

1 **Quality of periconceptional dietary intake and maternal and neonatal outcomes**

2

3 Lynn M. YEE, MD, MPH (1), Robert M. SILVER, MD (2), David M. HAAS, MD, MS (3), Samuel PARRY, MD

4 (4), Brian M. MERCER, MD (5), Jay IAMS, MD (6), Deborah WING, MD (7), Corette B. PARKER, DrPH (8),

5 Uma M. REDDY, MD, MPH (9), Ronald J. WAPNER, MD (10), William A. GROBMAN, MD, MBA (1)

6

7 1. Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, Feinberg School
8 of Medicine, Northwestern University

9 2. Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, University of
10 Utah, Salt Lake City, UT

11 3. Department of Obstetrics & Gynecology, Indiana University School of Medicine, Indianapolis, IN

12 4. Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, Perelman School
13 of Medicine, University of Pennsylvania, Philadelphia, PA

14 5. Department of Obstetrics & Gynecology, MetroHealth Medical Center, Case Western Reserve
15 University, Cleveland, OH

16 6. Department of Obstetrics & Gynecology, The Ohio State University, Columbus, OH

17 7. Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, University of
18 California-Irvine, Irvine, CA

19 8. RTI International, Research Triangle Park, NC

20 9. Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive
21 Science, Yale University, New Haven, CT

22 10. Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecology, Columbia
23 University, New York, NY

24

This is the author's manuscript of the article published in final edited form as:

Yee, L. M., Silver, R. M., Haas, D. M., Parry, S., Mercer, B. M., Iams, J., ... & Grobman, W. A. (2020). Quality of periconceptional dietary intake and maternal and neonatal outcomes. *American Journal of Obstetrics and Gynecology*. <https://doi.org/10.1016/j.ajog.2020.01.042>

25 CORRESPONDING AUTHOR:

26 Lynn M. Yee, MD, MPH

27 Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology

28 Northwestern University Feinberg School of Medicine

29 250 E. Superior Street, #5-2145

30 Chicago, IL 60611

31 Phone: 312-472-4685

32 Fax : 312-472-0511

33 lynn.yee@northwestern.edu

34

35 CONFLICT OF INTEREST: The authors report no conflicts of interest.

36

37 PRESENTATION: Presented in oral format at the 2019 39th Annual Meeting of the Society for Maternal-
38 Fetal Medicine (February 11-16, 2019).

39

40 FUNDING: LMY was supported by the NICHD K12 HD050121-11 at the time the study was performed.

41 Support for the NuMoM2b study was provided by grant funding from the *Eunice Kennedy Shriver*

42 National Institute of Child Health and Human Development: U10 HD063036, RTI International; U10

43 HD063072, Case Western Reserve University; U10 HD063047, Columbia University; U10 HD063037,

44 Indiana University; U10HD063041, University of Pittsburgh; U10 HD063020, Northwestern University;

45 U10 HD063046, University of California Irvine; U10 HD063048, University of Pennsylvania; and U10

46 HD063053, University of Utah. In addition, support was provided by respective Clinical and Translational

47 Science Institutes to Indiana University (UL1TR001108) and University of California Irvine

48 (UL1TR000153).

49

50 ABSTRACT WORD COUNT: 468

51 MANUSCRIPT WORD COUNT: 2959

Journal Pre-proof

52 CONDENSATION: Poor periconceptional dietary quality, common among US women, is associated with
53 adverse maternal and neonatal outcomes even after controlling for potential comorbidities.

54

55 SHORT TITLE: Periconceptional diet quality and obstetric outcomes

56

57 AJOG AT A GLANCE:

58 A. Why was the study conducted? Although disparities in periconceptional dietary quality exist, it is
59 unknown whether individual periconceptional diet quality is associated with obstetric outcomes.

60 B. What are the key findings? Poor periconceptional dietary quality is associated with greater
61 relative risk of cesarean delivery, hypertensive disorders, postpartum hemorrhage, NICU
62 admission, preterm birth, and low birthweight, whereas it is associated with lower risk of major
63 perineal laceration and macrosomia.

64 C. What does the study add to what we already know? Poor periconceptional dietary quality is
65 associated with adverse perinatal outcomes even after controlling for body mass index and
66 potential comorbidities.

67

68 **Key words:** dietary disparities, dietary quality, healthy eating index, periconceptional diet, pregnancy
69 diet, pregnancy outcome

70 **ABSTRACT**

71 **Background:** Periconceptional diet quality is commonly suboptimal and sociodemographic disparities in
72 diet quality exist. However, it is unknown whether individual periconceptional diet quality is associated
73 with obstetric outcomes.

74 **Objective:** Our objective was to assess differences in maternal and neonatal outcomes according to
75 maternal periconceptional diet quality.

76 **Study Design:** This is a secondary analysis of a large, multicenter prospective cohort study of 10,038
77 nulliparous women receiving obstetrical care at 8 United States centers. Women underwent three
78 antenatal study visits and had detailed maternal and neonatal data abstracted by trained research
79 personnel. In the first trimester (between 6 and 13 weeks), women completed the modified Block 2005
80 Food Frequency Questionnaire, a semiquantitative assessment of usual dietary intake for the 3 months
81 around conception. Responses were scored using the Healthy Eating Index-2010, which assesses
82 adherence to the 2010 Dietary Guidelines for Americans. Higher scores on the Healthy Eating Index
83 represent better adherence. Healthy Eating Index scores were analyzed by quartile; quartile 4
84 represents the highest dietary quality. Bivariable and multivariable analyses were performed to assess
85 associations between diet quality and outcomes. A sensitivity analysis in which markers of
86 socioeconomic status were included in the multivariable Poisson regression models was performed.

87 **Results:** In the cohort of 8,259 women with Healthy Eating Index data, the mean Healthy Eating Index
88 score was 63 (\pm 13) of 100. Women with the lowest quartile Healthy Eating Index scores were more
89 likely to be younger, non-Hispanic black and Hispanic, publicly insured, low income, and tobacco users.
90 They were more likely to have comorbidities (obesity, chronic hypertension, pregestational diabetes,
91 mental health disorders), a higher pre-pregnancy body mass index, and less education. Women with
92 lowest quartile scores experienced less frequent major perineal lacerations and more frequent
93 postpartum hemorrhage requiring transfusion and hypertensive disorders of pregnancy, which persisted

94 on multivariable analyses (controlling for age, body mass index, tobacco use, chronic hypertension,
95 pregestational diabetes mellitus, and mental health disorders) comparing women in each quartile to
96 quartile 4. Additionally, women in quartiles 1 and 2 experienced greater adjusted relative risk of
97 cesarean delivery compared to women in quartile 4. Neonatal outcomes also differed by dietary
98 quartile, with women in the lowest Healthy Eating Index quartile experiencing greater adjusted relative
99 risk of preterm birth, neonatal intensive care unit admission, small for gestational age infant, and low
100 birthweight, and lower risk of macrosomia; all neonatal findings also persisted in multivariable analyses.
101 The sensitivity analysis with inclusion of markers of socioeconomic status (race/ethnicity, insurance
102 status, marital status) in the multivariable models supported these findings.

103 **Conclusions:** Periconceptional diet quality among women in the United States is poor. Poorer
104 periconceptional dietary quality is associated with adverse maternal and neonatal outcomes even after
105 controlling for potential comorbidities and body mass index, suggesting periconceptional diet may be an
106 important social or biological determinant of health underlying existing health disparities.

107

108 **INTRODUCTION**

109 Overall dietary quality is poor for most Americans.^{1,2} Fewer than 3% of United States (US) adults
110 have ideal diet scores, and ample public health data suggest poor dietary quality is associated with
111 morbidity.¹⁻³ Moreover, racial, ethnic, and socioeconomic disparities in dietary quality are substantial for
112 nearly all measures, including diet scores, individual nutrient sources, and energy intake, and while
113 overall dietary quality in the US may be improving, these disparities are widening.^{1,2,4,5} Reproductive age
114 women planning pregnancy have similarly poor diets,^{1,6,7} despite potential fetal health implications.⁸
115 Multiple European-based studies show that women planning pregnancy are only marginally more likely
116 to comply with dietary recommendations and that dietary patterns changed little from before
117 pregnancy to early pregnancy.^{6,9,10} Thus, a woman's periconceptional diet is highly reflective of her
118 general nutritional patterns and dietary intake later in pregnancy.

119 In 2017, using data from a large cohort of US nulliparous women, Bodnar et al demonstrated
120 both that periconceptional dietary quality is suboptimal in US women and that racial, ethnic, and
121 sociodemographic disparities in dietary quality exist.¹¹ In this analysis, non-Hispanic white women had
122 the highest quality of periconceptional diet, whereas almost half of non-Hispanic black women had
123 dietary quality in the lowest quintile. Furthermore, although the quality of diet increased with greater
124 maternal education in all racial or ethnic groups, education was most strongly associated with diet
125 quality for white women.¹¹ Top sources of energy, overall, in this study were foods rich in sugars and
126 solid fats and included refined bread, soda, pasta, grain desserts, and alcohol.¹¹

127 Periconceptional dietary quality has been hypothesized to be an important determinant of
128 maternal and fetal outcomes,^{8,12} with suboptimal nutrition having a critical negative influence on fetal
129 growth, placentation, inflammation, and maternal metabolic regulation, and possibly leading to
130 differences in outcomes such as livebirth rate or birth weight.¹¹⁻¹⁵ Poor periconceptional dietary quality
131 may affect pregnancy outcomes via mechanisms such as micronutrient deficiency or relationship with

132 gestational weight gain. However, data to confirm this hypothesis are lacking, particularly in the US.
133 Thus, our objective was to assess if there is an association between periconceptional dietary quality and
134 maternal and neonatal outcomes.

135

136 **MATERIALS AND METHODS**

137 This is a secondary analysis of data from the Nulliparous Pregnancy Outcomes Study: Monitoring
138 Mothers-To-Be (nuMoM2b), which was a large, multicenter observational cohort study conducted at 8
139 US medical centers from 2010 to 2013.¹⁶ In this study, over 10,000 nulliparous women with singleton
140 pregnancies were enrolled for prospective study. Recruitment was conducted at geographically diverse
141 locations and was designed to sample a population reflective of the general US population. Women
142 were eligible for enrollment if they had a live singleton pregnancy, had no previous pregnancy that
143 progressed beyond 20 weeks of gestation, and were between 6 weeks 0 days and 13 weeks 6 days of
144 gestation at recruitment. Exclusion criteria included maternal age younger than 13 years, history of
145 three or more spontaneous abortions, current pregnancy complicated by suspected fatal fetal
146 malformation or known fetal aneuploidy, assisted reproduction with a donor oocyte, multifetal
147 reduction, or plan to terminate the pregnancy. Data were collected via multiple sources, including in-
148 person interviews, surveys completed by participants, and medical record review. Participants
149 completed three study visits with trained research personnel, with Visit 1 occurring between 6 weeks 0
150 days and 13 weeks 6 days of gestation. At least 30 days after delivery, trained and certified chart
151 abstractors reviewed the medical records of all participants and recorded final birth outcomes.¹⁶
152 Full details of the study protocol previously have been published.¹⁶

153 This analysis specifically addresses periconceptional dietary quality as the exposure of interest.
154 At Visit 1, women completed the modified Block 2005 Food Frequency Questionnaire, a
155 semiquantitative assessment of usual dietary intake for the 3 months around conception. The Block

156 questionnaire assesses 52 nutrients and 35 food groups from approximately 120 food and beverage
157 items. The questionnaire includes serial adjustment items to estimate portion size, and the instrument
158 has been validated in many populations. Details of the Block questionnaire have previously been
159 reported by Bodnar et al.¹¹

160 Answers to the Block questionnaire were scored using the Healthy Eating Index 2010 (HEI-2010),
161 or the HEI.^{17,18} The HEI, which is a measure used to assess how well a set of foods aligns with key
162 recommendations of the 2010 Dietary Guidelines for Americans, evaluates 12 key aspects of dietary
163 quality, including adequacy of intake of specific food groups and moderation of intake of less nutritious
164 foods. Higher scores represent better adherence to national guidelines, and an ideal score of 100
165 indicates that the reported food intake is consistent with the Dietary Guidelines recommendations.¹⁷
166 The mean HEI-2010 score for adult Americans in 2007-2008 was 54.3 out of 100, which indicated that
167 the average diet of adult Americans did not align with dietary recommendations.¹⁷ This analysis is
168 restricted to women with available HEI data.

169 We *a priori* selected 5 maternal and 5 neonatal outcomes of interest, each of which was chosen
170 based on the plausible relationship of these outcomes with periconceptional food quality.^{4,15,19-22}
171 Maternal outcomes included gestational diabetes mellitus (GDM), major perineal laceration (defined as
172 3rd or 4th degree perineal laceration), cesarean delivery, postpartum hemorrhage requiring a blood
173 transfusion, and hypertensive disorder of pregnancy. GDM diagnosis was based on clinical record review
174 using each site's local protocol for diagnosis. Postpartum hemorrhage was restricted to women who
175 required a transfusion in order to assess associations with the most severe version of this outcome.
176 Hypertensive disorder of pregnancy included antepartum gestational hypertension, or antepartum,
177 intrapartum, or postpartum (up to 14 days) preeclampsia, eclampsia, or superimposed preeclampsia, as
178 defined by the American College of Obstetricians and Gynecologists (ACOG).²³ Neonatal outcomes of
179 interest included preterm birth (<37 weeks of gestation), admission to the neonatal intensive care unit

180 (NICU), small-for-gestational age infant (defined as <10%ile by Alexander criteria²⁴), low birthweight
181 (defined as <2500g), and macrosomia (defined as >4000g).

182 Multiple maternal demographic and clinical characteristics were assessed as potentially
183 confounding factors. Demographic factors included maternal age, insurance status (public versus non-
184 public), marital status, household income (<200% or ≥200% of the poverty line), educational attainment
185 (some college or greater versus no college), and self-reported race and ethnicity (non-Hispanic white,
186 non-Hispanic black, Hispanic, Asian, and other). Clinical factors included body mass index (BMI, kg/m²) at
187 visit 1, tobacco use currently or before pregnancy, chronic hypertension (regardless of medication
188 status), pregestational diabetes mellitus, and any mental health disorder.

189 We examined differences between maternal baseline demographic and clinical characteristics
190 by HEI quartile using chi-squared and ANOVA tests, as appropriate. We then assessed differences
191 between maternal and neonatal outcomes by HEI quartile using chi-squared tests. HEI scores were
192 analyzed by quartile because such groupings best reflect clinically relevant categories of dietary quality
193 and are most consistent with existing literature. Analyses for the outcome of GDM excluded women
194 with pregestational diabetes mellitus. Using multivariable Poisson regression models, adjusted relative
195 risks were constructed to estimate the independent associations of HEI quartile with each outcome,
196 with HEI quartile 4 (highest level of food quality) as the referent, and each HEI quartile individually
197 compared to the referent. The multivariable model included potentially confounding variables that were
198 associated with HEI quartile on bivariable models with a p-value of <0.05. Although markers of
199 socioeconomic status differed by HEI quartile, these factors were (*a priori*) not used in multivariable
200 models because of likely collider bias related to the potential causal relationship between
201 socioeconomic factors, periconceptual dietary quality, and maternal and neonatal outcomes. Thus,
202 final models did not include race/ethnicity, insurance status, marital status, and educational attainment.

203 However, in order to confirm the primary findings, we performed a sensitivity analysis in which
204 race/ethnicity, insurance status, and marital status were included in the multivariable Poisson models.

205 All analyses were carried out in STATA release 15.0 (StataCorp, College Station, TX). All statistical
206 tests were two-tailed and considered significant at the $p < 0.05$ level. Each site's local governing
207 institutional review board approved the study and all women provided written informed consent prior
208 to participation.

209

210 RESULTS

211 The nuMoM2b cohort included 10,038 women, of whom 82% (N=8259) were eligible for
212 inclusion in this analysis. The mean HEI score was 63 with a standard deviation of 13 (Figure 1). Women
213 in the lowest quartile had scores less than 53.7, whereas quartile 2 included 53.8 to 63.7, quartile 3
214 included 63.8 to 72.7, and quartile 4 included women with scores 72.8 and greater. Women in the
215 lowest HEI quartile, representing poorest dietary quality, were younger, and more likely to be non-
216 Hispanic black or Hispanic, have public insurance, use tobacco, and have a lower household income
217 (Table 1). They were less likely to be married and have at least some college education. Women in the
218 lowest HEI quartile additionally had a higher mean pre-pregnancy BMI and were more likely to have
219 comorbidities, including chronic hypertension, pregestational diabetes, and mental health disorders.

220 Women in the lowest HEI quartile (quartile 1) experienced a greater frequency of postpartum
221 hemorrhage requiring transfusion ($p=0.02$) and hypertensive disorder of pregnancy ($p<0.001$), but a
222 significantly lower frequency of major perineal laceration ($p<0.001$) (Table 2). There were no differences
223 in frequency of GDM or cesarean delivery by HEI quartile on bivariable analyses. These findings largely
224 persisted on multivariable analyses (Table 3). For postpartum hemorrhage requiring transfusion and
225 hypertensive disorders, women in quartile 1 had greater relative risk of both outcomes (hemorrhage:
226 aRR 3.33, 95% CI 1.47-7.52; hypertension: aRR 1.16, 95% CI 1.02-1.31) compared to women in quartile 4.

227 Women in HEI quartile 1 also had lower relative risk of major perineal laceration (aRR 0.68, 95% CI 0.47-
228 0.98) compared to women in quartile 4. The adjusted relative risk of cesarean delivery was greater for
229 women with HEI quartile 1 (aRR 1.20, 95% CI 1.07-1.34) and quartile 2 (aRR 1.11, 95% CI 1.00-1.23) than
230 women in quartile 4. Women in quartile 3 of HEI did not differ from quartile 4 with respect to any
231 outcome, and risk of GDM was unassociated with HEI quartile.

232 Neonatal outcomes additionally differed by HEI quartile (Table 4). Women with lower HEI
233 quartiles experienced greater frequency of preterm birth ($p=0.014$), NICU admission ($p=0.009$), small-
234 for-gestational-age status ($p<0.001$), and low birthweight ($p=0.002$). Women with lower HEI quartiles
235 also experienced lower frequency of macrosomia ($p=0.025$). On multivariable analyses, all relationships
236 persisted for women in quartile 1 compared to quartile 4 (Table 5). Further, women in quartiles 1 and 2
237 had lower risk of macrosomia than women in quartile 4. The risk of NICU admission was elevated for
238 women in all quartiles compared to quartile 4.

239 Results of the sensitivity analysis with inclusion of race/ethnicity, insurance status, and marital
240 status in the multivariable models confirmed the primary analysis, in that the direction and magnitude
241 of associations remained consistent. Specifically, all point estimates for the relative risks in the
242 sensitivity analysis remained within 15% of the primary analysis with the exception of quartile 1
243 comparisons for small-for-gestational-age status and low birthweight, in which the risks both decreased
244 by 17% (Table 6).

245

246 **COMMENT**

247 *Principal findings*

248 Periconceptional dietary quality is associated with differences in demographic characteristics
249 among US pregnant women, but previous work had not addressed associations of dietary quality with
250 obstetric and perinatal outcomes. We identified that poor periconceptional dietary quality is associated

251 with multiple adverse maternal and neonatal outcomes, including postpartum hemorrhage,
252 hypertensive disorders of pregnancy, cesarean delivery, preterm birth, NICU admission, small-for-
253 gestational-age status, and low birthweight, even when accounting for comorbidities and BMI. In
254 contrast, women with poor dietary quality experienced lower risk of macrosomia. There is a dose-
255 response effect, such that women with the lowest dietary quality had the strongest associations with
256 adverse outcomes, whereas outcomes for women in the third quartile of dietary quality were similar to
257 those of women in the highest quartile.

258 *Results in Context*

259 There are several postulated mechanisms that may underlie these findings. First, poor
260 periconceptional dietary quality may lead to micronutrient deficiency, potentially interfering with
261 clotting factors that allow normal recovery in the context of obstetrical hemorrhage or other factors that
262 alter risk of placentally-mediated diseases. This hypothesis has been explored in small studies where
263 obese women had lower amounts of micronutrients despite energy-rich diets.²⁵ Second, greater intake
264 of low-quality foods has been previously associated with excessive weight gain.²⁶ Thus, periconceptional
265 dietary quality may affect outcomes via its influence on gestational weight gain.²⁷ For example, in an
266 Italian cohort, women with “prudent” dietary patterns before pregnancy had improved gestational
267 weight gain outcomes than women with worse dietary quality.²⁸ Third, food insecurity, or sufficient
268 access by all people at all times to enough food to lead an active, healthy life, may also play an
269 important role.²⁹ It is plausible that women in the lowest quartiles of periconceptional dietary quality
270 experienced poor quality due to food insecurity.

271 Although the landscape of racial, ethnic, and socioeconomic inequities in the US differ from
272 those of Western European countries, some of our findings mirror theirs. For example, in a Spanish
273 cohort of 787 women, early pregnancy HEI scores in the lowest quartile were associated with greater
274 odds of fetal growth restriction; the effect was most pronounced for the first versus fourth quartiles.¹⁵

275 Work from the Norwegian Mother and Child Cohort Study found that better quality mid-pregnancy diet
276 was associated with more optimal fetal growth outcomes and lower odds of preeclampsia, preterm
277 birth, and postpartum weight retention.^{19,20,22}

278 *Clinical and research implications*

279 These data suggest that health care providers who care for pregnant and preconception women
280 should include a basic assessment of dietary quality as a component of counseling about lifestyle factors
281 that may promote maternal and fetal health. Ample evidence suggests pregnancy is an opportunity for
282 improvement of healthy behaviors, that nutrition and lifestyle modification advice are well received by
283 women who seek preconception care, and that some interventions in this period may have long-lasting
284 maternal and child health benefits.^{12,30} ACOG addresses the importance of discussing diet in the context
285 of caring for women who are overweight or obese and additionally includes food access as one of
286 several social determinants of health to be screened.^{31,32} We propose that further attention to dietary
287 quality in the obstetric context may be worthwhile for clinical practice and future research.

288 There are several potential areas for future investigation. This analysis only addresses total HEI
289 scores as a reflection of adherence to national nutrition guidelines. Future work can also assess specific
290 dietary sources of nutrients, dietary sources of energy, components of the HEI, and the role of nutrient
291 supplementation. Additional methods of examining diet may include measures of food group diversity,
292 which has been shown to reflect micronutrient intake in a study of pregnant women.³³ Future work also
293 should investigate food security and the mechanisms between inequity and food quality. Future
294 investigations may also address whether interventions that improve dietary quality during pregnancy
295 are associated with improvements in perinatal outcomes. Finally, we must also understand the dietary
296 quality issues unique to women with comorbidities such as diabetes.

297 Importantly, race and ethnicity are socially mediated concepts that have previously been
298 associated with food quality. For this reason, we opted to not adjust for race and markers of

299 socioeconomic status in the primary analysis, due to the possibility of collider bias and the obscuring of
300 the potential effects of periconceptional food quality on outcomes. Moreover, results of the sensitivity
301 analysis supported the main analysis; in some cases the confidence intervals crossed unity, but given the
302 overall consistency of the adjusted relative risk point estimates, this appears to be largely a result of
303 reduced degrees of freedom once more variables are added into the regression. The etiologies of race
304 and socioeconomic status as drivers of adverse perinatal outcomes have not fully been elucidated, but
305 we theorize that suboptimal periconceptional and pregnancy food quality may be one mechanism.
306 Future work on dietary quality needs to address disparities by race, ethnicity, education, and
307 socioeconomic status in more depth in attempt to understand their role in contributing to differences in
308 adverse outcomes.

309 *Strengths and limitations*

310 A major strength of this study is the use of a large and diverse sample of US women that is
311 representative of the population at large. Moreover, the nuMoM2b cohort is extraordinarily well
312 characterized and includes detailed assessments that enhance the granularity and quality of data, in
313 contrast to data from vital statistics databases. The direct questioning of food quality via the HEI only a
314 short amount of time after the period of interest also enhances the quality and fidelity of dietary recall,
315 in contrast to investigations that use more generalized assessments, less standardized measurement
316 approaches, or require longer periods of recall.

317 However, there are several limitations to consider. This is an observational analysis, as are most
318 studies of dietary quality, and as such, findings can be affected by unmeasured confounding. Second,
319 although much data suggest pregnancy diet is likely to be very similar to periconceptional diet, the
320 association may be imprecise. Third, all estimates of typical dietary intake have inherent imperfections
321 due to misreporting or recall bias, although self-reported dietary data have sufficient fidelity to inform
322 policy and dietary guidelines.¹¹ Finally, nuMoM2b participants were interested in a longitudinal research

323 investigation that began in early pregnancy and were recruited from a large academically-affiliated
324 medical centers, and thus findings may not be fully generalizable.

325 *Conclusions*

326 In summary, US women have very poor dietary quality prior to pregnancy. Dietary quality
327 remains an important public health issue in the US and internationally, and is a major contributor to
328 morbidity and overall population health.³ Additionally, dietary inequities are pervasive and may have an
329 impact on perinatal health, which is an important area for ongoing study. These data demonstrate that
330 periconceptual dietary quality may be associated with adverse maternal and child health outcomes,
331 which can have both short- and long-term implications for the health of the family, including potential
332 intergenerational or epigenetic effects. These findings emphasize the critical nature of preconception
333 care, food-focused public health policies, and systems-level changes that promote healthy food choices,
334 particularly during important windows of opportunity such as pregnancy.

335 REFERENCES

- 336 1. Wang D, Leung C, Li Y, et al. Trends in dietary quality among adults in the United States, 1999
337 through 2010. *JAMA Intern Med* 2014;174:1587-94.
- 338 2. Rehm C, Penalvo J, Afshin A, Mozaffarian D. Dietary Intake Among US Adults, 1999-2012. *JAMA*
339 2016;315:2542-53.
- 340 3. Wang D, Li Y, Afshin A, et al. Global Improvement in Dietary Quality Could Lead to Substantial
341 Reduction in Premature Death. *J Nutr* 2019;149:1065-74.
- 342 4. Orr C, Keyserling T, Ammerman A, Berkowitz S. Diet quality trends among adults with diabetes
343 by socioeconomic status in the U.S.: 1999-2014. *BMC Endocr Disord* 2019;19:54.
- 344 5. Fang Zhang F, Liu J, Rehm C, Wilde P, Mande J, Mozaffarian D. Trends and Disparities in Diet
345 Quality Among US Adults by Supplemental Nutrition Assistance Program Participation Status.
346 *JAMA Netw Open* 2018;1:e180237.
- 347 6. Inskip H, Crozier S, Godfrey K, et al. Women's compliance with nutrition and lifestyle
348 recommendations before pregnancy: general population cohort study. *BMJ* 2009;338:b481.
- 349 7. Ramage S, McCargar L, Berglund C, Harber V, Bell R, Team ftAS. Assessment of Pre-Pregnancy
350 Dietary Intake with a Food Frequency Questionnaire in Alberta Women. *Nutrients* 2015;7:6155-
351 66.
- 352 8. Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: nutrition and lifestyle in the
353 preconception period and its importance for future health. *Lancet* 2018;391:1830-41.
- 354 9. Lundqvist A, Johansson I, Wennberg A, et al. Reported dietary intake in early pregnant
355 compared to non-pregnant women - a cross-sectional study. *BMC Pregnancy Childbirth* 2014;14.
356 10. Crozier S, Robinson S, Godfrey K, Cooper C, Inskip H. Women's dietary patterns change little
357 from before to during pregnancy. *J Nutri* 2009;139:1956-63.
- 358 11. Bodnar L, Simhan H, Parker C, et al. Racial or ethnic and socioeconomic inequalities in adherence
359 to National Dietary Guidance in a large cohort of US pregnant women. *J Acad Nutri Diet*
360 2017;117:867-77.
- 361 12. Baird J, Jacob C, Barker M, et al. Developmental Origins of Health and Disease: A Lifecourse
362 Approach to the Prevention of Non-Communicable Diseases. *Healthcare (Basel)* 2017;5:pji: E14.
- 363 13. Oliver M, Jaquiery A, Bloomfield F, Harding J. The effects of maternal nutrition around the time
364 of conception on the health of the offspring. *Soc Reprod Fertil Steril* 2007;64:397-410.
- 365 14. Gaskins A, Nassan F, Chiu Y, et al. Dietary patterns and outcomes of assisted reproduction. *Am J*
366 *Obstet Gynecol* 2019;220:567.e1-18.
- 367 15. Rodriguez-Bernal C, Rebagliato M, Iniguez C, et al. Diet quality in early pregnancy and its effects
368 on fetal growth outcomes: the Infancia y Medio Ambiente (Childhood and Environment) Mother
369 and Child Cohort Study in Spain. *Am J Clin Nutr* 2010;91:1659-66.
- 370 16. Haas D, Parker C, Wing D, et al. A description of the methods of the Nulliparous Pregnancy
371 Outcomes Study: monitoring mothers-to-be (nuMoM2b). *American Journal of Obstetrics and*
372 *Gynecology* 2015;212:539.e1-24.
- 373 17. Healthy Eating Index (HEI). 2019. (Accessed Accessed September 30, 2019, at
374 <https://www.fns.usda.gov/resource/healthy-eating-index-hei>.)
- 375 18. Guenther P, Kirkpatrick S, Reedy J, et al. The Healthy Eating Index-2010 is a valid and reliable
376 measure of diet quality according to the 2010 Dietary Guidelines for Americans. *J Nutr*
377 2014;144:399-407.
- 378 19. Torjusen H, Brantsaeter A, Haugen M, et al. Reduced risk of pre-eclampsia with organic
379 vegetable consumption: results from the prospective Norwegian Mother and Child Cohort
380 Study. *BMJ Open* 2014;4:e006143.

- 381 20. Englund-Ogge L, Brantsaeter A, Sengpiel V, et al. Maternal dietary patterns and preterm
382 delivery: results from large prospective cohort study. *BMJ* 2014;348:g1446.
- 383 21. Agrawal S, Fledderjohann J, Vellakkal S, Stuckler D. Adequately diversified dietary intake and
384 iron and folic acid supplementation during pregnancy is associated with reduced occurrence of
385 symptoms suggestive of pre-eclampsia or eclampsia in Indian women. *PLOS One*
386 2015;10:e0119120.
- 387 22. von Ruesten A, Brantsaeter A, Haugen M, et al. Adherence of pregnant women to Nordic dietary
388 guidelines in relation to postpartum weight retention: results from the Norwegian Mother and
389 Child Cohort Study. *BMC Public Health* 2014;14.
- 390 23. American College of O, Gynecologists, Task Force on Hypertension in P. Hypertension in
391 pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on
392 Hypertension in Pregnancy. *Obstet Gynecol* 2013;122:1122-31.
- 393 24. Alexander G, Himes J, Kaufman R, Mor J, Kogan M. A United States national reference for fetal
394 growth. *Obstet Gynecol* 1996;87:163-8.
- 395 25. Mohd-Shukri N, Duncan A, Denison F, et al. Health Behaviours during Pregnancy in Women with
396 Very Severe Obesity. *Nutrients* 2015;7:8431-43.
- 397 26. Boggs D, Rosenberg L, Rodriguez-Bernal C, Palmer J. Long-term diet quality is associated with
398 lower obesity risk in young African American women with normal BMI at baseline. *J Nutr*
399 2013;143:1636-41.
- 400 27. Uusitalo U, Arkkola T, Ovaskainen M, et al. Unhealthy dietary patterns are associated with
401 weight gain during pregnancy among Finnish women. *Public Health Nutr* 2009;12:2392-9.
- 402 28. Maugeri A, Barchitta M, Favara G, et al. Maternal Dietary Patterns Are Associated with Pre-
403 Pregnancy Body Mass Index and Gestational Weight Gain: Results from the "Mamma &
404 Bambino" Cohort. *Nutrients* 2019;11:1308-20.
- 405 29. Coleman-Jensen A, Rabbitt M, Gregory C, Singh A, for the United States Department of
406 Agriculture. Household food security in the United States in 2018. Economic Research Report
407 Number 270. US Department of Agriculture Economic Research Service; 2019.
- 408 30. Stephenson J, Patel D, Barrett G, et al. How do women prepare for pregnancy? Preconception
409 experiences of women attending antenatal services and views of health professionals. *PLOS One*
410 2014;9:e103085.
- 411 31. American College of Obstetricians and Gynecologists. Challenges for Overweight and Obese
412 Women, Committee Opinion No 591. *Obstet Gynecol* 2014;123:726-30.
- 413 32. American College of Obstetricians and Gynecologists. Importance of social determinants of
414 health and cultural awareness in the delivery of reproductive health care, Committee Opinion
415 No. 729. *Obstet Gynecol* 2018;131.
- 416 33. Komatowski B, Comstock S. Dietary diversity is inversely correlated with pre-pregnancy body
417 mass index among women in a Michigan pregnancy cohort. *PeerJ* 2018;6.
- 418

419

420 **Figure 1: Healthy Eating Index-2010 Score Distribution**

Journal Pre-proof

421 **Table 1: Demographic and clinical characteristics associated with Healthy Eating Index quartile**

	HEI quartile 1 (N=2065)	HEI quartile 2 (N=2065)	HEI quartile 3 (N=2065)	HEI quartile 4 (N=2064)	P value*
Maternal age, years	23.9 (\pm 5.2)	26.6 (\pm 5.5)	28.7 (\pm 5.1)	29.9 (\pm 4.5)	<0.001
Race/ethnicity					<0.001
Non-Hispanic white	987 (47.8)	1198 (58.1)	1472 (71.3)	1536 (74.4)	
Non-Hispanic black	496 (24.0)	277 (13.4)	113 (5.5)	58 (2.8)	
Hispanic	420 (20.3)	421 (20.4)	287 (13.9)	246 (11.9)	
Asian	31 (1.5)	68 (3.3)	107 (5.2)	142 (6.9)	
Other	131 (6.3)	99 (4.8)	85 (4.1)	82 (4.0)	
Public insurance	1037 (50.7)	604 (29.5)	313 (15.2)	174 (8.4)	<0.001
Household income <200% poverty line	782 (55.7)	567 (33.8)	341 (18.5)	241 (12.4)	<0.001
Married	630 (30.5)	1201 (58.2)	1571 (76.2)	1795 (87.0)	<0.001
Some college education or greater	1581 (82.0)	1532 (90.7)	1384 (96.5)	1182 (98.8)	<0.001
Body mass index, kg/m ²	27.1 (\pm 7.3)	26.9 (\pm 6.6)	25.9 (\pm 5.6)	24.9 (\pm 4.9)	<0.001
Ever used tobacco	1047 (50.7)	864 (41.9)	788 (38.3)	756 (36.6)	<0.001
Chronic hypertension	64 (3.3)	60 (3.0)	43 (2.2)	24 (1.2)	<0.001
Pregestational diabetes mellitus	39 (2.0)	33 (1.7)	29 (1.5)	16 (0.8)	0.018
Mental health disorder	433 (22.0)	356 (17.9)	339 (17.0)	289 (14.6)	<0.001

Data displayed as N (%) or mean (\pm standard deviation).

HEI, Healthy Eating Index; quartile 4 represents the best quality of periconceptual diet

* P-value for chi-squared or ANOVA test.

422

423

424 **Table 2: Maternal outcomes by Healthy Eating Index quartile**

	HEI quartile 1 (N=2065)	HEI quartile 2 (N=2065)	HEI quartile 3 (N=2065)	HEI quartile 4 (N=2064)	P value*
Gestational diabetes mellitus	89 (4.6)	92 (4.7)	84 (4.3)	80 (4.1)	0.758
Cesarean delivery	536 (27.2)	559 (28.1)	559 (28.1)	521 (26.3)	0.539
Major perineal laceration	47 (4.7)	83 (7.5)	102 (8.6)	113 (9.3)	<0.001
Postpartum hemorrhage requiring transfusion	28 (1.4)	18 (0.9)	15 (0.7)	10 (0.5)	0.02
Hypertensive disorder of pregnancy	510 (25.9)	481 (24.1)	445 (22.4)	401 (20.3)	<0.001

Data displayed as N (%).
 HEI, Healthy Eating Index; quartile 4 represents the best quality of periconceptional diet
 * P-value for chi-squared test.

425

426

427 **Table 3: Multivariable analysis of maternal outcomes by Healthy Eating Index quartile**

428

	HEI Q1 aRR (95% CI)	HEI Q2 aRR (95% CI)	HEI Q3 aRR (95% CI)	HEI Q4
Gestational diabetes mellitus	1.20 (0.86-1.65)	1.11 (0.82-1.49)	1.01 (0.75-1.36)	Ref
Cesarean delivery	1.20 (1.07-1.34)	1.11 (1.00-1.23)	1.07 (0.96-1.18)	Ref
Major perineal laceration	0.68 (0.47-0.98)	0.97 (0.73-1.28)	0.97 (0.75-1.26)	Ref
Postpartum hemorrhage requiring transfusion	3.33 (1.47-7.52)	2.07 (0.94-4.52)	1.59 (0.71-3.58)	Ref
Hypertensive disorder of pregnancy	1.16 (1.02-1.31)	1.11 (0.98-1.25)	1.05 (0.94-1.19)	Ref

Data displayed as adjusted relative risk (95% confidence interval), estimated through a Poisson regression model. HEI, Healthy Eating Index; quartile 4 represents the best quality of periconceptual diet and is the referent. Adjusted for age, body mass index, tobacco use, chronic hypertension, pregestational diabetes mellitus, and mental health disorder.

429

430 **Table 4: Neonatal outcomes by Healthy Eating Index quartile**

	HEI quartile 1 (N=2065)	HEI quartile 2 (N=2065)	HEI quartile 3 (N=2065)	HEI quartile 4 (N=2064)	P value*
Preterm birth (<37 weeks)	197 (9.5)	171 (8.3)	155 (7.5)	143 (6.9)	0.014
NICU admission	350 (18.0)	362 (18.3)	345 (17.5)	288 (14.6)	0.009
Small for gestational age (<10%ile)	252 (12.8)	218 (11.0)	174 (8.8)	187 (9.5)	<0.001
Low birth weight <2500g	158 (7.7)	129 (6.2)	105 (5.1)	111 (5.4)	0.002
Macrosomia >4000g	214 (10.4)	226 (10.9)	244 (11.8)	273 (13.2)	0.025

Data displayed as N (%).

HEI, Healthy Eating Index; quartile 4 represents the best quality of periconceptional diet. NICU, neonatal intensive care unit

* P-value for chi-squared test.

431

432

433 **Table 5: Multivariable analysis of neonatal outcomes by Healthy Eating Index quartile**

434

	HEI Q1 aRR (95% CI)	HEI Q2 aRR (95% CI)	HEI Q3 aRR (95% CI)	HEI Q4
Preterm (<37 weeks)	1.27 (1.01-1.60)	1.12 (0.90-1.40)	1.02 (0.81-1.27)	Ref
NICU admission	1.22 (1.04-1.42)	1.23 (1.06-1.42)	1.19 (1.03-1.38)	Ref
Small for gestational age (<10%ile)	1.24 (1.02-1.51)	1.11 (0.92-1.34)	0.91 (0.4-1.11)	Ref
Low birth weight <2500g	1.32 (1.02-1.71)	1.10 (0.85-1.42)	0.89 (0.68-1.16)	Ref
Macrosomia >4000g	0.60 (0.47-0.76)	0.78 (0.63-0.96)	0.85 (0.70-1.03)	Ref

Data displayed as adjusted relative risk (95% confidence interval), estimated through a Poisson regression model.

HEI, Healthy Eating Index; quartile 4 represents the best quality of periconceptional diet and is the referent. NICU, neonatal intensive care unit

Adjusted for age, body mass index, tobacco use, chronic hypertension, pregestational diabetes mellitus, and mental health disorder.

435

436

437 **Table 6: Sensitivity analyses including markers of socioeconomic status**

	HEI Q1 aRR (95% CI)	HEI Q2 aRR (95% CI)	HEI Q3 aRR (95% CI)	HEI Q4
Maternal outcomes				
Gestational diabetes mellitus	1.09 (0.78-1.53)	1.07 (0.79-1.35)	1.00 (0.74-1.35)	Ref
Cesarean delivery	1.12 (1.00-1.25)	1.07 (0.96-1.19)	1.06 (0.96-1.17)	Ref
Major perineal laceration	0.78 (0.53-1.14)	1.02 (0.77-1.35)	0.99 (0.77-1.28)	Ref
Postpartum hemorrhage requiring transfusion	3.32 (1.48-7.44)	1.98 (0.91-4.31)	1.57 (0.70-3.52)	Ref
Hypertensive disorder of pregnancy	1.13 (1.00-1.29)	1.10 (0.98-1.24)	1.05 (0.93-1.19)	Ref
Neonatal outcomes				
Preterm (<37 weeks)	1.11 (0.88-1.42)	1.07 (0.85-1.33)	0.99 (0.79-1.23)	Ref
NICU admission	1.18 (1.00-1.39)	1.21 (1.04-1.41)	1.18 (1.02-1.37)	Ref
Small for gestational age (<10%ile)	1.03 (0.83-1.27)	1.01 (0.83-1.23)	0.88 (0.72-1.07)	Ref
Low birth weight <2500g	1.09 (0.83-1.44)	1.01 (0.78-1.31)	0.86 (0.66-1.13)	Ref
Macrosomia >4000g	0.63 (0.49-0.81)	0.81 (0.65-0.99)	0.85 (0.70-1.04)	Ref
Data displayed as adjusted relative risks (95% confidence interval), estimated through a Poisson regression model.				
HEI, Healthy Eating Index; quartile 4 represents the best quality of periconceptional diet and is the referent. NICU, neonatal intensive care unit				
Adjusted for age, body mass index, tobacco use, chronic hypertension, pregestational diabetes mellitus, mental health disorder, race/ethnicity, insurance status, and marital status.				

438

