Residential Surrounding Greenness and Cognitive Decline: A 10-Year Follow-up of the Whitehall II Cohort

Carmen de Keijzer, Cathryn Tonne, Xavier Basagaña, Antònia Valentín, Archana Singh-Manoux, Jordi Alonso, Josep Maria Antó, Mark J. Nieuwenhuijsen, Jordi Sunyer, and Payam Dadvand

Table of Contents

Figure S1. Geographical distribution of the study population at three follow-ups.

Table S1. Information on the exposure assessment: NDVI and EVI images used for the exposure assessment and information on missing values.

Table S2. Description of Multiple Imputation.

Table S3. Comparison between participants with complete data and participants with a missing value for at least one covariate. Median global cognition z-score and NDVI (1st quartile, 3rd quartile).

Table S4. Correlations between A. NDVI in the 500 meter buffers at different follow-ups and B. between different NDVI and EVI in different buffer sizes.

Table S5. Sensitivity analyses. Difference (95% confidence interval) in global cognition and cognitive sub- z-scores at baseline and after 10 years of follow-up in association with a one interquartile range increase in residential surrounding greenness (NDVI).

Table S6. Sensitivity analyses - further adjustment for neighborhood factors. Difference (95% confidence interval) in global cognition z score at baseline and after 10 years of follow-up in association with a one interquartile range increase in residential surrounding greenness (NDVI).

Table S7. Sensitivity analysis – Inverse probability weighting. Difference (95% confidence interval) in global cognition z score over 10 years associated with a one interquartile range increase in residential surrounding greenness (NDVI).

Table S8. Difference (95% confidence interval) in global cognition and cognitive sub- z scores at baseline and after 10 years of follow-up in association with a one interquartile range increase in residential surrounding greenness (EVI).
Figure S 1. Geographical distribution of the study population at three follow-ups

Distribution of the study population over the UK

1997 - 1999  2002-2004  2007-2009
Table S1. Information on the exposure assessment: NDVI and EVI images used for the exposure assessment and information on missing values

| Follow-up  | Date image NDVI & EVI       | % cloud cover | 500 m buffer | 1000 m buffer |
|------------|-----------------------------|---------------|--------------|---------------|
| 1997-1999  | 24/05/2000 - 08/06/2000      | 23            | 97.94        | 96.23         |
| 2002-2004  | 25/05/2003 - 09/06/2003      | 23            | 97.60        | 94.85         |
| 2007-2009  | 24/05/2008 - 08/06/2008      | 7             | 96.62        | 94.16         |

Table S2. Description of Multiple Imputation

**Software used and key setting:** STATA 12 software (Stata Corporation, College Station, Texas) – Ice command (with 10 cycles)

**Number of imputed datasets created:** 25

**Variables included in the imputation procedure:**

**Variables used in the main analyses (complete observations of outcome and exposure, and covariates which could have missing values) together with other relevant covariates:**

A cognitive score (global cognition, reasoning, fluency or short-term memory score), age, gender, ethnicity, marital status, educational attainment, household assets (including house), employment grade, IMD income domain, smoking, alcohol consumption, general health questionnaire depression subscale, network score, social support of close person 1, physical activity level, general health status, average PM$_{2.5}$ in a 1000m buffer in year of follow-up, average PM$_{10}$ in a 1000m buffer in year of follow-up, and a greenness indicator (NDVI in the direct neighborhood or EVI in the direct neighborhood)

**Treatment of non-normally distributed variables:** matching.

**Treatment of binary/categorical variables:** logistic models.

**Statistical interactions included in imputation models:** none.
Table S 3. Comparison between participants with complete data and participants with a missing value for at least one covariate. Median global cognition z-score and NDVI (1st quartile, 3rd quartile)

|                | Participants with complete data on covariates | Participants with at least one missing value for a covariate | p-value* |
|----------------|-----------------------------------------------|-------------------------------------------------------------|----------|
| **1997-1999**  |                                               |                                                             |          |
| Global cognition z-score | 0.097 (-0.571, 0.712)                      | -0.261 (-1.142, 0.373)                                    | <0.001   |
| NDVI (500 m buffer) | 0.588 (0.502, 0.671)                         | 0.547 (0.454, 0.629)                                      | <0.001   |
| NDVI (1000 m buffer) | 0.598 (0.516, 0.683)                          | 0.558 (0.467, 0.641)                                      | <0.001   |
| **2002-2004**  |                                               |                                                             |          |
| Global cognition z-score | -0.135 (-0.753, 0.478)                      | -0.728 (-1.575, 0.054)                                    | <0.001   |
| NDVI (500 m buffer) | 0.604 (0.513, 0.698)                          | 0.574 (0.477, 0.658)                                      | <0.001   |
| NDVI (1000 m buffer) | 0.612 (0.522, 0.708)                          | 0.580 (0.485, 0.676)                                      | <0.001   |
| **2007-2009**  |                                               |                                                             |          |
| Global cognition z-score | -0.296 (-0.920, 0.299)                      | -0.740 (-1.594, -0.066)                                   | <0.001   |
| NDVI (500 m buffer) | 0.631 (0.546, 0.715)                          | 0.601 (0.511, 0.686)                                      | <0.001   |
| NDVI (1000 m buffer) | 0.642 (0.558, 0.727)                          | 0.608 (0.520, 0.701)                                      | <0.001   |

* Mann-Whitney test
Table S 4. Correlations between A. NDVI in the 500 meter buffers at different follow-ups and B. between different NDVI and EVI in different buffer sizes

| A. | NDVI 500m | 1997 – 1999 | 2002-2004 | 2007-2009 |
|----|-----------|-------------|-----------|-----------|
| 1997 – 1999 | 1 | | | |
| 2002-2004 | 0.690* | 1 | | |
| 2007-2009 | 0.686* | 0.810* | 1 | |

| B. | 1997-1999 | NDVI 500m | NDVI 1000m | EVI 500m | EVI 1000m |
|----|-----------|-----------|-----------|---------|-----------|
| NDVI 500m | 1 | | | | |
| NDVI 1000m | 0.957* | 1 | | | |
| EVI 500m | 0.896* | 0.867* | 1 | | |
| EVI 1000m | 0.865* | 0.912* | 0.954* | 1 | |

*p<0.001*
Table S 5. Sensitivity analyses. Difference (95% confidence interval) in global cognition and cognitive sub- scores at baseline and after 10 years of follow-up in association with a one interquartile range increase in residential surrounding greenness (NDVI).

|                  | NDVI (500 m buffer) | NDVI (1000 m buffer) |
|------------------|---------------------|----------------------|
|                  | N                   | Baseline             | Decline   | N                   | Baseline             | Decline   |
| Global score     |                     |                      |           |                     |                      |           |
| Main model       | 6387                | -0.012 (0.003, 0.037)| -0.011 (0.003, 0.039) | 5931                | 0.011 (0.003, 0.037) | 0.010 (0.003, 0.039) |
| A) No multiple imputation | 5931 | -0.007 (0.031) | 0.001 (0.023) | -0.010 (0.031) | 0.010 (0.023) |
| B) Excluding rural areas | 5655 | -0.008 (0.031) | 0.019 (0.020) | -0.011 (0.032) | 0.017 (0.021) |
| C) Only England | 6273                | -0.003 (0.040) | 0.014 (0.020) | -0.006 (0.040) | 0.013 (0.022) |
| D) Excluding non-white | 5844 | -0.006 (0.033) | 0.015 (0.024) | -0.008 (0.034) | 0.014 (0.026) |
|                  |                     | (0.007, 0.042)      |           | (0.007, 0.045)      | |
| Sub-scores       |                     |                      |           |                     |                      |           |
| Reasoning        |                     |                      |           |                     |                      |           |
| Main model       | 6411                | 0.021 (0.003, 0.038)| 0.033 (0.009, 0.041) | 5946                | 0.021 (0.003, 0.038) | 0.034 (0.003, 0.042) |
| A) No multiple imputation | 5946 | 0.003 (0.039) | 0.023 (0.019) | 0.015 (0.054) | 0.015 (0.023) |
| B) Excluding rural areas | 5676 | 0.003 (0.043) | 0.019 (0.021) | 0.017 (0.060) | 0.005 (0.041) |
| C) Only England | 6297                | 0.001 (0.037) | 0.019 (0.022) | 0.014 (0.053) | 0.008 (0.041) |
| D) Excluding non-white | 5863 | 0.001 (0.037) | 0.006 (0.038) | 0.010 (0.050) | 0.007 (0.041) |
|                  |                     | (0.006, 0.040)      |           | (0.006, 0.041)      | |
| Fluency          |                     |                      |           |                     |                      |           |
| Main model       | 6415                | -0.018 (0.002, 0.040) | 0.015 (0.004, 0.044) | 5952                | -0.004 (0.041) | 0.015 (0.025) |
| A) No multiple imputation | 5952 | -0.004 (0.041) | 0.021 (0.021) | -0.010 (0.036) | 0.015 (0.025) |
| B) Excluding rural areas | 5681 | -0.003 (0.045) | -0.001 (0.021) | -0.012 (0.040) | 0.002 (0.046) |
| C) Only England | 6301                | -0.003 (0.040) | 0.019 (0.021) | -0.007 (0.039) | 0.004 (0.045) |
| D) Excluding non-white | 5866 | -0.005 (0.038) | 0.016 (0.025) | 0.015 (0.029) | 0.008 (0.050) |
|                  |                     | (0.005, 0.045)      |           | (0.005, 0.048)      | |
| Short-term memory|                     |                      |           |                     |                      |           |
| Main model       | 6413                | -0.008 (0.003, 0.022) | -0.017 (0.007, 0.020) | 5946                | -0.035 (0.018) | -0.045 (0.011) |
| A) No multiple imputation | 5946 | -0.008 (0.020) | -0.014 (0.024) | -0.014 (0.026) | -0.037 (0.017) |
| B) Excluding rural areas | 5679 | -0.007 (0.023) | -0.003 (0.026) | -0.014 (0.017) | -0.011 (0.018) |
| C) Only England | 6299                | -0.004 (0.021) | -0.014 (0.023) | -0.014 (0.015) | -0.038 (0.017) |
| D) Excluding non-white | 5862 | -0.026 (0.029) | -0.007 (0.030) | -0.036 (0.022) | -0.031 (0.025) |

All estimates are from linear mixed effect models that included NDVI, age, age squared, age x NDVI, gender, ethnicity (white, non-white), marital status (married/cohabiting, yes or no), alcohol use (frequency of consumption in the year prior to filling in the questionnaire; sometimes, daily, or never), diet (intake of fruit and vegetables; daily or less than daily), smoking status (current, past, or never), education (lower secondary school or less, higher secondary school, and university or higher), employment grade (high, middle, or low), and the Index of Multiple Deprivation (IMD) income and employment scores.
Table S 6. Sensitivity analyses - further adjustment for neighborhood factors. Difference (95% confidence interval) in global cognition z score at baseline and after 10 years of follow-up in association with a one interquartile range increase in residential surrounding greenness (NDVI).

|                                | NDVI (500 m buffer) |                     | NDVI (1000 m buffer) |                     |
|--------------------------------|----------------------|---------------------|----------------------|---------------------|
|                                | Baseline  | Difference           | Baseline  | Difference           |
| **Main model**                 |           |                      |          |                      |
|                                | 0.012     | 0.020               | 0.011     | 0.021               |
|                                | (-0.007, 0.031) | (0.003, 0.037)     | (-0.010, 0.031) | (0.003, 0.039)     |
| **IMD**                        |           |                      |          |                      |
| Crime                          | 0.013     | 0.020               | 0.011     | 0.021               |
|                                | (-0.006, 0.033) | (0.003, 0.037)     | (-0.009, 0.034) | (0.004, 0.039)     |
| Barriers to housing and services score | 0.012     | 0.020               | 0.011     | 0.021               |
|                                | (-0.007, 0.031) | (0.003, 0.037)     | (-0.010, 0.031) | (0.004, 0.039)     |
| **Land use**                   |           |                      |          |                      |
| Road area density              | 0.015     | 0.020               | 0.015     | 0.022               |
|                                | (-0.007, 0.037) | (0.003, 0.038)     | (-0.010, 0.039) | (0.004, 0.040)     |
| Path area density              | 0.014     | 0.020               | 0.014     | 0.022               |
|                                | (-0.005, 0.034) | (0.003, 0.038)     | (-0.007, 0.035) | (0.004, 0.040)     |
| Domestic building density      | 0.015     | 0.020               | 0.014     | 0.022               |
|                                | (-0.006, 0.035) | (0.004, 0.038)     | (-0.009, 0.037) | (0.004, 0.040)     |
| Non-domestic building density  | 0.013     | 0.020               | 0.012     | 0.022               |
|                                | (-0.008, 0.034) | (0.003, 0.038)     | (-0.011, 0.034) | (0.004, 0.040)     |

All estimates are from linear mixed effect models that included NDVI, age, age squared, age x NDVI, gender, ethnicity (white, non-white), marital status (married/cohabiting, yes or no), alcohol use (frequency of consumption in the year prior to filling in the questionnaire; sometimes, daily, or never), diet (intake of fruit and vegetables; daily or less than daily), smoking status (current, past, or never), education (lower secondary school or less, higher secondary school, and university or higher), employment grade (high, middle, or low), and the Index of Multiple Deprivation (IMD) income and employment scores.
Table S 7. Sensitivity analysis – Inverse probability weighting. Difference (95% confidence interval) in global cognition z score over 10 years associated with a one interquartile range increase in residential surrounding greenness (NDVI).

|                     | NDVI (500 m buffer) | NDVI (1000 m buffer) |
|---------------------|---------------------|----------------------|
|                     | Baseline           | Difference           | Baseline           | Difference           |
| **Main analysis**   |                     |                      |                     |                      |
| Fully adjusted      | 0.012 (-0.007, 0.031) | 0.019 (0.002, 0.037) | 0.011 (-0.010, 0.032) | 0.020 (0.002, 0.038) |
| model               |                     |                      |                     |                      |
| **Weighted analyses** |                   |                      |                     |                      |
| Weights A)         | 0.010 (-0.010, 0.030) | 0.019 (0.000, 0.037) | 0.008 (-0.014, 0.030) | 0.019 (-0.001, 0.039) |
| Weights B)         | 0.008 (-0.012, 0.028) | 0.018 (-0.001, 0.036) | 0.006 (-0.017, 0.028) | 0.017 (-0.003, 0.037) |

\(^a\) Analysis restricted to those with a baseline observation for global cognition (N=5850)

(A) weights based on the inverse of the probability of completing the study
(B) weights based on the inverse of the probability of having complete data on cognitive scores

All estimates are from linear mixed effect models that included NDVI, age, age squared, age x NDVI, gender, ethnicity (white, non-white), marital status (married/cohabiting, yes or no), alcohol use (frequency of consumption in the year prior to filling in the questionnaire; sometimes, daily, or never), diet (intake of fruit and vegetables; daily or less than daily), smoking status (current, past, or never), education (lower secondary school or less, higher secondary school, and university or higher), employment grade (high, middle, or low), and the Index of Multiple Deprivation (IMD) income and employment scores.

Table S 8. Difference (95% confidence interval) in global cognition and cognitive sub-z scores at baseline and after 10 years of follow-up in association with a one interquartile range increase in residential surrounding greenness (EVI).

|                     | EVI (500 m buffer) | EVI (1000 m buffer) |
|---------------------|---------------------|----------------------|
|                     | Baseline           | Difference           | Baseline           | Difference           |
| **Global score**    |                     |                      |                     |                      |
| Global cognition    | 0.009 (-0.009, 0.026) | 0.020 (0.004, 0.036) | 0.003 (-0.016, 0.022) | 0.020 (0.003, 0.037) |
| **Sub-scores**      |                     |                      |                     |                      |
| Reasoning           | 0.003 (-0.013, 0.019) | 0.018 (0.004, 0.033) | 0.009 (-0.009, 0.027) | 0.019 (0.003, 0.034) |
| Fluency             | 0.009 0.023        |                      | 0.004 0.025        |                      |
| Short-term memory   | (-0.010, 0.029)    | (-0.005, 0.041)     | (-0.018, 0.025)    | (0.006, 0.045)      |
|                     | (-0.023, 0.026)    | (-0.027, 0.022)     | (-0.035, 0.017)    | (-0.034, 0.017)     |

All estimates are from linear mixed effect models that included EVI, age, age squared, age x EVI, gender, ethnicity (white, non-white), marital status (married/cohabiting, yes or no), alcohol use (frequency of consumption in the year prior to filling in the questionnaire; sometimes, daily, or never), diet (intake of fruit and vegetables; daily or less than daily), smoking status (current, past, or never), education (lower secondary school or less, higher secondary school, and university or higher), employment grade (high, middle, or low), and the Index of Multiple Deprivation (IMD) income and employment scores.