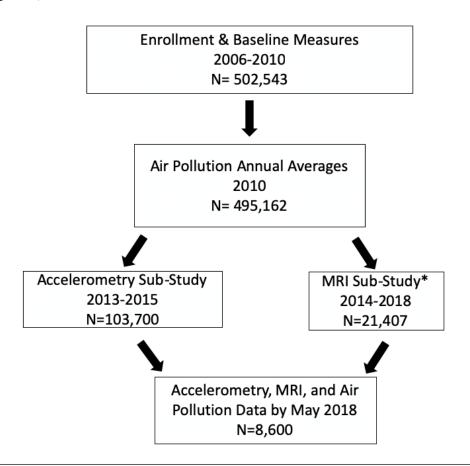
eFigure 1, Timeline of Instrument Collection and N's



\*MRI Measurements are ongoing. The latest measurement date as of the data download for this study, was May 2018

e Figure 2, Correlation Matrix of NO2 Measures Over Time

|                      | NO <sub>2</sub> | NO <sub>2</sub> | NO <sub>2</sub> | NO <sub>2</sub> |
|----------------------|-----------------|-----------------|-----------------|-----------------|
|                      | 2005            | 2006            | 2007            | 2010            |
| NO <sub>2</sub> 2005 | 1               | 0.99            | 0.98            | 0.87            |
| NO <sub>2</sub> 2006 |                 | 1               | 0.98            | 0.88            |
| NO <sub>2</sub> 2007 |                 |                 | 1               | 0.85            |
| NO <sub>2</sub> 2010 |                 |                 |                 | 1               |

## Legend

| 2363.13 |                         |  |  |  |
|---------|-------------------------|--|--|--|
|         | Both estimates via EU-  |  |  |  |
|         | wide air pollution maps |  |  |  |
|         | 2010 estimate via       |  |  |  |
|         | ESCAPE                  |  |  |  |

eTable 1a Sensitivity Analyses of Main Effects of Associations of NO2 and PM2.5 with Gray Matter Volume: Household income, Time between Imaging and Air Pollution, PA Season Measurement

|                   | Model 1   | Model 2  | Model 3   |
|-------------------|---|--|---|
|                   | standard set of covariates & sample reported in Table 2 N=8,600 | Restricting to population with household income data, controlling for standard set of covariates N=7,870 | Model 2, and controlling for time between imaging and air pollution, season, household income N=7,870 |
| NO <sub>2</sub>   | -0.042 (-0.068, -0.016)   | -0.036 (-0.063, -0.009)  | -0.034 (-0.061, -0.007)   |
| PM <sub>2.5</sub> | -0.033 (-0.052, -0.007)   | -0.029 (-0.051, -0.006)  | -0.025 (-0.048, -0.002)   |

eTable 1b Sensitivity Analyses of Main Effects of Associations Between NO2 and PM2.5 with Gray Matter Volume: Adjustments for BMI, Alcohol Intake, Smoking, and Other Medical Conditions

|                   |                     | ,                       | <u> </u>                     |                               |
|-------------------|---------------------|-------------------------|------------------------------|-------------------------------|
|                   | Model 1             | Model 2                 | Model 3                      | Model 4                       |
|                   | standard set of     | Restricting to sample   | Model 2, and controlling for | Model 3, and controlling for  |
|                   | covariates & sample | with smoking, BMI,      | BMI, Alcohol, and smoking    | history of heart attack, high |
|                   | reported in Table 2 | and alcohol intake      | N=8,456                      | blood pressure, and diabetes, |
|                   | N=8,600             | N=8,456                 |                              | and excluding those with any  |
|                   |                     |                         |                              | dementia                      |
|                   |                     |                         |                              | N=8,393                       |
| NO <sub>2</sub>   | -0.042 (-0.068, -   | -0.038 (-0.064, -0.011) | -0.034 (-0.060, -0.008)      | -0.037 (-0.063, -0.010)       |
| NO <sub>2</sub>   | 0.016)              |                         |                              |                               |
| DNA               | -0.033 (-0.052, -   | -0.031 (-0.053, -0.008) | -0.029 (-0.051, -0.007)      | -0.029 (-0.051, -0.006)       |
| PM <sub>2.5</sub> | 0.007)              |                         |                              |                               |

eTable 2a Sensitivity Analyses of Interaction Models: Associations of  $NO_2$  and  $PM_{2.5}$  absorbance with white matter hyperintensity volume, among participants with >30 minutes/week of vigorous physical activity: Household income, Time between Imaging and Air Pollution, PA Season Measurement

|                  | Model 1                | Model 2                           | Model 3  | Model 4                               |
|------------------|------------------------|-----------------------------------|--|---------------------------------------|
|                  | sample reported in     | Restricting to sample with        | Model 2 + controlling for times between imaging  | Model 3, but restricted to those with |
|                  | Table 3 & standard set | household income data and with    | and accelerometry, and imaging and air pollution | white matter hyperintensities<2.5 sd  |
|                  | of covariates          | acceleration before brain imaging | measurements, + season +household income         | above the mean                        |
|                  | N= 8,016               | N=6,549                           | N=6,549  | N=6,502                               |
| NO2              | 0.063 (0.015, 0.111)   | 0.064 (0.011, 0.117)              | 0.058 (0.006, 0.109)                             | 0.056 (0.005, 0.106)                  |
| PM2.5 absorbance | 0.071 (0.025, 0.116)   | 0.072 (0.022, 0.122)              | 0.065 (0.015, 0.115)                             | 0.060 (0.011, 0.109)                  |

eTable 2b Sensitivity Analyses of Interaction Models: Associations of NO<sub>2</sub> and PM<sub>2.5</sub> absorbance with white matter hyperintensity volume, Adjustments for BMI, Alcohol Intake, Smoking, and Other Medical Conditions

|            | Model 1                | Model 2                          | Model 3  | Model 4  |
|------------|------------------------|----------------------------------|--|--|
|            | Sample reported in     | Restricting to sample with       | Model 2, and controlling for BMI, Alcohol, and | Model 3, and controlling for history of heart  |
|            | Table 3 & standard set | smoking, BMI, and alcohol intake | smoking  | attack, high blood pressure, and diabetes, and |
|            | of covariates          | N=7,881                          | N=7,881  | excluding those with any dementia              |
|            | N= 8,016               |                                  |  | N=7,881  |
| NO2        | 0.063 (0.015, 0.111)   | 0.063 (0.015, 0.111)             | 0.061 (0.014, 0.109)                           | 0.049 (0.002, 0.096)                           |
| PM2.5      | 0.071 (0.025, 0.116)   | 0.075 (0.030, 0.120)             | 0.065 (0.021, 0.110)                           | 0.063 (0.019, 0.107)                           |
| absorbance |                        |                                  |  |  |

eTable 3 Associations of Air Pollution with Grey Matter Volume (N=8,600) and White Matter Hyperintensity Volume (n=8,016), by Age Categories

|                      | Age category  | Beta coefficients for Air | Beta coefficients for Air Pollution with |
|----------------------|---------------|---------------------------|--|
|                      |               | Pollution with Grey       | White Matter Hyperintensity Volume,      |
|                      |               | Matter Volume, by Age     | by Age                                   |
| PM <sub>2.5-10</sub> | <50           | -0.053 (-0.086, -0.020)   | 0.049 ( 0.012, 0.086)                    |
|                      | 50-60         | 0.012 (-0.014, 0.037)     | -0.024 (-0.053, 0.004)                   |
|                      | 61+           | -0.011 (-0.038, 0.016)    | -0.021 ( -0.052, 0.010)                  |
|                      | p-interaction | .01                       | .01                                      |

These effect estimates represent beta coefficients for associations of PM2.5-10 with grey matter and white matter hyperintensity volume by age. None of the other AP measures had measurable interactions with Age on any structural brain volume outcomes.