



Ultra-processed food intake is associated with children and adolescents with congenital heart disease clustered by high cardiovascular risk factors

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Abstract

The excessive intake of ultra-processed foods (UPF) is associated with an increase in cardiovascular risk. However, the effect of UPF intake on cardiovascular health in children and adolescents with congenital heart disease (CHD) is unknown. The aim of the present study was to describe UPF intake and evaluate associations with isolated cardiovascular risk factors and children and adolescents with CHD clustered by cardiovascular risk factors. A cross-sectional study was conducted involving 232 children and adolescents with CHD. Dietary intake was assessed using three 24-hour recalls. UPF were categorised using the NOVA classification. The cardiovascular risk factors evaluated were central adiposity, elevated high-sensitivity C-reactive protein (hs-CRP) and subclinical atherosclerosis. The clustering of cardiovascular risk factors (waist circumference, hs-CRP and carotid intima-media thickness) was performed, allocating the participants to two groups (high *v.* low cardiovascular risk). UPF contributed 40.69% (SD 6.21) to total energy intake. The main UPF groups were ready-to-eat and take-away/fast foods (22.2% energy from UPF). The multivariable logistic regression revealed that an absolute increase of 10% in UPF intake (OR = 1.90; 95% CI: 1.01;3.58) was associated with central adiposity. An absolute increase of 10% in UPF intake (OR = 3.77; 95% CI: 1.80, 7.87) was also associated with children and adolescents with CHD clustered by high cardiovascular risk after adjusting for confounding factors. Our findings demonstrate that UPF intake should be considered as a modifiable risk factor for obesity and its cardiovascular consequences in children and adolescents with CHD.

Keywords: Ultra-processed food: Obesity: CVD risk factors: Atherosclerosis: Cluster analysis: Congenital heart disease

Ultra-processed foods (UPF) are industrially produced ready-to-eat foods and beverages that generally have high fat and sugar content as well as low micronutrient content⁽¹⁾. Children can often have high UPF intake, accounting for more than 40% of the energy contribution of the diet⁽²⁾. Nearly 70% of schoolchildren consume at least one UPF product per day⁽³⁾. Previous studies have demonstrated that UPF intake is associated with low diet quality^(4,5) and unfavourable health outcomes, such as obesity^(6,7) and dyslipidaemia⁽⁸⁾ in children. UPF intake is also associated with a greater risk of mortality due to CVD in adults^(9,10).

Although CVD usually only appears in adulthood, the early identification of risk factors in childhood can assist in the establishment of measures for reducing cardiovascular mortality later in life⁽¹¹⁾. This is crucial for individuals with congenital heart

disease (CHD), who are at high risk of mortality in adulthood due to CVD⁽¹²⁾. Some studies report that the development of CVD begins in childhood in individuals with CHD who have risk factors, such as obesity^(13,14), inflammation^(13,15) and subclinical atherosclerosis⁽¹⁶⁾. This population also has unique clinical characteristics related to cardiovascular risk, such as an abnormal anatomy, altered haemodynamics, cyanosis, reperfusion injury and inflammation from heart procedures⁽¹⁷⁾.

Children and adolescents with CHD seem to have a diet with a large amount of UPF. One study found that this population has a high intake of added sugars and trans fatty acids⁽¹⁸⁾, which are often present in UPF^(4,5). However, no studies have explored UPF intake and associations with cardio-metabolic risk factors in children and adolescents with CHD. It is also important to analyse the combination of cardiovascular risk factors to enable

Abbreviations: CHD, congenital heart disease; cIMT, carotid intima-media thickness; hs-CRP, high-sensitivity C-reactive protein; UPF, ultra-processed food; WC, waist circumference.

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greater robustness in the identification of groups at high cardiovascular risk, since individuals can have multiple and interrelated cardiovascular risk factors⁽¹⁹⁾.

The hypothesis tested in this study is that UPF intake is associated with increased cardiovascular risk in children and adolescents with CHD. Therefore, the aim of the present study was to describe UPF intake and evaluate associations with isolated cardiovascular risk factors and children and adolescents with CHD clustered by high cardiovascular risk factors. UPF intake was also evaluated stratified by age group.

Methods

Study design and population

The present cross-sectional study is part of the follow-up study on atherosclerosis risk factors in children and adolescents with CHD 'The Floripa CHild (Congenital Heart disease and atherosclerosis in children and adolescents) Study', which was conducted from January to July 2017 involving children and adolescents with CHD who underwent surgery or interventional catheterisation for CHD and were in outpatient care at two referral hospitals in southern Brazil. The sample size was estimated with the aid of the OpenEpi[®] software considering the following criteria: (i) total population of children and adolescents with CHD in two cardiology outpatient care programmes (n 430); (ii) unknown prevalence of children and adolescents with CHD clustered by high cardiovascular risk factors (set at 50% to obtain the largest sample), (iii): type 1 error (α) of 0.05, type 2 error (β) of 0.20, 95% CI; (iv): losses or refusals (10%). Thus, 225 participants were needed for this study.

Children and adolescents between 5 and 18 years of age with CHD who underwent surgery or interventional catheterisation for CHD were included. The exclusion criteria were clinical conditions that interfered with the anthropometric assessment, genetic syndromes and chronic or acute inflammatory condition in the 15 d prior to the assessment. This study received approval from the Human Research Ethics Committee of The Joanna de Gusmão Children's Hospital (certificate number: 1-672-255/2016) and was conducted in accordance with the ethical precepts stipulated in the 1964 Declaration of Helsinki and later amendments. All parents and guardians signed a statement of informed consent before the study was initiated.

Dietary intake

Three non-consecutive 24-h food recalls using the multiple-pass method⁽²⁰⁾ were applied by trained dietitians. The dietitians received theoretical and practical training based on the guidelines of the multiple-pass method⁽²⁰⁾ supervised by a researcher dietitian with experience in the application of the method. Two 24-h recalls were applied on weekdays and one 24-h recall was applied on a weekend day. The 24-h recalls were applied to the individuals who spent more time at home with the children. The children and adolescents also assisted in the process. The first 24-h recall was applied in-person during the data collection and the second and third 24-h recalls were applied over the

telephone (mean time between the first and third 24-h dietary recalls was 7.3 weeks (SD: 3.21)).

Energy and nutrient intakes were estimated using the Nutrition Data System for Research (NDSR) grad pack 2017 (NCC Food and Nutrient Database, University of Minnesota). As the NDSR is North American software, we checked the nutritional equivalences of the foods available in the software based on Brazilian charts^(21–23) and typical Brazilian recipes were entered into the software. Other studies with Brazilians used this software to assess dietary intake^(24–26). Energy and nutrient intakes were adjusted for intra- and interpersonal variability using the Iowa State University method⁽²⁷⁾. Nutrients were adjusted to total energy intake using the residual method⁽²⁸⁾. Details on the assessment of dietary intake can be found in a previous study⁽¹⁸⁾. Intakes of energy (kcal/d and kJ/d), proteins (g/kg/d), carbohydrates (%E), total fat (%E), SFA (%E), MUFA (%E), PUFA (%E), *trans* fatty acids (%E), cholesterol (mg/d), Na (mg/d), total fibre (g/d), added sugars (g/d), Ca (mg/d), Fe (mg/d), P (mg/d), Zn (mg/d), Se (μ g/d), Mg (mg/d), K (mg/d), vitamin A (μ g/d), vitamin C (mg/d) vitamin D (μ g/d) and vitamin B₁₂ (μ g/d) were estimated.

Classification of ultra-processed food

Food and beverages recorded in the three non-consecutive 24-h recalls were categorised using the NOVA classification, which is based on the degree of processing: (1) unprocessed and minimally processed foods; (2) processed culinary ingredients; (3) processed foods and (4) UPF⁽¹⁾. This study focused only on the UPF group. UPF were defined as industrially produced ready-to-eat foods with many ingredients, rich in additives and with low micronutrient content. Examples of UPF are soda drinks, chips, sweet biscuits and breakfast cereals⁽¹⁾. UPF were divided into the following groups: (1) ready-to-eat and take-away/fast foods; (2) instant noodles; (3) chips; (4) sweetening products; (5) sweet biscuits/breakfast cereals; (6) chocolate; (7) industrially packaged breads; (8) soft drinks; (9) margarine; (10) salted crackers; (11) processed meats; (12) infant formula; (13) chocolate powders; (14) sweetened beverages and (15) candy. Details on the ultra-processed groups are described in Supplementary Table 1. Total UPF intake and the intake of the main groups were adjusted for intra- and interpersonal variability using the Iowa State University method⁽²⁷⁾ and total energy intake was adjusted using the residual method⁽²⁸⁾. UPF intake was expressed as the percentual of daily energy intake (%E/d). The dietary sources contributing to daily energy from UPF were also calculated.

Outcomes

The primary outcome of the study was children and adolescents with CHD clustered by high cardiovascular risk factors using two-stage cluster analysis. The purpose of cluster analysis was to group participants based on co-occurring of cardiovascular risk factors considering the characteristics of the sample. The cluster solution was based on interpretability of the cluster. Thus, cluster analysis was performed several times with multiple cardiovascular risk factors (lipid profile, glycaemic profile and anthropometric variables in continuous and/or categorical

variables) and interactions between cluster variables, as performed in previous studies^(18,29). The three most important cardiovascular risk factors in children and adolescents with CHD (waist circumference (WC; percentile), high-sensitivity C-reactive protein (hs-CRP; mg/l) and carotid intima-media thickness (cIMT; mm)) were used as continuous variables in the cluster analysis. Log-likelihood was used to measure distance. The Schwarz Bayesian information criterion was followed. To check the quality of the cluster, the maximum average silhouette (> 0.5) was used, which represents good cohesion and separation between clusters⁽³⁰⁾. Two clusters were identified based on cardiovascular risk factors: (1) children and adolescents with CHD clustered by high cardiovascular risk factors (i.e., highest values for WC, hs-CRP and cIMT) and (2) children and adolescents with CHD clustered by low cardiovascular risk factors (i.e., lowest values for WC, hs-CRP and cIMT). Details on the participants clustered by high cardiovascular risk factors are displayed in Supplementary Table 2.

The secondary outcomes were isolated cardiovascular risk factors (central adiposity, elevated hs-CRP and subclinical atherosclerosis). WC was measured at the iliac crest at the end of normal expiration using a nonelastic tape measure with an accuracy of 1 mm (TBW[®], São Paulo, Brazil) without applying any pressure to the body surface. WC percentiles according to sex and age were calculated⁽³¹⁾. Central adiposity was classified as \geq the 75th percentile according to age and sex⁽³²⁾. High-sensitivity CRP was determined by immunonephelometry (Dimension[®], Siemens). Elevated hs-CRP was considered ≥ 3 mg/l, representing high cardiovascular risk⁽³³⁾. cIMT was evaluated using carotid ultrasound (Toshiba, model Viamo[®], Japan) with a 7.5 MHz linear transducer and a depth of 4 cm and was determined by a paediatric cardiologist following 'The recommendations of the Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force'⁽³⁴⁾. The cIMT measurement was performed on the three clearest of six images collected in arterial diastole using semi-automated arterial edge-detection software (M'Ath[®], Metris SRL) with a digital reading of 100 points and expressed in millimetres (mm). Subclinical atherosclerosis was considered cIMT \geq the third tercile (mean: 0.592 mm (sd: 0.055)).

Covariates

The socio-demographic characteristics of interest were age (in years, categorised as children or adolescents), sex (female or male), household income (\leq the monthly minimum wage or $>$ the monthly minimum wage) and mother's schooling ($<$ 10 years or ≥ 10 years of formal study). The following clinical characteristics related to CHD were also evaluated: CHD (cyanotic or acyanotic), heart procedure (cardiac catheterisation or heart surgery), number of hospitalisations due to infection ($<$ three times or \geq three times) and post-operative time (years). A family history of obesity and early CVD (no or yes) was also investigated. Screen time (use of electronic devices) was categorised as $<$ 2 hours/d or ≥ 2 hours/d⁽³⁵⁾. Physical activity was assessed using Physical Activity Questionnaire for Children and categorised as insufficiently active (one to three points) or active (four to five points)⁽³⁶⁾. Passive smoking was assessed by the following

question posed to the participants: 'Does anyone in your home smoke?' Passive smoking was recorded when the participant answered affirmatively. BMI for age and by percentile were obtained using the WHO Anthro Plus software. Overweight and obesity were classified as \geq the 85th percentile⁽³⁷⁾.

Statistical analysis

The normality of continuous variables was evaluated using the Kolmogorov–Smirnov test, histograms and the CV. Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range. Categorical variables were expressed as absolute and relative frequencies. Either the chi-square or Fisher's exact test was used to examine differences in the clinical characteristics of the participants among terciles of the percentage of UPF in the diet. The sample was divided into two groups: lower intake ($<$ the median of UPF intake) and higher intake (\geq the median of UPF intake). Differences between these groups were investigated using the Student's *t* test. Logistic regression analysis was applied to evaluate the association between UPF intake and isolated cardiovascular risk factors as well as children and adolescents with CHD clustered by high cardiovascular risk factors. The results were expressed as OR and the respective 95% CI. The OR corresponded to an absolute increase of 10% of UPF in the diet. The multiple logistic regression analysis was adjusted for confounding factors, which were determined based on statistical significance in the simple regression analysis ($P < 0.20$) as well as previous studies on cardiovascular risk factors in children and adolescents with CHD. Adjusted Analysis 1 (all outcomes) – the analysis was adjusted for age (years), sex, physical activity (score) and mother's schooling. Adjusted Analysis 2 (central adiposity) – the analysis was further adjusted for type of CHD, post-operative time (years) and family history of CVD. Adjusted Analysis 2 (elevated hs-CRP) – the analysis was further adjusted for family history of CVD, number of hospitalisations due to infection and central adiposity. Adjusted Analysis 2 (subclinical atherosclerosis) – the analysis was further adjusted for family history of CVD, number of hospitalisations due to infection, central adiposity and elevated hs-CRP. Adjusted Analysis 2 (children and adolescents with CHD clustered by high cardiovascular risk factors) – the analysis was further adjusted for family history of CVD and number of hospitalisations due to infection. All analyses were conducted using the Statistical Package for the Social Sciences (SPSS version 23.0, IBM SPSS Inc.). Figures were created using GraphPad Prism version 8 (Graph Pad Software Inc.). An alpha level < 0.05 was considered statistically significant.

Results

Participant's characteristics

A total of 232 participants (52.6% girls) were included in the study (Supplementary Fig. 1). Mean age was 10.02 years (7.09–13.05). Post-operative time was 6.73 years (SD 3.84). Nineteen percent of the participants were overweight or obese based on BMI for age and 24.6% had central obesity based on WC. Table 1 displays the characteristics of the participants.

Table 1. Characteristic of study participants

Characteristics	All participants (n 232)		Children (n 111)		Adolescents (n 121)		P value
	n	%	n	%	n	%	
UPF intake							
Mean	40.69		41.75		39.72		
SD	6.21		6.55		5.74		
Sex							
Female	122	52.6	50	41.0	72	59.0	0.03
Male	110	47.4	61	55.5	49	44.5	
Household income†							
< monthly minimum wage	157	67.7	72	45.9	85	54.1	0.40
≥ monthly minimum wage	75	32.2	39	52.0	36	48.0	
Mother's schooling‡							
< 10 years	99	43.0	34	34.3	65	65.7	< 0.001
≥ 10 years	131	57.0	77	58.8	54	41.2	
Type of CHD							
Cyanotic	79	34.1	40	50.6	39	49.4	0.58
Acyanotic	153	65.9	71	46.4	82	53.6	
Heart procedure							
Cardiac catheterisation	41	17.7	19	46.3	22	53.7	0.87
Heart surgery	191	82.3	92	48.2	99	51.8	
Number of hospitalisations due to infection							
< 3 times	187	80.6	87	46.5	100	53.5	0.51
≥ 3 times	45	19.4	24	53.3	21	46.7	
BMI for age							
Adequate	188	81.0	94	50.0	94	50.0	0.19
Overweight/obesity	44	19.0	17	38.6	27	61.4	
Waist circumference§							
No central obesity	170	73.3	83	48.8	87	51.2	0.54
Central obesity	57	24.6	25	43.9	32	56.1	
Passive smoke							
No	172	75.1	29	50.9	28	49.1	0.65
Yes	57	24.9	80	46.5	92	53.5	
Physical activity¶							
Active	10	4.4	6	60.0	4	40.0	0.53*
Insufficiently active	217	95.6	103	47.5	114	52.5	
Screen time							
< 2 h	109	47.0	49	45.0	60	55.0	0.43
≥ 2 h	123	53.0	62	50.4	61	49.6	
Family history of CVD**							
No	177	77.6	85	48.0	92	52.0	0.75
Yes	51	22.4	23	45.1	28	54.9	
Family history of obesity							
No	147	64.5	73	49.7	74	50.3	0.41
Yes	81	35.5	35	43.2	46	56.8	

* P-value obtained by chi-square or Fisher's exact test.

† Brazilian minimum wage in February 2017 (US\$295.00).

‡ n = 2 participants did not report.

§ n = 5 participants did not evaluate.

|| n = 3 participants did not report.

¶ n = 5 participants did not report.

** n = 4 participants did not report.

Ultra-processed food intake

UPF accounted for a mean of 40.69% (SD 6.21) of total energy intake. The main food groups contributing to UPF intake were ready-to-eat and take-away/fast foods (22.2% of total energy), sweetening products (17.7% of total energy) and sweet biscuits/breakfast cereals (9.8% of total energy) (Fig. 1). Supplementary Table 3 shows the nutrient profile of the diet according to UPF intake. Compared with the lower intake group, higher UPF intake was associated with lower intakes of energy ($P < 0.001$), total fibre ($P < 0.001$) and K ($P = 0.002$) as well as

higher intakes of carbohydrates ($P < 0.001$), total fat ($P < 0.001$), SFA ($P < 0.001$), MUFA ($P < 0.001$), PUFA ($P < 0.001$), trans fatty acids ($P < 0.001$), cholesterol ($P < 0.001$), P ($P = 0.001$), Zn ($P < 0.001$), vitamin A ($P < 0.001$) and vitamin B₁₂ ($P = 0.04$).

Association between ultra-processed food and cardiovascular risk factors

The prevalence of cardiovascular risk factors among the children and adolescents was 24.6% for central adiposity, 12.5% for elevated hs-CRP and 33.2% for subclinical atherosclerosis.

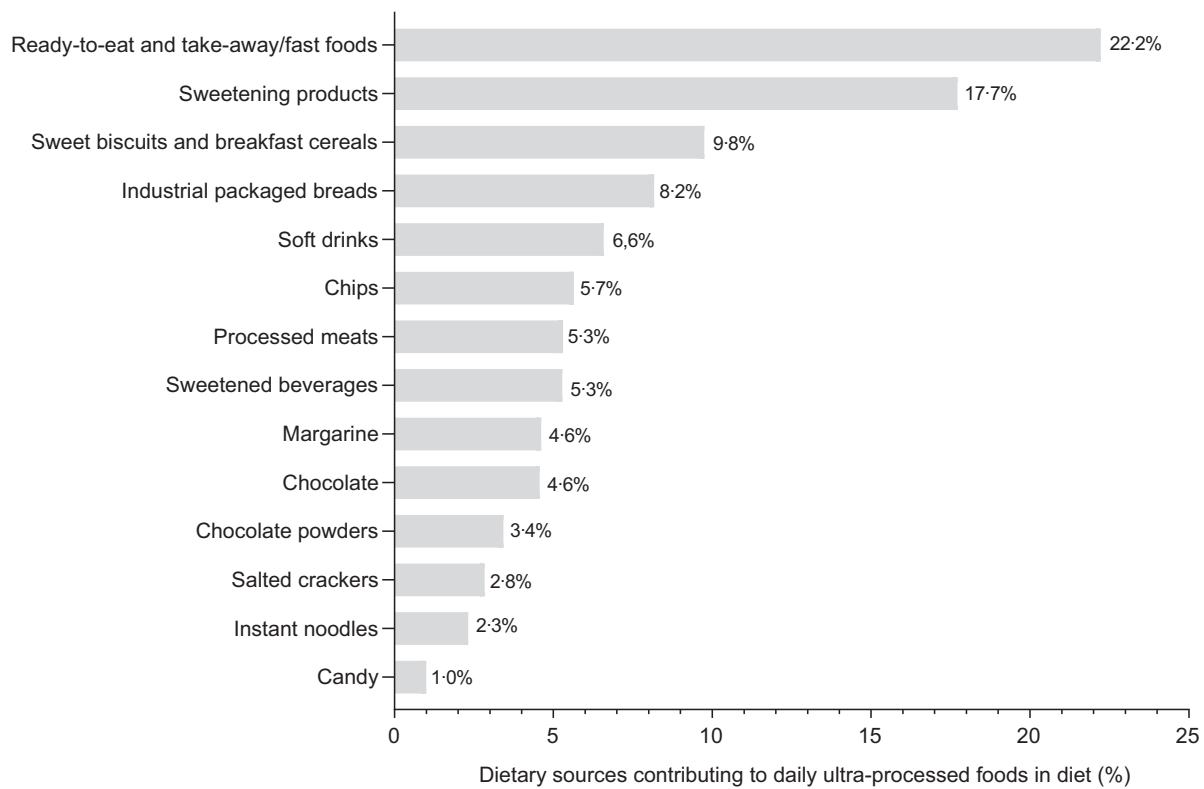


Fig. 1. Dietary sources contributing to daily energy from UPF in diet (%).

Associations between UPF intake and each isolated cardiovascular risk factors are displayed in Table 2. The multivariable logistic regression revealed that an absolute increase of 10 % of UPF in the diet was associated with an increased likelihood of central adiposity (OR = 1.90, 95 % CI: 1.01, 3.58). In the age group analyses, an absolute increase of 10 % of UPF was associated with central adiposity only in adolescents (children: OR = 1.39, 95 % CI: 0.58, 3.33; adolescents: OR = 4.66, 95 % CI: 1.60, 13.55). UPF intake was not associated with the elevated hs-CRP or subclinical atherosclerosis.

Association between ultra-processed food intake and children/adolescents with congenital heart disease clustered by high cardiovascular risk factors

In the cluster analysis, 22.3 % of the children and adolescents with CHD were clustered by high cardiovascular risk factors. The multivariable logistic regression revealed that an absolute increase of 10 % of UPF was associated with children and adolescents with CHD clustered by high cardiovascular risk factors (OR = 3.77, 95 % CI: 1.80, 7.87) (Table 3). In the adjusted multivariable analysis stratified by age group, an absolute increase of 10 % of UPF intake was associated with children clustered by high cardiovascular risk factors (OR = 5.98, 95 % CI: 1.38, 25.83) as well as adolescents clustered by high cardiovascular risk factors (OR = 5.18, 95 % CI: 1.71, 15.68).

Discussion

In the present cross-sectional study involving children and adolescents with CHD, UPF contributed to nearly half of total energy intake and the main UPF group was ready-to-eat and take-away/fast foods. An absolute increase of 10 % of UPF in the diet was associated with an increased likelihood of central adiposity in children and adolescents with CHD clustered by high cardiovascular risk factors. These findings underscore the need for early nutrition interventions focused on the reduction in UPF intake for groups at high cardiovascular risk, such as children and adolescents with CHD, which may be beneficial to cardiovascular health.

UPF accounted for nearly half of the total daily energy intake (40.7 %) of the children and adolescents with CHD. This figure is higher than the 29.6 % reported for Brazilian adolescents and adults⁽³⁸⁾ as well as the 33.2 % and 29.2 % reported for healthy Belgian children and adolescents, respectively⁽³⁹⁾, but similar to the 41.8 % and 47.8 %, respectively, reported for healthy Brazilian preschoolers and schoolchildren with a low socio-economic status⁽²⁾. The high UPF intake in the present study may be related to the fact that most children and adolescents with CHD are from low-income families. The main food groups contributing to UPF intake were ready-to-eat and take-away/fast foods, sweetening products and sweet biscuits/breakfast cereals. Healthy Brazilian adolescents also have high intakes of pizza, hamburgers and sandwiches⁽⁴⁰⁾, which are also defined as

Table 2. Associations between intake of UPF and cardiovascular risk factors

Cardiovascular risk factors	All participants (<i>n</i> 232)			Children (<i>n</i> 111)			Adolescents (<i>n</i> 121)		
	OR	95 % CI	<i>P</i> value	OR	95 % CI	<i>P</i> value	OR	95 % CI	<i>P</i> value
Central adiposity									
No of cases/non-cases	57/227			25/108			32/119		
Unadjusted	2.31	1.42, 3.76	0.001	2.17	1.11, 4.21	0.02	2.82	1.35, 5.90	0.01
Adjusted 1*	2.09	1.15, 3.81	0.02	1.48	0.64, 3.40	0.36	4.53	1.69, 12.16	0.003
Adjusted 2†	1.90	1.01, 3.58	0.04	1.39	0.58, 3.33	0.45	4.66	1.60, 13.55	0.01
Elevated hs-CRP [¶]									
No of cases/non-cases	29/230			11/111			18/119		
Unadjusted	1.28	0.70, 2.32	0.42	2.44	1.06, 5.59	0.04	0.75	0.30, 1.87	0.54
Adjusted 1*	1.82	0.87, 3.84	0.16	1.89	0.67, 5.39	0.23	2.27	0.57, 7.19	0.27
Adjusted 2‡	1.38	0.62, 3.14	0.43	1.74	0.51, 5.93	0.38	1.23	0.31, 4.86	0.76
Elevated cIMT ^{**}									
No of cases/non-cases	77/227			38/107			39/120		
Unadjusted	1.19	0.77, 1.85	0.43	1.19	0.66, 2.18	0.56	1.16	0.60, 2.25	0.66
Adjusted 1*	1.48	0.84, 1.10	0.18	1.59	0.71, 3.58	0.26	1.31	0.52, 3.29	0.57
Adjusted 2§	1.58	0.85, 2.92	0.15	1.50	0.62, 3.64	0.37	1.27	0.44, 3.65	0.66

CI, confidence interval; UPF, ultra-processed food; hs-CRP, high-sensitivity C-reactive protein; cIMT, carotid intima-media thickness.

OR of a 10 % increase in relative intake of ultra-processed in diet (% of total energy intake).

* Adjusted 1 is adjusted for age (years), sex, physical activity (score) and mother's schooling.

† Adjusted 2 for central adiposity = adjusted for age, sex, mother's schooling, physical activity (score), type of CHD, post-operative time (years) and family history for obesity.

‡ Adjusted 2 for elevated hs-CRP = adjusted for age, sex, mother's schooling, physical activity (score), type of CHD, post-operative time (years) and family history for CVD and number of hospitalisations due to infection, central obesity.

§ Adjusted 2 for elevated cIMT = adjusted for age, sex, mother's schooling, physical activity (score), type of CHD, post-operative time (years) and family history for CVD and number of hospitalisations due to infection, hs-CRP, central obesity.

|| Central adiposity: *n* = 5 missing data.

¶ Elevated hs-CRP: *n* = 2 missing data.

** Elevated cIMT: *n* = 5 missing data.

Table 3. Associations between intake of UPF and children and adolescents with CHD clustered by high cardiovascular risk factors

Participants clustered by cardiovascular risk factors‡	All participants (<i>n</i> 232)			Children (<i>n</i> 111)			Adolescents (<i>n</i> 121)		
	OR	95 % CI	<i>P</i> -value	OR	95 % CI	<i>P</i> -value	OR	95 % CI	<i>P</i> -value
No of cases/non-cases	49/220			7/104			42/116		
Unadjusted	1.72	1.05, 2.80	0.03	4.56	1.65, 12.52	0.003	2.02	1.03, 3.86	0.04
Adjusted 1*	3.43	1.63, 7.22	< 0.001	5.07	1.10, 23.40	0.04	5.03	1.62, 15.66	0.01
Adjusted 2†	3.77	1.80, 7.87	< 0.001	5.98	1.38, 25.83	0.02	5.18	1.71, 15.68	0.01

CI, confidence interval; UPF, ultra-processed food; CHD, congenital heart disease.

OR of a 10 % increase in relative intake of ultra-processed in diet (% of total energy intake).

* Adjusted 1 is adjusted for age (years), sex, physical activity (score) and mother's schooling.

† Adjusted 2 for clustering of cardiovascular risk factors = adjusted for age, mother's schooling, physical activity (score), type of CHD, post-operative time (years) and family history for CVD and number of hospitalisations due to infection.

‡ Participants clustered by cardiovascular risk factors: *n* = 12 missing data.

ready-to-eat and take-away/fast foods. Among children from lower income families, however, the UPF that contribute most to the energy of the diet were bread, biscuits and sweets⁽²⁾. Children and adolescents with CHD also have a high frequency of visits to fast food restaurants (approximately 35 % once a month and 13.7 % twice a month)⁽⁴¹⁾, which is in agreement with the main source of UPF found in our study.

The children and adolescents with CHD with higher UPF intake had lower intakes of energy, total fibre and K as well as higher intakes of carbohydrates, total fats, SFA, MUFA, PUFA, *trans* fatty acids, cholesterol, P, Zn, vitamin A and vitamin B₁₂. Several studies have shown that UPF intake is associated with a lower quality of nutrients in the diet, especially low fibre intake and high intakes of saturated fat, sugar and Na in healthy children^(4,5,39) and adolescents⁽⁴²⁾. However, our findings also

showed that participants with high UPF intake had higher intakes of micronutrients, such as P, Zn, vitamin A and vitamin B₁₂. These findings may be explained by the fortification of UPF with vitamins and minerals⁽⁴³⁾. A study on food items advertised by two Brazilian supermarket chains found that UPF have higher contents of fibre, vitamins and proteins compared with unprocessed and minimally processed foods⁽³⁷⁾. However, UPF often make claims on their front-of-pack labels, such as reduced content or absence of saturated fat, reduced energy content, 'light', 'whole grain and fibers', 'free-from' and 'low in lactose', and highlight the presence of ingredients and 'free-from gluten' or 'wheat-free'. Such claims can mislead consumers to unhealthy food choices by giving the impression that UPF are 'rich' in vitamins and minerals⁽⁴⁴⁾. Thus, the association between UPF and nutrient intake should be viewed with caution. An editorial

stated that the nutritional quality of a food product depends on its final composition and not merely on the intensity and complexity of its processing level⁽⁴⁵⁾.

UPF intake was associated with central adiposity in the present study, which is consistent with data from a cross-sectional study involving healthy Brazilian children with a low socio-economic status, which found that a 10% increase in UPF was associated with a 0.7-cm increase in WC⁽²⁾. Likewise, high UPF intake has been associated with obesity indicators in children⁽⁷⁾ and adolescents^(38,46). A prospective birth cohort with 9025 British children found that high UPF intake was associated with increased BMI, fat mass index and WC from 7 to 24 years of age compared with lower UPF intake⁽⁴⁷⁾. A review found that UPF were associated with increased fat mass in healthy children and adolescents⁽⁶⁾. Some points may explain this association, as UPF are commonly easy to prepare or ready to eat, palatable, have large portion sizes (encouraging higher intake) and have a high energy density⁽⁴⁸⁾. Moreover, UPF intake was inversely associated with satiety responsiveness⁽⁴⁹⁾. While the literature offers no studies that evaluated UPF intake in patients with CHD, a previous investigation with the same sample found that intakes of added sugars and trans fatty acids was associated with central obesity in children and adolescents with CHD⁽¹⁸⁾ and these nutrients are commonly found in large amounts in UPF^(4,5). Another point that could help explain the association between UPF intake and central adiposity is overprotective parenting of children and adolescents with CHD. Indeed, a review described that overprotective parenting is associated with obesity in patients with CHD⁽⁵⁰⁾. One form of overprotection is to satisfy children's wishes (e.g., permit the consumption of UPF), which may lead to the development of obesity. It is noteworthy that the association between UPF intake and central adiposity was only significant in adolescents in the present study, which may be explained by the fact that adolescents are exposed to risk factors for obesity for a longer period compared with children.

As atherosclerotic CVD had a multifactorial aetiology⁽⁵¹⁾, the use of a clustering approach to investigate the co-occurrence of several cardiovascular risk factors in children and adolescents⁽⁵²⁻⁵⁴⁾ is a promising method for the early identification of cardiovascular risk and the establishment of preventive measures considering a set of risk factors. Thus, an original aspect of this study was the fact that the participants were clustered by high cardiovascular risk factors considering WC, hs-CRP and cIMT together. Although no previous study has evaluated UPF intake with participants clustered by high cardiovascular risk factors, some studies found that UPF intake was positively associated with dyslipidaemia in children^(8,55), glycaemia in overweight and obese schoolchildren⁽⁵⁶⁾, metabolic syndrome in adolescents⁽⁵⁷⁾ as well as mortality from CVD⁽¹⁰⁾. Moreover, a meta-analysis that reviewed prospective cohort studies on UPF intake and health status in adults found that the highest UPF intake was associated with a 1.29-fold higher risk ratio of cardiovascular risk and a 1.34-fold higher risk ratio of cerebrovascular disease⁽⁵⁸⁾. However, most studies that describe the association between UPF intake and cardiovascular risk were developed using FFQ, which were often

not developed to assess the level of food processing; moreover, processing level classification errors could occur⁽⁴⁵⁾.

The prevention of acquired CVD should begin in childhood⁽¹¹⁾. One modelling approach found that a reduction in UPF intake could improve diet quality⁽⁵⁹⁾ and decrease cardiovascular mortality⁽⁶⁰⁾. Thus, the reduction in UPF intake in childhood could be a simple, effective strategy for the prevention of early CVD in patients with CHD. The present findings underscore the importance of guidelines for patients with CHD patients with recommendations to reduce the intake of UPF along with practical actions/strategies, such as interactive nutritional education, a reminder by paediatric cardiologists regarding the harmful effects of UPF and the involvement of families in reducing UPF intake in children and adolescents with CHD.

The present study has some limitations that should be taken into account. First, the generalisation of these results may be limited by clinical characteristics of the participants. Second, the participants had varied post-operative times (different times of exposure to cardiovascular risk factors), which may influence the results. However, we were careful in using post-operative time as a covariable in the regression analyses. Third, the intake of unhealthy foods, such as UPF, may have been underreported, especially in obese participants. Fourth, the lack of an assessment of maturation stage could be a limitation, as hormones can exert an effect on the outcomes of this study. To minimise the lack of this data, we stratified the analyses according to age group. Fifth, the inherent limitation of methods for evaluating dietary intake in children (information bias regarding food intake reported by parents who do not follow their children's diet). However, we took all methodological care to minimise this bias. Lastly, the cross-sectional design does not enable the determination of cause-and-effect relationships and we worked with secondary data. Thus, the fact that the sample size was calculated based on the aim of a previous study constitutes a limitation of the present investigation.

This study also has strengths that should be noted. Repeated 24-hour dietary recalls using the multiple-pass method were applied and adjusted for the intra- and inter-person variability and energy intake to minimise the occurrence of bias in the evaluation of dietary intake. We analysed participants clustered by high cardiovascular risk factors (WC, hs-CRP and cIMT), providing a more comprehensive view of these factors. The classification of the ultra-processed groups was reviewed by two researchers. Recipes that included UPF were included in the analysis, which led to greater accuracy in the estimates of the contribution of UPF to total energy from the diet.

In conclusion, children and adolescents with CHD had a high UPF intake, especially ready-to-eat and take-away/fast foods, sweetening products and sweet biscuits/breakfast cereals. Our findings also show that UPF intake was associated with children and adolescents with CHD clustered by high cardiovascular risk factors. The present findings underscore the importance of reducing UPF intake, which could contribute to preventing obesity and minimising the occurrence of isolated and combined cardiovascular risk factors in children and adolescents with CHD. Reducing UPF intake could also lead to a reduction in



the occurrence of early mortality from acquired CVD in adulthood.

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The authors declare no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit <https://doi.org/10.1017/S0007114522002240>

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