**Perfluoroalkyl Substances and Cognitive Function in Older Adults: Should We Consider Non-Monotonic Dose-Responses and Chronic Kidney Disease?**

Sung Kyun Park,1,2 Ning Ding,1 Dehua Han1

Supplemental Materials

**Table S1.** Detection rates andsurvey-weighted geometric mean (GM) and 95% confidence interval (95% CI), median and interquartile range (IQR), and range of serum concentrations of 10 perfluoroalkyl substances (ng/mL).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | % <Detection | GM (95% CI) | Median (IQR) | Range |
| PFBS | 98.4% | <LOD (<LOD) | <LOD (<LOD) | <LOD-0.8 |
| PFHxS | 0.9% | 1.84 (1.68-2.02) | 1.9 (1.1-2.9) | <LOD-47.8 |
| PFOS | 0.5% | 8.38 (7.69-9.13) | 9.3 (5.5-14.0) | 0.1-1403.0 |
| PFOSA | 98.5% | <LOD (<LOD) | <LOD (<LOD) | <LOD-0.6 |
| PFHpA | 79.6% | 0.08 (0.08-0.09) | <LOD (<LOD) | <LOD-1.1 |
| PFOA | 0.5% | 2.62 (2.45-2.80) | 2.7 (1.9-3.7) | <LOD-61.0 |
| PFNA | 1.2% | 0.95 (0.87-1.03) | 0.9 (0.7-1.4) | <LOD-80.8 |
| PFDeA | 12.7% | 0.23 (0.21-0.25) | 0.2 (0.1-0.4) | <LOD-17.8 |
| PFUA | 34.6% | 0.15 (0.13-0.16) | 0.1 (<LOD-0.2) | <LOD-43.9 |
| PFDoA | 85.7% | 0.08 (<LOD-0.08) | <LOD (<LOD) | <LOD-1.0 |

PFBS, perfluorobutane sulfonate; PFHxS, perfluorohexane sulfonate; PFOS, perfluorooctane sulfonate; PFOSA, perfluorooctane sulfonamide; PFHpA, perfluoroheptanoate; PFOA, perfluorooctanoate; PFNA, perfluorononanoate; PFDeA, perfluorodecanoate; PFUA, perfluoroundecanoate; PFDoA, perfluorododecanoate.

**Table S2.** Effect estimates ($βs$) and 95% Confidence Intervals (CIs) of composite z-score per doubling increase in serum perfluoroalkyl concentrations among 903 adults 60 years and older **with observed data**.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **n** | $β$ (95% CI) | ***P* value** |
| **PFOS** |  |  |  |
|  Model 1a | 643 | -0.018 (-0.069, 0.033) | 0.48 |
|  Model 2b | 588 | -0.016 (-0.072, 0.039) | 0.56 |
|  Model 3c | 587 | -0.027 (-0.084, 0.030) | 0.34 |
|  Model 4d | 587 | -0.027 (-0.083, 0.029) | 0.33 |
| **PFOA** |  |  |  |
|  Model 1a | 643 | 0.057 (-0.009, 0.12) | 0.09 |
|  Model 2b | 588 | 0.059 (-0.007, 0.12) | 0.08 |
|  Model 3c | 587 | 0.052 (-0.015, 0.12) | 0.12 |
|  Model 4d | 587 | 0.053 (-0.010, 0.12) | 0.10 |
| **PFHxS** |  |  |  |
|  Model 1a | 643 | 0.017 (-0.030, 0.064) | 0.47 |
|  Model 2b | 588 | 0.021 (-0.029, 0.072) | 0.39 |
|  Model 3c | 587 | 0.011 (-0.040, 0.063) | 0.66 |
|  Model 4d | 587 | 0.012 (-0.040, 0.063) | 0.64 |
| **PFNA** |  |  |  |
|  Model 1a | 643 | 0.057 (0.008, 0.11) | 0.02 |
|  Model 2b | 588 | 0.062 (0.016, 0.11) | 0.009 |
|  Model 3c | 587 | 0.052 (0.003, 0.10) | 0.04 |
|  Model 4d | 587 | 0.052 (0.006, 0.099) | 0.03 |

PFOS, perfluorooctane sulfonate; PFOA, perfluorooctanoate; PFHxS, perfluorohexane sulfonate; PFNA, perfluorononanoate.

a Model 1 was adjusted for age, sex, race/ethnicity, education, poverty-income ratio, health insurance, food security, smoking status, alcohol consumption, total recreational activity, and NHANES cycles. Complex survey designs were taken into account in the analyses.

bModel 2: Model 1 + smoking pack-years, serum cotinine (log-transformed)

cModel 3: Model 2 + fish and shellfish consumption.

dModel 4: Model 3 + CKD status.

**Table S3**. Effect modification by sex in the association between serum perfluoroalkyl concentrations and composite z-score.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Male** | **Female** |  *P* for interactionb |
| **N** | 443 | 460 |  |
| PFOS | -0.037 (-0.096, 0.021) | 0.016 (-0.028, 0.059) | 0.15 |
| PFOA | 0.022 (-0.062, 0.11) | 0.085 (0.012, 0.16)\* | 0.26 |
| PFHxS | 0.009 (-0.048, 0.066) | 0.031 (-0.018, 0.080) | 0.57 |
| PFNA | 0.036 (-0.041, 0.11) | 0.069 (0.027, 0.11)† | 0.42 |

aPooled effect estimates ($βs$) and 95% Confidence Intervals (CIs) of composite z-score per doubling increase in serum perfluoroalkyl concentrations **with 20 imputations**. All models were adjusted for age, race/ethnicity, education, poverty-income ratio, health insurance, food security, smoking status, alcohol consumption, total recreational activity, NHANES cycles, smoking pack-years, serum cotinine (log-transformed), fish and shellfish consumption, and chronic kidney disease status.

b*P* for interaction was computed from the cross-product term between sex and log2(perfluroalkyl).

\**P*<0.05, †*P*<0.005.

**Table S4**. Effect modification by chronic kidney disease (CKD) in the association between PFAS and composite z-score.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No** | **Yes** | *P* for interactionb |
| **N** | 613 | 290 |  |
| **PFOS** | -0.045 (-0.085, -0.004)\* | 0.059 (-0.016, 0.13) | 0.02 |
| **PFOA** | 0.026 (-0.059, 0.11) | 0.11 (0.012, 0.21)\* | 0.26 |
| **PFHxS** | -0.006 (-0.060, 0.048) | 0.068 (-0.004, 0.14) | 0.16 |
| **PFNA** | 0.032 (-0.012, 0.077) | 0.11 (0.010, 0.21)\* | 0.19 |

aPooled effect estimates ($βs$) and 95% Confidence Intervals (CIs) of composite z-score per doubling increase in serum perfluoroalkyl concentrations **with 20 imputations**. All models were adjusted for age, sex, race/ethnicity, education, poverty-income ratio, health insurance, food security, smoking status, alcohol consumption, total recreational activity, NHANES cycles, smoking pack-years, serum cotinine (log-transformed), fish and shellfish consumption.

b*P* for interaction was computed from the cross-product term between log2(perfluroalkyl) and CKD.

\**P*<0.05.