Received: 24 August 2020 | Revised: 26 October 2020 | Accepted: 13 November 2020

DOI: 10.1111/ijpo.12758

ORIGINAL RESEARCH

Pediatric OBESITY WILEY

A Prudent dietary pattern is inversely associated with liver fat content among multi-ethnic youth

Wei Perng[1,2,3] | Robyn Harte[1] | Brandy M. Ringham[1] | Ana Baylin[3] | Anna Bellatorre[1] | Ann Scherzinger[4] | Michael I. Goran[5] | Dana Dabelea[1,2,6]

[1]Lifecourse Epidemiology of Adiposity and Diabetes (LEAD) Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado

[2]Department of Epidemiology, Colorado School of Public Health, Aurora, Colorado

[3]Department of Nutritional Sciences, University of Michigan School of Public Health, Ann Arbor, Michigan

[4]Department of Radiology, University of Colorado School of Medicine, Aurora, Colorado

[5]Program for Diabetes and Obesity, The Saban Research Institute, Children's Hospital of Los Angeles, Los Angeles, California

[6]Department of Pediatrics, University of Colorado School of Medicine, Aurora, Colorado

Correspondence
Wei Perng, Department of Epidemiology, Colorado School of Public Health, 12474 East 19th Ave, Room 208, Aurora, CO 80045, USA.
Email: wei.perng@cuanschutz.edu

Funding information
National Institute of Diabetes and Digestive and Kidney Diseases, Grant/Award Numbers: KL2-TR002534, R01 DK068001

Summary

Objectives: To identify dietary patterns associated with hepatic fat fraction (HFF), a measure of liver fat content and risk factor for non-alcoholic fatty liver disease, in a prospective study of 397 multi-ethnic youth.

Methods: We obtained information on habitual dietary intake via the Block Kids Food Frequency Questionnaire at age 6 to 15 years ('T1') and 12 to 19 years ('T2'), and measured HFF using magnetic resonance imaging at T2. We derived dietary patterns via principal components analysis and examined associations with ln-transformed HFF using linear regression models that accounted for maternal education, gestational diabetes exposure and smoking habits; and child pubertal status, BMI and physical activity.

Results: At T1, none of the dietary patterns identified were associated with HFF measured at T2. At T2, a Prudent dietary pattern characterized by high fruit and vegetable intake was inversely associated with HFF (−0.08 [95% CI: −0.16, −0.00]). Similarly, increased adherence to the Prudent pattern across T1 and T2 corresponded with lower ln-HFF (−0.11 [−0.18, −0.04] units). On the other hand, adherence to a Western pattern comprising fried foods and refined carbohydrates at T2 correlated with higher HFF among non-Hispanic White participants (0.16 [0.06, 0.26]). These findings persisted after accounting for child BMI.

Conclusions: Even in healthy youth, a diet high in fruits and vegetables is associated with lower HFF, whereas a diet high in fried foods and refined carbohydrates is related to higher HFF. Dietary changes may serve as an early preventive measure to mitigate liver fat accrual.

KEYWORDS

adolescents, diet, epidemiology, hepatic fat fraction, non-alcoholic fatty liver disease

1 | INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of increasing rates of chronic liver disease in the United States.[1,2] This statistic spares no age group, especially in the wake of the childhood obesity pandemic: NAFLD affects approximately one in four youth with obesity and up to 10% of the general paediatric population.[3] Although NAFLD is clinically defined as liver fat content >5.5%,[4] the condition comprises a spectrum of liver pathology from relatively benign simple steatosis to the more pernicious non-alcoholic steatohepatitis (NASH), fibrosis/cirrhosis and hepatocellular carcinoma. Given that there is currently no effective treatment for NAFLD, identification of modifiable risk factors of liver fat accretion in a general population during early life is a public health prerogative.

Although most NALFD risk factors like race/ethnicity,[5] genetics,[6] age and adiposity[7] are difficult (some, impossible) to change, diet is a modifiable determinant of liver fat.[8] As summarized by a recent systematic review,[9] observational studies in adults found that excessive consumption of refined carbohydrates and unhealthy fats are associated with NAFLD risk. In addition, both observational studies and clinical trials have found that compliance with a Mediterranean dietary pattern, and consumption of foods high in polyunsaturated fats, fresh fruits and vegetables and fibre is protective against NAFLD.[8]

The literature surrounding dietary correlates of NAFLD in youth is less robust. In an analysis of 89 German children classified as overweight and 36 controls classified as non-overweight, Nier et al[10] reported higher total energy and carbohydrate intake, particularly intake from sugar-sweetened beverages, among participants with NAFLD. In a gene-by-environment analysis, Davis et al[11] detected a synergistic interaction of the *PNPLA3* genotype with carbohydrate and total sugar intake in relation to liver fat content among 153 Hispanic youth. In the same population, Cook et al[12] subsequently noted an inverse association between consumption of non-starchy vegetables and liver fat content among 175 youth classified as overweight. Finally, two studies that focused on the Mediterranean dietary pattern via the KIDMED index[13] reported inverse associations of this dietary index with NAFLD among youth classified as overweight/obese in Italy (n = 243)[14] and Turkey (n = 181).[15] These papers indicate detrimental effects of high carbohydrate intake and the beneficial effects of a diet high in fresh fruits and vegetables. However, the evidence in youth is hampered by relatively small sample sizes, which may result in lack of power to detect smaller but biologically relevant effects; cross-sectional designs, which preclude inference on temporality; the focus on specific foods or nutrients which is not reflective of real-life dietary intake; and ethnically homogenous populations, which limit generalizability.

Here, we addressed gaps in literature using data from 397 multiethnic youth. First, we used a data-driven approach to characterize dietary patterns at two sensitive periods of development from late childhood through adolescence: age 6 to 14 years and age 12 to 19 years. Next, we sought to identify dietary patterns at each timepoint that were associated with liver fat content, a direct metric of NAFLD risk.[4] Finally, we examined associations of change in adherence to dietary patterns with liver fat content.

2 | METHODS

2.1 | Study population

Study participants were from the Exploring Perinatal Outcomes among CHildren (EPOCH) study, a historical prospective cohort of youth whose mothers were members of the Kaiser Permanente of Colorado (KPCO) Health plan.[16,17] The original study sought to understand the long-term consequences of exposure to diabetes in utero. Thus, we enrolled 99 children exposed to maternal diabetes and a random sample of 505 unexposed youth. We carried out the first research visit (T1) when offspring were ~ 10 years of age (n = 604) and the second research visit (T2) when children were ~ 16 years of age (n = 414).

Of the 414 participants who attended both visits, we excluded 15 missing data on HFF at T2, followed by 2 without data on maternal diabetes status (an important covariate), yielding an analytic sample of 397 youth. This study was approved by the Colorado Multiple Institutional Review Board. Mothers provided informed consent and offspring provided written assent.

2.2 | Dietary assessment (exposure)

At the T1 and T2 visits, we used the Block Kids Food Frequency Questionnaire (FFQ),[18] which queried the frequency of intake of 83 foods consumed in the last week. Participants reported the frequency of consumption of small, medium, or large portions of each food or beverage ranging from '1 day' to 'every day'. We did not weight frequency of intake by portion size in light of evidence that children and adolescents have difficulty assessing portion size.[19,20]

Prior to statistical analyses, we consolidated the 83 items into 42 food groups based on their nutritional properties (Table S1). We estimated total daily energy intake using the United States Department of Agriculture Food Composition Database[21] and adjusted each food group by total energy intake using the residuals method.[22]

2.3 | Assessment of hepatic fat fraction (outcome)

As described,[23] hepatic imaging was performed at T2 via magnetic resonance imaging (MRI), using a modification of the Dixon method.[10,11] We calculated hepatic fat fraction (HFF) from the mean pixel signal intensity data for each flip angle acquisition. Given the low proportion of participants with clinical NAFLD (6.3% with HFF > 5.5%), we assessed HFF continuously following a natural log (ln) transformation.

2.4 | Covariates

Maternal pre-pregnancy body mass index (BMI; kg/m^2) was calculated using pre-pregnancy weight from medical records and measured height. All pregnant women at KPCO are routinely screened for GDM at 24 to 28 weeks using the standard two-step protocol.[24] At the first study visit (T1), mothers reported their education level and smoking habits during pregnancy via a questionnaire.[25]

At both research visits, we measured the participants' weight on a digital scale and height via a calibrated stadiometer. We calculated BMI and standardized it using the World Health Organization growth reference.[26] Participants reported their race/ethnicity at T1 as non-Hispanic White (51.9%), non-Hispanic Black (7.1%), Hispanic (36.0%),

TABLE 1 Bivariate associations of background characteristics with hepatic fat fraction (HFF) at age 11 to 16 years (T2) among 397 EPOCH youth

	N[a]	Mean ± SD HFF (%)	P-value[b]
Maternal perinatal characteristics			
Maternal pre-pregnancy BMI (kg/m^2)			.002
Underweight (<18.5 kg/m^2)	9	2.19 ± 0.90	
Normal weight (18.5-24.9 kg/m^2)	135	1.94 ± 1.28	
Overweight (25.0-29.9 kg/m^2)	79	2.53 ± 2.15	
Obese (>30 kg/m^2)	60	3.67 ± 5.52	
Maternal gestational diabetes mellitus (GDM)			.96
Yes	70	2.74 ± 4.59	
No	327	2.41 ± 2.64	
Maternal education level			.15
<High school	23	2.60 ± 2.18	
High school or equivalent	57	2.46 ± 2.30	
>High school	328	2.46 ± 3.22	
Mother smoked during pregnancy			.99
Yes	29	2.96 ± 5.54	
No	368	2.43 ± 2.79	
Child's characteristics at time of HFF assessment (T2)			
Sex			.13
Female	198	2.36 ± 2.20	
Male	199	2.70 ± 3.73	
Race/ethnicity			.002
Non-Hispanic White	206	2.01 ± 1.36	
Hispanic	143	3.25 ± 4.71	
Non-Hispanic other	48	2.10 ± 1.16	
Age			.02
12 to <16 years	108	3.05 ± 3.93	
16 to <17 years	1115	1.94 ± 1.37	
≥17 years	174	2.46 ± 3.22	
BMI *z*-score[c]			<.0001
<−2.0	8	1.93 ± 1.10	
≥−2.0 to ≤1.0	266	1.80 ± 1.01	
>1.0 to ≤2.0	91	3.16 ± 4.29	
>2.0	32	6.17 ± 6.21	
Pubertal status[d]			.78
Tanner stage = 2 or 3	23	3.57 ± 7.60	
Tanner stage = 4	150	2.39 ± 3.23	
Tanner stage = 5	218	2.41 ± 1.94	
Mean energy expenditure (METs over a 3-day period)			.31
Q1 (lowest)	98	2.71 ± 2.85	
Q2	96	2.35 ± 1.70	
Q3	97	2.50 ± 3.90	
Q4 (highest)	97	2.40 ± 3.51	

[a]Totals may not add up to 397 due to missing values.
[b]From a *P*-for-linear-trend for ordinal variables; from a Type 3 F test for a difference for categorical variables. HFF is ln-transformed in these models.
[c]According to the World Health Organization (WHO) growth reference for children 5 to 19 years of age.
[d]Based on pubic hair development in boys and breast development in girls.

or non-Hispanic other (5.0%). In the analysis, we combined non-Hispanic Black with non-Hispanic other into 'Other' due to small cell sizes.

Covariates at T2 included pubertal development based on Tanner stage of pubic hair development in boys and breast development in girls.[27] We obtained data on participants' physical activity levels at T2 using the 3-Day Physical Activity Recall Questionnaire (3DPAR), which captures habitual physical activity of adolescents based on a 3-day period[28] and has been validated against accelerometry.[29] We used these data to derive average energy expenditure (METs) as a proxy for physical activity.

2.5 | Data analysis

First, we assessed bivariate associations of maternal/perinatal and child characteristics with ln-HFF as well as NAFLD status to identify potential confounders to the association of interest. This step, in conjunction with our a priori knowledge of determinants of cardiometabolic health in youth informed covariate selection in the multivariable analysis.

Next, we created dietary patterns at T1 and T2, separately, using food frequencies derived from the FFQ. Using principal components analysis (PCA), we consolidated the food groups into principal components (factors) with an orthogonal rotation. Of the 42 factors generated by PCA, we retained the first three at T1 and the first two at T2 based on standard criteria of the Scree plot and eigenvalues >1,[30] and interpretability of the dietary patterns. We considered food groups with factor loadings ≥|0.30| to be a key contributor to a dietary pattern.[31,32]

In the main analysis, we examined associations of the dietary patterns at each time (*X*-variable) with ln-HFF (*Y*-variable) at T2 using a series of multivariable models to assess the impact of covariate adjustment on the estimate of association. Model 1 included maternal education and GDM exposure; and child's age, sex and race/ethnicity. Model 2 further accounted for energy expenditure at T2. Model 3 included Model 1 covariates plus BMI *z*-score at T2 to assess an effect of diet on HFF, independent of concurrent adiposity. Model 4 included Model 1 covariates plus pubertal status. In all models, adjustment for maternal pre-pregnancy BMI (kg/m^2) did not materially change findings. Thus, we did not include this variable in final models.

We also examined associations of key food groups (ie, those with factor loadings >|0.30|) within each factor with HFF, using Model 1 and estimating β (95% CI) for each 1-SD increment in food groups of interest. We noted consistency in the food group composition of Factors 1 and 2 across T1 and T2, so we also explored associations of change in the factor scores (which represents change in adherence to each dietary pattern over time) with HFF at T2 using Models 1 to 5 described.

We tested for interactions of the dietary patterns with GDM, sex, pubertal status and race/ethnicity. We found evidence of effect modification (*P*-interaction < .05) by race/ethnicity for one of the T2 dietary patterns, so we stratified these models by Hispanic ethnicity (Hispanic, non-Hispanic White, non-Hispanic other). Given the loss to follow-up between T1 and T2, we compared background characteristics of participants who were at both visits vs at the T1 visit only and did not find any marked differences (data available upon request).

TABLE 2 Composition of dietary patterns at age 6 to 14 years (T1) and 12 to 19 years (T2) among 397 youth in EPOCH

Food group	% Variance	Factor loading
T1 dietary patterns		
Factor 1 (Prudent)	6.5%	
Leafy greens		0.79
Salad dressing		0.74
Raw or cooked vegetables		0.66
Cruciferous vegetables		0.38
Fruit		0.36
Factor 2 (Western)	4.8%	
Fried potatoes		0.58
Margarine and butter		0.56
Ketchup		0.44
Sugar-sweetened beverages		0.41
Fast food		0.38
Beef		0.37
Crackers and cracker sandwiches		−0.46
Factor 3 (Breakfast foods)	4.0%	
Milk		0.56
Cereal		0.49
Cheese		−0.39
Fried packaged snacks		−0.38
T2 dietary patterns		
Factor 1 (Prudent)	8.8%	
Leafy greens		0.68
Vegetables		0.68
Fruit		0.58
Cruciferous vegetables		0.46
Nuts and seeds		0.46
Yoghourt		0.44
Stir-fried vegetables		0.40
Salad dressing		0.38
Sugar-sweetened beverages		−0.35
Fast food		−0.35
Beef		−0.36
Factor 2 (Western)	5.8%	
Fried potatoes		0.58
Ketchup		0.52
Beef		0.44
Fast food		0.42
Salad dressing		0.41
Fried packaged snacks		0.36
Cereal		−0.48

We carried out all analyses using SAS software (version 9.3; SAS Institute Inc., Cary, North Carolina).

3 | RESULTS

Mean ± SD age of participants at T1 was 10.5 ± 1.5 years (range:_ 6.0-13.9 years), and at T2 was 16.7 ± 1.2 years (range: 12.6-19.6 years). Half (49.9%) of the participants were female, and 48.1% (n = 287) were non-Hispanic White. Average (range) HFF was 2.5% (median: 1.9%, range: 0% to 38.2%), and 6.3% (n = 25 of 397) had NAFLD. Table 1 shows associations of background characteristics with ln-HFF. Key determinants/correlates of higher HFF were higher maternal pre-pregnancy BMI (P-for-trend = .002), male sex (P-difference = .13), race/ethnicity (Type 3 P-value = .002, with the highest HFF among Hispanic participants) and higher BMI z-score at T2 (P-for-trend < .0001). Table S2 shows the same characteristics, but stratified by NAFLD status (yes vs no).

Table 2 shows the composition of dietary patterns we retained at T1 and T2. At T1, we retained three factors (dietary patterns) from the PCA that accounted for 15.3% of the variability in the original food groups. The first factor, which we named the Prudent dietary pattern, was composed of leafy greens, vegetables and fresh fruit. The second factor was driven by fried potatoes, margarine and butter, sugar-sweetened beverages and fast food; thus, we named this factor the Western dietary pattern. Factor 3 was composed of breakfast foods (high intake of milk and cereal, low intake of cheese and fried snacks). At T2, we retained two factors that accounted for 14.6% of variability. Factor 1 at T2 resembled Factor 1 at T1, so we named it the Prudent dietary pattern. Factor 2 at T2 resembled Factor 2 from T1, so we named this factor the Western dietary pattern.

At T1, none of the dietary patterns were associated with ln-HFF (Table 3). At T2, Factor 1 was inversely associated with ln-HFF. In Model 1, each 1-unit increment in Factor 1 corresponded with 0.08 (0.00, 0.16) units lower ln-HFF, or an 8% (95% CI: 0%, 17%) decrease in HFF. Adjustment for physical activity (Model 2), BMI z-score (Model 3), and pubertal status (Model 4) at T2 did not change the findings. When we stratified by race/ethnicity due to evidence of a statistical interaction between Factor 2 at T2 and race/ethnicity, we found that among non-Hispanic White youth, each 1-unit increment in Factor 2 was associated with 0.16 (95% CI: 0.06, 0.26) units higher ln-HFF, or a 14% (95% CI: 4%, 25%) relative increase in HFF. This estimate persisted after adjustment for covariates in Models 2 to 4 (Table 3).

In Table 4, we show associations of key food groups within dietary patterns at T2 with ln-HFF. The only notable association was a positive association between fast food intake in Factor 1 and ln-HFF (0.10 [95% CI: 0.02, 0.17]). For Factor 2, fried potatoes (0.15 [95% CI: 0.03 0.27]) and fast food (0.25 [95% CI: 0.05, 0.44]) were positively related to ln-HFF in non-Hispanic White participants. Among Hispanic youth, fried/packaged snacks were inversely associated with ln-HFF (−0.24 [95% CI: −0.44, −0.05]).

Finally, we explored associations with respect to change in diet (Table 5). Each 1-unit increase in Factor 1 across the two research

TABLE 3 Associations of dietary patterns at 6 to 14 years (T1) and 12 to 19 years (T2) with hepatic fat fraction (HFF) at T2 among 397 EPOCH youth[a]

	β (95% CI) in ln-HFF per 1 unit of each dietary pattern factor score				
	Unadjusted	**Model 1**	**Model 2**	**Model 3**	**Model 4**
T1 dietary patterns					
All children	*n = 397*	*n = 397*	*n = 386*	*n = 397*	*n = 397*
Factor 1 (Prudent)	0.04 (−0.03, 0.11)	0.05 (0.02, 0.13)	0.06 (−0.02, 0.13)	0.03 (−0.04, 0.10)	0.05 (0.02, 0.13)
Factor 2 (Western)	0.04 (−0.03, 0.12)	0.03 (−0.05, 0.10)	0.03 (−0.05, 0.11)	−0.01 (−0.09, 0.06)	0.02 (−0.06, 0.10)
Factor 3 (Breakfast)	−0.02 (−0.09, 0.06)	−0.01 (−0.09, 0.07)	−0.02 (−0.10, 0.06)	0.02 (−0.05, 0.09)	−0.01 (−0.09, 0.07)
T2 dietary patterns					
All children	*n = 370*	*n = 370*	*n = 354*	*n = 370*	*n = 370*
Factor 1 (Prudent)	**−0.11 (−0.18, −0.03)**	**−0.08 (−0.16, 0.00)**	−0.07 (−0.16, 0.01)	−0.07 (−0.15, 0.01)	−0.08 (−0.16, 0.00)
Non-Hispanic White	*n = 195*	*n = 195*	*n = 190*	*n = 195*	*n = 239*
Factor 2 (Western)	**0.15 (0.05, 0.25)**	**0.16 (0.06, 0.26)**	**0.16 (0.06, 0.27)**	**0.15 (0.04, 0.25)**	**0.16 (0.06, 0.26)**
Hispanic	*n = 131*	*n = 131*	*n = 129*	*n = 131*	*n = 131*
Factor 2 (Western)	−0.06 (−0.20, 0.08)	−0.05 (−0.19, 0.09)	−0.06 (−0.20, 0.09)	−0.02 (−0.15, 0.11)	−0.05 (−0.19, 0.09)
Non-Hispanic other	*n = 44*	*n = 44*	*n = 42*	*n = 44*	*n = 239*
Factor 2 (Western)	−0.02 (−0.18, 0.15)	−0.02 (−0.17, 0.14)	0.01 (−0.16, 0.17)	−0.05 (−0.20, 0.11)	−0.01 (−0.17, 0.15)

Note: Model 1: Adjusted for maternal education level the year the child was born, in utero GDM exposure, and child's age, sex, and race/ethnicity. Model 2: Model 1 + physical activity levels at T2 (average energy expenditure over a 3-day period). Model 3: Model 1 + BMI z-score at T2. Model 4: Model 1 + pubertal status at T2 (Tanner stages 2 + 3, 4 and 5 based on pubic hair development in boys and breast development in girls).
Bolded values indicate statistical significance at alpha = 0.05.
[a]HFF is natural log (ln) transformed due to a non-normal distribution.

TABLE 4 Associations of dietary patterns at with hepatic fat fraction (HFF) at age 12 to 19 years among 397 EPOCH youth[a]

	Factor loading	β (95% CI)[b] per 1-SD intake of each food group
T2 factor 1 (Mediterranean)		
Leafy greens (+)	0.68	0.03 (−0.05, 0.10)
Vegetables (+)	0.68	−0.04 (−0.12, 0.04)
Fruit (+)	0.58	−0.07 (−0.14, 0.01)
Cruciferous vegetables (+)	0.46	0.03 (−0.05, 0.11)
Nuts and seeds (+)	0.46	−0.05 (−0.13, 0.02)
Yoghourt (+)	0.44	−0.05 (−0.12, 0.03)
Stir-fried vegetables (+)	0.40	0.00 (−0.08, 0.08)
Salad dressing (+)	0.38	0.06 (−0.02, 0.14)
Sugar-sweetened beverages (−)	−0.35	0.03 (−0.03, 0.11)
Beef (−)	−0.35	0.06 (−0.02, 0.14)
Fast food (−)	−0.36	**0.10 (0.02, 0.17)**
T2 factor 2 (Western)		
Non-Hispanic White		
Fried potatoes (+)	0.58	**0.15 (0.03, 0.27)**
Ketchup (+)	0.52	0.07 (−0.04, 0.19)
Beef (+)	0.44	0.10 (−0.03, 0.22)
Fast food (+)	0.42	**0.25 (0.05, 0.44)**
Salad dressing (+)	0.41	0.07 (−0.03, 0.16)
Fried packaged snacks (+)	0.36	0.16 (0.02, 0.30)
Cereal (−)	−0.48	−0.01 (−0.07, 0.06)
Hispanic		
Fried potatoes (+)	0.58	−0.07 (−0.22, 0.08)
Ketchup (+)	0.52	0.00 (−0.15, 0.16)
Beef (+)	0.44	0.06 (−0.09, 0.21)
Fast food (+)	0.42	0.22 (−0.08, 0.52)
Salad dressing (+)	0.41	0.05 (−0.08, 0.18)
Fried packaged snacks (+)	0.36	**−0.24 (−0.44, −0.05)**
Cereal (−)	−0.48	0.00 (−0.11, 0.10)
Non-Hispanic other		
Fried potatoes (+)	0.58	−0.08 (−0.26, 0.10)
Ketchup (+)	0.52	0.01 (−0.13, 0.15)
Beef (+)	0.44	−0.09 (−0.28, 0.10)
Fast food (+)	0.42	0.11 (−0.12, 0.34)
Salad dressing (+)	0.41	0.01 (−0.13, 0.14)
Fried packaged snacks (+)	0.36	**−0.18 (−0.34, −0.02)**
Cereal (−)	−0.48	−0.03 (−0.15, 0.09)

Bolded values indicate statistical significance at alpha = 0.05.
[a]HFF is natural log (ln) transformed due to a non-normal distribution.
[b]Estimates are adjusted for maternal education level the year the child was born, in utero GDM exposure and child's age at T1 and difference in age between T1 and T2, sex and race/ethnicity.

visits corresponded with 0.11 (95% CI: 0.04, 0.18) lower ln-HFF, which translates to a 12% (95% CI: 4%, 20%) relative decrease in HFF. This estimate persisted after adjustment for T2 covariates (Table 5, Models 2-4).

4 | DISCUSSION

In this study of 397 multi-ethnic youth in Colorado, we derived dietary patterns at median age 10.6 years (T1) and 16.8 years (T2) and examined their associations with MRI-assessed hepatic fat fraction (HFF) at T2. We identified three distinct dietary patterns at T1, and two dietary patterns at T2. Although none of the dietary patterns at T1 were associated with HFF, adherence to a Prudent dietary pattern at T2 corresponded with lower HFF. On the other hand, compliance with a Western dietary pattern at T2 was associated with higher HFF among non-Hispanic youth. Finally, we found that increased adherence to a Prudent dietary pattern across T1 and T2 was associated with lower HFF at T2. These associations were independent of concurrent adiposity.

4.1 | Associations of factor 1 (Prudent dietary pattern) at T2 with HFF

Our finding that a dietary pattern characterized by high intake of leafy greens, vegetables and fruits is inversely related to HFF aligns with studies in adults,[8] and two recent cross-sectional analyses in adolescents.[14,15] In one study of youth ~12 years of age, Cakir et al created a priori Mediterranean diet score based on the KIDMED index[13] to assess for differences in the diet score among youth with overweight/obesity and NAFLD (n = 106), youth with obesity but without NAFLD (n = 21) and healthy children with normal BMI (n = 54) in the Black Sea region of Turkey. Youth with NAFLD had the lowest score, followed by those who had obesity without NAFLD, then those who were healthy and normal weight. In the other study, which also used the KIDMED index, Della Corte et al[14] reported higher prevalence of 'low KIDMED score' (KIDMED index ≤3) in conjunction with greater severity of NAFLD among 243 Italian adolescents with obesity aged 10 to 17 years. One key strength of our study in comparison to current literature is that we assessed change in adherence to a Mediterranean-like diet over time, which not only lends credence to our findings of a protective effect, but also is a better reflection of the relevance of long-term diet trajectories in the development of chronic conditions like NAFLD.

Potential pathways and mechanisms underlying the protective effect of a Prudent diet against liver fat accretion include a potential effect of a Prudent diet on promotion of weight loss which, in turn, can reverse earlier stages of NAFLD[33]; physiological benefits of specific nutrients consumed in relatively high amounts when following a Prudent or Mediterranean-like diet, including but not limited to anti-inflammatory N-3 polyunsaturated fatty acids,[34] antioxidants like Vitamins C and E that combat oxidative stress pathways implicated in the progression across the spectrum of NAFLD severity.[35]

TABLE 5 Associations of change in factor 1 and factor 2 between age 6 to 14 years (T1) and 12 to 19 years (T2) with hepatic fat fraction (HFF) at T2 among EPOCH youth

		β (95% CI) for change in factor scores with HFF[a]	
	N	Factor 1 Prudent dietary pattern	Factor 2 Western dietary pattern
Unadjusted	368	**−0.12 (−0.19, −0.06)**	0.00 (0.06, 0.06)
Model 1	368	**−0.11 (−0.18, −0.04)**	0.02 (−0.04, 0.08)
Model 2	359	**−0.11 (−0.18, −0.04)**	0.02 (−0.04, 0.08)
Model 3	368	**−0.09 (−0.15, −0.02)**	0.04 (−0.02, 0.10)
Model 4	369	**−0.11 (−0.18, −0.04)**	0.02 (−0.04, 0.08)

Note: Model 1: Adjusted for maternal education level the year the child was born, in utero GDM exposure and child's age, sex and race/ethnicity. Model 2: Model 1 + physical activity levels at T2 (average energy expenditure over a 3-day period). Model 3: Model 2 + BMI *z*-score at T2. Model 4: Model 3 + pubertal status at T2 (Tanner stages 2 + 3, 4 and 5 based on pubic hair development in boys and breast development in girls).
Bolded values indicate statistical significance at alpha = 0.05.
[a]HFF is natural log (ln) transformed due to a non-normal distribution.

4.2 | Associations of factor 2 (Western diet) at T2 with HFF

The other dietary pattern associated with HFF was a Western dietary pattern at T2 that comprised high intake of high fat and fried foods, including fried potatoes, beef, fast food, salad dressing and fried/packaged snacks. The association of this dietary pattern with HFF differed by race/ethnicity such that greater adherence to this pattern was associated with higher HFF among non-Hispanic White youth only. When we explored associations with individual food groups with HFF, we found a positive relationship with respect to fried potatoes and fast food in non-Hispanic White participants. This association makes sense given that the fried potatoes food group included French fries, tater tots and hush puppies, and the fast food group comprised fast food, take-out, pizza, pizza pockets, hot dogs, corn dogs—all of which are sources of the unhealthy saturated and *trans* fats, and refined carbohydrates implicated in the pathogenesis of NAFLD.[9]

Among Hispanic youth, we observed an inverse association between fried/packaged snacks and HFF. This was unexpected given that foods in the fried/packaged snacks food groups were all calorie-dense and nutrient-poor foods, but could be a manifestation of the Hispanic paradox (aka the epidemiological paradox) wherein persons of Hispanic ethnicity exhibit more favourable health outcomes despite higher exposure to risk factors.[36] We also acknowledge that this association could be spurious, or an artefact of residual confounding by unmeasured variables.

Our finding that associations of Factor 2 differed by race/ethnicity has ramifications for understanding pathophysiology of obesity-related conditions that manifest with a cluster of cardiometabolic disturbances that are of particular concern in Hispanic persons, including NALFD, due to synergistic gene-diet interactions.[11]

4.3 | Strengths and limitations

Our study had several strengths. First, we characterized dietary patterns using a data-driven approach to assess eating habits and diet quality.[37] These dietary patterns likely reflect long-term intake, which is directly relevant to risk of chronic diseases like NAFLD, and may also reflect upstream social determinants of health for consideration in future studies. Second, we derived dietary patterns at two timepoints across the adolescent transition, which is a sensitive period for development of metabolic disease risk.[38] Third, our prospective design and rich data on confounders and precision covariates enhanced our ability to make inferences regarding the potential influence of diet on liver fat content.

One limitation to this study is potential reporting bias of dietary intake, which may be differential with respect to HFF given the correlation between HFF and obesity.[39] Second, we did not have liver fat content based on the gold standard (liver biopsy). However, MRI is the most sensitive non-invasive procedure available. Third, we only measured HFF at T2 so we were not able to assess the effect of diet on change in liver fat content over time.

5 | CONCLUSIONS

In this analysis of nearly 400 diverse young people representative of the general paediatric population in the United States (eg, the majority are normal BMI, with 30% classified as overweight/obese), compliance with a Prudent dietary pattern—both cross-sectionally, as well as increased adherence over time—is associated with lower HFF, whereas adherence to a Western dietary pattern is associated with higher HFF among non-Hispanic White youth. Although the effect sizes we detected were modest (ie, an 8% to 14% relative difference in HFF per 1 unit increment in dietary patterns) they have long-term ramifications given that cardiometabolic disease risk factors track from youth into adulthood.[40,41] Given that we were able to detect associations of holistic dietary habits with liver fat content in a relatively healthy paediatric cohort, our findings point towards the utility of dietary modifications to halt disease progression in the early, reversible stages of the liver disease spectrum. In addition to confirming our results, future studies should explore whether certain foods within the Prudent dietary pattern are more

relevant to protecting against hepatic fat accumulation, and whether the influence of diet operates through changes in body composition and/or tempo of pubertal maturation given the interrelations among adiposity gain, pubertal progression and biomarkers of metabolic health.

ACKNOWLEDGEMENTS

This work was supported by the NIH, National Institute of Diabetes, Digestive, and Kidney Diseases (R01 DK068001). Wei Perng is supported by KL2-TR002534. The funders had no role in the conceptualization, implementation or interpretation of this work.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Wei Perng conceptualized and designed the study, conducted the analysis, wrote the first draft of the article and revised it for important intellectual content. Dana Dabelea acquired the data, aided in data interpretation and revised the article for important intellectual content. Robyn Harte and Brandy M. Ringham generated the data, aided in conduct of the analysis and revised the article for important intellectual content. Ana Baylin contributed to the design of the analysis, aided in interpretation of the results and revised the article for important intellectual content. Anna Bellatorre aided in interpretation of the results and revised the article for important intellectual content. Ann Scherzinger contributed to generation and interpretation of data and revised the article for important intellectual content. Michael I. Goran contributed to the conception and design of the analysis, aided in interpretation of data and revised the article for important intellectual content. All authors gave final approval of the version of the article submitted and will do so for the version to be published.

ORCID

Wei Perng https://orcid.org/0000-0001-8552-6850

REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Diseases. Definition & Facts of NAFLD & NASH. [Online]. 2016; https://www.niddk.nih.gov/health-information/liver-disease/nafld-nash/definition-facts. Accessed February 21, 2018.
2. Doycheva I, Watt KD, Rifai G, et al. Increasing burden of chronic liver disease among adolescents and young adults in the USA: a silent epidemic. *Dig Dis Sci*. 2017;62(5):1373-1380.
3. Lavine JE, Schwimmer JB. Nonalcoholic fatty liver disease in the pediatric population. *Clin Liver Dis*. 2004;8(3):549-558. viii-ix.
4. Alderete TL, Toledo-Corral CM, Desai P, Weigensberg MJ, Goran MI. Liver fat has a stronger association with risk factors for type 2 diabetes in African-American compared with Hispanic adolescents. *J Clin Endocrinol Metab*. 2013;98(9):3748-3754.
5. Welsh JA, Karpen S, Vos MB. Increasing prevalence of nonalcoholic fatty liver disease among United States adolescents, 1988-1994 to 2007-2010. *J Pediatr*. 2013;162(3):496-500.e491.
6. Browning JD, Szczepaniak LS, Dobbins R, et al. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. *Hepatology*. 2004;40(6):1387-1395.
7. National Guideline Centre (UK). *Risk Factors for NAFLD*. London, England: National Institute for Health and Care Excellence (UK); 2016.
8. Papandreou D, Andreou E. Role of diet on non-alcoholic fatty liver disease: an updated narrative review. *World J Hepatol*. 2015;7(3):575-582.
9. Mirmiran P, Amirhamidi Z, Ejtahed H-S, Bahadoran Z, Azizi F. Relationship between diet and non-alcoholic fatty liver disease: a review article. *Iran J Public Health*. 2017;46(8):1007-1017.
10. Nier A, Conzelmann IB, Ozel Y, Bergheim I. Non-alcoholic fatty liver disease in overweight children: role of fructose intake and dietary pattern. *Nutrients*. 2018;10(9):1329. https://doi.org/10.3390/nu10091329.
11. Davis JN, Lê K-A, Walker RW, et al. Increased hepatic fat in overweight Hispanic youth influenced by interaction between genetic variation in PNPLA3 and high dietary carbohydrate and sugar consumption. *Am J Clin Nutr*. 2010;92(6):1522-1527.
12. Cook LT, O'Reilly GA, Goran MI, Weigensberg MJ, Spruijt-Metz D, Davis JN. Vegetable consumption is linked to decreased visceral and liver fat and improved insulin resistance in overweight Latino youth. *J Acad Nutr Diet*. 2014;114(11):1776-1783.
13. Serra-Majem L, Ribas L, Ngo J, et al. Food, youth and the Mediterranean diet in Spain. Development of KIDMED, Mediterranean diet quality index in children and adolescents. *Public Health Nutr*. 2004;7(7):931-935.
14. Della Corte C, Mosca A, Vania A, Alterio A, Iasevoli S, Nobili V. Good adherence to the Mediterranean diet reduces the risk for NASH and diabetes in pediatric patients with obesity: the results of an Italian study. *Nutrition*. 2017;39–40:8-14.
15. Cakir M, Akbulut UE, Okten A. Association between adherence to the Mediterranean diet and presence of nonalcoholic fatty liver disease in children. *Child Obes*. 2016;12(4):279-285.
16. Crume TL, Ogden L, West NA, et al. Association of exposure to diabetes in utero with adiposity and fat distribution in a multiethnic population of youth: the exploring perinatal outcomes among children (EPOCH) study. *Diabetologia*. 2011;54(1):87-92.
17. Crume TL, Ogden L, Maligie M, et al. Long-term impact of neonatal breastfeeding on childhood adiposity and fat distribution among children exposed to diabetes in utero. *Diabetes Care*. 2011;34(3):641-645.
18. Cullen KW, Watson K, Zakeri I. Relative reliability and validity of the block kids questionnaire among youth aged 10 to 17 years. *J Am Diet Assoc*. 2008;108(5):862-866.
19. Matheson DM, Hanson KA, McDonald TE, Robinson TN. Validity of children's food portion estimates: a comparison of 2 measurement aids. *Arch Pediatr Adolesc Med*. 2002;156(9):867-871.
20. Baranowski T, Domel SB. A cognitive model of children's reporting of food intake. *Am J Clin Nutr*. 1994;59(1 Suppl):212s-217s.
21. Haytowitz, DB, Ahuja, JKC, Wu, X, et al. USDA National Nutrient Database for Standard Reference, Legacy Release. Nutrient Data Laboratory, Beltsville Human Nutrition Research Center, ARS, USDA; 2019. https://data.nal.usda.gov/dataset/usda-national-nutrient-database-standard-reference-legacy-release. Accessed December 4, 2020.
22. Willett WC. Implications of total energy intake for epidemiologic analyses. *Nutritional Epidemiology*. Vol 30. New York, NY: Oxford University Press; 1998:279-298.
23. Bellatorre A, Scherzinger A, Stamm E, Martinez M, Ringham B, Dabelea D. Fetal overnutrition and adolescent hepatic fat fraction: the exploring perinatal outcomes in children study. *J Pediatr*. 2018;192:165-170.e161.
24. 2. Classification and diagnosis of diabetes. *Diabetes Care*. 2017;40(Suppl 1):S11-S24.
25. West NA, Crume TL, Maligie MA, Dabelea D. Cardiovascular risk factors in children exposed to maternal diabetes in utero. *Diabetologia*. 2011;54(3):504-507.

26. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ*. 2007;85(9):660-667.
27. Marshall WA, Tanner JM. Growth and physiological development during adolescence. *Annu Rev Med*. 1968;19:283-300.
28. Weston AT, Petosa R, Pate RR. Validation of an instrument for measurement of physical activity in youth. *Med Sci Sports Exerc*. 1997;29 (1):138-143.
29. Pate RR, Ross R, Dowda M, Trost SG, Sirard JR. Validation of a 3-day physical activity recall instrument in female youth. *Pediatr Exerc Sci*. 2003;15(3):257-265.
30. Dunteman G. *Principal Components Analysis*. Newbury Park, CA: Sage; 1989.
31. McNaughton SA, Ball K, Mishra GD, Crawford DA. Dietary patterns of adolescents and risk of obesity and hypertension. *J Nutr*. 2008;138 (2):364-370.
32. McCann SE, Marshall JR, Brasure JR, Graham S, Freudenheim JL. Analysis of patterns of food intake in nutritional epidemiology: food classification in principal components analysis and the subsequent impact on estimates for endometrial cancer. *Public Health Nutr*. 2001; 4(5):989-997.
33. Nobili V, Manco M, Devito R, et al. Lifestyle intervention and antioxidant therapy in children with nonalcoholic fatty liver disease: a randomized, controlled trial. *Hepatology*. 2008;48(1):119-128.
34. Lu W, Li S, Li J, et al. Effects of omega-3 fatty acid in nonalcoholic fatty liver disease: a meta-analysis. *Gastroenterol Res Pract*. 2016; 2016:1459790.
35. Hill DB, Devalaraja R, Joshi-Barve S, Barve S, McClain CJ. Antioxidants attenuate nuclear factor-kappa B activation and tumor necrosis factor-alpha production in alcoholic hepatitis patient monocytes and rat Kupffer cells, in vitro. *Clin Biochem*. 1999;32(7):563-570.
36. The Hispanic paradox. *Lancet*. 2015;385(9981):1918.
37. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002;13(1):3-9.
38. Schooling CM. Life course epidemiology: recognising the importance of puberty. *J Epidemiol Community Health*. 2015;69(8):820.
39. Lissner L, Troiano RP, Midthune D, et al. OPEN about obesity: recovery biomarkers, dietary reporting errors and BMI. *Int J Obes (Lond)*. 2007;31(6):956-961.
40. Camhi SM, Katzmarzyk PT, Broyles S, et al. Predicting adult body mass index-specific metabolic risk from childhood. *Metab Syndr Relat Disord*. 2010;8(2):165-172.
41. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation*. 2008;117(25):3171-3180.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Perng W, Harte R, Ringham BM, et al. A Prudent dietary pattern is inversely associated with liver fat content among multi-ethnic youth. *Pediatric Obesity*. 2021;16: e12758. https://doi.org/10.1111/ijpo.12758