Supplemental Material

Air Pollution and Performance-Based Physical Functioning in Dutch Older Adults

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**Supplemental material, Table S1.** Land-use regression models with model performance (leave-one-out cross-validation $R^2$, $R^2_{LOOCV}$)

| Exposure | Land-use regression model                                                                 | $R^2_{LOOCV}$ |
|----------|------------------------------------------------------------------------------------------|---------------|
| NO$_2$   | -7.80 + 1.18 × REGIONALESTIMATE + 2.30 × 10$^{-5}$ × POP$_{5000}$ + 2.46 × 10$^{-6}$ × TRAFLOAD$_{50}$ + 1.06 × 10$^{-4}$ × ROADLENGTH$_{1000}$ + 9.84 × 10$^{-5}$ × HEAVYTRAFOAD$_{25}$ + 12.19 × DISTINVNEARC1 + 4.47 × 10$^{-7}$ × HEAVYTRAFOAD$_{25,500}$ | 0.81          |
| NO$_x$   | 3.25 + 0.74 × REGIONALESTIMATE + 4.22 × 10$^{-6}$ × TRAFLOAD$_{50}$ + 6.36 × 10$^{-4}$ × POP$_{1000}$ + 2.39 × 10$^{-6}$ × HEAVYTRAFOAD$_{500}$ + 71.65 × DISTINVMAJOR1 + 0.21 × MAJORROAD_LENGTH$_{25}$ | 0.82          |
| PM$_{2.5}$ abs | 0.07 + 2.95 × 10$^{-9}$ × TRAFLOAD$_{500}$ + 2.93 × 10$^{-3}$ × MAJORROAD_LENGTH$_{50}$ + 0.85 × REGIONALESTIMATE + 7.90 × 10$^{-9}$ × HLDRES$_{5000}$ + 1.72 × 10$^{-5}$ × HEAVYTRAFOAD$_{50}$ | 0.89          |
| PM$_{10}$ | 23.71 + 2.16 × 10$^{-8}$ × TRAFMAJORLOAD$_{500}$ + 6.68 × 10$^{-6}$ × POP$_{5000}$ + 0.02 × MAJORROAD_LENGTH$_{50}$ | 0.60          |
| PM$_{2.5}$ | 9.46 + 0.42 × REGIONALESTIMATE + 0.01 × MAJORROAD_LENGTH$_{50}$ + 2.28 × 10$^{-9}$ × TRAFMAJORLOAD$_{1000}$ | 0.61          |
| PM$_{coarse}$ | 7.59 + 5.02 × 10$^{-9}$ × TRAFLOAD$_{1000}$ + 1.38 × 10$^{-7}$ × PORT$_{5000}$ + 5.38 × 10$^{-5}$ × TRAFNEAR | 0.38          |

DISTINVMAJOR1: inverse distance (m$^{-1}$) to the nearest road of the local road network; DISTINVNEARC1: Inverse distance to the nearest road; HEAVYTRAFOAD$_X$: Total heavy-duty traffic load of all roads in X m buffer (sum of (heavy-duty traffic intensity * length of all segments)); HLDRES$_X$: Sum of high density and low density residential land in X m buffer; MAJORROAD_LENGTH$_X$: Road length of major roads in X m buffer; POP$_X$: Number of inhabitants in X m buffer; PORT: port in X m buffer; REGIONALESTIMATE: Regional estimate; ROADLENGTH$_X$: Road length of major roads in X m buffer; TRAFLOAD$_X$: Total traffic load of all roads in X m buffer (sum of (traffic intensity * length of all segments)); TRAFMAJORLOAD$_X$: Total traffic load of major roads in X m buffer (sum of (traffic intensity * length of all segments)); TRAFNEAR: Traffic intensity on nearest road;
**Supplementary material, Table S2.** Distribution of baseline performance scores by participant characteristics (N=1,762 participants).

| Covariate                        | Performance-based | Self-reported |
|----------------------------------|-------------------|---------------|
|                                  | N     | Mean (std) | p-value<sup>a</sup> | N     | Mean (std) | p-value<sup>a</sup> |
| Age at performance measurement  |       |           |                          |       |           |                          |
| ≤ 65 years                       | 606   | 12.8 (2.5) | <0.0001                  | 630   | 33.9 (2.8) | <0.0001                  |
| 65 – 70 years                    | 676   | 12.4 (2.8) |                          | 714   | 33.4 (3.6) |                          |
| 70 – 75 years                    | 905   | 11.9 (2.9) |                          | 946   | 33.1 (3.6) |                          |
| 75 – 80 years                    | 750   | 10.8 (3.3) |                          | 801   | 32.3 (4.2) |                          |
| 80 – 85 years                    | 559   | 9.3 (3.7)  |                          | 598   | 30.5 (5.4) |                          |
| > 85 years                       | 609   | 7.0 (3.6)  |                          | 716   | 27.0 (7.0) |                          |
| Female sex                       |       |           | <0.0001                  |       |           | <0.0001                  |
| Male                             | 1896  | 11.1 (3.3) |                           | 1985  | 32.8 (4.1) |                           |
| Female                           | 2209  | 10.5 (3.9) |                           | 2420  | 30.9 (5.8) |                           |
| Educational level                |       |           | <0.0001                  |       |           | <0.0001                  |
| Low                              | 1892  | 10.1 (3.8) |                           | 2073  | 30.8 (5.8) |                           |
| Medium                           | 1409  | 11.1 (3.6) |                           | 1494  | 32.2 (4.6) |                           |
| High                             | 804   | 11.9 (3.2) |                           | 838   | 33.3 (3.7) |                           |
| Smoking                          |       |           | 0.0009                   |       |           | <0.0001                  |
| Never smoker                     | 1264  | 10.4 (4.0) |                           | 1382  | 31.0 (5.8) |                           |
| Ex-smoker                        | 2169  | 10.9 (3.6) |                           | 2298  | 32.1 (4.6) |                           |
| Current smoker                   | 672   | 11.2 (3.3) |                           | 725   | 32.1 (5.2) |                           |
| Alcohol consumption              |       |           | <0.0001                  |       |           | <0.0001                  |
| Non drinker                      | 572   | 9.0 (4.1)  |                           | 651   | 28.8 (6.8) |                           |
| Light drinker                    | 2143  | 10.8 (3.7) |                           | 2287  | 31.8 (5.0) |                           |
| Moderate drinker                 | 1147  | 11.7 (3.2) |                           | 1209  | 33.0 (3.9) |                           |
| Excessive drinker                | 243   | 11.7 (3.3) |                           | 258   | 32.9 (3.9) |                           |
### Supplementary material, Table S2. (continued)

| Covariate                          | Performance-based |                     | Self-reported     |                     |
|------------------------------------|-------------------|---------------------|-------------------|---------------------|
|                                    | N     | Mean (std) | p-value<sup>a</sup> | N     | Mean (std) | p-value<sup>a</sup> |
| Physical activity past 2 weeks     |       |            |                   |       |            |                   |
| < 78 min/day                       | 905   | 9.9 (4.0)  | <0.0001           | 1024  | 30.0 (6.7) | <0.0001           |
| 78 – 199 min/day                   | 2126  | 11.0 (3.6) |                   | 2257  | 32.1 (4.6) |                   |
| ≥ 199 min/day                      | 1074  | 11.1 (3.5) |                   | 1124  | 32.6 (4.1) |                   |
| Depression                         |       |            | <0.0001           |       |            | <0.0001           |
| No                                 | 3572  | 11.1 (3.5) |                   | 3793  | 32.3 (4.6) |                   |
| Yes                                | 533   | 9.1 (4.1)  |                   | 612   | 28.5 (6.8) |                   |
| Chronic diseases                   |       |            | <0.0001           |       |            | <0.0001           |
| 0                                  | 979   | 12.4 (2.8) |                   | 1033  | 34.0 (2.9) |                   |
| 1                                  | 1509  | 11.3 (3.3) |                   | 1613  | 32.6 (4.1) |                   |
| 2 or more                          | 1617  | 9.4 (3.9)  |                   | 1759  | 29.6 (6.2) |                   |

<sup>a</sup> F-test taking into account the correlation between repeated observations within the same participant.
**Supplementary material, Table S3.** Residential exposure to air pollution – Pearson correlations between pollutants.

|       | NO₂  | NOₓ  | PM₂.₅ abs | PM₂.₅ | PM₁₀ | PM coarse |
|-------|------|------|-----------|-------|------|-----------|
| NO₂   | 1.00 | 0.91 | 0.88      | 0.43  | 0.87 | 0.89      |
| NOₓ   | 1.00 | 0.86 | 0.43      | 0.88  | 0.87 |           |
| PM₂.₅ abs | 1.00 | 0.69 | 0.92      | 0.36  |      |           |
| PM₂.₅ | 1.00 |      | 0.48      | 0.36  |      |           |
| PM₁₀  | 1.00 |      | 0.90      |       |      |           |
| PM coarse |      |      |           |       |      | 1.00      |
**Supplementary material, Table S4.** Distribution of daily average air pollution concentrations on the days of the physical performance test for all study participants.

| Pollutant     | Mean (SD) | Min | Median | Max | IQR |
|---------------|-----------|-----|--------|-----|-----|
| NO$_2$ ($\mu$g/m$^3$) | 18.6 (7.1) | 7.4 | 17.1   | 47.8| 11.1|
| PM$_{10}$ ($\mu$g/m$^3$) | 23.9 (10.1) | 6.7 | 21.9   | 69.0| 15.0|
Supplemental material, Table S5. Adjusted \(^a\) associations \(^b\) between performance-based physical functioning and residential air pollution exposure from linear mixed model analyses with additional adjustment for air pollution concentrations during the week preceding the performance test \(^c\).

| Pollutant | Increment | Mean difference | (95% CI)                | p-value |
|-----------|-----------|-----------------|-------------------------|---------|
| NO\(_2\)  | 8.9 \(\mu g/m^3\) | -0.22 | (-0.42; -0.02) | 0.028 |
| NO\(_x\) | 13.5 \(\mu g/m^3\) | -0.20 | (-0.36; -0.03) | 0.019 |
| PM\(_{2.5abs}\) | 0.31 \(10^{-5} m^3\) | -0.12 | (-0.29; 0.06) | 0.182 |
| PM\(_{2.5}\) | 1.4 \(\mu g/m^3\) | 0.18 | (-0.05; 0.41) | 0.130 |
| PM\(_{10}\) | 1.5 \(\mu g/m^3\) | -0.21 | (-0.36; -0.07) | 0.004 |
| PM\(_{coarse}\) | 0.8 \(\mu g/m^3\) | -0.18 | (-0.31; -0.05) | 0.008 |

\(^a\) Adjusted for age, sex, education level, smoking, alcohol consumption, depression, physical activity, area-level socio economic status defined as the status score of the four-position postcode, air pollution concentrations on the day of the performance test, and cross-products of time since baseline with education, alcohol consumption, and depression.

\(^b\) Associations are presented as mean difference in physical performance score with 95% confidence intervals (CI) for an interquartile range increase in air pollution exposure and were derived from models with exposure and exposure-time since baseline interaction.

\(^c\) Associations with NO\(_2\) and NO\(_x\) were adjusted for NO\(_2\) concentrations on the day of the test, all other associations were adjusted for PM\(_{10}\) concentrations on the day of the test.

\(^d\) N=1,676 participants, n = 4,005 observations for NO\(_2\) and NO\(_x\) and N=1,674 participants, n = 3,974 observations for all other associations due to some missings for air pollution concentrations on the test day.
Supplemental material, Table S6 Adjusted \(^a\) associations \(^b\) between physical performance (performance-based and self-reported) and residential air pollution exposure from linear mixed model analyses, restricted to participants who completed all three cycles of data collection.

| Pollutant     | Increment | Mean difference | (95% CI)     | p-value | Mean difference | (95% CI)     | p-value |
|---------------|-----------|-----------------|--------------|---------|-----------------|--------------|---------|
| NO\(_2\)      | 8.9 \(\mu g/m^3\) | -0.26           | (-0.49; -0.04) | 0.022   | 0.12            | (-0.18; 0.42) | 0.441   |
| NO\(_x\)      | 13.5 \(\mu g/m^3\) | -0.21           | (-0.40; -0.03) | 0.027   | 0.15            | (-0.10; 0.40) | 0.242   |
| PM\(_{2.5}\)abs | 0.31 \(10^{-3}m^3\) | -0.17           | (-0.37; 0.03)  | 0.092   | 0.07            | (-0.20; 0.33) | 0.610   |
| PM\(_{2.5}\)   | 1.4 \(\mu g/m^3\)   | 0.16            | (-0.11; 0.43)  | 0.251   | -0.09           | (-0.44; 0.27) | 0.627   |
| PM\(_{10}\)    | 1.5 \(\mu g/m^3\)   | -0.24           | (-0.41; -0.07) | 0.005   | 0.11            | (-0.11; 0.34) | 0.319   |
| PM\(_{coarse}\) | 0.8 \(\mu g/m^3\)    | -0.21           | (-0.36; -0.05) | 0.008   | 0.12            | (-0.08; 0.33) | 0.236   |

\(^a\) Adjusted for age, sex, education level, smoking, alcohol consumption, depression physical activity, area-level socio economic status defined as the status score of the four-position postcode, and cross-products of time since baseline with education, alcohol consumption and depression.

\(^b\) Associations are presented as mean difference in physical performance score with 95% confidence intervals (CI) for an interquartile range increase in air pollution exposure and were derived from models with exposure and exposure-time since baseline interaction.

\(^c\) N=1,022 participants, n = 3,066 observations

\(^d\) N=1,165 participants, n = 3,495 observations
**Supplemental material, Table S7.** Adjusted \(^a\) associations \(^b\) between physical performance (performance-based and self-reported) and residential air pollution exposure from linear mixed model analyses, restricted to participants who did not change address between three years prior to the 2005/2006 cycle and the last completed cycle.

| Pollutant | Increment | Performance-based \(^c\) | | | Self-reported \(^d\) | |
|---|---|---|---|---|---|---|
| | | Mean difference | (95% CI) | p-value | Mean difference | (95% CI) | p-value |
| NO\(_2\) | 8.9 µg/m\(^3\) | -0.38 | (-0.60; -0.15) | 0.001 | 0.17 | (-0.12; 0.46) | 0.252 |
| NO\(_x\) | 13.5 µg/m\(^3\) | -0.27 | (-0.46; -0.09) | 0.004 | 0.28 | (0.03; 0.52) | 0.026 |
| PM\(_{2.5}\) abs | 0.31 10\(^{-5}\)m\(^1\) | -0.25 | (-0.44; -0.05) | 0.014 | 0.06 | (-0.20; 0.31) | 0.662 |
| PM\(_{2.5}\) | 1.4 µg/m\(^3\) | 0.03 | (-0.23; 0.29) | 0.823 | -0.19 | (-0.52; 0.15) | 0.276 |
| PM\(_{10}\) | 1.5 µg/m\(^3\) | -0.29 | (-0.46; -0.13) | 0.001 | 0.14 | (-0.07; 0.36) | 0.188 |
| PM\(_{coarse}\) | 0.8 µg/m\(^3\) | -0.24 | (-0.39; -0.09) | 0.001 | 0.18 | (-0.01; 0.38) | 0.069 |

\(^a\) Adjusted for age, sex, education level, smoking, alcohol consumption, depression, physical activity, area-level socio economic status defined as the status score of the four-position postcode, and cross-products of time since baseline with education, alcohol consumption and depression.

\(^b\) Associations are presented as mean difference in physical performance score with 95% confidence intervals (CI) for an interquartile range increase in air pollution exposure and were derived from models with exposure and exposure-time since baseline interaction.

\(^c\) N=1,247 participants, n = 3,042 observations

\(^d\) N=1,287 participants, n = 3,218 observations
Supplemental material, Table 8. Post hoc sensitivity analyses of residual confounding of the association between air pollution and performance-based physical functioning due to an unmeasured binary confounder (U).

| Outcome | Performance-based physical functioning |
|---------|---------------------------------------|
| Exposure contrast | 4th vs 1st quartile of NO₂ exposure |
| Effect estimate (exposure – outcome) | -0.46 points |
| Difference in outcome per year | -0.30 points |

**Sensitivity analysis specifications and results**

*Hypothetical relation of U to cognitive outcome (U - outcome)*

| Difference in cognitive outcome, U = 1 vs U = 0 | -0.6 points | -1.5 points |
| Years apart in age associated with the same difference in outcome | 2 years | 5 years |

*Resulting relation of U to exposure required to produce the reported effect estimate*

| Difference in the prevalence of U, high vs low exposure a | 77% | 31% |
| Equivalent minimum relative odds (OR) of high exposure, U = 1 vs U = 0 b | 59.2 | 3.6 |

a For details on the method used please see Vanderweele TJ and Arah OA. 2011. Unmeasured confounding for general outcomes, treatments, and confounders: Bias formulas for sensitivity analyses. Epidemiology 22(1):42-52.

b Prevalence differences are absolute not relative differences. Given the difference in U prevalence shown, the minimum OR of high exposure is the smallest OR across all possible pairs of U prevalence.
Supplemental material, Table S9. Adjusted\(^a\) associations\(^b\) between physical performance (performance-based and self-reported) and residential air pollution exposure from linear mixed model analyses without exposure-time since baseline interaction terms.

| Pollutant | Increment  | Mean difference | (95% CI)          | p-value | Mean difference | (95% CI)          | p-value |
|-----------|------------|-----------------|-------------------|---------|-----------------|-------------------|---------|
| NO\(_2\)  | 8.9 μg/m\(^3\) | -0.22           | (-0.40; -0.04)    | 0.014   | 0.21            | (-0.06; 0.47)     | 0.121   |
| NO\(_x\)  | 13.5 μg/m\(^3\) | -0.17           | (-0.32; -0.02)    | 0.022   | 0.23            | (0.01; 0.46)      | 0.037   |
| PM\(_{2.5}\) abs | 0.31 \(10^{-5}\) m\(^-1\) | -0.12           | (-0.27; 0.04)     | 0.142   | 0.10            | (-0.14; 0.33)     | 0.413   |
| PM\(_{2.5}\)  | 1.4 μg/m\(^3\) | 0.08            | (-0.13; 0.28)     | 0.456   | -0.16           | (-0.46; 0.15)     | 0.311   |
| PM\(_{10}\)   | 1.5 μg/m\(^3\) | -0.19           | (-0.32; -0.06)    | 0.005   | 0.17            | (-0.03; 0.36)     | 0.096   |
| PM\(_{coarse}\) | 0.8 μg/m\(^3\) | -0.16           | (-0.29; -0.04)    | 0.008   | 0.20            | (0.02; 0.38)      | 0.031   |

\(^a\) Adjusted for age, sex, education level, smoking, alcohol consumption, depression, physical activity, area-level socio economic status defined as the status score of the four-position postcode, and cross-products of time since baseline with education, alcohol consumption and depression.

\(^b\) Associations are presented as mean difference in physical performance score with 95% confidence intervals (CI) for an interquartile range increase in air pollution exposure.

\(^c\) N=1,695 participants, n = 4,105 observations

\(^d\) N=1,758 participants, n = 4,405 observations
Supplemental material, Figure S1. Flow-chart of the study sample.

LASA participants 2005/2006 measurement cycle: 
N = 2,165

Estimated air pollution levels at 2005/2006 measurement cycle home address: 
N = 2,133

Physical functioning data from the 2005/2006, 2008/2009 and/or 2011/12 measurement cycles: 
N = 1,937

Complete data on potential confounders from 2005/2006 cycle: 
N = 1,762

| Measurement Cycle | Performance-based physical functioning: | N | Self-reported physical functioning: |
|-------------------|----------------------------------------|---|-----------------------------------|
| 2005/2006         |                                        | 1,616 | 1,746 |
| 2008/2009         |                                        | 1,366 | 1,455 |
| 2011/2012         |                                        | 1,123 | 1,204 |
Supplemental material, Figure S2. Adjusted associations between self-reported physical functioning and quartiles of residential air pollution exposure from linear mixed model analyses with p-values of F-tests for equality of means and trend tests using quartile midpoints (N=1,758 participants, n=4,405 observations).
Adjusted for age, sex, education level, smoking, alcohol consumption, depression, physical activity, area-level socio economic status defined as the status score of the four-position postcode, and cross-products of time since baseline with education, alcohol consumption and depression.

Associations are presented as mean difference in physical performance score in the different quartiles as compared to the 1st quartile with 95% confidence intervals and were derived from models with exposure and exposure-time since baseline interaction.
**Supplemental material, Figure S3.** Adjusted\(^a\) **sex-specific associations** \(^b\) between performance-based physical functioning and residential air pollution exposure from linear mixed model analyses with exposure-sex interaction terms (N=1,735 participants, n=4,039 observations). Grey dots represent females, white dots represent males.

\(^a\) Adjusted for age, education level, smoking, alcohol consumption, depression, physical activity, area-level socio economic status defined as the status score of the four-position postcode, and cross-products of time since baseline with education, alcohol consumption and depression.

\(^b\) Associations are presented as mean difference in physical performance score with 95% confidence intervals (CI) for an interquartile range increase in air pollution exposure and were derived from models with exposure and exposure-time since baseline interaction.