Evaluation of Preconception Dietary Patterns in Women Enrolled in a Multisite Study

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ABSTRACT

Background: Diet indices are widely used in nutritional research across communities but do not "capture" the full extent of diet variability across multiple countries. Empirically derived dietary patterns can provide additional information because they reflect combinations of foods potentially associated with health outcomes. Limited studies have evaluated preconception dietary patterns in heterogeneous populations.

Objectives: In the multisite Nutritional Intervention Preconception and During Pregnancy to Maintain Healthy Glucose Metabolism and Offspring Health (NiPPeR) study, the secondary aims included: *1)* derive pooled and site-specific preconception dietary patterns, and 2) evaluate these patterns using anthropometric measures and metabolic biomarkers.

Methods: Women planning pregnancy (*n* = 1720) in the United Kingdom, Singapore, and New Zealand completed interviewer-administered harmonized FFQs and lifestyle questionnaires at recruitment. Across-cohort ("pooled") and site-specific dietary patterns were derived, and associations between dietary pattern scores and BMI, waist-to-hip ratio, plasma lipids, and glycemia assessed using multivariable linear regression, expressing results as SD change in outcome per SD change in dietary pattern score.

Results: The pooled analysis identified 3 dietary patterns: "Vegetables/Fruits/Nuts" ("Healthy"), "Fried potatoes/Processed meat/Sweetened beverages" ("Less Healthy"), and "Fish/Poultry/Noodles/Rice" ("Mixed"). The "Healthy" and "Less Healthy" pooled pattern scores were highly correlated with their corresponding site-specific dietary pattern scores ("Healthy": ρ = 0.87–0.93; "Less Healthy": ρ = 0.65–0.88). Women with higher scores for the "Healthy" pooled pattern had a lower waist-to-hip ratio (standardized β: −0.10; 95% CI: −0.18, −0.01); those with higher scores for the "Less Healthy" pooled pattern had a higher BMI (standardized β: 0.17; 95% CI: 0.09, 0.24), higher LDL cholesterol (standardized β: 0.10; 95% CI: 0.01, 0.19), and less optimal glucose profiles. However, we noted higher adherence to the "Healthy" pooled pattern with higher BMI.

Conclusions: The "Healthy" and "Less Healthy" pooled patterns were comparable to the corresponding site-specific patterns. Although the associations between these patterns and objective anthropometric/metabolic measures were largely in the expected directions, future studies are required to confirm these findings. This trial is registered at clinicaltrials.gov (NCT02509988). *Curr Dev Nutr* 2022;6:nzac106.

Introduction

Unlike diet quality indices, comparing exploratory (data-driven) dietary patterns across multiple countries or ethnic groups is more complex (1). Nevertheless, these exploratory dietary patterns remain informative because they provide insights into existing overall diets that could be associated with health outcomes (2, 3). Several studies involving healthy adults (4), the elderly (5), and pregnant women (6) have adopted harmonization methods to enable generalizable exploratory dietary patterns to be defined across various countries or study populations. However, it remains uncertain whether the harmonized patterns adequately represent the populations in question and whether harmonizing these patterns will result in the loss of site-specific dietary information. This led 1 study to internally validate the harmonized "plant-based" exploratory dietary pattern against self-reported vegetarian status, and externally validate the harmonized pattern against the modified Alternative Healthy Eating Index (6). To date, harmonized exploratory dietary patterns have mostly been evaluated using subjective self-reported measures (6) or have yet to be evaluated when they were generated using data from validated country- or site-specific FFQs (4, 5).

Biomarkers have been commonly used in validating dietary patterns in single population studies (7). For example, whereas increasing adherence to the "Healthy"/"Prudent" patterns tended to be associated with more favorable metabolic biomarker profiles (2, 8–12), increasing adherence to the "Less Healthy"/"Western" patterns was associated with less favorable biomarker profiles (8, 11–13). Biomarkers have the benefit of being objective because they are unaffected by self-reporting bias (7). Additionally, they have been shown to reveal ethnic-specific differences in associations between diet and health outcomes, likely due to biological differences in metabolism or the subtle differences in diets across ethnic groups (2, 9). To our knowledge, biomarkers have not previously been used for validating harmonized dietary patterns in women planning pregnancy. Given the emerging evidence on the links between preconception nutrition and subsequent pregnancy/offspring health outcomes, studies examining dietary patterns during the preconception phase are of interest (14, 15).

We leveraged a multisite preconception study, the NiPPeR (Nutritional Intervention Preconception and During Pregnancy to Maintain Healthy Glucose Metabolism and Offspring Health) study, to harmonize baseline dietary data from women planning pregnancy across 3 sites. Following this, we evaluated the derived harmonized (pooled) and site-specific dietary patterns using multiple objective measurements including anthropometric measures and metabolic biomarkers. Additionally, we evaluated whether the pooled dietary patterns led to the loss of site-specific dietary information and if these patterns adequately represent the populations in question. These are secondary outcomes of interest in the NiPPeR study.

Methods

Study design and participants

All information used for this study was collected at recruitment to the NiPPeR study, prior to start of any intervention. The NiPPeR study is a double-blind randomized trial that compared the effects of a standard nutritional drink with the effects of a nutritional supplement containing standard preconception/pregnancy micronutrients (folic acid, iron, calcium, iodine, β-carotene) with an enriched supplement (additionally containing *myo*-inositol, vitamin D, riboflavin, vitamin B-6, vitamin B-12, zinc, and the probiotics *Lactobacillus rhamnosus* and *Bifidobacterium animalis* spp. *lactis*). The primary outcome was the maintenance of healthy glucose concentrations during pregnancy (16).

Participants were healthy women, aged 18–38 y, who were planning pregnancy in Southampton, United Kingdom (UK), Singapore (SG), or Auckland, New Zealand (NZ). Women were excluded if they: *1*) were already known to have diabetes (type 1 or type 2); *2*) were taking oral steroids or anticonvulsant medication; *3*) were seeking assisted fertility treatment (apart from clomiphene and letrozole); *4*) were taking hormonal contraceptives; *5*) were seeking treatment for HIV or hepatitis B or C in the past month; or *6*) had known serious food allergies. Further details of the NiPPeR trial have been published elsewhere (16). Standardized protocols for data and sample collection were applied across sites.

The NiPPeR study has been granted ethical approval by the Research Ethics Committees at each of the 3 study sites: Health Research Authority NRES Committee South Central Research Ethics Committee (REC), reference 15/SC/0142 (United Kingdom); the Health and Disability Ethics Committee (HDEC), reference 15/NTA/21 (New Zealand); and the National Healthcare Group Domain Specific Review Board (NHG DSRB), reference 2015/00205 (Singapore). The trial is an academic-led study registered at clinicaltrials.gov (NCT02509988), Universal Trial Number U1111-1171-8056. Information sheets were provided to potential participants ahead of them being approached for consent by research staff. Participation was on a voluntary (unpaid) basis, and participants provided written informed consent for future use of their data in published research including the analyses described in this article. This study was conducted in compliance with the protocol, Good Clinical Practice, and the applicable regulatory requirements.

Dietary assessment

Validated semiquantitative FFQs for adults from the UK (100 item) (17), SG (92 item) (18), and NZ (83 item) (19) were harmonized for the NiPPeR study. This was done by comparing the items from the 3 FFQs and aligning them across sites. Categorizing the FFQ items into either core or site-specific food groups produced a total of 41 core food groups that were largely similar across all 3 sites (**Supplemental Table 1**). FFQ items that were unique to each site or to only 2 sites were also identified and

grouped into site-specific food groups. In total, there were 51, 47, and 53 food groups belonging to the UK, SG, and NZ FFQs, respectively. This classification process and the administration approach of the FFQs were discussed and agreed by the investigators from all 3 sites prior to the dietary assessment. Further details can be found in the **Supplemental Text**.

Across all 3 sites, usual dietary intakes during the month preceding enrollment were assessed using the harmonized semiquantitative FFQs, which were administered in-person by trained research staff. For each food item, participants were asked to indicate their frequency of consumption in an open-ended format (with options of Never, Frequency per month, Frequency per week, or Frequency per day) of standard portions of foods and beverages. Subsequently, responses for all FFQ line items were standardized to daily intakes. Total daily energy intakes were calculated for each participant using site-specific food composition databases to accommodate the distinct aspects of the site-specific food items. The exclusion of dietary misreporting using energy intakes was discussed and agreed by all investigators. The lower limit (500 kcal) was based on existing literature (20), whereas the upper limit (7000 kcal) was based on energy intakes of obese women enrolled in the Healthy Mums and Babies (HUMBA) trial (A Brown, unpublished results, 2019) (21).

Sociodemographic and lifestyle factors

Trained research staff conducted in-person interviews with enrolled participants following recruitment. Information including sociodemographic (e.g., age, annual household income) and lifestyle behaviors (e.g., alcohol consumption, smoking status, physical activity, and sedentary behaviors) were collected. Ethnicity was categorized into 5 groups: White, Chinese, Malay, South Asian, and a fifth "Other ethnicity" group (including Polynesians, Blacks, and other Asians). Participants were asked about the number of days they engaged in moderate and vigorous physical activity in the past 7 d. Additionally, participants also reported the number of days and average amount of time spent on sedentary behaviors (sitting time at leisure, viewing television, and use of electronic devices in the past 7 d and sitting time at work in an average working day). Total sitting time was derived as the total daily time spent sitting at work and sitting at leisure for the past week. Total screen time was derived as the total daily time spent on viewing television and using electronic devices for the past week.

Anthropometric and metabolic measures

During the first preconception visit, weight (Seca 899 scales) and height (Leicester height measure) were measured to the nearest 0.1 kg and 0.1 cm, respectively, for calculation of BMI (in kg/m^2), together with measurements of waist and hip circumferences (centimeters), used for calculation of waist-to-hip ratio. Anthropometric measures were taken in triplicate and the mean value for each measure was recorded.

Plasma glucose (fasting, 30-min, and 120-min) in a 75-g oral glucose load tolerance test and glycated hemoglobin (HbA1c) were measured by a single laboratory at each site, with uniform external quality assurance as per the Royal College of Pathologists of Australasia Quality Assurance Program. Serum concentrations of fasting insulin, high-sensitivity C-reactive protein (hs-CRP), and fasting plasma lipids (triglycerides, HDL cholesterol, and LDL cholesterol) were batch analyzed in a single laboratory (cobas; Roche Diagnostics). The updated homeostasis model assessment for insulin resistance (HOMA2-IR) was calculated using fasting plasma glucose and fasting serum insulin (22).

Statistical analyses

Derivation of pooled and site-specific dietary patterns.

Factor analysis was used to derive the underlying preconception dietary patterns. The Kaiser–Meyer–Olkin measure of sampling adequacy and Bartlett test of sphericity were first performed to determine if the data were suitable for factor analysis (23). Varimax rotation was next performed to ensure that the factors derived were independent of one another and to improve factor interpretability (24). The choice of the number of factors to retain was based on the break point of the scree plot, an eigenvalue >1, and factor interpretability. Factor loadings, estimated using the principal factor method, are the correlation coefficients of each food group and the derived dietary pattern; hence, higher factor loadings indicate a greater contribution of a particular food group to that derived pattern. For simplicity, only food groups with factor loadings ≥0.25 were presented. Subsequently, dietary pattern scores for each participant were calculated by summing the standardized intake of food groups (frequency/day) weighted by their regressed factor loadings, giving each participant a score for each derived pattern. A higher dietary pattern score to a specific dietary pattern indicates greater adherence to that derived pattern. The measures of suitability of data for factor analysis and scree plots of the pooled and site-specific dietary pattern analyses are shown in **Supplemental Figure 1**.

Two sets of dietary pattern analyses were conducted: 1) pooled analysis using FFQs from all 3 sites and based on the 41 core food groups; and 2) site-specific analyses using FFQs from each site and based on all food groups, including site-specific food groups. Unlike existing studies, which typically use a single approach—either a pooled dietary pattern analysis (using the same number of harmonized food groups) or a study-specific dietary pattern analysis (using a different number of food groups for each study) —we decided to use both approaches. This enabled us to examine 1) if harmonizing patterns led to the loss of site-specific information, and 2) if the harmonized (pooled) patterns adequately represent the populations in question by calculating Spearman correlations between the pooled and site-specific dietary pattern scores.

Evaluation of the pooled and site-specific dietary patterns.

Each anthropometric and metabolic measure was first log$_e$ transformed to achieve an approximately normal distribution. To allow comparisons across these objective measures, these transformed values were then standardized before further analyses. Multivariable linear regression models were used to examine the associations between dietary pattern scores and each anthropometric and metabolic measure. The models were adjusted for site (only for pooled patterns), ethnicity, daily energy intakes, highest educational attainment, smoking status, parity, days of moderate and vigorous physical activity, and family history of diabetes, along with mutually adjusting for other dietary patterns. In the models involving anthropometric measures (BMI and waist-to-hip ratio), they were mutually adjusted for in the analyses. For example, when examining the associations between dietary pattern scores and BMI,

Table 1 Characteristics of 1720 women planning pregnancy in the NiPPeR cohort at baseline[1]

	All	UK	SG	NZ
Number of women	1720	460	660	600
Age ± SD,[2] y	31 ± 4	30 ± 4	31 ± 4	31 ± 4
BMI ± SD,[2] kg/m^2	26 ± 6	27 ± 6	24 ± 6	27 ± 7
Overweight/obese, %	51.7	55.7	50.0	50.4
Ethnic origin, %				
White	46.9	93.9	—	62.5
Chinese	26.7	0.2	63.0	7.0
South Asian (Indian, Pakistani, Bangladeshi)	7.0	2.4	8.3	9.2
Malay	9.5	0.2	24.7	—
Other (Polynesians, Blacks, and other Asians)	9.8	3.3	3.9	21.3
Nulliparous, %	68.0	65.4	65.9	72.2
Bachelor's degree and above, %	61.9	50.9	60.3	72.0
Household income quintiles, %				
Q1 + Q2 (lowest income bracket)	17.4	7.1	32.0	8.9
Q3	22.0	15.4	28.8	19.7
Q4 + Q5 (highest income bracket)	60.6	77.5	39.2	71.5
Current smoker, %	7.3	9.8	6.8	5.8
No alcohol consumption in past 3 month, %	31.1	15.9	53.8	17.8
Instances of moderate or vigorous physical activity in the past week,[3] d/wk	3 (2, 5)	3 (1, 5)	2 (1, 5)	4 (2, 6)
Daily total screen time in the past week,[3] h	3 (2, 4)	3 (2, 4)	3 (2, 4)	3 (2, 4)
Daily total sitting time in the past week,[3] h	7 (3, 8)	6 (3, 8)	7 (4, 9)	6 (4, 8)
Estimated daily energy intake,[3] kcal	1955 (1593, 2425)	1853 (1570, 2221)	1850 (1476, 2339)	2158 (1788, 2671)

[1]Missing values for BMI ($n = 3$), overweight/obese were based on Asian BMI cutoffs for SG participants and non-Asian BMI cutoffs for UK and NZ participants. For Asians (including Chinese, Indians, Pakistani, Bangladeshi, Malay, mixed Asian), BMI ≥23 to <27.5 was defined as overweight and BMI ≥27.5 was defined as obese. For non-Asians (including white Caucasian, Polynesian, black, mixed Asian–non-Asian), BMI ≥25 to <30 was defined as overweight and ≥30 was defined as obese. Household income quintiles ($n = 117$); current smoker ($n = 4$); instances of moderate/vigorous physical activity ($n = 10$); daily total screen time ($n = 17$); daily total sitting time ($n = 12$). NiPPeR, Nutritional Intervention Preconception and During Pregnancy to Maintain Healthy Glucose Metabolism and Offspring Health; NZ, New Zealand; Q, quintile; SG, Singapore; UK, United Kingdom.
[2]Values presented are mean ± SD.
[3]Values presented are median (25th percentile, 75th percentile).

waist-to-hip ratio was included as a covariate. This was performed because for any given BMI there could be differences in abdominal adiposity, which can be accounted for by adjusting for waist-to-hip ratio in the model (25). Additionally, studies have shown that adjusting for BMI is useful when examining the association between abdominal adiposity (measured by waist circumference) and morbidity (25).

The standardized β estimates and their corresponding P values (denoted by asterisks) of these models were visualized using heat maps for ease of comparison across the pooled and site-specific dietary patterns. All analysis was performed using Stata 14.2 (StataCorp LLC), and heat maps were produced using the package *ggplot2* in R (R Foundation). Statistical tests were 2-sided, and P values <0.05 indicated statistical significance.

Results

Of the 1729 women recruited, 9 were excluded due to missing dietary data ($n = 1$) or implausible daily energy intakes of <500 kcal/d or >7000 kcal/d ($n = 8$), leaving 1720 women for the subsequent analyses (**Supplemental Figure 2**).

Characteristics of the participants
The characteristics of NiPPeR participants across the 3 sites are shown in **Table 1**. Of the 1720 women, 46.9% were of White ethnicity, 26.7%

of Chinese ethnicity, and the remainder from the other 3 ethnic groups. The mean age of the women was 31 y and close to half of the women were overweight or obese (51.7%). The majority of the women have higher education qualifications (61.9%), were from higher income households (60.6%), were nulliparous (68.0%) and only a small proportion of women were current smokers (7.3%) (Table 1).

Pooled and site-specific preconception dietary patterns
Based on the pooled analysis, 3 pooled dietary patterns were identified: "Vegetables/Fruits/Nuts" (referred to as "Healthy" subsequently), "Fried potatoes/Processed meat/Sweetened beverages" (referred to as "Less Healthy" subsequently), and "Fish/Poultry/Noodles/Rice" (referred to as "Mixed" subsequently) (**Table 2**). The pooled "Healthy" pattern was characterized by higher intakes of a variety of vegetables (including salad), a variety of fruits and nuts, but lower intakes of rice and noodles/pasta (**Table 3**). The pooled "Less Healthy" pattern was characterized by higher intakes of chips and fries, processed meat, sweetened beverages, and white bread (**Table 4**). The pooled "Fish/Poultry/Noodles/Rice" pattern was characterized by higher intakes of oily fish, white fish, poultry, leafy vegetables, eggs, noodles/pasta, and rice. The common variances explained by these 3 patterns were 46%, 23%, and 18%, respectively.

Based on site-specific analyses, 3 major dietary patterns were also observed at each site (Table 2). For simplicity, these site-specific patterns were referred to as "Healthy", "Less Healthy", and "Mixed"

Table 2 Characteristics of pooled and site-specific dietary patterns in the NiPPeR cohort[1]

	Pooled analysis[2]	UK[3]	SG[3]	NZ[3]
n	1720	460	660	600
Number of food groups	41	51	47	53
Number of factors	3	3	3	3
Sum of common variance explained by 3 factors, %	87	52	69	56
Dietary patterns identified				
"Healthy" pattern	Vegetables/Fruits/Nuts	Vegetables/Nuts/Fruits	Vegetables/Nuts/Fruits	Vegetables/Nuts/Fruits
"Less Healthy" pattern	Fried potatoes/Processed meat/Sweetened beverages	Processed meat/Red meat/Sweetened beverages	Fried foods/Processed meat/Sweetened beverages	Processed meat/Red meat/International takeaways/Sweetened beverages
"Mixed" pattern	Fish/Poultry/Noodles/Rice	Pastries/cakes/Fried potatoes/Confectionery	Fish/Red meat/Mushroom/Noodles	Fried snacks/Dried/canned/ citrus fruits/Fruit juices

[1]NiPPeR, Nutritional Intervention Preconception and During Pregnancy to Maintain Healthy Glucose Metabolism and Offspring Health; NZ, New Zealand; SG, Singapore; UK, United Kingdom.
[2]Pooled analysis includes participants from UK, SG, and NZ. Forty-one core food groups that included only foods common to all 3 countries were used for deriving dietary patterns.
[3]Site-specific food groups were added to the analysis on top of the 41 core food groups, resulting in 51, 47, and 53 food groups for UK, SG, and NZ.

subsequently. The "Healthy" patterns were "Vegetables/Nuts/Fruits" in all 3 countries (Table 3). The "Less Healthy" patterns were: UK "Processed meat/Red meat/Sweetened beverages"; SG "Fried foods/ Processed meat/Sweetened beverages"; and NZ "Processed meat/Red meat/International takeaways/Sweetened beverages" (Table 4). The third pooled and site-specific patterns were collectively known as "Mixed" pattern due to the heterogeneity observed across these site-specific patterns. In SG, an Asian-like diet ("Fish/Red meat/ Mushroom/Noodles") was identified; diets made up of discretionary foods were identified in the UK ("Pastries/Cakes/Fried potatoes/ Confectionery") and NZ ("Fried snacks/Dried/canned, Citrus fruits/Fruit juices"). Factor loadings of the food groups that made up these site-specific "Mixed" patterns are shown in **Supplemental Table 2**.

The pooled "Healthy" and "Less Healthy" pattern scores had moderate to strong correlations with the site-specific "Healthy" ($\rho = 0.87$–0.93) and "Less Healthy" ($\rho = 0.65$–0.88) dietary pattern scores, respectively (**Supplemental Table 3**). The pooled "Mixed" pattern score was strongly correlated to the SG "Mixed" score but correlated weakly with the UK "Mixed" and NZ "Mixed" scores.

Evaluation of the pooled and site-specific dietary patterns
Women with increasing adherence to the pooled "Healthy" pattern had a higher BMI but a lower waist-to-hip ratio (**Figure 1**). These findings were mirrored by significant associations of increasing adherence to the UK "Healthy" pattern with higher BMI and increasing adherence to the SG "Healthy" pattern with a lower waist-to-hip ratio. No significant associations were observed between the pooled or site-specific "Healthy" patterns and fasting glucose, 30-min glucose, 120-min glucose, HbA1c, HOMA-IR, hs-CRP, and plasma lipids (**Supplemental Table 4**).

In contrast, women with increasing adherence to the pooled "Less Healthy" pattern had a higher 30-min glucose, HOMA2-IR, LDL cholesterol, and BMI (Figure 1). These associations were mirrored in the site-specific "Less Healthy" patterns, with slight variations in standardized coefficients and statistical significance. For example, women with increasing adherence to the UK "Less Healthy" pattern additionally had higher 120-min glucose and hs-CRP, and those with increasing

adherence to the "Less Healthy" SG pattern had higher concentrations of fasting glucose. Notably, a significant inverse association between the "Less Healthy" NZ pattern and HDL cholesterol was observed. No significant associations were observed between the pooled or site-specific "Less Healthy" patterns with HbA1c, triglycerides, and waist-to-hip ratio (**Supplemental Table 5**).

Women with increasing adherence to the pooled "Mixed" pattern were likely to have higher 120-min glucose concentrations (**Supplemental Figure 3**). In general, the associations observed for the site-specific "Mixed" patterns were unlike that of the pooled "Mixed" pattern. For example, whereas higher adherence to the UK "Mixed" pattern was significantly associated with higher HOMA2-IR and BMI, higher adherence to the SG "Mixed" pattern was associated with higher fasting, 30-min glucose concentrations, and BMI. Conversely, women with higher adherence to the NZ "Mixed" pattern had significantly lower 30-min glucose concentrations. No significant associations between the site-specific "Mixed" patterns were found for HbA1c, hs-CRP, plasma lipids, and waist-to-hip ratio (**Supplemental Table 6**).

Discussion

In this multisite study of women planning pregnancy, we identified 3 pooled dietary patterns ("Healthy," "Less Healthy," and "Mixed") using a harmonized approach. Three site-specific preconception dietary patterns each in the UK, SG, and NZ were identified, of which the "Healthy" and "Less Healthy" site-specific patterns were strongly correlated with the respective pooled patterns. In general, the associations between the pooled and site-specific "Healthy"/"Less Healthy" patterns with objective anthropometric and metabolic measures were in the expected directions. However, we noted higher adherence to the "Healthy" pooled and UK patterns with higher BMI and no significant association between the "Healthy"/"Less Healthy" pooled and site-specific patterns with other metabolic measures.

Pooled and site-specific preconception dietary patterns
Characterized by higher intakes of fruits and vegetables, the pooled "Healthy" pattern of the NiPPeR study appeared similar to healthy

Table 3 Factor loadings of food groups of the "Healthy" pooled and site-specific patterns[1]

	"Healthy" patterns			
	Pooled	UK	SG	NZ
Common variance explained, %	46	24	25	19
Food groups				
Salad	0.58	0.31	0.35	0.59
Root vegetables	0.56	0.47	0.53	0.52
Peas, green beans, legumes, and pulses	0.55	0.50	0.55	0.32
Other vegetables and gourds	0.52	0.49	0.39	0.52
Tomatoes	0.50	0.45	0.58	0.34
Bananas	0.49	—	0.39	—
Potatoes and starchy vegetables	0.46	—	0.42	0.34
Yoghurt	0.43	0.29	0.29	—
Cheese	0.42	—	—	0.26
Apples and pears	0.42	0.40	0.38	—
Grapes, berries, stone fruits, and tropical fruits	0.41	0.39	0.38	—
Nuts	0.38	0.40	0.46	0.35
Breakfast cereals	0.38	—	0.27	—
Citrus fruits and fruit juices	0.38	—	0.34	—
Leafy vegetables	0.34	0.68	0.48	0.57
Hot beverages	0.34	—	—	—
Dried and canned fruits	0.25	0.34	0.24	—
Noodles and pasta	− 0.27	—	—	—
Rice	− 0.42	—	—	—
White bread	—	− 0.30	—	—
Wholemeal/multigrain/brown bread	0.36	—	—	—
Eggs	—	0.44	—	0.34
Oily fish, white fish, shellfish, and other seafood	0.35	—	0.26	—
Onions (UK and NZ only)	0.46	—	0.26	—
Frying fats and oils (UK and NZ only)	0.31	—	—	—
Cream (UK and NZ only)	0.31	—	—	—
Gravy, stock, and seasonings (UK and NZ only)	0.30	—	—	—
Mushroom (UK and SG only)	0.28	—	—	—
Steamed snacks/dim sum/ethnic bread (SG and NZ only)	0.33	—	—	—
Avocado (NZ only)	—	—	—	0.25
Water (NZ only)	—	—	—	0.25

[1]Values are correlation coefficients between each food variable and the dietary pattern. For simplicity, only food groups with absolute values ≥0.25 are listed. NZ, New Zealand; SG, Singapore; UK, United Kingdom.

exploratory dietary patterns in women planning pregnancy in Australia and the United Kingdom (e.g., "Fruit and Low-fat Dairy" and "Prudent") (26, 27). In parallel, the pooled "Less Healthy" pattern of the NiPPeR study, which consisted mostly of foods high in fat, sugar, and refined carbohydrates (e.g., "Meat, High-fat & Sugar," and "High-fat/sugar/takeaway") was similarly observed in Australian, Spanish, and Canadian women planning pregnancy (14, 26, 28, 29). Additionally, the pooled "Healthy" and "Less Healthy" patterns were also largely similar to the site-specific "Healthy" and "Less Healthy" patterns, respectively. This suggests that key dietary information was retained in the pooled dietary patterns.

Characterized by higher intakes of animal protein, typical staple foods (e.g., rice and noodles/pasta), leafy vegetables, and eggs, the pooled "Mixed" pattern in the NiPPeR study shared similarities with patterns rich in vegetables, animal protein foods (e.g., "Vegetables and Meat" and "High-protein/fruit") consumed by women residing in Spain, Australia, and Brazil (14, 29, 30). Of note, the pooled "Mixed" pattern in the NiPPeR study was likely driven by the larger proportion of participants from SG, relative to UK and NZ participants. Clear differ-

ences among the "Mixed" site-specific patterns were observed on closer examination. Whereas the SG "Mixed" pattern was characterized by higher intake of animal proteins, fish, and a variety of vegetables, the UK and NZ "Mixed" patterns had higher intakes of energy-dense foods with refined carbohydrates. In addition, the NZ "Mixed" pattern was made up of food groups such as citrus fruits, fruit juices, and dried or canned fruits. These site-specific consumption patterns have been previously reported in other women of comparable age to those enrolled in the NiPPeR study [UK: "Snacking" (31), "Sugary foods, dairy" (32), and NZ: "Refined and processed," "Sweet and savoury snacking" (33)], reflecting the cultural and regional differences in intakes of specific foods.

Evaluation of the pooled and site-specific dietary patterns
Consistent with several studies examining the associations between exploratory dietary patterns and anthropometric measures (9–11), women with higher adherence to the pooled and site-specific "Healthy" patterns had a lower waist-to-hip ratio. Conversely, those with higher adherence to the pooled and site-specific "Less Healthy" patterns had

Table 4 Factor loadings of food groups of the "Less Healthy" pooled and site-specific patterns[1]

	"Less Healthy" patterns			
	Pooled	UK	SG	NZ
Common variance explained, %	23	15	23	22
Food groups				
Chips and fries	0.48	—	0.55	0.52
Crisps and savory snacks	0.45	0.36	0.41	0.35
Ham, bacon, sausage, and other processed meat	0.43	0.59	0.54	0.55
Sweetened beverages	0.37	0.27	0.36	0.36
Pastries and cakes	0.36	—	0.51	—
Chocolate	0.35	0.29	0.35	—
White bread	0.34	—	0.33	0.46
Pizza	0.33	—	0.33	0.50
Other meats (pork, lamb, beef)	0.31	0.43	—	0.53
Sweet biscuits and cookies	0.29	0.34	—	0.29
Potatoes and starchy vegetables	0.28	—	—	0.37
Poultry	—	0.34	—	0.36
Salad	—	0.33	—	—
Diet drinks	—	0.25	—	—
Other vegetables and gourds	−0.33	—	—	—
Tofu/beancurd/vegetarian foods	−0.46	—	—	—
Sweet and savory spreads	0.34	—	—	—
Ice cream	—	—	0.34	—
Savory biscuits and crackers	0.31	—	—	—
Sweet biscuits and cookies	0.30	—	—	—
Cheese	—	—	0.27	—
Noodles and pasta	—	—	0.45	—
Oily fish, white fish, shellfish, and other seafood	0.35	—	—	—
Buns	—	—	—	0.30
Liver and offal (UK and SG only)	0.35	—	—	—
Fried snacks/dim sum/ethnic bread (SG and NZ only)	0.57	—	—	—
Steamed snacks/dim sum/ethnic bread (SG and NZ only)	0.32	0.25	—	—
International takeaways (NZ only)	—	0.40	—	—
Sweets/candies (UK and NZ only)	—	0.27	—	—

[1]Values are correlation coefficients between each food variable and the dietary pattern. For simplicity, only food groups with absolute values ≥0.25 are listed. NZ, New Zealand; SG, Singapore; UK, United Kingdom.

a higher BMI. Contrary to expectations, increasing adherence to the pooled and UK "Healthy" patterns was associated with higher BMI. It is possible that intakes of energy-dense potatoes and starchy vegetables of the pooled "Healthy" pattern and intakes of dried and canned fruits and frying fats/oils of the UK "Healthy" pattern contributed to weight gain and hence a higher BMI observed (34, 35). With respect to the metabolic measures, women with higher adherence to the pooled and site-specific "Less Healthy" patterns had less favorable plasma glucose and lipid profiles and higher concentrations of hs-CRP, which has been reported by previous studies (8, 11). Women with higher adherence to these "Less Healthy" patterns generally have higher intakes of refined grains, sugary foods and drinks, and fried foods high in saturated and *trans* fat, contributing to a poorer glycemic and insulinemic response and higher levels of observed inflammation (8).

In contrast, differing associations were observed for the pooled and site-specific "Mixed" patterns, which are largely attributed to differences among these dietary patterns as aforementioned. Whereas the UK and SG "Mixed" patterns were associated with less favourable metabolic profiles (higher BMI, higher insulin resistance, fasting and 30-min glucose), the NZ "Mixed" was associated with lower 30-min glucose concentrations. This might reflect intakes of beans and legumes as part of the NZ

"Mixed" pattern that could have enhanced the glycemic and insulinemic response (36). Future diet-related investigations might explore whether these pooled and site-specific "Mixed" patterns play a role in subsequent maternal and child health outcomes.

Collectively known as metabolic risk biomarkers, the objective anthropometric and metabolic measures examined in this study are typically used to predict risk of chronic cardiometabolic diseases in individuals (37). Given this, the associations observed for the "Less Healthy" patterns were not unexpected because higher adherence to suboptimal diets are known to be associated with increased cardiometabolic risks (8). Taken together, the associations between the pooled "Healthy" and "Less Healthy" patterns were generally in the expected directions.

Strengths and limitations
Strengths of our study include combining previous harmonization methods to examine preconception diets as a whole and using multiple objective anthropometric and metabolic measures to strengthen our findings. Additionally, this study adds to the growing evidence on the overall diets of women planning pregnancy. However, this study was limited in several ways.
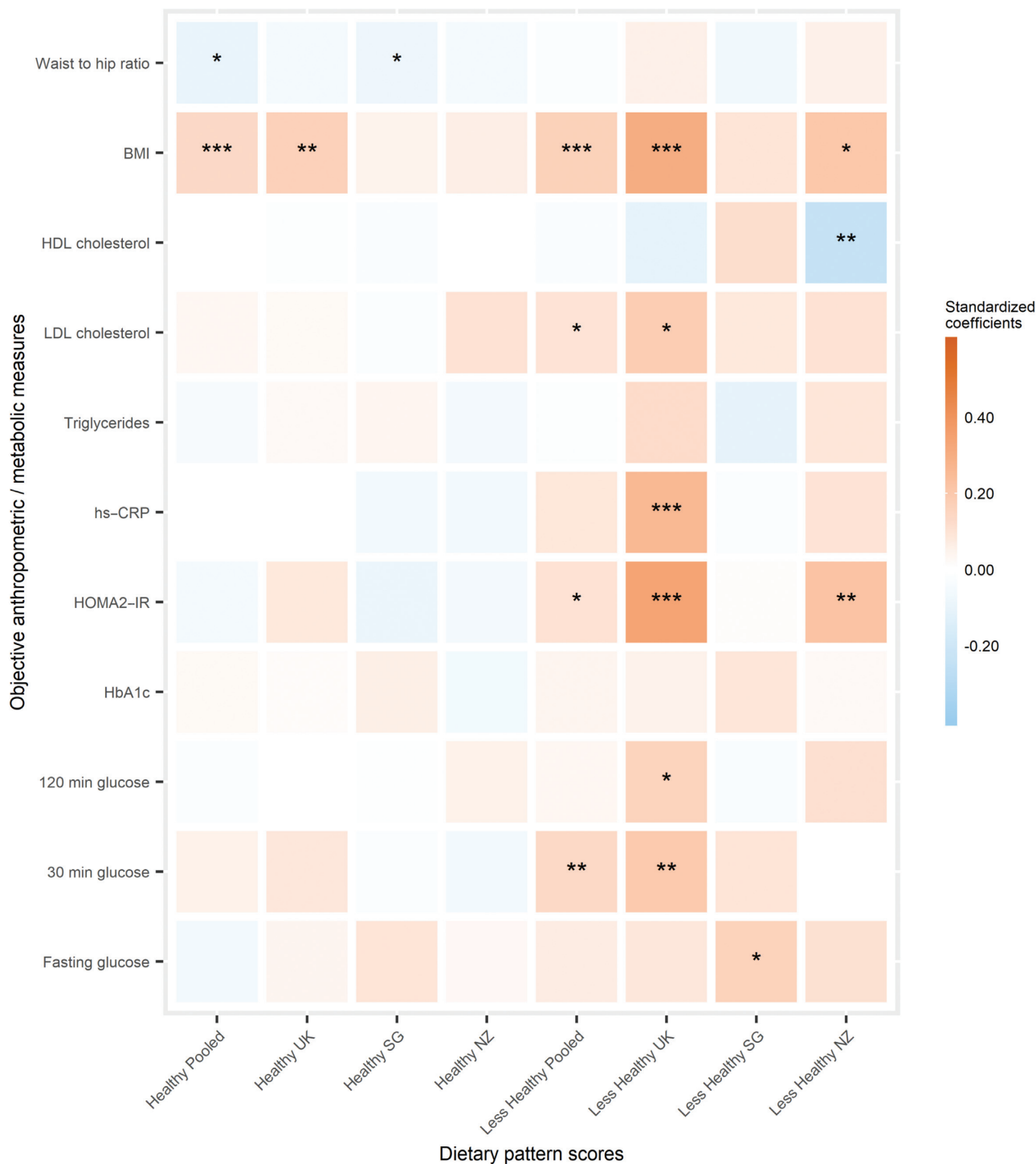
FIGURE 1 Visual representation of the cross-sectional associations between the pooled and site-specific "Healthy" and "Less Healthy" dietary pattern scores with objective anthropometric and metabolic measures. Cells with asterisks indicate that the standardized β coefficients were statistically significant: $*P < 0.05$; $**P < 0.01$; $***P < 0.001$. HbA1c, glycated hemoglobin; HOMA2-IR, updated homeostasis model assessment for insulin resistance; hs-CRP, high-sensitivity C-reactive protein; NZ, New Zealand; SG, Singapore; UK, United Kingdom.

First, self-reported food intakes, measured using FFQs, are prone to overestimation, as observed by several studies (38, 39). However, FFQs have been found to be useful in ranking participants' dietary intakes and are commonly used to examine habitual

dietary intakes and their associations with health outcomes (40, 41).

Second, due to the cross-sectional nature of this study, we were unable to ascertain temporal associations between preconception dietary

patterns and the objective anthropometric and metabolic measures. Nevertheless, except for BMI, the associations observed were in the expected directions and were consistent with previous studies. However, reverse causation could have occurred because approximately half of the participants in the NiPPeR study were either overweight or obese. Women with higher BMI could have consumed healthier diets to lose weight during the preconception period. For others who did not change their usual diets, it is expected that higher adherence to "Less Healthy" diets was associated with less favorable metabolic risk biomarker profiles (e.g., higher concentrations of hs-CRP).

Third, the NiPPeR study was not designed to recruit representative samples from each country. Despite this, the results presented here provide valuable insights into preconception dietary patterns across the 3 sites.

Fourth, information on the degree of pregnancy planning, which can be assessed using the London Measure of Unplanned Pregnancy (42), was not collected in this study. Women with a higher degree of pregnancy planning could have higher adherence to "Healthy" dietary patterns and thus have a more favorable anthropometric and metabolic profile.

Fifth, we noted that several food groups loaded in >1 dietary pattern. This is not unusual given the complexity of dietary intakes and highlights the importance of examining dietary patterns that consist of multiple food groups instead of single food groups in isolation. However, the cross-loading of foods on different patterns suggests that these dietary patterns should ideally be regenerated for the analytic sample of interest to fully represent their existing consumption patterns. Future studies could consider using diet indices, generated from a predefined list of foods and beverages, to complement findings from dietary patterns.

Conclusion and future research

Despite differences in country of residence and ethnicity, similar preconception "Healthy" and "Less Healthy" pooled and site-specific dietary patterns were identified. In general, these patterns have expected associations with objective anthropometric and metabolic measures, providing a basis for future diet-related investigations. However, future studies involving similar populations are required to confirm these findings.

Acknowledgments

Data Availability

A Trial Consultative Panel, comprising senior representatives from the academic institutions undertaking the study and the industry partner, has been set up and will consider associated studies requesting access to data and materials. The data underlying this article will be shared on reasonable request to the corresponding author.

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