



# HOKKAIDO UNIVERSITY

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| Title            | Determinants and Temporal Trends of Perfluoroalkyl Substances in Pregnant Women : The Hokkaido Study on Environment and Children's Health                                    |
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Table S1. Crude regression coefficients (ß) and 95% confidence intervals in multivariable linear regression model by PFAS in pregnant women.

|                                 | PFHxS                        | PFOS                         | PFOA                         | PFNA                         | PFDA                         | PFUnDA                       | PFDoDA                       | PFTTrDA                      |
|---------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Age at delivery (years)         |                              |                              |                              |                              |                              |                              |                              |                              |
| <25                             | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          |
| 25~29                           | 0.087(-0.009,0.184)          | <b>0.128(0.049,0.207)</b>    | 0.031(-0.049,0.11)           | 0.031(-0.049,0.11)           | 0.043(-0.04,0.126)           | <b>0.144(0.057,0.23)</b>     | 0.071(-0.013,0.155)          | 0.041(-0.041,0.123)          |
| 30~34                           | 0.031(-0.062,0.124)          | 0.021(-0.055,0.097)          | 0.026(-0.051,0.102)          | 0.026(-0.051,0.102)          | 0.035(-0.045,0.114)          | <b>0.167(0.083,0.25)</b>     | <b>0.112(0.031,0.193)</b>    | <b>0.083(0.004,0.161)</b>    |
| >=35                            | 0.034(-0.066,0.135)          | 0.028(-0.054,0.11)           | 0.018(-0.064,0.101)          | 0.02(-0.062,0.103)           | 0.053(-0.033,0.139)          | <b>0.181(0.091,0.271)</b>    | <b>0.089(0.002,0.177)</b>    | <b>0.093(0.009,0.178)</b>    |
| p for trend                     | 0.559                        | <b>0.048</b>                 | <b>&lt;0.001</b>             | 0.88                         | 0.383                        | <b>0.001</b>                 | <b>0.042</b>                 | <b>0.01</b>                  |
| Preprgnancy BMI                 |                              |                              |                              |                              |                              |                              |                              |                              |
| <18.5                           | -0.022(-0.088,0.043)         | 0.047(-0.006,0.1)            | 0.036(-0.041,0.113)          | <b>0.066(0.012,0.119)</b>    | 0.034(-0.022,0.089)          | 0.023(-0.035,0.082)          | 0.049(-0.008,0.106)          | 0.029(-0.026,0.084)          |
| 18.5~24.9                       | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          |
| >=25                            | -0.007(-0.096,0.082)         | -0.069(-0.141,0.004)         | -0.097(-0.203,0.009)         | -0.044(-0.117,0.029)         | -0.036(-0.113,0.04)          | <b>-0.081(-0.161,-0.001)</b> | <b>-0.175(-0.252,-0.097)</b> | <b>-0.167(-0.243,-0.092)</b> |
| Parity                          |                              |                              |                              |                              |                              |                              |                              |                              |
| 0                               | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          |
| 1                               | <b>-0.223(-0.276,-0.169)</b> | <b>-0.183(-0.226,-0.14)</b>  | <b>-0.458(-0.517,-0.398)</b> | <b>-0.202(-0.246,-0.159)</b> | <b>-0.108(-0.154,-0.062)</b> | 0.015(-0.033,0.064)          | 0.001(-0.047,0.048)          | 0.003(-0.043,0.049)          |
| >=2                             | <b>-0.226(-0.297,-0.156)</b> | <b>-0.298(-0.355,-0.241)</b> | <b>-0.631(-0.71,-0.552)</b>  | <b>-0.27(-0.328,-0.213)</b>  | <b>-0.136(-0.197,-0.075)</b> | 0.026(-0.038,0.091)          | -0.013(-0.076,0.05)          | 0.019(-0.042,0.08)           |
| p for trend                     | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | 0.382                        | 0.741                        | 0.528                        |
| Education level (years)         |                              |                              |                              |                              |                              |                              |                              |                              |
| <=9                             | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          |
| 10~12                           | -0.119(-0.267,0.028)         | <b>0.125(0.004,0.245)</b>    | -0.128(-0.302,0.046)         | 0.088(-0.032,0.209)          | <b>0.176(0.05,0.302)</b>     | <b>0.226(0.093,0.358)</b>    | 0.088(-0.042,0.217)          | 0.079(-0.046,0.204)          |
| 13~16                           | -0.047(-0.194,0.101)         | <b>0.16(0.04,0.28)</b>       | -0.057(-0.231,0.117)         | <b>0.152(0.031,0.272)</b>    | <b>0.239(0.114,0.365)</b>    | <b>0.292(0.16,0.424)</b>     | <b>0.146(0.017,0.275)</b>    | <b>0.142(0.017,0.267)</b>    |
| >16                             | 0.081(-0.078,0.241)          | <b>0.3(0.17,0.431)</b>       | 0.126(-0.062,0.315)          | <b>0.303(0.172,0.434)</b>    | <b>0.315(0.178,0.451)</b>    | <b>0.356(0.213,0.5)</b>      | <b>0.186(0.046,0.327)</b>    | <b>0.138(0.002,0.273)</b>    |
| p for trend                     | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>&lt;0.001</b>             | <b>0.003</b>                 |
| Cotinine Level in 3rd trimester |                              |                              |                              |                              |                              |                              |                              |                              |
| Non-smoker (<0.22 ng/mL)        | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          | ref                          |
| Passive smoker (0.22-11.49)     | -0.02(-0.072,0.032)          | 0.059(0.016,0.101)           | 0.058(-0.003,0.119)          | -0.021(-0.064,0.022)         | -0.019(-0.063,0.026)         | -0.012(-0.059,0.034)         | -0.025(-0.071,0.02)          | 0.008(-0.036,0.052)          |

ng/ml)

|                                    |                           |                          |                           |                            |                              |                             |                              |                     |
|------------------------------------|---------------------------|--------------------------|---------------------------|----------------------------|------------------------------|-----------------------------|------------------------------|---------------------|
| Active smoker (>11.49 ng/mL)       | -0.001(-0.094,0.093)      | -0.038(-0.115,0.039)     | -0.002(-0.113,0.109)      | <b>-0.123(-0.2,-0.045)</b> | <b>-0.108(-0.189,-0.028)</b> | <b>-0.164(-0.248,-0.08)</b> | <b>-0.094(-0.176,-0.012)</b> | -0.02(-0.1,0.059)   |
| p for trend                        | 0.658                     | 0.383                    | 0.307                     | <b>0.008</b>               | <b>0.024</b>                 | <b>0.004</b>                | <b>0.032</b>                 | 0.893               |
| Alcohol consumption history        |                           |                          |                           |                            |                              |                             |                              |                     |
| No                                 | ref                       | ref                      | ref                       | ref                        | ref                          | ref                         | ref                          | ref                 |
| Yes                                | 0.012(-0.013,0.037)       | 0.003(-0.017,0.024)      | 0.012(-0.017,0.042)       | -0.007(-0.028,0.014)       | <b>-0.026(-0.047,-0.004)</b> | -0.017(-0.039,0.006)        | -0.009(-0.031,0.013)         | 0.002(-0.019,0.023) |
| Annual housed income (million yen) |                           |                          |                           |                            |                              |                             |                              |                     |
| <3                                 | ref                       | ref                      | ref                       | ref                        | ref                          | ref                         | ref                          | ref                 |
| 3~5                                | -0.004(-0.071,0.063)      | 0.04(-0.014,0.095)       | 0.006(-0.072,0.085)       | 0.038(-0.017,0.093)        | <b>0.058(0,0.115)</b>        | 0.043(-0.017,0.103)         | 0.03(-0.028,0.089)           | 0.001(-0.055,0.058) |
| >5                                 | <b>0.081(0.011,0.151)</b> | <b>0.107(0.05,0.164)</b> | <b>0.107(0.025,0.189)</b> | <b>0.112(0.055,0.17)</b>   | <b>0.086(0.026,0.146)</b>    | <b>0.086(0.024,0.149)</b>   | 0.061(0,0.122)               | 0.047(-0.012,0.106) |
| p for trend                        | <b>0.008</b>              | <b>&lt;0.001</b>         | <b>0.004</b>              | <b>&lt;0.001</b>           | 0.06                         | 0.06                        | <b>0.047</b>                 | 0.076               |

PFHxS, prfluorohexane sulfonate; PFOS, perfluorooctane sulfonate; PFOA, perfluorooctanoic acid; PFNA, perfluorononanoic acid; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid; PFDoDA, perfluorododecanoic acid; PFTrDA, perfluorotridecanoic acid; BMI, body mass index; Bold represented p value <0.05.

Table S2. Pregnant women's blood collection period and sample size at each period.

| 1      | 2      | 3      | 4      | 5             | 6      | 7      | 8      | 9      | 10     | 11     | 12     | 13      | 14     |
|--------|--------|--------|--------|---------------|--------|--------|--------|--------|--------|--------|--------|---------|--------|
| 2003.8 | 2004.2 | 2004.8 | 2005.2 | 2005.8        | 2006.2 | 2006.8 | 2007.2 | 2007.8 | 2008.2 | 2008.8 | 2009.2 | 2009.8  | 2010.1 |
| 2004.1 | 2004.7 | 2005.1 | 2005.7 | <b>2006.1</b> | 2006.7 | 2007.1 | 2007.7 | 2008.1 | 2008.7 | 2009.1 | 2009.7 | 2009.12 | 2012.7 |
| n=92   | n=188  | n=155  | n=154  | n=154         | n=124  | n=166  | n=140  | n=150  | n=161  | n=142  | n=153  | n=256   | n=88   |

Table S3. Maternal basic characteristics before and after Jan 2006.

|                                 | before | after | p-value      |
|---------------------------------|--------|-------|--------------|
|                                 | N      | N     |              |
| Age at delivery (years)         |        |       |              |
| <25                             | 58     | 125   | <b>0.002</b> |
| 25~29                           | 258    | 349   |              |
| 30~34                           | 297    | 585   |              |
| >=35                            | 130    | 321   |              |
| Preprgnancy BMI                 |        |       |              |
| <18.5                           | 121    | 264   | 0.213        |
| 18.5~24.9                       | 552    | 1002  |              |
| >=25                            | 70     | 114   |              |
| Parity                          |        |       |              |
| 0                               | 326    | 636   | 0.127        |
| 1                               | 307    | 511   |              |
| >=2                             | 110    | 233   |              |
| Education level (years)         |        |       |              |
| <=9                             | 26     | 38    | 0.266        |
| 10~12                           | 324    | 555   |              |
| 13~16                           | 314    | 619   |              |
| >16                             | 79     | 168   |              |
| Cotinine Level in 3rd trimester |        |       |              |
| Non-smoker (<0.22 ng/mL)        | 249    | 680   | 0.001        |

|                                    |     |     |       |
|------------------------------------|-----|-----|-------|
| Passive smoker (0.22-11.49 ng/mL)  | 415 | 602 |       |
| Active smoker (>11.49 ng/mL)       | 79  | 98  |       |
| Alcohol consumption history        |     |     |       |
| No                                 | 320 | 592 | 0.940 |
| Yes                                | 423 | 788 |       |
| Annual housed income (million yen) |     |     |       |
| <3                                 | 136 | 286 | 0.385 |
| 3~5                                | 339 | 621 |       |
| >5                                 | 268 | 473 |       |

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BMI, body mass index.