24	8.04	**0.000**	0.51	0.15	1.78	0.292
Stage Tanner 4 – 5	1.44	0.96	2.16	0.080	0.64	0.33	1.23	0.183
Consumption of school meals (no)	1.35	0.97	1.89	0.072	0.72	0.43	1.23	0.233
Maternal Obesity (yes)	1.19	0.87	1.65	0.281	0.93	0.52	1.66	0.818
Age (years)	1.18	0.91	1.56	0.210	1.30	0.91	1.56	0.244

Adolescent Obesity: ≥ 2 z score BMI

Maternal Obesity: BMI ≥30 kg/m2

Table 5: Association between Z score BMI and macronutrients and food group with and without adjusting by misreporting status GOCS Study 2014-2015.

	MODEL 1 (n: 882)				MODEL 2 (n:858)				MODEL 3 (n:782)				MODEL 4 (n:345)			
	Coef β	p value	95% Conf.	Interval	Coef β	p value	95% Conf.	Interval	Coef β	p value	95% Conf.	Interval	Coef β	p value	95% Conf.	Interval
Fat (% of total EI)	-0.00	0.634	-0.015	0.009	0.00	0.681	-0.009	0.014	0.02	**0.001**	0.007	0.029	0.02	**0.034**	0.001	0.037
Carbohydrates (% of total EI)	-0.01	0.306	-0.016	0.005	-0.01	0.120	-0.018	0.002	-0.02	**0.001**	-0.025	-0.006	-0.01	0.101	-0.030	0.003
Proteins (% of total EI)	0.04	**0.000**	0.020	0.070	0.04	**0.002**	0.014	0.062	0.01	0.375	-0.012	0.033	-0.01	0.686	-0.046	0.030
Saturated fat (% of total EI)	-0.03	0.056	-0.052	0.001	-0.02	0.226	-0.042	0.010	0.02	0.193	-0.008	0.040	0.03	0.137	-0.009	0.064
Sodium (mg/1000 kcal)	0.00	**0.000**	0.000	0.001	0.00	**0.000**	0.000	0.001	0.00	**0.031**	0.000	0.000	0.00	0.537	0.000	-0.000
Added sugars (% of total EI)	-0.01	**0.044**	-0.022	-0.000	-0.01	**0.040**	-0.022	-0.001	-0.01	0.205	-0.016	0.004	0.01	0.267	-0.007	0.027
Yogurts (%EI)	-0.01	0.500	-0.025	0.012	-0.01	0.294	-0.028	0.008	-0.02	**0.013**	-0.037	-0.004	-0.02	0.114	-0.051	0.006
Vegetables (%EI)	0.05	**0.001**	0.021	0.077	0.05	**0.001**	0.019	0.073	0.02	0.143	-0.006	0.044	0.03	0.302	-0.023	0.075
Processed meats (%EI)	0.01	0.246	-0.006	0.023	0.01	0.359	-0.007	0.020	0.01	**0.039**	0.001	0.027	0.02	**0.044**	0.001	0.041
Juice and soft drink (%EI)	0.01	0.127	-0.003	0.022	0.01	0.298	-0.006	0.018	0.01	0.350	-0.006	0.016	0.02	**0.030**	0.002	0.041
Cookies and cake (%EI)	-0.00	0.255	-0.012	0.003	0.00	0.454	-0.011	0.005	0.00	0.304	-0.004	0.011	0.01	0.145	-0.003	0.020

Model 1: model crude

Model 2: adjusted by age, sex, tanner, maternal education, maternal BMI

Model 3: model 2 + adjusted by misreporting (UnR, OvR)

Model 4: model 2 only PR

Supplemental file 1: Reference and cut-off values used to identify misreporting among adolescents

	n	CVrEI (%)*	CVpER† (%)	CVmTEE‡ (%)	Plausibility range (% rEI/pER)
Girls	448	27.4	4.8	8.2	78.4 to 121.6
Boys	434	26.3	4.2	8.2	79.1 to 120.9

CV, coefficient of variation, EI, energy intake; ER, energy requirement; TEE, total energy expenditure.
* Intra-individual variation of EI (24-h recall, GOCS).
†Error in predicted energy expenditure requirements, according to Huang et al and DRI (19, 24).
‡Day-to-day variation and measurement error for TEE based on the double labelled water technique (23).

Supplemental Files 2
S2. Description of the foods that composed each of the 21 food groups. GOCS Study, Chile 2014-2015.

Food groups	Food composition
Milk	Fluid whole milk (3% fat), whole milk powder, reduced fat milk (2% fat), skim milk, skim milk powder, Flavored milk purchased ready-to-drink
Yogurts	Yogurt, fermented milk
Cheeses	Gouda cheese, ricotta cheese, cream cheese, cheddar cheese,
Meat	Steak beef, ground beef, beef ribs, pork chop, pork ribs, pork loin, poultry, chicken, turkey, fish, viscera (all cooking methods)
Processed meats	Ham, bologna, turkey breast, chicken breast, salami, Sausage, sausages, frankfurters, meatballs ready for consumption, nuggets, hamburger ready for consumption (only meat).
Junk food	Pizzas, sandwiches of meat or hamburger ready to eat, french fries, wonton, egg roll, chilean hot dog, *sopaipillas, tacos, empanadas.* Mainly, street food or fast food
Juice and soft drinks	Juice or flavored drink, purchased ready-to-drink, juice or flavored drink, dry mix – unprepared, Soda pop or soft drink regular or diet
Bread	French bread, bun bread, white bread with salt
Ready to eat cereal	Breakfast cereals
Rice, potato and pasta	Rice, cooked potatoes, mashed potatoes, pasta and dishes pasta.
Vegetables	Lettuce, cabbage, raw salad, others load vegetables. Pumpkin, carrot, cucumber, tomato, among others.
Fruits	Pineapple, banana, orange, apple, pear, papaya, mango, watermelon, tangerine, grape, blueberry, strawberry, blackberry, fruit salad, fruit juices
Eggs	Fried eggs, scrambled eggs, omelet, boiled eggs, egg white, egg yolk
Homemade dishes	Typical chilean food or meals prepared at home, restaurants or schools; that require a longer preparation time and made with natural foods. For instance: Beans, lentils, chickpeas, white beans, legumes-based preparations, vegetables stews with or without meat, *cazuela, charquican, chapsui, humitas, pastel de choclo* among others.
Cracker and salt snack	Crackers, saltine or soda, salty chips - snack type, cheese balls, puffs or twists, potato chips
Chocolates and confectionary	Chocolate candy, chocolate candy bar, sweets based on milk, lollipop, candy, caramel, jams, *dulce de leche*

Cookies and Cake	Cookies and bars, granola bars, sweet biscuit and cookie stuffed, cookie sandwich, cookies commercial packaged, Cakes, cheesecake, cake sponge, doughnut, muffins, pies fruit, cupcake, cake purchased ready-to-eat
Desserts and ice cream	Pudding, flan, mousse, gelatin dessert, chilean desserts, fruit canned with syrup, ice cream and frozen desserts, Popsicle
Sugar	White sugar, chocolate powder
Butter and margarine	Salted butter, unsalted butter, salted margarine, unsalted margarine, light margarine
Mayonnaise, ketchup	Mayonnaise or mayo type dressing, ketchup, mustard, soy sauce

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8.2 SEGUNDO MANUSCRITO

"DIETARY PATTERNS AMONG CHILEAN ADOLESCENTS FROM THE GROWTH AND OBESITY COHORT STUDY INDICATE POOR DIETARY QUALITY".

Key words: Dietary patterns, Adolescents, Overweight, Exploratory Factor Analysis

Abbreviations

GOCS, Growth and Obesity Cohort Study

LAC, Latin America and the Caribbean

SSBs, sugar-sweetened beverages

WHO, World Health Organization

DP, dietary patterns

24HR, 24-hour recalls

BMI, body mass index

EFA, exploratory factor analysis

EI, energy intake

EER, estimated energy requirements

OR, odds ratios

CI, confidence interval

SES, socioeconomic status

Abstract

Diet during adolescence can have lasting effects on nutritional status, health, and development; however, evidence during this period from Latin America countries is limited. We hypothesized that dietary patterns with low-quality nutrition are associated with overweight. We collected data for 882 Chilean adolescents from the Growth and Obesity Cohort Study (mean age 12 years, sd=0.7). Socio-demographic, dietary, and weight status data were obtained during clinical visits. Dietary intake was assessed through 24-h recalls, and dietary patterns were obtained through exploratory factor analysis. Logistic regression models adjusted for potential confounding variables were used to examine the association between dietary patterns and body weight. Four dietary patterns accounted for 24.9% of the dietary behaviors: "Breakfast/*Once*," "Meat and Vegetables," "Western," and "Sweet Snack." "Breakfast/*Once*," "Western," and "Sweet Snack" patterns provided higher energy and excess nutrients, which has been associated with chronic diseases (sodium, saturated fat, added sugars). Moreover, adolescents with a higher adherence to "Western" or "Sweet Snack" patterns (third tertile) had odds of being classified as overweight (OR= 1.67; 95% CI: 1.103–2.522 and OR= 1.86; 95% CI: 1.235–2.792; respectively) than those with lower adherence (first tertile); adherence to the "Meat & Vegetables" pattern was also associated with overweight (OR= 1.83; 95% CI: 1.219–2.754). These dietary patterns were associated with higher caloric intake and overconsumption of nutrients of public health concern. Three of the four main dietary patterns were associated with overweight. These results can contribute to the development of regulatory actions to tackle the current obesity problem in Chile.

Key words: dietary pattern; adolescent; overweight; exploratory factor analysis

1. Introduction

Adolescence is a critical stage in life, and it is characterized by an accelerated growth rate and multiple physical and social changes that prepare a person for adulthood [1]. Diet quality during this period is important, as it can affect an adolescent's nutritional status and can have long-lasting effects on their future feeding behavior, nutritional status, early life health, and on the development of their offspring [2-4]. Nonetheless, diet during this period is not well studied and there is a need for further evidence [5].

The rising trend of overweight and obesity in children and adolescents has plateaued in many high-income countries (HIC) and industrialized low to middle income countries (LMIC), albeit at high levels [6]. In the last few decades, in Latin America and the Caribbean (LAC) regions, there has been a shift towards diets based mostly on foods with added sugar and salt, refined carbohydrates, grain-based desserts, and savory snacks [7]. In combination with a decline in physical activity, these diets have led to a rapid increase in childhood obesity in LAC countries [5, 7, 8].

Among LAC countries, Chile has one of the highest prevalence rates (up to 31%) of overweight and obesity in children and adolescents [5, 8] . In addition, Chile has the highest measured per capita sales of sugar-sweetened beverages (SSBs); junk food; salted snacks; and foods high in added sugar, saturated fats, and sodium [7] among LAC countries. There is now evidence that dietary patterns, rather than individual nutrients or

foods, contribute to disease trajectories [9-13]. However, how the consumption of different foods is integrated within specific dietary patterns, particularly in LAC countries where there is great cultural and dietary diversity, is unclear [14].

Adolescents' diets have been less studied than those of adults, or have been extrapolated from adult data [5], and the evidence for dietary patterns is particularly scarce for LAC countries [14, 15]. We hypothesized that dietary patterns with low-quality nutrition (high in saturated fat, added sugars, and sodium) are associated with overweight. Thus, the aim of the present study was to describe the dietary patterns in a cohort of low-middle income adolescents from Chile, which has one of the highest prevalences of obesity in LAC countries, and to examine the associations of these diets with socio-demographic factors and excess body weight. The data were collected before the implementation of a set of regulatory actions to prevent obesity (warning labels, marketing, and control of food sold in schools) [16], and therefore, can serve as a baseline for assessing the effect of the regulations.

2. Methods

2.1 Study population

Our study sample was obtained from adolescents participating in the Growth and Obesity Chilean Cohort Study (GOCS). Briefly, GOCS is a population-based ambispective cohort

of 1,195 children, born in 2002–2003, from six low-middle income counties from the southeast area of Santiago, Chile. Participants were children who were born at term (37–42 weeks); had a birthweight of between 2,500 and 4,500 g; and were free from conditions that could affect their growth, such as food allergies, and genetic and metabolic diseases. Details of the design, objectives, and recruitment strategies of the GOCS have been described elsewhere [17, 18]. GOCS contains data on anthropometric measurements and sexual maturation evaluations collected every six months since 2006 [19]. Dietary assessments were carried out in person during clinic visits in 2013 with the use of 24-h recalls (24HR).

The present study used data collected during the 8–9-year follow-up. In the present study, all adolescents were evaluated in 2014–2015, with at least one 24HR per participant (n = 913), and anthropometric measurements were obtained during the same clinic visit (n = 882). We excluded 31 adolescents (21 boys and 11 girls) because no anthropometric measurements were available. The final sample of this study included 882 adolescents. There were no differences in age and energy intakes between the total sample and the excluded participants (i.e., mean ages 12.07 vs 12.02 years and energy intake 1828 vs 1827 mean kilocalories/day, respectively).

The study protocol was approved by the Institutional Reviewer Board from the Institute of Nutrition and Food Technology, University of Chile. Parents/caregivers provided informed consent before data collection.

2.2 Dietary data collection

Dietary data were obtained through two non-consecutive 24HR interviews on different weekdays, weekends, and seasons, following the "Multiple Pass Method" [20]. About 60% of the second recalls were collected 6 months after the first recall. The interviews were conducted in person by trained dieticians in the presence of the person responsible for preparing and serving meals to the adolescents to avoid food misreporting. Dietary intake data included the time of the meal and in-between meals; names of dishes, and cooking methods; and a list of food, beverages, and serving sizes (household measures), and was obtained with the aid of a photo atlas from the National Survey of Food Consumption of Chile [21]. Energy and nutrient intakes from 24HRs were calculated using the Nutrition Data System for Research (NDSR) program (version of 20014, NCC, University of Minnesota, Minneapolis, USA), which uses the United States Department of Agriculture (USDA) database as the main food composition table. Therefore, all foods and beverages listed in the 24HR interviews were matched with those in the NDSR database through their general description (i.e., name, preparation, and cooking method). Energy and macronutrient values available in the Chilean Food Composition table [22], local food industry composition tables, and/or nutrition food labels were compared to values described by the software. A concordance rate between 80 and 120% for each parameter analyzed was required to accept food harmonization. Chilean preparations, such as *charquican, cazuela,* and *sopaipillas*, were added as recipes to the NDSR because they are commonly consumed by Chilean adolescents and were not in the software database. We observed 24HRs with values over 3,500 kcal and under 500 kcal [23], which

were revised to rule out digitalization errors. We did not exclude any participant with these values.

In total, 1,053 different foods were reported in two 24HRs, but 993 were consumed by at least 5% of the sample. These food items were collapsed into 29 food categories on the basis of their nutritional value, coefficient correlation between groups, commonality values, food preparation methods, and Chilean dietary behaviors **(Supplemental files)**.

2.3 Anthropometric measurements

Anthropometric measurements were obtained using validated techniques, and they were duplicated by two trained dietitians using standard procedures (one for each sex, intra-, and inter-class correlation > 0.9) [19]. Body weight was measured with a standardized scale (TANITA BC-418) with 0.1 kg precision, and height was measured using a longitudinal stadiometer (SECA 222) ranging from 6 to 230 cm in capacity and a precision of 0.1 cm. Body mass index (BMI) was defined using the standard formula: weight (kg) divided by height squared (m^2). The BMI z-score was calculated according to the World Health Organization (WHO) definition for age and sex, and it was used to classify the adolescents' body weight status as underweight (≤ -1 SD), normal weight (< -1 SD and < +1 SD), overweight (≥ +1 SD and < +2SD), and obese (≥ +2 SD) [24]. We used the term overweight (outcome variable) when referring to overweight and obesity nutritional status combined.

2.4 Covariates

2.4.1 Sexual maturation

A pediatric endocrinologist evaluated the adolescents' breast and genital development and classified them according to the Tanner stages. Girls were evaluated according to their breast development through inspection and palpation using the Tanner scale. Boys were evaluated according their genitalia development through palpation using the Prader orchidometer [25].

2.4.2 Maternal self-reported information

The following information was obtained: (i) Maternal highest education level (≥ 12 y or < 12 y), (ii) children's school administrative status (private or public), (iii) hours of sleep (meeting or not meeting the recommendations ≥ 9 h/day or < 9 h/day), and (iv) participation in the school feeding program (yes or no).

The school feeding program aims to provide daily food services (breakfast, lunch, *once* [a typical Chilean meal served sometime between 5–9 pm, comparable to teatime], snacks, and dinner, as appropriate) to all students from vulnerable sections of society in

Chile's public schools. In the present study, 30% of the adolescents were reported to be beneficiaries of the school feeding program.

2.4.3 Maternal weight status

A trained dietitian measured the participants' mothers' weights and heights to calculate their BMI and classify their weight status according to the WHO guidelines[26].

2.5 Statistical analysis

Firstly, we used statistical modeling techniques incorporated into the Multiple Source Method online platform, which were used to estimate the usual intake of each food group in grams [27]. Exploratory factor analysis (EFA) was used to identify the dietary patterns from 29 food groups. Initially, factors with Eigenvalues greater than or equal to 1.0 were retained. In the second stage, the screen plot was visually inspected, and it suggested the retention of four factors. Varimax orthogonal rotation was applied for better interpretation of the factor loading matrix and to ensure independence of the factors derived. Factor loadings greater than or equal to 0.25 were considered to contribute to the pattern [28]. The retained patterns were named according to their interpretability, the characteristics of the food in each dietary pattern, and the commonalities observed, which reflect the level of linkage between the variable (food group) and the extracted factor. For each

participant, the factor score of each dietary pattern was calculated using the regression scoring method [29]. The dietary pattern scores were then stratified into tertiles and used as independent variables. The Kruskal–Wallis, χ_2, Pearson's, and Mann–Whitney U tests were used to investigate the associations between the adherence to dietary patterns and weight status, Tanner stages, socio-demographic variables, and maternal variables (bivariate analyses).

We also used the Multiple Source Method to estimate the usual intake of energy and critical nutrients of public health concern (i.e., sodium, added sugars, saturated fats) [30]. Individual usual nutrient intakes were expressed in grams or micrograms per 1000 kcal of energy, or as total percentage of energy intake.

Median and inter-quartile ranges were provided according to factor score tertiles. The associations between usual nutrient intakes and adherence to dietary patterns were calculated by applying the Kruskal–Wallis and Dunn tests.

Misreporting of energy intake was estimated with the following equation: EI (energy intake) – EER (estimated energy requirements)/EER × 100 [31]. This variable was adjusted for in all regression models. Logistic regression models were used to investigate the association between adherence to each dietary pattern and overweight (dummy variable defined herein as overweight [yes or no]) with covariates adjusted. Odds ratios (OR) and 95% confidence intervals (95% CI) were provided. All analyses were performed

using STATA software version 15 (College Station, TX, StataCorp, 2007) with significance values established for all tests at $p < 0.05$ (5%).

3. Results

3.1 Demographics and lifestyle characteristics

The sample from GOCS included 882 respondents (mean age 12 years, SD = ±0.7), of which 50.8% were female. The majority of the adolescents were classified as overweight or obese (51.6%). Almost half of the participants (49.7%) were classified into the fourth and fifth Tanner stages of sexual maturation. More than 60% of the participants slept for more than 9 h/day and studied at private schools. In relation to the maternal socio-demographic and weight status, over half (65.5%) of the participant mothers did not have more than 12 years of study, and 41% were classified as overweight or obese (**Table 1**).

3.2 Identification of dietary patterns

Exploratory factor analysis allowed the identification of four dietary patterns: (i) "Breakfast/*Once*" consisting of tea, sugar, bread, margarine/butter, and cold cuts (positive loadings); (ii) "Meats and Vegetables" consisting of meats, vegetables, and salad dressing (positive loadings); (iii) "Western" consisting of processed meats, soft drinks, rice, pastas,

potatoes, mayonnaise, ketchup (positive loadings) and milk, homemade dishes, and chocolate powder (negative loadings); and (iv) "Sweet Snack" consisting of flavored milk, cookies, and cakes (positive loadings), and yoghurts and ready-to-eat cereals (negative loadings). These patterns resulted in a total intake variance of 7.4%, 6.4%, 5.6%, and 5.4%, respectively (**Table 2)**.

3.3 Adherence to dietary patterns, socio-demographics, weight status, and maternal variables

The frequency of adherence (%) to dietary patterns and the bivariate relationships with socio-demographics and weight status, i.e., pubertal and maternal weight statuses, are shown in **Table 3**. Adherence to the "Breakfast/*Once*" pattern was higher among underweight and obese adolescents ($p = 0.01$). Adherence to the "Meats and Vegetables" pattern was higher among adolescents who were not recipients of the school feeding program ($p = 0.04$). The adherence to the "Western" pattern was higher among male adolescents ($p = 0.04$) and those who did not participate in the school feeding program ($p = 0.04$). Adherence to the "Sweet Snack" pattern was higher in adolescents that partook in the school feeding program ($p = 0.01$).

3.4 Nutrient intake and adherence to dietary patterns

Associations between nutrient intake and adherence to dietary patterns are shown in **Table 4.** Adolescents with higher adherence to the "Breakfast/*Once,*" "Western," and "Sweet Snack" patterns (third tertile) had a higher energy intake than those who showed lower adherence (first tertile). The contribution of saturated fats was significantly higher in the "Western" pattern, whereas added sugars accounted for a significantly higher percentage of energy contribution for adolescent "Sweet Snack" consumers. The "Meats & Vegetables" and "Breakfast/*Once*" patterns were associated with lower intakes of saturated fats but a higher intake of sodium.

3.5 Adherence to dietary patterns and overweight

When adjusted for covariates (i.e., sex, age, Tanner status, misreporting, maternal obesity, and education level), adolescents with higher adherence to the "Meats and Vegetables," "Western," and "Sweet Snack" patterns had higher odds of being classified as overweight than those with lower adherence (OR = 1.83, 95% CI: 1.21–2.75; OR = 1.67, 95% CI: 1.10–2.52 and OR = 1.86, 95% CI: 1.23–2.79, respectively). The "Breakfast/*Once*" pattern was not significantly associated with overweight **(Table 5)**.

3.6 Sensitivity Analyses

We tested other combinations of food groups that had low factor loadings (e.g., we combined the eggs and cheeses groups, and confectionary, desserts and ice cream groups; for their commonalities) but their communalities and factor loadings did not improve, indeed, the consistency of the findings remained the same (data not shown).

4. Discussion

The present study identified four major dietary patterns among Chilean adolescents: "Breakfast/*Once,*" "Meats & Vegetables." "Western," and "Sweet Snack" pattern. All dietary patterns identified in this sample were associated with either a high caloric intake or overconsumption of a nutrient of public health concern, such as saturated fats and added sugars or sodium. Moreover, the "Western" and "Sweet Snack" patterns showed a positive association with overweight; however, the "Meats & Vegetables" pattern was also associated with overweight; these adolescents may have been consuming natural food in an attempt to combat their health problems.

In this population, the "Breakfast/*Once"* pattern showed the highest percentage of dietary variance. This pattern describes a very typical diet of the Chilean population [21]; it accounts for two of the four main meals in Chile, i.e., breakfast, lunch, "*once,*" and dinner. In Chile, it has been recently observed that dinner is being increasingly replaced by *once* and, currently, only one in four Chileans over 18 years of age eat dinner [21]. This may

have a potential effect on the shortfall of quality nutrients, as dinner in some cultures often includes a variety of healthy meats, vegetables, integral cereals, and fruits [32]. In this study, adolescents with a higher adherence to the "Breakfast/*Once*" pattern had higher energy and sodium intakes, and obese adolescents showed a higher adherence to this pattern. Bread, which is one of the main components of this pattern and a major source of energy and sodium intake, is the most consumed food among Chileans (i.e., 86.5 kilograms/person/year), particularly among low-income individuals [21, 33, 34]. The Latin American Study of Nutrition and Health also observed that refined-grain products, such as bread, are a major source energy in Latin American countries; however, Chile had a higher percentage (25.13%) of energy contribution through refined-grains than Colombia (11.71%) [35], which has a lower obesity prevalence in adolescents [8].

Studies have shown that dietary patterns with high factor loadings, e.g. the bread group, have higher energy densities and positive associations with overweight [36-38]. We found that foods groups of this pattern (white bread, sugar, margarine, cold cut, tea) provide low quality nutrition, similar to "traditional breakfast" patterns found by Oliveira et al. in Brazilian adults [39]; however, we did not find this food group to be associated with overweight. This might require further study, as our sample was homogenous in terms of socioeconomic status (SES), and this pattern is a dietary behavior typical of the Chilean population [21]. However, our findings that this pattern explained the higher variability of diet is worrying, because adolescence is a stage critical of rapid growth, and to maintain this behavior could lead to negative health consequences in adult life [4].

The “Meats & Vegetables” pattern was the second most relevant in this population. This pattern could be considered healthier because it has a higher factor loading of natural foods, such as vegetables and meats. Furthermore, this pattern was more frequent among those not participating in the school feeding program (based on SES) and whose mothers had a higher education level. The latter is in agreement with previous reports that high SES individuals have healthier dietary behaviors than their counterparts with lower SES [21]. Also, in line with the literature, we found an inverse association between adherence to the “Meats and Vegetables” dietary pattern and energy intake [12, 37, 40]. In contrast with this finding and that of other studies that show a likely protective role against obesity [15, 41], we found that the “Meats & Vegetables” pattern was associated with a higher odds of being classified as overweight. In Mexican adolescents, the “high animal protein” pattern also was positively associated with BMI [42]. In addition, the evidence suggests that plant, but not animal proteins, offer a protective effect in the prevention of excess weight [43, 44]. We believe this is explained by reverse causality [45], whereby overweight adolescents have either already changed their diet to a more healthy one before the assessment or they under-report unhealthy food and over-report healthy food [46].

The “Meats & Vegetables” pattern was mainly composed of natural foods, and we did not expect it to be associated with high sodium and low saturated fat intakes. Negative factor loadings of processed meats, cold cut, and junk food may explain the low intake of saturated fat, and the addition of salt (higher factor loadings of oil, lemon, salt, and vinegar foods) to salads, which is in line with recent analyses of the National Survey of Food Consumption [21], could also explain the high sodium intake. These results are

different from those found for American children and adolescents, where the main sources sodium were pizza, Mexican dishes, sandwiches, breads, cold cuts, soups, savory snacks, etc. [47]. Assessing sodium intake using 24HR is a challenge for epidemiological studies, because intake is likely to be incorrectly estimated or not accurately recalled. We used household measures together with a photo atlas [21] and up-to-date labelling of food to aid in the accurate estimation of sodium intake. These results highlight the need for consumer awareness and educational activities, in conjunction with other salt-reduction strategies, to address this public health problem [48].

"Western" and "Sweet Snack" patterns were characterized by unhealthy and processed foods of low nutritional quality, with the exception of the meats group and the rice, pastas, and potatoes group, which are good sources of protein and carbohydrates and are staple Chilean foods [21]. It is important to note that the "Western" pattern was characterized by a high negative loading of the homemade dishes group, which could indicate that adolescents who have high scores for this pattern consume more ready-to-eat or ready-to-heat foods than vegetable soups and legume stews with proteins (animal or vegetable). Such dishes require a longer cooking time but are nutritionally balanced and culturally appropriate for adolescents, according to Chilean dietary guidelines [32, 49]. These results are consistent with the evidence for the increase in expenditure on ready-to-eat meals, SSBs, and away-from-home foods in Chile in recent years [50, 51]. There is evidence that consumption of SSBs promotes weight gain in children and adults; therefore, discouraging the consumption of SSBs is an important way to help children achieve and maintain a healthy body weight [52]. As expected, adolescents with higher adherence to the "Western" and "Sweet Snack" patterns had higher energy intakes,

although the nutrient sources differed between these patterns (i.e., saturated fat for the "Western" and sugars for the "Sweet Snack" patterns) in line with the patterns found for Australian adolescents [37]. According to a systematic review on empirical dietary patterns [41] and other studies in Brazil [36], Mexico [42] and Colombia [53], dietary patterns named "Snack" and "Western" (characterized by processed foods of low nutritional quality) were also associated with an increased risk of overweight in children and adolescents; these results are in line with our findings. This is important because the objective of front labeling and the control of food marketing aimed at children in Chile is to regulate the consumption of unhealthy food groups (including processed meat, soft drinks, cookies, and cakes) and to inform consumers, through a warning symbol on packaged products, that they are high in energy, saturated fats, total sugars, or sodium [16].

Dietary patterns were, in general, homogeneously distributed among the study sample. We observed that boys had higher adherence scores for "Western" patterns than girls, probably because girls under-report these types of foods, and because girls are more vulnerable to social aesthetic standards [54]. We also observed that participation in the school feeding program protected adolescents from the "Western" dietary pattern, probably because this program provides beneficiaries with a free breakfast and lunch that includes fresh fruits and vegetables, as well as fulfilling nutrient requirements based on dietary guidelines [49, 55]. However, participation in the school feeding program did not protect individuals from the "Sweet Snack" pattern, which is probably because snacks are also available inside schools, in addition to main meals [56].

The limitations of the study should be considered when interpreting the results. The present study used EFA, a method that involves decision-making by researchers at various stages of the modeling process, such as decision on grouping and the number of factors to be selected. For this reason, widely-used nutritional epidemiology procedures were applied and validated to counterbalance these weaknesses [57] and several sensitivity analyses confirmed the validity of our findings. Although we used 24HRs, which might be subject to recall bias and do not estimate the usual dietary intake, 61% of the sample underwent a second measurement within 6 months. This allowed us to estimate the usual intake, adjusting for intra-individual variance according to the Multiple Source Method, and to increase the reliability of the results [27]. The interviews were reported by parents or caregivers who had access to the school feeding program menus, which complemented the dietary data and followed the "Multiple-Pass Method." The study population was somewhat homogeneous in terms of SES, and the inclusion of more variety may have had an effect on the differences between groups [58]. Analyses of the adherence to dietary patterns and overweight status were not adjusted for physical activity due to a lack of information, but it was possible to adjust the final models for the Tanner pubertal stage (i.e., a relevant confounding factor among adolescents) [1]. Finally, dietary misreporting is a common problem among adolescents; however, our analyses took into account potential misreporting [46].

5. Conclusion

In a sample of low-middle income adolescents from Chile, a country with one the highest prevalences of obesity worldwide, we found that common dietary patterns are related to high consumption of calories and nutrients of public health concern. We did not identify dietary patterns that could be considered healthy, indicating that intake of healthy foods among this age group is random and does not conform to an organized pattern. Our results are of concern and demonstrate poor dietary quality during a period that can have long-lasting implications for both the individual and their potential offspring. It is important to evaluate whether the ongoing obesity prevention policies will be able to modify these unhealthy behaviors among a traditionally resistant age-group.

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Authors contributions

A.M.A carried out the study and data analyses and drafted the manuscript, contributed towards study concepts and design, and approved the final version of the manuscript submitted for publication. R.M.F. participated in data analyses, interpretation, and manuscript preparation. C.C.A. participated in the design and coordination of the study, the acquisition of data, and helped to interpret and draft the manuscript. X.P.M. and X.C.S. participated in the preparation of the manuscript. All authors read and approved the final manuscript to be published.

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Sponsors were not involved in study design, collection, analysis and interpretation of data; manuscript writing or submission decision.

Declarations of Interest

The authors declare no conflict of interest.

Table 1. Anthropometric, sociodemographic, and maternal characteristics of 882 Chilean adolescents, GOCS Study 2014-2015.

Variables		n	%
Sex			
	Male	434	49.2
	Female	448	50.8
Tanner Stage¥			
	1	54	6.1
	2	222	25.2
	3	144	16.3
	4	257	29.1
	5	182	20.6
	Missing	23	2.6
Weight status (BMI-for-age *z* score)*			
	Underweight	43	4.9
	Normal Weight	383	43.5
	Overweight	275	31.2
	Obesity	180	20.4
Sleep (hours)			
	≥9 hours	236	26.8
	< 9 hours	532	60.3
	Missing	114	12.9
Maternal Obesity †			
	No	520	59.0
	Yes	338	38.3
	Missing	24	2.7
Maternal education (years)			
	≥12 years	578	65.5
	< 12 years	280	31.8
	Missing	24	2.7

* BMI-for-age *z* score: underweight ≤ -1 SD, normal < -1 SD and < +1 SD, overweight ≥+1 SD and < +2SD, obesity ≥ +2 SD (24).

† Maternal obesity=BMI≥30 kg/m2

¥ Tanner status: Girls were evaluated according to their breast development and Boys were evaluated according their genitalia development (25)

Table 2: Factor loadings*, explained variance and eigenvalues of the four major dietary patterns practiced by GOCS adolescents (n:882), Chile 2014-2015.

Food groups	Breakfast/*Once*	Meats & Vegetables	Western	Sweet snack
Milk	-0.22	0.00	**-0.32**	-0.12
Flavored milk	-0.24	-0.20	0.06	**0.28**
Yogurt	-0.10	0.03	0.01	**-0.73**
Cheeses	0.06	-0.06	0.16	0.11
Meats	-0.16	**0.50**	**0.29**	0.07
Cold cuts	**0.27**	-0.15	**0.27**	0.00
Processed meats	0.01	-0.20	**0.41**	-0.07
Junk Food	-0.18	-0.23	0.11	0.09
Flavored juices	-0.22	0.16	-0.07	0.24
Soft drink	-0.07	0.03	**0.41**	0.14
Tea and coffee	**0.73**	0.04	-0.11	0.08
Bread	**0.64**	-0.04	0.18	0.11
Ready to eat cereal	-0.09	0.03	-0.02	**-0.77**
Rice, pastas, potatoes	0.02	0.16	**0.47**	-0.05
Vegetables	0.09	**0.81**	-0.01	0.00
Fresh fruit	0.08	0.16	-0.23	0.05
Eggs	0.02	0.04	0.00	-0.07
Homemade dishes	0.14	-0.11	**-0.62**	0.01
Soups	-0.10	0.18	-0.19	0.13
Cracker and salt snack	-0.14	-0.11	0.16	0.03
Confectionery and chocolate	-0.07	0.02	-0.03	0.17
Cookies	-0.23	-0.07	-0.11	**0.29**
Cakes	-0.09	0.03	-0.19	**0.25**
Desserts and ice cream	0.05	0.08	0.01	-0.03
Sugar	**0.70**	0.10	-0.12	0.08
Chocolate powder	-0.19	-0.03	**-0.27**	0.01
Margarine and butter	**0.49**	-0.08	0.05	-0.09
Oil, lemon, salt, vinegar (for salad)	0.00	**0.79**	0.03	-0.07
Mayonnaise and ketchup	-0.01	0.04	**0.31**	0.06
% of explained variance	**7.42**	**6.42**	**5.64**	**5.43**
% of accumulated explained variance	**7.42**	**13.84**	**19.48**	**24.90**
Eigenvalues	**2.16**	**1.88**	**1.63**	**1.55**

*Factor loadings |0.20| are shown in bold for readability purposes. Bartlet sphericity test (BSS) = $p < 0.0001$, KMO: 0.52

Table 3: Adherence (%) according to sociodemographic, anthropometric, and maternal nutrition status of 882 Chilean adolescents, GOCS Study 2014-2015 Chile.

Variables		**Breakfast/*Once***							**Meats & Vegetables**						
		T1*		**T2***		**T3***		**P†**	**T1**		**T2**		**T3**		**P**
		%	**n**	**%**	**n**	**%**	**n**		**%**	**n**	**%**	**n**	**%**	**n**	
Sex	Male	30.2	131	34.1	148	35.7	155	0.126	35.5	154	33.4	145	31.1	135	0.292
	Female	36.4	163	32.6	146	31.0	139		31.3	140	33.3	149	35.5	159	
Tanner stage¥	1-3	31.4	132	33.6	141	35.0	147	0.617	36.0	151	32.9	138	31.2	131	0.243
	4-5	34.4	151	33.0	145	32.6	143		30.8	135	34.2	150	35.1	154	
Weight status‡	Underweight	30.2	13	23.3	10	46.5	20	**0.013**	32.6	14	32.6	14	34.9	15	0.167
	Normal Weight	36.2	139	30.0	115	33.9	130		37.0	142	34.6	133	28.4	109	
	Overweight	33.1	91	40.0	110	26.9	74		31.3	86	33.1	91	35.6	98	
	Obese	28.3	51	32.8	59	38.9	70		28.9	52	31.1	56	40.0	72	
Sleep Hours	≥9 hours	33.5	79	34.8	82	31.8	75	0.727	32.2	76	37.3	88	30.5	72	0.324
	<9 hours	35.7	190	32.0	170	32.3	172		34.6	184	31.8	169	33.7	179	
School administrative status	Public	30.6	101	32.4	107	37.0	122	0.186	34.9	115	32.7	108	32.4	107	0.728
	Private	34.8	189	34.1	185	31.1	169		32.2	175	34.1	185	33.7	183	
School feeding program£	Yes	32.6	91	33.3	93	34.1	95	0.939	37.3	104	35.1	98	27.6	77	**0.042**
	No	33.7	203	33.3	201	33.0	199		31.5	190	32.5	196	36.0	217	
Maternal obesity (BMI ≥30kg/m2)	Yes	36.5	100	32.7	113	30.8	125	0.069	33.3	113	33.1	114	33.7	111	0.966
	No	29.6	190	33.4	170	37.0	160		33.4	173	33.7	172	32.8	175	

Maternal education years	≥12 years	35.3	204	32.7	189	32.0	185	0.304	31.8	184	32.9	190	35.3	204	0.076
	<12 years	30.0	84	35.7	100	34.3	96		38.2	107	33.6	94	28.2	79	

* Tertile adherence

† X_2 Pearson tests, p value <0.05

‡ Weight status, BMI-for-age *z* score: underweight ≤ -1 SD, normal < -1 SD and < +1 SD, overweight ≥+1 SD and < +2SD, obesity ≥ +2 SD (24).

£ School feeding program: adolescents receive some food services of feeding program (yes or no).

¥ Tanner status: girls were evaluated according to their breast development and boys were evaluated according their genitalia development [24]

Table 3 (continuation): Adherence (%) according to sociodemographic, anthropometric, and maternal nutrition status of 882 Chilean adolescents, GOCS Study 2014-2015 Chile.

Variables		Western							Sweet snack						
		T1 *		T2*		T3*		P†	T1		T2		T3		P
Sex	Male	29.3	127	35.7	155	35.0	152	**0.040**	33.9	147	31.8	138	34.3	149	0.627
	Female	37.3	167	31.0	139	31.7	142		32.8	147	34.8	156	32.4	145	
Tanner status¥	1-3	32.4	136	36.0	151	31.7	133	0.324	33.3	140	32.9	138	33.8	142	0.900
	4-5	33.9	149	31.2	137	34.9	153		33.9	149	33.7	148	32.4	142	
Weight status‡	Underweight	27.9	12	41.9	18	30.2	13	0.675	34.9	15	27.9	12	37.2	16	0.408
	Normal Weight	35.4	136	30.5	117	34.1	131		35.9	138	30.5	117	33.6	129	
	Overweight	31.6	87	34.2	94	34.2	94		33.1	91	34.2	94	32.7	90	
	Obese	32.8	59	36.1	65	31.1	56		27.8	50	39.4	71	32.8	59	
Sleep Hours	≥9 hours	33.9	80	32.2	76	33.9	80	0.663	33.5	79	31.4	74	35.2	83	0.611
	<9 hours	32.7	174	35.5	189	31.8	169		34.8	185	33.7	179	31.6	168	
School administrative status	Public	34.6	114	31.5	104	33.9	112	0.670	31.5	104	37.9	125	30.6	101	0.082
	Private	32.8	178	34.4	187	32.8	178		34.4	187	30.6	166	35.0	190	
School feeding program£	Yes	36.9	103	35.5	99	27.6	77	**0.046**	27.6	77	32.3	90	40.1	112	**0.007**
	No	31.7	191	32.3	195	36.0	217		36.0	217	33.8	204	30.2	182	
Maternal obesity	No	35.2	183	33.7	175	31.2	162	0.197	33.1	172	34.2	178	32.7	170	0.719
	Yes	30.2	102	33.4	113	36.4	123		33.7	114	31.7	107	34.6	117	

Maternal education years	≥12 years	33.0	191	35.3	204	31.7	183	0.265	35.1	203	32.5	188	32.4	187	0.561
	<12 years	33.2	93	30.4	85	36.4	102		31.4	88	34.6	97	33.9	95	

* Tertile adherence

† X_2 Pearson tests, p value <0.05

‡ Nutritional status, BMI-for-age *z* score: underweight ≤ -1 SD, normal < -1 SD and < +1 SD, overweight ≥+1 SD and < +2SD, obesity ≥ +2 SD (24).

£ School feeding program: adolescents receive some food services of feeding program (yes or no).

¥ Tanner status: girls were evaluated according to their breast development and boys were evaluated according their genitalia development [24]

Table 4: Median nutrient intake according to tertile* of adherence to dietary patterns in GOCS adolescents (n:882)

		Saturated fat % IE§			Added sugars % IE§			Sodium mg/1000 kcal			Energy (kcal)		
		Median	**IQR†**	**P‡**	**Median**	**IQR***	**P**	**Median**	**IQR***	**P**	**Median**	**IQR***	**P**
Breakfast/*Once*"	tertile 1	9.8	1.8	0.001 abc	18.3	6.6	0.285	1468	286	0.001 ab	1754	504	0.017 c
	tertile 2	9.6	2.1		17.4	6.8		1535	261		1758	464	
	tertile 3	9.0	2.4		17.3	6.4		1515	254		1819	427	
Meats & Vegetables	tertile 1	9.7	2.2	0.001 bc	17.5	6.5	0.949	1478	257	0.017 ab	1809	478	0.194 c
	tertile 2	9.6	2.2		17.9	6.3		1521	286		1763	442	
	tertile 3	9.1	2.1		17.4	7.3		1530	277		1781	464	
Western	tertile 1	9.5	2.0	0.077 bc	17.5	6.8	0.404	1488	304	0.424 b	1738	441	0.001 bc
	tertile 2	9.4	2.2		18.2	7.3		1514	272		1733	429	
	tertile 3	9.7	2.5		17.2	6.2		1526	247		1913	417	
Sweet Snack	tertile 1	9.6	2.1	0.215 a	16.5	6.5	0.001 bc	1528	263	0.001 bc	1704	470	0.001 bc
	tertile 2	9.5	2.3		16.8	6.5		1553	288		1887	446	
	tertile 3	9.5	2.6		19.3	6.2		1460	258		1754	504	

* Tertile 1 lower adherence, tertile 3 higher adherence

§ IE, energy intake day

†Interquartile range (IQR)

‡Kruskal–Wallis test and Dunn's test post hoc, P value <0.05

a Significant difference between tertile 1 and 2 of the factor scores.

b Significant difference between tertile 1 and 3 of the factor scores.

c Significant difference between tertile 2 and 3 of the factor scores.

Table 5: Crude odds ratio and adjusted odds ratio of overweight, according to tertile¶ of dietary pattern practiced by GOCS adolescents. Chile, 2014-2015

	Crude model			Adjusted Model 1§			Adjusted Model 2|		
	OR†	95% CI*		OR†	95% CI*		OR†	95% CI*	
Breakfast/*Once*									
tertile 1*	Ref‡			Ref			Ref		
tertile 2	1.45	1.045	2.003*	1.28	0.903	1.815	1.25	0.839	1.875
tertile 3	1.03	0.744	1.420	0.90	0.634	1.274	1.03	0.689	1.529
Meats & Vegetables									
tertile 1	Ref			Ref			Ref		
tertile 2	1.13	0.818	1.562	1.15	0.810	1.620	1.07	0.717	1.583
tertile 3	1.55	1.119	2.146*	1.68	1.180	2.390*	1.83	1.219	2.754*
Western									
tertile 1	Ref			Ref			Ref		
tertile 2	1.19	0.864	1.651	1.14	0.802	1.608	1.07	0.720	1.603
tertile 3	1.06	0.764	1.459	1.00	0.701	1.418	1.67	1.103	2.522*
Sweet Snack									
tertile 1	Ref			Ref			Ref		
tertile 2	1.39	1.003	1.920*	1.53	1.077	2.160*	1.51	1.013	2.235*
tertile 3	1.12	0.807	1.541	1.19	0.839	1.680	1.86	1.235	2.792*

* 95% Confidence Intervals, value p <0.05.
† OR: odds ratio, CI: confidence interval
‡ Ref: reference
§ Model 1: adjusted for sex, age, tanner, maternal obesity, maternal education (n:816)
| Model 2: adjusted for sex, age, tanner, maternal obesity, maternal education and misreporting (n:816)
¶ Tertile 1 lower adherence, tertile 3 higher adherence

Supplemental Files

S1. Description of the foods that composed each of the 29 food groups included in the factor analysis. GOCS Study, Chile 2014-2015.

Food groups	Food composition
Milk	Fluid whole milk (3% fat), whole milk powder, reduced fat milk (2% fat), skim milk, skim milk powder
Flavored milk	Mixtures and milk drinks, strawberry, chocolate and other flavors, purchased ready-to-drink
Yogurts	Yogurt, fermented milk
Cheeses	Gouda cheese, ricotta cheese, cream cheese, cheddar cheese,
Meat	Steak beef, ground beef, beef ribs, pork chop, pork ribs, pork loin, poultry, chicken, turkey, fish, viscera (all cooking methods)
Cold cuts	Ham, bologna, turkey breast, chicken breast, salami
Processed meats	Sausage, sausages, frankfurters, meatballs ready for consumption, nuggets, hamburger ready for consumption (only meat).
Junk food	Pizzas, sandwiches of meat or hamburger ready to eat, french fries, wonton, egg roll, chilean hot dog, *sopaipillas, tacos, empanadas*. Mainly, street food or fast food
Sweetened beverages	Juice or flavored drink, purchased ready-to-drink, juice or flavored drink, dry mix - unprepared
Soft drinks	Soda pop or soft drink regular or diet
Coffee and tea	Coffee, instant coffee, herbal tea, tea bag
Bread	French bread, bun bread, white bread with salt
Ready to eat cereal	Breakfast cereals
Rice, potato and pasta	Rice, cooked potatoes, mashed potatoes, pasta and dishes pasta.
Vegetables	Lettuce, cabbage, raw salad, others load vegetables. Pumpkin, carrot, cucumber, tomato, among others.
Fruits	Pineapple, banana, orange, apple, pear, papaya, mango, watermelon, tangerine, grape, blueberry, strawberry, blackberry, fruit salad, fruit juices
Eggs	Fried eggs, scrambled eggs, omelet, boiled eggs, egg white, egg yolk
Homemade dishes	Typical chilean food or meals prepared at home, restaurants or schools; that require a longer preparation time and made with natural foods. For instance: Beans, lentils, chickpeas, white beans, legumes-based preparations, vegetables stews with or without meat, *cazuela, charquican, chapsui, humitas, pastel de choclo* among others.
Soup	Dry soup, bouillon, consommé.
Cracker and salt snack	Crackers, saltine or soda, salty chips - snack type, cheese balls, puffs or twists, potato chips
Chocolates and confectionary	Chocolate candy, chocolate candy bar, sweets based on milk, lollipop, candy, caramel, jams, *dulce de leche*

Cookies	Cookies and bars, granola bars, sweet biscuit and cookie stuffed, cookie sandwich, cookies commercial packaged
Cake	Cakes, cheesecake, cake sponge, doughnut, muffins, pies fruit, cupcake, cake purchased ready-to-eat
Desserts and ice cream	Pudding, flan, mousse, gelatin dessert, chilean desserts, fruit canned with syrup, ice cream and frozen desserts, Popsicle
Sugar	White sugar
Chocolate powder	Cocoa powder, chocolate powder
Butter and margarine	Salted butter, unsalted butter, salted margarine, unsalted margarine, light margarine
Salt, lemon, vinegar to salad	Soybean oil, sunflower oil, vegetal oil, olive oil, salt, vinegar, lemon juice to salad
Mayonnaise, ketchup	Mayonnaise or mayo type dressing, ketchup, mustard, soy sauce

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8.3 TERCEIRO MANUSCRITO

“PRUDENT PATTERN IS ASSOCIATED TO AGE AT MENARCHE IN ADOLESCENTS WITH EXCESS WEIGHT FROM GROWTH AND OBESITY CHILEAN COHORT STUDY”

Abstract

Background: Timing of pubertal development is an important health issue that can impact the increasing in morbidity and mortality in adult life and future generations. The age at menarche is a late marker of puberty. Several studies have associated nutrients or foods with age at menarche, but there are few evidences on this relation with overall diet, such as empirical dietary patterns.

Objective: To analyze the association between dietary patterns and age at menarche in a prospective cohort of Chilean girls of low-middle income families.

Methods: A total of 602 Chilean girls have been followed from 2006 to the present in the Growth and Obesity Cohort Study. Starting in 2013, diet was assessed via a 24-h recall. Our analyses included 270 girls (mean 11.6 years, DS=0.49) with data on prospective diet, anthropometric measures and age at menarche during clinical visits. Dietary patterns were obtained through exploratory factor analysis. Cox regression models adjusted for potential confounding variables were used to associate dietary patterns with age at menarche.

Results: The findings revealed three dietary patterns accounting for 19.5% of the variance in the diet: "Breakfast/*Once*", "Prudent" and "Western". Girls with excess weight in the highest vs lowest tertile of "Prudent" pattern had a later age at menarche (HR: 0.51; 95% CI: 0.31-0.85). No significant association was found in girls with normal weight. "Breakfast/*Once"* and "Western" patterns were not associated with age at menarche.

Conclusion: Healthy dietary patterns during puberty in excess weight girls could modulate the age at menarche. Then, following dietary guidelines could influence timing of puberty in girls with excess weight during pubertal phase.

Introduction

The timing of pubertal development is an important health problem that has consequences on the increased morbidity and mortality in adult life (1, 2). Nutritional factors, such as overweight and obesity, have been linked with timing of puberty. Particularly in girls a rapid weight gain during childhood has been related to an early age at menarche and other markers of puberty(3-7). For this reason, there is an increased interest on studying the relation between dietary factors and timing of puberty.

As an example, girls who consumed more animal proteins and less vegetable proteins during childhood had an earlier at menarche (8-10). Specific foods sources of animal proteins have been investigated, but the evidence is still inconsistent. Studies in US and Iran girls have observed that a higher frequency of cow's milk consumption increase the probability of early menarche (11, 12). Another study with US girls did not corroborate this association (13). A higher frequency of red meat intake during childhood in Colombian girls was associated with an earlier age at menarche, whereas a higher intake of fish was associated with later menarche (14).

Furthermore, the consumption of Sugar-sweetened Beverages (SSBs) at 9-14 years old have also been associated with earlier menarche in US girls (15). Another prospective study conducted in African American and Caucasian girls from the United States observed that a higher consumption of caffeinated and artificially sweetened beverages at 9-10 years was associated with an increased risk of early menarche (16).

However, diet is a complex factor, where foods are eaten in a structured way. During meals or snacks foods interact among themselves facilitating or hindering the absorption of nutrients (17, 18). Diet is modulated by individual preferences, beliefs or cultural traditions, as well as geographic, environmental, social and economic factors (17). Therefore, studying

the overall diet is essential to understand the relationship between nutrients, foods, and puberty.

Few evidences associating puberty in adolescents with of overall diet, such as empirical dietary patterns, have been reported. A cross sectional study conducted among 365 Korean girls aged 9–12 years found that "Shellfish and Processed meat" pattern (composed by bread, processed meats and shellfish) was positive associated with sexual maturation assessed by tanner scale (19, 20). Another population-based study among 2033 Shanghai girls found that "Unhealthy" patterns composed by dessert/snacks, soft drinks, and fried food was associated with precocious puberty. Only one prospective study conducted in 263 girls from Mexico City in a birth cohort evidenced that "Vegetables and Lean proteins" pattern composed by vegetables, potato, legumes, chicken, organ meat (diet evaluated during early childhood, 1-5 years) was associated with delayed breast development, but they did not found association whit age at menarche (21).

The Growth and Obesity Cohort Study (GOCS) started the follow-up in 2006, but dietary assessment was included in 2013. In previous GOCS analyses, we found that yogurt intake > 125 mL was associated with later age at menarche (4.6 months) compared to no consumption (22). However, we did not explore how other foods or how dietary patterns can influence puberty markers. Therefore, the aim of this study was to identify and assess the association between dietary patterns and age at menarche in a prospective cohort of Chilean girls of low to middle-low income families.

Materials and methods

Study population

The study population consists of participants in the Growth and Obesity Cohort Study (GOCS) from Santiago, Chile. Briefly, GOCS is a population-based ambispective cohort of 1195 children, whom were born in 2002-2003 in six counties from the Southeast area of Santiago, Chile. Participants were singletons who were born at term (37–42 weeks), had a birth weight ≥2500 and <4500 g, and were free from conditions that could affect growth. The GOCS children represented middle-low and low-income families from public nursery schools, which provide free education and meals (i.e., breakfast and lunch). The details of the study design, protocol and baseline were described elsewhere (23, 24). From the total of 1195 children, 602 girls provided follow-up information during childhood and puberty and were considered for the current study. Repeated anthropometric and sexual maturation measurements were collected in the GOCS participants since 2006. Since 2013 dietary intake of participants was collected at a 6-month basis in clinic visits with a 24-hour dietary recall (24HR). Sociodemographic and maternal characteristics were collected by trained research assistants through a structured questionnaire.

For the present study, we included girls who had at least one 24HR and anthropometric measurements (n=458). For the analyses that consider age at menarche, we excluded 188 girls who reported their first menses before the start of dietary intake measurements. Therefore, the final sample was composed by 270 girls **(Supplemental file).**

The study protocol was approved by the Ethics Committee of the Institute of Nutrition and Food Technology, University of Chile. Informed consent was obtained from all parents or guardians of adolescents before beginning data collection.

Dietary intake

Dietary data was obtained by two non-consecutive 24HR (57% of sample provided a second 24HR). The interviews were collected in different days of the week and weekends and different seasons. We used the "Multiple Pass Method" (25), and a photographic atlas from the National Survey of Food Consumption of Chile (26). Trained dietitians collected the 24HR from the child, however the parent/caregiver that was responsible for preparing the meals was present to complement the information provided by the adolescent.

Foods and meals provided by the School Feeding Program (SFP) were added in this study in order to estimate the consumption among the beneficiaries of the program (27). Usual measures (e.g., cups, units and spoons) reported in each 24HR were converted into units of weight or volume, as per the standardization and quantification of the foods, according to Chilean publications and other standard regional recipes (26, 28). The Nutrition Data System for Research (NDSR) software (version of 2014, NCC, University of Minnesota, Minneapolis) was used to determine the nutrient content of each food and beverage consumed. This program uses the United States Department of Agriculture (USDA) database as the main food composition table. For this reason, all foods and beverages reported on the 24HR were matched in the NDS-R database through general description (i.e., name, type and mode of preparation). Energy and macronutrient values available in Chilean food composition tables (TCA) (29), local food industry composition tables and/or nutrition labels were compared to values described in the software. A concordance rate between 80 and 120% for each parameter analyzed was required to accept food harmonization. Some Chilean preparations (e.g., *charquican, cazuela, sopaipillas* and *Chilean hot dog*) and other industrialized foods were added as they were commonly consumed and were not in the software database.

A total of 1053 different food items were reported in each 24HR and 993 were consumed by at least 5% of the sample. These food items were classified into 30 food categories based on their nutritional value, correlation coefficient between groups, communalities values, food preparation, and Chilean dietary behaviors. In addition, evidence of potentially relevant groups for pubertal development (i.e., whole-milk, low-fat milk and non-fat milk, yogurt, red meat, poultry and fish, processed meat and soft drinks) were taken into account **(Supplemental files)**.

Energy misreporting

Misreporting of energy intake was estimated by the following equation: EI (energy intake) – EER (estimated energy requirements)/EER x 100 (30). This variable was used to adjust all the regression models.

Outcome: age at menarche

Around 7 years old, girls had pubertal staging assessed by a single pediatric endocrinologist (31). Age at menarche was self-reported. Mothers and girls were advised to call researchers, and telephonic follow-up was performed every 6 months starting at breast Tanner stage 4 (B4). A questionnaire was developed to differentiate vaginal infections or other genitourinary conditions from first menses (32).

Age at menarche was considered as the time in months from birth to the age of menarche, and the outcome was defined as attaining menarche. Girls who did not reach menarche by the end of follow-up were re-evaluated at 30th March 2018 (n = 5).

Covariates

Weight and height were measured every 6–12 months during follow-up visits with the use of standardized techniques by trained dietitians as described elsewhere (33). For the purpose of these analyses, the measurements assessed closer to the age at menarche were considered. Body mass index (BMI) was calculated using the standardized formula of weight (kg) divided by height squared (m^2) and BMI z-scores were calculated based on age and sex of the participants according to World Health Organization Growth Reference (WHO) (34). Excess weight was defined as a combination of both overweight (1≥ z score BMI <2) and obesity (≥ 2 z score).

Participants' mothers self-reported information on education level (dichotomized as ≥12 or <12 years) and age at menarche. A trained dietitian also measured the mother's current height and weight to calculate BMI according to WHO cutoffs for adults (35). Time spent on TV during the days of the week and weekend (≥ 2 or < 2hours/day) for the adolescents, hours of sleep (≥ 9 or < 9hours/day) (36) and attendance on the School Feeding Program (yes or no) were provided at clinic visits by participants using a semi-structured questionnaire.

Statistical analysis

We have already reported dietary patterns of the participants elsewhere (37), but due to important sex differences in dietary patterns we considered important identify dietary patterns in girls, separately(38).

Statistical modeling techniques incorporated into the Multiple Source Method online platform were used to estimate usual intake in grams for each group food (39). Exploratory factor analysis (EFA) was used to identify the dietary patterns from the 30 food groups (all girls were included, n = 458). Initially, factors with Eigenvalues greater than or equal to 1.0

were retained and the screen plot was visually inspected, suggesting the retention of four factors. Varimax orthogonal rotation was applied to improve the interpretability of the factor loading matrix and to ensure the independence of the factors derived. Factor loadings greater than or equal to |0.30| were considered to contribute to the pattern (40). The retained patterns were named according to their interpretability, the characteristics of food in each dietary pattern, and food culture. Communalities were observed; which reflect the level of linkage between the variable (food group) and the extracted factor. For each participant a factor score of each dietary pattern was calculated using regression scoring method (41). The dietary pattern scores were then stratified in tertiles and used as independent variables (exposure).

To compare adherence (%) to the dietary patterns according to sociodemographic, anthropometric, and maternal nutrition status, chi-square test for categorical variables and one-way ANOVA for continuous variables were used.

Survival curves, Kaplan Meier estimator and Test of Log-Rank were determined for each covariable. To examine the proportionality assumption of weight status, sociodemographic and maternal characteristic (variables that the evidence has associated with timing of puberty) time-to event analyses were performed. Multivariate Cox proportional hazards models were used for assess the relationship between adherence to a dietary pattern (in tertiles) and age at menarche, estimating failure curves (e.g., expected proportion of girls who had their menarche over time). Schoenfeld residuals were used to evaluate the proportional hazards assumption. Hazard ratio (HRs) and 95% confidence intervals (CIs) were computed and the second and third tertile with first tertile (reference) of each dietary pattern were compared. Covariables such as mother's menarche age (years) and BMI (kg/m2), maternal education (< 12 and ≥12 years) including misreporting of energy intake (percentage) were used as adjust in the analysis. Models were stratified according to

weight status in order to meet the assumption of proportional hazards (42). All statistical analyses were performed using STATA software version 15 with 95% confidence interval and significance level established for all tests at $p<0.05$.

Results

The estimated mean age at menarche was 12.6 (SD=0.83 years). Almost half of the participants (46.3%) presented excess weight. In relation to maternal socio-demographic characteristics, weight status and age at menarche, one out of three mothers reported less than 12 years of education, nearly a third were obese and at least one out five self-reported an age at menarche < 11 years old (**Table 1**).

Exploratory factor analysis allowed the identification of three dietary patterns: (i) "Breakfast or *Once*" ("*Once*" is a typical Chilean meal served between 5-9pm in comparison to tea time) consisting of tea, sugar, bread, margarine/butter and cold cuts (positive loadings) and flavored milk (negative loading); (ii) "Prudent" consisting of white meats (poultry and fish), fruits, vegetables, oil, lemon, salt, and vinegar for salad dressings (positive loadings) and processed meats (negative loadings); (iii) "Western" consisting of soft drinks, junk-food, cookies and cakes, and soups (positive loadings) and yogurt, and ready to-eat cereal (negative loadings). These patterns explained a variance on total intake of 7%, 6.4% and 6% respectively (**Table 2)**.

Figure 1 shows the probability of having menarche according to variables associated with puberty, according to the evidences. We found that girls with excess weight have their menarche before that those with normal weight (p=0.0001). On the other hand, girls with mothers that had their menarche later than 15 years old, had their menarche later than their counterparts (p=0.0183).

After adjusting for maternal education, maternal obesity, mother`s age at menarche and energy intake misreporting significant associations were found as follows: girls with excess weight in the highest tertile of scores for a "Prudent" dietary pattern had 51% less probability of reaching menarche (HR: 0.51; 95% CI: 0.31-0.85) than those with lower adherence (i.e., first tertile). There was no association between "Breakfast/*Once*" or "Western" dietary pattern and menarche age **(Table 4).**

Discussion

In this prospective study of Chilean adolescents, 3 major dietary patterns were identified for girls before their age at menarche: "Breakfast/*Once*", "Prudent" and "Western". Part of our findings were in the expected direction with evidence from other studies. To support this, girls with higher adherence to the "Prudent" dietary pattern had a significantly later age at menarche, compared to the ones with lower adherence. "Breakfast/*Once*" and "Western" dietary patterns were not associated with age at menarche.

In this subsample of GOCS girls mean age at menarche was 12.6 years (DS=0.83). Pereira et al. (2019) in a recent study with the total sample reported a median age of 11.9 years (IQR= 11.2-12.6) (32). This difference could be justified because dietary data were obtained after 2013, when many girls had already reported their first menarche. GOCS girls have a high obesity prevalence, and we found that girls with excess weight had an earlier menarche compared with normal weight girls. Earlier age of menarche and childhood obesity have been supported by prospective evidences. Potential mechanisms of obesity may promote gonadal axis initiation in essence related to insulin resistance and hyperinsulinemia,

hyperandrogenism and leptin (6, 7, 43, 44). There is no clear evidence on association between pre-pubertal body composition and onset-of-puberty markers (i.e., pubarche or thelarche age) or to puberty duration that influence on late markers of age of menarche (44).

"Breakfast/Once" was the only dietary pattern with HR of risk but no statistical significance was detected for the subsample. However, in the total sample (dietary data prospective and retrospective) data were statistical significant (data not shown). This dietary pattern had high loading factors for bread, cold cut, sugar, margarine, tea and coffee. Some of these groups might be associated with earlier menarche due to the presence of caffeine on coffees and teas (especially black teas). Studies suggested that caffeine might alter specific brain regions, which include the hypothalamic-pituitary-adrenocortical axis that is important to regulate pubertal timing (45, 46). A prospective study with African-American and Caucasian girls found that consumption of caffeinated soft-drinks were positively associated with risk on early menarche (RR for 1 serving/d increment: 1.43; 95% CI: 1.08, 1.88). Coffees and teas were not investigated because the consumption was low in this population (16). Besides, Chileans families have the habit to consume hot tea with added table sugar and bread (26). These items present a high-glycemic index (47) that may be linked to hormone regulations and other biological mechanisms associated to earlier menarche (3). For this reason, these results should be interpreted with cautions, because it could be due to lack of statistical power.

The "Western" dietary pattern was characterized by high factors loading on energy-dense, added sugars, solid fats and sodium food sources. Cross-sectional evidences from Korea (19) and Shanghai (48) have shown positive association with "Unhealthy" or "Shellfish and Processed meat patterns", respectively, and puberty. One of the main differences with our findings is that these studies evaluated an onset puberty marker

(development breast). Besides, the cross-sectional design of the studies does not allow to infer causality. Due to the age of menarche being associated with the intake of SSBs we expected to find associations with the "Western" pattern (15). Studies have shown that Chilean individuals have a high intake of SSB (49) and industrialized foods (such as cookies and cakes) (26, 50), which present high glycemic index (47).This could be linked to the onset of puberty pathway glycemic index- hyperinsulinemia-SHBG and IGF-1 (15). Moreover, in Chile, street foods are prepared with processed meats. A study including Colombia girls (14) showed associations between red meats and earlier age at menarche, proposing a pathway mechanism on iron and zinc (51). Since the "Western" pattern was not associated with age at menarche, this discrepancy may be explained because dietary patterns evaluate the overall diet, not specific or single foods. Diet is multidimensional, and the various aspects of diet captured by the different components may have different and important effects on health outcomes (17, 52). Besides, the timing of dietary assessment was different on the studies. Some authors suggest that critical exposures that predict puberty, such as diet, may occur earlier in childhood (10). Considering that, our dietary data were assessed close to the age at menarche.

The findings that a "Prudent" pattern (characterized by low-energy, lean proteins. vitamins, minerals and fiber food sources) was associated with a later age at menarche only in excess weight adolescents is consistent with the results found by Jansen et al (21). This study targeted Mexican adolescents. "Vegetables and Lean Proteins" pattern was related to late breast development, but not with age of menarche. Studies that support the findings of this current study indicate that an increase intake on plant-based proteins during mild-childhood has been related to later menarche age (8, 9). Other researches have seen that a particular vegetable component, which includes dietary fiber and isoflavones, was associated

with later menarche age (53, 54). Differences between studies were found. The Mexican study evaluated the timing of the dietary assessment in the course of childhood from 1 to 5 years. It was associated with breast development, a marker of onset of puberty. The present study assessed dietary intake during pre-menarche phase and associated it with a late marker of puberty. As previously mentioned, a critical moment of exposure was assessed and this could have influenced the outcome of puberty (10, 44). Statistical significance was found only in overweight girls and this controversy may be explained because higher weight status is associated with early age at menarche (44). Thus, a "Prudent" pattern may be a protective factor for childhood obesity and earlier menarche (55). Girls were 10-13 years old at the beginning of dietary assessment. There is a probability for their puberty begins with breast development. Reverse causality may occur only if early maturing and overweight girls adhere more to a "Prudent" pattern as a result of their physical changes (56).

This study has several strengths. First, the longitudinal design can estimate the time order of the casual relationship between peripubertal diet and age of menarche. Few studies had aimed to assess EFA considering food groups and the epidemiological evidence associated to age at menarche using nutritional epidemiological validated procedures. This counterbalance the weaknesses on studies that focus on nutrients and foods. Also, it considered to estimate EFA in a sample of girls, only, because dietary factors can change according to sex (i.e., girls are more concerned about body image) (17, 56). Although the 24HR can provide recall bias, the interviews were reported together with parents/caregivers and a complete list of foods from the School Nutrition Program was provided. Also, the "Multiple-Pass Method" (MPM) was applied to certify that all foods were listed properly by the adolescents and there was no missing information. In addition, usual intake adjusted for

intra-individual variance according to the MPM was estimated to increase the reliability of the results. Nevertheless, limitations should be noted. The results cannot be generalized to girls from high socio-economic level and the sample size was based on date availability rather than power. In order to obtain a prospective data on age of menarche, girls who had their menarche before the dietary assessment were excluded. Those girls were slightly younger at the 4th Tanner stage (mean=10.9 years old) and menarche (mean=11.2 years old) compared to the ones included. This difference could have potentially introduced selection bias, but not affected the internal validity of the results. Besides, the findings with total sample were relatively the same (data not shown).

Conclusions

The GOCS study found that excess weight girls that adhere most to a "Prudent" dietary pattern had a significantly later age at menarche than those with less adherence. From a public health perspective these findings are in line for meeting the current dietary guidelines. Girls with excess weight during pubertal phase that follow dietary guidelines could have influence in timing of puberty. Further investigations are needed to understand the relationship between nutrients, foods and how these interact at timing of puberty.

Table 1. Anthropometric, sociodemographic, and maternal characteristics of GOCS girls.

Girls	**n**	**Mean or %**	**SD**
Age at Tanner stage 4 visit, years	270	12.21	0.87
Age at menarche, years	270	12.55	0.83
Age at R24h visit, years	270	11.63	0.49
Weight before menarche, kg	270	49.11	11.60
Height before menarche, cm	270	152.20	6.40
BMI-for-age *z* score before menarche	270	0.76	1.20
Weight status (BMI-for-age *z* score) ‡			
Under weight	17	6.30	
Normal	128	47.41	
Overweight	82	30.37	
Obesity	43	15.93	
School Feeding Program (SFP)			
Yes	98	36.3	
No	172	63.7	
Television watching (hours/day)			
< 2 hours	147	54.44	
≥2 hours	71	26.3	
missing	52	19.26	
Sleep (hours)			
<9 hours	165	61.11	
≥9 hours	72	26.67	
missing	33	12.22	
Mothers			
Maternal education (years)			
≥12 years	168	62.22	
< 12 years	99	36.66	
missing	3	0.01	
Maternal obesity †			
No	169	62.59	
Yes	94	34.81	
missing	7	2.59	
Age at menarche (years)			
≤11	49	18.15	
12 - 14	150	55.56	
≥15	34	12.59	
missing	37	13.70	

‡ Weight status, BMI-for-age *z* score: underweight ≤ -1 SD, normal < -1 SD and < +1 SD, overweight ≥+1 SD and < +2SD, obesity ≥ +2 SD (24).

† Maternal obesity=BMI≥30 kg/m2

Table 2: Factor loadings*, explained variance and eigenvalues of the four major dietary patterns practiced by GOCS girls

Food groups	**Breakfast/*Once***	**Prudent**	**Western**
Low fat milk	-0.14	0.07	0.09
Whole fat milk	-0.04	0.12	0.07
Yogurt	-0.10	-0.03	**-0.64**
Cheeses	0.26	-0.19	-0.14
Flavored milk	**-0.31**	-0.22	-0.14
Red meat	0.07	0.18	-0.08
White_meat	-0.09	**0.34**	0.13
Processed meats	0.08	**-0.33**	0.06
Cold cuts	**0.43**	-0.14	-0.21
Junk Food	-0.23	-0.13	**0.34**
Flavored juices	-0.21	0.09	0.04
Soft drink	-0.01	-0.16	**0.37**
Tea and coffee	**0.64**	0.07	0.26
Breads	**0.72**	-0.04	-0.14
Ready-to-eat cereal	-0.10	-0.08	**-0.61**
Rice, pastas, potatoes	0.16	-0.05	-0.10
Vegetables	0.06	**0.73**	0.04
Fresh fruits	0.02	**0.41**	-0.17
Eggs	-0.02	0.18	-0.16
Homemade dishes	0.00	0.20	-0.09
Crackers and salt snacks	-0.12	-0.20	0.18
Confectionery and chocolates	-0.04	-0.06	0.16
Cookies and cakes	-0.21	-0.07	**0.40**
Desserts and ice creams	0.11	0.18	0.02
Sugar	**0.56**	0.20	**0.34**
Chocolate powder	-0.26	0.15	0.03
Margarine and butter	**0.52**	-0.10	0.00
Oil, lemon, salt, vinegar (for salad)	-0.03	**0.65**	0.06
Mayonnaise and ketchup	0.10	0.07	0.04
Soups	-0.05	0.16	**0.33**
% of explained variance	0.07	0.06	0.06
% of accumulated explained variance	0.07	0.14	0.19
Eigenvalues	2.22	1.89	1.70

Factor loadings |0.30| are shown in bold for readability purposes. Bartlett sphericity test (BSS) = $p < 0.0001$. KMO 0.54

Table 3: Adherence (%) according to sociodemographic, anthropometric, and maternal nutritional status of 270 GOCS girls

Variables		**Breakfast/*Once***			**Prudent**			**Western**		
	n	T1¶	T2	T3	T1	T2	T3	T1	T2	T3
Excess weight status‡										
No	145	32.41	35.17	32.41	33.79	36.55	29.66	34.48	29.66	35.86
Yes	125	39.20	28.80	32.00	31.2	36.00	32.8	34.4	38.4	27.2
p-value†			0.42			0.84			0.21	
School feeding program£										
Yes	98	32.65	35.71	31.63	29.59	45.92	24.49	33.67	39.8	26.53
No	172	37.21	30.23	32.56	34.30	30.81	34.88	34.88	30.23	34.88
p-value			0.62			**0.04**			0.21	
Television watching (hours/day)										
< 2 hours	147	36.73	36.73	26.53	35.37	34.69	29.93	36.73	37.41	25.85
≥2 hours	71	38.03	28.17	33.80	21.13	45.07	33.8	32.39	25.35	42.25
p-value	52		0.38			0.09			**0.04**	
Sleep (hours)										
≥9 hours	72	31.94	34.72	33.33	30.56	41.67	27.78	38.89	38.89	22.22
<9hours	165	39.39	32.73	27.88	33.33	35.15	31.52	33.94	32.12	33.94
p-value			0.52			0.63			0.19	
Maternal education (years)										
≥12 years	168	37.50	30.95	31.55	33.33	36.31	30.36	37.5	32.74	29.76
<12 years	99	31.31	35.35	33.33	31.31	36.36	32.32	30.3	35.35	34.34
			0.57			0.93			0.48	
Maternal obesity†										
No	169	37.28	28.99	33.73	31.95	34.91	33.14	30.77	33.73	35.5
Yes	94	32.98	38.30	28.72	31.91	39.36	28.72	41.49	32.98	25.53
p-value			0.30			0.71			0.14	

Mother`s age at menarche (years)										
	≤11 years	49	32.65	42.86	24.49	28.57	40.82	30.61	30.61	34.69	34.69
	12-14 years	150	38.00	29.33	32.67	35.33	34.67	30	36	35.33	28.67
	≥15 years	34	44.12	20.59	35.29	32.35	35.29	32.35	38.24	20.59	41.18
p-value		37		0.26			0.92			0.43	

¶ Tertile 1 lower adherence, Tertile 3 higher adherence percentage

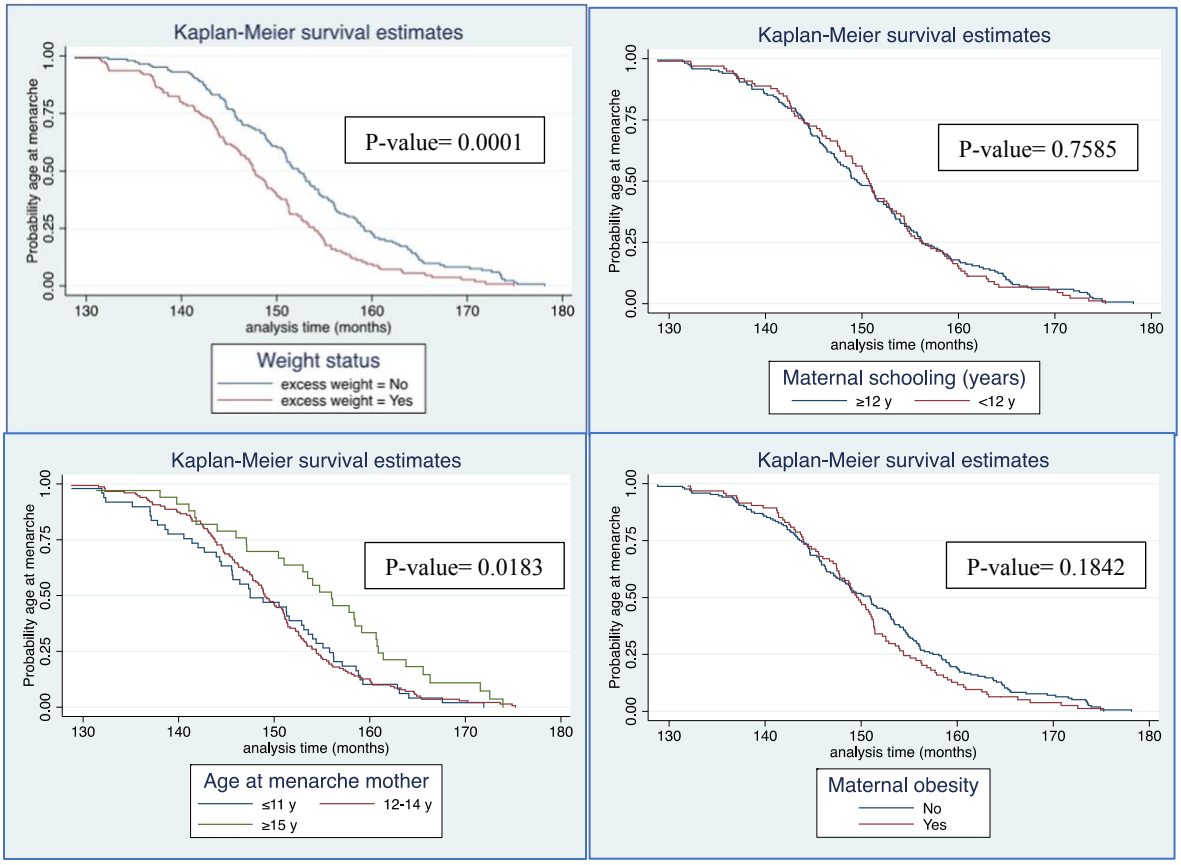
† X_2 Pearson tests, p-value <0.05

‡ Weight status, BMI-for-age *z* score: normal < +1 SD, overweight ≥+1 SD (24).

£ School feeding program: adolescents receive some food services of feeding program (yes or no).

† Maternal obesity=BMI≥30 kg/m_2

Figure 1: Kaplan–Meier Survival plots for age at menarche according to weight status and maternal characteristic in 270 GOCS girls



‡ Weight status, BMI-for-age *z* score: excess weight ≥+1 SD (24).
† Maternal obesity= BMI ≥30 kg/m2

Table 4: HRs and 95% CIs for associations with age at menarche according to tertile¶ of dietary pattern practiced by GOCS girls. Chile.

		Crude Model			Adjusted Model 1§			Adjusted Model 2|		
	Median age at menarche	**HR**	**95% Conf. Interval**		**HR**	**95% Conf. Interval**		**HR**	**95% Conf. Interval**	
Breakfast/*Once*										
First tertile	12.59	Ref‡			Ref			Ref		
Second tertile	12.54	1.06	0.79	1.42	1.24	0.79	1.96	1.52	0.94	2.46
Third tertile	12.50	0.94	0.70	1.27	0.72	0.45	1.16	1.31	0.82	2.10
Prudent										
First tertile	12.34	Ref			Ref			Ref		
Second tertile	12.50	0.85	0.63	1.14	0.66	0.41	1.05	0.61	0.37	1.01
Third tertile	12.73	0.75	0.56	1.03	0.92	0.57	1.48	**0.51**	**0.31**	**0.85**
Western										
First tertile	12.46	Ref			Ref			Ref		
Second tertile	12.54	1.02	0.76	1.36	1.14	0.71	1.82	0.73	0.46	1.16
Third tertile	12.54	0.82	0.61	1.11	0.83	0.52	1.32	1.04	0.63	1.71

* 95% Confidence Intervals, p-value <0.05.
† HR: Hazard ratio, CI: confidence interval
‡ Ref: reference
¶ Tertile 1 lower adherence, tertile 3 higher adherence
§ Model 1: Normal status (underweight and normal status) adjusted for: maternal menarche, maternal education, maternal obesity, misreporting (n:119)
| Model 2: Excess weight status (overweight and obesity status) adjusted for: maternal menarche, maternal education, maternal obesity, misreporting (n:112)

Supplemental Files

S1. Description of the foods that composed each of the 30 food groups included in the factor analysis. GOCS Study, Chile 2014-2015.

Food groups	**Food composition**
Low fat milk	skim milk, skim milk powder, reduced fat milk (2% fat),
Whole fat milk	Fluid whole milk (3% fat), whole milk powder.
Flavored milk	Mixtures and milk drinks, strawberry, chocolate and other flavors, purchased ready-to-drink
Yogurts	Yogurt, fermented milk
Cheeses	Gouda cheese, ricotta cheese, cream cheese, cheddar cheese,
White meat	poultry, chicken, turkey, fish, viscera (all cooking methods)
Red meat	Steak beef, ground beef, beef ribs, pork chop, pork ribs, pork loin,
Cold cuts	Ham, bologna, turkey breast, chicken breast, salami
Processed meats	Sausage, sausages, frankfurters, meatballs ready for consumption, nuggets, hamburger ready for consumption (only meat).
Junk food	Pizzas, sandwiches of meat or hamburger ready to eat, french fries, wonton, egg roll, chilean hot dog, *sopaipillas, tacos, empanadas*. Mainly, street food or fast food
Sweetened beverages	Juice or flavored drink, purchased ready-to-drink, juice or flavored drink, dry mix - unprepared
Soft drinks	Soda pop or soft drink regular or diet
Coffee and tea	Coffee, instant coffee, herbal tea, tea bag
Bread	French bread, bun bread, white bread with salt
Ready to eat cereal	Breakfast cereals
Rice, potato and pasta	Rice, cooked potatoes, mashed potatoes, pasta and dishes pasta.
Vegetables	Lettuce, cabbage, raw salad, others load vegetables. Pumpkin, carrot, cucumber, tomato, among others.
Fruits	Pineapple, banana, orange, apple, pear, papaya, mango, watermelon, tangerine, grape, blueberry, strawberry, blackberry, fruit salad, fruit juices
Eggs	Fried eggs, scrambled eggs, omelet, boiled eggs, egg white, egg yolk
Homemade dishes	Typical chilean food or meals prepared at home, restaurants or schools; that require a longer preparation time and made with natural foods. For instance: Beans, lentils, chickpeas, white beans, legumes-based preparations, vegetables stews with or without meat, *cazuela, charquican, chapsui, humitas, pastel de choclo* among others.

Soup	Dry soup, bouillon, consommé.
Cracker and salt snack	Crackers, saltine or soda, salty chips - snack type, cheese balls, puffs or twists, potato chips
Chocolates and confectionary	Chocolate candy, chocolate candy bar, sweets based on milk, lollipop, candy, caramel, jams, *dulce de leche*
Cookies and Cake	Cookies and bars, granola bars, sweet biscuit and cookie stuffed, cookie sandwich, cookies commercial packaged, Cakes, cheesecake, cake sponge, doughnut, muffins, pies fruit, cupcake, cake purchased ready-to-eat
Desserts and ice cream	Pudding, flan, mousse, gelatin dessert, chilean desserts, fruit canned with syrup, ice cream and frozen desserts, Popsicle
Sugar	White sugar
Chocolate powder	Cocoa powder, chocolate powder
Butter and margarine	Salted butter, unsalted butter, salted margarine, unsalted margarine, light margarine
Oil, lemon, salt, vinegar (for salad)	Soybean oil, sunflower oil, vegetal oil, olive oil, salt, vinegar, lemon juice to salad
Mayonnaise, ketchup	Mayonnaise or mayo type dressing, ketchup, mustard, soy sauce

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9 CONSIDERAÇÕES FINAIS

Este trabalho contribui principalmente para o avanço do conhecimento acerca da relação entre padrões de dieta, excesso de peso e sua possível relação com idade da menarca. Além disso, padrões de dieta em adolescentes chilenos são pela primeira vez reportados.

Observou-se alta prevalência do relato implausível entre adolescentes chilenos, principalmente do subrelato. Entre os fatores associados ao subrelato a obesidade foi o principal preditor, mas diferente ao esperado, o subrelato foi maior entre meninos. Além disso o relato implausível foi seletivo para alguns grupos de alimentos, como vegetais, *junk food*, chocolates, e gerou associações espúrias entre dieta e IMC. Dessa forma, considerar o relato implausível de energia em adolescentes chilenos, principalmente o subrelato; é essencial no momento de investigar associações entre dieta e desfechos em saúde na epidemiologia nutricional.

Os padrões identificados nos adolescentes participantes de GOCS refletem a atual cultura alimentar chilena, principalmente de famílias de nível socioeconômico médio a médio-baixo; observando-se ingestão de alimentos com alto teor de energia, gorduras saturadas, sódio e açúcares de adição em todos os padrões identificados. Esses achados ratificam as atuais políticas públicas de prevenção e controle da obesidade, como a rotulagem frontal e a publicidade dos alimentos industrializados, dirigidas principalmente para crianças e adolescentes. Entretanto, os resultados também indicam alguns vazios dessas políticas, como o alto consumo dos alimentos comercializados principalmente nas ruas ou fora das escolas (grupo *junk food* composto principalmente por salgados, pizzas, *hot dog*, *sopaipillas*, entre outros) que não são alvos de intervenções. Por outro lado, o grupo pão, principal contribuinte à ingestão de energia, é culturalmente aceitável e faz parte do padrão alimentar dos adolescentes, mas seu consumo em grandes quantidades tem relação pode estar associado o excesso de peso. Portanto,

é imprescindível considerar estes achados nas atuais políticas de saúde e incluir a educação alimentar nas escolas e famílias principalmente de nível socioeconômico baixo a médio-baixo.

Documentou-se pela primeira vez uma associação inversa entre padrões de dieta e idade de menarca. Especificamente, meninas com excesso de peso que aderem mais ao padrão *"Prudent"* tinham menor risco de apresentar uma idade de menarca precoce, comparadas com aquelas que aderem menos. Esses achados são relevantes, primeiro pelo desenho longitudinal, que permite inferir certo grau de causalidade, porque a coleta de dados dietéticos foi em media um ano antes da menarca; e segundo porque a evidência epidemiológica dos grupos de alimentos que compõem este padrão (frango, peixe, vegetais, frutas) é relativamente consistente com nossos resultados. Espere-se que os resultados deste estudo fomentem a realização de pesquisas futuras entre dieta, usando indicadores globais de alimentação como padrões de dieta, em outras etapas da vida (alimentação durante a gestação, primeira infância ou pré-puberal) e outros marcadores de início e duração da puberdade.

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ANEXOS

ANEXO 1- Termo de Consentimento Livre e Esclarecido GOCS III

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UNIVERSIDAD DE CHILE
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UNIVERSIDAD DE LAS NACIONES UNIDAS
UNIDAD DE INVESTIGACION Y DOCENCIA

CONSENTIMIENTO INFORMADO

Titulo del Proyecto: Relaciones entre crecimiento temprano, adiposidad, maduración ósea como determinantes del inicio y progresión de pubertad y estado metabólico en niños Chilenos
Investigador Principal: Dra. Camila Corvalán
Fuente de Financiamiento: FONDECYT

Los niños que son obesos y que inician la pubertad (que maduran sexualmente) más temprano pueden tener más riesgo de presentar cuando adultos enfermedades crónicas como obesidad, diabetes, problemas de colesterol, etc.

Se ha propuesto que la velocidad de crecimiento en los primeros años de vida podría relacionarse con la posibilidad de que un niño se vuelva obeso. El crecimiento en los primeros años de vida también se ha asociado con la posibilidad de un inicio más temprano de la pubertad.

El objetivo de este estudio es evaluar en niños chilenos la importancia que tiene el crecimiento temprano en la edad de inicio de la pubertad y en la aparición de problemas de salud durante la adolescencia (Ej.: diabetes y aumento del colesterol)

¿Quiénes pueden participar en este estudio? Pueden participar todos los niños y niñas que pertenezcan al estudio "Crecimiento y Obesidad Infantil" (ECO). No

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pueden participar del estudio los niños que tengan alguna enfermedad que pueda alterar su crecimiento o desarrollo.

¿Tengo necesariamente que participar en este estudio? Si acepto participar ¿puedo cambiar de opinión o retirarme? La participación en este estudio es totalmente voluntaria. Si usted está de acuerdo y permite que su hijo (a) participe, puede retirarlo del estudio en cualquier momento. Si Ud. decide que no participe, ésto no tendrá ninguna consecuencia negativa para usted ni para su hijo (a). Si Ud. decide que se retire del estudio después de que se le hayan tomado algunas mediciones a su hijo (a), Ud. podrá solicitar que esta información sea desechada y no utilizada en los análisis posteriores.

¿Por qué debiera considerar la participación de mi hijo o hija en este estudio? Este estudio nos ayudará a conocer mejor cuáles son los factores que favorecen que el niño madure más tempranamente, o que presente obesidad o una enfermedad crónica. Este conocimiento permitiría hacer mejores programas de salud para prevenir estas enfermedades.

Si decido que mi hijo(a) participe en el estudio, ¿Qué estudios le van a hacer y para qué servirán esos estudios? Si Ud. está de acuerdo con que su hijo(a) participe en este estudio, se le visitará en su casa y se le invitará a venir al INTA alternadamente cada 6 meses durante 4 años. Lo que se hará es lo siguiente:

1. *En su hogar:*
   1.1 Una nutricionista entrenada medirá el cuerpo de su hijo (a) (es decir, peso, talla, circunferencias, etc.) y el espesor de la piel de diferentes partes del cuerpo como el brazo, abdomen, etc. Estas mediciones durarán alrededor de 15 minutos y no causarán dolor o daño a su hijo(a).
   1.2 Una persona entrenada y del mismo sexo que su hijo (a) evaluará el desarrollo de caracteres sexuales de su hijo(a) (botón mamario y tamaño testicular) a través de un examen físico. Esta evaluación dura 5 minutos y

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no causa ningún daño, aunque puede causarle un poco de vergüenza a su hijo (a).

2. *Cuando acuda Ud. (u otra persona de su confianza) con su hijo(a) al INTA (El Libano 5524, Comuna de Macul)*
   2.1 Las mismas mediciones que en su hogar
   2.2 Una enfermera entrenada hará una ecografía de la mano izquierda de su hijo (a), para saber si los huesos están madurando normalmente. Este estudio dura 10 minutos y no tiene ningún riesgo.

3. *Cuando en las niñas aparezca el botón mamario y cuando la mama alcance tamaño adulto, y en los niños cuando los testículos alcancen* 4 y 10 cc adicionalmente, se hará lo siguiente: una enfermera entrenada tomará una muestra de sangre (20 ml, equivalente a una y media cuchara sopera) del brazo de su hijo (a). En esta sangre se medirán algunos indicadores relacionados con riesgo metabólico tales como glicemia, insulina, colesterol y triglicéridos y hormonas de maduración biológica como estrógenos y testosterona. Para estas mediciones es necesario que su hijo(a) esté en ayuno total (sin tomar ni comer nada) por a lo menos 8 horas.

Para ponernos de acuerdo en el dia que se realizarán estas mediciones, nosotros nos comunicaremos telefónicamente con UD. En las visitas a la casa, la evaluación de su hijo(a) se realizará en una habitación con privacidad. Cuando deba asistir al INTA pondremos a su disposición un transporte que traerá a su hijo(a) y al acompañante al INTA. En el INTA, las mediciones se realizarán en una habitación del policlínico también en forma privada.Una vez finalizadas las mediciones, se le proporcionará una colación a ambos y se los llevará de vuelta.
Si lo desea, usted está invitada a asistir a estas evaluaciones.

¿Qué molestias o daños podría experimentar mi hijo, o hija, y que harán los investigadores si sufre un daño en este estudio?

- Las evaluaciones del desarrollo sexual en su hijo (a) no le causarán ningún daño, aunque le puede producir un poco de vergüenza.
- Las tomas de muestra de sangre del brazo de su hijo(a) en ocasiones pueden causar un moretón en la zona de punción.

¿Qué harán los investigadores con la información obtenida? Toda la información que obtengamos durante este estudio será estrictamente confidencial. Esta información sólo será utilizada por los investigadores del proyecto y no estará disponible para otros fines. Su hijo(a) será identificada por un número y no por su nombre. En el caso que la información obtenida se utilice en medios científicos, nos aseguraremos que estos datos se mantendrán anónimos y no tendrán aplicación en otro proyecto o por personas ajenas al presente estudio. Las muestras de sangre serán guardadas en un refrigerador ubicado en el INTA bajo la responsabilidad del investigador principal del proyecto (Camila Corvalán). Una vez recolectadas todas las muestras, éstas serán trasladadas al laboratorio del Dr. Germán Iñiguez (IDIMI, U de Chile) y del Departamento de Nutrición de la Universidad Católica para su posterior análisis. Si Ud. lo autoriza el resto de muestra de sangre se guardará para potenciales análisis futuros. Los resultados no afectarán en modo alguno la participación de su hijo(a) en la escuela o la atención médica que su hijo(a) reciba.

¿En qué términos este estudio podría beneficiar a otras personas? La información que se obtenga en este estudio permitirá identificar algunos factores que favorecen o protegen frente al desarrollo de la obesidad y otras enfermedades crónicas, permitiendo acciones preventivas personalizadas.

¿Recibiré algún beneficio por permitir que mi hijo, o hija, participe en este estudio? Ud. recibirá un informe escrito que describa los resultados de los exámenes que se le realicen a su hijo (a). Las personas del estudio le informarán si su hijo(a):

1. tiene exceso de peso en cada evaluación

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2. tiene su maduración sexual alterada en cada evaluación
3. tiene niveles altos de azúcar o grasa en la sangre, máximo 6 meses después que se tome la muestra de sangre

Su hijo(a) será derivada al consultorio correspondiente si se detecta algún problema de salud.

¿Recibiré algún pago por permitir que mi hijo, o hija, participe en este estudio? Ud recibirá, en la primera visita anuales al Inta, $ 5000 por la participación de su hijo (a) en este estudio

¿Se cobrará a mi o a FONASA o a mi isapre el costo de las determinaciones de laboratorio o el traslado relativo a este estudio? Ni usted, ni FONASA o su isapre tendrán que pagar por la participación de su hijo (a) en este estudio. Cuando tenga que llevar a su hijo (a) a evaluación médica en el INTA, tampoco tendrá que pagar por el traslado ni la consulta. Ud. tampoco tendrá que cancelar el costo del transporte desde y hacia el INTA cuando se realicen las mediciones a su hijo (a).

Una vez que haya autorizado que mi hijo, o hija, participe en el estudio ¿A quién tendría que dirigirme para averiguar más detalles acerca del estudio o reclamar por un posible mal trato recibido? En cualquier momento del estudio UD. podrá dirigirse a la Dra. Camila Corvalán 978-1453 o al Dr. Gerardo Weisstaub 978- 1412, cuyo lugar de trabajo se encuentra en Avda. El Líbano 5524. INTA-Universidad de Chile. Santiago. Chile. Si UD. tiene dudas o consultas sobre sus derechos como participantes en este estudio, UD. puede dirigirse a Ana María Pino, Presidenta del Comité de Ética del INTA (Fono: 9781418).

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CONSENTIMIENTO ESCRITO Nº __ __ __ __

Santiago, ____ del mes de_____ del año 2____

Yo _____

Domicilio en_____Nº_____Comuna_____

Teléfono_____ Celular_____

En relación con mi hijo/a (nombre) _____Declaro:

- haber sido informado por el personal de terreno respecto de los objetivos, proyecciones y procedimientos del estudio "Relaciones entre crecimiento temprano, adiposidad, maduración ósea como determinantes del inicio y progresión de pubertad y estado metabólico en niños Chilenos"

- conocer que la información que entregue será confidencial; que se me informará del resultado en el caso que los exámenes no den un resultado normal

- conocer que la participación en este estudio no implica ninguna obligación por parte de los ejecutores del estudio, no compromete ninguno de los derechos por servicios de salud que actualmente percibo ni me hace acreedor a nuevos beneficios.

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En relación con ello, acepto que se realicen las siguientes mediciones en mi hijo:

	Acepto	No acepto
Medición del cuerpo de mi hijo (a) Ej. Peso, talla y la cantidad de grasa (dos veces al año, durante 4 años)		
Evaluación del desarrollo de mi hijo(a) a través del examen físico realizado por personal entrenado (dos veces al año, durante 4 años).		
Medición de la maduración ósea (una vez al año, durante 4 años).		
Obtener una muestra de sangre (20ml) para medir azúcar, grasa y hormonas en la sangre (dos veces en los 4 años).		
Guardar el resto de muestra de sangre para análisis futuros relacionados con crecimiento y maduración		

Firma de uno de los padres (padre o madre) _____

Firma del profesional: _____

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ASENTIMIENTO ESCRITO Nº __ __ __ __

Santiago, ____ del mes de_____ del año 20____

Yo _____, tengo _____años y vivo con mi_____

Personal de la Universidad de Chile vino a mi casa y habló conmigo, me explicaron que los mismos investigadores que han realizado los estudios anteriores en los que he participado están haciendo un nuevo estudio para saber por qué algunos adolescentes empiezan la pubertad antes y les gustaría que yo aceptara participar de ese estudio.

Entendí que ellos se pusieron de acuerdo con mi madre para visitarme en mi casa, pesarme y medirme y evaluar si han crecido o ha aparecido vello en mis genitales. Entendí también que una vez al año iré al INTA donde me harán las mismas mediciones y además estudiarán los huesos de mi muñeca. También me explicaron que me tomarán una muestra de sangre. Esto me podrá doler un poco, pero ayudará a evaluar cómo está mi salud.

Me dijeron que nadie aparte del equipo de investigación involucrado en el estudio sabrá mi nombre y que todas las evaluaciones serán sin costo para mis padres, y que puedo decidir no participar o abandonar el estudio en cualquier momento. Mis padres o el equipo de investigación del estudio no se enojarán si decido no participar o retirarme.

Acepto No acepto Participar del estudio cientifico que están haciendo algunos doctores del INTA sobre algunas cosas que pueden hacer que tenga mi pubertad antes y que se dañe mi salud

Firma (o asentimiento) del niño/a:_____

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ANEXO 2- Termo de Consentimento Livre e Esclarecido GOCS IV

Instituto de Nutrición y Tecnología de los Alimentos
Avda. El Líbano 5524, Macul, Casilla 138, Correo 11, Santiago - Chile
www.inta.cl

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COMITÉ DE ÉTICA
INSTITUTO DE NUTRICIÓN Y TECNOLOGÍA DE LOS ALIMENTOS

CONSENTIMIENTO INFORMADO PARA MADRES O PERSONAS RESPONSABLES DE NIÑAS PARTICIPANTES ESTUDIO ECO

Titulo del Proyecto: "Determinantes tempranos de riesgo de cáncer de mama" y "Predictores del desarrollo de la glándula mamaria y volumen fibroglandular de la mama en la pubertad"

Investigadores Principales: Prof. Ricardo Uauy (INTA) y Prof. Karin Michels (Universidad de Harvard, EEUU)

Nombre de las instituciones patrocinantes: World Cancer Research Fund y National Institute of Health.

El objetivo de esta investigación es estudiar la relación entre ciertas características de la niñez sobre tres marcadores de riesgo de cáncer de mama: 1) La composición de la mama; 2) La edad de inicio de la pubertad (que es la edad en la cual comienza la maduración sexual); y 3) La edad de inicio de la menstruación.

¿Quiénes pueden participar en este estudio?
En este estudio podrán participar todas las niñas que actualmente participan en el estudio "Efecto del momento del rebote adiposo y el crecimiento temprano sobre: crecimiento, adiposidad y factores de riesgo de enfermedades crónicas, en prepúberes chilenos"(ECO).

Este estudio se realizará entre los años 2011 y 2015. La participación de su hija requerirá de alrededor de 2 visitas al año por un periodo de cuatro años al INTA (Av. El Líbano 5524, Comuna de Macul). Cada visita durará cerca de 3 horas.

¿Por qué debiera considerar la participación de mi hija en este estudio?
Para colaborar en un estudio para aprender sobre cómo algunos procesos que ocurren en la niñez (por ejemplo, el peso al nacer, la ganancia de peso durante la niñez, la maduración sexual y los cambios hormonales asociados a ella, etc.) y la exposición a algunas sustancias ambientales podrían determinar el riesgo de desarrollar cáncer de mama en el futuro.

¿Tengo necesariamente que participar en este estudio? Si acepto que mi hija participe, ¿puedo cambiar de opinión o retirarme?
La participación en este estudio es totalmente voluntaria. Si usted está de acuerdo y permite que su hija participe, puede retirar a su hija en cualquier momento que lo desee. Su decisión de participar (o no participar) en el estudio no afectará de ninguna manera la participación de su hija en el estudio ECO.

Si decido que mi hija participe, ¿Qué procedimientos le van a hacer y para qué servirán esos estudios?

Si Ud. está de acuerdo con que su hija participe, el estudio requiere:

1. Las mediciones que Usted ya ha autorizado en el proyecto ECO (visitas cada seis meses al INTA y mediciones de peso, talla, pliegues corporales, ecografía ósea, evaluación del desarrollo puberal, medición en sangre de algunos marcadores metabólicos y hormonales).

2. Adicionalmente para este estudio se agregarán:
   a. Análisis en la muestra de sangre ya autorizada: marcadores inflamatorios y algunas características genéticas relacionadas con el desarrollo de la mama.
   b. Consultas sobre la dieta de su hija en algunas de las visitas. Esta entrevista la realizará una persona del estudio capacitada y tomará aproximadamente 40 minutos.
   c. Toma de una muestra de orina de 6 ml (aproximadamente 1 y media cucharaditas) para medición de algunas sustancias ambientales). Esta será realizada por un profesional de la salud.
   d. Medición de la composición corporal de su hija con una máquina de DEXA cuando finalice su desarrollo mamario. Esta medición la realizará personal entrenado del equipo; el procedimiento llevará unos 30 minutos.
   e. Llamadas telefónicas para verificar la fecha de la primera menstruación. Estas llamadas serán realizadas por personal del equipo cada tres meses.

En el INTA, las mediciones se realizarán en una habitación del policlínico en forma privada. Si lo desea, usted está invitada a asistir a estas evaluaciones.

¿Qué molestias o daños podría experimentar mi hija, y que harán los investigadores para disminuir el riesgo?

No hay daño, sólo la molestia del tiempo necesario para los exámenes. La medición de composición corporal de su hija con la máquina de DEXA no le causará ningún daño, la expone a una radiación ...s inferior a la de una radiografía de tórax normal.

¿Qué harán los investigadores para asegurar que la información que recolectarán sobre mi hija no caerá en manos equivocadas?

Toda la información que obtengamos durante este estudio será estrictamente confidencial. Esta información sólo será utilizada por los investigadores del proyecto y no estará disponible para otros fines. Su hija será identificada por un número y no por su nombre. Los resultados del estudio sólo podrán ser publicados con fines científicos. La identidad de su hija va a permanecer en el anonimato. Los resultados no serán incluidos en los registros médicos y no afectará en modo alguno la participación de su hija en la escuela o la atención médica que su hija reciba.

¿Recibiré algún beneficio por permitir que mi hija participe en este estudio?
Usted recibirá el mismo informe escrito que describa íntegramente los resultados de los exámenes que se le realicen. Las personas del estudio le informarán si su hija:
1. tiene exceso de peso.
2. presenta maduración sexual alterada
3. tiene niveles altos de azúcar o grasa en la sangre.

Su hija será derivada al consultorio correspondiente si se detecta algún problema de salud.

¿En qué términos este estudio podría beneficiar a otras personas?
Al participar en este estudio, su hija estará ayudando a generar conocimientos y datos acerca de los determinantes del riesgo de cáncer de mama en Chile.

¿Qué harán los investigadores si mi hija sufre algún daño durante el estudio?
Su hija no sufrirá ningún daño por el proyecto.

¿Recibiré algún pago por permitir que mi hija, participe en este estudio?
Ud. recibirá la compensación y el regalo del estudio ECO.

¿Se cobrará a mi o FONASA o ISAPRE el costo de las determinaciones de laboratorio relativas a este estudio?
No habrá ningún costo para usted de ninguna de las mediciones y evaluaciones que se le hagan a su hija. Ni su ISAPRE o FONASA tendrán que pagar nada por la participación de su hija en este estudio.

Una vez que haya autorizado que mi hija, participe en el estudio ¿A quién tendría que dirigirme para averiguar más detalles acerca del estudio o reclamar por un posible mal trato recibido?
Si usted tiene cualquier pregunta, comentario o sugerencia sobre el proyecto, por favor, póngase en contacto con la Dra. Ana Pereira, quien está a cargo del trabajo de campo de este estudio. Su número de teléfono es 9781402 y su dirección de correo electrónico es apereira@inta.uchile.cl. Si usted tiene alguna pregunta o inquietud acerca de sus derechos como participante en este estudio, puede comunicarse con la Dra. Ana María Pino. La Dra. Pino es la presidenta del Comité de Ética del INTA. Su número de teléfono es 978-1418.

CONSENTIMIENTO ESCRITO Nº __ __ __ __

Santiago, ____ del mes de_____ del año 201__

Yo.....

En relación con mi hija (nombre) .....Declaro:

- haber sido informado por el personal de terreno respecto de los objetivos, proyecciones y procedimientos del estudio **"Determinantes tempranos de riesgo de cáncer de mama".**
- conocer que la información que entregue será confidencial y que se me informará del resultado de as evaluaciones.
- conocer que la participación en este estudio no implica ninguna obligación por parte de los ejecutores del estudio, no compromete ninguno de los beneficios de salud que actualmente percibo ni me hace acreedor a nuevos beneficios.

En relación con ello, acepto que se realicen las mediciones propuestas en mi hija.

_____
Firma de la persona encargada de la niña

_____
Firma del profesional

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ASENTIMIENTO ESCRITO Nº __ __ __ __

Santiago, Mes____ Día _____ Año____

Yo,....., tengo.....años y vivo con.....

La gente de la Universidad de Chile me explicó que están realizando un estudio para evaluar algunas características de los niños y ver si se relaciona con la posibilidad de cáncer de mama en la edad adulta. Ellos me invitaron a participar en este estudio.

Entendí que en las visitas al INTA, consultarán a mi mamá sobre mi alimentación, me tomarán una muestra de orina y me realizarán una medición con una máquina llamada DXA. También me explicaron que ninguna de estas mediciones me producirá dolor.

Me dijeron que nadie aparte del equipo de investigación involucrado en el estudio sabrá mi nombre y que todas las evaluaciones serán sin costo para mis padres, y que puedo decidir no participar o abandonar el estudio en cualquier momento. Mis padres o el equipo de investigación del estudio no se enojarán si decido no participar o retirarme.

Acepto ☐ No acepto ☐ participar en este estudio sobre los determinantes de la infancia de riesgo de cáncer de mama.

Firma (o asentimiento) de la niña: _____

Firma del profesional _____

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ANEXO 3- Manual de procedimentos para coleta de dados antropométricos

6. TOMA DE MEDIDAS ANTROPOMÉTRICAS

MEDICIÓN DE PESO

- **Preescolar/Escolar/Adolescente y adulto:**
  - Instrumento para utilizar: Balanza digital portátil SECA 803 o TANITA BC-418

Técnica de medición: Previo a la medición, localice una superficie plana horizontal y firme para colocarla. Sin alfombras. La persona debe pesarse con la menor cantidad de ropa posible y sin zapatos. Se pide a la persona que suba a la balanza, colocando los pies en paralelo en el centro, de frente al examinador. Debe estar erguido, con la vista al frente, sin moverse y con los brazos que caigan naturalmente a los lados. Realice la lectura del número que indica la pantalla digital y registre, kilos y gramos separados por un punto y con 3 decimales, por ejemplo 56.500.

Un grupo de los participantes se evalúa el peso junto a la evaluación de composición corporal en EL EQUIPO Body composition analyser TANITA BC-418.

MEDICIÓN DE TALLA

- **Talla escolares, adolescentes y adultos.**
  - Instrumento por utilizar: Estadiómetro portátil modelo seca 213 con capacidad de 20-210 cm, graduación de 1 mm.

Técnica de medición: Previo a la medición, busca una superficie firme y plana perpendicular al piso, coloca el estadiómetro en el piso en el ángulo que forman la pared y el piso.

Pedir al sujeto que quede descalzo, sin calcetines ni accesorios y/o peinados en el cabello. Pedir al sujeto que se acomode al estadiómetro dando la espalda al instrumento, que mantenga una posición de pie con el cuerpo erguido, los talones en contacto directo con la base del equipo y juntos, la parte

distal de los pies con un ángulo de 45°. Pídale al participante que se mantenga recta/o, mirando directamente al frente, con la línea de visión y la cabeza paralelos al piso "plano de Frankfort" (ver figura 1)

En caso de los niños arrodíllese al lado derecho del tallímetro (ver figura 2), en su rodilla derecha solamente, para que tenga el máximo de movilidad. Ubíquese al frente del tallímetro, coloque los pies lo más juntos posible, tenga en cuenta que pueden presentarse niño o niñas que probablemente no pueden juntar totalmente los pies (por sobrepeso, etc.), de igual manera verifique que no se empine y que los pies se encuentren contra la parte posterior en la pared del tallímetro Con la mano derecha justo encima de los tobillos del niño o niña y su mano izquierda sobre las rodillas y empújelas cuidadosamente contra la superficie, de igual manera, asegúrese de que las piernas estén rectas y que los talones y las pantorrillas estén pegadas a la superficie.

Tanto para adultos como niños coloque su mano izquierda abierta sobre el mentón y cierre su mano gradualmente. Asegúrese de que los hombros estén en posición de descanso y que las manos estén rectas a lado y al lado del cuerpo y que la cabeza, omoplatos y glúteos estén pegadas a la parte posterior del tallímetro. Con su mano derecha baje el tope móvil superior del tallímetro, hasta apoyarlo contra la cabeza. La presión que ejerza sobre la cabeza alterará la medida, así que no debe hacer demasiada presión.

Para finalizar revisen la posición del participante y repitan cualquier paso que se considere necesario.

Registrar el dato observado en centímetros con un decimal (ejemplo: 164.3 cm).

Figura N° 1

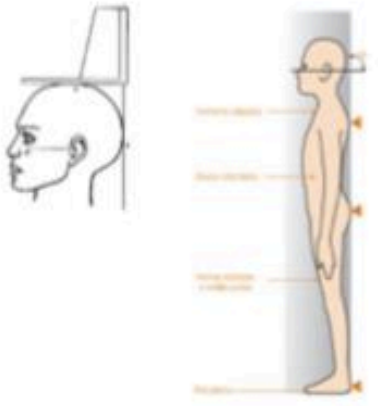
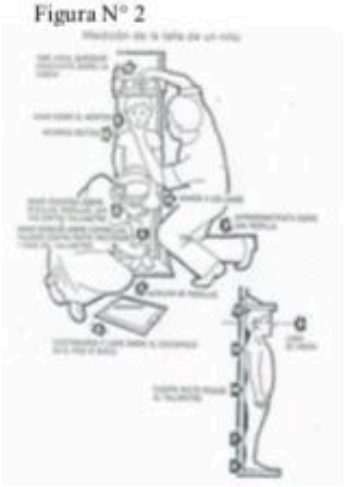


Figura N° 2



ANEXO 4- Modelo de formulário Antropometria

ANTROPOMETRIA

Folio _____

Peso al nacimiento (KG) _____

Talla nacimiento (CM) _____

Observaciones dato nacimiento

_____

TRAYECTORIA DE ANTROPOMETRIA INCONSISTENTE
TOMAR MEDIDAS CON ESPECIAL CUIDADO

Formulario antropometria ECO
- ○ Se hizo
- ○ Rechaza
- ○ No se hizo
- ○ Pendiente

Por que no se realizo medicion de antropometria o esta incompleto _____

Con que tipo de ropa se realiza el pesaje?
- ○ Ropa interior (calzon y/o calceta)
- ○ Ropa liviana (calcetas + calzas + beatle o camiseta manga larga o corta)
- ○ Ropa gruesa (calcetas + calzas + beatle o camiseta manga larga o corta + blusa manga larga o corta + jeans o buzo sin poleron)

Peso 1 en Kg _____

Peso 2 en Kg _____

Promedio de pesos _____

Diferencia entre pesos _____
(Si la diferencia es mayor a 0.5, tomar tercera medicion)

Peso 3 en Kg _____

Talla 1 (EN CENTIMETROS) _____

Talla 2 (EN CENTIMETROS) _____

Diferencia entre tallas tomadas _____
(Diferencia de talla sobre 0.5 tomar tercera medida)

Promedio Talla _____

Talla 3 (EN CENTIMETROS) _____

Talla Sentado (EN CENTIMETROS) _____

Talla Sentado 2 (EN CENTIMETROS) _____

Unidad de datos

PESO

Promedio de Peso _____

Medidas con que se calculo promedio de peso
- ○ Peso de tanita
- ○ Peso antro 1 y Peso antro 2
- ○ Peso antro 2 y Peso antro 3
- ○ Peso antro 1 y Peso antro 3
- ○ Peso 1, peso 2 y peso 3
- ○ Basado en unica medida registrada

TALLA

Promedio de Talla _____

Medidas con que se calculo promedio de talla
- ○ Talla 1 y talla 2
- ○ Talla 2 y talla 3
- ○ Talla 1 y talla 3
- ○ Talla 1, talla 2, talla 3
- ○ Basado en unica medida registrada

IMC

IMC segun promedios _____

PUNTAJE Z

WAZ (peso para la edad) _____

HAZ (altura para la edad) _____

BAZ (imc para la edad) _____

WHZ (peso para la talla) _____

ANEXO 5- Modelo de formulário Avaliação puberal

TANNER

Folio _____

Formulario de tanner
- ○ Se hizo
- ○ Rechaza
- ○ No se hizo
- ○ Pendiente

Porque no se evaluo tanner _____

Encuesta tanner hombre

Encuesta Tanner hombres
- ○ No corresponde
- ○ Si se realizo
- ○ Si se realizo, pero esta incompleto
- ○ No se hizo, pero se debio hacer.

Por que no se realizo encuesta de tanner _____

Tienes bigotes o vellos en la cara por lo que necesitas afeitarte ○ Si ○ No

Durante este ultimo tiempo has tenido un cambio de voz ○ Si ○ No

Tienes vello axilar ○ Si ○ No

Confirmacion fin de pubertad

Se confirma fin de pubertad simil tanner 4

Confirmacion de pubertad simil Tanner 4 ○ No Confirmado ○ Confirmado

Observaciones de la encuesta de tanner hombre _____

Tanner evaluado por el nino
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99

Tanner evaluado por Acompanante
- ○ 0
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99

Quien evalua el tanner
- ○ Mama
- ○ Papa
- ○ Hermano/a
- ○ Abuelo/a
- ○ Tio/a
- ○ Tutor
- ○ Otros

Observacion quien evaluo el tanner _____ (especifique "otro")

Tanner Mama derecha
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 99

Tanner Mama Izquierda
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 99

Medicion Testiculo Derecho (tomar medida en MILIMETROS CUBICOS) _____

Medicion Testiculo Izquierdo (Tomar medida en MILIMETROS CUBICOS) _____

Tanner Final
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99

Vello Axilar
- ○ Yes
- ○ No

Vello Facial
- ○ Yes
- ○ No

Olor Axilar
- ○ Yes
- ○ No

Desodorante
- ○ No usa
- ○ Si usa

TANNER DE CUERPO

MEDICION TESTICULO IZQUIERDO (CORREGIDO)
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 8
- ○ 10
- ○ 12
- ○ 15
- ○ 20
- ○ 25
- ○ 99

MEDICION TESTICULO DERECHO (CORREGIDO)
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 8
- ○ 10
- ○ 12
- ○ 15
- ○ 20
- ○ 25
- ○ 99

Tanner de cuerpo (segun medidas)
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99 (indeterminado)

Tanner de cuerpo final (corregido y aprobado)
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99 (indeterminado)

Debut de tanner de cuerpo?
- ○ No
- ○ Si
- ○ Indeterminado

TANNER DE VELLO PUBICO

Tanner de vello pubico (segun medidas)
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99 (indeterminado)

Tanner de vello pubico final (corregido y aprobado)
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 99 (indeterminado)

Debut de tanner de vello pubico?
- ○ No
- ○ Si
- ○ Indeterminado

VALIDACION DE TANNER

Requiere validacion?
- ○ No
- ○ Si

Motivo de validacion
- ☐ Involucion
- ☐ Error en la medicion

Origen de validacion
- ☐ Error de tanner de cuerpo
- ☐ Error de tanner de vello pubico

RESOLUCION
- ○ Se cambia el valor para ajustarse a la secuencia
- ○ Se mantiene el valor acorde a las mediciones
- ○ Se deja en blanco (no se consideran las mediciones de esta visita)

Fecha de resolucion de la validacion _____

Justificacion de la validacion _____

Aprobado por Ana Pereira y Camila Corvalan
- ○ No
- ○ Si
- ○ En espera

MENARQUIA

Folio	_____
evaluacion de menarquia	○ No corresponde ○ Si se realizo ○ Si se realizo, pero esta incompleto ○ No se hizo, pero se debio hacer.
Por que no se realizo Enc. menarquia o esta incompleta	_____
Fecha en que se realiza la encuesta	_____
Fecha de cuando sangro	_____
Fecha de menarquia	_____
Cuantos dias duro el sangrado	_____
Volumen de Sangrado (medido en Usa Tollitas o protectos)	○ Usa Toallitas ○ Usa Protector ○ No usa Toallitas,/protector
Volvio a sangrar	○ Yes ○ No
Cuantas veces a vuelto a sangrar	○ 1 vez ○ 2 veces o mas
Frecuencia de sangrado	○ Ciclo Normal (ciclo menstrual entre 21 y 34 dias) ○ Oligomenorrea (ciclo menstrual mayor o igual a 35 dias) ○ Polimenorrea (ciclo menstrual menor a 21 dias) ○ Irregular ○ No sabe/no responde
Tipo de sangrado	○ Irregular ○ Regular
Sangra solo al orinar	○ Yes ○ No
Sangra solo al defecar	○ Yes ○ No
Sangra solo al limpiarse	○ Yes ○ No
Color del sangrado	○ Chocolate ○ Rojo
Algun sintoma	○ Yes ○ No
especificaciones del sangrado	_____
Recibe atencion por algun especialista	○ Yes ○ No

posible menarquia	_____
Observaciones	_____
recibe atencion de endocrinologo	_____
Confirmacion de menarquia	○ No Confirmada ○ Confirmada

ANEXO 6- Parecer Comité de Ética em Pesquisa da Faculdade de Saúde Publica da Universidade de São Paulo

USP - FACULDADE DE SAÚDE PÚBLICA DA UNIVERSIDADE DE SÃO PAULO - FSP/USP

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Dieta, estado nutricional e risco cardiometabólico em adolescentes chilenos
Pesquisador: Angela Graciela Martínez Arroyo
Área Temática:
Versão: 1
CAAE: 04256118.1.0000.5421
Instituição Proponente: Faculdade de Saúde Pública da Universidade de São Paulo - FSP/USP
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.179.870

Apresentação do Projeto:
Trata-se de um estudo transversal aninhado a um estudo longitudinal chamado Growth and Obesity Cohort Study (GOCS), iniciado em 2006. Serão utilizados os dados dos adolescentes acompanhados entre os anos 2014 e 2015.Foram convidados a participar do
estudo GOCS todas as crianças que estavam frequentando creches da "Junta Nacional de Jardines Infantiles" (JUNJI) da área Sudeste da cidade de
Santiago no ano 2006 e cumpriram os seguintes critérios de inclusão: 1) gravidez simples, 2) idade gestacional superior a 37 semanas, 3) peso ao
nascer normal (entre 2.500 e 4.500 gramas), 4) ausência de doença física ou psicológica que poderia afetar seriamente o crescimento. Do total de
1953 crianças convidadas e elegíveis, 1.196 concordaram em participar desse estudo.

Objetivo da Pesquisa:
Objetivo Primário:
Investigar a associação entre dieta, estado nutricional e risco cardiometabólico em adolescentes chilenos.
Objetivo Secundário:
- Caracterizar a população de estudo segundo variáveis sociodemográficas, estado nutricional e risco cardiometabólico;
- Descrever a ingestão

Endereço: Av. Doutor Arnaldo, 715
Bairro: Cerqueira Cesar **CEP:** 01246-904
UF: SP **Município:** SAO PAULO
Telefone: (11)3061-7779 **Fax:** (11)3061-7779 **E-mail:** cep@fsp.usp.br

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habitual de energia, macro e micronutrientes (açúcares de adição, gorduras saturadas, sódio) segundo variáveis sociodemográficas e estado
nutricional;
• Identificar os alimentos e/ou grupos de maior contribuição na ingestão de energia, açúcar de adição, gordura saturada e sódio;
• Identificar padrões de dieta e avaliar sua associação com o estado nutricional e risco cardiometabólico.

Avaliação dos Riscos e Benefícios:
Existem riscos mínimos envolvidos com a pesquisa, pois serão utilizados para a análise apenas dados secundários.
Dentre os benefícios, destaca-se que este estudo pode auxiliar a avaliar e reorientar as políticas e programas de promoção da saúde no Chile.

Comentários e Considerações sobre a Pesquisa:
Estudo original e relevante, uma vez o aumento da prevalência da obesidade é um problema de saúde pública em muitos países e deve ser abordado com urgência já que pode afetar a saúde imediata, nível educacional e a qualidade de vida dos indivíduos.
A Profa. Dra. Camila Corvalán Aguilar, do Instituto de Nutrición y Tecnología de Alimentos (INTA)da Universidade do Chile autorizou a utilização dos dados de ingestão de alimentos, de antropometria e do estado metabólico das crianças participantes do Estudo Chileno de Crescimento e Obesidade (ECO).

Considerações sobre os Termos de apresentação obrigatória:
Os termos de apresentação obrigatória estão adequados.

Conclusões ou Pendências e Lista de Inadequações:
Aprovação do projeto.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1208007.pdf	03/12/2018 15:31:43		Aceito

Endereço: Av. Doutor Arnaldo, 715
Bairro: Cerqueira Cesar **CEP:** 01.246-904
UF: SP **Município:** SAO PAULO
Telefone: (11)3061-7779 **Fax:** (11)3061-7779 **E-mail:** coep@fsp.usp.br

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Continuação do Parecer: 3.179.870

Declaração de Pesquisadores	Carta_CC.docx	03/12/2018 15:31:01	Angela Graciela Martinez Arroyo	Aceito
Folha de Rosto	AngelaMartinezPlataformaBrasil.pdf	03/12/2018 15:24:36	Angela Graciela Martinez Arroyo	Aceito
Projeto Detalhado / Brochura Investigador	projeto_final.pdf	29/08/2018 15:29:19	Angela Graciela Martinez Arroyo	Aceito

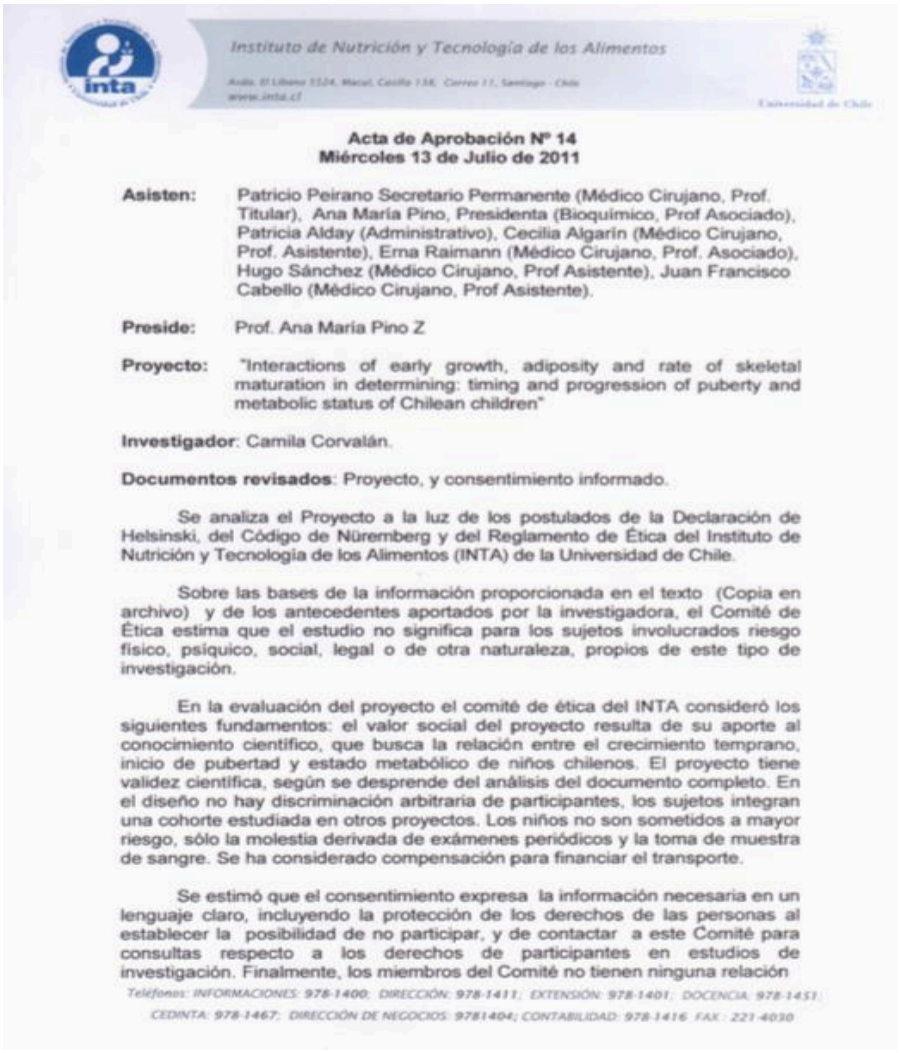
Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

SAO PAULO, 01 de Março de 2019

Assinado por:
Kelly Polido Kaneshiro Olympio
(Coordenador(a))

ANEXO 7- Parecer Comité de Ética em Pesquisa do *Instituto de Nutrición y Tecnologia de los Alimentos, Universidad de Chile*



Instituto de Nutrición y Tecnología de los Alimentos

Avda. El Líbano 5524, Macul, Casilla 138, Correo 11, Santiago - Chile
www.inta.cl

Universidad de Chile

Acta de Aprobación Nº 14
Miércoles 13 de Julio de 2011

Asisten: Patricio Peirano Secretario Permanente (Médico Cirujano, Prof. Titular), Ana María Pino, Presidenta (Bioquímico, Prof Asociado), Patricia Alday (Administrativo), Cecilia Algarín (Médico Cirujano, Prof. Asistente), Erna Raimann (Médico Cirujano, Prof. Asociado), Hugo Sánchez (Médico Cirujano, Prof Asistente), Juan Francisco Cabello (Médico Cirujano, Prof Asistente).

Preside: Prof. Ana María Pino Z

Proyecto: "Interactions of early growth, adiposity and rate of skeletal maturation in determining: timing and progression of puberty and metabolic status of Chilean children"

Investigador: Camila Corvalán.

Documentos revisados: Proyecto, y consentimiento informado.

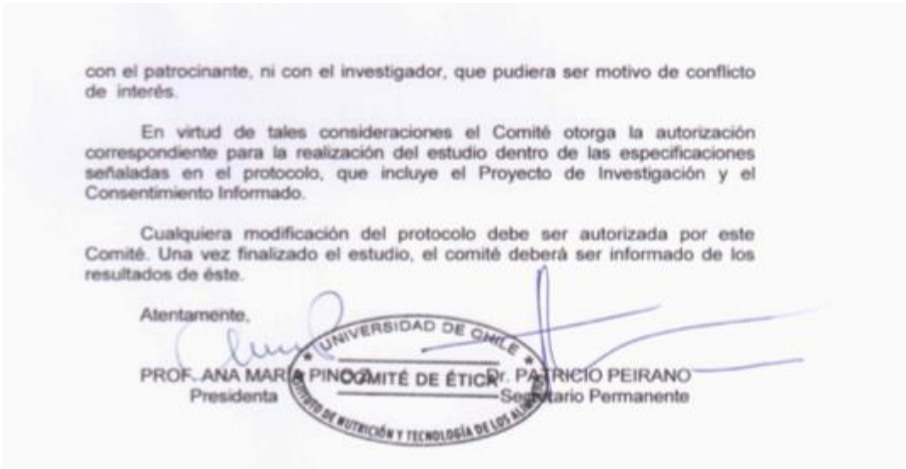
Se analiza el Proyecto a la luz de los postulados de la Declaración de Helsinski, del Código de Nüremberg y del Reglamento de Ética del Instituto de Nutrición y Tecnología de los Alimentos (INTA) de la Universidad de Chile.

Sobre las bases de la información proporcionada en el texto (Copia en archivo) y de los antecedentes aportados por la investigadora, el Comité de Ética estima que el estudio no significa para los sujetos involucrados riesgo físico, psíquico, social, legal o de otra naturaleza, propios de este tipo de investigación.

En la evaluación del proyecto el comité de ética del INTA consideró los siguientes fundamentos: el valor social del proyecto resulta de su aporte al conocimiento científico, que busca la relación entre el crecimiento temprano, inicio de pubertad y estado metabólico de niños chilenos. El proyecto tiene validez científica, según se desprende del análisis del documento completo. En el diseño no hay discriminación arbitraria de participantes, los sujetos integran una cohorte estudiada en otros proyectos. Los niños no son sometidos a mayor riesgo, sólo la molestia derivada de exámenes periódicos y la toma de muestra de sangre. Se ha considerado compensación para financiar el transporte.

Se estimó que el consentimiento expresa la información necesaria en un lenguaje claro, incluyendo la protección de los derechos de las personas al establecer la posibilidad de no participar, y de contactar a este Comité para consultas respecto a los derechos de participantes en estudios de investigación. Finalmente, los miembros del Comité no tienen ninguna relación

Teléfonos: INFORMACIONES: 978-1400; DIRECCIÓN: 978-1411; EXTENSIÓN: 978-1401; DOCENCIA: 978-1451; CEDINTA: 978-1467; DIRECCIÓN DE NEGOCIOS: 9781404; CONTABILIDAD: 978-1416 FAX : 221-4030



con el patrocinante, ni con el investigador, que pudiera ser motivo de conflicto de interés.

En virtud de tales consideraciones el Comité otorga la autorización correspondiente para la realización del estudio dentro de las especificaciones señaladas en el protocolo, que incluye el Proyecto de Investigación y el Consentimiento Informado.

Cualquiera modificación del protocolo debe ser autorizada por este Comité. Una vez finalizado el estudio, el comité deberá ser informado de los resultados de éste.

Atentamente,

UNIVERSIDAD DE CHILE
INSTITUTO DE NUTRICIÓN Y TECNOLOGÍA DE LOS ALIMENTOS

PROF. ANA MARÍA PINO
Presidenta
COMITÉ DE ÉTICA

Dr. PATRICIO PEIRANO
Secretario Permanente

Instituto de Nutrición y Tecnología de los Alimentos

Avda. El Líbano 5524, Macul, Casilla 138, Correo 11, Santiago - Chile
www.inta.cl

Acta de Aprobación Nº 12
Miércoles 13 de Junio de 2012

Asisten: Patricio Peirano, Secretario Permanente (Médico-cirujano, Prof titular), Ana María Pino, Presidenta (Bioquímico, Prof Asociado), Dra. Cecilia Algarín (Médico-cirujano, Prof. Asistente), Dra. Erna Raiman (Médico Cirujano, Prof Asociado), Patricia Alday (Representante de la Comunidad), Dr Juan Francisco Cabello (Médico-cirujano, Prof. Asistente), Marcela Castillo (Psicóloga, Prof. Asistente).

Preside: Prof. Ana María Pino

Proyecto: "Predictores del desarrollo de la glándula mamaria y volumen fibroglandular de la mama en la pubertad".

Investigadora: Dra Karin Michels (Universidad de Harvard).

Documentos revisados: Proyecto y consentimiento informado del proyecto "Determinantes tempranos de riesgo de cáncer de mama" (WCRF, IR: Dr R Uauy), y consentimiento conjunto.

Se analiza el Proyecto a la luz de los postulados de la Declaración de Helsinski, del Código de Nüremberg y del Reglamento de Ética del Instituto de Nutrición y Tecnología de los Alimentos (INTA) de la Universidad de Chile.

En la evaluación del proyecto el comité de ética del INTA consideró los siguientes fundamentos: el valor social del proyecto resulta de su aporte al conocimiento científico. El proyecto tiene validez científica, según se desprende del análisis del documento completo, incluyendo los antecedentes de los investigadores.
Las participantes corresponden a la cohorte de niñas del proyecto "Crecimiento y obesidad (ECO)"; se autorizó una forma de consentimiento informado común para los proyectos de World Research Cancer Found y el actual de NIH (Dr R Uauy). Se estimó que el consentimiento expresa la información necesaria en un lenguaje claro, incluyendo la protección de los derechos de las personas al establecer la posibilidad de no participar, y de contactar a este Comité para consultas respecto a los derechos de participantes en estudios de investigación.

Finalmente, los miembros del Comité no tienen ninguna relación con el patrocinante, ni con el investigador, que pudiera ser motivo de conflicto de interés.

Sobre la base de la información proporcionada en el texto (Copia en archivo), el Comité de Ética estima que el estudio no representa para los sujetos involucrados riesgo de tipo psíquico, social, legal o de otra naturaleza, propios de este tipo de investigación.

En virtud de tales consideraciones el Comité otorga la autorización correspondiente para la realización del estudio dentro de las especificaciones señaladas en el protocolo, que incluye el Proyecto de Investigación y el correspondiente Consentimiento Informado.

Cualquiera modificación del protocolo debe ser autorizada por este Comité. Una vez finalizado el estudio, el comité deberá ser informado de los resultados de éste.

Atentamente,

Prof. Ana María Pino Z
Presidenta

Dr. Patricio Peirano
Secretario Permanente

UNIVERSIDAD DE CHILE
COMITÉ DE ÉTICA
INSTITUTO DE NUTRICIÓN Y TECNOLOGÍA DE LOS ALIMENTOS

ANEXO 8: Folha de rosto referente à submissão manuscrito 1

---------- Forwarded message ---------
De: **Journal of Adolescent Health** <em@editorialmanager.com>
mailto:regina.fisberg@gmail.com is 12:37
Subject: Journal of Adolescent Health - Acknowledgement of receipt of your submission
To: Regina Mara Fisberg <regina.fisberg@gmail.com>

Dear Professor Fisberg,

Your submission entitled "Misreporting of energy intake and factors associated among adolescents from the Growth and Obesity Chilean Cohort Study (GOCS)" has been received by the Journal of Adolescent Health. Your manuscript has been assigned tracking number JAH-2019-00504. Please refer to this number when communicating with the editorial office about your paper.

You will be able to check on the progress of your paper by logging on to the Editorial System of the journal as an author. The URL is https://www.editorialmanager.com/jah/.

If you have not heard anything further regarding the status of your manuscript submission within 14 DAYS OF SUBMISSION, please check the EM site to make certain that you have not missed any communication from the editorial office.

Thank you for submitting your work to the Journal of Adolescent Health.

Kind regards,

Journal of Adolescent Health

ANEXO 9: Folha de rosto referente à submissão manuscrito 2

From: Nutrition Research <EviseSupport@elsevier.com>
Date: October 10, 2019 at 4:28:56 PM GMT-3
To: angela.martinez@uv.cl
Subject: Track your co-authored submission to Nutrition Research
Reply-To: EviseSupport@elsevier.com

Dear Professor Martinez Arroyo,

Submission no: NR_2019_900
Submission title: Dietary patterns of Chilean adolescents from the Growth and Obesity Cohort Study indicate poor dietary quality.
Corresponding author: Dr Regina Mara Fisberg
Listed co-author(s): Professor Angela Martinez Arroyo, Dr Camila Corvalan Aguilar, Professor Ximena Palma Molina, Professor Ximena Ceballos Sanchez

Dr Fisberg has submitted a manuscript to Nutrition Research and listed you as a co-author. This email is to let you know we will be in contact with updates at each decision stage of the submission process.

The link below takes you to a webpage where you can sign in to our submission system using your existing Elsevier profile credentials or register to create a new profile. You will then have the opportunity to tailor these updates and view reviewer and editor comments once they become available.

http://www.evise.com/profile/api/navigate/NR?resourceUrl=%2Fco-author%2F%3Fdgcid%3Dinvite_email_coauthoroutreach02715317%23%2FNR%2Fsubmission%2FNR_2019_900

If you are not a co-author of this manuscript, please contact Researcher Support at: https://service.elsevier.com

Thank you very much for your submission and we will be in touch as soon as we have any news to share.

Nutrition Research

ANEXO 10: Curriculum lattes

Regina Mara Fisberg

Bolsista de Produtividade em Pesquisa do CNPq - Nível 1D

Endereço para acessar este Cv: http://lattes.cnpq.br/3405418847290218
Última atualização do currículo em 24/06/2019

Graduada em Nutrição pela Universidade São Camilo (1984), mestre em Ciências Biológicas pela Universidade Federal de São Paulo (1989), doutora em Ciências Biológicas pela Universidade Federal de São Paulo (1994) e livre-docente em Saúde Pública pela Faculdade de saúde Pública da USP (2005). Sua carreira de pesquisadora orientadora (já formou 18 mestres e 8 doutores) foi feita no Departamento de Nutrição da Faculdade de Saúde Pública da USP, com ênfase em Técnicas e Métodos na Avaliação Nutricional de População, atuando principalmente nos seguintes temas: epidemiologia nutricional, consumo alimentar, dieta e recomendações nutricionais. De vários projetos pesquisa, realizados com apoio das agencias de fomento nacionais e internacionais e em colaboração com outros pesquisadores, resultaram 8 livros e mais de 150 publicações de artigos científicos (índice H=20 ISI). É bolsista de produtividade em pesquisa nível 1D, do CNPq, desde 2003 e líder do diretório de grupos de pesquisa. É membro do corpo editorial da Revista Brasileira de Epidemiologia e da Revista de Nutrição e tem atuado como revisor regular em revistas nacionais e internacionais. Integra o Grupo de Trabalho sobre Nutrição e Alimentos para Fins Especiais (GTNFSDU) do Codex Alimentarius, da ANVISA, entre 2011 e 2017. Participa ativamente em funções de gestão científica e acadêmica da Universidade, sendo representante da categoria professor Associado 3 no Departamento de Nutrição e na Congregação. Foi presidente da Comissão de Graduação da Faculdade de Saúde Pública entre 2005 e 2011 e Chefe de Departamento entre 2014 e 2016. **(Texto informado pelo autor)**

Identificação

Nome	Regina Mara Fisberg
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Graduada em Nutrição e Dietética pela Universidad de Valparaíso, Chile (2005). Mestre em Nutrição e Alimentos com menção em Promoção da Saúde e Prevenção de Doenças Crônicas associadas à Nutrição, Instituto de Nutrición y Tecnologa de los Alimentos (INTA)´, Universidad de Chile (2010). Professora Facultad de Farmacia da Universidad de Valparaíso, Chile (desde 2006). Bolsista de "Becas de Doctorado en el Extranjero, BECAS CHILE, CONICYT, convocatoria 2015". Atualmente doutoranda do Programa de Nutrição em Saúde Pública da Faculdade de Saúde Pública da USP. **(Texto informado pelo autor)**

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2015	Doutorado em andamento em Doutorado em Ciências.. Universidade de São Paulo, USP, Brasil. Título: Padrões de dieta e ingestão de nutrientes em crianças de Santiago, Chile: relação com estado nutricional e perfil metabólico, Orientador: Regina Mara Fisberg. Coorientador: Marcela Reyes Jedlicki. Bolsista do(a): Becas Chile, CONICYT, Chile. Palavras-chave: estudo tranversais; crianças; risco metabolico; padrões de dieta. Grande área: Ciências da Saúde Grande Área: Ciências da Saúde / Área: Nutrição / Subárea: Saúde Coletiva. Grande Área: Ciências da Saúde / Área: Nutrição / Subárea: Epidemiologia. Setores de atividade: Alimentação.
2010 - 2013	Mestrado em Nutricion y Alimentos. Universidad de Chile, UC, Chile. Título: Association between metabolic syndrome and breast density in premenopausal Chilean women,Ano de Obtenção: 2013. Orientador: Maria Luisa Garmendia.