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The consumption of ultra-processed foods was associated with adiposity, but not with metabolic indicators in a prospective cohort study of Chilean preschool children

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Abstract

Background Increasing consumption of ultra-processed foods (UPF) has been identified as a risk factor for obesity and various diseases, primarily in adults. Nonetheless, research in children is limited, especially regarding longitudinal studies with metabolic outcomes. We aimed to evaluate the longitudinal association between consumption of UPF, adiposity, and metabolic indicators in Chilean preschool children.

Methods We conducted a prospective analysis of 962 children enrolled in the Food and Environment Chilean Cohort (FECHIC). Dietary data were collected in 2016 at age 4 years with 24-h recalls. All reported foods and beverages were classified according to the NOVA food classification, and the usual consumption of UPF in calories and grams was estimated using the Multiple Source Method. Adiposity (*z*-score of body mass index [BMI *z*-score], waist circumference [WC], and fat mass [in kg and percentage]) and metabolic indicators (fasting glucose, insulin, HOMA-IR, triglycerides, total cholesterol, and cholesterol fractions) were measured in 2018, at the age of 6 years. Linear regression models ((0) crude, (1) adjusted for covariables, and (2) adjusted for covariables plus total caloric intake) were used to evaluate the association between UPF and outcomes. All models included inverse probability weights to account for the loss to the follow-up.

Results At 4 years, usual consumption of UPF represented 48% of the total calories and 39% of the total food and beverages grams. In models adjusted for covariables plus caloric intake, we found a positive association between UPF and BMI *z*-score (for 100 kcal and 100 g, respectively: $b = 0.24$ [95%CI 0.16–0.33]; $b = 0.21$ [95%CI 0.10–0.31]), WC in cm ($b = 0.89$ [95%CI 0.41–1.37]; $b = 0.86$ [95%CI 0.32–1.40]), log-fat mass in kg $b = 0.06$ [95%CI 0.03–0.09]; $b = 0.04$ [95%CI 0.01–0.07]), and log-percentage fat mass ($b = 0.03$ [95%CI 0.01–0.04]; $b = 0.02$ [95%CI 0.003–0.04]), but no association with metabolic indicators.

Conclusions In this sample of Chilean preschoolers, we observed that higher consumption of UPF was associated with adiposity indicators 2 years later, but not with metabolic outcomes. Longer follow-up might help clarify the natural history of UPF consumption and metabolic risks in children.

Keywords Ultra-processed food , Adiposity, Metabolic markers, Children, Child diet

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Background

Childhood obesity has become an escalating health concern worldwide. According to the 2019 projections by the World Obesity Federation, it is anticipated that by 2025, approximately 206 million children and adolescents aged 5–19 years will be affected by obesity, mainly due to increasing rates in emerging countries [1]. In Latin America, 7% of children under 5 years of age and 20–25% of children and adolescents up to 19 years are estimated to living with overweight or obesity [2]. In Chile, data from a survey including students in the public education system in 2019 revealed that 26.5 and 24.9% of preschool children (kinder) presented overweight and obesity, respectively [3]. Childhood obesity tends to persist over time and is associated with metabolic disturbances, which increasingly manifest at younger ages [4]. Several determinants are associated with childhood obesity, with changes in eating patterns being described as one of the main ones.

During the last decades, the food system has changed in different countries, and traditional diets have been increasingly replaced by ultra-processed foods (UPF) [5]. UPF are industrial formulations made mainly of substances extracted or derived from foods (e.g., sugar and fats), with little or no whole food in their composition and which typically contain added additives such as flavorings, colorings, and other additives used to modify the sensory attributes of the final product [6]. Children and adolescents have been described as the primary consumers of UPF in national surveys from Australia [7], Canada [8], the USA [9], Mexico [10], and Chile [11]. In developed countries such as the UK and the USA, UPF represents more than 60% of the calories consumed in children's and adolescents' diets [12, 13]. In some Latin American countries such as Chile and Mexico, it is more than one-third of the total calories consumed by children 1–19 years old [10, 11]. Non-representative studies in Brazil and Chile have reported that more than 40% of the total caloric intake comes from UPF in preschoolers at 4 years old [14, 15].

Nationally representative data from food purchases and consumption from different countries showed that high amounts of UPF in diets are related to higher amounts of sugar and sodium, high energy density, and lower quantities of protein, micronutrients, and fiber [5, 16–20]. In adults, systematic reviews and meta-analyses indicated a direct association between UPF consumption and overweight, obesity, metabolic syndrome, diabetes, and all-cause mortality [21–24]. However, evidence regarding health impacts in children is still scarce and inconsistent [25]. A recent systematic review of the effects of UPF, as defined by NOVA, on obesity and cardiometabolic comorbidities in children and adolescents showed that higher consumption of UPF was associated with greater adiposity in most studies. In the case of metabolic indicators, studies available are only a few and mostly from Brazil. Moreover, results have shown conflicting results [25]. For instance, prospective studies with children aged between 3 and 6 years found a direct relationship between the consumption of UPF and total cholesterol [26, 27], LDL cholesterol [26], and triglycerides [27], but not with the glycemic profile [14].

Given the extent of the public health burden related to poor nutrition in children and the exponential increase in the consumption of UPF, a better understanding of the effects of UPF on indicators of metabolic risk in children is crucial. To our knowledge, no previous study on this topic has been conducted in Chile, so we aimed to prospectively evaluate the association between the consumption of ultra-processed foods, adiposity, and metabolic indicators in a sample of low-to-middle-income Chilean preschool children after 2 years of follow-up.

Methods

Study design and subjects

We used data from the Food and Environment Chilean Cohort (FECHIC), a cohort of 962 Chilean low-to-middle-income preschoolers from Southeast Santiago, Chile, started in 2016. Mothers were recruited in public schools to participate in the study with their 4- to 6-year-old children. Details on the recruitment and inclusion criteria are available elsewhere [28]. Briefly, the inclusion criteria were mothers as the primary caregivers for food purchases and childcare, absence of mental illness in the mother and child, and of other diseases with an impact on food consumption and child development, besides children of non-twin gestation, born at term and with normal birth weight. The present study included children with dietary data at baseline (year 2016, average age: 4.9 years) and anthropometric, body composition, or metabolic indicators measured after 2 years (year 2018, average age: 6.1 years).

Dietary intake

At baseline, trained dietitians collected 24-h dietary recalls (24HR) following the United States Department of Agriculture (USDA) Automated Multiple-Pass method [29]. They used a photographic atlas to help estimate portion sizes accurately [30], and recorded data on portion size, type of preparation, type of food, and product brand and flavor in the case of packaged foods, as well as the source of the food and eating location. This information was entered into SER-24, a software developed by the Center for Research in Food Environment and Prevention of Obesity and Non-Communicable Diseases (CIAPEC), INTA, that includes over 6000 foods and beverages

and 1400 standard recipes of traditional Chilean dishes and estimates nutrient intake using the Food Composition Table of the USDA [28, 31]. The mother was the primary respondent and reported 1 day of their child's food consumption in a face-to-face interview. Children were present during the interview and complemented the information for the eating occasions when the respondent was absent (e.g., school time). In the case of receiving meals from the School Feeding Program, these preparations were also recorded to link them to the recipes and nutrient contents of the food providers. A second dietary recall was collected within 30 days in a random subsample of 20.1% of participants.

Food consumption according to the NOVA food classification system

Briefly, the NOVA classification considers the extent and purpose of industrial processing and classifies all foods and beverages into four groups: group 1—natural or minimally processed foods (MPF); group 2—processed culinary ingredients (PCI); group 3—processed foods (PF); and group 4—ultra-processed foods (UPF). Examples of UPF include industrialized sodas, toddler milk, confectionaries, chocolates, ice cream, hamburgers, reconstituted meat products, pizzas and other frozen dishes, instant soups, and packaged bakery products, among others [6]. We identified UPF based on food descriptions, food categories and type of food, whether packaged or unpackaged, brand, and flavor, when available. Simple preparations included in the software SER-24 (e.g., cooked rice) were classified based on their main component. Other homemade recipes were disaggregated into their components, and each of them was individually classified. Food classification was carried out by a postgraduate dietitian at CIAPEC and reviewed by a second dietitian. Disagreements (0.4%) were discussed and resolved by consensus. To verify the interrater agreement, a third dietitian independently classified a random subset of 5% of SER-24 records ($n=306$). We found an agreement of 97.4% and a kappa coefficient of 0.95, indicating almost perfect agreement between the raters. More details about the methodology applied were published elsewhere [32].

We calculated the consumption of UPF in calories and in grams for each participant. Most published studies used the caloric share of UPF; however, presenting UPF grams allowed us to consider the consumption of low or non-calorie UPF, such as artificially sweetened beverages commonly consumed by Chilean children at this age [33].

Exclusion of outliers in dietary data

We identified outliers using two techniques: comparing the total calories consumed and the energy requirements of each participant and considering the extremes in the distribution of UPF (both in calories and grams).

We estimated the energy requirements with the Dietary Reference Intake (DRI) equation according to age and sex [34], using sedentary and very active levels of physical activity to calculate the lower and the higher cutoff points, respectively [35]. We used the subsample with two dietary recalls to calculate the standard deviation (SD) for the ratio (in %) between reported energy intake (rEI) and predicted energy requirement (pER), using the formula provided by Huang [36]. The formula considers the pooled coefficient of variation (CV) of the rEI (CVrEI = 32.6%, calculated for our sample [37]), the number of days of dietary assessment ($d=2$), the CV of the pER (CVpER = 12.1%, calculated with the mean and SD for the total energy of 3- to 18-year-old boys and girls described in the DRI [34]), and the coefficient of variation in the measured total energy expenditure (CVmTEE = 8.2%, obtained from literature [36, 37]). The value of SD for our sample was 27.3%, and we defined implausible diets as those in which reported energy was from < -3 or $+3$ SD away from predicted energy requirements (i.e., < 18.1% or > 181.9% of the pER).

Additionally, diets under the 1st and above the 99th percentile of UPF consumption in calories and grams were excluded (UPF consumption < 42 kcal or > 1478.5 kcal and < 27 g or > 1554.5 g).

Of the 1154 records collected at the beginning of the study, 15 were considered implausible, and 30 were considered extreme UPF consumption. Then, the estimates of usual consumption included 743 children with a unique and 183 with two measures of 24HR.

Usual consumption of UPF

We estimated the usual consumption of UPF using the Multiple Source Method (MSM). This method assumes that the 24HR is not biased for the usual consumption and models the probability of consumption—with logistic regression—and the amount consumed in a day of consumption—with linear regression—allowing the incorporation of covariates and is based on the premise that habitual consumption is equal to the probability of consumption times the usual amount consumed. Usual consumption can be estimated for dietary components that have frequent or daily consumption (e.g., nutrients), but also for those that have episodic consumption (e.g., food categories), as long as at least two measurements for a part of participants are available [38]. A minimum of 50 individuals with at least two 24HR is required to apply statistical methods to account for within- and

between-person variation and estimate the usual consumption for food groups consumed almost every day [39].

The MSM was applied using free access online software developed by the Department of Epidemiology of the German Institute of Human Nutrition Potsdam-Rehbrücke, available at https://nugo.dife.de/msm/. Covariables included for the estimates were sex, age, baseline body mass index (BMI) *z*-score for sex and age, and maternal variables (age, BMI, work outside the home, and education level).

Outcomes

All outcomes were measured after approximately 2 years of follow-up when the children were, on average, 6.1 years old.

Anthropometric indicators

We used data collected by trained dietitians following standard procedures. Height was measured using a portable stadiometer (Seca 217, to the nearest 0.1 cm), and weight was measured using a digital electronic scale (Seca 803 or 813, precision of 0.1 kg). Weight and height were taken in duplicate, and we used their average to calculate BMI. We compared the BMI of each child with the World Health Organization (WHO) growth references specific for age and sex [40] to obtain their *z*-score value (BMI *z*-score). Waist circumference (WC) was measured with a metal tape (Lufkin W 606 PM, USA, precision 0.1 cm) and taken in duplicate. A third measurement was required if the difference between both measurements was greater than 0.5 cm. We calculated the average WC for each child in cm.

Body composition

Body composition was estimated using the bioelectrical impedance (BIA) method using Tanita BC-418 (Tanita Corp.) and following the manufacturer's recommendations. The child's age, sex, and height were entered manually. Children stood barefoot on the appliance while holding the handles for approximately 30 s. We used predicted values of fat mass (kg) and percentage of fat mass calculated by the device using impedance, weight, height, and age with standard calibrated equations based on data from dual-energy X-ray absorptiometry [41].

Metabolic indicators

A nursing team collected the blood samples from the children after 8 to 12 h of fasting. We used the serum triglycerides, total cholesterol, high-density cholesterol (HDL-c), and low-density cholesterol (LDL-c) levels as lipid profile variables. For the glycemic profile, we used fasting glucose, insulin, and the HOMA-IR (acronym in English for homeostatic model to assess insulin resistance). Triglycerides, total cholesterol, and HDL-c were measured using enzymatic colorimetric assays. LDL-c was calculated using the Friedewald formula [42]. All lipid profile markers were expressed in mg/dl. Glycemia was measured by the enzymatic colorimetric method and expressed in mg/dL, and insulin by electrochemiluminescent immunoassay and expressed in μU/ml. HOMA-IR was calculated as insulin (μU/ml) × glucose (mmol/l) /22.5. All metabolic outcomes were considered continuous variables in the analysis.

Covariables in the association models

Directed acyclic graphs (DAGs) were used to represent the structures of the causal networks that link exposure (consumption of UPF) and the outcomes of interest (adiposity and metabolic profile) and support the identification of confounding variables in the associations studied [43]. Given that we have two primary groups of outcomes (adiposity and metabolic indicators), we constructed two separate DAGs using the online application DAGitty (Fig. 1) [44].

Considering the DAGs, to estimate the total effect of the consumption of ultra-processed foods at 4 years on adiposity and metabolic responses at 6 years of age, the minimally sufficient adjustment set of variables included socioeconomic status (SES), maternal BMI and age, sex, age, and children's television time (displayed in white in Fig. 1).

To approximate SES, we considered in the models mother's educational level, categorized as "low" (less than high school), "medium" (at least high school), or "high" (more than high school), and whether they worked outside the home ("yes" or "no"), considering that in Chile the unemployment rate is higher in poor than in non-poor [45] and women with higher educational levels more often work outside the home [46]. We also included other maternal variables such as maternal age (self-reported) and BMI (calculated using maternal weight and height measurements collected by trained dietitians).

Among the variables for the children, we considered sex (male or female), age (in months), and television time. To estimate the total hours children spent watching television on weekdays, we summed the time spent watching TV before and after school and in the evening based on information provided by the mothers.

Full completeness was obtained for all covariates except maternal BMI, for which data for 4.2% of the total sample were missing. All covariables included in the models were measured at baseline.

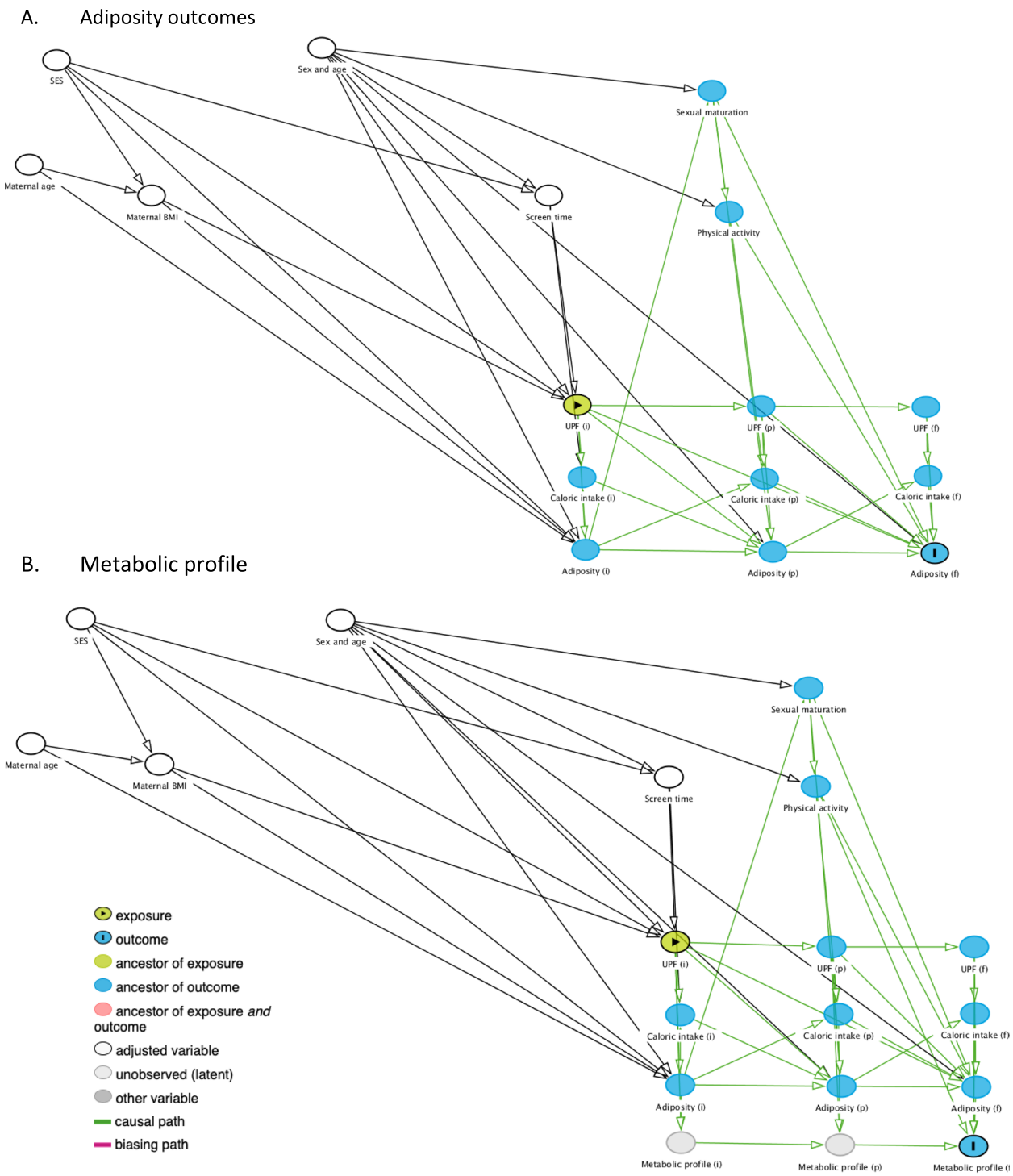

Fig. 1 Conceptual framework for the relationship between UPF consumption at 4 years and adiposity (**A**) and metabolic indicators (**B**) at 6 years. Notes: UPF – ultra-processed foods, SES – socioeconomic status, BMI – body mass index, (i) – initial values at 4 years, (p) – other values during the study period, (f) – final values at 6 years

Statistical analysis

Descriptive analyses were presented using mean and SD for quantitative variables and absolute and relative frequency for qualitative variables.

All participants whose dietary reports did not fulfill the above exclusion criteria and who provided data for at least one or more health outcomes were included in the association models. The proportion of loss to follow-up was 23.7% for anthropometric indicators, 33.5% for body composition, and 39.9% for metabolic indicators. We compared the characteristics of participants included and lost in the analysis by presenting the percentual difference between them and applying a *T*-test for quantitative and chi-square for qualitative variables, and differential loss related to maternal educational level was identified. Given the loss to follow-up and to address the potential selection bias, we incorporated the stabilized inverse probability of censuring weights (SW) in all models. This method creates a pseudo-population with characteristics comparable to the initial population to simulate random censuring of covariates of interest [47]. We calculated different SW for anthropometric, body composition, and metabolic indicators since the number of participants in each analysis differed. The calculation of SW uses as a numerator the probability of censuring (i.e., proportion of participants lost in the follow-up) and as a denominator the probability of censuring based on the covariables included in the model [47, 48]. The probability of censorship was obtained with logistic regression with loss of follow-up as the response variable (yes or no), and the covariates included were sex, age, and initial BMI *z*-score of the child, and maternal age, BMI, work outside the home, and educational level of the mother. Using SW results in the same estimate as unstabilized inverse probability weights, but typically in narrower 95% confidence intervals and increased statistical efficiency [47, 48]. SW were included in all regression analysis using the option pweight.

We used linear regression models to investigate the associations between the consumption of UPF at 4 years (in 100 cal and grams), adiposity, and metabolic indicators at 6 years. We reported regression coefficients and 95% confidence intervals (95% CI) for crude and adjusted models.

The model 1 was adjusted for covariables presented in the DAG: socioeconomic status (represented by maternal education and work outside the home), maternal BMI and age, and sex, age, and television time of children. The model 2 was adjusted for the same covariables plus caloric intake. The coefficient is then interpreted as the effect of substituting 1 unit of UPF with 1 unit of non-UPF, maintaining a constant caloric intake [49, 50].

Given the low prevalence of missing data in the covariates (less than 5% and in only one variable), we assumed that missing data were completely at random and performed regressions with complete case analysis [51]. The goodness-of-fit of the models was evaluated via graphical analysis of the residuals and inflation factors of variance. The distribution of residues was not random for insulin, HOMA-IR, triglycerides, fat mass, and fat mass percentage, so the final models included the log-transformed version of these variables. As sensibility analysis, we considered models without SW and models with quartiles of UPF as the exposure variable. All analyses were conducted using Stata v18.0 (College Station, TX).

Results

The baseline characteristics of all FECHIC children and sub-samples with anthropometric, body composition, and metabolic indicators are presented in Table 1. The characteristics of the children included in each evaluation were similar to those of the reference cohort. At the start of the FECHIC cohort study, the children had an average age of 4.9 ± 0.5 years old, were comparable by sex (51.9% girls), and had a mean BMI *z*-score of 1. The mothers were 31.4 ± 6.7 years old, and most had a medium education level (55.1%). Children lost in the follow-up presented differences primarily related to their mothers' educational level; more children from mothers of low education level were lost for anthropometric indicators ($p = 0.003$) and body composition ($p < 0.001$), and more children from mothers of high education level were lost for metabolic outcomes ($p < 0.001$).

Estimated usual consumption of UPF

Table 2 shows the estimated usual consumption of each NOVA food group at baseline (4 years of age). Children consumed approximately 48% of their diet by calories from UPF and 39% of their diet by grams from UPF. Among the NOVA groups, UPF contributed the highest percentage of children's calories, while MPF contributed the highest percentage of grams to children's diet (57.0%).

Adiposity and metabolic outcomes

A description of the outcomes included in the study is available in Table 3. After 2 years of follow-up, the mean BMI *z*-score was 1.1 ± 1.3, and the mean fat mass percentage was 24.2 ± 5.3%. The mean fasting blood glucose was 81.8 mg/dL.

Associations between consumption of UPF and adiposity and metabolic indicators

Tables 4 and 5 present the associations between the usual consumption of UPF at 4 years and adiposity and metabolic indicators at 6 years, considering the three types

Table 1 Baseline description of the reference cohort and the participants evaluated and lost for each outcome. FECHIC, 2016

Variables	Reference ($n=962$)	Anthropometric indicators				Body composition				Metabolic indicators			
		Included ($n=734$)	Lost ($n=228$)	Diff. in %	*p*-value	Included ($n=639$)	Lost ($n=323$)	Diff. in %	*p*-value	Included ($n=578$)	Lost ($n=384$)	Diff. in %	*p*-value
Child characteristics													
Sex, *n* (%)					0.792				0.728				0.642
Male	463 (48.1)	355 (48.4)	108 (47.4)	−2.1		305 (47.7)	158 (48.9)	2.5		282 (48.8)	181 (47.1)	−3.5	
Female	499 (51.9)	379 (51.6)	120 (52.6)	1.9		334 (52.3)	165 (51.1)	−2.3		296 (51.2)	203 (52.9)	3.3	
Age in years, mean (SD)	4.9 (0.5)	4.9 (0.5)	4.8 (0.5)	−2.1	0.148	4.9 (0.5)	4.8 (0.5)	−2.0	0.082	4.9 (0.5)	4.8 (0.5)	−2.0	0.213
BMI *z*-score, mean (SD)	1.0 (1.2)	1.0 (1.2)	1.1 (1.2)	9.1	0.163	1.0 (1.2)	1.1 (1.2)	10.0	0.217	1.0 (1.2)	1.1 (1.2)	10.0	0.469
Weight status, *n* (%)					0.444				0.463				0.715
Normal weight	509 (52.9)	396 (53.9)	113 (49.6)	−8.0		344 (53.8)	165 (51.1)	−5.0		308 (53.2)	201 (52.3)	−1.7	
Over-weight	277 (28.8)	209 (28.5)	68 (29.8)	4.6		185 (29.0)	92 (28.5)	−1.7		169 (29.2)	108 (28.1)	−3.8	
Obesity	176 (18.3)	129 (17.6)	47 (20.6)	17.0		110 (17.2)	66 (20.4)	18.6		101 (17.5)	75 (19.6)	12.0	
Maternal characteristics													
Age in years, mean (SD)	31.4 (6.7)	31.6 (6.7)	30.5 (6.6)	−3.6	0.024	31.7 (6.7)	30.8 (6.5)	−2.8	0.057	31.6 (6.6)	31.0 (6.8)	−1.9	0.225
BMI, mean (SD)	28.8 (5.5)	28.7 (5.6)	29.0 (5.1)	1.0	0.549	28.7 (5.6)	28.8 (5.3)	0.3	0.871	28.7(5.6)	28.8 (5.3)	0.3	0.823
Work out-side of home, *n* (%)	483 (50.2)	362 (49.3)	117 (51.3)	4.1	0.598	315 (49.3)	164 (50.8)	3.0	0.665	275 (47.6)	204 (53.1)	11.6	0.092
Education level, *n* (%)					0.003				< 0.001				< 0.001
Low	173 (18.0)	118 (16.1)	55 (24.1)	49.7		100 (15.6)	73 (22.6)	44.9		96 (16.6)	77 (20.1)	21.1	
Medium	530 (55.1)	425 (57.9)	105 (46.1)	−20.4		380 (59.5)	150 (46.4)	−22.0		352 (60.9)	178 (46.3)	−24.0	
High	259 (26.9)	191 (26.0)	68 (29.8)	14.6		159 (24.9)	100 (31.0)	24.5		130 (22.5)	129 (33.6)	49.3	

Notes: *BMI* Body mass index

Children nutritional status was evaluated with WHO cutoffs for BMI for sex and age (BMI > 1 SD defined as overweight and BMI > 2 SD, as obesity) [40]. Maternal education level was categorized as low: less than high school, medium: at least high school, and high: completed superior education. Maternal BMI was missing for 4.2% of the total sample. *P*-value for *T*-test is shown for age and BMI of children and mothers; and *p*-value for chi-square is showed for sex, weight status, work outside of home, and education level

Table 2 Estimated usual dietary consumption at 4 y according to NOVA food system classification ($n=893$). FECHIC, 2016

NOVA	Consumption in calories			Consumption in grams		
	Mean (SD)	Min–Max	%	Mean (SD)	Min–Max	%
Group 1. MPF	424.5 (122.9)	126.9–941.2	34.9	791.4 (250.1)	269.5–2002.7	57.0
Group 2. PCI	103.4 (24.8)	55.0–207.0	8.5	14.5 (4.0)	7.4–30.6	1.0
Group 3. PF	169.0 (43.6)	74.3–351.8	13.9	65.1 (21.5)	23.0–142.6	4.7
Group 4. UPF	577.2 (133.2)	263.3–972.6	47.5	539.0 (109.4)	261.3–933.9	38.8
Total	1214.5 (66.9)	1008.3–1407.4	100.0[a]	1397.5 (159.1)	950.6–2040.3	100.0[a]

Notes: *MPF* Minimally processed foods, *PCI* Processed culinary ingredients, *PF* Processed foods, *UPF* Ultra-processed foods, *SD* Standard deviation, *Min* Minimal value, *Max* Maximal value

[a] The usual consumption was estimated using the MSM for each food group and total diet; then, the sum of calories and grams for food groups is close but not identical to the estimated values for total calories and total grams of diet

Table 3 Description of anthropometric, body composition, and metabolic indicators at 6 years. FECHIC, 2018

Outcomes	Mean	SD
Anthropometric indicators ($n=734$)		
BMI *z*-score	1.1	1.3
WC, cm	59.5	5.3
Body composition ($n=690$)		
Fat mass, kg	6.4	2.8
Fat mass, %	24.2	5.3
Metabolic indicators ($n=578$)		
Blood glucose, mg/dl	81.1	8.1
Insulinemia, µU/ml	7.5	3.5
HOMA-IR	1.5	0.7
Total cholesterol, mg/dl	164.3	26.0
HDL cholesterol, mg/dl	46.4	10.8
LDL cholesterol, mg/dl	99.4	21.5
Triglycerides, mg/dl	92.6	37.6

Notes: *BMI* Body mass index, *WC* walst circumference, *HOMA-IR* Homeostasis model assessment of insulin resistance, *LDL* Low-density lipoprotein, *HDL* High-density lipoprotein

of models (crude, adjusted for covariables, adjusted for covariables plus total caloric intake). We did not find an association between UPF and adiposity in crude and covariable adjustment models. However, when UPF was adjusted for covariables plus total caloric intake, we observed a positive association of small magnitude with BMI *z*-score (respectively for 100 kcal and 100 g of UPF: $b=0.24$ [95% CI 0.16–0.33]; $b=0.21$ [95% CI 0.10–0.31]), WC ($b=0.89$ [95% CI 0.41–1.37]; $b=0.86$ [95% CI 0.32–1.40]), log-fat mass ($b=0.06$ [95% CI 0.03–0.09]; $b=0.04$ [95% CI 0.01–0.07]), and log-percentage fat mass ($b=0.03$ [95% CI 0.01–0.04]; $b=0.02$ [95% CI 0.003–0.04]). For metabolic outcomes, the coefficients of UPF and their 95% CI for both 100 cal and 100 g were close to null values for all models.

Sensitivity analysis

The results obtained in models without SW (Additional file 1: Tables S1 and S2) and in models with the consumption of UPF in quartiles (Additional file 1: Tables S3 and S4) were consistent with those obtained in main analysis.

Discussion

In this study, we found a high consumption of UPF in terms of calories and grams in a sample of low- and middle-income preschoolers from Santiago, Chile. We also found a positive association between the consumption of UPF at the age of 4 years and several markers of adiposity measured at 6 years old. However, we did not find an association between UPF consumption and metabolic indicators after 2 years of follow-up.

We remark that we found associations only in models that included a total caloric intake adjustment. In nutritional epidemiology, an energy adjustment is used to study the consumption of nutrients or foods in terms of total energy. The underlying reason is that interventions at the individual or population level usually aim to modify the consumption of certain nutrients or foods, with changes in the composition of the diet, but not in the overall amount of food consumed. The energy adjustment also controls for the confounding effect resulting from the association between total energy intake with physical activity, differences in body size, and metabolic efficiency [49, 50]. On this basis, we consider the estimates that include the energy adjustment as the more reliable in our study. Analysis that takes into account the total calories by using the caloric share of UPF is the most prevalent in studies focused on investigating UPF and health outcomes [52]. The fact our results showed associations between UPF and adiposity markers only when adjusting for total calories provides further support to suggest that the relative contribution of UPF in the diet is more important than their absolute amount, and the health

Table 4 Associations between the consumption of ultra-processed foods (in calories and grams) at 4 years, anthropometric indicators ($n=762$), and body composition at 6 years ($n=690$). FECHIC, 2018

Adiposity outcomes	Per 100 cal of UPF			Per 100 g of UPF		
	β	95% CI		*β*	95% CI	
Anthropometric indicators						
BMI *z*-score						
Model 0 – Crude	−0.02	−0.09	0.05	0.07	−0.03	0.16
Model 1 – Covariables	−0.01	−0.09	0.06	0.03	−0.07	0.12
Model 2 – Covariables + caloric intake	0.24	0.16	0.33	0.21	0.10	0.31
WC, cm						
Model 0 – Crude	−0.43	−0.84	−0.03	−0.03	−0.54	0.48
Model 1 – Covariables	−0.35	−0.75	0.06	−0.08	−0.59	0.43
Model 2 – Covariables + caloric intake	0.89	0.41	1.37	0.86	0.32	1.40
Body composition						
Fat mass (log −), kg						
Model 0 – Crude	−0.02	−0.04	0.01	−0.02	−0.05	0.01
Model 1 – Covariables	−0.01	−0.03	0.01	−0.01	−0.03	0.02
Model 2 – Covariables + caloric intake	0.06	0.03	0.09	0.04	0.01	0.07
Fat mass (log −), %						
Model 0 – Crude	−0.01	−0.03	−0.001	−0.02	−0.03	−0.0005
Model 1 – Covariables	−0.01	−0.03	0.01	−0.005	−0.02	0.01
Model 2 – Covariables + caloric intake	0.03	0.01	0.04	0.02	0.003	0.04

Notes: *UPF* Ultra-processed foods, *BMI* Body mass index, *WC* Waist circumference. Stabilized inverse probability weights were included in all models. Model 1: adjusted for children´s sex, age, and screen time, and mothers' BMI, age, educational level, and work outside home status. Model 2: adjusted for all covariates from model 1 plus usual total caloric intake

effects observed are a consequence of a displacement of traditional dietary patterns [53].

In the present study, we found that almost half of the calories of preschool children were derived from UPF, in line with the findings of previous studies with similar populations [14, 15]. We also found that consumption of UPF during preschool years was positively associated with increases in BMI *z*-score and WC after 2 years of follow-up. Similarly, a study with 307 children of low socioeconomic status from Brazil found that the consumption of UPF in 4 year-old children predicted a higher increase in WC at 8 years old [14]. On the other hand, our findings do not align with the results of a previous study conducted on 7-year-old children from Portugal. In Portuguese children, there was no association between UPF and BMI *z*-score and WC *z*-score after 3 years of follow-up [54]. One potential explanation for the discrepancy in results is the difference in the amount of UPF consumed between both populations. Chilean children consumed more UPF than did Portuguese children. The percentage of grams and calories from UPF in the diet of Chilean children was 39 and 48%, while in Portuguese children, UPF represented 25 and 31% of the total grams and calories consumed, respectively. Another potential explanation is the age difference of the participants between studies. Our study followed children from 4 to 6 years, when they were starting the adipose rebound [55], while the study from Portugal followed children between 7 and 10 years old. Age and duration of follow-up could be a relevant factor. For example, a prior study from the Avon Longitudinal Study of Parents and Children that assessed longitudinal associations between UPF and adiposity trajectories from 7 to 24 years old showed that differences in BMI and fat mass by UPF consumption become more accentuated starting adolescence, another critical period for development [56].

Regarding metabolic indicators, we did not find an association with any included indicator. A recent review assessing the effect of UPF on metabolic syndrome components in children and adolescents based on nine cohort studies found mixed results. Some longitudinal studies have reported a positive association between UPF and blood lipids, but not with blood glucose; it is important to highlight that only a few prospective studies on metabolic outcomes in children are available in the literature to date [57]. Our results suggest that adiposity indicators could be altered before we observe metabolic marker alterations. However, metabolic alterations associated with adiposity during childhood are an increasingly common problem. A study with more than 26,000

Table 5 Association between the consumption of ultra-processed foods (in calories and grams) at 4 years and metabolic indicators at 6 years ($n=628$). FECHIC, 2018

Metabolic indicators	Per 100 cal of UPF			Per 100 g of UPF		
	β	95% CI		*β*	95% CI	
Blood glucose, mg/dl						
Model 0 – Crude	−0.30	−0.83	0.22	0.25	−0.37	0.87
Model 1 – Covariables	−0.34	−0.86	0.17	0.08	-0.57	0.72
Model 2 – Covariables + caloric intake	−0.28	−0.91	0.35	0.27	−0.43	0.97
Insulinemia (log −), µU/ml						
Model 0 – Crude	−0.02	−0.04	0.01	0.02	−0.01	0.06
Model 1 – Covariables	−0.02	−0.05	0.01	−0.01	−0.04	0.03
Model 2 – Covariables + caloric intake	0.01	−0.02	0.05	0.02	−0.01	0.06
HOMA-IR (log −)						
Model 0 – Crude	−0.02	−0.05	0.004	−0.01	−0.04	0.02
Model 1 – Covariables	−0.02	−0.05	0.005	−0.004	−0.04	0.03
Model 2 – Covariables + caloric intake	0.01	−0.02	0.05	0.03	−0.01	0.06
Total cholesterol, mg/dl						
Model 0 – Crude	−0.25	−1.88	1.37	−0.10	−2.13	1.93
Model 1 – Covariables	−0.23	−1.88	1.43	0.04	−2.06	2.15
Model 2 – Covariables + caloric intake	0.22	−1.90	2.35	0.44	−1.89	2.76
LDL cholesterol, mg/dl						
Model 0 – Crude	0.62	−0.04	1.27	0.70	−0.12	1.53
Model 1 – Covariables	0.52	−0.16	1.20	0.65	−0.25	1.55
Model 2 – Covariables + caloric intake	0.10	−0.80	1.01	0.31	−0.70	1.33
HDL cholesterol, mg/dl						
Model 0 – Crude	−0.48	−1.79	0.83	−0.46	−2.10	1.18
Model 1 – Covariables	−0.41	−1.75	0.93	−0.57	−2.31	1.17
Model 2 – Covariables + caloric intake	0.18	−1.51	1.87	−0.15	−2.03	1.74
Triglycerides (log −), mg/dl						
Model 0 – Crude	−0.01	−0.04	0.01	−0.01	−0.04	0.02
Model 1 – Covariables	−0.01	−0.03	0.01	0.001	−0.03	0.03
Model 2 – Covariables + caloric intake	0.002	−0.03	0.03	0.02	−0.01	0.04

Notes: *HOMA-IR* Homeostasis model assessment of insulin resistance, *LDL* Low-density lipoprotein, *HDL* High-density lipoprotein. Stabilized inverse probability weights were included in all models. Model 1: adjusted for children´s sex, age, and screen time, and mothers' BMI, age, educational level, and work out of home status. Model 2: adjusted for all covariates from model 1 plus usual total caloric intake

children with obesity (average: 12.6 ± 2.9 years) from European countries found metabolic alterations in more than half of the participants, the most prevalent being high blood pressure (34%), dyslipidemias (32%), and less common alterations in glucose metabolism (3.3%) [58]. Similar results were also described in Mexico [59]. The results of these studies could indicate that alterations in blood pressure and lipid metabolism occur early in children with obesity. It is proposed that, with respect to glucose parameters, alterations may occur in the late stage of the development of metabolic alterations [60, 61]. There is also evidence of the role of diet in metabolic risk from an early age. In a population-based cohort analyzing diet trajectories from ages 2–3 to 11–12 years, individuals who consistently adhered to an "unhealthy" diet trajectory showed compromised cardiovascular function and poorer metabolic health when compared to children consistently following a "healthy" diet, again suggesting that adolescence would be a critical period for observing the emergence of metabolic traits [62].

Various UPF characteristics have been examined to explain their detrimental impact on health. The most explored explanation revolves around the inadequate nutritional profile of UPF, characterized by a higher density of added sugars and saturated fats, and a lower density of vitamins and minerals compared to non-ultra-processed foods [16]. However, the nutritional imbalance in UPF seems incapable of fully explaining the observed effects. Findings from different studies have shown that the association between consumption of UPF and health

outcomes persists even after adjusting for the nutritional profile of the diet [63, 64]. UPF manufacturing often involves processed and refined ingredients that lack the natural food matrix, leading to reduced satiety and heightened glycemic response [65]. Additionally, UPF tend to have a higher energy density due to their ingredients and low water content, making them easy to consume rapidly in terms of volume and calories, facilitating excessive intake [66, 67]. Furthermore, UPF typically exhibit a lower protein density, and it has been hypothesized that this lower protein content could lead individuals to overconsume other foods and, consequently, excess energy [68]. Another hypothesis considered to explain these associations beyond the nutritional profile is that the widespread consumption of UPF may result in increased intake of substances that are rare or absent in nature, such as food additives [69].

The consumption of UPF by children is a matter of concern. We know that children are the main consumers of these products in several countries, with the percentage of consumption higher than that observed in adults [70]. In fact, media marketing that encourages increased consumption of UPF targets children, given their high vulnerability. Additionally, eating habits built during childhood tend to persist throughout life [71]; therefore, becoming accustomed to consuming high levels of sugars, sodium, and fats is worrisome. Moreover, children have a lower body size; thus, they have a higher risk of exposure to critical levels of substances found in UPF. Thus, several countries, mostly in the Latin-American region, have adopted food-based guidelines with messages advising against the consumption of UPF [72–75]. In Brazil, dietary guidelines for children under 2 years of age explicitly recommend offering MPF and avoiding UPF [76]. Additionally, in Brazil, the legislation of the school feeding program prohibits the provision of UPF for children under 3 years of age and mandates that at least 75% of resources be allocated to the acquisition of MPF [77]. While not explicitly incorporating the concept of UPF into its regulations, Chile has one of the most comprehensive frameworks to protect children from packaged foods and beverages high in nutrients of concern, such as sugar, salt, and saturated fats (mostly UPF). The Chilean Food-Labeling and Advertising Law implemented in 2016 (after our dietary data collection) mandates the inclusion of warning labels "high in" on the front of the package, restricts the marketing of regulated foods to children under 14 years of age, and prohibits selling or offering of these foods in schools [78]. These measures should be reinforced and globally promoted to create environments in which children have restricted or no access to UPF given the risks associated with their consumption.

Our study has several strengths, including its longitudinal design, detailed dietary information that includes specific brand names of packaged foods, objective measurements of adiposity and metabolic profiles, and the estimation of usual consumption of UPF employing statistical methods to account for within-person variability in food consumption. However, some limitations should also be considered for interpreting our results. In observational studies, there is an inherent measurement error in the dietary data, which refers to the difference between the reported dietary intake and the true usual dietary intake. However, we attempted to select only plausible reports by excluding diets very far from the estimated considered children's sex and age, and we also excluded diets with extreme values of UPF (< p1 and > p99). We also gathered dietary information using the standardized 24-h dietary recall technique, deemed the method with the least misreporting in children [79], and included children in the interviews which could reduce errors due to lack of awareness of parents regarding children's dietary consumption. Additionally, we applied a statistical method to estimate the usual consumption of UPF; however, our estimate could not represent the usual consumption over the entire follow-up period. Still, dietary recalls can be subjected to social desirability bias, which may lead to the underestimation of UPF and bias in the associations toward the null. The proportion of loss on the follow-up was significant, especially for metabolic indicators, and we found differential losses related to mothers' education. However, maternal education was not associated with outcomes, except glycemia (data not shown), so the estimates should not be importantly modified with the observed differential loss to follow-up; besides, we applied inverse probability of censoring weights to adjust all analyses to make more correct inferences considering the characteristics of our initial sample. Although we controlled for potential confounders, we cannot rule out unmeasured or residual confounding as this was an observational study. Finally, the findings might lack broad generalizability because our sample consisted of preschoolers attending public schools in Santiago's low- to middle-income region.

Conclusions

We observed that a higher consumption of UPF was associated with adiposity indicators in this sample of Chilean preschoolers. Our results suggest the need for a longer exposure time for metabolic effects to emerge, so strategies to prevent the consumption of UPF aimed at schoolchildren could still improve these trajectories. Therefore, policies promoting food environments that facilitate the consumption of minimally processed

foods and make it difficult for children to access UPF should be encouraged.

Abbreviations

24HR	24-H Diet Recall
BMI	Body mass index
CIAPEC	Center of Research in Food Environment and Prevention of Obesity and Non-Communicable Diseases
CV	Coefficient of variation
DAG	Directed acyclic graph
DRI	Dietary Reference Intake
FECHIC	Food and Environment Chilean Cohort
HDL-c	High-density cholesterol
HOMA-IR	Homeostatic Model to Assess Insulin Resistance
INTA	Institute of Nutrition and Food Technology
LDL-c	Low-density cholesterol
MPF	Minimally processed foods
MSM	Multiple Source Method
pER	Predicted energy requirement
PCI	Processed culinary ingredients
PF	Processed foods
rEI	Reported energy intake
SES	Socioeconomic status
SW	Stabilized inverse probability of censuring weights
UPF	Ultra-processed food
USDA	United States Department of Agriculture
WC	Waist circumference
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-024-03556-z.

Additional file 1: Tables S1-S4. Table S1 – Associations between the consumption of UPF at 4 y, anthropometric indicators, and body composition at 6 y without considering SW. Table S2 – Associations between the consumption of UPF at 4 y and metabolic indicators at 6 y without considering SW. Table S3 – Associations between quartiles of consumption of UPF at 4 y, anthropometric indicators and body composition at 6 y. Table S4 – Associations between quartiles of consumption of UPF at 4 y and metabolic indicators at 6 y

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Authors' contributions
Conceptualization: CZ and CC. Methodology: CZ and CC. Investigation: CZ. Funding acquisition: LST, MR and CC. Supervision: CC. Writing—original draft: CZ. Writing—review and editing: CZ, NR, LST, MR, and CC. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The original study was approved by the ethics committee of the Institute of Nutrition and Food Technology (INTA), University of Chile (Nº 7–2016, Nº 19–2017). All mothers signed an informed consent form on behalf of their children. The ethics committee of the Faculty of Medicine, University of Chile, also approved the current analyses (Nº 159–2021).

Consent for publication
All authors approve the publication of the final manuscript.

Competing interests
The authors declare that they have no competing interests. CC is a Guest Editor in BMC Medicine, for the article collection "Food Environments and Health".

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