

## Short Communication

# The biomarker-based validity of a brief-type diet history questionnaire for estimating eicosapentaenoic acid and docosahexaenoic acid intakes in pregnant Japanese women

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**Objectives:** Maternal docosahexaenoic acid (DHA) intakes is important for brain development in fetuses. Accurate assessment of EPA and DHA intakes is required in clinical settings to identify women with deficiency of these nutrients and provide an appropriate intervention for them. We examined the validity and reproducibility of a brief-type self-administered diet history questionnaire (BDHQ) for evaluating EPA and DHA intakes of pregnant Japanese women, to establish an easily administered dietary assessment tool. **Methods:** A total of 105 women in the second trimester and 102 women in the third trimester were studied at a university hospital in Tokyo, between November 2010 and February 2012. The reference values for the validation study were plasma concentrations of EPA and DHA. For the reproducibility study, 54 women completed the BDHQ twice, within a 4-week period in the second trimester. **Results:** Energy-adjusted intakes of EPA, DHA, and EPA+DHA were significantly associated with the corresponding plasma concentrations ( $r_s=0.354$ ,  $r_s=0.305$ , and  $r_s=0.327$  in the second trimester;  $r_s=0.391$ ,  $r_s=0.316$ , and  $r_s=0.358$  in the third trimester, respectively). Intraclass correlation coefficients for the two-time BDHQ were 0.543 (EPA), 0.611 (DHA), and 0.581 (EPA+DHA). In the Bland-Altman plots, the intakes of EPA, DHA, and EPA+DHA in the two-time BDHQ showed that the values for most participants were in the accepted range of agreement. **Conclusions:** BDHQ has an acceptable validity level for assessing EPA and DHA intakes among Japanese women in the second and third trimesters.

**Key Words:** diet history questionnaire, docosahexaenoic acid, eicosapentaenoic acid, pregnant women, validation

## INTRODUCTION

The human brain is highly enriched in the long chain omega 3 fatty acid, docosahexaenoic acid (DHA) which accumulates during fetal and postnatal development.<sup>1</sup> Another long chain omega 3 fatty acid, eicosapentaenoic acid (EPA) together with DHA have been implicated in reducing the severity of depression in mothers.<sup>2</sup> Therefore, these fatty acids have been the focus of recent research. Intake of sufficient amounts of EPA and DHA is beneficial for maintaining appropriate blood concentration since a major part of EPA and DHA is sourced from foods. However, insufficient intakes of EPA and DHA in most pregnant Japanese women have been previously shown.<sup>3,4</sup> At present, clinical assessment of EPA and DHA intakes in routine pregnancy medical checkups is not conducted in many general hospitals in Japan. This is because dietary assessments conducted by dietitians are expensive and time consuming, and an easily administered dietary assessment tool has not been established yet.

A self-administered diet history questionnaire (DHQ), which contains questions regarding 150 food and beverage items, was developed in Japan to assess dietary intake over the previous month.<sup>5</sup> This DHQ has accepted validity and reproducibility with regard to EPA and DHA intakes among pregnant women without pregnancy-associated nausea.<sup>3</sup> However, it is difficult to use this questionnaire as an assessment tool in clinical settings as it is highly time consuming. To address this problem, a brief-type self-administered diet history questionnaire

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Manuscript received 25 January 2014. Initial review completed 12 June 2014. Revision accepted 18 August 2014.

doi: 10.6133/apjcn.2015.24.2.10

(BDHQ) was developed as a short version of the DHQ;<sup>6</sup> this questionnaire takes only 10-15 minutes to answer. In non-pregnant Japanese adults, the nutrient intake estimates from the BDHQ show relatively high correlation coefficients with those from a reference method.<sup>5</sup> However, for the BDHQ to be applied to pregnant women, a separate validation study of the BDHQ specific to pregnancy is needed because most pregnant women are likely to make a conscious change of their dietary habits for themselves and their babies, and their dietary intake would be affected by pregnancy-associated physical conditions such as nausea and temporary change in appetite and preference.<sup>7</sup>

The aim of the present study was to evaluate the relative validity of the BDHQ for estimating EPA and DHA intakes in pregnant Japanese women by comparing these with their corresponding plasma concentrations. We also compared EPA and DHA intakes estimated from two-time BDHQ to assess its reproducibility. If the BDHQ is utilizable during pregnancy, it might facilitate routine nutritional assessment in clinical settings of Japan.

## Material and Methods

### Participants

This validation study was conducted at a university hospital in Tokyo between November 2010 and March 2012. Healthy Japanese women with single pregnancies were surveyed at 19-23 weeks of gestation and 35-36 weeks of gestation. The women at 19-23 weeks of gestation were recruited for this validation study at their routine antenatal medical checkups during their second trimester. The women at 35-36 weeks of gestation were recruited when they were at 19-23 weeks of gestation to participate in our other longitudinal study. To avoid participants' burden, patients with hypertension, diabetes, or psychiatric disorder were excluded. In addition, women aged <20 years, those with poor reading ability in Japanese, and those who took supplements including EPA and DHA were also excluded.

To identify the accurate week of pregnancy gestation, all participants underwent ultrasonography at 8-12 weeks of gestation. All participants were provided with detailed information about the study protocol, and each gave written informed consent. The research ethics committee of the Graduate School of Medicine at the University of Tokyo approved the study procedures (No. 3197).

Participants answered questionnaires, including the BDHQ, while waiting for a medical checkup at 19-23 weeks of gestation or 35-36 weeks of gestation. Non-fasting blood samples were drawn during the routine blood tests of normal pregnancy-related health examination. Participants answered questionnaires either on the same day as their blood sample collection or within a 7-day period after the sample collection.

To assess the reproducibility of the BDHQ, pregnant women at 15-19 weeks of gestation were recruited between November 2010 and March 2011. These participants completed the BDHQ twice during their second trimester, once at recruitment and again, 4 weeks later.

### Diet history questionnaire

The BDHQ, a short version of the DHQ, was designed to

assess dietary intake over a month.<sup>6</sup> The DHQ is a 22-page semi-quantitative questionnaire that assesses dietary intake on the basis of the reported consumption frequency and portion size of 150 food and beverage items. The questionnaire takes 30-40 minutes to answer. In contrast, the BDHQ is a 4-page fixed-portion questionnaire that assesses dietary intake on the basis of the reported consumption frequency of 58 different food and beverage items. It takes only 10-15 minutes to answer. Most food and beverage items were selected from the food list of the DHQ as these items are commonly consumed in Japan. Standard portion sizes for women were derived from the primary data provided by the National Nutrition Survey of Japan and various recipe books for Japanese dishes.<sup>8</sup> The BDHQ includes questions regarding not only frequency of consumption of the selected foods, but also the usual cooking methods and general dietary behavior.

The EPA and DHA intakes were calculated from the six options for fish consumption: "squid, octopus, shrimp, and clam," "small fish with bones," "dried fish and salted fish," "canned tuna," "oily fish," and "lean fish." The seven frequency responses to each item listed ranged from "more than twice per day" to "almost never." Estimates for energy, EPA, and DHA intakes were based on the Japanese Standard of Food Composition Tables.<sup>9</sup> We calculated energy-adjusted intakes of EPA, DHA, and EPA plus DHA by the density method, as using energy-adjusted values of nutrients is recommended in epidemiological studies to reduce intra-individual measurement errors.

We excluded participants who reported an extremely unrealistic energy intake from the analysis (i.e., a reported energy intake of less than half the energy requirement for the lowest physical activity category or more than 1.5 times the energy requirement for moderate physical activity, according to the "Dietary Reference Intakes for Japanese").<sup>10,11</sup>

In a previous study with non-pregnant Japanese women, the correlation coefficients between energy-adjusted intakes from the BDHQ and the corresponding serum phospholipid concentrations were  $r=0.33$  for EPA,  $r=0.27$  for DHA, and  $r=0.31$  for EPA plus DHA, respectively.<sup>12</sup>

### Biological markers

Within 8 hours of collection, blood samples were centrifuged for 10 minutes at 3,000 rpm to separate plasma. The plasma samples were stored at  $-80^{\circ}\text{C}$  until analysis. The samples were measured within 6 months of collection. EPA and DHA concentrations were assayed using gas chromatography. The reference values for plasma EPA and DHA concentrations are 11.6-107.2  $\mu\text{g/mL}$  and 48.6-152.4  $\mu\text{g/mL}$ , respectively. Assays were conducted at the Mitsubishi Kagaku Bio-Chemical Laboratories, Tokyo, Japan.

### General questionnaires and data processing

We collected demographic and lifestyle information including age, gestational age, smoking status, and supplement use with a self-administered questionnaire. Participants were also asked if they had pregnancy-associated nausea in the previous month. Pre-pregnancy body mass index (BMI) was calculated from self-reported

pre-pregnancy weight and height. The BMI was classified according to World Health Organization criteria: underweight (BMI <18.5 kg/m<sup>2</sup>), normal weight (BMI=18.5–24.9 kg/m<sup>2</sup>), and overweight or obese (BMI ≥25.0 kg/m<sup>2</sup>).

### Statistical analyses

We assumed the level of validity between the estimated intakes provided via the BDHQ and the corresponding plasma concentrations, with 80% power and a 5% significance level. A sample size of more than 85 was required to detect a minimally acceptable level of  $r=0.30$ .<sup>13</sup> Associations between intakes and plasma concentrations of EPA, DHA, and EPA plus DHA were analyzed using Spearman's rank correlation coefficient.

We calculated the intraclass correlation coefficients (ICCs) of EPA, DHA, and EPA plus DHA intakes estimated from the two-time BDHQ. The calculations were performed after log-transformation of the intake data because of the right-skewed distribution. Bland-Altman plots were used to illustrate the difference between the two-time BDHQ against the mean intakes of EPA, DHA, and EPA plus DHA by the two-time BDHQ. The upper and lower lines represented the upper and lower 95% limits of agreement (mean difference±1.96 SD).

Statistical analyses were conducted using Statistical Package for Social Sciences for Windows, version 15.0 (SPSS Japan Inc.). All statistical tests were two-tailed. Values of  $p<0.05$  were considered statistically significant.

## RESULTS

### Validation study

Of the 147 women recruited for the validation study in the second trimester, 131 (89.1%) provided written informed consent. We excluded 26 women for the following reasons: 9 had missing data; 9 had insufficient blood collection; 2 had a severely under-reported energy intake, and 6 took DHA supplements. Our final analysis was therefore conducted using data from 105 healthy pregnant women in the second trimester (71.4%). Of the 140 women who met the inclusion criteria for the validation study of the third trimester, 38 women were excluded for the following reasons; 12 had missing data; 13 had insufficient blood collection; 5 had a severely under-reported energy intake, and 8 took DHA supplements. Our analysis in the third trimester was conducted using data obtained from 102 healthy pregnant women (72.8%).

Table 1 shows the characteristics of the participants. The mean age was 34.7 years in the second and third trimesters. Twenty-nine participants (27.6%) in the second trimester and 38 (37.2%) in the third trimester reported having pregnancy-associated nausea. The median (interquartile range) daily intakes of EPA and DHA were 165 (101–262) mg/day and 297 (195–452) mg/day in the second trimester and 174 (121–252) mg/day and 316 (227–432) mg/day in the third trimester, respectively. Sixty-two participants (59.0%) in the second trimester and 53 (51.2%) in the third trimester had EPA plus DHA intake

**Table 1.** Characteristics of participants

	Validation study		Reproducibility study (n=54)
	Second trimester (n=105)	Third trimester (n=102)	
Age (years), mean (SD)	34.7 (4.1)	34.7 (4.4)	34.6 (3.6)
Parity: Primigravida, n (%)	71 (68)	55 (54)	35 (65)
Education, n (%)			
High school	7 (7)	10 (10)	6 (11)
Junior or technical college	44 (42)	41 (40)	19 (35)
College or university	54 (51)	51 (50)	29 (54)
Household income (Japanese yen/year), n (%)			
<5,000,000	12 (11)	19 (19)	9 (17)
5,000,000 - 9,000,000	52 (50)	43 (42)	27 (50)
>9,000,000	41 (39)	40 (39)	18 (33)
Height (cm), mean (SD)	159 (5.0)	160 (5.4)	160 (5.5)
Pre-pregnancy BMI (kg/m <sup>2</sup> ), mean (SD)	20.3 (2.6)	20.9 (2.7)	20.5 (2.7)
BMI <18.5, n (%)	31 (30)	11 (11)	12 (22)
BMI=18.5-24.9, n (%)	67 (64)	81 (79)	38 (70)
BMI ≥25.0, n (%)	7 (7)	10 (10)	4 (7)
Regular smoker during pregnancy, n (%)	0 (0)	3 (3)	0 (0)
Having pregnancy-associated nausea, n (%)	29 (28)	38 (37)	12 (22)
Gestational age (weeks), mean (SD)	20.1 (1.0)	35.3 (0.5)	
Gestational age at 1st survey (weeks), mean (SD)			16.1 (1.4)
Gestational age at 2nd survey, (weeks), mean (SD)			20.5 (1.2)
Dietary intakes, median (interquartile range)			
Energy (kcal/day)	1,464 (1,279-1,694)	1,449 (1,270-1,752)	
EPA (mg/day)	165 (101-262)	174 (121-252)	
(% of energy)	0.10 (0.07-0.15)	0.11 (0.08-0.15)	
DHA (mg/day)	297 (195-452)	316 (227-432)	
(% of energy)	0.18 (0.13-0.26)	0.19 (0.15-0.26)	
EPA+DHA (mg/day)	467 (298-726)	486 (346-704)	
(% of energy)	0.28 (0.20-0.41)	0.31 (0.23-0.42)	
Plasma concentrations, median (interquartile range)			
EPA (µg/mL)	25 (16-35)	28 (17-43)	
DHA (µg/mL)	110 (93-130)	150 (121-186)	

BMI: body mass index; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid.

**Table 2.** Dietary intakes estimated from the two-time BDHQ and the intraclass correlation coefficients (n=54)

	1st BDHQ		2nd BDHQ		1st BDHQ + 2nd BDHQ intraclass correlation coefficient
	Median (interquartile range)		Median (interquartile range)		
Energy (kcal/day)	1,515	(1,277-1,814)	1,490	(1,354-1,854)	0.705
EPA (mg/day) <sup>†</sup>	182	(127-317)	197	(140-263)	0.543
DHA (mg/day) <sup>†</sup>	323	(224-529)	359	(250-467)	0.611
EPA+DHA (mg/day) <sup>†</sup>	507	(347-847)	558	(377-746)	0.581

BDHQ: brief-type self-administered diet history questionnaire; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid.

<sup>†</sup>The intraclass correlation coefficients were calculated after log-transformation of the variables to achieve normal distribution.

of less than 500 mg/day.

The daily and energy-adjusted intakes of EPA, DHA, and EPA plus DHA correlated positively with the corresponding plasma concentrations (EPA;  $r_s=0.352$  and  $r_s=0.354$ , DHA;  $r_s=0.284$  and  $r_s=0.305$ , EPA plus DHA;  $r_s=0.318$  and  $r_s=0.327$  in the second trimester, EPA;  $r_s=0.432$  and  $r_s=0.391$ , DHA;  $r_s=0.292$  and  $r_s=0.316$ , EPA plus DHA;  $r_s=0.359$  and  $r_s=0.358$  in the third trimester, respectively). Even though participants with pregnancy-associated nausea were excluded, the correlation coefficients of EPA, DHA, and EPA plus DHA did not show a significant change.

### Reproducibility study

Of the 62 women recruited for the reproducibility study, 56 (90.3%) provided written informed consent. We excluded 2 women from the analysis because they severely under-reported their energy intake in the first BDHQ. Therefore, the data for 54 participants (87.0%) were included in the final analysis. Of the 54 women, 35 participated in both the validation study and reproducibility study.

The ICCs between the intakes from the two-time BDHQ were 0.543 for EPA, 0.611 for DHA, and 0.581 for EPA plus DHA (Table 2). The Bland-Altman plots of each intake of EPA, DHA, and EPA plus DHA showed good agreement between the two-time BDHQ among most of participants (Figure 1).

### DISCUSSION

The present study is the first to validate the use of an easily administered dietary assessment questionnaire for estimating EPA, DHA, and EPA plus DHA intakes among pregnant Japanese women, which can be used in clinical settings.

The results revealed a positive correlation between daily and energy-adjusted intakes and plasma concentrations of EPA, DHA, and EPA plus DHA. In dietary validation studies, correlation coefficients  $>0.50$  are considered as close correlation,  $0.30-0.50$  as acceptable, and  $<0.30$  as poor.<sup>14</sup> Accordingly, the BDHQ had an acceptable validity level for daily intakes of EPA and EPA plus DHA, and energy-adjusted intakes of EPA, DHA, and EPA plus DHA. However, the correlation coefficient of the daily DHA intake was slightly lower than the acceptable level. A similar result was found in the validation study of the DHQ for pregnant women.<sup>3</sup> One reason for this could be a selective transfer of DHA, through the placenta from the mother to the fetus, for fetal brain development.<sup>15</sup> Such a placental nutrient transport might have attenuated the correlation between intakes and biomarkers.<sup>16</sup> Addi-

tionally, the low correlation coefficients might have been affected by the physiological hemodilution occurring during pregnancy and small variations in fish consumption among young Japanese women.<sup>17</sup> Considering these possible effects on the present results, we believe that the BDHQ had an acceptable level of validity for assessing daily DHA intakes in the pregnancy period.

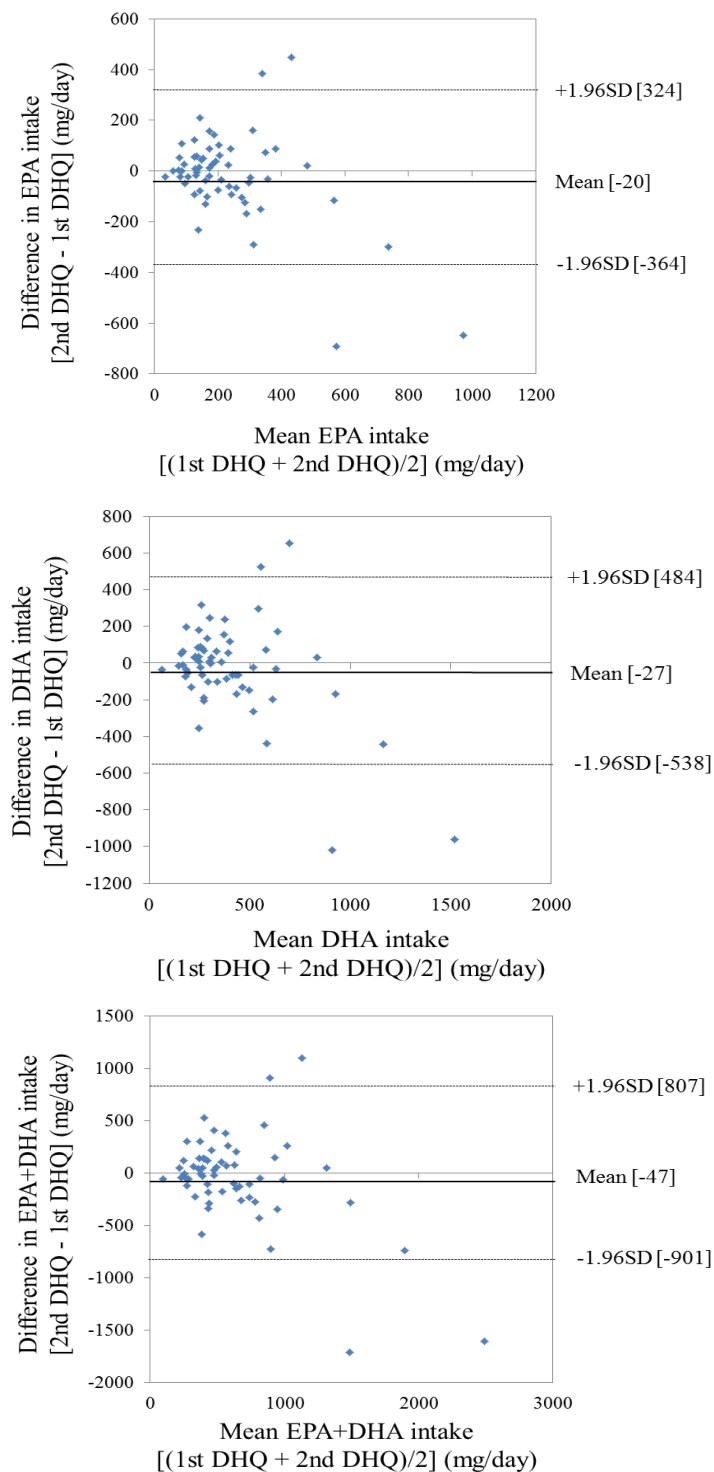
The validation study of the DHQ, which is the original version of the BDHQ, showed the validity of EPA and DHA only among the pregnant women without nausea.<sup>3</sup> Nausea and vomiting during pregnancy often affect food craving and aversion.<sup>7</sup> Changing food selections due to nausea may cause a perception gap in food consumption. However, the present study showed similar results of the correlation coefficients even though the women with nausea were excluded. The impact of nausea on the nutrition status depends on the type and degree of nausea symptom.<sup>18</sup> Although the present study indicated that the BDHQ is applicable regardless of the possibility of nausea, a careful interpretation of the dietary intakes of the women with nausea is required for appropriate interpretation of the results.

The ICCs for EPA, DHA, and EPA plus DHA exceeded 0.50. Correlation coefficients in the reproducibility study of the dietary assessment questionnaire were considered good in the range of  $0.50-0.70$ .<sup>19</sup> Additionally, the Bland-Altman plots also showed agreement of the EPA and DHA intakes in the two-time BDHQ among most participants. Both results indicated the BDHQ had good reproducibility of EPA, DHA, and EPA plus DHA intakes. The dietary habits in the pregnancy period are likely to change because of the physical condition, especially pregnancy-associated nausea.<sup>7</sup> Therefore, we implemented the reproducibility study in the second trimester, when the dietary intakes would be relatively stable due to a reduction of nausea and vomiting in most pregnant women.<sup>20</sup> In addition, the 4-week interval might be an appropriate period to assess measurement error of the dietary questionnaire, rather than to measure changes in the women's dietary habits according to gestational progression.

Mean energy intakes of our participants were much lower than the estimated energy requirement (1,950-2,250 kcal/day in the second trimester and 2,150-2,450 kcal/day in the third trimester).<sup>21</sup> We presumed that this was partly due to under-reporting of dietary intakes, because women are likely to underreport their intakes.<sup>22,23</sup> More than half of the participants took less than 500 mg/day of EPA plus DHA, although Ministry of Health, Labour and Welfare of Japan recommends more than 1,000 mg/day.<sup>21</sup> Even taking into consideration the under-reporting of dietary

intakes, the EPA plus DHA intakes of our participants were low. From the viewpoint of fetal brain development and prevention of maternal depression, pregnant women are recommended to take adequate consumption of fish, especially smaller fish including salmon and sardine, which contains relatively low amounts of methylmercury. Healthcare providers would need to provide an accurate nutritional guidance for pregnant women, especially those with low intake of EPA and DHA, to take sufficient amount of EPA and DHA.

The current study had three limitations. First, participant characteristics may have been biased because the research was conducted at an urban-based university hospital. Second, we did not use erythrocyte levels of EPA and DHA, which reflect long-term intake. However, we believe that plasma is a reasonable biomarker because the correlations between the plasma levels and erythrocyte levels of EPA and DHA are strong.<sup>24</sup> Third, we could not conduct a validation study in the first trimester because dietary research is difficult due to



**Figure 1.** Bland-Altman plot comparing dietary intake estimated from the two-time BDHQ. BDHQ: brief-type self-administered diet history questionnaire. The difference between EPA, DHA, or EPA plus DHA intakes estimated from the two-time BDHQ for each person (y-axis) is plotted against the mean intake of EPA, DHA, or EPA plus DHA averaged from the two-time BDHQ (x-axis). The mean differences and the upper and lower 95% limits of agreement are shown by dotted lines.

severe pregnancy-associated nausea and vomiting.

This study confirmed that the BDHQ has acceptable validity for assessing daily and energy-adjusted intakes of EPA, DHA, and EPA plus DHA among pregnant Japanese women in the second and third trimesters. The BDHQ would be useful for identifying pregnant women with deficiencies of these intakes in clinical settings and providing them with individual advice based on the assessment.

#### ACKNOWLEDGEMENTS

This work was supported by Urakami Foundation for Food and Food Culture Promotion, 2011 and Fumiko Yamaji professional nursing education, 2011. We are deeply grateful to the participants and the hospital staff for their cooperation.

#### AUTHOR DISCLOSURES

None of the authors have a conflict of interest.

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### 基于生物标志物用于估计日本女性孕期二十碳五烯酸和二十二碳六烯酸摄入简易饮食史问卷的效度

**目的：**孕妇二十二碳六烯酸（DHA）的摄入对胎儿大脑发育很重要。在临床上建立一个准确测定 EPA 和 DHA 的摄入量的方法，可以筛选出缺乏这些营养素的妇女，以便进行适当的干预。我们检测了一个简易的自我管理的饮食史问卷（BDHQ）评价日本孕妇的 EPA 和 DHA 摄入量的效度和可重复性，以便建立一个易于管理的膳食评估工具。**方法：**在 2010 年 11 月至 2012 年 2 月期间对东京大学附属医院的 105 名孕中期妇女和 102 名孕晚期妇女进行了研究。以 EPA 和 DHA 的血浆浓度作为有效性研究的参考值。以 54 名妇女在孕中期 4 周内完成两次 BDHQ 作为重复性研究的参考值。**结果：**校正能量的 EPA、DHA、EPA+DHA 摄入量与其血浆浓度显著相关（孕中期： $r_s=0.354$ 、 $r_s=0.305$ 、 $r_s=0.327$ ；孕晚期： $r_s=0.391$ 、 $r_s=0.316$ 、 $r_s=0.358$ ）。两次 BDHQ 的组内相关系数分别为 0.543（EPA），0.611（DHA）和 0.581（EPA+DHA）。Bland-Altman 图显示，两次 BDHQ 中大多数参与者的 EPA、DHA 和 EPA+DHA 摄入量在许可值的可接受范围内。**结论：**BDHQ 在评估日本妇女孕中期和孕晚期 EPA 和 DHA 摄入量时，其效度在可接受范围内。

**关键词：**饮食史问卷调查、二十二碳六烯酸、二十碳五烯酸、孕妇、验证