**Supplemental Material**

**Air Pollution-Associated Changes in Biomarkers of Diabetes Risk**

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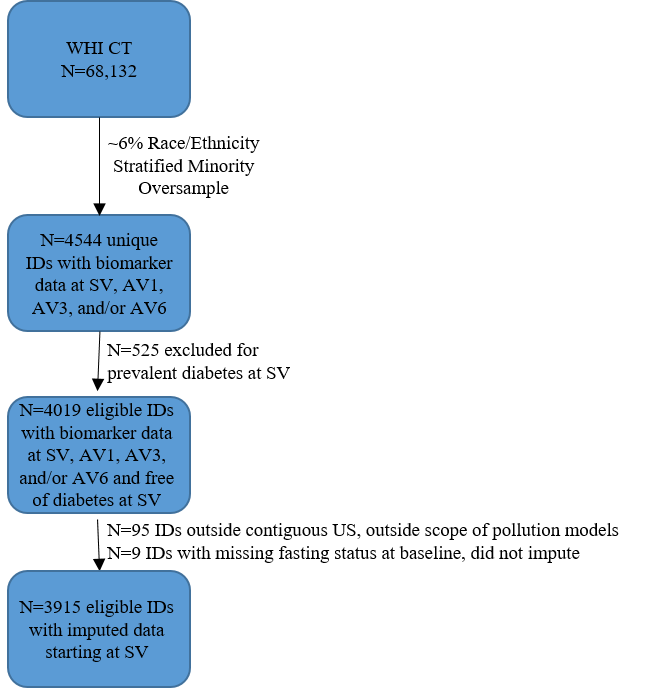
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**Abbreviations**. AV, annual visit; HOMA-IR, homeostasis model assessment-insulin resistance; NOx, nitrogen oxides; PM10 and PM2.5, particulate matter ≤ 10 and ≤ 2.5 μm in diameter; SV, screening visit; TG:HDL-C, ratio of triglycerides to high-density lipoprotein cholesterol; TyG, triglycerides-glucose index. See main text for cited definitions.

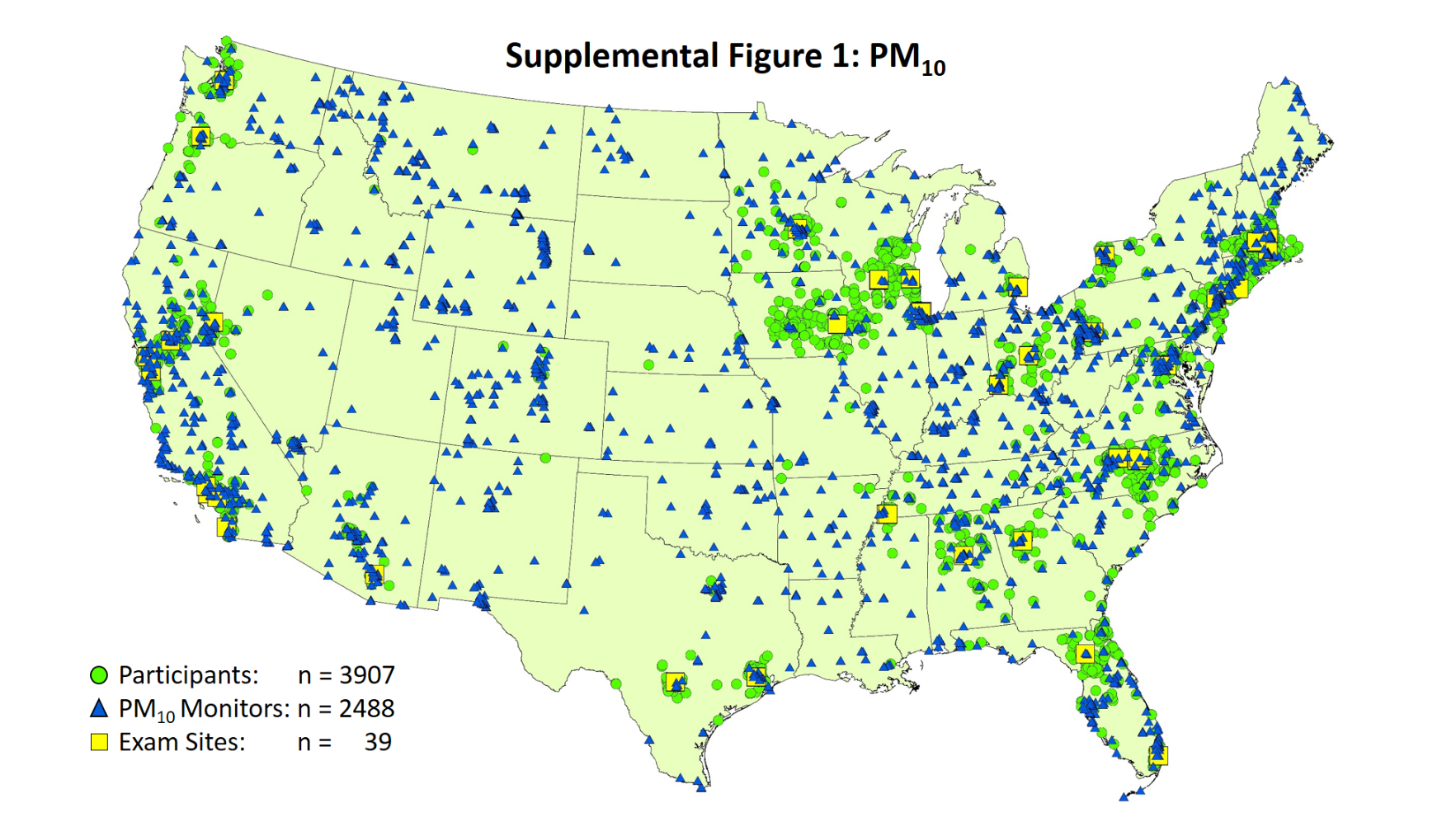
Table S1. Unweighted demographic, behavioral, clinical, and contextual characteristics at screening

(1993-1998), Women’s Health Initiative Clinical Trials

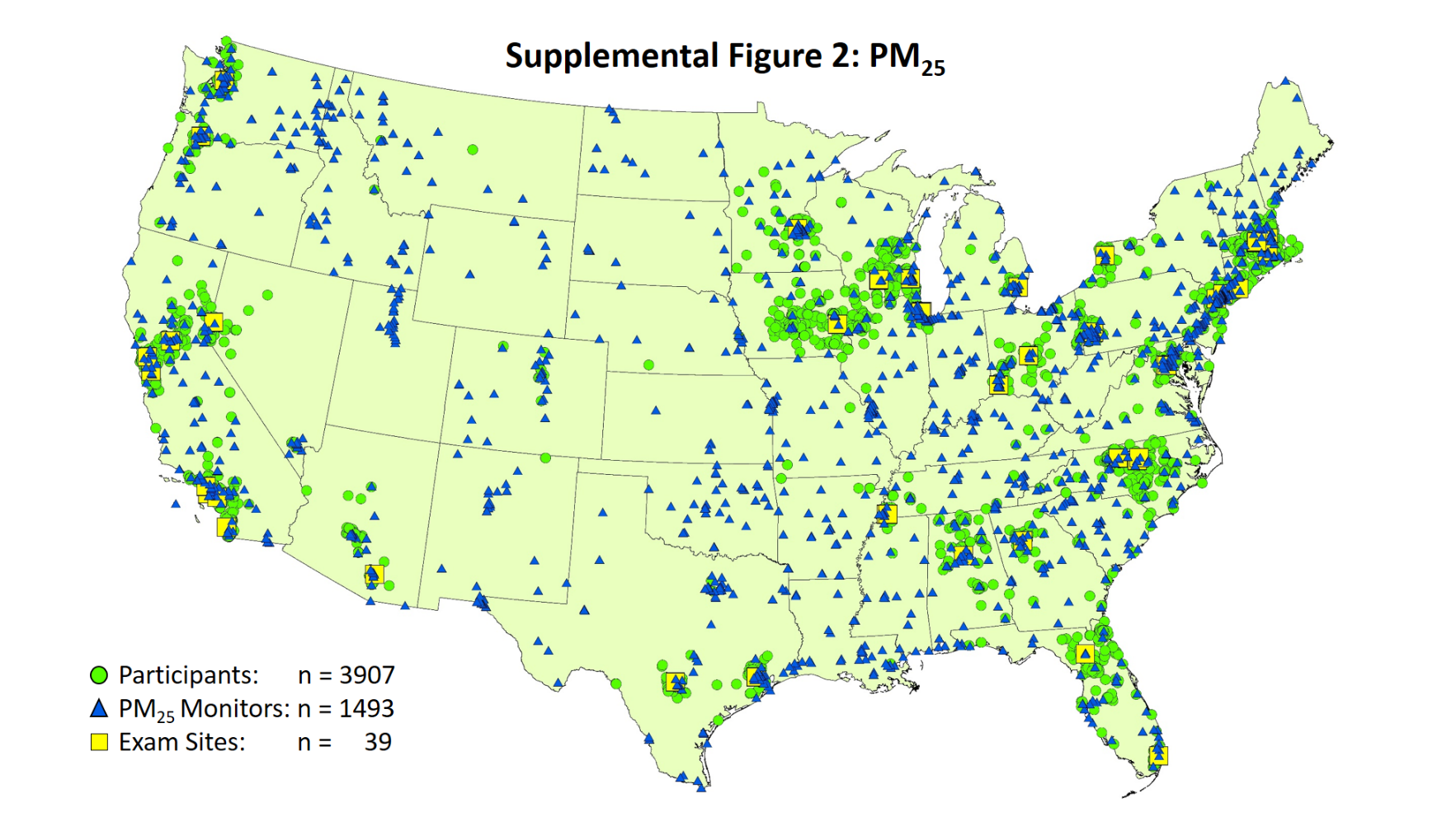
|  |  |
| --- | --- |
| Characteristics | Mean (SD) or % |
| Age, years | 62.2 (7.1) |
| Race/ethnicity (%) Non-Hispanic White | 52.1 |
| Non-Hispanic Black | 24.9 |
| Hispanic | 12.6 |
| Others | 10.4 |
| Less than college graduate (%) | 66.0 |
| Area-level SES | -1.5 (5.6) |
| Examination season (%) Spring | 28.4 |
| Summer | 26.2 |
| Fall | 24.2 |
| Winter | 21.2 |
| Examination day on weekday (%) | 95.6 |
| Family history of diabetes (%) | 36.0 |
| Current smoker (%) | 8.9 |
| Current alcohol use (%) | 51.8 |
| Total energy expenditure, MET-hrs/week | 10.3 (13.0) |
| Body Mass Index, kg/m2 | 29.2 (6.0) |
| Glucose, mg/dLa | 94.4 (10.3) |
| Insulin, uIU/mL | 11.3 (6.6) |
| HOMA-IR | 2.7 (1.8) |
| TG:HDL-C | 2.8 (2.3) |
| TyG | 8.7 (0.5) |
| PM10 (μg/m3) 2-day b | 28.8 (11.2) |
| 365-day b | 28.1 (3.8) |
| 12-month c | 21.3 (5.3) |
| PM2.5 (μg/m3) 12-month c | 12.3 (3.1) |
| NOx (ppb) 2-day b | 39.0 (30.0) |
| 365-day b | 38.4 (16.4) |
| Note: CI, confidence interval; HOMA-IR, homeostatic model assessment of insulin resistance; MET, metabolic equivalent; NOx, nitrous oxide; PM2.5, particulate matter ≤2.5 μm in diameter; PM10, particulate matter ≤10 μm in diameter; ppb, parts per billion; SES, socioeconomic status; TG:HDL-C, triglyceride to high-density lipoprotein cholesterol ratio; TyG, triglyceride-glucose index; uIU, micro international units  a Excluded extremely low glucose values (<50 mg/dL, n=2)  b Daily mean concentrations spatially estimated using national-scale, log normal, ordinary kriging  c Monthly mean concentrations spatiotemporally estimated using generalized, additive mixed  models and land use regression | |

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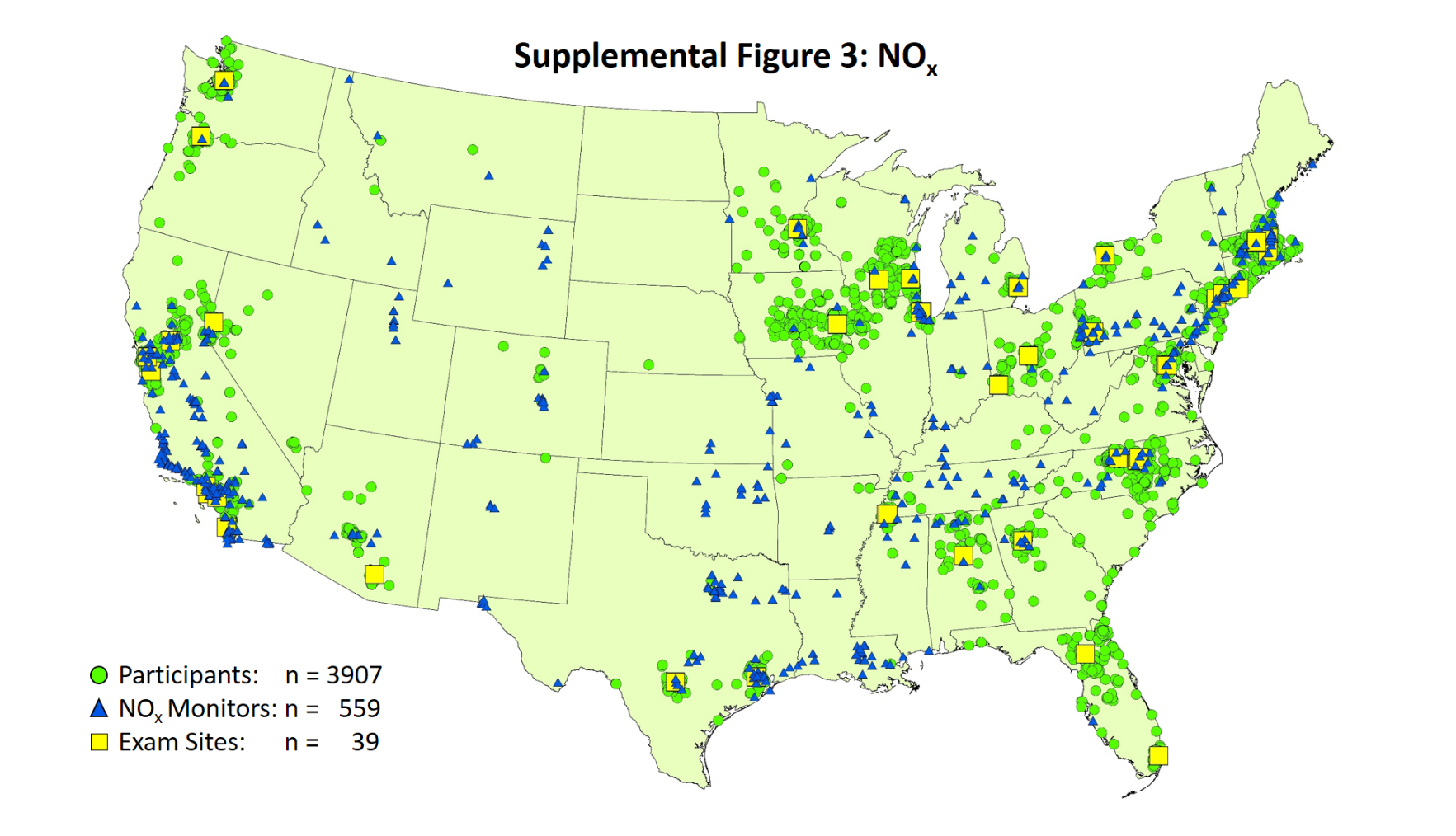
**Figure S1. Flowchart of included participants**

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**Figure S2.** Map of geocoded addresses of non-diabetic participants, PM10 air pollution monitors, and exam sites (1993–2004). Exam sites followed 60 to 187 sampled participants. Participant addresses were a median of 7.5 km away from the nearest PM10 monitor.



**Figure S3.** Map of geocoded addresses of non-diabetic participants, PM2.5 air pollution monitors, and exam sites (1993–2004). Exam sites followed 60 to 187 sampled participants. Participant addresses were a median of 7.4 km away from the nearest PM2.5 monitor.



**Figure S4.** Map of geocoded addresses of non-diabetic participants, NOx air pollution monitors, and exam sites (1993–2004). Exam sites followed 60 to 187 sampled participants. Participant addresses were a median of 15.0 km away from the nearest NOx monitor.

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**Figure S5.** Scatterplots of participant-specific glucose homeostasis measures (glucose; insulin; HOMA-IR; TG:HDL-C; TyG), mean air pollution concentrations (daily PM10; monthly PM2.5; daily NOx), and daily mean meteorological measures (temperature; dew point; barometric pressure) with kernel-smoothed moving averages, by exam year (1993-2004), after excluding values ≥ 3 standard deviations from the mean. At the screening visit (pink) and annual visits 1, 3, or 6 (yellow; green; blue), mean (standard deviation) measures of glucose homeostasis, air pollution concentrations, and meteorological measures were:

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **Glucose**  **(mg/dl)** | | **Insulin**  **(uIU/ml)** | | **HOMA-IR** | | **TG:HDL-C** | | **TyG** | |
| SV | 94.3 | (10.3) | 11.3 | (6.6) | 2.7 | (1.8) | 2.8 | (2.2) | 8.7 | (0.5) |
| AV1 | 93.2 | (9.7) | 10.8 | (6.0) | 2.5 | (1.6) | 2.8 | (2.5) | 8.7 | (0.5) |
| AV3 | 92.7 | (10.5) | 12.0 | (6.8) | 2.8 | (1.8) | 2.8 | (2.3) | 8.7 | (0.5) |
| AV6 | 95.1 | (10.9) | 9.4 | (6.5) | 2.3 | (1.8) | 2.7 | (2.0) | 8.7 | (0.5) |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **PM10**  **(ug/m3)** | | **PM2.5**  **(ug/m3)** | | **NOx**  **(ppb)** | |
| SV | 28.8 | (11.2) | 12.2 | (4.2) | 39.0 | (30.0) |
| AV1 | 28.1 | (10.9) | 12.9 | (4.7) | 37.2 | (29.9) |
| AV3 | 28.0 | (10.6) | 14.9 | (6.0) | 36.0 | (30.2) |
| AV6 | 27.0 | (10.5) | 14.7 | (6.0) | 32.1 | (25.7) |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Visit** | **Temperature**  **(◦C)** | | **Dewpoint**  **(◦C)** | | **BarometricPressure**  **(kPa)** | |
| SV | 14.1 | (9.2) | 7.4 | (9.3) | 101.6 | (0.6) |
| AV1 | 14.5 | (9.3) | 8.0 | (9.3) | 101.6 | (0.6) |
| AV3 | 14.3 | (9.2) | 7.8 | (9.2) | 101.7 | (0.6) |
| AV6 | 14.5 | (9.2) | 8.1 | (9.3) | 101.7 | (0.5) |

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**Table S2.** Unadjustedpercent change in biomarkers of diabetes risk (95% confidence interval) per unit increase in air pollution concentration (1993-2004), Women’s Health Initiative Clinical Trials

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Measure | Fasting glucose |  | PM10 *a* | | | PM2.5 *a* | NOx *a* | |
| N | 2-day | 365-day | 12-month | 12-month | 2-day | 365-day |
| Fasting Glucose | All | 3915 | -0.1 (-0.4, 0.2) | -0.4 (-1.7, 1.0) | -0.4 (-1.4, 0.6) | -1.2 (-2.3, 0.0) | -0.2 (-0.6, 0.2) | -0.5 (-1.4, 0.3) |
| Normal | 2902 | 0.1 (-0.3, 0.4) | -0.7 (-1.9, 0.5) | -0.8 (-1.7, 0.1) | -1.2 (-2.3, -0.1) | -0.2 (-0.5, 0.2) | -0.5 (-1.2, 0.3) |
| Impaired | 1013 | 0.0 (-0.3, 0.3) | 0.0 (-1.3, 1.3) | -0.1 (-1.0, 0.9) | -0.1 (-1.2, 0.9) | 0.0 (-0.3, 0.3) | 0.0 (-0.5, 0.6) |
|  |  |  |  |  |  |  |  |  |
| Fasting Insulin | All | 3915 | -1.0 (-1.8, -0.2) | -1.5 (-5.9, 3.1) | 2.3 (-1.6, 6.5) | 2.9 (-1.9, 7.9) | -0.2 (-1.3, 0.9) | -2.3 ( -5.5, 0.9) |
| Normal | 2902 | -1.1. (-1.9, -0.2) | -3.5 (-7.9, 1.2) | 0.8 (-3.3, 4.9) | 2.5 (-2.3, 7.5) | -0.2 (-1.3, 0.9) | -2.5 (-6.1, 1.2) |
| Impaired | 1013 | -0.2 (-2.3, 1.9) | 3.9 (-2.6, 10.9) | 6.2 (0.4, 12.2) | 4.3 (-2.4, 11.5) | 0.4 (-1.8, 2.8) | -1.1 (-4.8, 2.7) |
|  |  |  |  |  |  |  |  |  |
| HOMA-IR | All | 3915 | -0.9 (-1.9,0.0) | -2.1. (-6.5, 2.6) | 0.6 (-3.1, 4.5) | 0.8 (-4.1, 5.9) | -0.4 (-1.8, 1.0) | -2.7 (-5.6, 0.3) |
| Normal | 2902 | -0.9 (-2.1, 0.3) | -5.0 (-9, -0.9) | -0.8 (-5.1, 3.6) | 0.8 (-4.0, 5.7) | -0.3 (-1.7, 1.1) | -2.2 (-5.7, 1.4) |
| Impaired | 1013 | 0.0 (-2.2, 2.3) | 5.5 (-3.0, 14.7) | 6.7 (0.4, 13.3) | 2.0 (-5.2, 9.7) | 0.0 (-2.6, 2.6) | -1.4 (-5.3, 2.6) |
|  |  |  |  |  |  |  |  |  |
| TG:HDL-C | All | 3915 | 0.1 (-0.9, 1.1) | 2.1. (-2.5, 7.0) | -1.4 (-5.7, 3.1) | 0.6 (-4.3, 5.6) | -0.8 (-1.8, 0.3) | -0.4 (-3.2, 2.5) |
| Normal | 2902 | -0.2 (-1.2, 0.9) | 0.7 (-3.8, 5.5) | -2.3 (-6.9, 2.5) | 0.9 (-4, 6.2) | -0.9 (-2.0, 0.2) | -0.6 (-3.4, 2.3) |
| Impaired | 1013 | 0.8 (-1.1, 2.7) | 5.1 (-3.6, 14.5) | 1.1 (-5.5, 8.1) | -0.1 (-7.3, 7.7) | -0.2 (-2.6, 2.3) | 0.4 (-3.9, 4.9) |
|  |  |  |  |  |  |  |  |  |
| TyG | All | 3915 | -0.1 (-1.0, 0.7) | 0.0 (-4.3, 4.6) | -2.8 (-6.6, 1.1) | 1.2 (-2.5, 5) | -0.5 (-1.4, 0.5) | -0.8 (-3.4, 1.9) |
| Normal | 2902 | -0.2 (-1.1, 0.6) | -0.8 (-5.1, 3.8) | -4.0 (-8.0, 0.2) | 1.2 (-2.7, 5.3) | -0.6 (-1.5, 0.3) | -0.8 (-3.6, 2.1) |
| Impaired | 1013 | 0.4 (-1.4, 2.1) | 2.6 (-4.5, 10.3) | 0.1 (-5.7, 6.3) | 1.4 (-4.6, 7.8) | 0.0 (-2.5, 2.6) | 0.1 (-3.7, 4.1) |
| Note: HOMA-IR, homeostatic model assessment of insulin resistance; NOx, nitrous oxide; PM2.5, particulate matter ≤2.5 μm in diameter; PM10, particulate matter ≤10 μm in diameter; TG:HDL-C, triglyceride to high-density lipoprotein cholesterol ratio; TyG, triglyceride-glucose index.  *a* PM: 10 ug/m3 increase; NOx: IQR increase (2-day: 28.4 ppb; 365-day: 20.3 ppb)  *b P* < 0.05  *c P*interaction < 0.05 | | | | | | | | |

Figure S6: Sketch of P-value function for associations between 12-month PM2.5 and biomarkers of diabetes risk.

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For a list of all the investigators who have contributed to WHI science, please visit: https://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator %20Long%20List.pdf