# SUPPLEMENTAL MATERIALS

**Table S1** Serum concentrations (in ng/mL) of PFAS in midlife women from the Study of Women’s Health Across the Nation Multi-Pollutant Study, baseline (1999-2000).a

|  |  |  |
| --- | --- | --- |
| **PFAS** | **% >LOD** | **Median (IQR) in ng/mL** |
| PFHxS | 99.6 | 1.5 (1.0-2.4) |
| PFOS | NA | 24.7 (17.6-36.0) |
| n-PFOS | 100 | 17.4 (12.4-25.0) |
| Sm-PFOS | 99.8 | 7.3 (4.7-11.2) |
| n-PFOA | 99.9 | 4.1 (2.9-5.8) |
| Sb-PFOA | 18.0 | <LOD |
| PFNA | 97.2 | 0.6 (0.4-0.8) |
| PFDA | 40.6 | <LOD (<LOD-0.3) |
| PFDoDA | 3.5 | <LOD |
| PFUnDA | 31.6 | <LOD (<LOD-0.2) |
| EtFOSAA | 99.0 | 1.2 (0.7-2.2) |
| MeFOSAA | 99.7 | 1.5 (0.9-2.3) |

a Limit of detection (LOD) is 0.1 ng/mL for all PFAS. PFOS represents the sum of n-PFOS and Sb-PFOS.

**Table S2** Percent change and 95% confidence interval (95% CI) of free leptin index, leptin, sOB-R, adiponectin, and HMW adiponectin per doubling increase in serum concentrations of PFOS, n-PFOS, Sm-PFOS, n-PFOA, PFNA, PFHxS, EtFOSAA and MeFOSAA.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Free leptin index | Leptin, ng/mL | sOB-R, ng/mL | Adiponectin, μg/mL | HMW adiponectin, μg/mL |
|  | Percent change  (95% CI) , % | Percent change  (95% CI) , % | Percent change  (95% CI) , % | Percent change  (95% CI), % | Percent change  (95% CI) , % |
| PFOS |  |  |  |  |  |
| Model 1 | 14.7 (7.7, 22.3)\*\*\* | 13.6 (7.8, 19.7)\*\*\* | -1.0 (-3.1, 1.1) | 0.9 (-2.5, 4.3) | 0.2 (-3.5, 4.1) |
| Model 2 | 5.2 (0.05, 10.6)\* | 5.7 (1.5, 10.2)\*\* | 0.5 (-1.5, 2.6) | 3.1 (-0.1, 6.5) | 2.5 (-1.2, 6.4) |
| n-PFOS |  |  |  |  |  |
| Model 1 | 12.4 (5.4, 19.9)\*\* | 11.6 (5.9, 17.7)\*\*\* | -0.7 (-2.8, 1.5) | 1.1 (-2.3, 4.6) | 0.8 (-3.0, 4.7) |
| Model 2 | 4.9 (-0.2, 10.3) | 5.5 (1.2, 9.9)\* | 0.5 (-1.5, 2.6) | 2.9 (-0.4, 6.3) | 2.6 (-1.1, 6.5) |
| Sm-PFOS |  |  |  |  |  |
| Model 1 | 15.3 (9.3, 21.6)\*\*\* | 13.8 (8.9, 18.9)\*\*\* | -1.3 (-3.1, 0.5) | 0.4 (-2.4, 3.3) | -0.5 (-3.7, 2.7) |
| Model 2 | 4.7 (0.4, 9.2)\* | 5.2 (1.6, 8.9)\*\* | 0.4 (-1.3, 2.2) | 2.9 (0.2, 5.8)\* | 2.0 (-1.2, 5.2) |
| n-PFOA |  |  |  |  |  |
| Model 1 | 16.0 (8.5, 24.0)\*\*\* | 13.1 (7.0, 19.5)\*\*\* | -2.5 (-4.7, -0.3)\* | -1.9 (-5.3, 1.6) | -3.2 (-7.0, 0.8) |
| Model 2 | 6.2 (0.8, 11.9)\* | 5.1 (0.7, 9.8)\* | -1.0 (-3.1, 11.7) | 0.3 (-3.0, 3.8) | -1.0 (-4.7, 2.9) |
| PFNA |  |  |  |  |  |
| Model 1 | 4.6 (-1.8, 11.4) | 3.1 (-2.1, 8.3) | -1.3 (-3.4, 0.8) | 0.2 (-3.1, 3.6) | -1.1 (-4.7, 2.7) |
| Model 2 | 6.0 (1.0, 11.3)\* | 4.4 (0.3, 8.7)\* | -1.6 (-3.5, 0.4) | -0.09 (-3.2, 3.1) | -1.3 (-4.8, 2.3) |
| PFHxS |  |  |  |  |  |
| Model 1 | -1.2 (-5.8, 3.7) | 0.0 (-3.9, 4.0) | 1.2 (-0.4, 2.8) | 0.7 (-1.8, 3.3) | 1.9 (-0.9, 4.9) |
| Model 2 | -0.6 (-4.2, 3.2) | 0.5 (-2.5, 3.6) | 1.1 (-0.5, 2.6) | 0.6 (-1.8, 3.1) | 1.8 (-0.9, 4.7) |
| EtFOSAA |  |  |  |  |  |
| Model 1 | 9.8 (5.4, 14.3)\*\*\* | 7.5 (3.9, 11.1)\*\*\* | -2.1 (-3.4, -0.7)\*\* | -0.5 (-2.6, 1.7) | -1.5 (-3.9, 0.9) |
| Model 2 | 4.2 (1.0, 7.5)\* | 2.9 (0.3, 5.7)\* | -1.2 (-2.5, 0.09) | 0.8 (-1.2, 2.9) | -0.3 (-2.6, 2.1) |
| MeFOSAA |  |  |  |  |  |
| Model 1 | 8.9 (3.1, 15.1)\*\* | 7.9 (3.1, 13.0)\*\* | -0.9 (-2.8, 0.9) | -1.0 (-3.8, 2.0) | 0.5 (-2.8, 3.8) |
| Model 2 | 5.2 (0.8, 9.8)\* | 4.8 (1.2, 8.6)\*\* | -0.4 (-2.2, 1.4) | -0.1 (-2.9, 2.7) | 1.2 (-2.0, 4.5) |

Model 1 was adjusted for age, race, study site, education, smoking status, physical activity and menopausal status.

Model 2: Model 1 + BMI

\*\*\**P*<0.0001, \*\**P*<0.01, \**P*<0.05

**Table S3** Percent change and 95% confidence interval (95% CI) of free leptin index, leptin, sOB-R, adiponectin, and HMW adiponectin by quartiles of serum concentrations of PFOS, n-PFOS, Sm-PFOS, n-PFOA, PFNA, PFHxS, EtFOSAA and MeFOSAA.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Free leptin index | Leptin, ng/mL | sOB-R, ng/mL | Adiponectin, μg/mL | HMW adiponectin, μg/mL |
|  | Percent change  (95% CI) , % | Percent change  (95% CI) , % | Percent change  (95% CI) , % | Percent change  (95% CI), % | Percent change  (95% CI) , % |
| PFOS |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (2.0-17.5) | Ref | Ref | Ref | Ref | Ref |
| Q2 (17.6-24.6) | 1.38 (-12.39, 17.31) | 4.23 (-7.60, 17.57) | 2.81 (-2.17, 8.04) | 3.66 (-4.06, 12.00) | 2.65 (-5.96, 12.05) |
| Q3 (24.7-36.0) | 25.29 (8.13, 45.17)\*\* | 22.17 (8.19, 37.95)\*\* | -2.49 (-7.25, 2.52) | 1.62 (-6.02, 9.88) | -2.44 (-10.69, 6.58) |
| Q4 (36.1-376.0) | 36.53 (17.16, 59.09)\*\*\* | 32.67 (16.94, 50.52)\*\*\* | -2.82 (-7.75, 2.37) | 0.48 (-7.35, 8.97) | -0.04 (-8.81, 9.57) |
| Model 2 |  |  |  |  |  |
| Q1 (2.0-17.5) | Ref | Ref | Ref | Ref | Ref |
| Q2 (17.6-24.6) | -0.75 (-11.45, 11.23) | 2.50 (-6.70, 12.61) | 3.28 (-1.48, 8.26) | 4.46 (-3.00, 12.49) | 3.78 (-4.65, 12.95) |
| Q3 (24.7-36.0) | 5.14 (-6.33, 18.02) | 5.72 (-3.89, 16.29) | 0.55 (-4.14, 5.47) | 6.28 (-1.41, 14.56) | 2.04 (-6.35, 11.19) |
| Q4 (36.1-376.0) | 14.53 (1.56, 29.15)\* | 14.78 (3.95, 26.74)\*\* | 0.22 (-4.64, 5.32) | 5.14 (-2.75, 13.68) | 4.82 (-4.13, 14.61) |
| n-PFOS |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (1.4-12.3) | Ref | Ref | Ref | Ref | Ref |
| Q2 (12.4-17.4) | 7.99 (-6.66, 24.93) | 10.58 (-1.94, 24.70) | 2.40 (-2.54, 7.59) | 4.72 (-3.04, 13.10) | 4.51 (-4.22, 14.03) |
| Q3 (17.5-25.0) | 17.00 (0.91, 35.66)\* | 16.88 (3.46, 32.05)\* | -0.10 (-4.99, 5.04) | 5.78 (-2.18, 14.38) | 4.58 (-4.28, 14.27) |
| Q4 (25.1-250.0) | 34.89 (15.72, 57.24)\*\* | 32.09 (16.40, 49.88)\*\*\* | -2.08 (-7.04, 3.15) | 0.29 (-7.51, 8.75) | 0.83 (-8.01, 10.51) |
| Model 2 |  |  |  |  |  |
| Q1 (1.4-12.3) | Ref | Ref | Ref | Ref | Ref |
| Q2 (12.4-17.4) | 0.96 (-9.86, 13.09) | 4.66 (-4.69, 14.92) | 3.66 (-1.09, 8.64) | 6.69 (-0.88, 14.84) | 6.65 (-1.96, 16.02) |
| Q3 (17.5-25.0) | 0.84 (-10.16, 13.19) | 3.49 (-5.92, 13.83) | 2.63 (-2.16, 7.65) | 10.00 (2.05, 18.57)\* | 9.00 (0.04, 18.76) |
| Q4 (25.1-250.0) | 15.64 (2.58, 30.37)\* | 16.35 (5.40, 28.44)\*\* | 0.61 (-4.25, 5.73) | 4.33 (-3.48, 12.77) | 5.16 (-3.79, 14.94) |
| Sm-PFOS |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (<LOD-4.7) | Ref | Ref | Ref | Ref | Ref |
| Q2 (4.8-7.2) | 3.31 (-10.98, 19.90) | 5.48 (-6.72, 19.26) | 2.10 (-2.95, 7.41) | -0.14 (-7.74, 8.08) | 0.56 (-8.06, 9.99) |
| Q3 (7.3-11.2) | 20.33 (3.51, 39.89)\* | 20.38 (6.32, 36.30)\*\* | 0.04 (-4.96, 5.30) | 2.46 (-5.42, 11.00) | 0.03 (-8.63, 9.52) |
| Q4 (11.3-126.0) | 47.23 (25.96, 72.09)\*\*\* | 40.22 (23.28, 59.48)\*\*\* | -4.76 (-9.69, 0.43) | -2.56 (-10.31, 5.87) | -3.69 (-12.32, 5.79) |
| Model 2 |  |  |  |  |  |
| Q1 (<LOD-4.7) | Ref | Ref | Ref | Ref | Ref |
| Q2 (4.8-7.2) | -5.04 (-15.50, 6.72) | -1.52 (-10.57, 8.44) | 3.70 (-1.18, 8.83) | 2.27 (-5.20, 10.32) | 3.30 (-5.28, 12.66) |
| Q3 (7.3-11.2) | 2.79 (-8.69, 15.70) | 5.84 (-4.01, 16.70) | 2.97 (-1.94, 8.13) | 6.85 (-1.05, 15.39) | 4.36 (-4.42, 13.95) |
| Q4 (11.3-126.0) | 9.80 (-2.99, 24.29) | 10.01 (-0.68, 21.86) | 0.19 (-4.81, 5.45) | 5.00 (-3.11, 13.80) | 3.95 (-5.19, 13.97) |
| n-PFOA |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (<LOD-2.8) | Ref | Ref | Ref | Ref | Ref |
| Q2 (2.9-4.1) | 5.52 (-9.18, 22.59) | 5.39 (-6.90, 19.30) | -0.12 (-5.08, 5.09) | 0.27 (-7.39, 8.57) | 1.10 (-7.59, 10.61) |
| Q3 (4.2-5.8) | 19.46 (2.06, 39.83)\* | 15.33 (1.26, 31.36)\* | -3.46 (-8.48, 1.84) | -3.24 (-10.99, 5.19) | -5.96 (-14.43, 3.35) |
| Q4 (5.9-56.5) | 45.11 (23.66, 70.29)\*\*\* | 33.92 (17.33, 52.86)\*\*\* | -7.71 (-12.59, -2.56)\*\* | -6.09 (-13.73, 2.22) | -8.90 (-17.23, 0.27) |
| Model 2 |  |  |  |  |  |
| Q1 (<LOD-2.8) | Ref | Ref | Ref | Ref | Ref |
| Q2 (2.9-4.1) | -2.96 (-13.68, 9.08) | -1.59 (-10.66, 8.40) | 1.41 (-3.38, 6.44) | 2.49 (-5.04, 10.61) | 3.56 (-5.07, 12.98) |
| Q3 (4.2-5.8) | -2.22 (-13.59, 10.64) | -2.15 (-11.65, 8.37) | 0.07 (-4.92, 5.32) | 1.75 (-6.13, 7.82)) | -0.89 (-9.60, 8.65) |
| Q4 (5.9-56.5) | 16.52 (2.77, 32.11)\* | 11.63 (0.63, 23.84)\* | -4.20 (-9.05, 0.91) | -0.65 (-8.46, 7.82) | -3.62 (-12.22, 5.82) |
| PFNA |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (<LOD-0.4) | Ref | Ref | Ref | Ref | Ref |
| Q2 (0.5) | 3.55 (-12.15, 22.06) | 5.75 (-7.67, 21.11) | 2.12 (-3.39, 7.94) | -4.98 (-12.85, 3.61) | -6.85 (-15.53, 2.73) |
| Q3 (0.6-0.7) | 12.95 (-1.73, 29.83) | 14.85 (2.39, 28.84)\* | 1.68 (-2.98, 6.57) | -0.54 (-7.56, 7.02) | 0.82 (-7.19, 9.53) |
| Q4 (0.8-5.0) | 12.24 (-2.57, 29.31) | 7.69 (-4.18, 21.02) | -4.06 (-8.53, 0.63) | -0.34 (-7.49, 7.36) | -3.03 (-10.87, 5.48) |
| Model 2 |  |  |  |  |  |
| Q1 (<LOD-0.4) | Ref | Ref | Ref | Ref | Ref |
| Q2 (0.5) | 5.18 (-7.39, 19.45) | 7.92 (-3.41, 19.18) | 2.01 (-3.20, 7.51) | -5.33 (-12.86, 2.84) | -7.05 (-15.43, 2.17) |
| Q3 (0.6-0.7) | 8.61 (-2.50, 20.99) | 11.21 (1.72, 21.58)\* | 2.39 (-2.06, 7.06) | 0.61 (-6.22, 7.93) | 2.30 (-5.59, 10.84) |
| Q4 (0.8-5.0) | 20.10 (7.65, 33.99)\*\* | 13.97 (4.12, 24.75)\*\* | -5.11 (-9.30, -0.72)\* | -1.79 (-8.54, 5.47) | -4.37 (-11.84, 3.73) |
| PFHxS |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (<LOD-0.9) | Ref | Ref | Ref | Ref | Ref |
| Q2 (1.0-1.4) | -0.33 (-14.40, 16.06) | 3.87 (-8.39, 17.77) | 4.21 (-1.03, 9.73) | 7.51 (-0.78, 16.50) | 10.57 (0.97, 21.08)\* |
| Q3 (1.5-2.4) | 20.22 (3.76, 39.29)\* | 20.73 (6.93, 36.32)\*\* | 0.42 (-4.46, 5.56) | -0.06 (-7.52, 8.01) | 1.74 (-6.81, 11.07) |
| Q4 (2.5-46.5) | -5.46 (-19.24, 10.65) | -2.13 (-14.05, 11.44) | 3.53 (-1.85, 9.20) | 3.34 (-4.89, 12.29) | 7.38 (-2.25, 17.94) |
| Model 2 |  |  |  |  |  |
| Q1 (<LOD-0.9) | Ref | Ref | Ref | Ref | Ref |
| Q2 (1.0-1.4) | 3.15 (-8.37, 16.12) | 6.88 (-3.06, 17.84) | 3.62 (-1.33, 8.82) | 6.56 (-1.33, 15.08) | 9.90 (0.66, 19.99)\* |
| Q3 (1.5-2.4) | 10.35 (-1.60, 23.75) | 12.48 (2.34, 23.62)\* | 1.93 (-2.78, 6.87) | 2.03 (-5.29, 9.92) | 3.91 (-4.56, 13.12) |
| Q4 (2.5-46.5) | -2.96 (-14.15, 9.69) | -0.002 (-9.61, 10.63) | 3.05 (-2.04, 8.40) | 2.76 (-5.10, 11.27) | 7.11 (-2.19, 17.30) |
| EtFOSAA |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (<LOD-0.6) | Ref | Ref | Ref | Ref | Ref |
| Q2 (0.7-1.1) | 32.64 (14.25, 53.98)\*\* | 24.01 (9.61, 40.29)\*\* | -6.51 (-11.12, -1.65)\*\* | 1.03 (-6.66, 9.35) | -2.84 (-11.17, 6.27) |
| Q3 (1.2-2.2) | 41.24 (21.46, 64.24)\*\*\* | 29.04 (13.91, 41.19)\*\*\* | -8.64 (-13.20, -3.84)\*\* | -6.62 (-13.80, 1.16) | -7.40 (-15.42, 1.38) |
| Q4 (2.3-112.5) | 43.71 (23.14, 67.71)\*\*\* | 32.24 (16.39, 50.26)\*\*\* | -7.98 (-12.68, -3.03)\*\* | 0.43 (-7.47, 9.00) | -4.68 (-13.12, 4.59) |
| Model 2 |  |  |  |  |  |
| Q1 (<LOD-0.6) | Ref | Ref | Ref | Ref | Ref |
| Q2 (0.7-1.1) | 16.95 (4.06, 31.45)\*\* | 11.76 (1.48, 23.10)\* | -4.44 (-8.94, 0.29) | 4.51 (-3.13, 12.75) | 0.37 (-7.99, 9.48) |
| Q3 (1.2-2.2) | 19.42 (6.10, 34.41)\*\* | 12.23 (1.78, 23.76)\* | -6.02 (-10.50, -1.31)\* | -2.59 (-9.80, 5.19) | -3.66 (-11.78, 5.20) |
| Q4 (2.3-112.5) | 16.57 (3.24, 31.62)\* | 11.13 (0.51, 22.86)\* | -4.67 (-9.34, 0.24) | 5.98 (-2.06, 14.68) | 0.39 (-8.28, 9.88) |
| MeFOSAA |  |  |  |  |  |
| Model 1 |  |  |  |  |  |
| Q1 (<LOD-0.9) | Ref | Ref | Ref | Ref | Ref |
| Q2 (1.0-1.4) | 43.99 (24.03, 67.18)\*\*\* | 35.76 (20.03, 53.55)\*\*\* | -5.72 (-10.39, -0.81)\* | -7.50 (-14.53, 0.12) | -11.37 (-18.95, -3.09)\*\* |
| Q3 (1.5-2.3) | 29.19 (11.30, 49.95)\*\* | 25.91 (11.34, 42.38)\*\* | -2.54 (-7.35, 2.53) | -0.95 (-8.47, 7.19) | -1.66 (-10.05, 7.51) |
| Q4 (2.4-14.4) | 31.78 (12.69, 54.10)\*\* | 27.20 (11.79, 44.73)\*\* | -3.48 (-8.48, 1.80) | -1.92 (-9.72, 6.56) | 0.64 (-8.36, 10.52) |
| Model 2 |  |  |  |  |  |
| Q1 (<LOD-0.9) | Ref | Ref | Ref | Ref | Ref |
| Q2 (1.0-1.4) | 19.93 (6.67, 34.85)\*\* | 16.60 (8.85, 28.43)\*\* | -2.78 (-7.39, 2.05) | -3.44 (-10.53, 4.22) | -7.79 (-15.47, 0.59) |
| Q3 (1.5-2.3) | 10.17 (-1.98, 23.83) | 10.48 (0.32, 21.66)\* | 0.28 (-4.46, 5.25) | 2.98 (-4.56, 11.12) | 2.03 (-6.45, 11.27) |
| Q4 (2.4-14.4) | 16.12 (2.73, 31.26)\* | 14.37 (3.37, 26.54)\*\* | -1.51 (-6.38, 3.62) | 1.16 (-6.59, 9.56) | 3.48 (-5.51, 13.33) |

Model 1 was adjusted for age, race, study site, education, smoking status, physical activity and menopausal status.

Model 2: Model 1 + BMI

\*\*\**P*<0.0001, \*\**P*<0.01, \**P*<0.05

**Table S4** Percent change and 95% confidence interval (95% CI) of free leptin index, leptin, sOB-R, adiponectin, and HMW adiponectin per doubling increase in serum concentrations of PFOS, n-PFOS, Sm-PFOS, n-PFOA, PFNA, PFHxS, EtFOSAA and MeFOSAA stratified by overweight/obesity.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Percent change in free leptin index, % | | Percent change in leptin, % | | Percent change in  sOB-R, % | | Percent change in total adiponectin, % | | Percent change in HMW adiponectin, % | |
|  | Obesity  (N=769) | Non-obesity  (N=469) | Obesity (N=769) | Non-obesity  (N=469) | Obesity (N=769) | Non-obesity  (N=469) | Obesity (N=769) | Non-obesity  (N=469) | Obesity (N=769) | Non-obesity  (N=469) |
| PFOS | 12.0  (4.9, 19.6)\*\* | 9.1  (-1.2, 20.4) | 11.3  (5.5, 17.4)\*\*\* | 9.4  (0.7, 18.9)\* | -0.7  (-3.3, 2.0) | 0.3  (-3.1, 3.8) | 4.5  (0.1, 9.1)\* | -3.4  (-8.2, 1.6) | 3.8  (-1.0, 8.8) | -4.0  (-9.8, 2.2) |
| P for interaction | 0.003 | | 0.0006 | | 0.72 | | 0.05 | | 0.13 | |
| n-PFOS | 10.8  (3.6, 18.5)\*\* | 8.0  (-2.1, 19.2) | 10.3  (4.4, 16.4)\*\* | 8.3  (-0.3, 17.7) | -0.4  (-3.1, 2.3) | 0.3  (-3.1, 3.8) | 4.4  (-0.008, 9.1) | -3.0  (-7.8, 2.1) | 4.2  (-0.7, 9.3) | -3.5  (-9.3, 2.6) |
| P for interaction | 0.01 | | 0.004 | | 0.96 | | 0.06 | | 0.10 | |
| Sm-PFOS | 11.7  (5.6, 18.1)\*\* | 8.4  (-0.04, 17.5) | 11.0  (6.1, 16.1)\*\*\* | 8.3  (1.2, 16.0)\* | -0.7  (-2.9, 1.6) | -0.6  (-2.8, 2.8) | 4.1  (0.4, 8.0)\* | -2.8  (-6.8, 1.4) | 2.8  (-1.2, 7.0) | -3.4  (-8.2, 1.6) |
| P for interaction | 0.0001 | | <0.0001 | | 0.47 | | 0.04 | | 0.20 | |
| n-PFOA | 13.7  (5.8, 22.2)\*\* | 5.9  (-3.9, 16.7) | 10.4  (4.1, 17.1)\*\* | 5.5  (-2.8, 14.5) | -2.9  (-5.7, 0.04) | -0.4  (-3.7, 3.0) | 1.5  (-3.2, 6.4) | -4.2  (-8.9, 0.8) | -0.7  (-5.7, 4.6) | -4.7  (-10.4, 1.3) |
| P for interaction | 0.0003 | | 0.0005 | | 0.04 | | 0.62 | | 0.71 | |
| PFHxS | 4.7  (-0.4, 10.1) | -3.9  (-10.6, 3.3) | 4.5  (0.3, 8.9)\* | -2.0  (-7.8, 4.2) | -0.2  (-2.2, 1.9) | 1.9  (-0.6, 4.5) | 0.2  (-3.0, 3.5) | -0.4  (-4.1, 3.4) | 1.2  (-2.4, 4.9) | 0.6  (-3.9, 5.3) |
| P for interaction | 0.04 | | 0.01 | | 0.90 | | 0.96 | | 0.43 | |
| PFNA | 5.4  (-1.5, 12.9) | 7.5  (-1.8, 17.8) | 2.9  (-2.7, 8.7) | 6.5  (-1.3, 15.0) | -2.4  (-5.1, 0.3) | -0.9  (-4.0, 2.2) | 4.3  (-0.1, 9.0) | -5.4  (-9.8, -0.9)\* | 3.3  (-1.6, 8.4) | -7.1  (-12.2,  -1.7)\* |
| P for interaction | 0.45 | | 0.72 | | 0.22 | | 0.02 | | 0.22 | |
| EtFOSAA | 6.5  (2.1, 11.2)\*\* | 6.8  (0.5, 13.5)\* | 5.3  (1.7, 9.0)\*\* | 4.4  (-0.9, 9.9) | -1.2  (-2.9, 0.5) | -2.2  (-4.3, -0.2)\* | 1.6  (-1.2, 4.4) | -2.4  (-5.4, 0.7) | 0.4  (-2.6, 3.5) | -3.2  (-6.8, 0.6) |
| P for interaction | 0.009 | | 0.009 | | 0.22 | | 0.32 | | 0.90 | |
| MeFOSAA | 3.7  (-2.4, 10.2) | 9.3  (1.1, 18.3)\* | 2.8  (-2.1, 8.0) | 9.2  (2.2, 16.7)\*\* | -0.9  (-3.3, 1.6) | -0.1  (-2.8, 2.6) | 1.3  (-2.6, 5.4) | -2.8  (-6.7, 1.3) | 3.2  (-1.1, 7.8) | -2.1  (-6.9, 2.8) |
| P for interaction | 0.45 | | 0.46 | | 0.70 | | 0.68 | | 0.22 | |

The models were adjusted for age, race, study site, education, smoking status, physical activity and menopausal status.

\*\*\*P<0.0001, \*\*P<0.01, \*P<0.05

7 women missing information on body mass index.

Overweight/obesity was defined as BMI25 kg/m2 for White and Black women, and BMI23 kg/m2 for Chinese and Japanese women.

**Table S5** Percent change and 95% confidence interval (95% CI) of free leptin index, leptin, sOB-R, adiponectin, and HMW adiponectin per doubling increase in serum concentrations of PFOS, n-PFOS, Sm-PFOS, n-PFOA, PFNA, PFHxS, EtFOSAA and MeFOSAA stratified by menopausal status.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Percent change in free leptin index, % | | Percent change in leptin, % | | Percent change in  sOB-R, % | | Percent change in total adiponectin, % | | Percent change in HMW adiponectin, % | |
|  | Pre-/early peri- menopause (N=773) | Late peri-/post menopause (N=250) | Pre-/early peri- menopause (N=773) | Late peri-/post menopause (N=250) | Pre-/early peri- menopause (N=773) | Late peri-/post menopause (N=250) | Pre-/early peri- menopause (N=773) | Late peri-/post menopause (N=250) | Pre-/early peri- menopause (N=773) | Late peri-/post menopause (N=250) |
| PFOS | 16.92 (7.67, 26.97)\*\* | 14.31  (-1.84, 33.12) | 14.53 (6.96, 22.62)\*\* | 15.61 (1.95, 31.10) | -2.05  (-4.72, 0.69) | 1.13  (-3.77, 6.29) | -0.24  (-4.40, 4.11) | 3.33  (-4.74, 12.09) | -1.16  (-5.75, 3.65) | 4.14  (-5.37, 14.62) |
| P for interaction | <0.0001 | | <0.0001 | | 0.08 | | 0.12 | | 0.01 | |
| n-PFOS | 14.87  (5.63, 24.91)\*\* | 10.50  (-5.16, 28.75) | 12.76  (5.19, 20.88)\*\* | 12.13  (-1.17, 27.24) | -1.83  (-4.55, 0.96) | 1.48  (-3.45, 6.65) | -0.11  (-4.34, 4.31) | 4.36  (-3.79, 13.20) | -0.54  (-5.23, 4.38) | 5.43  (-4.20, 16.03) |
| P for interaction | 0.0006 | | 0.0003 | | 0.09 | | 0.11 | | 0.01 | |
| Sm-PFOS | 16.46  (8.77, 24.70)\*\*\* | 18.97  (4.15, 35.90)\* | 14.28  (7.99, 20.94)\*\*\* | 18.93  (6.58, 32.71)\*\* | -1.88  (-4.10, 0.41) | -0.03  (-4.32, 4.44) | 0.02  (-3.46, 3.64) | 0.03  (-6.89, 7.46) | -1.60  (-5.42, 2.38) | 0.07  (-8.04, 8.88) |
| P for interaction | <0.0001 | | <0.0001 | | 0.04 | | 0.18 | | 0.02 | |
| n-PFOA | 18.91 (9.33, 29.33)\*\*\* | 14.72  (-2.73, 35.28) | 15.29  (7.52, 23.61)\*\*\* | 13.98  (-0.57, 30.65) | -3.05  (-5.74,  -0.28)\* | -0.64  (-5.85, 4.85) | -4.44  (-8.50,  -0.20)\* | 3.90  (-4.86, 13.46) | -5.11  (-9.60,  -0.40)\* | 5.50  (-4.88, 17.01) |
| P for interaction | <0.0001 | | <0.0001 | | 0.02 | | 0.01 | | 0.001 | |
| PFHxS | -1.29  (-7.23, 5.02) | -5.87  (-16.25, 5.79) | 0.28  (-4.74, 5.58) | -4.60  (-13.41, 5.11) | 1.60  (-0.47, 3.71) | 1.35  (-2.42, 5.27) | 0.27  (-2.87 | 2.28  (-3.88, 8.83) | 1.37  (-2.16, 5.03) | 3.63  (-3.68, 11.49) |
| P for interaction | 0.41 | | 0.57 | | 0.18 | | 0.55 | | 0.11 | |
| PFNA | 6.41  (-1.85, 15.37) | 7.68  (-8.56, 26.81) | 5.33  (-1.50, 12.63) | 4.94  (-8.37, 20.20) | -1.02  (-3.65, 1.68) | -2.54  (-7.58, 2.77) | 0.46  (-3.63, 4.71) | 0.25  (-8.11, 9.37) | -0.57  (-5.07, 4.14) | -1.07  (-10.71, 9.61) |
| P for interaction | 0.16 | | 0.22 | | 0.20 | | 0.37 | | 0.13 | |
| EtFOSAA | 11.99  (6.30, 17.98)\*\*\* | 13.85 (3.33, 25.44)\*\* | 9.02  (4.40, 13.84)\*\*\* | 12.19 (3.54, 21.57)\*\* | -2.65  (-4.33,  -0.94)\*\* | -1.46  (-4.55, 1.73) | -2.12  (-4.72, 0.56) | 4.02  (-1.25, 9.58) | -2.69  (-5.57, 0.29) | 2.99  (-3.15, 9.52) |
| P for interaction | <0.0001 | | <0.0001 | | 0.004 | | 0.05 | | 0.08 | |
| MeFOSAA | 10.18 (2.52, 18.41)\*\* | 10.84  (-2.53, 26.04) | 8.44  (2.15, 15.12)\*\* | 10.51  (-0.64, 22.91) | -1.57  (-3.91, 0.82) | -0.30  (-4.39, 3.97) | -1.63  (-5.21, 2.09) | -0.50  (-7.10, 6.57) | 0.50  (-3.57, 4.75) | -1.59  (-9.24, 6.69) |
| P for interaction | 0.004 | | 0.004 | | 0.18 | | 0.48 | | 0.94 | |

The models were adjusted for age, race, study site, education, smoking status, physical activity and menopausal status.

\*\*\*P<0.0001, \*\*P<0.01, \*P<0.05

7 women missing information on body mass index.

Overweight/obesity was defined as BMI25 kg/m2 for White and Black women, and BMI23 kg/m2 for Chinese and Japanese women.



**Figure S1** A flow chart of the study design.



**Figure S2** Correlation structure of PFAS included in the analysis.



**Figure S3** Dose-response relationships and 95% confidence interval (95% CI) bands for A. sm-PFOS, and B. EtFOSAA withleptin, holding all other PFAS at median serum concentrations, estimated by Bayesian kernel machine regression. The model was adjusted for age, race, study site, education, smoking status, physical activity, menopausal status, and waist circumference.



**Figure S4** Cumulative effects of perfluoroalkyl and polyfluoroalkyl substances (PFAS) mixtures on **leptin**, estimated by Bayesian kernel machine regression. This plot shows the estimated exposure-response relations and 95% confidence intervals (95% CIs) when all PFAS concentrations are held at a certain percentile, compared to when PFAS concentrations are held at the 10th percentile. The models were adjusted for age, race, study site, education, smoking status, physical activity, menopausal status, and waist circumference.



**Figure S5** Dose-response relationships and 95% confidence interval (95% CI) bands for A. sm-PFOS, B. n-PFOA, and C. EtFOSAA with free leptin index, holding all other PFAS at median serum concentrations, estimated by Bayesian kernel machine regression. The model was adjusted for age, race, study site, education, smoking status, physical activity, menopausal status, and body mass index.



**Figure S6** Cumulative effects of perfluoroalkyl and polyfluoroalkyl substances (PFAS) mixtures on **free leptin index**, estimated by Bayesian kernel machine regression. This plot shows the estimated exposure-response relations and 95% confidence intervals (95% CIs) when all PFAS concentrations are held at a certain percentile, compared to when PFAS concentrations are held at the 10th percentile. The models were adjusted for age, race, study site, education, smoking status, physical activity, menopausal status, and body mass index.