SUPPLEMENTARY DATA

**Supplementary Table 1.** Diagnostic thresholds for IR and higher degrees of impaired glucose metabolism.

| Category | Test FPG | 2-h PG |
|---|---|---|
| Normal | <110 mg/dl (<6.1 mmol/l) | <140 mg/dl (<7.8 mmol/l) |
| i-IFG | 110-125 mg/dl (6.1-7.0 mmol/l) | - |
| i-IGT | - | 140-199 mg/dl (7.8-11.0 mmol/l) |
| Diabetes | ≥126 mg/dl (≥7.0 mmol/l) | ≥200 mg/dl (≥11.1 mmol/l) |

FPG: fasting plasma glucose; 2-h PG: plasma glucose, 2 h after OGTT; i-IFG: isolated impaired fasting glucose; i-IGT: isolated impaired glucose tolerance.

**Supplementary Table 2.** Final covariate selection by outcome variable.

| Outcome | Personal characteristics* | | | | | | Socio-economic covariates† | | Lifestyle covariates‡ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Smoking | BMI | Waist-hip-ratio | Month of blood withdrawal | Education | Income | Pack-years smoked | Physical activity | Alcohol intake |
| HOMA-IR | ● | ● | ● | ● | ● | ● | | | ● | | |
| Glucose | ● | ● | ● | ● | ● | ● | | | ● | | |
| Insulin | ● | ● | ● | ● | ● | ● | | | | | |
| HbA1c | ● | ● | ● | ● | ● | ● | | ● | ● | | ● |
| Leptin | ● | ● | ● | ● | ● | ● | ● | | | ● | |
| hs-CRP | ● | ● | ● | ● | ● | ● | | | | ● | |

HOMA-IR: homeostasis model assessment-insulin resistance; HbA1c: hemoglobin A1c; hs-CRP: high sensitivity C-reactive protein.

*Inclusion by a-priori definition for all outcomes.

†Inclusion of socio-economic covariates if model fit increased (decrease in the Bayesian Information Criterion). Occupational status and socio-economic status (calculated as a combination of education and income) did not improve the model fit of any outcome.

‡Inclusion of lifestyle covariates (after inclusion of socio-economic covariates) if model fit increased (decrease in the Bayesian Information Criterion). Years smoked did not improve the model fit of any outcome.

SUPPLEMENTARY DATA

**Supplementary Table 3.** Annual average concentrations of air pollutants and traffic indicators stratified by state of glucose metabolism (non-diabetes: N = 2,125; pre-diabetes: N = 496; diabetes: N= 323).

| Variable | Subgroup | Mean | SD | 5% | Median | 95% | 5th-95th percentile | p-value* |
|---|---|---|---|---|---|---|---|---|
| $PM_{10}$ ($\mu g/m^3$) | Non-diabetes | 20.4 | 2.4 | 16.4 | 20.5 | 24.3 | 7.9 | 0.60 |
| | Pre-diabetes | 20.3 | 2.4 | 16.4 | 20.5 | 24.2 | 7.8 | |
| | Diabetes | 20.6 | 2.4 | 16.6 | 20.6 | 25.0 | 8.4 | |
| $PM_{coarse}$ ($\mu g/m^3$) | Non-diabetes | 6.2 | 1.1 | 4.9 | 6.1 | 8.4 | 3.5 | 0.49 |
| | Pre-diabetes | 6.2 | 1.1 | 4.8 | 6.1 | 8.5 | 3.7 | |
| | Diabetes | 6.3 | 1.1 | 5.0 | 6.1 | 8.5 | 3.5 | |
| $PM_{2.5}$ ($\mu g/m^3$) | Non-diabetes | 13.5 | 0.8 | 12.5 | 13.4 | 15.3 | 2.8 | 0.06 |
| | Pre-diabetes | 13.6 | 0.9 | 12.5 | 13.4 | 15.5 | 3.0 | |
| | Diabetes | 13.6 | 0.9 | 12.4 | 13.5 | 15.4 | 3.0 | |
| $PM_{2.5}$abs ($10^{-5}$/m) | Non-diabetes | 1.7 | 0.2 | 1.5 | 1.7 | 2.0 | 0.5 | 0.95 |
| | Pre-diabetes | 1.7 | 0.2 | 1.5 | 1.7 | 2.0 | 0.5 | |
| | Diabetes | 1.7 | 0.2 | 1.5 | 1.7 | 2.0 | 0.5 | |
| $NO_2$ ($\mu g/m^3$) | Non-diabetes | 18.7 | 3.8 | 13.8 | 18.2 | 25.6 | 11.9 | 0.11 |
| | Pre-diabetes | 18.7 | 3.8 | 13.5 | 18.3 | 25.5 | 12.1 | |
| | Diabetes | 19.1 | 3.7 | 14.0 | 18.9 | 26.0 | 12.0 | |
| $NO_x$ ($\mu g/m^3$) | Non-diabetes | 32.7 | 7.3 | 23.8 | 31.4 | 47.1 | 23.2 | 0.17 |
| | Pre-diabetes | 32.4 | 7.2 | 23.3 | 31.0 | 45.5 | 22.2 | |
| | Diabetes | 33.2 | 7.0 | 24.7 | 31.9 | 47.8 | 23.0 | |
| Traffic intensity on the nearest road (veh/day) per 1,000 | Non-diabetes | 0.2 | 0.3 | 0.1 | 0.1 | 0.8 | 0.8 | 0.52 |
| | Pre-diabetes | 0.2 | 0.3 | 0.1 | 0.1 | 0.8 | 0.8 | |
| | Diabetes | 0.1 | 0.3 | 0.1 | 0.1 | 0.7 | 0.6 | |
| Traffic load within 100 m on major roads (veh/day*m), per 10,000 | Non-diabetes | 41.8 | 106.6 | 0.0 | 0.0 | 255.7 | 255.7 | 0.87 |
| | Pre-diabetes | 39.5 | 92.2 | 0.0 | 0.0 | 228.3 | 228.3 | |
| | Diabetes | 35.1 | 87.0 | 0.0 | 0.0 | 202.1 | 202.1 | |

$PM_{10}$: particulate matter (PM) with diameter < 10 μm; $PM_{coarse}$: $PM_{10}$ - $PM_{2.5}$; $PM_{2.5}$: PM with diameter < 2.5 μm; $PM_{2.5}$abs: the soot content (absorbance) of $PM_{2.5}$; $NO_x$: sum of nitrogen monoxide and nitrogen dioxide; $NO_2$: nitrogen dioxide.

*Kruskal-Wallis rank sum test (to test for differences between the subgroups).

**Supplementary Table 4.** Association between long-term air pollution, traffic indicators and biomarkers presented as %-change* (with 95% CI) from geometric mean per 5th-95th percentile difference increase in air pollutants (basic confounder model).

| Pollutant Exposure | Increment[†] | HOMA-IR | | | |
|---|---|---|---|---|---|
| | | **All**<br>% change ( 95% CI) | **Non-diabetes**<br>% change (95% CI) | **Pre-diabetes**<br>% change (95% CI) | **Diabetes**<br>% change (95% CI) |
| PM$_{10}$ (µg/m$^3$) | 7.9 | **15.3 (3.8; 28.1)** | 9.5 (-2.4; 22.9) | **40.9 (9.6; 81.2)** | 3.8 (-28.2; 50.0) |
| PM$_{coarse}$ (µg/m$^3$) | 3.6 | **20.0 (7.7; 33.6)** | 11.4 (-1.0; 25.4) | **67.0 (30; 114.5)** | 10.7 (-23.9; 61.1) |
| PM$_{2.5}$ (µg/m$^3$) | 2.8 | 10.5 (-0.6; 22.7) | 1.1 (-10.2; 13.7) | 23.7 (-2.8; 57.4) | 33.3 (-6.4; 89.8) |
| PM$_{2.5}$abs (10$^{-5}$/m) | 0.5 | **13.9 (3.5; 25.2)** | 7.9 (-2.7; 19.7) | **58.4 (26.1; 98.8)** | 0.0 (-28.5; 40.0) |
| NO$_x$ (µg/m$^3$) | 22.9 | **21.0 (9.3; 33.9)** | **11.9 (0.1; 25)** | **70.6 (34.2; 116.9)** | 19.5 (-16.7; 71.6) |
| NO$_2$ (µg/m$^3$) | 11.9 | **18.6 (7.3; 31.1)** | 8.3 (-2.9; 20.9) | **63.2 (28.8; 106.7)** | 23.5 (-13.2; 75.9) |
| Traffic intensity on the nearest road (veh/day), per 1,000 | 7.5 | -4.5 (-12.0; 3.7) | -5.4 (-13.4; 3.3) | 16.8 (-4.9; 43.5) | -10.9 (-35.6; 23.3) |
| Traffic load within 100m on major roads (veh/day*m), per 10,000 | 243.6 | 5.9 (-2.1; 14.5) | 00. (-8; 8.6) | **49.8 (21.8; 84.3)** | 27.6 (-7.0; 75.1) |
| | | Glucose | | | |
| PM$_{10}$ (µg/m$^3$) | 7.9 | 1.0 (-0.7; 2.6) | 0.5 (-0.5; 1.5) | -0.4 (-3.4; 2.7) | -0.3 (-8.0; 8.1) |
| PM$_{coarse}$ (µg/m$^3$) | 3.6 | 1.4 (-0.3; 3.1) | 0.6 (-0.4; 1.7) | 1.2 (-1.8; 4.4) | 3.3 (-4.9; 12.2) |
| PM$_{2.5}$ (µg/m$^3$) | 2.8 | **1.7 (0.1; 3.4)** | 0.7 (-0.3; 1.8) | 1.5 (-1.4; 4.5) | 0.3 (-7.3; 8.4) |
| PM$_{2.5}$abs (10$^{-5}$/m) | 0.5 | 0.6 (-0.9; 2.1) | 0.6 (-0.3; 1.5) | 0.7 (-2.1; 3.6) | -0.5 (-7.5; 7.2) |
| NO$_x$ (µg/m$^3$) | 22.9 | 1.3 (-0.3; 2.9) | 0.8 (-0.2; 1.8) | 1.8 (-1.1; 4.9) | 1.2 (-6.6; 9.6) |
| NO$_2$ (µg/m$^3$) | 11.9 | **1.7 (0.1; 3.3)** | 0.7 (-0.2; 1.7) | 1.8 (-1.1; 4.8) | 2.9 (-4.8; 11.2) |
| Traffic intensity on the nearest road (veh/day), per 1,000 | 7.5 | -0.1 (-1.4; 1.2) | 0.7 (-0.1; 1.5) | 1.1 (-1.4; 3.7) | -1.9 (-8.7; 5.4) |
| Traffic load within 100m on major roads (veh/day*m), per 10,000 | 243.6 | 0.2 (-1; 1.4) | -0.4 (-1.2; 0.3) | **3.2 (0.6; 5.8)** | **8.0 (0.7; 15.8)** |
| | | Insulin | | | |
| PM$_{10}$ (µg/m$^3$) | 7.9 | **14.0 (3.0; 26.1)** | 8.9 (-2.8; 21.9) | **40.9 (10.4; 80.0)** | 4.2 (-27.1; 48.9) |
| PM$_{coarse}$ (µg/m$^3$) | 3.6 | **18.1 (6.5; 30.9)** | 10.6 (-1.5; 24.2) | **64.5 (29; 109.8)** | 7.3 (-25.4; 54.4) |
| PM$_{2.5}$ (µg/m$^3$) | 2.8 | 8.6 (-1.9; 20.1) | 0.4 (-10.6; 12.6) | 21.8 (-3.7; 53.9) | 32.8 (-5.7; 87.1) |
| PM$_{2.5}$abs (10$^{-5}$/m) | 0.5 | **13.0 (3.2; 23.8)** | 7.2 (-3.2; 18.6) | **56.9 (25.8; 95.8)** | 0.6 (-27.4; 39.3) |
| NO$_x$ (µg/m$^3$) | 22.9 | **19.3 (8.2; 31.5)** | 11.0 (-0.5; 23.7) | **67.1 (32.3; 111.1)** | 18.2 (-16.7; 67.9) |
| NO$_2$ (µg/m$^3$) | 11.9 | **16.5 (5.9; 28.3)** | 7.5 (-3.4; 19.8) | **59.9 (27.0; 101.3)** | 20.2 (-14.7; 69.2) |
| Traffic intensity on the nearest road (veh/day), per 1,000 | 7.5 | -4.4 (-11.6; 3.5) | -6.0 (-13.8; 2.4) | 15.6 (-5.4; 41.2) | -9.3 (-33.8; 24.3) |
| Traffic load within 100m on major roads (veh/day*m), per 10,000 | 243.6 | 5.6 (-2.0; 13.9) | 0.4 (-7.5; 8.9) | **45.0 (18.4; 77.4)** | 18.0 (-13.2; 60.5) |

PM$_{10}$: particulate matter (PM) with diameter < 10 µm; PM$_{coarse}$: PM$_{10}$ - PM$_{2.5}$; PM$_{2.5}$: PM with diameter < 2.5 µm; PM$_{2.5}$abs: the soot content (absorbance) of PM$_{2.5}$; NO$_x$: sum of nitrogen monoxide and nitrogen dioxide; NO$_2$: nitrogen dioxide; HOMA-IR: homeostasis model assessment-insulin resistance.

*Adjusted for age, sex, and BMI.
[†] Corresponds to the difference between the 5th-95th percentile of the corresponding exposure.

# SUPPLEMENTARY DATA

**Supplementary Table 5.** Association of exposure to air pollution, traffic indicators on biomarkers presented as %-change* (with 95% CI) from geometric mean per 5th-95th percentile difference increase in air pollutants (basic confounder model).

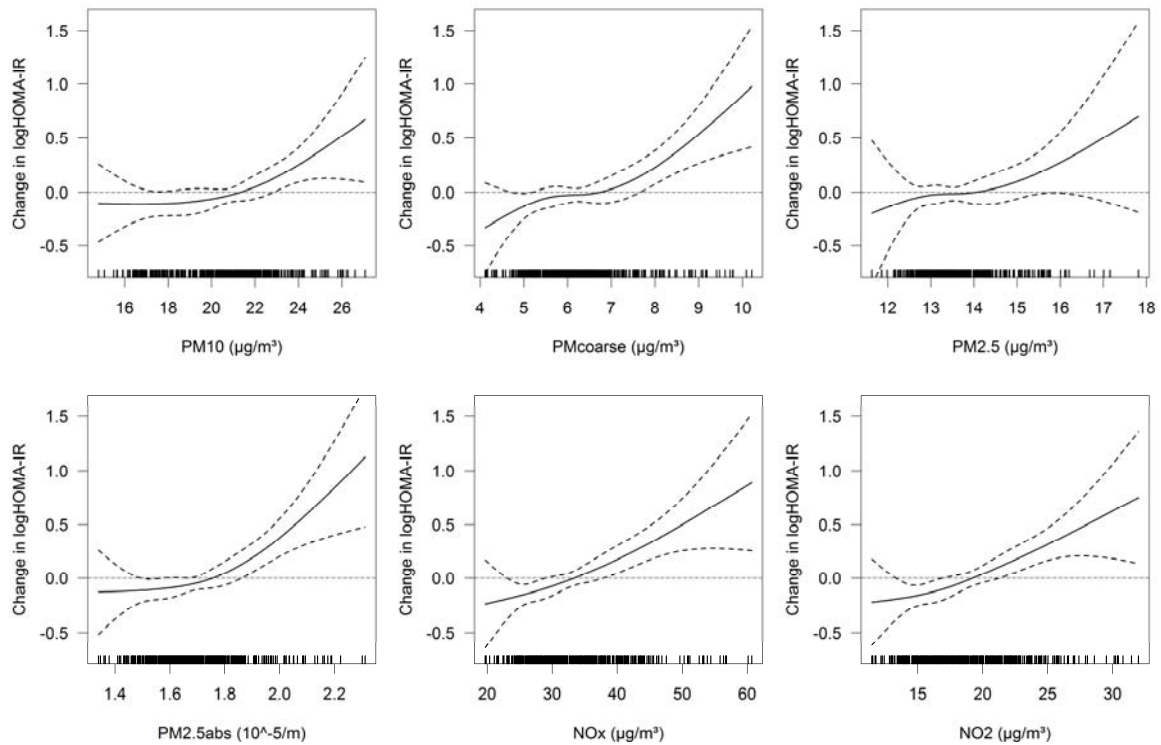| Pollutant Exposure | Increment[†] | HbA1c | | | |
|---|---|---|---|---|---|
| | | **All**<br>% change ( 95% CI) | **Non-diabetes**<br>% change (95% CI) | **Pre-diabetes**<br>% change (95% CI) | **Diabetes**<br>% change (95% CI) |
| $PM_{10}$ ($\mu g/m^3$) | 7.9 | 0.8 (-0.2; 1.9) | 0.3 (-0.4; 1.1) | -0.8 (-2.5; 0.8) | 2.7 (-2.6; 8.3) |
| $PM_{coarse}$ ($\mu g/m^3$) | 3.6 | 0.6 (-0.4; 1.6) | 0.3 (-0.5; 1.0) | -0.3 (-2.0; 1.4) | 1.9 (-3.5; 7.5) |
| $PM_{2.5}$ ($\mu g/m^3$) | 2.8 | **1.1 (0.1; 2.1)** | 0.5 (-0.2; 1.3) | 0.6 (-1.0; 2.2) | 1.2 (-3.8; 6.5) |
| $PM_{2.5}$abs ($10^{-5}$/m) | 0.5 | 0.2 (-0.7; 1.2) | 0.3 (-0.4; 0.9) | -0.5 (-2.0; 1.0) | 0.3 (-4.4; 5.2) |
| $NO_x$ ($\mu g/m^3$) | 22.9 | 0.7 (-0.3; 1.6) | 0.5 (-0.2; 1.2) | 0.3 (-1.3; 1.9) | 0.2 (-4.9; 5.5) |
| $NO_2$ ($\mu g/m^3$) | 11.9 | **0.9 (0.0; 1.9)** | 0.7 (0.0; 1.4) | 0.6 (-1.0; 2.2) | -0.3 (-5.2; 4.9) |
| Traffic intensity on the nearest road (veh/day), per 1,000 | 7.5 | 0.1 (-0.7; 0.9) | 0.2 (-0.4; 0.7) | 1.0 (-0.4; 2.3) | 1.8 (-2.8; 6.6) |
| Traffic load within 100m on major roads (veh/day*m), per 10,000 | 243.6 | -0.1 (-0.9; 0.6) | -0.3 (-0.8; 0.3) | 0.7 (-0.7; 2.1) | 2.3 (-2.3; 7.0) |
| | | **Leptin** | | | |
| $PM_{10}$ ($\mu g/m^3$) | 7.9 | 7.2 (-1.2; 16.3) | 5.6 (-4.1; 16.4) | 15.9 (-3.1; 38.7) | -0.6 (-20.7; 24.6) |
| $PM_{coarse}$ ($\mu g/m^3$) | 3.6 | 7.1 (-1.5; 16.5) | 3.8 (-6.0; 14.6) | 17.9 (-1.5; 41.2) | 7.2 (-14.8; 35.0) |
| $PM_{2.5}$ ($\mu g/m^3$) | 2.8 | 6.9 (-1.5; 16.0) | 3.5 (-6.2; 14.2) | 16.8 (-1.6; 38.6) | 8.2 (-13.0; 34.4) |
| $PM_{2.5}$abs ($10^{-5}$/m) | 0.5 | 2.0 (-5.3; 9.8) | -0.8 (-9.1; 8.2) | **22.5 (4.0; 44.2)** | -4.6 (-22.4; 17.2) |
| $NO_x$ ($\mu g/m^3$) | 22.9 | **13.1 (4.6; 22.4)** | 9.0 (-0.7; 19.6) | **31.5 (10.7; 56.2)** | 16.6 (-6.5; 45.5) |
| $NO_2$ ($\mu g/m^3$) | 11.9 | **15.8 (7.2; 25.2)** | **11.8 (2.0; 22.5)** | **26.0 (6.3; 49.4)** | 22.3 (-1.5; 51.8) |
| Traffic intensity on the nearest road (veh/day), per 1,000 | 7.5 | -2.5 (-8.5; 3.9) | -2.7 (-9.5; 4.7) | 5.1 (-9.2; 21.6) | 0.4 (-17.7; 22.6) |
| Traffic load within 100m on major roads (veh/day*m), per 10,000 | 243.6 | -2.0 (-8.0; 4.3) | -2.0 (-8.7; 5.3) | 4.2 (-10.3; 20.9) | 9.5 (-9.9; 33.0) |
| | | **hs-CRP** | | | |
| $PM_{10}$ ($\mu g/m^3$) | 7.9 | 10.4 (-2.0; 24.3) | 4.2 (-9.1; 19.3) | **38.6 (4.7; 83.6)** | 8.0 (-27.7; 61.3) |
| $PM_{coarse}$ ($\mu g/m^3$) | 3.6 | 5.0 (-7.0; 18.5) | -1.7 (-14.5; 13.0) | **34.2 (1.2; 78.0)** | 7.3 (-28.7; 61.5) |
| $PM_{2.5}$ ($\mu g/m^3$) | 2.8 | 10.6 (-1.8; 24.5) | 8.1 (-5.9; 24.1) | 11.1 (-15.1; 45.4) | 21.2 (-17.6; 78.2) |
| $PM_{2.5}$abs ($10^{-5}$/m) | 0.5 | 7.1 (-3.7; 19.2) | 1.8 (-9.9; 14.9) | 22.9 (-4.9; 59.0) | 23.5 (-14.2; 77.9) |
| $NO_x$ ($\mu g/m^3$) | 22.9 | **14.6 (2.2; 28.5)** | 8.3 (-4.9; 23.5) | **38.6 (5.7; 81.8)** | 30.1 (-12.2; 92.8) |
| $NO_2$ ($\mu g/m^3$) | 11.9 | **14.7 (2.4; 28.3)** | 5.3 (-7.4; 19.8) | **36.3 (4.4; 78.0)** | **52.4 (3.9; 123.4)** |
| Traffic intensity on the nearest road (veh/day), per 1,000 | 7.5 | 5.6 (-3.7; 15.8) | 3.1 (-7.0; 14.3) | 8.8 (-13.7; 37.1) | 31.0 (-7.9; 86.4) |
| Traffic load within 100 m on major roads (veh/day*m), per 10,000 | 243.6 | 0.2 (-8.3; 9.5) | 0.7 (-8.7; 11.1) | 4.1 (-17.7; 31.6) | -0.9 (-29.8; 40.0) |

HbA1c: hemoglobin A1c; hs-CRP: high sensitivity C-reactive protein; $PM_{10}$: particulate matter (PM) with diameter < 10 µm; $PM_{coarse}$: $PM_{10}$ - $PM_{2.5}$; $PM_{2.5}$: PM with diameter < 2.5 µm; $PM_{2.5}$abs: the soot content (absorbance) of $PM_{2.5}$; $NO_x$: sum of nitrogen monoxide and nitrogen dioxide; $NO_2$: nitrogen dioxide.

*Adjusted for age, sex, and BMI.

[†] Corresponds to the difference between the 5th-95th percentile of the corresponding exposure.
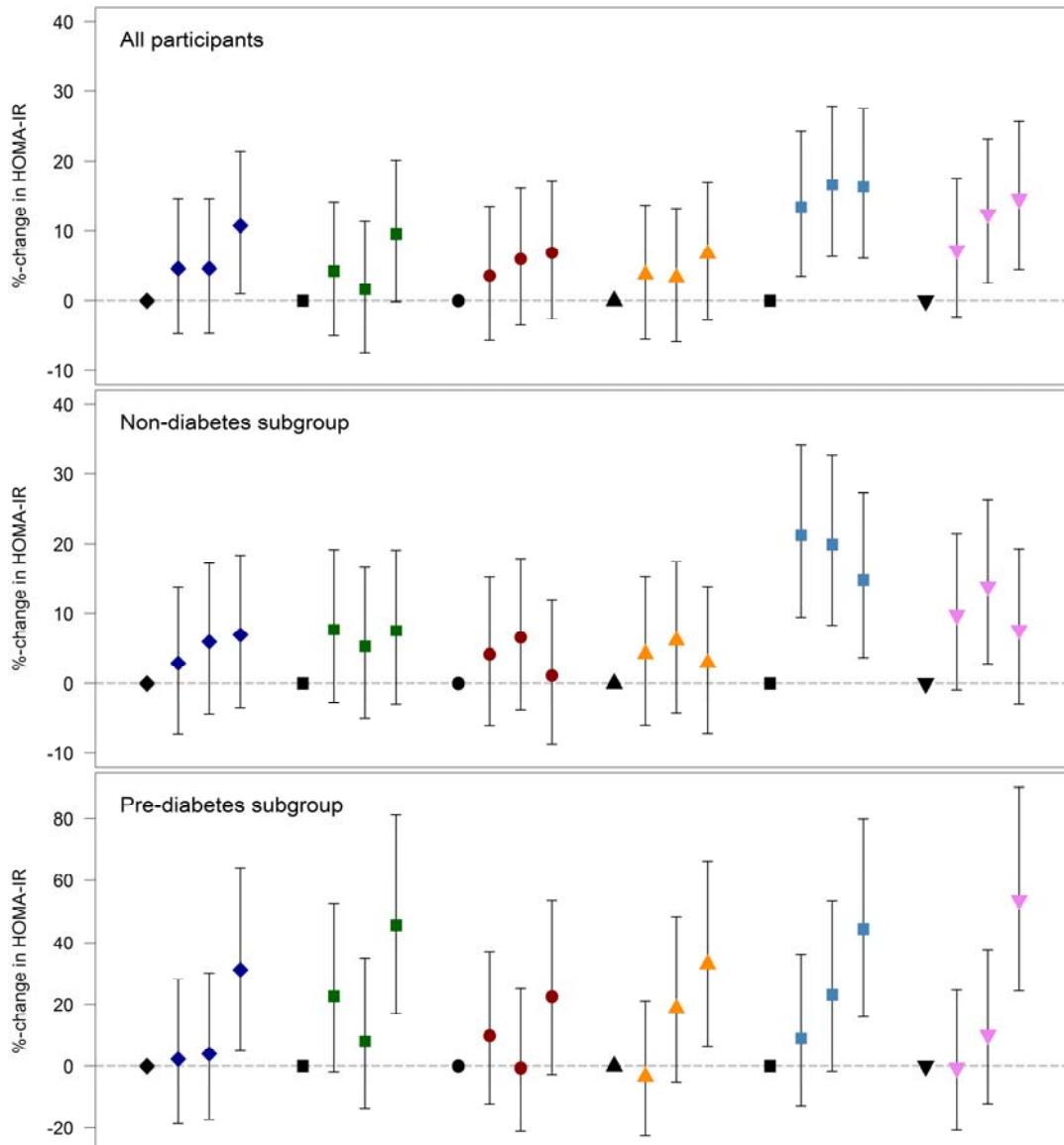
# SUPPLEMENTARY DATA

**Supplementary Figure 1.** Dose-response function for air pollutants (restricted cubic spline with 3 degrees of freedom) and HOMA-IR, adjusted for age, sex, BMI, waist-hip ratio, smoking status, month of blood withdrawal, and pack-years smoked (pre-diabetes group, n=496).
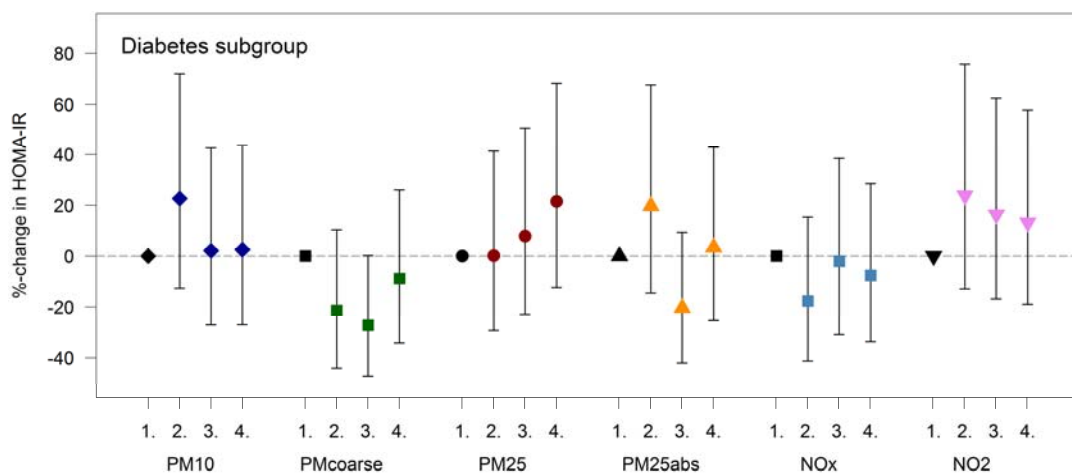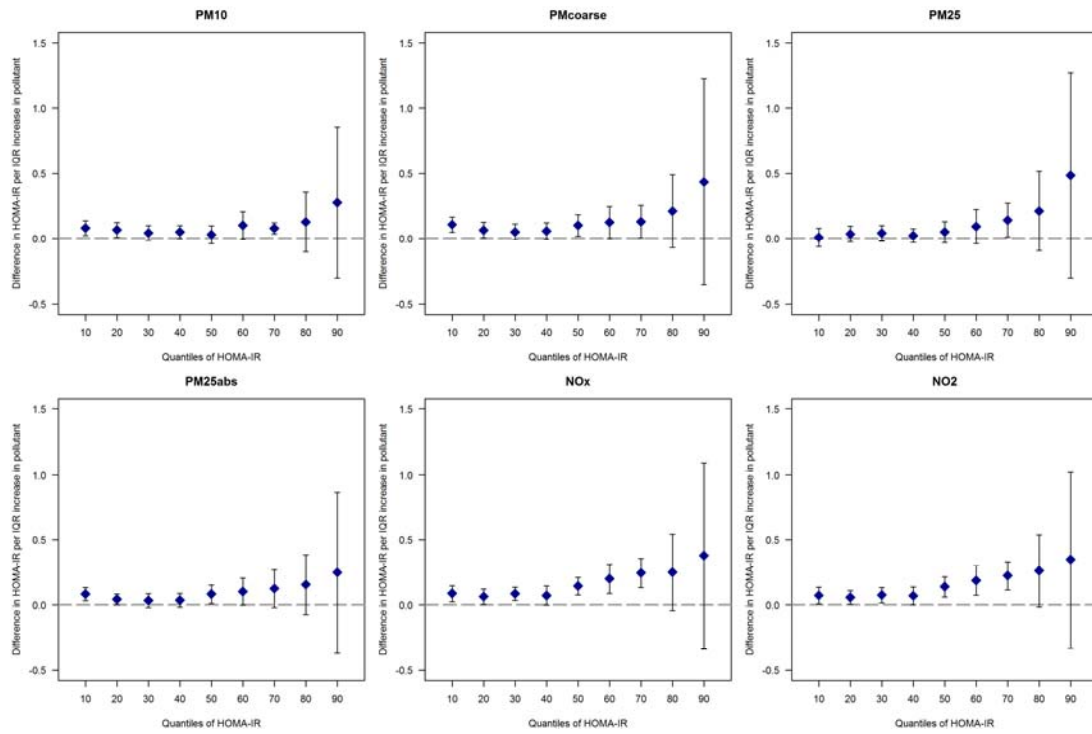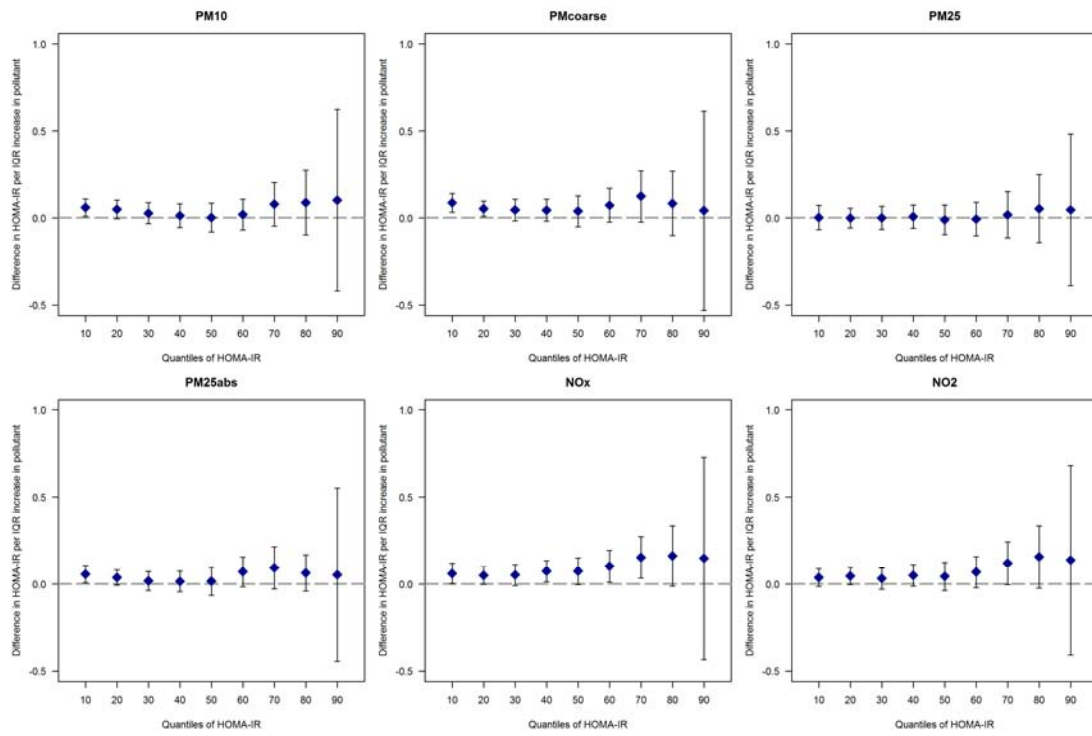


HOMA-IR: homeostasis model assessment-insulin resistance; $PM_{10}$: particulate matter (PM) with diameter < 10 μm; $PM_{coarse}$: $PM_{10}$ - $PM_{2.5}$; $PM_{2.5}$: PM with diameter < 2.5 μm; $PM_{2.5}$abs: the soot content (absorbance) of $PM_{2.5}$; $NO_x$: sum of nitrogen monoxide and nitrogen dioxide; $NO_2$: nitrogen dioxide.

SUPPLEMENTARY DATA

**Supplementary Figure 2.** Association between HOMA-IR and quartiles of air pollutant exposure (1. quartile is reference) adjusted for age, sex, BMI, waist-hip ratio, smoking status, month of blood withdrawal, and pack-years smoked.

Diabetes subgroup

%-change in HOMA-IR

PM10    PMcoarse    PM25    PM25abs    NOx    NO2

# SUPPLEMENTARY DATA

**Supplementary Figures 3a) – d).** Absolute difference in HOMA IR with 95% CI associated with an interquartile range increase in air pollutant exposure according to the deciles of HOMA IR adjusted for age, sex, BMI, waist-hip ratio, smoking status, and pack-years smoked*.
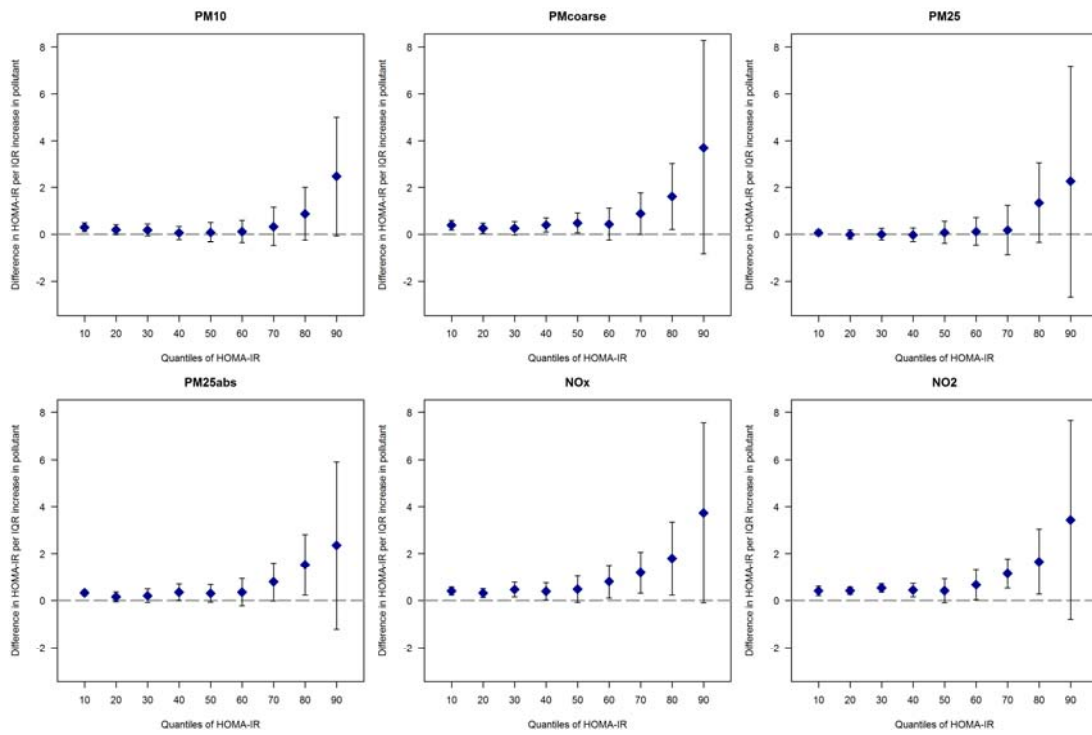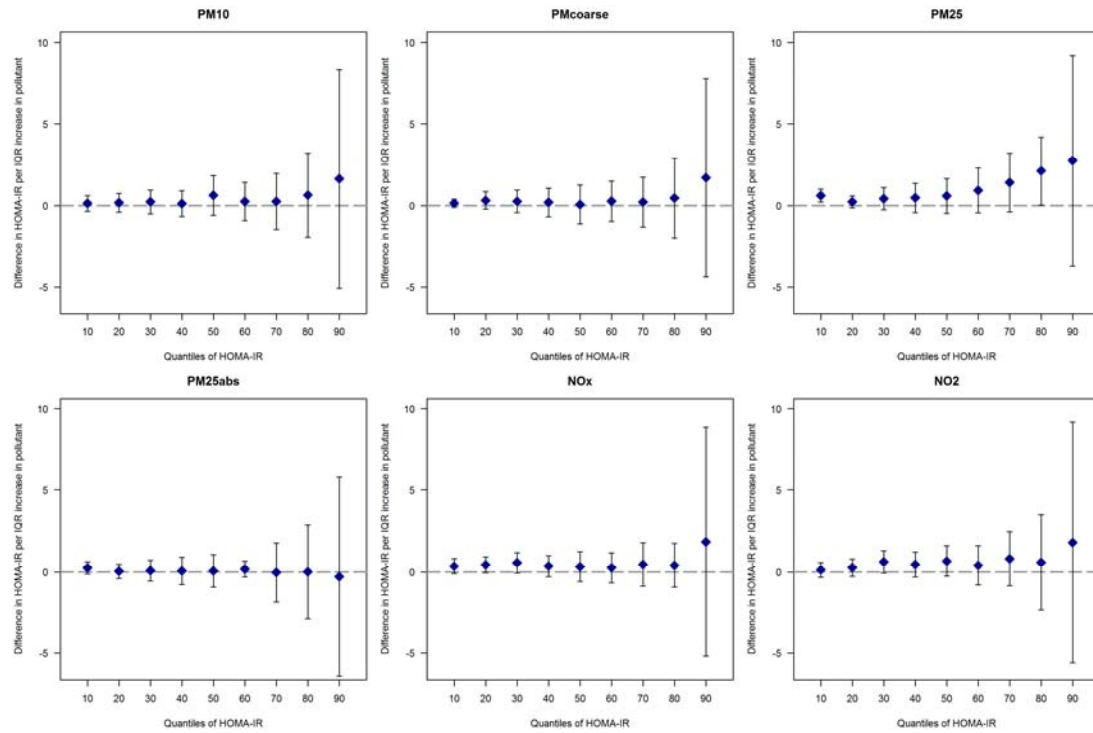
a) All participants

b) Non-diabetic participants



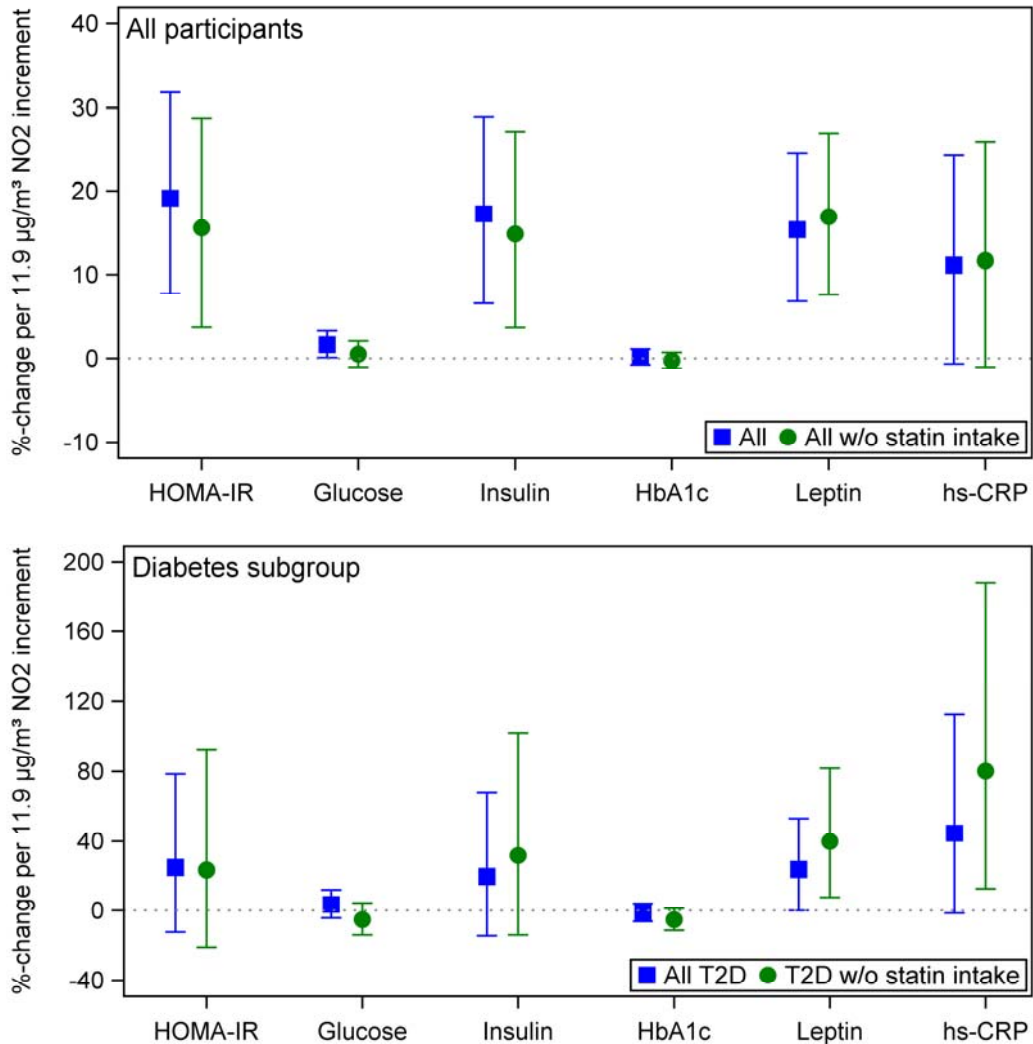c) Pre-diabetic participants

### d) Diabetic participants



*We did not adjust for month of blood withdrawal as models partly did not converge. However, the air pollutant estimates of the default used mean regression models were almost similar when adjusted or not adjusted for month.

**Supplementary Figure 4.** Association between $NO_2$ and biomarkers presented as %-change* (with 95% CI) from geometric mean per 11.9 μg/m³ increment in $NO_2$ for all participants (top) and diabetic individuals (bottom).



$NO_2$: nitrogen dioxide; HOMA-IR: homeostasis model assessment-insulin resistance; HbA1c: hemoglobin A1c; hs-CRP: high sensitivity C-reactive protein.

*Adjusted for age, sex, smoking, BMI, waist-hip ratio, month of blood withdrawal, selected socio-economic- and lifestyle variables (see Online Supplementary Table 2).