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Effects of *in utero* exposure to polychlorinated biphenyls, methylmercury, and
 polyunsaturated fatty acids on birth size

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31 Highlights

- The risk of small for gestational age by weight decreased with increasing hair
 mercury concentration.
- The concentrations of mercury in maternal hair had no association with birth
- 35 weight.
- The concentrations of polychlorinated biphenyls in maternal blood had no association with birth size.
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- 39

40 Abstract

41

The adverse effects of *in utero* exposure to polychlorinated biphenyls (PCBs) 42 or methylmercury (MeHg), and the beneficial effects of nutrients from maternal fish 43 intake might have opposing influences on fetal growth. In this study, we assessed the 44 effects of in utero exposure to PCBs and MeHg on birth size in the Japanese population, 45 which is known to have a high frequency of fish consumption. The concentrations of 46 47 PCBs and polyunsaturated fatty acids in maternal blood, and the total mercury in hair (as a biomarker of MeHg exposure) were measured during pregnancy and at delivery. 48 Maternal intakes of fish (subtypes: fatty and lean) and shellfishes were calculated from 49 a food frequency questionnaire administered at delivery. Newborn anthropometric 50 measurement data were obtained from birth records. The associations between chemical 51 exposures and birth size were analyzed by using multiple regression analysis with 52 adjustment for confounding factors among 367 mother-newborn pairs. The birth weight 53 was 3073 ± 37 g (mean \pm SD). The incidence of babies small for gestational age (SGA) 54 by weight was 4.9%. The median concentrations of total PCBs and hair mercury were 55 108 ng/g lipid and 1.41 µg/g, respectively. There was no overall association between 56 57 mercury concentrations and birth weight, birth length, chest circumference, and head circumference. We observed that the risk of SGA by weight decreased with increasing 58 mercury concentration in regression analyses with adjustment for polyunsaturated fatty 59 60 acids. Our results suggest that the beneficial effect of essential nutrition may mask the adverse effects of MeHg on birth size. The concentrations of PCBs had no association 61 with birth size. 62

63 Keywords: polychlorinated biphenyls, methylmercury, birth size, small for gestational 64 age, *in-utero* exposure, polyunsaturated fatty acids

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67 **1. Introduction**

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Newborn anthropometric measurements (weight, length, and head and chest 69 circumference) reflect fetal growth in utero, and are reported to predict infant survival, 70 71 growth, morbidity, and neurobehavioral performance in early life (Kajantie et al., 2005; Barker, 2006). In Japan, public health concerns have been raised about a marked 72 increase in the prevalence of babies with low birth weight, from 4.2% to 8.3% between 73 74 1980 and 2000 (Takimoto et al., 2005). Birth cohort studies reported discrepant findings about the association between maternal intake of fish/seafood during pregnancy and 75 birth size: some found a significant positive association (Olsen et al., 1990, 1993; Olsen 76 and Secher, 2002; Thorsdottir et al., 2004; Drouillet-Pinard et al., 2010; Brantsaeter et 77 al., 2012; Leventakou et al., 2014), whereas others found a null or negative association 78 (Rylander et al., 2000; Oken et al., 2004; Guldner et al., 2007; Halldorsson et al., 2007; 79 Mendez et al., 2010; Heppe et al., 2011). 80

81 A plausible explanation is that fish/seafood is a nutrient source of polyunsaturated fatty acids for the mother and, at the same time, exposes the fetus to 82 polychlorinated biphenyls (PCBs) (Grandjean et al., 2001; Halldorsson et al., 2008; 83 Papadopoulou et al., 2013) and methylmercury (MeHg) (Drouillet-Pinard et al., 2010; 84 van Wijngaarden et al., 2014; Vejrup et al., 2014). The adverse effects of in utero 85 exposure to environmental contaminants and the positive effects of the nutrients from 86 87 fish might have opposing influences on fetal growth (Grandjean et al., 2001; Halldorsson et al., 2008; Papadopoulou et al., 2013). PCBs are classified as persistent 88 organic pollutants as they are lipophilic, stable, and show widespread contamination in 89 90 the environment, food web, and human tissues (Sonneborn et al. 2008). Hg in fish muscle is mostly present in the form of MeHg, which is bioconcentrated up through the 91 aquatic food web, eventually resulting in exposure through the human diet (van 92 Wijngaarden et al., 2014). Fetal exposure to PCBs and MeHg in utero has the potential 93 for serious health concerns because these pollutants can cross the placental and blood-94 brain barriers to reach the immature fetal organs and tissues, which are particularly 95 susceptible to the effects of these toxins (Zahir et al. 2005; National Research Council 96 2000; Wojtyniak et al., 2010; Casas et al., 2015). 97

The toxic mechanism of action of PCBs has not yet been fully elucidated; 98 however, it is suspected that their estrogenic activity may play a role (Decastro et al., 99 100 2006). Experimental studies have demonstrated that PCBs display endocrine-disrupting effects in their ability to stimulate estrogen and can also function as xenoestrogens 101 (Bonefeld-Jorgensen et al., 2001; Cooke et al., 2001). Estrogenic and antiestrogenic 102 PCBs may have opposite associations with infant anthropometrics (Cooke et al., 2001). 103 Other adverse effects induced by PCBs include dioxin-like activities such as activation 104 of aryl hydrocarbon receptors (Van den Berg et al., 2006), and the potential toxic effects 105 induced by dioxin-like PCB congeners may be stronger than those of non-dioxin-like 106 (NDL) congeners (Giesy and Kannan, 1998). On the other hand, in our previous study, 107 we found that fish/seafood consumption was associated with the concentration of NDL 108 congeners (Miyashita et al., 2015). PCB 153 has been the most frequently used 109 indicator of the effects on fetuses of exposure to PCBs in epidemiological studies. In 110 previous studies, specific PCB congeners 153, 156, 118, 74, and 77 had potential 111 estrogenic and antiestrogenic activities (Cooke et al., 2001; Decastro et al., 2006) and 112 significant associations with birth size (Wojtyniak et al., 2010; Casas et al., 2015). 113

Epidemiological studies have previously reported inconsistent findings about 114 the effect of prenatal exposure to PCBs at background levels on birth weight: some 115 found significant inverse associations (Patandin et al., 1998; Rylander et al., 1998; 116 Karmaus and Zhu, 2004; Sagiv et al., 2007; Halldorsson et al., 2008; Sonneborn et al., 117 2008; Tan et al., 2009; Brucker-Davis et al., 2010; Papadopoulou et al., 2013), whereas 118 others found a null or positive association (Vartiainen et al., 1998; Grandjean et al., 119 2001; Gladen et al., 2003; Longnecker et al., 2005; Givens et al., 2007; Khanjani and 120 Sim, 2007; Wolff et al., 2007; Murphy et al., 2010; Lopez-Espinosa et al., 2011; Kezios 121 et al., 2012; Lignell et al., 2013; Hisada et al., 2014). In populations exposed to 122 relatively high MeHg levels because of high consumption of contaminated seafood or 123 accidental poisoning, epidemiologic studies have reported that prenatal MeHg exposure 124 can lead to harmful effects on children's health such as impaired neurobehavioral 125 development, congenital malformations, and restriction of fetal growth (National 126 Research Council 2000). However, limited epidemiological studies reported no 127 conclusive evidence on the effects of low-level MeHg exposure on birth size 128 (Drouillet-Pinard et al., 2010; Gundacker et al., 2010; Ramirez et al., 2000; Ramon et al., 129 2009; van Wijngaarden et al., 2014; Vejrup et al., 2014; Zahir et al. 2005). 130

Moreover, a balance of the opposite effects of contaminants and fish/seafood 131 intakes across populations consuming different types of fish/seafood may have resulted 132 in the discrepant finding among the previous birth cohort studies (Mahaffey, 2004; 133 134 Halldorsson et al., 2008; Ramon et al., 2009). A meta-analysis study including 19 European cohorts described that the most pronounced effect on birth weight was 135 observed for fatty fish, which is known to be a main source of long-chain 136 137 polyunsaturated fatty acids (LCPUFAs) (Leventakou et al., 2014). Systematic reviews have suggested that maternal intake of omega-3 fatty acid supplements during 138 pregnancy is associated with small but significant increases in infant birth size 139 (Makrides et al., 2006; Szajewska et al., 2006; Salvig and Lamont, 2011). However, in 140 some Asian countries, including Japan, where there is a high frequency of fish 141 consumption (Miyashita et al., 2015), there is insufficient evidence about the effect of in 142 utero exposure to PCBs and MeHg on birth size. 143

Thus, the aim of this study is to assess the effects of prenatal exposure to PCBs and MeHg on newborn anthropometric measurements, as well as the incidence of babies born small for gestational age (SGA), taking into account the biomarker of LCPUFAs among Japanese pregnant women.

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150 **2. Materials and Methods**

152 **2.1. Study population**

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The subjects in this study were all currently enrolled in the Hokkaido Study on 153 Environment and Children's Health. A total of 514 pregnant Japanese women were 154 recruited at the Sapporo Toho Hospital in Hokkaido, Japan, from July 2002 to 155 September 2005 (Kishi et al., 2013). An overview of this study is shown in Figure 1. 156 157 During their last trimester, the subjects completed a self-administered questionnaire on demographic characteristics, socioeconomic status, tobacco smoking and alcohol habits, 158 and frequency of consumption during pregnancy of food items such as shoreline fish 159 (e.g., saury, Pacific herring, or mackerel), pelagic fish (e.g., tuna, bonito, or salmon), 160 beef, pork, chicken, milk, and eggs. The medical records for 504 mother-newborn pairs 161 were used to gather information on delivery characteristics, including maternal height, 162 maternal prepregnancy weight, pregnancy complications, gestational age, infant sex, 163 parity, congenital anomalies, and newborn anthropometric measurements. 164

Within 5 days after delivery, the mothers completed a food frequency 165 questionnaire (FFQ) to estimate their fish/seafood intake and history of synthetic hair 166 waving (n = 430). The FFQ provided information about the frequency and portion size 167 for maternal fish intake (Supplementary Table 1). The estimated daily fish intake 168 (g/day) was calculated from the FFQ (Yasutake et al., 2003). We divided maternal fish 169 intake to four subtypes: fatty fish, lean fish, shellfishes, and whole. The fatty fish group 170 consisted of tuna, salmon, yellowtail, sardine, mackerel, saury, eel, Atka mackerel, 171 shishamo smelt, pacific herring, and trout. The lean fish group included bonito, sea 172 173 bream, flatfish, flounder, horse mackerel, carp, sweetfish, crucian carp, and Pacific cod. The shellfishes group included cuttlefish, octopus, crab, shrimp, shellfish, and fish 174 products (Leventakou et al., 2014). 175

This study was conducted with written informed consent from all subjects and was approved by the institutional ethics board for epidemiological studies at the Hokkaido University Graduate School of Medicine.

180 **2.2. Exposure assessment**

A 40-mL blood sample was taken from the maternal peripheral vein during the 181 last trimester. In subjects with pregnancy-related anemia, the samples were taken during 182 183 hospitalization immediately after delivery. Consequently, 356 samples were taken during pregnancy and 148 samples were taken after delivery. All samples were stored at 184 -80°C until needed for analysis. The extraction, purification, and analysis of PCBs from 185 186 whole blood specimens were performed by using a previously reported method (Iida and Todaka, 2003; Todaka et al., 2008a,b). The concentrations of PCBs were analyzed 187 at the Fukuoka Institute of Health and Environmental Sciences by using high-resolution 188 gas chromatography/high-resolution mass spectrometry of 5-g blood samples. To 189 evaluate the accuracy and reliability of the PCB analysis, quality control studies were 190 completed and compared against those done at three other laboratories. The average 191 variation among the concentrations of PCBs in human blood samples was considered 192 acceptable if it was within 10% (Kajiwara et al., 2008, 2009). The concentrations of 70 193 PCBs congeners were measured in 426 blood samples and adjusted for lipids (pg/g 194 lipid). The sample values below the detection limit for the 70 PCBs congeners were 195 assigned a value of one-half the detection limit. The remaining samples were not 196

analyzed because of unavailable or insufficient sample volumes (<5 g) for measurement. 197 198 PCB congeners were separated into four groups based on their suggested biological activities and the effect of exposure to them due to fish intake: estrogenic, antiestrogenic, 199 dioxin-like, and NDL PCBs (Cooke et al., 2001). The estrogenic group included 200 congeners 4, 10, 5, 8, 15, 17, 18, 31, 44, 47, 48, 52, 70, 99, 101, 136, 153, and 188. The 201 antiestrogenic group included congeners 77, 110, 105, 114, 126, 156, 171, and 169. The 202 dioxin-like PCBs included congeners 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 203 169, and 189 (Van den Berg et al., 2006). NDL PCBs had 58 congeners excluding the 204 12 dioxin-like PCBs from all 70 congeners measured in our study (Supplementary Table 205 2) (Miyashita et al., 2015). Additionally, we used the specific PCB congeners 153 (main 206 contributor), 156, 118, 74, and 77 as biomarkers of exposure to PCBs. 207

Maternal hair was collected within 5 days after delivery (n = 430). For the 1 cm 208 of hair closest to the scalp, the concentrations of total Hg were determined by using the 209 oxygen combustion-gold amalgamation method with the MD-1 atomic absorption 210 detector (Nippon Instruments Co., Ltd., Osaka, Japan) at the National Institute for 211 Minamata Disease (Yasutake et al., 2003). The total Hg concentration in hair was used 212 as a convenient biomarker of MeHg exposure (van Wijngaarden et al., 2014) because 213 >90% of the total Hg in hair is MeHg that is covalently bound to the cysteine residue of 214 hair protein (National Research Council, 2000). 215

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217 2.3. Maternal polyunsaturated fatty acid assessment

The fatty acid levels in maternal whole blood were determined by using gas 218 chromatography-mass spectrometry (GC-MS) as described in detail in our previous 219 220 study (Nakashima et al., 2013). Briefly, whole blood lipid was extracted from 25 µL blood (Folch et al., 1957), mixed with 1.2 mL methanol, 75 µL acetyl chloride, and 75 221 µL of 10 µg/100 µL tricosanoic acid ethyl ester/methanol (internal standard). After 222 adding *n*-hexane (500 μ L) and centrifugation of the sample, the upper organic layer was 223 collected and transferred into another vial. The *n*-hexane extraction was repeated once, 224 and then the concentration of fatty acid methyl ester in the *n*-hexane layer was measured 225 with GC-MS. Finally, nine fatty acid species were measured including the omega-6 226 fatty acids, palmitoleic and oleic acids, linoleic acid, and arachidonic acid (AA), and the 227 acids, α -linolenic acid, eicosapentaenoic omega-3 fattv acid (EPA), 228 and docosahexaenoic acid (DHA). The detection rates for eight fatty acids were >99.0% and 229 that for EPA was 97.8% (Kishi et al., 2015). We used EPA + DHA, AA, omega-3 fatty 230 acids, and omega-6 fatty acids as biomarkers of maternal LCPUFAs (van Wijngaarden 231 et al., 2014; Vejrup et al., 2014). 232

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234 2.4. Statistical analyses

Some subjects were excluded from analyses because of pregnancy-induced 235 hypertension (n = 11), diabetes mellitus (n = 1), fetal heart failure (n = 1), and multiple 236 births (n = 7). The final study population comprised 367 mother-newborn pairs with 237 completed questionnaire data and birth records, whose PCB and hair Hg concentrations 238 were measured (Figure 1). SGA by weight was defined as a birth weight less than the 239 10th percentile for the gestational age at delivery, based on growth charts specific for 240 newborn sex and maternal parity for birth size standards by gestational age for Japanese 241 neonates. SGA by length was defined as birth length less than the 10th percentile for the 242 gestational age at delivery, based on growth charts for birth size standards by gestational 243

age for Japanese neonates (Itabashi et al., 2014). Associations between subject 244 characteristics and concentrations of PCBs and hair Hg were evaluated by using the 245 Mann-Whitney U-test and Spearman's rank correlation coefficient. Associations 246 between subject characteristics and birth size were evaluated by using Student's t-test, 247 248 Pearson correlation, Spearman's rank correlation coefficient, and one-way analysis of variance. For linear regression analyses, we used log₁₀-transformed values for 249 concentrations of PCBs and hair Hg, as well as LCPUFAs, because these variables 250 251 displayed a skewed distribution. Associations between PCBs or hair Hg (expressed as continuous concentrations) and newborn anthropometric measurements were evaluated 252 by using linear regression analyses. For logistic regression analyses, we used 253 concentrations of PCBs and hair Hg, divided into quartiles, to evaluate potential 254 nonlinear relationships. The associations between PCBs or hair Hg and the incidence of 255 babies born SGA by weight and length were evaluated by using logistic regression 256 analyses. All regression analyses were conducted with or without adjustment of 257 factors-chosen for their significant associations with exposure and birth size in this 258 study (p < 0.05)—and possible confounding factors as reported in previous studies 259 (Drouillet-Pinard et al., 2010; Halldorsson et al., 2008; Ramon et al., 2009; 260 Papadopoulou et al., 2013; van Wijngaarden et al., 2014; Vejrup et al., 2014). 261 Specifically, the adjusted factors included maternal age (continuous), height 262 (continuous), prepregnancy weight (continuous), smoking during pregnancy (yes/no), 263 264 alcohol consumption during pregnancy (yes/no), household income (less than or greater than 5 million Yen annually), blood sampling period (during pregnancy or after 265 delivery), birth order (first-born or later children) reported as maternal parity, infant sex, 266 267 gestational age, maternal LCPUFAs, and total 70 PCBs or hair Hg. The logistic regression analysis for SGA by weight was not adjusted for birth order, infant sex, and 268 gestational age, because SGA by weight was defined based on growth charts for birth 269 size standards by gestational age specific for newborn sex and maternal parity. 270 Furthermore, the logistic regression analysis for SGA by length was not adjusted for 271 gestational age, because SGA by length was defined based on growth charts for birth 272 size standards by gestational age. 273

A p-value of <0.05 was considered statistically significant. Statistical analyses
 were performed by using the Statistics Package for Social Sciences (version 19.0J; IBM,
 Armonk, NY, USA) software for Windows.

277 **3. Results**

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The subjects' characteristics are described in Table 1. The percentage of babies 279 born SGA by weight was 4.9% and that of babies SGA by length was 11.7%. Table 2 280 shows the distribution of maternal biomarkers of fatty acid. The median concentration 281 of the total 70 PCBs in the maternal blood was 108 ng/g lipid (Supplementary Table 2). 282 The distributions of PCB concentrations are shown in Table 3. The geometric mean 283 284 concentrations of estrogenic, antiestrogenic, dioxin-like, and NDL PCBs were 27.9, 3.98, 10.9, and 93.8 ng/g lipid, respectively, and that of hair Hg was 1.34 μ g/g. The 285 concentrations of total PCBs significantly increased with maternal age and intake of fish, 286 EPA + DHA, and omega-3 fatty acids during pregnancy. The concentrations of hair Hg 287 significantly increased with fish intake during pregnancy (Table 4). The concentrations 288 of the total 70 PCBs and hair Hg in subjects with no history of parity; high household 289 income; frequent consumption of pelagic fish, beef, or milk (2once/week); or for 290 non-SGA babies by weight were significantly higher than those in subjects with a 291 history of parity; low income; infrequent consumption of pelagic fish, beef, or milk; or 292 SGA babies by weight, respectively (Table 4). The newborn anthropometric 293 measurements significantly increased with maternal height, prepregnancy weight, male 294 295 sex, birth by vaginal delivery, and increasing gestational age (Supplementary Table 3). Incidences of SGA babies by weight and length significantly reduced with increased 296 297 maternal prepregnancy weight and male sex (Supplementary Table 4).

We found no associations between the concentrations of estrogenic PCBs, 298 antiestrogenic PCBs, dioxin-like PCBs, NDL PCBs, or hair Hg and newborn 299 300 anthropometric measurements of birth weight, length, chest circumference, and head circumference in the multiple linear regression models with or without adjustment for 301 factors (Supplementary Table 5). As shown in Table 5, we found no significant 302 associations of SGA by weight with any quartile of estrogenic, antiestrogenic, 303 dioxin-like, or NDL PCB levels, for all models. We also found no significant 304 associations between the incidence of SGA by length and levels of estrogenic PCBs, 305 antiestrogenic PCBs, dioxin-like PCBs, NDL PCBs, and hair Hg in all models. The 306 adjusted odds ratios (ORs) for SGA by weight among the third (OR: 0.12, 95% 307 confidence interval [95% CI]: 0.02-0.68), and fourth quartiles (OR: 0.17, 95% CI: 308 0.04–0.79) for hair Hg significantly reduced as compared with those in the first quartile 309 310 (reference) with a significant trend (Table 5). The overall results analyzed by using regression analyses remained statistically significant after adjusting for omega-3 fatty 311 acids (Table 5, Supplementary Table 5), and EPA + DHA, AA, omega-6 fatty acids, fish 312 intake, fatty fish intake, and frequent consumption of pelagic fish, beef, and milk (data 313 not shown). Additionally, we found no interaction effect of PCBs or Hg and omega-3 314 fatty acids on SGA risk (Table 5), as well as EPA + DHA, AA, and omega-6 fatty acids 315 on birth weight, birth length, chest circumference, head circumference, and SGA risk 316 (data not shown). 317

PCB 153, 156, 118, and 74 were detected in all subjects, and PCB 77 was detected in 64% of the subjects. The median concentrations of PCB 153, 156, 118, 74, and 77 were 21.4, 1.95, 5.78, 3.12, and 0.011 ng/g lipid, respectively. The contribution rates of PCB 153, 156, 118, 74, and 77 according to total PCBs were 20.3%, 1.8%, 5.4%, 3.0%, and 0.01%, respectively. PCB 153 was the main contributor to PCB exposure in this study (Supplementary Table 2). In congener-specific analyses, after sample values below the detection limit were assigned a value of one-half the detection
limit, associations between PCB 153, 156, 118, 74, or 77 and birth size were evaluated
by regression analyses with adjustment for confounding factors. There were no
associations between concentrations of specific PCB congeners and newborn
anthropometric measurements or the incidence of babies born SGA in any of the
regression analyses (data not shown).

332 4. Discussion

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334 **Prenatal exposure to PCBs and birth size**

We found that prenatal exposure to PCBs, including antiestrogenic PCBs as well as specific PCB congeners, has no association with newborn anthropometric measurements at birth, or the incidence of babies born SGA after adjusting for confounding factors, including hair Hg, demographic characteristics, socioeconomic status, and maternal level of LCPUFAs. Similar results were obtained when examining only subjects with a normal birth weight and gestation period.

Median concentrations of PCB 153 have been reported with a wide range, from 341 10.7 ng/g lipid weight in a Poland cohort to 450 ng/g lipid in the maternal serum of a 342 Faroe Island cohort (Grandjean et al., 2001; Hertz-Picciotto et al., 2005; Sonneborn et 343 al., 2008; Wojtyniak et al., 2010). Concerning the exposure levels among the general 344 population in Japan, the maternal PCB 153 level of 21.0 ng/g lipid in this study seemed 345 346 to be comparable to that of 15.9 ng/g lipid (Nakamura et al., 2008) and 16.0 ng/g lipid (Hisada et al., 2014) measured in pregnant women in previous studies. Hisada (2014) 347 described that no association was observed between prenatal exposure to PCBs and 348 birth size, and the levels of PCB exposure among the general population in this study 349 was considerably lower than that among European (Wojtyniak et al., 2010) and 350 American populations (Hertz-Picciotto et al., 2005), in which a significant negative 351 association with prenatal exposure to PCBs and birth size was found. Therefore, one of 352 the reasons for the inconsistent results may be the difference in PCB exposure level. 353 Murphy (2010) reported no association between prenatal exposure to antiestrogenic 354 355 PCBs and birth weight of newborns of fish anglers, which is consistent with our findings. The estrogenic/antiestrogenic activities of PCBs have been demonstrated in in 356 vitro and in vivo models; however, their affinity for estrogens and xenoestrogens are two 357 to five times lower than that of natural hormones (Decastro et al. 2006). This suggests 358 that the concentrations of estrogenic/antiestrogenic PCBs in our study may not be at 359 levels too low to see any adverse effects on birth size but rather indicate a true 360 biological effect. 361

A European meta-analysis with a pooled dataset including populations with a 362 low PCB exposure described that birth weight reduced because of PCB 153 in cord 363 serum (El Majidi et al., 2012; Casas et al., 2015). However, a systematic analysis of 20 364 365 epidemiological studies described that the observed discrepancies in the concentrationresponse relation between prenatal PCB exposure and birth weight could not be 366 attributed conclusively to a difference in biological PCB levels (El Majidi et al., 2012). 367 In fact, in Inuit children exposed to high concentrations of PCBs, a lack of association 368 between PCB 153 in cord blood and birth size was observed (Dallaire et al., 2014). As 369 one of the possible explanations, the beneficial nutrients from fish/seafood intake may 370 have an opposite action to the toxic effects of PCBs (Mahaffey, 2004; Halldorsson et al., 371 2008; Ramon et al., 2009). In the Danish National Birth Cohort of subjects with 70 ng/g 372 lipid of the median PCB 153 and 5 g/day of median fatty fish intake from the FFQ, 373 inverse associations were observed between maternal PCB levels and birth weight 374 (Halldorsson et al., 2008). In a Faroe Island cohort of subjects, higher concentrations of 375 PCB 153 and PUFAs than that in our study were found, and a negative effect of 376 377 maternal EPA and no effect of PCB exposure on birth weight were observed (Grandjean et al., 2001). We found no association between maternal levels of LCPUFAs and birth 378

weight, birth length, chest circumference, and head circumference or SGA risk in this 379 380 study. However, our previous study on the same cohort suggested that maternal EPA might affect infant chest circumference (Jia et al., 2014). It is difficult to compare our 381 results with those of other studies because of substantial differences in the exposure 382 383 levels, profiles of fish/seafood intake, and contribution rate of fish/seafood to the overall PCB exposure level. However, we have provided additional data to support the finding 384 that low exposure to PCBs is likely insufficient to cause a negative effect on fetal 385 386 growth taking into account maternal LCPUFAs.

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388 Prenatal exposure to MeHg and birth size

Our findings suggest that prenatal exposure to MeHg has no association with newborn anthropometric measurements, although the incidence of babies born SGA by weight may reduce with higher concentrations of Hg in hair. The maternal hair Hg level of 1.41 μ g/g at delivery in our population was comparable to that of 1.96 μ g/g (Suzuki et al., 2010) and 1.62 μ g/g in pregnant women (Sakamoto et al., 2012), and that of 1.43 μ g/g in nonpregnant women from the general population in Japan (Yasutake et al., 2003), in which the effect on birth size was not evaluated.

Our finding is consistent with the results of several epidemiological studies that 396 also showed a lack of significant association between parental exposure to MeHg and 397 398 birth weight (Drouillet-Pinard et al., 2010; Gundacker et al., 2010; Ramirez et al., 2000; Ramon et al., 2009; van Wijngaarden et al., 2014). However, two different studies 399 described adverse effects from prenatal exposure to MeHg in relation to birth size 400 401 taking into account maternal fish intake (Ramon et al., 2009; Vejrup et al., 2014). In a study in Spain in which the subjects had a mean total Hg of 9.4 µg/L in cord blood and a 402 mean fish intake of 36 g/day, the concentrations of total Hg increased with reduced birth 403 weight and increased the risk of being born SGA for length but not SGA for weight 404 405 (Ramon et al., 2009). One possible explanation for the inconsistent findings is that the subjects of our study more frequently consumed fatty fish than the subjects of the 406 Spanish study. Fatty fish is known to be the main source of PUFAs (Leventakou et al., 407 2014). In study in the Republic of Seychelles on subjects with a mean hair MeHg of 5.9 408 $\mu g/g$ and a median omega-3 fatty acid level of 30 $\mu g/mL$, no association was observed 409 between MeHg or PUFAs and birth weight (van Wijngaarden et al., 2014). In a 410 Norwegian study of subjects with 1.45 µg/day median estimated dietary Hg and 6 g/day 411 fatty fish intake, a positive effect of maternal fish/seafood intake and a negative effect of 412 Hg exposure on birth weight were observed (Vejrup et al., 2014). Our study subjects had 413 23.3 g/day median fatty fish intake and 43 µg/mL median omega-3 fatty acids, which 414 were higher than that found in the Seychelles and Norwegian studies. The beneficial 415 effect of essential nutrition in our study may mask the adverse effects of MeHg on birth 416 size, as observed in the Norwegian study. 417

On the other hand, our finding that the risk of SGA by weight reduced at higher 418 concentrations of Hg in hair remained significant after adjustment for the concentrations 419 of LCPUFAs. A plausible physiological mechanism underlying our findings should be 420 investigated. To our knowledge, no previous studies have reported a reasonable 421 assumption about the direct protective role of low MeHg exposure in utero on fetal 422 growth. As another possible explanation, the association between higher Hg in hair and 423 reduced risk of SGA by weight may be confounded by an unobserved common factor. 424 In fact, biochemical observations showed that selenium, one of the essential 425

micronutrients for fetal growth, plays a protective role against Hg toxicity (Zahir et al., 426 427 2005; Chen et al., 2006). Because our findings of the impact of prenatal MeHg exposure on fetal growth even at low levels are not conclusive, we consider continuous risk 428 assessment as important among our population in which the fourth quartile included 429 subjects (n = 59) with hair Hg concentrations >2.2 μ g/g, which corresponds to the 430 provisionally tolerable MeHg intake level as set by the Food and Agriculture 431 Organization and the World Health Organization in 2006 (1.6 µg/kg body weight/week) 432 433 (FAO/WHO, 2006).

434

435 Strengths and limitations

The strengths of this study are as follows: (1) the assessment of biomarkers of 436 LCPUFAs; (2) the detection of 70 congeners of PCBs that were reported as the most 437 predominant congeners in the Japanese population (Todaka et al., 2008ab); (3) a high 438 PCB detection rate of 98.8%, and the ability to group and analyze them based on 439 bioactivities such as estrogen/antiestrogen, and dioxin-like effects; (4) various 440 demographic, socioeconomic, behavioral, and dietary data were collected prospectively, 441 minimizing recall error; and (4) evaluation with multiple linear models adjusted for 442 confounding effects between demographic characteristics, socioeconomic status, 443 maternal diet, and PCB or Hg contamination in fish/seafood. We propose that additional 444 studies be conducted to assess whether exposure to PCBs and MeHg in the general 445 446 population is at levels insufficient to cause impaired fetal growth in humans. The mothers included in this study were older at delivery, had heavier weight at 447 prepregnancy, had lower smoking rate during pregnancy, and had a later sampling 448 period than mothers who were not included in analysis. However, we considered that 449 the potential selection bias was limited because we found no difference in PCB and Hg 450 exposure levels between the mothers included and those not included in this study. The 451 children included in this study had a higher gestational age, weight, length, chest 452 circumference, and head circumference, and lower SGA for length at birth than those 453 children who were not included in the analysis. A potential selection bias may have 454 resulted from the effect on healthy children, in whom the influence of contaminants on 455 birth size may have been underestimated. We cannot exclude the possibility that our 456 findings occur by chance because of the small number of babies born SGA. A further 457 study with a larger sample size is needed to evaluate the effects of prenatal exposure to 458 459 PCBs and MeHg on the later growth of children.

461 Conclusion

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462 No overall association was found between mercury concentrations and birth weight, length, chest circumference, and head circumference. We observed that the risk 463 of SGA by weight reduced with increasing mercury concentration in hair in regression 464 analyses with adjustment for polyunsaturated fatty acids. In Japanese pregnant women, 465 who are known to have a high frequency of fish consumption, the beneficial effect of 466 essential nutrition may mask the adverse effects of MeHg on birth size, as was observed 467 in a previous European study. On the other hand, we cannot exclude the possibility that 468 prenatal MeHg exposure may adversely influence fetal growth even at low levels; 469 therefore, a follow-up study is needed to evaluate the effect of prenatal MeHg exposure 470 471 on the later growth of children. The concentrations of estrogenic, antiestrogenic, dioxin-like, and NDL PCBs had no association with birth weight, length, chest 472

473 circumference, head circumference, and SGA risk.

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474

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- 766

| Maternal characteristics Age at delivery (years)30.8 ± 4.8° 30.8 ± 4.8°Age at delivery (years)30.8 ± 4.8°Prepregnancy maternal weight (kg)52.5 ± 8.0°Parity0180 (49.0)1146 (39.8)235 (9.5)36 (1.6)Blood sampling period6 (1.6)<28 weeks21 (5.7)28 to <36 weeks148 (40.3)≥36 weeks78 (21.3)After delivery120 (32.7)History of chemical hair waving No260 (70.8)Yes100 (22.7)Education level (years)50≤97 (1.9)10-12147 (40.1)13-16208 (56.7)≥175 (1.4)Annual household income (million yen)61 (16.6)3 to <5183 (49.9)5 to <778 (21.3)Z25 (69.5)Yes112 (30.5)Caffeine intake during pregnancy No255 (69.5)Yes112 (30.5)Caffeine intake during pregnancy NoNosmoker305 (83.1)≤Once/week171 (46.6)≥Once/week171 (46.6)≥Once/week90 (24.7)Pork <once td="" week<=""><once td="" week<="">274 (75.3)≥Once/week337 (91.8)Eg<once td="" week<=""><once td="" week<="">337 (91.8)Eg<once td="" week<=""><once td="" week<="">333 (00.160)Fish intake (g/day)38.8 (0.0, 400)Fash intake (g/day)38.8 (0.0, 400)Fash intake (g/day)38.</once></once></once></once></once></once> | Characteris | tics | n (%) |
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| Arge at derivery (years) 30.5 ± 3.6 Prepregnancy maternal weight (kg) $158 \pm 5.4^{\circ}$ Prepregnancy maternal weight (kg) $2.5 \pm 8.0^{\circ}$ Parity 0 $180 (49.0)$ 1 $146 (39.8)2$ $35 (9.5)3$ $6 (1.6)Blood sampling period (1.6)-28 weeks 21 (5.7)28 to <36 weeks 148 (40.3)\geq 36 weeks 178 (21.3)After delivery 120 (32.7)History of chemical hair waving 0 00 (70.8)Yes 107 (29.2)Education level (years) \leq 9 7 (1.9)10-12$ $147 (40.1)13-16$ $208 (56.7)\geq 17 5 (1.4)Annual household income (million yen) < 3\leq 3 10 < 5 183 (49.9)5 to <7$ $78 (21.3)\geq 7 78 (21.3)Tobacco smoking during pregnancy No 255 (69.5)Yes 112 (30.5)Caffeine intake during pregnancy No 255 (69.5)Yes 20nce/week 198 (54.0)\geq 0nce/week 196 (53.4)Beef 0nce/week 171 (46.6)\geq 0nce/week 274 (75.3)\geq 0nce/week 337 (91.8)Egg 0nce/week 337 (91.8)Egg 0nce/week 356 (97.3)Fish intake from food frequency questionnairesFish intake (g/day) 38.8 (0.0, 400)Faty fish 23.3 (0.0, 160)Shurflish 11.1 (0.0, 200)Whale 00 (0.0, 6.70)$ | A go of dolin | | $20.9 \pm 4.9a$ |
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| Frequency of food consumption during pregnancyShoreline fish $\geq Once/week$ 198 (54.0) $\geq Once/week$ 169 (46.0)Pelagic fish $\geq Once/week$ 171 (46.6) $\geq Once/week$ 196 (53.4)Beef $< Once/week$ 274 (75.3) $\geq Once/week$ 90 (24.7)Pork $< Once/week$ 274 (75.3) $\geq Once/week$ 90 (24.7)Chicken $< Once/week$ 30 (8.2) $\geq Once/week$ 30 (8.2) $\geq Once/week$ 337 (91.8)Egg $< Once/week$ 314 (85.6)Milk $< Once/week$ 314 (85.6)Milk $< Once/week$ 356 (97.3)Fish intake from food frequency questionnairesFish intake (g/day)38.8 (0.0, 400)Fatty fish23.3 (0.0, 160)Lean fish0.0 (0.0, 66.7)Shellfish11.1 (0.0, 200)Whale0.0 (0.0, 6.7) | Carrenne int | ake during pregnancy (ing/day) | 120 (1.30, 646 |
| | Frequency of Shoreline fi | of food consumption during pregnancy sh | |
| $ \geq \text{Once/week} \qquad 169 (46.0) $ $ Pelagic fish \\ < \text{Once/week} \qquad 171 (46.6) \\ \ge \text{Once/week} \qquad 196 (53.4) $ $ Beef \\ < \text{Once/week} \qquad 274 (75.3) \\ \ge \text{Once/week} \qquad 90 (24.7) $ $ Pork \\ < \text{Once/week} \qquad 90 (24.7) \\ Pork \\ < \text{Once/week} \qquad 90 (24.7) \\ Chicken \\ < \text{Once/week} \qquad 30 (8.2) \\ \ge \text{Once/week} \qquad 337 (91.8) \\ Egg \\ < \text{Once/week} \qquad 53 (14.4) \\ \ge \text{Once/week} \qquad 314 (85.6) \\ Milk \\ < \text{Once/week} \qquad 10 (2.7) \\ \ge \text{Once/week} \qquad 356 (97.3) \\ Fish intake from food frequency questionnaires \\ Fish intake (g/day) \qquad 38.8 (0.0, 400) \\ Fatty fish \\ \text{Lean fish} \qquad 0.0 (0.0, 66.7) \\ Shellfish \qquad 11.1 (0.0, 200) \\ Whale \qquad 0.0 (0.0, 6.7) \\ \end{cases} $ | | <once td="" week<=""><td>198 (54.0)</td></once> | 198 (54.0) |
| Pelagic fish171 (46.6) $\geq Once/week$ 171 (46.6) 196 (53.4)Beef $< Once/week$ 196 (53.4)Beef $< Once/week$ 90 (24.7)Pork $< Once/week$ 90 (24.7)Pork $< Once/week$ 90 (24.7)Chicken $< Once/week$ 30 (8.2) $ \ge Once/weekSonce/week337 (91.8)Egg< Once/week53 (14.4) \ge Once/weekMilk< Once/week10 (2.7) \ge Once/weekMilk< Once/week356 (97.3)Fish intake from food frequency questionnairesFish intake (g/day)Fish intake (g/day)38.8 (0.0, 400) 11.1 (0.0, 200) 00 (0.0, 66.7)Shellfish11.1 (0.0, 200) 00 (0.0, 67.0)$ | | ≥Once/week | 169 (46.0) |
| Independent $\langle Once/week \\ \geq Once/week \\ 0nce/week \\ 0nce/week \\ 274 (75.3) \\ 0 (24.7$ | Pelagic fish | | |
| $\begin{array}{c} \\ \ge Once/week \\ \ge Once/week \\ \\ Beef \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $ | erugie iisii | <once td="" week<=""><td>171 (46.6)</td></once> | 171 (46.6) |
| Beef $\begin{array}{c} \leq Once/week \\ \leq Once/week \\ \geq Once/week \\ \geq Once/week \\ \leq Once/week \\ \leq Once/week \\ \geq Once/week \\ \geq Once/week \\ \geq Once/week \\ \geq Once/week \\ \leq O$ | | | 1/1(+0.0) 106(52.4) |
| Beef < Once/week 274 (75.3) $\geq Once/week$ 90 (24.7) Pork < Once/week 274 (75.3) $\geq Once/week$ 90 (24.7) Chicken < Once/week 30 (8.2) $\geq Once/week$ 337 (91.8) Egg < Once/week 53 (14.4) $\geq Once/week$ 314 (85.6) Milk < Once/week 10 (2.7) $\geq Once/week$ 356 (97.3) Fish intake from food frequency questionnaires Fish intake (g/day) 38.8 (0.0, 400) Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.7) | | ≥Once/week | 196 (53.4) |
| | веег | | |
| $ \ge Once/week \qquad 90 (24.7) $ Pork $ < Once/week \qquad 274 (75.3) $ $ \ge Once/week \qquad 90 (24.7) $ Chicken $ < Once/week \qquad 30 (8.2) $ $ \ge Once/week \qquad 337 (91.8) $ Egg $ < Once/week \qquad 53 (14.4) $ $ \ge Once/week \qquad 314 (85.6) $ Milk $ < Once/week \qquad 10 (2.7) $ $ \ge Once/week \qquad 356 (97.3) $ Fish intake from food frequency questionnaires Fish intake (g/day) \qquad 38.8 (0.0, 400) Fatty fish $ 23.3 (0.0, 160) $ Lean fish $ 0.0 (0.0, 66.7) $ Shellfish $ 11.1 (0.0, 200) $ Whale $ 0.0 (0.0, 6.7) $ | | <once td="" week<=""><td>274 (75.3)</td></once> | 274 (75.3) |
| Pork $274 (75.3)$ $90 (24.7)Chicken90 (24.7)Chicken30 (8.2)\geq Once/week337 (91.8)Egg337 (91.8)Egg314 (85.6)Milk2Once/week40nce/week314 (85.6)Milk2Once/week2Once/week356 (97.3)Fish intake from food frequency questionnairesFish intake (g/day)38.8 (0.0, 400)Fatty fish23.3 (0.0, 160)Lean fish0.0 (0.0, 66.7)Shellfish11.1 (0.0, 200)Whale0.0 (0.0, 6.7)$ | | ≥Once/week | 90 (24.7) |
| $\begin{array}{c} < Once/week \\ \geq Once/week \\ @ 0 (24.7) \\ \end{array}$ Chicken $\begin{array}{c} < Once/week \\ @ 0 (24.7) \\ \end{array}$ $\begin{array}{c} 30 (8.2) \\ 337 (91.8) \\ \end{array}$ Egg $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/week \\ @ 0nce/week \\ @ 0nce/week \\ \end{array}$ $\begin{array}{c} < Once/week \\ @ 0nce/week \\ @ 0nce/$ | Pork | | |
| $ \begin{array}{c} \geq 0 \text{nce/week} & 2/4 (10.5) \\ \geq 0 \text{nce/week} & 90 (24.7) \\ \hline \text{Chicken} & & & & & \\ & \geq 0 \text{nce/week} & & & & & \\ & \geq 0 \text{nce/week} & & & & & \\ & & \geq 0 \text{nce/week} & & & & & \\ & & \geq 0 \text{nce/week} & & & & & \\ & & & \geq 0 \text{nce/week} & & & & & \\ & & & & & & \\ & & & & & & $ | | <once td="" week<=""><td>274 (75 3)</td></once> | 274 (75 3) |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | | >Once/week | 90(247) |
| Clincken $30 (8.2)$ $\geq Once/week$ $337 (91.8)$ Egg $\bigcirc Once/week$ $\geq Once/week$ $314 (85.6)$ Milk $\bigcirc Once/week$ $\land Once/week$ $314 (85.6)$ Milk $\bigcirc Once/week$ $\land Once/week$ $10 (2.7)$ $\supseteq Once/week$ $356 (97.3)$ Fish intake from food frequency questionnaires Fish intake (g/day) Fatty fish $23.3 (0.0, 160)$ Lean fish $0.0 (0.0, 66.7)$ Shellfish $11.1 (0.0, 200)$ Whale $0.0 (0.0, 6.7)$ | Chielese | _Oneo/ week | JU (27.7) |
| | Chicken | ·O / 1 | 20 (0.2) |
| $ \begin{tabular}{ c c c c c } & & & & & & & & & & & & & & & & & & &$ | | <once td="" week<=""><td>30 (8.2)</td></once> | 30 (8.2) |
| Egg <once td="" week<=""> 53 (14.4) \geqOnce/week 314 (85.6) Milk <once td="" week<=""> 10 (2.7) \geqOnce/week 356 (97.3) Fish intake from food frequency questionnaires Fish intake (g/day) Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70)</once></once> | | ≥Once/week | 337 (91.8) |
| | Egg | | |
| $ \begin{tabular}{ c c c c c } \hline & & & & & & & & & & & & & & & & & & $ | | <once td="" week<=""><td>53 (14.4)</td></once> | 53 (14.4) |
| Milk $314'(83.0)'$ Milk \geq Once/week $10(2.7)$ \geq Once/week $356'(97.3)'$ Fish intake from food frequency questionnaires $38.8(0.0, 400)'$ Fatty fish $23.3(0.0, 160)'$ Lean fish $0.0(0.0, 66.7)'$ Shellfish $11.1(0.0, 200)'$ Whale $0.0(0.0, 6.70)'$ | | >Once/week | 314 (85.6) |
| NHK $<$ Once/week $10 (2.7)$ \geq Once/week $356 (97.3)$ Fish intake from food frequency questionnairesFish intake (g/day) $38.8 (0.0, 400)$ Fatty fish $23.3 (0.0, 160)$ Lean fish $0.0 (0.0, 66.7)$ Shellfish $11.1 (0.0, 200)$ Whale $0.0 (0.0, 6.70)$ | M;11z | | 517 (05.0) |
| $< Once/week$ 10 (2.7) $\geq Once/week$ 356 (97.3) Fish intake from food frequency questionnaires 56 (97.3) Fish intake (g/day) 38.8 (0.0, 400) Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | WIIIK | ·O / 1 | 10 (2.7) |
| \geq Once/week 356 (97.3) Fish intake from food frequency questionnaires 58.8 (0.0, 400) Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.7) | | <once td="" week<=""><td>10 (2.7)</td></once> | 10 (2.7) |
| Fish intake from food frequency questionnaires 38.8 (0.0, 400) Fish intake (g/day) 23.3 (0.0, 160) Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | | ≥Once/week | 356 (97.3) |
| Fish intake from food frequency questionnaires 38.8 (0.0, 400) Fish intake (g/day) 38.8 (0.0, 160) Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | | | |
| Fish intake (g/day) 38.8 (0.0, 400 Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | | from food frequency questionnaires | |
| Fatty fish 23.3 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | Fish intake | (/1) | 38.8 (0.0.400) |
| raty isin 25.5 (0.0, 160) Lean fish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | Fish intake | (g/dav) | 20.010.0. 100 |
| Lean Iish 0.0 (0.0, 66.7) Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | Fish intake Fish intake | (g/day) | 22.2 (0.0. 1(0) |
| Shellfish 11.1 (0.0, 200) Whale 0.0 (0.0, 6.70) | Fish intake Fish intake Fatty fish | (g/day) | 23.3 (0.0, 160) |
| Whale 0.0 (0.0, 6.70) | Fish intake Fish intake Fatty fish Lean fish | (g/day) | 23.3 (0.0, 160) 0.0 (0.0, 66.7) ¹ |
| | Fish intake Fish intake Fatty fish Lean fish Shellfish | (g/day) | 23.3 (0.0, 160) 0.0 (0.0, 66.7) 11.1 (0.0, 200) |
| | Fish intake Fish intake Fatty fish Lean fish Shellfish Whale | (g/day) | 23.3 (0.0, 160) 0.0 (0.0, 66.7) 11.1 (0.0, 200) 0.0 (0.0, 6.70) |

| Male | 173 (47.1) |
|----------------------------------|-----------------------------|
| Female | 194 (52.9) |
| Type of delivery | |
| Vaginal birth | 292 (79.3) |
| Cesarean section | 76 (20.7) |
| Gestational age at birth (weeks) | $39.0\pm1.4^{\rm a}$ |
| Birth weight (g) | 3073 ± 37^{a} |
| Length (cm) | $48.1 \pm 1.9^{\text{a}}$ |
| Chest circumference (cm) | $31.5 \pm 1.6^{\mathrm{a}}$ |
| Head circumference (cm) | 33.3 ± 1.3^{a} |
| SGA by weight | 18 (4.9) |
| SGA by length | 43 (11.7) |

769 770 771

^aMedian (minimum, maximum). SGA: small for gestational age.

| | Minimum | 25th | 50th | 75th | Maximum |
|---------------------|---------|------|------|------|---------|
| EPA + DHA | 3.0 | 20.5 | 32.2 | 47.8 | 163 |
| AA | 2.8 | 43.5 | 61.2 | 89.7 | 219 |
| Omega-3 fatty acids | 4.1 | 28.2 | 43.4 | 63.9 | 188 |
| Omega-6 fatty acids | 16.1 | 581 | 798 | 1030 | 2840 |

Table 2. Concentrations of LCPUFA ($\mu g/mL$) in maternal blood (n = 367).

773 LCPUFA: long-chain polyunsaturated fatty acids; EPA: eicosapentaenoic acid; DHA:

docosahexaenoic acid; AA: arachidonic acid; Omega-3 fatty acids: EPA, DHA, α -linolenic acid (ALA); Omega-6 fatty acids: AA, linoleic acid (LA).

Table 3. Concentrations of polychlorinated biphenyls in maternal blood (PCBs; ng/g lipid) and hair mercury ($\mu g/g$) in maternal samples (n = 367).

| | | | Percentil | e | |
|----------------------------------|---------|------|-----------|------|---------|
| | Minimum | 25th | 50th | 75th | Maximum |
| Estrogenic PCBs ^a | 3.88 | 19.5 | 28.7 | 40.0 | 147 |
| Antiestrogenic PCBs ^b | 0.63 | 2.75 | 4.13 | 5.60 | 21.7 |
| Dioxin-like PCBs ^c | 1.74 | 7.51 | 11.2 | 15.6 | 49.8 |
| Non-dioxin-like PCBs | 16.0 | 64.8 | 95.7 | 133 | 445 |
| Hair Hg | 0.24 | 0.96 | 1.41 | 1.89 | 4.73 |

^aPCB 52, 49, 47, 44, 70, 95, 101, 99, 110, and 153 (Cooke, 2001).

^bPCB 37, 77, 81, 126, 169, 114, 105, and 156 (Cooke, 2001). ^cPCB 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, and 189 (Van den Berg et al., 2006).

784 785 Table 4. Total polychlorinated biphenyls (PCBs) and hair mercury (Hg) levels in relation to maternal and infant characteristics and polyunsaturated fatty acids (n = 367)

| poryunsaturated ratty actus ($II = 507$) | | Total PCB | s (ng/g lipid) | Hair Hg (ug | y/g) |
|--|---|-----------------------|--------------------|-----------------------|--------------------------------------|
| Characteristics | | r | Median (min, max) | r | Median (min, max) |
| Maternal characteristics | | | | | , <i>i</i> , <i>i</i> |
| Age at delivery (years) | | 0.415 ^a ** | | 0.094^{a} | |
| Height (cm) | | 0.079^{a} | | -0.055ª | |
| Prepregnancy weight (kg) | | 0.016 ^a | | -0.029 ^a | |
| Parity | 0 | | 115 (19.6, 495)* | | 1.41 (0.30, 3.73)* |
| | ≥1 | | 102 (17.8, 354) | | 1.38 (0.24, 4.73) |
| Blood sampling period | During pregnancy | | 110 (17.8, 363) | | 1.41 (0.24, 4.73) |
| | After delivery | | 104 (27.4, 495) | | 1.40 (0.30, 4.30) |
| History of chemical hair waving | No | | 108 (17.8, 495) | | 1.37 (0.24, 4.35) |
| | Yes | | 109 (19.6, 362) | | 1.46 (0.30, 4.73) |
| Education level (years) | ≤12 | | 99.0 (17.8, 363) | | 1.33 (0.24, 4.35) |
| | >12 | | 111 (19.6, 495) | | 1.42 (0.30, 4.73) |
| Annual household income (million yen) | <5 | | 102 (17.8, 362)* | | 1.28 (0.24, 4.73)* |
| · · · · | ≥5 | | 123 (27.4, 495) | | 1.47 (0.30, 4.33) |
| Tobacco smoking during pregnancy | Nonsmoker | | 110 (17.8, 362) | | 1.41 (0.30, 4.35) |
| 6 6 6 6 6 | Smoker | | 954 (196, 495) | | 1.39(0.24, 4.73) |
| Alcohol consumption during pregnancy | No | | 100 (17.8, 354) | | 1 33 (0 31 4 03) |
| ruon danne programe | Yes | | 113 (27 8 405) | | 1.33(0.31, 4.03) 1.42(0.24, 4.73) |
| Caffeine intake (mg/day) | 105 | 0.017 ^a | 115 (27.0, 495) | -0.005 ^a | 1.42 (0.24, 4.75) |
| | | | | | |
| Frequency of food consumption during pr | regnancy | | | | |
| Shoreline fish | <once td="" week<=""><td></td><td>101 (17.8, 362)</td><td></td><td>1.31 (0.31, 4.35)</td></once> | | 101 (17.8, 362) | | 1.31 (0.31, 4.35) |
| | ≥Once/week | | 113 (19.6, 495) | | 1.46 (0.24, 4.73) |
| Pelagic fish | <once td="" week<=""><td></td><td>106 (17.8, 362)</td><td></td><td>1.24 (0.24, 4.03)**</td></once> | | 106 (17.8, 362) | | 1.24 (0.24, 4.03)** |
| | ≥Once/week | | 109 (27.4, 495) | | 1.49 (0.32, 4.73) |
| Beef | <once td="" week<=""><td></td><td>108 (17.8, 363)</td><td></td><td>1.34 (0.24, 4.73)*</td></once> | | 108 (17.8, 363) | | 1.34 (0.24, 4.73)* |
| | ≥Once/week | | 107 (19.6, 495) | | 1.51 (0.30, 3.69) |
| Pork | <once td="" week<=""><td></td><td>85.9 (19.6, 302)</td><td></td><td>1.54 (0.66, 4.03)</td></once> | | 85.9 (19.6, 302) | | 1.54 (0.66, 4.03) |
| | ≥Once/week | | 109 (17.8, 495) | | 1.39 (0.24, 4.73) |
| Chicken | <once td="" week<=""><td></td><td>108 (31.3, 362)</td><td></td><td>1.30 (0.37, 4.03)</td></once> | | 108 (31.3, 362) | | 1.30 (0.37, 4.03) |
| | ≥Once/week | | 108 (17.8, 495) | | 1.41 (0.24, 4.73) |
| Egg | <once td="" week<=""><td></td><td>102 (59.0, 213)</td><td></td><td>1.28 (1.19, 1.49)</td></once> | | 102 (59.0, 213) | | 1.28 (1.19, 1.49) |
| N (11) | ≥Once/week | | 108 (17.8, 495) | | 1.41 (0.24, 4.73) |
| Milk | <once td="" week<=""><td></td><td>74.9 (30.2, 354)**</td><td></td><td>1.24 (0.45, 3.09)</td></once> | | 74.9 (30.2, 354)** | | 1.24 (0.45, 3.09) |
| | ≥Once/week | | 111 (17.8, 495) | | 1.42 (0.24, 4.73) |
| Food frequency questionnaires at delivery | y | | | | |
| Fish intake (g/day) | | 0.187 ^a ** | | 0.215 ^a ** | |
| Fatty fish (g/day) | | 0.141ª** | | 0.210 ^a ** | |
| Shellfish (g/day) | | 0.087^{a} | | 0.084^{a} | |
| LCPUFA in maternal blood | | | | | |
| EPA + DHA | | 0.182 ^a ** | | 0.056ª | |
| АА | | 0.048ª | | -0.077ª | |
| Omega-3 fatty acids | | 0.155 ^a ** | | 0.022ª | |
| Omega-6 fatty acids | | 0.073ª | | -0.018ª | |
| | | | | | |
| Infant characteristics | Mala | | 111 (07.4.2.2) | | 1 41 (0 04 4 07) |
| Sex | Iviale | | 111 (27.4, 362) | | 1.41 (0.24, 4.35) |
| | remaie | | 104 (17.8, 495) | | 1.39 (0.30, 4.73) |
| Type of delivery | Vaginal birth | | 109 (17.8, 363) | | 1.43 (0.24, 4.73) |
| | Cesarean section | | 97.0 (19.6, 495) | 0.045 | 1.24 (0.30, 4.35) |
| Gestational age (weeks) | | 0.025 ^a | | 0.017 ^a | |
| SGA by weight | No | | 108 (17.8, 495) | | 1.42 (0.30, 4.73)* |
| | Yes | | 98.7 (51.0, 223) | | 0.92 (0.24, 2.62) |
| SGA by length | No | | 109 (17.8, 495) | | 1.41 (0.24, 4.73) |
| | Yes | | 97 (19.6, 247) | | 1.24 (0.46, 3.55) |

786 ^ar: Spearman's rank correlation coefficient.

787 788 *p<0.05, **p<0.01 by Mann–Whitney U-test and Spearman's rank correlation test. LCPUFA: long-chain polyunsaturated fatty acids, EPA: eicosapentaenoic acid, DHA: docosahexaenoic acid, AA: arachidonic acid.

| | | SGA by weight | | | SGA by length | | |
|----------------------|-------------|-------------------|-------------------------|-------------------------|------------------|-------------------------|-------------------------|
| | | Crude | Adjusted 1 ^a | Adjusted 2 ^a | Crude | Adjusted 1 ^b | Adjusted 2 ^b |
| | | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | | OR (95% CI) |
| Estrogenic PCBs | Quartile 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | Quartile 2 | 0.41 (0.10-1.65) | 0.51 (0.11-2.30) | 0.56 (0.12-2.58) | 1.21 (0.53-2.79) | 1.48 (0.60-3.67) | 1.57 (0.62-4.00) |
| | Quartile 3 | 0.27 (0.05-1.34) | 0.40 (0.07-2.24) | 0.42(0.07-2.41) | 0.38 (0.13-1.14) | 0.36 (0.11-1.17) | 0.37 (0.11–1.22) |
| | Quartile 4 | 0.85 (0.27-2.62) | 1.95 (0.46-8.18) | 1.88 (0.45-7.83) | 1.00 (0.42-2.36) | 0.81 (0.28-2.29) | 0.68 (0.23-2.03) |
| | p for trend | 0.662 | 0.694 | 0.696 | 0.509 | 0.334 | 0.197 |
| | P for | | | | | | |
| | interaction | | | 0.335 | | | 0.211 |
| Antiestrogenic PCBs | Quartile 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | Quartile 2 | 0.99 (0.28-3.54) | 1.16 (0.29-4.68) | 1.31 (0.32-5.34) | 1.31 (0.56-3.05) | 1.44 (0.58-3.57) | 1.53 (0.61–3.84) |
| | Quartile 3 | 0.57 (0.13-2.47) | 0.99 (0.20-4.87) | 1.07 (0.21-5.47) | 0.50 (0.18-1.42) | 0.52 (0.17-1.63) | 0.50 (0.16-1.57) |
| | Quartile 4 | 1.00 (0.28-3.58) | 1.95 (0.44-8.55) | 1.89 (0.43-8.29) | 1.10 (0.46-2.65) | 1.07 (0.38-2.98) | 0.94 (0.32-2.73) |
| | p for trend | 0.824 | 0.523 | 0.511 | 0.71 | 0.718 | 0.550 |
| | P for | | | | | | |
| | interaction | | | 0.317 | | | 0.249 |
| Dioxin-like PCBs | Quartile 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | Quartile 2 | 1.23 (0.36-4.18) | 1.54 (0.39-6.05) | 1.93 (0.48–7.77) | 1.34 (0.57–3.13) | 1.62 (0.64-4.09) | 1.79 (0.70-4.56) |
| | Quartile 3 | 0.38 (0.07-2.02) | 0.66 (0.11-4.06) | 0.64 (0.10-4.01) | 0.60 (0.22-1.62) | 0.68 (0.22-2.07) | 0.62 (0.20-1.94) |
| | Quartile 4 | 1.01 (0.28-3.62) | 2.20 (0.48–10.1) | 2.01 (0.44–9.19) | 1.01 (0.42–2.47) | 1.01 (0.35-2.90) | 0.83 (0.28-2.48) |
| | p for trend | 0.669 | 0.570 | 0.560 | 0.617 | 0.714 | 0.260 |
| | P for | | | | | | |
| | interaction | | | 0.155 | | | 0.096 |
| Non-dioxin like PCBs | Quartile 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | Quartile 2 | 0.48 (0.12–1.97) | 0.56 (0.12–2.59) | 0.57 (0.12–2.65) | 1.71 (0.73–3.99) | 1.99 (0.79–5.01) | 2.02 (0.79-5.17) |
| | Quartile 3 | 0.81 (0.24–2.77) | 1.36 (0.32–5.69) | 1.47 (0.34–6.42) | 0.47 (0.15–1.42) | 0.49 (0.15–1.64) | 0.49 (0.14–1.66) |
| | Quartile 4 | 0.64 (0.18–2.36) | 1.21 (0.24–6.22) | 1.18 (0.23-5.96) | 1.21 (0.50–2.97) | 1.00 (0.33-3.05) | 0.88 (0.28-2.76) |
| | p for trend | 0.654 | 0.759 | 0.752 | 0.697 | 0.483 | 0.345 |
| | P for | | | | | | |
| | interaction | | | 0.417 | | | 0.461 |
| Hair Hg | Quartile 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | Quartile 2 | 0.28 (0.07–1.04) | 0.24 (0.06–1.00) | 0.22 (0.05–0.94)* | 0.68 (0.29–1.62) | 0.69 (0.27–1.76) | 0.71 (0.27–1.84) |
| | Quartile 3 | 0.18 (0.04–0.86)* | 0.12 (0.02–0.68)* | 0.11 (0.02–0.64)* | 0.60 (0.25–1.47) | 0.58 (0.22–1.54) | 0.57 (0.21–1.55) |
| | Quartile 4 | 0.28 (0.07–1.05) | 0.17 (0.04–0.79)* | 0.16 (0.03-0.77)* | 0.69 (0.29–1.64) | 0.65 (0.24–1.76) | 0.61 (0.22–1.73) |
| | p for trend | 0.023 | 0.014 | 0.014 | 0.359 | 0.362 | 0.324 |
| | P for | | | 0.965 | | | 0.562 |
| | interaction | | | | | | |

Table 5. Odds ratios for babies born small for gestational age (n = 367).

791 The odds ratios (OR) and 95% confidence intervals (95% CI) for babies born small for gestational age (SGA) were calculated by using the first quartile as the reference category.

- p for trend: linear trend across quartiles.
- Adjusted 1ª: adjusted for maternal age, maternal height, prepregnancy maternal weight, tobacco smoking during pregnancy, alcohol consumption during pregnancy, household income, blood sampling
- period, and total PCBs or hair Hg.
- 792 793 794 795 796 797 798 799 800 Adjusted 2^a: adjusted for omega-3 fatty acids in addition to the adjusted factors in Adjusted 1^a
- Adjusted 1^b: adjusted for maternal age, maternal height, prepregnancy maternal weight, tobacco smoking during pregnancy, alcohol consumption during pregnancy, household income, blood sampling
- period, parity, infant sex, and total PCBs or hair Hg.
- Adjusted 2^{b} : adjusted for omega-3 fatty acids in addition to the adjusted factors in Adjusted 1^{b}
- P for interaction: introduced for interaction terms of quartile PCBs or quartile Hg, and quartile omega-3 fatty acids, in addition to the adjusted factors in Adjusted 2^a or Adjusted 2^b.
- *p<0.05.
- 801



806 Supplementary Material

807

808 Supplementary Table 1. Food frequency questionnaire.

Question 1: Frequency of fish consumption (choose one of the following options)

1. Often. Please indicate the number of fish servings per day.

2. Sometimes. Please provide an estimated frequency of fish consumption.

3. Rarely

4. Never

Question 2: Portion size of fish in one serving (choose one of the following options)

1. <50 g

- 2. 50–100 g
- 3. 100–150 g
- 4. 150–200 g
- 5. >200 g
- 6. Unknown

Question 3: Type of fish frequently consumed (choose as many of the following as applicable)

Tuna, bonito, salmon, yellowtail, sea bream, flatfish, flounder, sardine, mackerel, saury, horse mackerel, eel, carp, sweetfish, crucian carp, cuttlefish, octopus, crab, shrimp, shellfish, whale, fish products, Atka mackerel, shishamo smelt, Pacific cod, Pacific herring, trout

Supplementary Table 2. Analysis results of 70 PCB congeners (ng/g lipid) (n = 367).

| | Dete | Detect | M 1: (254 | 22'44'55'- HexaCB(# 153) | Total 70 I | ° CBs |
|--|-------|--------|------------------------|--------------------------------|--------------|--------------|
| PCB congeners | ction | 10n | Median $(25tn - 75tb)$ | · · · · | | Contri |
| | limit | (%) | 75ui) | r | r | bution |
| | | (70) | | 1 | 1 | rate |
| | | | | | | (%) |
| 245-TriCB(#29) | 0.01 | 32.4 | 0.01 (0.01–0.03) | 0.090 | 0.075 | 0.02 |
| 244'-TriCB(#28) | 0.01 | 99.7 | 1.08 (0.78–1.50) | 0.373** | 0.393** | 0.99 |
| 344'-TriCB(#37) | 0.01 | 21.8 | 0.01 (0.01–0.01) | 0.070 | 0.126* | 0.27 |
| 22'55'-TetraCB(#52) | 0.01 | 94.8 | 0.62 (0.36–0.90) | 0.1/9** | 0.225** | 0.58 |
| 22'45'-TetraCB(#49) | 0.01 | 92.1 | 0.17 (0.09–0.26) | 0.122* | 0.197** | 0.16 |
| 22'44'-TetraCB(#47) | 0.01 | 91.3 | 0.34 (0.20-0.50) | 0.186** | 0.263** | 0.31 |
| 22'35'-TetraCB(#44) | 0.01 | 84.2 | 0.27 (0.10-0.38) | 0.113* | 0.149** | 0.22 |
| 23'4'6-TetraCB(#71) | 0.01 | 86.4 | 0.10 (0.04–0.17) | -0.017 | 0.022 | 0.10 |
| 234'5-TetraCB(#63) | 0.01 | 93.5 | 0.05 (0.03–0.07) | 0.542** | 0.572** | 0.05 |
| 244'5-TetraCB(#74) | 0.01 | 100 | 3.12 (2.20-4.55) | 0.867** | 0.862** | 3.03 |
| 23'4'5-TetraCB(#/0) | 0.01 | 87.5 | 0.15 (0.09–0.20) | 0.20/** | 0.205** | 0.13 |
| 23'44'-TetraCB(#66) | 0.01 | 100 | 0.64 (0.43–0.98) | 0.643** | 0.652** | 0.63 |
| 233'4'-/2344'TetraCBs(#56/60) | 0.01 | 98.1 | 0.27 (0.18–0.40) | 0.568** | 0.577** | 0.25 |
| 22'35'6-PentaCB(#95) | 0.01 | 96.7 | 0.37 (0.22–0.56) | 0.318** | 0.341** | 0.35 |
| 22'355'-PentaCB(#92) | 0.01 | 97.0 | 0.26 (0.16–0.41) | 0.5/8** | 0.599** | 0.27 |
| 22'455'-PentaCB(#101) | 0.01 | 99.5 | 0.64 (0.42–0.91) | 0.552** | 0.588** | 0.62 |
| 22'44'5-PentaCB(#99) | 0.01 | 100 | 3.97 (2.66–5.51) | 0.893** | 0.888** | 3.72 |
| 234′56-PentaCB(#117) | 0.01 | 98.9 | 0.25 (0.17–0.36) | 0.714** | 0.769** | 0.24 |
| 22'345'-PentaCB(#87) | 0.01 | 97.5 | 0.25 (0.18–0.35) | 0.529** | 0.590** | 0.24 |
| 22'344'-PentaCB(#85) | 0.01 | 93.5 | 0.09 (0.05–0.13) | 0.411** | 0.458** | 0.09 |
| 233'4'6-PentaCB(#110) | 0.01 | 89.9 | 0.17 (0.10–0.26) | 0.338** | 0.379** | 0.16 |
| 233'4'5-PentaCB(#107) | 0.01 | 99.2 | 0.28 (0.17–0.43) | 0.734** | 0.776** | 0.28 |
| 22'355'6-HexaCB(#151) | 0.01 | 99.2 | 0.32 (0.22–0.53) | 0.641** | 0.659** | 0.36 |
| 22'33'56'-HexaCB(#135) | 0.01 | 97.0 | 0.14 (0.09–0.23) | 0.628** | 0.628** | 0.15 |
| 22'34'56-HexaCB(#147) | 0.01 | 93.7 | 0.12 (0.07–0.18) | 0.693** | 0.694** | 0.12 |
| 22'344'6-/22'34'5'6-HexaCB(#139/149) | 0.01 | 91.3 | 0.24 (0.13–0.37) | 0.486** | 0.479** | 0.23 |
| 22'33'56-HexaCB(#134) | 0.01 | 35.7 | 0.01 (0.01–0.02) | 0.030 | 0.044 | 0.01 |
| 233'55'6-HexaCB(#165) | 0.01 | 0 | | | | |
| 22'34'55'-HexaCB(#146) | 0.01 | 100 | 2.99 (2.02–4.32) | 0.973** | 0.960** | 2.89 |
| 22'33'46'-HexaCB(#132) | 0.01 | 85.0 | 0.11 (0.06–0.17) | 0.376** | 0.354** | 0.11 |
| 22'44'55'-HexaCB(#153) | 0.01 | 100 | 21.4 (14.5–31.2) | | 0.982** | 20.3 |
| 22'3455'-HexaCB(#141) | 0.01 | 83.1 | 0.09 (0.05–0.16) | 0.471** | 0.495** | 0.10 |
| 22'344'5-HexaCB(#137) | 0.01 | 100 | 0.77 (0.52–1.06) | 0.949** | 0.949** | 0.70 |
| 22'33'45'-HexaCB(#130) | 0.01 | 100 | 0.66 (0.44–0.96) | 0.909** | 0.917** | 0.63 |
| 233'4'5'6-HexaCB(#164) | 0.01 | 100 | 3.99 (2.63–5.91) | 0.842** | 0.872** | 3.91 |
| 22'344'5'-HexaCB(#138) | 0.01 | 100 | 11.9 (7.84–16.7) | 0.974** | 0.967** | 11.1 |
| 22'33'44'-HexaCB(#128) | 0.01 | 99.5 | 0.32 (0.20–0.48) | 0.662** | 0.714** | 0.33 |
| 22'33'566'-HptaCB(#179) | 0.01 | 86.4 | 0.07 (0.04–0.13) | 0.503** | 0.515** | 0.08 |
| 22'33'55'6-HptaCB(#178) | 0.01 | 99.7 | 1.31 (0.90–1.90) | 0.915** | 0.935** | 1.32 |
| 22'344'56-HptaCB(#182) | 0.01 | 100 | 6.06 (3.86–8.52) | 0.940** | 0.965** | 5.93 |
| 22'344'5'6-HptaCB(#183) | 0.01 | 99.7 | 1.65 (1.09–2.42) | 0.928** | 0.945** | 1.64 |
| 22'344'56-HptaCB(#181) | 0.01 | 71.1 | 0.03 (0.01–0.05) | 0.379** | 0.399** | 0.03 |
| 22'33'4'56-HptaCB(#177) | 0.01 | 99.7 | 1.45 (0.99–2.13) | 0.907** | 0.938** | 1.45 |
| 22'33'455'-HptaCB(#172) | 0.01 | 98.9 | 0.68 (0.44–1.01) | 0.858** | 0.904** | 0.68 |
| 22'344'55'-HptaCB(#180) | 0.01 | 100 | 13.0 (8.63–19.4) | 0.892** | 0.935** | 12.9 |
| 233'44'5'6-HptaCB(#191) | 0.01 | 90.7 | 0.16 (0.11–0.25) | 0.727** | 0.759** | 0.16 |
| 22'33'44'5-HptaCB(#170) | 0.01 | 100 | 4.57 (3.05–6.42) | 0.879** | 0.923** | 4.46 |
| 22'33'55'66'-OctaCB(#202) | 0.01 | 99.7 | 0.49 (0.31–0.73) | 0.828** | 0.810** | 0.48 |
| 22'33'45'66'-OctaCB(#200) | 0.01 | 91.6 | 0.09 (0.06–0.15) | 0.714** | 0.708** | 0.10 |
| 22'33'45'66'-/22'33'455'6-OctaCB(#201/198) | 0.01 | 100 | 1.88 (1.22–2.71) | 0.881** | 0.880^{**} | 1.82 |

| 22'344'55'6-OctaCB(#203) | 0.01 | 100 | 1.63 (1.07-2.37) | 0.859** | 0.850** | 1.58 |
|------------------------------|------|------|------------------|---------|---------|------|
| 22'33'44'56-OctaCB(#195) | 0.01 | 100 | 0.42 (0.30-0.63) | 0.877** | 0.857** | 0.41 |
| 22'33'44'55'-OctaCB(#194) | 0.01 | 100 | 1.64 (1.11–2.37) | 0.866** | 0.871** | 1.57 |
| 233'44'55'6-OctaCB(#205) | 0.01 | 87.2 | 0.07 (0.05-0.10) | 0.619** | 0.631** | 0.07 |
| 22'33'455'66'-NonaCB(#208) | 0.01 | 98.1 | 0.22 (0.14-0.33) | 0.737** | 0.707** | 0.22 |
| 22'33'44'566'-NonaCB(#207) | 0.01 | 96.2 | 0.11 (0.07-0.17) | 0.694** | 0.656** | 0.11 |
| 22'33'44'55'6-NonaCB(#206) | 0.01 | 99.7 | 0.54 (0.38-0.75) | 0.827** | 0.816** | 0.51 |
| 22'33'44'55'66'-DecaCB(#209) | 0.01 | 100 | 0.46 (0.33-0.61) | 0.776** | 0.763** | 0.42 |
| 344'5-TeCB(#81) | 0.01 | 0 | | | | |
| 33'44'-TeCB(#77) | 0.01 | 64.3 | 0.01 (0.01-0.01) | 0.266** | 0.328** | 0.01 |
| 33'44'5-PentaCB(#126) | 0.01 | 96.5 | 0.03 (0.02-0.05) | 0.726** | 0.763** | 0.03 |
| 33'44'55'-HexaCB(#169) | 0.01 | 94.6 | 0.02 (0.02-0.03) | 0.777** | 0.817** | 0.02 |
| 2'344'5-PetaCB(#123) | 0.01 | 98.1 | 0.11 (0.07-0.15) | 0.727** | 0.750** | 0.10 |
| 23'44'5-PetaCB(#118) | 0.01 | 100 | 5.78 (3.82-8.22) | 0.896** | 0.902** | 5.43 |
| 2344'5-PetaCB(#114) | 0.01 | 98.9 | 0.34 (0.23-0.48) | 0.880** | 0.887** | 0.32 |
| 233'44'-PetaCB(#105) | 0.01 | 100 | 1.40 (0.98-2.06) | 0.847** | 0.859** | 1.35 |
| 23'44'55'-HexaCB(#167) | 0.01 | 99.7 | 0.69 (0.46-0.98) | 0.945** | 0.950** | 0.65 |
| 233'44'5-HexaCB(#156) | 0.01 | 100 | 1.95 (1.32-2.72) | 0.931** | 0.932** | 1.82 |
| 233'44'5'-HexaCB(#157) | 0.01 | 99.7 | 0.48 (0.33-0.66) | 0.916** | 0.910** | 0.45 |
| 233'44'55'-HptaCB(#189) | 0.01 | 99.2 | 0.24 (0.17-0.34) | 0.811** | 0.803** | 0.22 |
| Total PCBs | | | 108 (72.7–149) | | | |

r was calculated by using Spearman's rank correlation coefficient. *p < 0.05, **p < 0.01.

| C1 | | Birth w | eight (g) | Length (c | m) | Chest | famam an () | Head | Forman () |
|----------------------------|--|----------------------|--------------------------------------|--------------------------------|----------------------------------|---------|----------------------------------|------------------|-------------------------------|
| Characteristics | | | $M_{con} \pm SD$ | | $M_{con} \pm SD$ | circum | Interence (cm) $M_{con} + SD$ | circum | terence (cm) Moon \pm SD |
| Maternal characteristics | | 1 | Wiedii ± SD | 1 | Wiedli ± 5D | 1 | Wieali ± 5D | 1 | We all \pm SD |
| Age at delivery (years) | , | -0.010^{a} | | _0.033ª | | 0.021ª | | 0 023ª | |
| Height (cm) | | -0.010 0.127ª* | | -0.035 0.153ª** | | 0.123a | k | 0.025 0.116a* | |
| Pre-pregnancy weight | (kg) | 0.127 0.162ª* | | 0.135 0.140 ^a ** | | 0.125 | 4 | 0.106a* | |
| Parity | 0 | 0.102 | 3055 ± 375 | 0.140 | 48.1 ± 2.0 | 0.119 | 31.4 + 1.7 | 0.100 | 332 + 14 |
| 1 anty | >1 | | 3002 ± 373 | | 48.1 ± 2.0 48.2 ± 1.0 | | 31.4 ± 1.7 31.6 ± 1.4 | | 33.2 ± 1.4 |
| Education loval (voors) | ≤ 1 | | 3092 ± 308 | | 40.2 ± 1.9 | | 31.0 ± 1.4 21.4 ± 1.6 | | 33.4 ± 1.3 |
| Education level (years) | $\sum 12$ | | 3030 ± 364 3086 ± 363 | | 46.0 ± 1.6 48.2 ± 2.0 | | 31.4 ± 1.0 21.6 \pm 1.5 | | 33.2 ± 1.3 22.4 ± 1.2 |
| A | ~12 | | 3080 ± 303 | | 46.2 ± 2.0 | | 31.0 ± 1.5 21.5 ± 1.5 | | 33.4 ± 1.3 |
| (million ven) | 5 s | | 3064 ± 303 3052 ± 385 | | 46.1 ± 2.0 48.2 ± 1.7 | | 31.3 ± 1.3 21.5 ± 1.7 | | 33.3 ± 1.3 |
| | ≥5 . Na a ana alam | | 3032 ± 383 | | 40.2 ± 1.7 | | 51.5 ± 1.7 | | 33.3 ± 1.3 |
| lobacco smoking di | uring Nonsmoker | | 3085 ± 384 | | 48.2 ± 2.0 | | 31.5 ± 1.6 | | 33.4 ± 1.4 |
| pregnancy | Smoker | | 3019 ± 299 | | 47.9 ± 1.5 | | 31.4 ± 1.2 | | 33.1 ± 1.2 |
| Alcohol consum | ption No | | 3059 ± 386 | | 48.0 ± 2.0 | | 31.4 ± 1.7 | | 33.3 ± 1.4 |
| during pregnancy | V | | 2107 + 225 | | 49.2 + 1.7 | | 217 + 12 | | 224 + 12 |
| Caffeine intake (ma/da | Yes | 0.072 | 3107 ± 333 | 0.043b | 48.3 ± 1.7 | 0.001 | 51./±1.2 | 0.001 | 33.4 ± 1.3 |
| Carrenne intake (ing/da | (y) | -0.072 | | -0.043 | | -0.091 | | -0.001 | |
| Frequency of food of | consumption durir | ıg | | | | | | | |
| pregnancy | ~ / . | | | | | | | | |
| Shoreline fish | <once td="" week<=""><td></td><td>3096 ± 341</td><td></td><td>48.2 ± 1.7</td><td></td><td>31.5 ± 1.4</td><td></td><td>33.4 ± 1.3</td></once> | | 3096 ± 341 | | 48.2 ± 1.7 | | 31.5 ± 1.4 | | 33.4 ± 1.3 |
| | ≥Once/week | | 3047 ± 404 | | 48.0 ± 2.2 | | 31.5 ± 1.7 | | 33.2 ± 1.3 |
| elagic fish | <once td="" week<=""><td></td><td>3060 ± 380</td><td></td><td>48.0 ± 1.8</td><td></td><td>31.4 ± 1.5</td><td></td><td>33.3 ± 1.3</td></once> | | 3060 ± 380 | | 48.0 ± 1.8 | | 31.4 ± 1.5 | | 33.3 ± 1.3 |
| | ≥Once/week | | 3086 ± 365 | | 48.2 ± 2.0 | | 31.6 ± 1.6 | | 33.3 ± 1.4 |
| Beef | <once td="" week<=""><td></td><td>3061 ± 384</td><td></td><td>48.0 ± 1.8</td><td></td><td>31.5 ± 1.6</td><td></td><td>33.3 ± 1.3</td></once> | | 3061 ± 384 | | 48.0 ± 1.8 | | 31.5 ± 1.6 | | 33.3 ± 1.3 |
| | ≥Once/week | | 3112 ± 334 | | 48.3 ± 2.4 | | 31.6 ± 1.4 | | 33.3 ± 1.3 |
| Pork | <once td="" week<=""><td></td><td>3061 ± 384</td><td></td><td>48.0 ± 1.8</td><td></td><td>31.5 ± 1.6</td><td></td><td>33.3 ± 1.3</td></once> | | 3061 ± 384 | | 48.0 ± 1.8 | | 31.5 ± 1.6 | | 33.3 ± 1.3 |
| | ≥Once/week | | 3112 ± 334 | | 48.3 ± 2.4 | | 31.6 ± 1.4 | | 33.3 ± 1.3 |
| Chicken | <once td="" week<=""><td></td><td>2969 ± 325</td><td></td><td>$47.5\pm1.5\texttt{*}$</td><td></td><td>31.2 ± 1.5</td><td></td><td>33.1 ± 1.2</td></once> | | 2969 ± 325 | | $47.5\pm1.5\texttt{*}$ | | 31.2 ± 1.5 | | 33.1 ± 1.2 |
| | ≥Once/week | | 3083 ± 374 | | 48.2 ± 2.0 | | 31.5 ± 1.6 | | 33.3 ± 1.3 |
| Egg | <once td="" week<=""><td></td><td>3002 ± 384</td><td></td><td>47.5 ± 2.9</td><td></td><td>31.3 ± 1.7</td><td></td><td>33.2 ± 1.4</td></once> | | 3002 ± 384 | | 47.5 ± 2.9 | | 31.3 ± 1.7 | | 33.2 ± 1.4 |
| | ≥Once/week | | 3085 ± 369 | | 48.2 ± 1.7 | | 31.5 ± 1.5 | | 33.3 ± 1.3 |
| Milk | <once td="" week<=""><td></td><td>3094 ± 410</td><td></td><td>48.3 ± 1.7</td><td></td><td>31.5 ± 1.2</td><td></td><td>33.3 ± 1.4</td></once> | | 3094 ± 410 | | 48.3 ± 1.7 | | 31.5 ± 1.2 | | 33.3 ± 1.4 |
| | \geq Once/week | | 3074 ± 370 | | 48.1 ± 1.9 | | 31.5 ± 1.6 | | 33.3 ± 1.3 |
| Food frequency question | onnaire at deliverv ⁱ | , | | | | | | | |
| Fish intake (α/day) | simane at derivery | 0.000 | | 0.025 | | _0.021 | | _0.087 | |
| Fatty fish intake (g/day) | <i>d</i>) | 0.000 | | 0.025 | | 0.067 | | -0.007 | |
| Shallfish (g/day) |) | 0.037 | | 0.030 | | 0.007 | | 0.074 | |
| Eatty agid in maternal 1 | bloodb | 0.015 | | 0.045 | | -0.030 | | -0.074 | |
| | bioou | 0.062 | | 0.024 | | 0.049 | | 0.049 | |
| | | -0.003 | | -0.034 | | -0.048 | | -0.048 | |
| AA Omago 2 fetter - 11 | | -0.101 | | -0.0/8 | | -0.103 | | -0.073 | |
| Omega-6 fatty acids | | -0.075 | | -0.053 | | -0.063 | | -0.04/ | |
| Omega-0 latty acids | | -0.009 | | -0.074 | | -0.008 | | -0.040 | |
| Infant characteristics | | | | | | | | | 33.7 |
| Sex | Male | | $3132\pm362^{\boldsymbol{\ast\ast}}$ | | $48.4\pm2.1\textit{**}$ | | $31.7 \pm 1.4 \texttt{*}$ | | 1.3** |
| | Female | | 3022 ± 373 | | 47.8 ± 1.8 | | 31.3 ± 1.7 | | 32.9 ± 1.3 |
| Type of delivery | Vaginal birth | | 3119 ± 343** | | $48.3 \pm 1.9 **$ | | $31.7 \pm 1.4 **$ | | 33.3 ± 1.3 |
| | Cesarean section | | 2900 ± 423 | | 47.2 ± 1.9 | | 30.9 ± 1.9 | | 33.3 ± 1.6 |
| | | 0.467 ^a * | - | 0.395 ^a ** | - | 0.421ª* | ** | 0.221ª* | * |
| Gestational age (weeks | 5) | * | | | | | | | |

nth d subject cha acteristics (n 816 Table 3 Relatio ətri = 367) Su ----1 1 ₁h **.**+. nte - 4

^ar: Pearson correlation coefficient.

^hr: Spearman's rank correlation coefficient. *p < 0.05, **p < 0.01 by the Pearson correlation and Spearman's rank correlation test and one-way analysis of variance.

| | | SGA by weight | | SGA by length | | |
|---|---|--|--|---------------------------------------|---------------------------------------|--|
| Characteristics | | No | Yes | No | Yes | |
| | | n (%) | n (%) | n (%) | n (%) | |
| Maternal characteristics | | | | | | |
| Age at delivery (years) | | $30.8\pm4.8^{\rm a}$ | $30.9\pm4.5^{\rm a}$ | $30.8\pm4.8^{\rm a}$ | 30.8 ± 4.8^{a} | |
| Height (cm) | | 158 ± 5.3^{a} | $157\pm6.7^{\rm a}$ | $158\pm5.2^{\rm a}$ | $158\pm6.5^{\rm a}$ | |
| Pre-pregnancy weight (kg) | | $52.7\pm8.0^{\rm a}$ | $47.9\pm5.7^{a*}$ | $52.9\pm7.9^{\rm a}$ | $49.7\pm7.8^{a\ast}$ | |
| Parity | 0 | 169 (93.9) | 11 (6.1) | 156 (86.7) | 24 (13.3) | |
| | ≥1 | 180 (96.3) | 7 (3.7) | 168 (89.8) | 19 (10.2) | |
| Education level (years) | ≤12 | 143 (92.9) | 11 (7.1) | 129 (83.8) | 25 (16.2)* | |
| | >12 | 206 (96.7) | 7 (3.3) | 195 (91.5) | 18 (8.5) | |
| Annual household income (million ven) | <5 | 232 (95.1) | 12 (4 9) | 212 (86.9) | 32 (13 1) | |
| (inition yell) | >5 | 232 (95.1) | 12(4.9) | 112 (01.1) | 32(13.1) | |
| Tobacco smoking during | | 117 (95.1) | 0 (4.9) | 112 (91.1) | 11 (0.9) | |
| pregnancy | Nonsmoker | 289 (94.8) | 16 (5.2) | 270 (88.5) | 35 (11.5) | |
| | Smoker | 60 (96.8) | 2 (3.2) | 54 (87.1) | 8 (12.9) | |
| Alcohol consumption during | No | 243 (05.3) | 12 (4 7) | 220 (80.8) | 26(10.2) | |
| pregnancy | Ves | 243(93.3) | 12(4.7) | 229 (09.0) | 20(10.2) | |
| Caffeine intake (mg/day) | 105 | 100(94.0) 117(150.646) ^b | 0(3.4) 128 (2.00, 395) ^b | 93(64.6) 115(150,646) ^b | 17(13.2) 135(200/427) ^b | |
| Carrenie intake (ing/day) | | 117 (1.50, 0+0) | 120 (2.00, 575) | 115 (1.50, 040) | 133 (2.00, 427) | |
| Frequency of food consumpti | on during pream | ancy | | | | |
| Shoreline fish | <once td="" week<=""><td>101 (06 5)</td><td>7 (2 5)</td><td>179 (90.0)</td><td>20(10,1)</td></once> | 101 (06 5) | 7 (2 5) | 179 (90.0) | 20(10,1) | |
| Shorenne fish | <once td="" week<=""><td>191 (90.3)</td><td>(3.3)</td><td>178 (89.9)</td><td>20(10.1)</td></once> | 191 (90.3) | (3.3) | 178 (89.9) | 20(10.1) | |
| Pelagic fish | <u>Conce/week</u> | 158 (95.5) | 10 (5.8) | 140(80.4) | 25 (15.0) | |
| Tetagle fish | <once td="" week<=""><td>101 (94.2) 188 (95.9)</td><td>10 (5.8) 8 (4 1)</td><td>147 (80.0)</td><td>24 (14.0) 19 (9 7)</td></once> | 101 (94.2) 188 (95.9) | 10 (5.8) 8 (4 1) | 147 (80.0) | 24 (14.0) 19 (9 7) | |
| Beef | <once td="" week<=""><td>259 (94.5)</td><td>15 (5.5)</td><td>242 (88.3)</td><td>32 (11.7)</td></once> | 259 (94.5) | 15 (5.5) | 242 (88.3) | 32 (11.7) | |
| | ≥Once/week | 87 (96 7) | 3 (3 3) | 79 (87 8) | 11(122) | |
| Pork | - <once td="" week<=""><td>30 (100)</td><td>0 (0)</td><td>27 (90.0)</td><td>3 (10.0)</td></once> | 30 (100) | 0 (0) | 27 (90.0) | 3 (10.0) | |
| | ≥Once/week | 319 (94.7) | 18 (5.3) | 297 (88.1) | 40 (11.9) | |
| Chicken | <once td="" week<=""><td>52 (98.1)</td><td>1 (1.9)</td><td>48 (90.6)</td><td>5 (9.4)</td></once> | 52 (98.1) | 1 (1.9) | 48 (90.6) | 5 (9.4) | |
| | \geq Once/week | 297 (94.6) | 17 (5.4) | 276 (87.9) | 38 (12.1) | |
| Egg | <once td="" week<=""><td>10 (100)</td><td>0 (0)</td><td>9 (90.0)</td><td>1 (10.0)</td></once> | 10 (100) | 0 (0) | 9 (90.0) | 1 (10.0) | |
| | ≥Once/week | 338 (94.9) | 18 (5.1) | 314 (88.2) | 42 (11.8) | |
| Milk | <once td="" week<=""><td>48 (94.1)</td><td>3 (5.9)</td><td>43 (84.3)</td><td>8 (15.7)</td></once> | 48 (94.1) | 3 (5.9) | 43 (84.3) | 8 (15.7) | |
| | ≥Once/week | 301 (95.3) | 15 (4.7) | 281 (88.9) | 35 (11.1) | |
| Food frequency questionnaire | at delivery ^b | | | | | |
| Fish intake (g/day) | e at derivery | 40.0 (0.83, 400) | 41.7 (1.67, 100) | 37.5 (0.83, 250) | 50.0 (1.67, 400) | |
| Fatty fish intake (g/day) | | 25.0 (0.00, 160) | 20.0 (1.11, 75.0) | 25.0 (0.00, 160) | 20.0 (0.00, 133) | |
| Shellfish (g/day) | | 11.1 (0.00, 200) | 12.2 (0.00, 32) | 11.1 (0.00, 100) | 7.5 (0.00, 200) | |
| Fatty acid in maternal blood ^b | | | | | | |
| EPA + DHA | | 31.8 (2.96, 163) | 33.1 (9.44, 110) | 31.7 (2.96, 163) | 33.2 (5.47, 121) | |
| AA | | 60.8 (2.77, 219) | 90.2 (9.20, 158) | 61.9 (2.77, 219) | 57.8 (3.71, 187) | |

821 Supplementary Table 4. Relation between small for gestational age (SGA) status and subject characteristics (n = 367).

| Omega-3 fatty acids | | 43.5 (4.09, 188) | 41.4 (12.0, 144) | 43.2 (4.09, 179) | 45.2 (6.09, 188) |
|-------------------------|------------------|------------------------|----------------------|--------------------|------------------|
| Omega-6 fatty acids | | 790 (16.1, 2836) | 911 (68.2, 1552) | 798 (16.1, 2836) | 811 (36.7, 2104) |
| Infant characteristics | | | | | |
| Sex | Male | 165 (95.4) | 8 (4.6) | 161 (93.1) | 12 (6.9)** |
| | Female | 184 (94.8) | 10 (5.2) | 163 (84.0) | 31 (16.0) |
| Type of delivery | Vaginal birth | 278 (95.5) | 13 (4.5) | 259 (89.0) | 32 (11.0) |
| | Cesarean section | 71 (93.4) | 5 (6.6) | 65 (85.5) | 11 (14.5) |
| Gestational age (weeks) | | $39.0 \pm 1.4^{\rm a}$ | $39.2\pm1.6^{\rm a}$ | 39.0 ± 1.4^{a} | 39.2 ± 1.1^{a} |

823 ^aMean \pm SD.

824 825 ^bMedian (minimum, maximum).

*p<0.05, **p<0.01 by the t-test and χ^2 test. SGA: small for gestational age, LCPUFA: long-chain polyunsaturated fatty acids, EPA: eicosapentaenoic acid, DHA: docosahexaenoic acid, AA: arachidonic acid. 826

828 829 Supplementary Table 5. Regression coefficients between newborn anthropometric measurements and concentrations of PCBs and Hg (n = 367).

| | | Birth weight (g) | Length (cm) | Chest circumference (cm) | Head circumference (cm) |
|----------------------|------------|-------------------|--------------------|--------------------------------|-------------------------|
| | | B (95% CI) | B (95% CI) | B (95% CI) | B (95% CI) |
| Estrogenic PCBs | Crude | 0.68 (-175–176) | 0.33 (-0.58-1.24) | 0.55 (-0.18-1.28) | -0.24 (-0.87-0.38) |
| | Adjusted 1 | -95.6 (-273-82.2) | 0.18 (-0.80-1.17) | 0.32 (-0.46–1.11) | -0.24 (-0.94-0.46) |
| | Adjusted 2 | -80.1 (-259–98.8) | 0.28 (-0.72-1.28) | 0.38 (-0.40–1.17) | -0.27 (-0.98–0.43) |
| Antiestrogenic PCBs | Crude | -8.61 (-178–161) | 0.08 (-0.80-0.96) | 0.30 (-0.40-1.00) | -0.17 (-0.78–0.43) |
| - | Adjusted 1 | -86.8 (-258-84.1) | -0.09 (-1.04-0.85) | 0.05 (-0.71-0.80) | -0.16 (-0.83-0.51) |
| | Adjusted 2 | -87.3 (-258-83.5) | -0.07 (-1.02–0.89) | 0.04 (-0.72–0.79) | -0.23 (-0.90–0.45) |
| Dioxin-like PCBs | Crude | -3.83 (-172–164) | 0.31 (-0.56-1.18) | 0.43 (-0.26–1.13) | -0.06 (-0.660.54) |
| | Adjusted 1 | -131 (-301-38.5) | 0.01 (-0.93-0.95) | 0.09 (-0.66-0.84) | -0.10 (-0.77-0.57) |
| | Adjusted 2 | -119 (-290–52.1) | 0.09 (-0.87–1.05) | 0.14 (-0.62–0.89) | -0.16 (-0.84-0.51) |
| Non-dioxin-like PCBs | Crude | -23.8 (-197–149) | 0.19 (-0.71–1.08) | 0.40 (-0.32-1.12) | -0.27 (-0.89–0.35) |
| | Adjusted 1 | -122 (-305-61.8) | 0.07 (-0.95-1.08) | 0.15 (-0.66-0.96) | -0.33 (-1.05-0.40) |
| | Adjusted 2 | -104 (-289–81.4) | 0.17 (-0.86–1.21) | 0.22 (-0.60–1.04) | -0.36 (-1.09–0.38) |
| Hair Hg | Crude | 121 (-53.8–296) | 0.36 (-0.55–1.27) | 0.46 (-0.27-1.19) | -0.26 (-0.88-0.37) |
| ··· 0 | Adjusted 1 | 160 (-3.34-323) | 0.27(-0.64-1.17) | 0.32 (-0.41–1.04) | -0.19 (-0.83-0.46) |
| | Adjusted 2 | 140 (-24.2–304) | 0.24(-0.68-1.16) | 0.24 (-0.48–0.97) | -0.24 (-0.89–0.41) |
| | | | | | |

830 831 832 833 834 Adjusted 1: adjusted for maternal age, maternal height, pre-pregnancy maternal weight, tobacco smoking during pregnancy, alcohol consumption during pregnancy, household income, blood sampling period, parity, gestational age, infant sex and log₁₀-transformed PCBs or log₁₀-transformed Hg. Adjusted 2: adjusted for omega-3 fatty acids in addition to adjustment factors in Adjusted 1 B: partial regression coefficient, CI: confidence interval,