

# Harmonization of Food-Frequency Questionnaires and Dietary Pattern Analysis in 4 Ethnically Diverse Birth Cohorts<sup>1–3</sup>

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## Abstract

**Background:** Canada is an ethnically diverse nation, which introduces challenges for health care providers tasked with providing evidence-based dietary advice.

**Objectives:** We aimed to harmonize food-frequency questionnaires (FFQs) across 4 birth cohorts of ethnically diverse pregnant women to derive robust dietary patterns to investigate maternal and newborn outcomes.

**Methods:** The NutriGen Alliance comprises 4 prospective birth cohorts and includes 4880 Canadian mother-infant pairs of predominantly white European [CHILD (Canadian Healthy Infant Longitudinal Development) and FAMILY (Family Atherosclerosis Monitoring In early Life)], South Asian [START (SouTh Asian birth cohORT)-Canada], or Aboriginal [ABC (Aboriginal Birth Cohort)] origins. CHILD used a multiethnic FFQ based on a previously validated instrument designed by the Fred Hutchinson Cancer Research Center, whereas FAMILY, START, and ABC used questionnaires specifically designed for use in white European, South Asian, and Aboriginal people, respectively. The serving sizes and consumption frequencies of individual food items within the 4 FFQs were harmonized and aggregated into 36 common food groups. Principal components analysis was used to identify dietary patterns that were internally validated against self-reported vegetarian status and externally validated against a modified Alternative Healthy Eating Index (mAHEI).

**Results:** Three maternal dietary patterns were identified—"plant-based," "Western," and "health-conscious"—which collectively explained 29% of the total variability in eating habits observed in the NutriGen Alliance. These patterns were strongly associated with self-reported vegetarian status (OR: 3.85; 95% CI: 3.47, 4.29;  $r^2 = 0.30$ ,  $P < 0.001$ ; for a plant-based diet), and average adherence to the plant-based diet was higher in participants in the fourth quartile of the mAHEI than in the first quartile (mean difference: 46.1%;  $r^2 = 0.81$ ,  $P < 0.001$ ).

**Conclusion:** Dietary data collected by using FFQs from ethnically diverse pregnant women can be harmonized to identify common dietary patterns to investigate associations between maternal dietary intake and health outcomes. *J Nutr* 2016;146:2343–50.

**Keywords:** FFQ, food frequency questionnaire, harmonization, multiethnic, PCA, prospective cohort, principal component analysis, dietary patterns, ethnicity

## Introduction

Methodologic advances in dietary measurement in large epidemiologic studies, such as the development of valid and reproducible semiquantitative FFQs (1, 2), have facilitated the study of associations between dietary intake and health and disease outcomes, such as cancer and cardiovascular disease. This is

often approached with a "reductionist" lens by examining associations between specific food items (3–6), single nutrients (5, 7), or sources of nutrients (8, 9) and health outcomes. This approach is reflective of public health approaches to food and nutrient recommendations. It has advanced our understanding and treatment of specific nutrient deficiency syndromes (e.g.,

folate fortification to prevent neural tube defects) and facilitated the identification and removal of particularly harmful components of food from the food supply (e.g., removal of partially hydrogenated vegetable oils). However, long-term diet is likely a stronger determinant of diet-related chronic disease risk than the consumption of any single food item or nutrient (10), and thus single-food (e.g., coffee) or single-nutrient studies (e.g., dietary cholesterol) are often misleading (11, 12) because they fail to capture the complex interplay between foods and nutrients consumed as meals over long periods of time. To overcome the limitations of single-nutrient or single-food studies, the empirical derivation of dietary patterns—defined as “the quantities, proportions, variety or combinations of different foods and beverages in diets, and the frequency with which they are habitually consumed” (13)—has been proposed as a method to characterize exposure that more accurately reflects how we consume foods or nutrients, and these patterns can be assessed for their associations with health and disease (14–18).

Canada is an ethnically diverse nation (19), which introduces challenges for health care providers tasked with providing evidence-based dietary advice, because much of what we know about diet and disease is rooted in studies in white European populations. Dietary choice is closely tied to ethnicity (e.g., foods, cooking methods, and eating habits) (20), and the degree to which an individual or community consumes ethnically traditional foods can be influenced by immigration, acculturation, and duration of residency in a host country (21).

In preparation for investigations into the role of maternal nutrition on maternal and newborn outcomes in a multiethnic birth cohort consortium, we developed an approach to derive harmonized dietary patterns in pregnant women. This article describes the methods used to derive and to validate dietary patterns identified at a single time point in the cross-sectional analysis of a prospective birth cohort and outlines the unique challenges faced and the methodologic approaches used to address them.

## Methods

### Study population

The NutriGen Alliance is a multiethnic birth cohort consortium composed of 4 ethnically diverse cohorts of pregnant women representing several geographic regions across Canada. These cohorts were assembled to understand the early-life determinants of cardiometabolic risk, allergy,

and asthma. Each cohort enrolled pregnant women in their second or third trimester and will follow the mother and infant from pregnancy through delivery and into childhood. The NutriGen Alliance provides a platform to investigate the joint influences of dietary intake, genetics, and the gut microbiome on the development of maternal and infant health outcomes in a Canadian context. As of February 2016, 5000 women with dietary data have been enrolled across the 4 cohort studies. There are 3047 pregnant women from the Canadian Healthy Infant Longitudinal Development (CHILD)<sup>15</sup> Study (22), representing 5 ethnic groups [white European (74%), East or South East Asian (12%), Aboriginal (4%), South Asian (3%), and African or other (12%) origin] recruited from 6 urban and rural Canadian cities (Vancouver, British Columbia; Edmonton, Alberta; Winnipeg, Manitoba; Morden, Manitoba; Winkler, Manitoba; Toronto, Ontario). There are 839 pregnant women included from the Family Atherosclerosis Monitoring In early life (FAMILY) Study (23), representing 5 ethnic groups [white European (74%), East or South East Asian (1%), Aboriginal (1%), South Asian (1%), and African or other (4%) origin] recruited from the Greater Hamilton Area, Ontario. There are 1006 South Asian mothers from the South Asian birth cohort (START) (24) recruited from the Peel Region, Ontario, and 108 of an anticipated 300 Aboriginal mothers from the Aboriginal Birth Cohort (ABC) (25) recruited from the Six Nations Reserve, Ontario. Comprehensive clinical and dietary data from all pregnant women were collected from all 4 cohorts. Ethical approval was obtained for each study independently, and informed consent was obtained from all individual participants included in the study.

For this analysis, women who did not satisfactorily complete the FFQ [i.e., did not answer  $\geq 10$  questions ( $\sim 6\%$ )] or who reported an implausible energy intake ( $<500$  or  $>6500$  kcal/d) were excluded. One individual reported an implausibly high intake of a single food item (i.e., 64 servings of lettuce/d). The exclusion of this participant's FFQ, or replacement of the implausible reported value with a value equal to the 99th percentile of the “plausible” values (12 servings/d), produced identical dietary patterns; as such, the implausible value was included. The final number of women included in our analysis was 4880 (Supplemental Table 1).

### Assessment of dietary intake and dietary patterns

**FFQs.** In the CHILD study, maternal diet was assessed by using a semiquantitative FFQ, adapted from the Fred Hutchinson Cancer Center tool (26). In the FAMILY, START, and ABC cohorts, semiquantitative FFQs developed for the Study of Health and Risk in Ethnic Groups (SHARE) Study (27) were used to assess maternal dietary intake during pregnancy, modified to capture ethnicity-specific foods (SHARE-based FFQs). ABC, FAMILY, and START FFQs were analyzed by using a database linked to the Canadian Nutrient File; the CHILD FFQ was analyzed by using the USDA nutrient database, modified for a Canadian setting (28), allowing estimation of energy intake. The development and validation of these tools have been described previously (29–31).

**Frequency of consumption and serving size.** The included FFQs used different serving size reference portions and frequency of consumption options. The CHILD FFQ provided respondents with categorical frequency options from which to choose (e.g., never to  $>2$  servings/d), whereas in the SHARE-based FFQs, response categories were open-ended. Thus, we harmonized serving sizes of the SHARE-based FFQs to those in CHILD FFQ (Supplemental Table 2) (32, 33). Detailed steps describing the calculations and methods used to harmonize serving sizes across the cohorts are presented in Supplemental Table 3.

**Food groupings.** To create common food groups across the cohorts, individual FFQ items from each study were aggregated into groups of foods of similar nutrient profile and type (e.g., poultry, leafy greens, legumes, etc.). In some cases, food groups contained only a single item that uniquely reflected a particular dietary pattern (e.g., French fries reflect fast- and convenience-food consumption; Supplemental Table 4). We grouped foods in a way that has been used in previous dietary pattern analysis studies that examined associations between dietary habits and cardiometabolic conditions, allergies, or common clinical biomarkers

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<sup>3</sup> Supplemental Tables 1–8 and Supplemental Figure 1 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://jn.nutrition.org>.

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<sup>15</sup> Abbreviations used: ABC, Aboriginal Birth Cohort; CHILD, Canadian Healthy Infant Longitudinal Development; DNBC, Danish National Birth Cohort; FAMILY, Family Atherosclerosis Monitoring In early life; mAHEI, modified Alternative Healthy Eating Index; MoBa, Norwegian Mother and Child Cohort Study; PCA, principal components analysis; SHARE, Study of Health and Risk in Ethnic Groups; START, South Asian birth cohort.

(e.g., fasting plasma glucose, cholesterol, and TGs) (32–35). For example, bacon, breakfast sausages, low-fat and regular hotdogs, lunchmeats, and canned meats were combined into a single category called “processed meats.”

### Dietary pattern analysis

To identify dietary patterns within the FFQ data, we used the “psych” package (version 1.5.6) within R (version 3.1.2) to perform a principal components analysis (PCA) with an orthogonal varimax rotation (16). The statistical details of PCA as a means to reduce the dimensionality of the FFQ are beyond the scope of this article, but we refer interested readers to several excellent reviews (10, 33, 36–39). The number of dietary patterns retained was determined by visual inspection of scree plots in conjunction with eigenvalues ( $>1.0$ ) and principal component interpretability (15, 40, 41). Three sensitivity analyses of dietary patterns were conducted (by using the same PCA approach as described) but limiting the sample to: 1) women diagnosed with type 2 diabetes before their current pregnancy ( $n = 107$ ; with or without hypertension), 2) women diagnosed with hypertension before their current pregnancy ( $n = 190$ ; with or without type 2 diabetes), and 3) those without type 2 diabetes ( $n = 4720$ ) or hypertension ( $n = 4632$ ) before their current pregnancy.

We labeled each dietary pattern (i.e., groups of foods with similarly high factor loadings) with a descriptor that reflected the highly loaded food groups (e.g., “Western” compared with “prudent” patterns). The PCA scores for each pattern obtained for each individual represented how closely their food choices reflected each of the empirically derived dietary patterns, with a higher score reflecting a greater degree of adherence to that dietary pattern. Dietary pattern scores were adjusted to the mean total population energy intake by using the residual method (42, 43).

### Dietary pattern adherence score

We created a dietary pattern adherence score that would more intuitively represent an individual’s degree of adherence to each of the identified dietary patterns. To do this, “cardinal food groups” that characterized each dietary pattern were defined as those food groups with an absolute factor (dietary pattern) loading score  $\geq 0.30$  (Supplemental Table 5) (44, 45). Daily servings of each of the cardinal food groups were converted into quintiles, by using the distribution of servings within the study population, and assigned “quintile scores” from 1 (<20th percentile) to 5 ( $\geq 80$ th percentile) (Supplemental Table 6). These quintile scores for each of the food groups were summed to derive a numerical indicator of how closely an individual’s diet reflected a given pattern. For example, “processed foods” had an absolute loading score  $\geq 0.30$  (0.55) for the “Western” diet but not for “plant-based” ( $-0.22$ ) or “health-conscious” (0.13) dietary patterns. In this case, the quintile score for “processed foods” contributed to the total score for the Western dietary pattern but not to the plant-based or health-conscious dietary patterns. An individual’s score for that specific diet was divided by the maximum score possible for the diet and multiplied by 100 to quantify the degree to which an individual adheres to each of the given dietary patterns (on a scale of 1–100) (Table 1).

### Internal and external validation of dietary pattern scores

PCA summary scores were internally validated against self-reported vegetarian practice by using a logistic regression model. It was hypothesized that higher plant-based diet scores would be associated with higher odds of self-reported vegetarian status. PCA summary scores were externally validated against the modified Alternative Healthy Eating Index (mAHEI) (46) by comparing differences in mean scores between extreme quartile groups for PCA dietary patterns. An mAHEI diet score was calculated for each participant. Participants received 10 points for each of the following food items they consumed above (healthful foods) or below (less-healthful foods) a threshold:  $\geq 5$  servings vegetables,  $\geq 4$  servings fruit,  $\geq 1$  serving nuts or soy proteins,  $\geq 3$  servings whole grains, a ratio of  $\geq 4$  servings fish to 1 serving meat and eggs, and  $\leq 0.5$  servings of less-healthy foods (i.e., fried foods and processed meats); intermediate intakes were scored proportionally between 0 and 10. The maximum mAHEI score was 60. For this analysis, “processed meats” was included

in the mAHEI “fried foods” category to capture *trans*-fat consumption. The mAHEI category for “alcohol consumption” was not included in this analysis of pregnant women. A design feature of the mAHEI [and other indexes, such as the Healthy Eating Index (47)] is that it rewards the consumption of “healthy” foods (5 items contribute to the score) more heavily than the avoidance of “unhealthy” foods (1 item contributes to the score); however, this feature does not preclude its usefulness as a valuable external validation tool for our derived dietary patterns. To do this, we compared mean plant-based, health-conscious, and Western diet scores between individuals in the lowest mAHEI-points quartile (i.e.,  $<15$  points, “least healthy”) and those in the fourth mAHEI quartile (i.e.,  $\geq 45$  points, “most healthy”). Differences in mean scores between diet groups were used to assess validity (e.g., higher plant-based scores were expected in those in the fourth mAHEI quartile than in those in the first quartile and higher Western scores were expected in those in the first mAHEI quartile than in those in the fourth quartile).

## Results

### PCA-derived patterns

Overall, 4880 valid FFQs were harmonized across 4 cohorts (Supplemental Table 1). The dimensionality of the food-group matrix was reduced from the 152–167 items queried within each individual study FFQ to 36 harmonized food groups (Supplemental Table 4), and 93 food items were common to all 4 instruments. A total of 59 and 70 foods were unique to CHILD and START FFQs, respectively; 64 were unique to the FAMILY FFQ; and 6 were unique to the ABC FFQ (Figure 1). The PCA identified 3 primary dietary patterns within the NutriGen Alliance with eigenvalues of 4.02, 3.20, and 3.05, which collectively explained 29% of the diet variability within the harmonized FFQ data set. The dietary patterns were classified as “plant-based,” “Western,” and “health-conscious” to emphasize the prominent food groups that defined each pattern. These categorizations reflect previously described dietary patterns in large cohort studies (Supplemental Table 5) (32–35, 48). In sensitivity analyses, the PCA-derived dietary patterns within subgroups of mothers who reported prepregnancy diabetes ( $n = 107$ ) or hypertension ( $n = 190$ ) were similar (e.g., plant-based, Western, and health-conscious) to those derived with the entire sample population or to those groups without hypertension ( $n = 4632$ ) or type 2 diabetes ( $n = 4720$ ).

The number of food groups with a loading factor  $\geq |0.30|$  were 10 for the plant-based, 13 for the Western, and 14 for the health-conscious patterns. The plant-based pattern was characterized by vegetables, legumes, fermented dairy, whole grains, nonmeat dishes, and a lack of red meat; the Western pattern had a high loading of sweets, red and processed meats, French fries, starchy vegetables, condiments, and sweet drinks; and the health-conscious pattern was characterized by seafood, poultry, and red meats; eggs; cruciferous vegetables; leafy greens; fruit; refined grains; stir-fried dishes; and condiments.

The dietary PCA scores for each individual were as follows:  $-1.8$  to  $6.1$  (plant-based),  $-3.7$  to  $6.6$  (Western), and  $-2.8$  to  $9.1$  (health-conscious). When adjusted for total energy intake by using the residual method (49) to a mean total energy intake of 2000 kcal/d (equal to the mean energy intake of mothers in the NutriGen Alliance), the range of loading scores for dietary patterns were  $-2.2$  to  $5.5$  (plant-based),  $-5.4$  to  $4.7$  (Western), and  $-4.0$  to  $7.8$  (health-conscious). Negative values indicate that an individual’s dietary pattern is not generally reflective of the specific PCA-derived pattern (i.e., plant-based, Western, or health-conscious), and positive values indicate that an individual’s dietary pattern is generally reflective of the specific PCA-derived pattern.

**TABLE 1** Quantification of quintile dietary scores for each individual within the NutriGen Alliance cohort

Step	Description
1. Identify characteristic food groups for each diet	Identify the food groups in each dietary pattern that load most strongly (i.e., $\geq 0.30$ ) and characterize them (e.g., "processed meat" for the Western diet; see Supplemental Table 5).
2. Assign quintile scores for consumption frequency	Convert the serving frequencies for each characteristic food group to quintiles, from 1 to 5. This will give individuals in the lowest (<20%) and highest ( $\geq 80\%$ ) consumption frequencies for any food group a score of 1 and 5, respectively.
3. Calculate the participant quintile diet score for each diet	For each diet, sum the quintile scores of the foods that characterize the diet (identified in step 1). For foods that are inversely associated with a diet (e.g., "meat" in the "prudent" diet), individuals with a quintile score of 1, 2, 3, 4, or 5 would receive 5, 4, 3, or 2 points or 1 point, respectively, for that food group for that diet. When complete, each participant will have a total quintile score for each of the diets identified (e.g., plant-based, Western, and "health-conscious").
4. Calculate the maximum quintile score for each diet	Multiply the total number of characteristic foods for each diet by 5. This is the maximum score for that diet. For example, the plant-based diet has 10 characteristic food groups; multiplied by 5 this gives a maximum score of 50 [e.g., 10 (food items) $\times$ 5 (maximum points for each food item) = 50 (maximum possible score)].
5. Determine relative adherence to dietary patterns	Divide each person's diet scores (step 3) by the maximum scores for each diet (step 4). This will reflect how closely each person's reported dietary patterns match each of the identified dietary patterns on a scale from 0% to 100%. For example, a person with scores of 34% plant-based, 75% Western, and 47% health-conscious would suggest that their diet is most similar to the Western pattern, with foods common to the prudent and health-conscious patterns consumed less frequently.

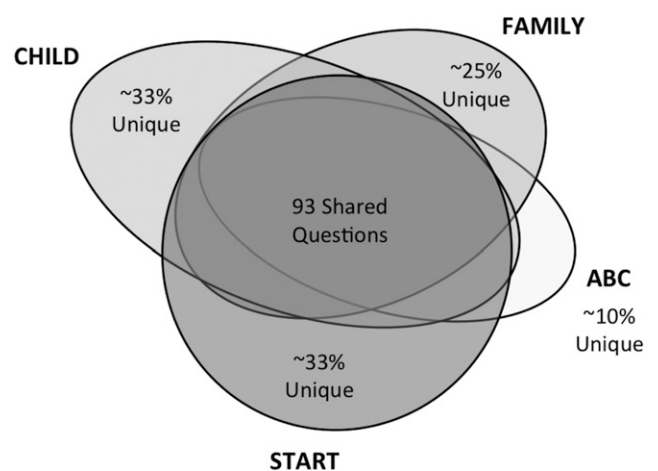
In a second PCA, indicators for each ethnicity were included in the PCA to estimate the effect of ethnicity on the derived dietary patterns (Supplemental Table 7). "Other vegetables" no longer loaded at  $\geq 0.30$  within the health-conscious dietary pattern, but the dietary patterns were equivalent to those observed in the original PCA reported in Supplemental Table 5. Univariate regression showed that the summary scores from the PCA that did not include ethnicity correlated strongly with the summary scores when ethnicity was included: plant-based ( $r^2 = 0.97$ ,  $P < 0.001$ ), Western ( $r^2 = 0.94$ ,  $P < 0.001$ ), and health-conscious ( $r^2 = 0.96$ ,  $P < 0.001$ ).

### Diet scores

The maximum adherence diet scores for the plant-based, Western, and health-conscious diets were 50, 65, and 70 total quintile points, respectively. Energy-adjusted PCA scores were well correlated with the energy-adjusted, quintile-based diet scores ( $r^2$  values: plant-based = 0.75,  $P < 0.001$ ; Western = 0.47,  $P < 0.001$ ; health-conscious = 0.51,  $P < 0.001$ ).

By using this scoring method, the plant-based diet had a mean adherence of 57.1%, the Western diet had a mean adherence of 58.6%, and the health-conscious diet had a mean adherence of 59.2% (Supplemental Table 8). There were clear differences between the 4 major ethnic groups (i.e., those with  $\geq 200$  participants) with respect to average dietary pattern scores. South Asians most closely adhered to the plant-based diet (mean  $\pm$  SD score:  $77.9\% \pm 12.5\%$ ), whereas East and South East Asians were least adherent ( $47.7\% \pm 10.3\%$ ). The Western diet was most strongly adhered to by Aboriginal people ( $63.3\% \pm 9.2\%$ ) and least strongly by South Asians ( $47.6\% \pm 9.5\%$ ). The health-

conscious diet was strongly followed by East or South East Asians ( $66.9\% \pm 9.2\%$ ) and least strongly adhered to by South Asians ( $51.5\% \pm 10.1\%$ ).



**FIGURE 1** Venn diagram of the similarity and differences between the food items queried within individual study cohorts (i.e., ABC, CHILD, FAMILY, and START) that comprise the NutriGen Alliance cohort ( $n = 4880$ ). Unlisted similarities of foods questioned between studies are  $\leq 10\%$  similar. ABC, Aboriginal Birth Cohort Study; CHILD, Canadian Healthy Infant Longitudinal Development Study; FAMILY, Family Atherosclerosis Monitoring In earlyLY life Study; START, South Asian birth cohort Study.

## Validation assessments

**Internal validity.** To assess the internal validity and robustness of the harmonized NutriGen dietary patterns, we also derived the patterns within each of the individual cohorts separately (ABC, CHILD, FAMILY, and START) and found that the cohort-specific dietary patterns reflected those of the harmonized NutriGen cohort. CHILD presented 2 primary diets: ovopescetarian (plant-based with fish and eggs) and Western; FAMILY presented 2 primary diets: health-conscious and Western; START presented 3 primary diets: plant-based, Western, and health-conscious; and ABC presented 2 primary diets: health-conscious and Western.

The unadjusted and energy-adjusted PCA summary scores were validated against the self-reported dichotomous variable “vegetarian status” (which included self-reports of lactovegetarians, ovovegetarians, vegetarians, and vegans). For the unadjusted PCA scores, a single-unit increase in the plant-based diet PCA score was associated with 3-fold greater odds of self-reporting as a “vegetarian” or being a nonconsumer of meat (OR: 3.35; 95% CI: 3.03, 3.68;  $r^2 = 0.26$ ,  $P < 0.001$ ), whereas a single-unit increase in either the Western (OR: 0.36; 95% CI: 0.31, 0.42;  $r^2 = 0.08$ ,  $P < 0.001$ ) or health-conscious (OR: 0.60; 95% CI: 0.53, 0.68;  $r^2 = 0.02$ ;  $P < 0.001$ ) diets were negatively associated with self-reported vegetarian status. For energy-adjusted PCA scores, the plant-based diet was similarly positively associated with self-reported vegetarian status (OR: 3.85; 95% CI: 3.47, 4.29;  $r^2 = 0.30$ ,  $P < 0.001$ ), and both the Western (OR: 0.29; 95% CI: 0.24, 0.34;  $r^2 = 0.08$ ,  $P < 0.001$ ) and health-conscious (OR: 0.67; 95% CI: 0.59, 0.75;  $r^2 = 0.01$ ,  $P < 0.001$ ) diets were negatively associated with self-reported vegetarian status.

**External validity.** Individuals in the lowest (least healthy) mAHEI quartile had a lower adherence to the plant-based (mean diet score:  $35.8\% \pm 7.9\%$  in quartile 1 compared with  $81.8\% \pm 11.2\%$  in quartile 4;  $r^2 = 0.81$ ,  $P < 0.001$ ) and health-conscious ( $41.8\% \pm 8.7\%$  in quartile 1 compared with  $56.0\% \pm 13.6\%$  in quartile 4;  $r^2 = 0.23$ ,  $P < 0.001$ ) dietary patterns than those in the highest (most healthy) mAHEI quartiles (Supplemental Figure 1). Individuals in the lowest mAHEI quartile adhered more strongly to the Western dietary pattern ( $57.7\% \pm 12.9\%$  in quartile 1 compared with  $52.9\% \pm 15.0\%$  in quartile 4;  $r^2 = 0.02$ ,  $P < 0.001$ ) than those in the highest mAHEI quartile.

## Discussion

This study describes, to our knowledge, a novel application of a methodologic approach to harmonize dietary data collected with cohort-specific, independently validated FFQs across 4 ethnically diverse birth cohorts. This effort represents an exemplar readily extensible to settings outside of Canada. Such harmonization efforts are increasingly common (50) for other types of data, and directed criteria and guidelines have been developed (i.e., PhenX Toolkit, available from: <https://www.phenxtoolkit.org>) to facilitate the pooling of maternal and infant data across birth cohorts (51).

We identified 3 unique dietary patterns, which we named “plant-based,” “Western,” and “health-conscious,” that closely resemble previously documented patterns in a cohort of the Toronto Nutrigenomics and Health Study, a multiethnic cohort of young Canadian men and women residing in the Greater Toronto area ( $n = 1153$ ) (52). In this study, 3 patterns—prudent, Western, and Eastern—were identified by using a single semiquantitative

FFQ and explained 16% of the dietary variance, which is less than the 29% that our harmonized analysis explained. Although dietary pattern studies typically identify 2 major dietary patterns (14, 15, 53), the similarity of the NutriGen and Toronto Nutrigenomics and Health Study dietary patterns likely reflects a similar ethnic composition of the cohorts.

In the present study, we faced the challenge of post hoc harmonization. An excellent example of forward thinking on harmonization is provided by the merger of FFQ data collected from 2 birth cohorts: the Danish National Birth Cohort (DNBC;  $n = 70,183$ ) and the Norwegian Mother and Child Cohort Study (MoBa;  $n = 87,000$ ) (54). Despite some unique regional items within each FFQ, food items were comparable and aggregated into common higher-order food groups (e.g., fruit, legumes, etc.). The harmonization was aided by a high degree of ethnic homogeneity and cooperation between the DNBC and MoBa study teams during MoBa’s development, which facilitated the development of an FFQ that was very similar to the DNBC FFQ. Nevertheless, we show that retrospective harmonization across diverse ethnic cohorts is possible (27). Furthermore, we were well powered to detect small differences (i.e., 3–4%) in dietary pattern adherence, even within ethnic groups in which one may expect homogeneity of dietary intakes (Supplemental Table 8).

The NutriGen Alliance dietary patterns showed good internal and external validity. The plant-based score was strongly associated with self-reported vegetarian status, although even this association is likely diluted because “vegetarian” was inconsistently defined across the cohorts: for example, in the CHILD cohort, pregnant women “reported abstinence from meats,” whereas in the FAMILY, START, and ABC cohorts a “vegetarian” status question was asked. A single-unit increase in the plant-based score increased the odds of being a vegetarian (i.e., non-meat eater) by >3-fold; conversely, a unit increase in the Western diet reduced these odds by ~70%. The health-conscious diet score was less useful at predicting vegetarian status: a single-unit increase reduced the likelihood of vegetarian status by ~40%. Our analyses suggest that 3 dietary patterns can accurately discriminate between groups who consume distinct dietary patterns (i.e., vegetarians from non-vegetarians).

Our external validation against the mAHEI (46), which has been used previously to assess diet quality in pregnant women (55), found that mAHEI score was associated with greater adherence to the plant-based and health-conscious dietary patterns and lower adherence to the Western diet, which confirms alignment of our dietary patterns with external methods for assessing diet quality. Total energy was adjusted for in the analysis to reduce confounding and random error due to differences in food intake resulting from differences in body size, metabolic efficiency, and physical activity. In some studies, it may be desirable to not account for energy if excess food energy is causally implicated in the relation between certain foods or diets and specific outcomes (e.g., when modeling the association between high-energy sugar-sweetened beverages and obesity). However, it is often desirable to isolate the effect of a specific food item or nutrient from its unspecific contribution to total energy intake when assessing diet-disease associations (e.g., the unique contribution of *trans* fat from other energy-containing nutrients of the foods in which it is contained). In a comparison of dietary patterns derived with and without energy adjustment, Northstone et al. (43) found that “white bread” was positively loaded on the “processed diet” in an unadjusted model but, after energy-adjustment, was negatively loaded for the “health-conscious diet.” Balder et al. (56) proposed that, in an energy-adjusted model, the avoidance of high-energy foods in favor of

low-energy healthy alternatives (i.e., choosing lower-energy-dense brown bread rather than high-energy-dense white bread) is a salient feature of “health-conscious” diets; therefore, energy-unadjusted and -adjusted models characterize similar dietary patterns and are therefore comparable. In the present study, the likelihood of vegetarian status according to participant plant-based, Western, and health-conscious dietary pattern scores were comparable in unadjusted and energy-adjusted models. It has been recommended that energy adjustment be performed post-PCA (43, 56) to simplify the interpretation of the results.

A salient feature of our cohort was its ethnic diversity. Downstream dietary pattern analyses within diverse cohorts often require adjustment for ethnicity (16, 57), which is most often accomplished by including ethnicity as a covariate in multivariable models. An alternative approach is to include ethnicity in the PCA when deriving dietary patterns, which would help account for the tight conceptual linking of diet and culture. In the present study, including ethnicity in the PCA only marginally affected the dietary patterns (Supplemental Table 7), and these dietary pattern scores derived with ethnicity correlated strongly with those derived without including ethnicity in the PCA ( $r^2 \geq 0.94$ ). However, adjusting for ethnicity in the PCA makes it impossible to assess whether the associations between dietary patterns and health outcomes are modified by ethnicity. Thus, leaving ethnicity out of the PCA derivation of dietary patterns gives maximum flexibility to the researcher in future analyses of dietary patterns and health outcomes.

We developed a diet score to simplify the interpretation of the dietary patterns. Individual summary scores for each principal component reflect how closely each person follows a given dietary pattern (e.g., prudent, Western, and health-conscious), but factor loading scores are difficult to interpret because the score and the range of scores vary across dietary patterns. However, by only focusing on foods that contribute strongly to each dietary pattern (i.e., “cardinal features” with loading scores  $\geq 0.30$ ) and by calculating a diet score ranging from 1% (minimal adherence) to 100% (full adherence) for each of the diets, the dietary patterns scores have the straightforward interpretation of how closely dietary habits reflects each of the empirically derived plant-based, Western, and health-conscious diets. Because this intuitive approach loses little information, and there is a strong correlation between diet scores and PCA scores, the derived dietary scores can be used in place of the summary scores for regression analyses for easier interpretability and presentation of results.

Our study has some limitations. Maternal diet was collected by using a single administration of a self-completed FFQ. Although these instruments have been validated, recall bias and measurement error are acknowledged limitations of these tools. However, given the prospective nature of our planned analyses (i.e., the association between maternal food choices and future maternal and infant health) and the large number of individuals involved, we anticipate that random error will be comparable to other prospective cohort studies that have used this method of assessment. This problem can be attenuated if multiple measures of diet are available (58). In addition, scree plots identified 3 patterns—with eigenvalues  $>3.0$  each that collectively explained 29% of the dietary variability—of several possible patterns detected by the PCA. Minor patterns, which explain a smaller degree of variation, were not retained. Future studies may need to increase the number of dietary patterns to characterize less-common dietary patterns in their study population of interest. We addressed the issue of reverse confounding such that a pre-existing medical condition, such as prepregnancy diabetes or

hypertension, may influence dietary intake in pregnancy by conducting a sensitivity analysis in those women with type 2 diabetes or hypertension. Our analyses showed that, within each subgroup, the PCA-derived dietary patterns did not differ substantially from each other or from our patterns derived by using the complete sample. In addition, although nutrients were not the focus of the present study, future analyses in these 4 harmonized birth cohorts that focus on macro- and micro-nutrient analyses will require harmonization of the nutrient data when different nutrient databases were used.

In conclusion, this study addressed a novel challenge, the merging and harmonization of multiple FFQ data sets collected from pregnant women of diverse ethnicities with the use of an established methodology for dietary pattern analysis. We showed a valid approach to merge both similar and distinct FFQ data sets to investigate how maternal diet during pregnancy contributes to maternal and infant health and disease.

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