Carbohydrate and fiber intake and the risk of premenstrual syndrome

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Abstract

Background/Objectives—Women with premenstrual syndrome (PMS) are encouraged to reduce sugar and increase fiber intake to reduce symptoms. However, research supporting these recommendations is limited, and their role in PMS development is unclear. This study examines the relation between carbohydrate and fiber intake and the risk of PMS nested within the prospective Nurses' Health Study II cohort.

Subjects/Methods—Carbohydrate and fiber intake were assessed at baseline and three additional times during follow-up by food frequency questionnaire. Incident cases of PMS were identified by self-reported PMS diagnosis during 14 years of follow-up and validated by supplemental questionnaire (n=1,234). Women were classified as controls if they did not report PMS diagnosis during follow-up and confirmed minimal or no premenstrual symptoms (n=2,426). We estimated relative risks (RR) and 95% confidence intervals (CI) using multivariable logistic regression.

Results—Total carbohydrate intake two to four years before reference year was not associated with PMS development (RR quintile 5 versus 1 = 0.99; 95% CI = 0.74-1.33). Intakes of specific carbohydrates or fibers were not associated with PMS development, except maltose. Adjusting for body mass index, smoking, and other factors, women with the highest maltose intake (median =
3.0 g/day) had a RR of 1.45 (95% CI = 1.11-1.88) compared to those with the lowest intake (median = 1.2 g/day).

Conclusions—Overall, carbohydrate and fiber consumption was not associated with risk of PMS. As this is the first study to suggest that maltose may be associated with PMS development, further replication is needed.

Keywords
Premenstrual syndrome; dietary carbohydrates; prospective studies; epidemiology

INTRODUCTION

Up to 20% of reproductive aged women meet clinical diagnostic criteria for premenstrual syndrome (PMS), (1,2) a cyclical menstrual disorder, where women experience physical and emotional symptoms during the late luteal phase of their menstrual cycle that abate within a few days following the onset of menses. While the etiology of PMS is still largely unknown, an interaction between hormonal, neural, genetic, psychosocial, and dietary factors likely contributes (3).

Because of the limited efficacy of pharmaceutical treatments for PMS, there is a need for identifying preventive and modifiable risk factors such as diet. Both the Association of Reproductive Health Professionals and the American Congress of Gynecology and Obstetrics suggest that women with PMS frequently consume small portions of complex carbohydrates, which are high in fiber, and reduce intake of sugar to improve symptom severity (4,5). However, these recommendations are based on limited empirical evidence (6). A few retrospective studies examining the relation between consumption of carbohydrates and premenstrual symptoms have reported inconsistent findings (7-9). Among retrospective studies, the temporality of carbohydrate intake versus PMS onset may be difficult to determine. Thus, it is unknown whether higher carbohydrate and sugar intake relative to complex carbohydrate and fiber intake contribute to PMS development, or instead reflects dietary changes in response to symptoms. No previous study has prospectively evaluated whether carbohydrate intake is associated with risk of developing PMS.

Therefore, we evaluated the relation between carbohydrate intake and the development of PMS in the Nurses’ Health Study II (NHS2) PMS Sub-Study, a case-control study nested within the prospective NHS2.

METHODS

Study Population

The NHS2 is a prospective cohort study that follows 116 429 female nurses aged 25-42 years at the first mailed questionnaire in 1989. Information on health-related behaviors and medical history have been updated biennially and diet quadrennially for over 25 years (10). Response rates have been at least 89% for all questionnaire cycles. The Institutional Review Board at Brigham and Women’s Hospital in Boston, MA approved the original NHS2 study protocol.
Classification of PMS cases and controls

The NHS2 PMS Sub-Study (10,11), includes a subset of premenopausal women free of PMS prior to baseline in 1991. Over 14 years of follow-up, 4,108 participants reported new clinician-made diagnoses of PMS and the diagnosis year was used as the reference year. Women that did not report a diagnosis of PMS during follow-up were randomly assigned a reference year between 1991 and 2005, of which 3,248 were frequency matched to cases based on age and reference years. To limit the possibility that PMS-like symptoms were due to another condition we excluded women with extremely irregular menstrual cycles or a history of cancer (except non-melanoma skin cancer), endometriosis, infertility, or hysterectomy prior to their reference year. Additionally, because of our interest in diet, those with implausible caloric intakes (i.e., those below 500 kcal and above 3,500 kcal) were also excluded (13). These potential cases and controls were mailed a modified version of the Calendar of Premenstrual Experiences questionnaire (11,12) assessing occurrence, timing, and personal impact of 26 premenstrual symptoms in the specified two-year period before their reference year to confirm case and control status (10).

PMS cases included 1,257 women who met clinical diagnostic guidelines for PMS. Specifically, case criteria included: 1) ≥1 physical and ≥1 emotional premenstrual symptoms; 2) an overall symptom severity of “moderate” or “severe” OR a “moderate” or “severe” effect of symptoms on at least one life activity or relationship; 3) symptoms begin ≤14 days prior to the onset of menses; 4) symptoms end ≤4 days after the onset of menses; and 5) no symptoms are present in the week after the end of menses (10). Controls included 2,463 women who had no or minimal symptoms that did not affect daily functioning. Control criteria included: 1) confirmed no PMS diagnosis; 2) either no premenstrual symptoms OR an overall symptom severity of “minimal” or “mild”; and 3) either “no effect” or a “mild” effect of symptoms on life activities and relationships. Women who did not meet either case or control criteria were not included in these analyses to minimize the likelihood for misclassification of the outcome.

Assessment of carbohydrate intake

Women completed a semi-quantitative 131-item food frequency questionnaire (FFQ) beginning in 1991 and subsequently every four years thereafter to assess intakes of total carbohydrates, glycemic index and load, dietary insulin index, total sugar and sugar subtypes (natural, added, sucrose, fructose, lactose, maltose, and glucose), total fiber and fiber subtypes (vegetable, legume, cereal, and fruit), whole and refined grains, bran, germ, and starch. We calculated each woman’s nutrient intakes by multiplying the reported consumption frequency of a specified portion and the nutrient content for each food item and summing across all foods and supplements. We then adjusted nutrient intakes for total caloric intake using the residual method (13).

Similar FFQs are valid in assessing carbohydrate intake (13, 14). The correlation for total carbohydrate intake (energy-adjusted) measured by the FFQ and by two 1-week diet records was 0.59 (13). Similarly, the correlation for total carbohydrate intake (energy-adjusted) measured by the FFQ and by three 4-day weighed food records was 0.55 and 0.53 for sugar, 0.40 for starch, 0.67 for fiber, 0.40 for glycemic index, and 0.38 for glycemic load (14).
For each participant, we evaluated carbohydrate intake at both baseline (1991) and two to four years before her specific reference year. Dietary information was available for 3,660 Sub-Study participants at baseline and 3,638 women two to four years prior to reference year.

**Assessment of covariates**

Information on other potential PMS risk factors and diet were collected on biennial questionnaires, including age, weight, reproductive history (e.g., pregnancies, tubal ligation, oral contraceptive use), and smoking status. Height and menstrual cycle characteristics were only assessed on the 1989 questionnaire. The menstrual cycle questionnaire assessed history of depression and antidepressant use and a separate questionnaire in 2001 assessed childhood trauma (15). Lastly, the FFQ given every four years assessed intakes of other nutrients such as vitamin D and calcium from foods and supplements.

**Statistical analysis**

We calculated age-adjusted means and standard deviations (continuous variables) and frequencies (categorical variables) using generalized linear modeling to obtain distributions of demographic and lifestyle characteristics between cases and controls.

We used logistic regression to estimate relative risks (RR) of PMS adjusting for age and 95% confidence intervals (CI) across quintiles of carbohydrate intake compared to the lowest quintile. In multivariable regression models we controlled for age, reference year, age at menarche, body mass index (BMI; weight [kg]/height [m²]), physical activity, ever use of oral contraceptives, parity (pregnancies lasting ≥6 months), smoking status and quantity (pack-years), ever use of antidepressants, significant childhood trauma, alcohol intake, vitamin D from dietary sources and total intake of vitamins B₆, B₁₂, B₁, B₂, folate, iron, zinc, potassium, and calcium. Analyses of risk associated with baseline carbohydrate intake included covariates assessed at baseline. For analyses of carbohydrate intake two to four years before reference year, we included covariates assessed two to four years before reference year as well. In additional models, we mutually adjusted carbohydrate subtypes for one another. We used the Mantel extension test for trend to assess for linear trends across quintiles using the median value of each carbohydrate quintile as a continuous variable in regression models.

We further assessed whether the relationship between carbohydrates and PMS differed by age at diagnosis/reference year (<40 versus ≥40 years) and smoking (past/never versus current) via stratified analyses. We evaluated multiplicative interaction using likelihood ratio tests comparing models with interaction terms (stratification factor × indicators of macronutrient quintile) and without interaction terms.

We used SAS 9.3 (SAS Institute Inc., Cary, NC, USA) to conduct all analyses, where p-values <0.05 (two-tailed) were considered statistically significant.
RESULTS

Cases were younger, heavier at baseline in 1991 and at age 18, more likely to have used oral contraceptives, smoked, have been diagnosed with depression, used antidepressants, and had significant childhood trauma compared to controls (Table 1). Additionally, cases had lower intakes of vitamin D (from food sources) and calcium, and higher intakes of vitamins B<sub>6</sub> and B<sub>12</sub> at baseline. Very few women in our study used fiber supplements (<3%).

Total carbohydrate intake two to four years prior to the reference year was not associated with PMS development (Table 2). For example, the RR for the highest quintile of intake (median = 273.0 g/day) compared to the lowest quintile of intake (median = 185.0 g/day) was 0.99 (95% CI = 0.74-1.33). Similarly, glycemic index and glycemic load were not associated with the development of PMS. While higher dietary insulin index was associated with lower risk of developing PMS in age-adjusted models, results adjusted for covariates were attenuated and no longer significant.

Total sugar, added sugars, natural sugars, sucrose, fructose, and glucose were not associated with the development of PMS (Table 3). High lactose intake was associated with lower risk of PMS in age-adjusted analyses but after controlling for additional confounders such as BMI, smoking, and additional covariates, results were no longer significant. Maltose intake was linearly related to PMS risk (p for trend = 0.005). Women with the highest intake (median = 3.0 g/day) had a 45% higher risk of developing PMS compared to women with the lowest intake (median = 1.2 g/day) (95% CI = 1.11-1.88). The higher risk associated with maltose remained significant when adjusting for other types of sugar (RR quintile 5 versus quintile 1 = 1.43; 95% CI = 1.10-1.87, p for trend = 0.005; Supplementary Table 1).

Total fiber, vegetable fiber, cereal fiber, and fruit fiber were not associated with PMS development (Table 4). Fiber from legume sources appeared to have a u-shaped association with PMS development, with lower risk of developing PMS in the third and fourth quintiles of intake compared to the first quintile. Comparison of models with and without the inclusion of cubic spline terms indicate a significant non-linear trend (p=0.04).

Intake of whole grains and refined grains were not associated with PMS development (Table 5). Additionally, intake of bran, germ, and starch were not linearly associated with PMS development.

Analyses evaluating carbohydrate intake at baseline in 1991 did not materially differ from the results shown. As BMI may potentially lie within the causal path between carbohydrates and PMS, the analyses were repeated without adjusting for BMI and estimates were unchanged. Analyses stratified by age and smoking status did not suggest effect modification of relative risks; statistical tests of interactions were all non-significant (all p for interaction >0.05).

Additional post hoc analyses were performed to address the possibility of residual confounding, particularly in the model assessing maltose. These models evaluated the effect of controlling for continuous alcohol intake rather than categorical, as well as adjusting for beer. Neither of these variables affected the estimate from the primary analysis.
DISCUSSION

To our knowledge, this is one of the first studies to prospectively evaluate how carbohydrate and fiber intake are associated with the development of PMS. Overall, we found little evidence that carbohydrate intake is related to PMS, though high intake of the sugar maltose was positively associated with risk.

Prior research of the relation between carbohydrate intake and PMS has been limited to consideration of the prevalence and/or severity of symptoms. Among these previous studies, findings have been inconsistent. Nagata and colleagues (2004) evaluated the relationship of carbohydrates and premenstrual symptoms among 189 Japanese women aged 19-34 years (7). After controlling for age, smoking status, and other factors, the authors found that total intake of carbohydrates was not significantly associated with the total Menstrual Distress Questionnaire score (r = -0.12; p >0.05) in the premenstrual phase. Johnson and colleagues assessed macronutrient intake in healthy, normally menstruating women (n=26) without complaints of menstrual distress (not necessarily PMS) and found that percentage of kilocalories from carbohydrates was positively associated with negative affect (r = 0.51; p <0.01) and behavior change (r = 0.42; p <0.05) (8). Murakami and colleagues found an inverse association of glycemic index and premenstrual symptoms in Japanese dietetic students (n=640) aged 18-22 years (p for trend=0.016) though no association with glycemic load or fiber (16).

Cross and colleagues evaluated energy intakes during different phases of the menstrual cycle, including intake of carbohydrates, among women with PMS (17). They found statistically significant increases in intake of total carbohydrates (44.6% versus 45.6% of kilocalories, p = 0.05) and simple sugars (18.9% versus 20.9%; p <0.001) from the postmenstrual to the premenstrual phase among women with PMS but not among women without PMS. In addition, there was a non-significant decrease in intake of complex carbohydrates (25.6% versus 24.6% of kilocalories; p = 0.07). Two previous studies have assessed the association between intake of foods with high sugar contents in women with PMS or premenstrual symptom severity and found increases in both consumption premenstrually and increased symptom severity (9,17). Collectively, these findings support the hypothesis that women experiencing menstrual symptoms may alter their carbohydrate intake, perhaps in response to carbohydrate cravings. Thus, the associations reported in retrospective studies may be influenced by reverse causation.

While our findings for carbohydrates and sugars were generally null, we did observe higher risk of PMS development in women with higher intake of maltose. Maltose is a sugar found commonly in alcohols such as beer and foods such as yams, candy bars, tomato sauce, and cereals. As associations of maltose with PMS have not been reported previously, this finding may be due to chance. However, in post hoc analyses, we found that women who consumed at least one serving of sweet potato or yam per week compared to never had an 26% higher risk of developing PMS (95% CI=0.92-1.7), suggesting that associations may be similar for foods very high in maltose.
Some previous studies have suggested that women with PMS consume higher intakes of alcohol compared to controls (18), including beer (19). However, the positive association between maltose and PMS found in our study is unlikely to be driven by alcohol, as we controlled for alcohol intake. Additionally, cases and controls had similar age-adjusted intakes of alcohol at baseline (3.1 g/day versus 3.1 g/day) and a previous analysis in the NHS2 found no association with alcohol intake and PMS development (RR = 1.19; 95% CI = 0.84-1.67) within the same PMS Sub-Study cohort (20). A mechanism for an association between maltose and PMS is unknown, and it is unclear whether the association was due to chance; thus, additional prospective studies are needed to confirm this finding.

Our study was nested within a large prospective cohort. Prospective charting of menstrual symptoms is infeasible in the context of large studies, as it is time intensive and cost prohibitive to collect diaries repeatedly from thousands of women. However, we used strict criteria to classify PMS cases and verify controls had minimal symptoms that had no impact on function (10). Though some non-differential misclassification of PMS is possible, its potential impact on findings is minimized, as we compared women at the two ends of the symptom spectrum and excluded women who met neither case nor control criteria. Recall of symptom experience is likely to be accurate at the two extremes, those who regularly experience severe symptoms that impair daily functioning and those who regularly experience few, if any symptoms. Therefore, PMS status is unlikely to be misclassified between these two groups (10). Secondly, PMS was determined prospectively by report of clinician-made diagnoses, which was then confirmed by retrospective questionnaire; this approach has been shown to be comparable to reported prospective charting in a validation study (11).

In conclusion, we did not observe evidence of an association of carbohydrate intake with PMS risk. High sugar intake and low fiber intake were also not associated with the development of PMS. While high intake of the sugar maltose was associated with higher risk of PMS, additional prospective studies are needed to confirm this association.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Age-standardized characteristics of premenstrual syndrome cases and controls at baseline (n=3 660); NHS2 PMS Sub-study, 1991-2005.

| Characteristics | Cases (n=1 234) | Controls (n=2 426) | p-value $^3$ |
|-----------------|----------------|-------------------|--------------|
| Age, years      | 33.9 (4.2)     | 34.5 (3.9)        | <0.001       |
| Body mass index (kg/m$^2$) |                |                   |              |
| At baseline (1991) | 24.6 (5.2)     | 23.7 (4.7)        | <0.001       |
| At age 18        | 21.4 (3.3)     | 21.1 (3.1)        | 0.02         |
| Age at menarche, years | 12.4 (1.4)     | 12.5 (1.4)        | 0.05         |
| Age at first birth, years$^2$ | 25.9 (3.9)     | 26.1 (3.7)        | 0.09         |
| Number of full-term pregnancies (≥6 months) | 1.6 (1.2) | 1.6 (1.2) | 0.36 |
| Physical activity, METS/week | 22.9 (60.2) | 23.6 (55.6) | 0.74 |
| Pack-years of cigarette smoking | 8.3 (64.7) | 4.8 (50.2) | 0.09 |
| Alcohol intake, g/day | 3.1 (6.5) | 3.1 (5.7) | 0.99 |
| Total kilocalorie intake, kcal/day | 1 826 (537) | 1 813 (520) | 0.62 |
| Vitamin D intake food sources, IU/day$^d$ | 255 (119) | 267 (123) | 0.01 |
| Total vitamin B$_6$ intake, mg/day$^d$ | 8.6 (26.3) | 5.8 (15.6) | <0.001 |
| Total vitamin B$_{12}$ intake, mg/day$^d$ | 10.1 (14.2) | 9.4 (8.5) | 0.04 |
| Total thiamin intake, mg/day$^d$ | 3.6 (8.2) | 3.2 (6.0) | 0.09 |
| Total riboflavin intake, mg/day$^d$ | 4.1 (8.2) | 3.6 (5.7) | 0.07 |
| Total iron intake, mg/day$^d$ | 24.9 (23.3) | 25.8 (24.8) | 0.35 |
| Total zinc intake, mg/day$^d$ | 15.9 (10.7) | 15.7 (10.3) | 0.59 |
| Total potassium intake, mg/day$^d$ | 2 925 (499) | 2 897 (501) | 0.17 |
| Total calcium intake, mg/day$^d$ | 1 030 (403) | 1 063 (421) | 0.03 |

| %     | %     | p-value $^3$ |
|-------|-------|--------------|
| History of tubal ligation | 15 | 16 | 0.66 |
| Oral contraceptive use | | | |
| Ever | 85 | 77 | <0.001 |
| Current | 12 | 11 | 0.33 |
| Duration > 4 years | 43 | 37 | 0.001 |
| Smoking status | | | |
| Current | 13 | 7 | <0.001 |
| Past | 27 | 17 | <0.001 |
| Previously diagnosed with depression | 18 | 8 | <0.001 |
| Previously used antidepressant | 15 | 7 | <0.001 |
| History of childhood trauma | 18 | 9 | <0.001 |

$^1$ All characteristics, except age, standardized to the age distribution of participants in 1991
Limited to parous women

Calculated using generalized linear model

Energy adjusted values
Table 2

Age-adjusted and multivariate relative risks (RR)\(^1\) and 95% confidence intervals (CI) for dietary carbohydrate intakes 2-4 years prior to reference year and risk of premenstrual syndrome (n=3 638); NHS2 PMS Sub-Study, 1991-2005.

|                      | Q1  | Q2  | Q3  | Q4  | Q5  | p-trend |
|----------------------|-----|-----|-----|-----|-----|---------|
| **Total carbohydrate** |     |     |     |     |     |         |
| Range, g/day\(^2\)    | ≤197.0 | 197.1-215.0 | 215.1-231.0 | 231.1-251.0 | ≥251.1 |
| Case: Control Ratio   | 239:412 | 243:506 | 244:503 | 259:502 | 237:493 |
| RR                   |     |     |     |     |     |         |
| Age-adjusted         | Ref | 0.82 | 0.82 | 0.88 | 0.82 | 0.19    |
| Multivariate         | Ref | 0.89 | 0.94 | 1.07 | 0.99 | 0.66    |
| 95% CI\(^3\)         | 0.69-1.15 | 0.73-1.22 | 0.81-1.40 | 0.74-1.33 |         |
| **Glycemic index**   |     |     |     |     |     |         |
| Range\(^2\)          | ≤51.2 | 51.3-53.1 | 53.2-54.7 | 54.8-56.5 | ≥56.6  |
| Case: Control Ratio   | 239:448 | 231:488 | 253:484 | 248:523 | 250:473 |
| RR                   |     |     |     |     |     |         |
| Age-adjusted         | Ref | 0.88 | 0.97 | 0.87 | 0.95 | 0.64    |
| Multivariate         | Ref | 1.06 | 1.15 | 1.16 | 1.19 | 0.20    |
| 95% CI\(^3\)         | 0.82-1.36 | 0.89-1.48 | 0.89-1.52 | 0.89-1.99 |         |
| **Glycemic load**    |     |     |     |     |     |         |
| Range\(^2\)          | ≤104.0 | 104.1-115.1 | 115.2-125.1 | 125.2-137.9 | ≥138.0 |
| Case: Control Ratio   | 234:413 | 233:490 | 267:512 | 250:498 | 238:503 |
| RR                   |     |     |     |     |     |         |
| Age-adjusted         | Ref | 0.83 | 0.90 | 0.87 | 0.81 | 0.14    |
| Multivariate         | Ref | 0.98 | 1.06 | 1.12 | 1.07 | 0.48    |
| 95% CI\(^3\)         | 0.76-1.27 | 0.82-1.37 | 0.85-1.47 | 0.80-1.42 |         |
| **Dietary insulin index** |     |     |     |     |     |         |
| Range\(^2\)          | ≤39.8 | 39.9-42.1 | 42.2-44.0 | 44.1-46.4 | ≥46.5  |
| Case: Control Ratio   | 218:385 | 259:439 | 226:483 | 256:556 | 263:553 |
| RR                   |     |     |     |     |     |         |
|       | Q1  | Q2  | Q3  | Q4  | Q5  | p-trend |
|-------|-----|-----|-----|-----|-----|---------|
| Age-adjusted | Ref | 1.03| 0.80| 0.79| 0.81| 0.01    |
| Multivariate | Ref | 1.13| 0.92| 0.93| 1.05| 0.88    |
| 95% CI |     | 0.87-1.46 | 0.70-1.20 | 0.71-1.21 | 0.80-1.38 |   |

1 Adjusted for age (years, continuous), reference year (1991-92, 93, 94-96, 97-98, 99-2000, 01-02, 03-04), age at menarche (years, continuous), current body mass index (≤9.9, 20.0-22.4, 22.5-24.9, 25.0-27.4, 27.5-29.9, ≥30 kg/m²), physical activity (<3, 3-8, 9-18, 19-26, 27-41, ≥42 METs per week), oral contraceptive use (none, 1-23, 24-71, 72-119, ≥120 months), parity (nulliparous, 1-2, 3-4, ≥5 pregnancies lasting at least 6 months), smoking (never, past 1-14, past 15-34, past 35+, current 1-14, current 15-34, current 35+ cigarettes/day), previous use of antidepressants (never, ever), childhood trauma score (5, 6-10, 11-15, 16-20, 21-25), alcohol intake (quintiles), intake of vitamin D from food sources (quintiles), and intake for vitamins B₆, B₁₂, B₁, B₂, folate, iron, zinc, potassium, and calcium (quintiles).

2 Quintile ranges are for 1991 questionnaire cycle. Quintile cutpoints were determined separately for each questionnaire cycle and will vary slightly by year.

3 95% CI is for multivariable model.
Table 3

Age-adjusted and multivariate relative risks (RR) and 95% confidence intervals (CI) for dietary sugar intakes 2-4 years prior to reference year and risk of premenstrual syndrome (n=3 638); NHS2 PMS Sub-Study, 1991-2005.

|                | Q1     | Q2   | Q3   | Q4   | Q5     | p-trend |
|----------------|--------|------|------|------|--------|---------|
| **Total sugar**|        |      |      |      |        |         |
| Range, g/day²  | 80.2   | 80.3-96.1 | 96.2-111.2 | 111.3-131.1 | ≥131.2 |         |
| Case: Control Ratio | 252:452 | 262:485 | 226:506 | 271:521 | 211:452 |         |
| Age-adjusted RR | Ref    | 0.96 | 0.79 | 0.92 | 0.81 | 0.08    |
| Multivariate RR | Ref    | 1.05 | 0.89 | 1.04 | 0.84 | 0.22    |
| 95% CI³        | 0.82-1.33 | 0.69-1.15 | 0.81-1.34 | 0.63-1.10 |         |
| **Added sugar**|        |      |      |      |        |         |
| Range, g/day²  | 82.2   | 32.3-42.3 | 42.4-53.4 | 53.5-71.3 | ≥71.4 |         |
| Case: Control Ratio | 242:438 | 262:511 | 260:572 | 233:484 | 225:411 |         |
| Age-adjusted RR | Ref    | 0.92 | 0.81 | 0.85 | 0.96 | 0.85    |
| Multivariate RR | Ref    | 1.03 | 0.91 | 0.97 | 1.01 | 0.99    |
| 95% CI³        | 0.81-1.30 | 0.71-1.15 | 0.75-1.25 | 0.76-1.34 |         |
| **Natural sugar**|        |      |      |      |        |         |
| Range, g/day²  | 85.2   | 35.3-46.0 | 46.1-56.4 | 56.5-69.7 | ≥69.8 |         |
| Case: Control Ratio | 225:399 | 256:483 | 264:492 | 248:546 | 229:496 |         |
| Age-adjusted RR | Ref    | 0.94 | 0.96 | 0.81 | 0.82 | 0.03    |
| Multivariate RR | Ref    | 1.00 | 0.98 | 0.81 | 0.77 | 0.09    |
| 95% CI³        | 0.77-1.30 | 0.74-1.31 | 0.59-1.11 | 0.54-1.11 |         |
| **Sucrose**    |        |      |      |      |        |         |
| Range, g/day²  | 29.7   | 29.8-36.9 | 37.0-44.0 | 44.1-54.1 | ≥54.2 |         |
| Case: Control Ratio | 242:458 | 266:510 | 254:535 | 248:475 | 212:438 |         |
| RR             |        |      |      |      |        |         |
| Fructose | Lactose | Maltose | Glucose |
|----------|---------|---------|---------|
| **Range, g/day** | **Case: Control Ratio** | **RR** | **95% CI** |
| ≤ 14.3 | 240:483 | Age-adjusted Ref | 0.97 | 0.89 | 0.97 | 0.90 | 0.41 |
| 14.4-18.6 | 257:486 | Multivariate Ref | 1.04 | 0.93 | 1.04 | 0.91 | 0.53 |
| 18.7-23.1 | 246:519 | 95% CI² | 0.82-1.31 | 0.73-1.18 | 0.81-1.34 | 0.70-1.19 | |
| 23.2-29.6 | 239:483 | **Age-adjusted Ref** | 1.02 | 0.91 | 0.95 | 1.00 | 0.85 |
| 231:445 | Multivariate Ref | 1.14 | 0.92 | 1.02 | 0.96 | 0.52 |
| 0.89-1.45 | 0.72-1.18 | 95% CI² | 0.80-1.32 | 0.73-1.24 | |
| ≤ 6.9 | 219:413 | **Age-adjusted Ref** | 0.99 | 0.98 | 1.02 | 0.74 | 0.005 |
| 7.0-12.2 | 231:430 | Multivariate Ref | 1.04 | 1.13 | 1.07 | 0.73 | 0.08 |
| 12.3-18.0 | 267:505 | 95% CI² | 0.79-1.37 | 0.83-1.54 | 0.75-1.53 | 0.48-1.12 | |
| 18.1-27.6 | 262:472 | **Age-adjusted Ref** | 1.09 | 1.09 | 1.18 | 1.31 | 0.01 |
| 243:596 | Multivariate Ref | 1.17 | 1.21 | 1.32 | 1.45 | 0.005 |
| 0.91-1.49 | 0.94-1.55 | 95% CI² | 1.03-1.70 | 1.11-1.88 | |
| ≤ 1.2 | 196:444 | **Age-adjusted Ref** | 1.09 | 1.09 | 1.18 | 1.31 | 0.01 |
| 253:518 | Multivariate Ref | 1.17 | 1.21 | 1.32 | 1.45 | 0.005 |
| 0.91-1.49 | 0.94-1.55 | 95% CI² | 1.03-1.70 | 1.11-1.88 | |
| ≤ 14.0 | 251:501 | **Age-adjusted Ref** | 1.09 | 1.09 | 1.18 | 1.31 | 0.01 |
| 255:489 | Multivariate Ref | 1.17 | 1.21 | 1.32 | 1.45 | 0.005 |
| 0.91-1.49 | 0.94-1.55 | 95% CI² | 1.03-1.70 | 1.11-1.88 | |
|          | Q1  | Q2  | Q3  | Q4  | Q5  | p-trend |
|----------|-----|-----|-----|-----|-----|---------|
| Age-adjusted | Ref | 1.03| 1.01| 1.02| 0.94| 0.55    |
| Multivariate | Ref | 1.14| 1.07| 1.08| 0.91| 0.33    |
| 95% CI     |     | 0.90-1.45 | 0.84-1.36 | 0.84-1.39 | 0.69-1.19 |     |

1 Adjusted for age, reference year, age at menarche, body mass index, physical activity, oral contraceptive use, parity, smoking, previous use of antidepressants, childhood trauma score, alcohol intake, intake of vitamin D from food sources, and intake for vitamins B6, B12, B1, B2, folate, iron, zinc, potassium, and calcium. Please see footnote to table 2 for variable categorizations.

2 Quintile ranges are for 1991 questionnaire cycle. Quintile cutpoints were determined separately for each questionnaire cycle and will vary slightly by year.

3 95% CI is for multivariable model.
Table 4

Age-adjusted and multivariate relative risks (RR) \(^{1}\) and 95% confidence intervals (CI) for dietary fiber intakes 2-4 years prior to reference year and risk of premenstrual syndrome (n=3 638); NHS2 PMS Sub-Study, 1991-2005.

|                  | Q1   | Q2     | Q3     | Q4     | Q5     | p-trend |
|------------------|------|--------|--------|--------|--------|---------|
| **Total fiber**  |      |        |        |        |        |         |
| Range, g/day \(^2\) | ≤4.0 | 14.1-16.4 | 16.5-18.7 | 18.8-21.9 | ≥22.0 |         |
| Case: Control Ratio | 233:454 | 238:478 | 247:518 | 253:499 | 251:467 |         |
| RR Age-adjusted  | Ref  | 1.00   | 0.95   | 1.02   | 1.10   | 0.36    |
| RR Multivariate  | Ref  | 1.05   | 0.99   | 1.08   | 1.11   | 0.50    |
| 95% CI \(^3\)    | 0.81-1.36 | 0.75-1.29 | 0.81-1.44 | 0.81-1.53 |         |
| **Vegetable fiber** |      |        |        |        |        |         |
| Range, g/day \(^2\) | ≤4.1 | 4.2-5.4 | 5.5-6.8 | 6.9-8.8 | ≥8.9  |         |
| Case: Control Ratio | 244:480 | 239:515 | 257:518 | 241:475 | 241:428 |         |
| RR Age-adjusted  | Ref  | 0.93   | 1.02   | 1.05   | 1.16   | 0.08    |
| RR Multivariate  | Ref  | 0.93   | 1.05   | 1.02   | 1.03   | 0.68    |
| 95% CI \(^3\)    | 0.73-1.18 | 0.82-1.35 | 0.78-1.33 | 0.77-1.38 |         |
| **Legume fiber** |      |        |        |        |        |         |
| Range, g/day \(^2\) | ≤0.1 | 0.2-0.5 | 0.6-0.8 | 0.9-1.3 | ≥1.4  |         |
| Case: Control Ratio | 245:437 | 233:487 | 225:502 | 247:530 | 272:460 |         |
| RR Age-adjusted  | Ref  | 0.86   | 0.81   | 0.85   | 1.10   | 0.11    |
| RR Multivariate  | Ref  | 0.83   | 0.78   | 0.78   | 1.02   | 0.41    |
| 95% CI \(^3\)    | 0.65-1.06 | 0.61-0.99 | 0.61-0.99 | 0.80-1.30 |         |
| **Cereal fiber** |      |        |        |        |        |         |
| Range, g/day \(^2\) | ≤3.5 | 3.6-4.5 | 4.6-5.6 | 5.7-7.2 | ≥7.3  |         |
| Case: Control Ratio | 213:368 | 221:441 | 249:483 | 263:581 | 276:543 |         |
| RR                |      |        |        |        |        |         |
| Q1 | Q2   | Q3   | Q4   | Q5   | p-trend |
|----|------|------|------|------|---------|
| Age-adjusted Ref | 0.86 | 0.89 | 0.78 | 0.87 | 0.28    |
| Multivariate Ref  | 0.94 | 1.10 | 1.00 | 1.14 | 0.24    |
| 95% CI $^3$       | 0.72-1.22 | 0.84-1.43 | 0.76-1.31 | 0.87-1.51 | |

**Fruit fiber**

| Range, g/day$^2$ | Q1 | Q2   | Q3   | Q4   | Q5   | p-trend |
|-----------------|----|------|------|------|------|---------|
| 1-1.5           | 0.98 | 0.87 | 1.12 | 1.03 | 0.63 |
| 1.6-2.3         | 1.00 | 0.85 | 1.15 | 0.95 | 0.59 |
| 2.4-3.4         | 0.93-1.54 | 0.74-1.21 | 0.89-1.50 | 0.72-1.27 | |

1. Adjusted for age, reference year, age at menarche, body mass index, physical activity, oral contraceptive use, parity, smoking, previous use of antidepressants, childhood trauma score, alcohol intake, intake of vitamin D from food sources, and intake for vitamins B$_6$, B$_12$, B$_1$, B$_2$, folate, iron, zinc, potassium, and calcium. Please see footnote to table 2 for variable categorizations.

2. Quintile ranges are for 1991 questionnaire cycle. Quintile cutpoints were determined separately for each questionnaire cycle and will vary slightly by year.

3. 95% CI is for multivariable model.
Table 5

Age-adjusted and multivariate relative risks (RR) and 95% confidence intervals (CI) for dietary grain intakes 2-4 years prior to reference year and risk of premenstrual syndrome (n=3,638); NHS2 PMS Sub-Study, 1991-2005.

|                | Q1 | Q2  | Q3  | Q4  | Q5  | p-trend |
|----------------|----|-----|-----|-----|-----|---------|
| Whole grains   |    |     |     |     |     |         |
| Range, g/day   | ≤7.9 | 8.0-13.7 | 13.8-20.4 | 20.5-30.3 | ≥30.4 |         |
| Case: Control Ratio | 210:419 | 227:437 | 264:499 | 259:530 | 262:531 |         |
| RR Age-adjusted | Ref | 1.04 | 1.07 | 0.98 | 0.99 | 0.67 |
| Multivariate    | Ref | 1.03 | 1.08 | 1.05 | 1.09 | 0.58 |
| 95% CI         | 0.79-1.33 | 0.83-1.39 | 0.80-1.37 | 0.83-1.43 |         |
| Refined grains  |    |     |     |     |     |         |
| Range, g/day   | ≤4.7 | 44.8-54.9 | 55.0-64.6 | 64.7-77.4 | ≥77.5 |         |
| Case: Control Ratio | 212:376 | 241:466 | 245:479 | 263:535 | 261:560 |         |
| RR Age-adjusted | Ref | 0.90 | 0.90 | 0.87 | 0.81 | 0.08 |
| Multivariate    | Ref | 0.99 | 1.05 | 1.10 | 1.12 | 0.31 |
| 95% CI         | 0.77-1.28 | 0.81-1.36 | 0.85-1.42 | 0.85-1.47 |         |
| Bran            |    |     |     |     |     |         |
| Range, g/day   | ≤1.3 | 1.4-2.9 | 3.0-4.8 | 4.9-8.3 | ≥8.4 |         |
| Case: Control Ratio | 204:387 | 246:480 | 251:501 | 267:554 | 254:494 |         |
| RR Age-adjusted | Ref | 0.98 | 0.96 | 0.92 | 0.98 | 0.85 |
| Multivariate    | Ref | 0.91 | 0.92 | 1.01 | 1.09 | 0.23 |
| 95% CI         | 0.71-1.18 | 0.71-1.19 | 0.77-1.32 | 0.82-1.44 |         |
| Germ            |    |     |     |     |     |         |
| Range, g/day   | ≤0.3 | 0.4-0.6 | 0.7-0.9 | 1.0-1.4 | ≥1.5 |         |
| Case: Control Ratio | 227:408 | 248:516 | 235:469 | 250:495 | 262:528 |         |
| RR             |     |     |     |     |     |         |
|       | Q1      | Q2      | Q3      | Q4      | Q5      | p-trend |
|-------|---------|---------|---------|---------|---------|---------|
| Age-adjusted | Ref | 0.86    | 0.90    | 0.90    | 0.89    | 0.65    |
| Multivariate | Ref | 0.77    | 0.92    | 0.91    | 0.86    | 0.80    |
| 95% CI | 0.60-0.99 | 0.71-1.19 | 0.70-1.18 | 0.67-1.12 |

### Starch

| Range, g/day | Case: Control Ratio | RR  |
|-------------|---------------------|-----|
| ≤63.1       | 219:393             | Ref | 0.93 |
| 63.2-73.3   | 237:453             | 0.94 | 0.94 |
| 73.4-82.5   | 253:485             | 0.79 | 0.79 |
| 82.6-94.2   | 239:541             | 0.90 | 0.90 |
| ≥94.3       | 274:544             | 0.20 | 0.20 |

|       | 95% CI |     |
|-------|--------|-----|
| RR    | 0.73-1.21 | 0.82-1.37 |
|       | 0.72-1.22 | 0.89-1.52 |

1. Adjusted for age, reference year, age at menarche, body mass index, physical activity, oral contraceptive use, parity, smoking, previous use of antidepressants, childhood trauma score, alcohol intake, intake of vitamin D from food sources, and intake for vitamins B6, B12, B1, B2, folate, iron, zinc, potassium, and calcium. Please see footnote to table 2 for variable categorizations.

2. Quintile ranges are for 1991 questionnaire cycle. Quintile cutpoints were determined separately for each questionnaire cycle and will vary slightly by year.

3. 95% CI is for multivariable model.