



## Dietary intake of fish and n-3 polyunsaturated fatty acids and risks of perinatal depression: The Japan Environment and Children's Study (JECS)

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### ABSTRACT

The results of several epidemiological studies and clinical trials investigating the effects of n-3 polyunsaturated fatty acids (PUFAs) on antenatal and postnatal depression remain controversial. We investigated the possible association of dietary intake of fish and n-3 PUFAs with the risks of maternal and paternal psychological distress during pregnancy and of maternal postpartum depression in Japan. From a dataset comprising 104,102 maternal registrations and 52,426 paternal registrations in The Japan Environment and Children's Study, this study analyzed complete data on questionnaires for 75,139, 79,346, and 77,661 women during early pregnancy, mid-late pregnancy, and after pregnancy, respectively, and for 41,506 male partners. Multivariable logistic regression showed reduced risk of psychological distress in the second and third quintiles for fish intake in early pregnancy and in the second to fifth quintile in mid-late pregnancy. No reductions were observed for n-3 PUFA intake in early pregnancy but in the second to fourth quintile in mid-late pregnancy. For postpartum depression, reductions were observed in the second to fourth quintile for fish intake but only in the first quintile for n-3 PUFA intake. As for paternal psychological distress, only the fourth quintile for fish intake showed a significant

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Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; K6, Kessler Psychological Distress Scale; CI, confidence interval; EPA, eicosapentaenoic acid; OR, odds ratio; PUFAs, polyunsaturated fatty acids; DHA, docosahexaenoic acid

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reduced risk but none were shown for n-3 PUFA intake. In conclusion, fish intake was associated with some reduced risk of psychological distress during pregnancy, even for male partners. The associations were weaker for n-3 PUFA intake than for fish intake.

## 1. Introduction

Recent meta-analyses of observational studies (Grosso et al., 2016) and clinical trials (Mocking et al., 2016; Sarris et al., 2016) revealed that n-3 polyunsaturated fatty acids (PUFAs) might have both preventive and therapeutic effects on depression. The meta-analysis of observational studies showed a significant linear dose-response relationship between fish intake and risk of depression (Grosso et al., 2016). Also, the highest intake level of both total n-3 PUFAs and long-chain n-3 PUFAs (i.e., eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) showed a decreased risk of depression compared with the lowest intake, and dose-response analysis revealed a J-shaped association (Grosso et al., 2016). Of the two later meta-analyses of intervention studies, the first revealed a significant moderate to strong effect in favor of n-3 PUFAs (Sarris et al., 2016) and the other reported a beneficial overall effect of n-3 PUFA supplementation in patients meeting the diagnostic criteria for major depressive disorder (Mocking et al., 2016).

The association of dietary n-3 PUFA consumption and depression is controversial, however, in the case of pregnant women, who are believed to be vulnerable to depression because of decreased n-3 PUFA levels during fetal growth (Rees et al., 2005). Some studies have reported beneficial effects of dietary intake of n-3 PUFAs and/or fish on antenatal and/or postnatal depression (da Rocha and Kac, 2012; Golding et al., 2009; Miyake et al., 2013; Shiraishi et al., 2015), while others have shown no effects (Browne et al., 2006; Miyake et al., 2006; Sontrop et al., 2008; Strom et al., 2009). These mixed and inconclusive findings may be attributable to differences in study design, sample size, duration of follow-up, participant background factors, and/or the tools used to assess depression, suggesting that further research is required. Of the three studies reported from Japan (Miyake et al., 2006, 2013; Shiraishi et al., 2015), the study that prospectively examined the effect of n-3 PUFA intake on the risk of postpartum depression revealed no clear inverse association (Miyake et al., 2006). In the other two cross-sectional studies, while one found an independent association of increased consumption of fish, EPA, and DHA with a lower prevalence of depressive symptoms (Miyake et al., 2013), the other found no beneficial effects of n-3 PUFA intake on these symptoms (Shiraishi et al., 2015).

Most of the relevant research to date has focused on maternal perinatal depression, because until recently it was widely believed that only women are affected by depression during pregnancy. Emerging evidence now indicates that their male partners are also affected by depression in the antenatal and postnatal periods. In Japan, one study showed that 15.1% of male partners showed depressive symptoms during mid-pregnancy and 18.9% during late-pregnancy (Hagino et al., 2006), while another study showed that 6.8% were affected at, on average, 29.9 weeks of pregnancy (Watabe and Asaka, 2016). However, scientific research on the predictors of depressive symptoms in men during pregnancy is still scarce, and as far as we know associations with dietary intake of fish and n-3 PUFAs ( $\alpha$ -linolenic acid + EPA + docosapentaenoic acid + DHA) have not been investigated. In this study, we investigated the association in women and their male partners during pregnancy, using data from The Japan Environment and Children's Study (JECS).

## 2. Methods

### 2.1. Study population

The methods of JECS have been described in detail elsewhere (Kawamoto et al., 2014; Michikawa et al., in press). Briefly, JECS is a nationwide government-funded birth cohort study that is evaluating the impact of various environmental factors on children's health and development. The pregnant women participating in JECS were recruited from 15 areas in Japan between January 2011 and March 2014 (Kawamoto et al., 2014; Michikawa et al., in press). The present study is based on the jecs-ag-20160424 dataset that was released in June 2016 and the allbirth\_reviced001\_ver001 dataset that was released in October 2016. The full dataset is for 104,102 maternal registrations, 6648 of which we excluded because of multiple registration in the study and/or multiple births (Fig. 1). We also excluded data for 29 pregnancies in women who withdrew from the study and for women who gave incomplete answers on the questionnaires, leaving the following for final analysis: data for 75,139 pregnancies in the first trimester, 79,346 pregnancies in the second or third trimester, and 77,661 pregnancies in the postpartum period. Similarly, 2747 of the 52,426 male partners registered in the dataset were excluded because of multiple entries for different pregnancies and/or multiple births by their partner (in such case data for only one birth was used for analysis), leaving 49,679 subjects. We excluded a further 9 subjects who withdrew and 8164 subjects who gave incomplete answers on the questionnaires. This left data for 41,506 male partners for the final analysis (Fig. 1).

The study protocol was approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and by the Ethics Committee of the University of Toyama. Written informed consent was obtained from all participating women and their male partners.

### 2.2. Measurements

See Supplementary Methods for details of the following measurements used: self-administered questionnaires; Kessler Psychological Distress Scale (K6); Edinburgh Postnatal Depression Scale (EPDS); and dietary intake of fish and n-3 PUFAs.

### 2.3. Statistical analysis

Data are expressed as the means  $\pm$  SD or median unless stated otherwise. To estimate the risks of psychological distress and postpartum depression for each level of fish intake and n-3 PUFA intake, we categorized the participants according to quintile for fish intake or n-3 PUFA level. We then performed logistic regression analysis to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Tests for trend involved assigning categorical numbers to quintile distributions for fish intake and n-3 PUFA intake and evaluating these as continuous variables. Psychological distress during pregnancy was analyzed with adjustment for age, energy intake, number of previous deliveries, pre-pregnancy BMI, highest educational level, annual household income, marital status, alcohol intake, smoking status, morning sickness, physical activity, history of anxiety disorder, history of depression, and employment status. Presence of neonatal physical anomaly was added for analysis of postpartum depression. For male partners, marital status, morning sickness, and physical activity were excluded from the adjustment and the female partner's psychological distress status was added. The association of change in dietary intake of fish and n-3

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