

Note to readers with disabilities: *EHP* strives to ensure that all journal content is accessible to all readers. However, some figures and Supplemental Material published in *EHP* articles may not conform to [508 standards](#) due to the complexity of the information being presented. If you need assistance accessing journal content, please contact ehpsubmissions@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

Supplemental Material

Midlife Residential Greenness and Late-Life Cognitive Decline among Nurses' Health Study Participants

Marcia Pescador Jimenez, Maude Wagner, Francine Laden, Jaime E. Hart, Francine Grodstein, and Peter James

Table of Contents

Table S1. Demographic characteristics and green space exposure of Nurses' Health Study participants with complete information on the outcome cognitive function and cognitive decline, and initial cohort invited to participate in the study of cognitive function.

Table S2. Association between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, further adjusting for Physical Activity and Body Mass Index (n=16,962).

Table S3. Association between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, at a 1230m buffer (n=16,962).

Table S4. Association between annual average greenness at midlife (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, at a 270m buffer (n=16,962).

Table S5. Association between annual average greenness in the immediate year prior to the first cognitive assessment (NDVI) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study (n=16,861).

Table S6. Association between annual average greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) excluding participants in the lowest 10% of the distribution of cognitive performance in the Nurses' Health Study, at a 270m buffer (n=15,478).

Table S7. Association between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) removing participants who had just moved to the address for less than 2 years (N=13,945) and who changed their address during the follow-up period (N=13,588), Nurses' Health Study, at a 270m buffer.

Table S8. Longitudinal association between midlife exposure to greenness (NDVI, 1986-1994) and cognitive decline (1995-2008) among women in the Nurses' Health Study, at a 1230m buffer (n=16,962).

Table S9. Longitudinal association between annual average greenness at midlife (NDVI, 1986-1994) and cognitive decline (1995-2008) among women in the Nurses' Health Study, at a 270m buffer (n=16,962).

Table S10. Longitudinal association between annual greenness in the immediate year prior to the first cognitive assessment (NDVI) and cognitive decline (1995-2008) among women in the Nurses' Health Study (n=16,861).

Table S11. Longitudinal association between annual average greenness (NDVI, 1986-1994) and cognitive decline (1995-2008) excluding participants in the lowest 10% of the distribution of cognitive performance in the Nurses' Health Study, at a 270m buffer (n=15,478).

Table S12. Longitudinal association between midlife exposure to greenness (NDVI, 1986-1994) and cognitive decline (1995-2008) excluding participants who had just moved to the address for less than 2 years (N=13,945) or who changed their address during the follow-up period (N=13,588), Nurses' Health Study, at a 270m buffer.

Table S13. Association of midlife exposure to greenness (NDVI, 1986-1994) with baseline cognitive function and cognitive decline of global cognition (1995-2008), stratified by: neighborhood socioeconomic status, population density, and apolipoprotein E ϵ 4 (apoE ϵ 4) carriers, the Nurses' Health Study (n=16,962).

Table S14. Association of midlife exposure to greenness (NDVI, 1986-1994) with baseline cognitive function and cognitive decline of global cognition (1995-2008), stratified by: apolipoprotein E ϵ 4 (apoE ϵ 4) carriers, restricted to women without any APOE- ϵ 2 allele, the Nurses' Health Study (n=15,709).

Figure S1. Study timeline.

Figure S2. Directed Acyclic Graph of the hypothesized association.

Figure S3. Non-linear associations between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, at a 270m buffer.

Figure S4. Estimated trajectories of global cognition over time for the lowest and highest midlife exposure to greenness (NDVI, 1986-1994) among women in the Nurses' Health Study (n=16,962).

Additional File- Excel Document

Table S1. Demographic characteristics and green space exposure of Nurses' Health Study participants with complete information on the outcome cognitive function and cognitive decline, and initial cohort invited to participate in the study of cognitive function.

	Initial sample (n=19,395)	Analytical Sample ^a (n=16,962)
Age, mean, y	74.26 ± 2.30	74.23 ± 2.29
Participant's Education, % (n)		
Bachelor's degree	16.45 (3,190)	16.44 (2,789)
Master's or Doctoral degree	5.68 (1102)	5.84 (990)
Husband's Education, % (n)		
Some High School	4.97 (963)	5.11 (866)
High School graduate	33.80 (6,555)	34.24 (5,807)
College graduate	21.61 (4,191)	22.04 (3,738)
Graduate school	15.83 (3,071)	15.96 (2,707)
Missing	21.60 (4,190)	20.43 (3,466)
Marital Status, married, % (n)	69.65 (13,508)	70.76 (12,003)
Low mental health score, % (n)	3.94 (764)	3.82 (648)
Antidepressant use, % (n)	4.79 (929)	5.67 (961)
APOE-ε4 carriers (at least one allele), % (n) ^b	6.23 (1,209)	7.02 (1,190)
Census tract median income	44,049 ± 16,240	43,787 ± 15,949
Census tract home value	126,847 ± 88,366	125,122 ± 85,882
Population density (num per sq km)	1,308.47 ± 2,751.27	1,302.87 ± 2,790.52

Values are expressed as mean ±SD, unless otherwise specified.

^aThis sample includes participants with complete information on cognitive function score.

^bApolipoprotein E (APOE)-ε4.

Table S2. Association between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, further adjusting for Physical Activity and Body Mass Index (n=16,962)^a

Models^b	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition (N=16,168)	0.02 (0.01, 0.04)
Verbal Memory (N=16,168)	0.01 (-0.01, 0.02)

^a NDVI – Normalized Difference Vegetation Index

^b Linear mixed models were used, including an intercept that represents the mean cognitive level at baseline.

Table S3. Association between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, at a 1230m buffer (n=16,962) ^a

Models^b	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.02 (0.01, 0.04)
Plus socio-economic indicators	0.03 (0.02, 0.04)
Plus neighborhood socioeconomic indicators	0.03 (0.02, 0.05)
Plus depression + antidepressants	0.03 (0.02, 0.04)
Verbal Memory	
Age-adjusted	0.01 (-0.004, 0.02)
Plus socio-economic indicators	0.01 (-0.001, 0.02)
Plus neighborhood socioeconomic indicators	0.01 (0.003, 0.03)
Plus depression + antidepressants	0.01 (-0.0002, 0.03)

^a NDVI – Normalized Difference Vegetation Index

^b Linear mixed models were used, including an intercept that represents the mean cognitive level at baseline.

Table S4. Association between annual average greenness at midlife (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, at a 270m buffer (n=16,962)^a

Models ^b	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.03 (0.02, 0.04)
Plus socio-economic indicators	0.03 (0.02, 0.04)
Plus neighborhood socioeconomic indicators	0.03 (0.02, 0.04)
Plus depression + antidepressant use *	0.03 (0.02, 0.04)
Verbal memory	
Age-adjusted	0.02 (0.01, 0.03)
Plus socio-economic indicators	0.02 (0.01, 0.03)
Plus neighborhood socioeconomic indicators	0.02 (0.01, 0.03)
Plus depression + antidepressant use	0.02 (0.01, 0.03)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline.

Table S5. Association between annual average greenness in the immediate year prior to the first cognitive assessment (NDVI) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study (n=16,861)^a

Models ^b	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.03 (0.02, 0.04)
Plus socio-economic indicators	0.03 (0.02, 0.04)
Plus neighborhood socioeconomic indicators	0.03 (0.02, 0.04)
Plus depression + antidepressant use *	0.03 (0.02, 0.04)
Verbal memory	
Age-adjusted	0.01 (-0.004, 0.02)
Plus socio-economic indicators	0.01 (-0.003, 0.02)
Plus neighborhood socioeconomic indicators	0.01 (-0.01, 0.02)
Plus depression + antidepressant use	0.01 (-0.01, 0.02)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline.

Table S6. Association between annual average greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) excluding participants in the lowest 10% of the distribution of cognitive performance in the Nurses' Health Study, at a 270m buffer (n=15,478)^a

Models ^b	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.02 (0.01, 0.03)
Plus socio-economic indicators	0.02 (0.01, 0.03)
Plus neighborhood socioeconomic indicators	0.02 (0.01, 0.03)
Plus depression + antidepressant use *	0.02 (0.01, 0.03)
Verbal memory	
Age-adjusted	0.01 (0.001, 0.02)
Plus socio-economic indicators	0.01 (-0.00, 0.02)
Plus neighborhood socioeconomic indicators	0.01 (-0.001, 0.02)
Plus depression + antidepressant use	0.01 (-0.002, 0.02)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline.

Table S7. Association between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) removing participants who had just moved to the address for less than 2 years (N=13,945) and who changed their address during the follow-up period (N=13,588), Nurses' Health Study, at a 270m buffer ^a

Models	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)	
	Removing participants who moved to the address less than 2 yrs	Removing participants who changed their address during the follow-up period
Global cognition		
Age-adjusted	0.03 (0.02, 0.04)	0.03 (0.02, 0.04)
Plus socio-economic indicators	0.03 (0.02, 0.04)	0.03 (0.02, 0.04)
Plus neighborhood socioeconomic indicators	0.03 (0.01, 0.04)	0.03 (0.01, 0.04)
Plus depression + antidepressant use	0.03 (0.01, 0.04)	0.03 (0.01, 0.04)
Verbal memory		
Age-adjusted	0.02 (0.00, 0.03)	0.02 (0.01, 0.03)
Plus socio-economic indicators	0.02 (0.00, 0.03)	0.02 (0.01, 0.03)
Plus neighborhood socioeconomic indicators	0.02 (0.00, 0.03)	0.02 (0.003, 0.03)
Plus depression + antidepressant use	0.02 (0.00, 0.03)	0.02 (0.003, 0.03)

^a NDVI – Normalized Difference Vegetation Index

Table S8. Longitudinal association between midlife exposure to greenness (NDVI, 1986-1994) and cognitive decline (1995-2008) among women in the Nurses' Health Study, at a 1230m buffer (n=16,962)^a

Models^b	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.003 (0.001, 0.006)
Plus socio-economic indicators	0.003 (0.001, 0.006)
Plus neighborhood socioeconomic indicators	0.003 (0.001, 0.006)
Plus depression + antidepressants	0.003 (0.001, 0.006)
Verbal Memory	
Age-adjusted	0.002 (-0.001, 0.005)
Plus socio-economic indicators	0.002 (-0.001, 0.005)
Plus neighborhood socioeconomic indicators	0.002 (-0.001, 0.005)
Plus depression + antidepressants	0.002 (-0.001, 0.005)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline and a slope parameter that represents the mean annual rate of cognitive decline over time.

Table S9. Longitudinal association between annual average greenness at midlife (NDVI, 1986-1994) and cognitive decline (1995-2008) among women in the Nurses' Health Study, at a 270m buffer (n=16,962) ^a

Models ^b	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.003 (0.001, 0.006)
Plus socio-economic indicators	0.003 (0.001, 0.006)
Plus neighborhood socioeconomic indicators	0.003 (0.001, 0.006)
Plus depression + antidepressant use *	0.003 (0.001, 0.006)
Verbal memory	
Age-adjusted	0.002 (-0.00, 0.005)
Plus socio-economic indicators	0.002 (-0.00, 0.005)
Plus neighborhood socioeconomic indicators	0.002 (-0.00, 0.005)
Plus depression + antidepressant use	0.002 (-0.00, 0.005)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline and a slope parameter that represents the mean annual rate of cognitive decline over time.

Table S10. Longitudinal association between annual greenness in the immediate year prior to the first cognitive assessment (NDVI) and cognitive decline (1995-2008) among women in the Nurses' Health Study (n=16,861)^a

Models ^b	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.004 (0.001, 0.006)
Plus socio-economic indicators	0.004 (0.001, 0.006)
Plus neighborhood socioeconomic indicators	0.004 (0.001, 0.006)
Plus depression + antidepressant use *	0.004 (0.001, 0.006)
Verbal memory	
Age-adjusted	0.004 (0.001, 0.006)
Plus socio-economic indicators	0.004 (0.001, 0.006)
Plus neighborhood socioeconomic indicators	0.004 (0.001, 0.006)
Plus depression + antidepressant use	0.004 (0.001, 0.006)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline and a slope parameter that represents the mean annual rate of cognitive decline over time.

Table S11. Longitudinal association between annual average greenness (NDVI, 1986-1994) and cognitive decline (1995-2008) excluding participants in the lowest 10% of the distribution of cognitive performance in the Nurses' Health Study, at a 270m buffer (n=15,478)^a

Models ^b	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)
Global cognition	
Age-adjusted	0.004 (0.001, 0.006)
Plus socio-economic indicators	0.004 (0.001, 0.006)
Plus neighborhood socioeconomic indicators	0.004 (0.001, 0.006)
Plus depression + antidepressant use *	0.004 (0.001, 0.006)
Verbal memory	
Age-adjusted	0.003 (0.00, 0.006)
Plus socio-economic indicators	0.003(-0.00, 0.006)
Plus neighborhood socioeconomic indicators	0.003 (-0.00, 0.006)
Plus depression + antidepressant use	0.003 (-0.00, 0.006)

^aNDVI – Normalized Difference Vegetation Index

^bLinear mixed models were used, including an intercept that represents the mean cognitive level at baseline and a slope parameter that represents the mean annual rate of cognitive decline over time.

Table S12. Longitudinal association between midlife exposure to greenness (NDVI, 1986-1994) and cognitive decline (1995-2008) excluding participants who had just moved to the address for less than 2 years (N=13,945) or who changed their address during the follow-up period (N=13,588), Nurses' Health Study, at a 270m buffer ^a

Models	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)	
	Removing participants who moved to the address less than 2 yrs	Removing participants who changed their address during the follow-up period
Global cognition		
Age-adjusted	0.003 (0.00, 0.005)	0.002 (-0.00, 0.005)
Plus socio-economic indicators	0.003 (0.00, 0.005)	0.002 (-0.00, 0.005)
Plus neighborhood socioeconomic indicators	0.003 (0.00, 0.005)	0.002 (-0.00, 0.005)
Plus depression + antidepressant use *	0.003 (0.00, 0.005)	0.002 (-0.00, 0.005)
Verbal memory		
Age-adjusted	0.003 (-0.001, 0.006)	0.002 (-0.001, 0.005)
Plus socio-economic indicators	0.003 (-0.001, 0.006)	0.002 (-0.001, 0.005)
Plus neighborhood socioeconomic indicators	0.003 (-0.001, 0.006)	0.002 (-0.001, 0.005)
Plus depression + antidepressant use	0.003 (-0.001, 0.006)	0.002 (-0.001, 0.005)

^a NDVI – Normalized Difference Vegetation Index

Table S13. Association of midlife exposure to greenness (NDVI, 1986-1994) with baseline cognitive function and cognitive decline of global cognition (1995-2008), stratified by: neighborhood socioeconomic status, population density, and apolipoprotein E ε4 (apoE ε4) carriers, the Nurses' Health Study (n=16,962).^{a,b,c}

	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)
Neighborhood Socioeconomic Status		
Low (N=5657)	0.03 (0.01, 0.05)	0.006 (0.001, 0.01)
Medium (N=5649)	0.02 (-0.001, 0.04)	0.0001 (-0.004, 0.01)
High (N=5656)	0.02 (-0.002, 0.04)	0.005 (0.0006, 0.009)
Interaction p-value	0.38	0.49
Population Density		
Low (N=5595)	0.01 (-0.01, 0.03)	-0.001 (-0.01, 0.004)
Medium (N=5580)	0.03 (0.004, 0.05)	0.005 (-0.001, 0.01)
High (N=5584)	0.05 (0.02, 0.07)	0.004 (-0.002, 0.01)
Interaction p-value	0.73	0.19
ApoE ε4 carriers		
Non-carriers (N=15020)	0.03 (0.02, 0.04)	0.004 (0.001, 0.01)
Carriers (N=1942)	0.02 (-0.02, 0.06)	0.01 (0.0004, 0.02)
Interaction p-value	0.90	<0.001

^a NDVI – Normalized Difference Vegetation Index

^b Linear mixed models were used, including an intercept that represents the mean cognitive level at baseline and a slope parameter that represents the mean annual rate of cognitive decline over time.

^c Data from this table is represented in Figure 1.

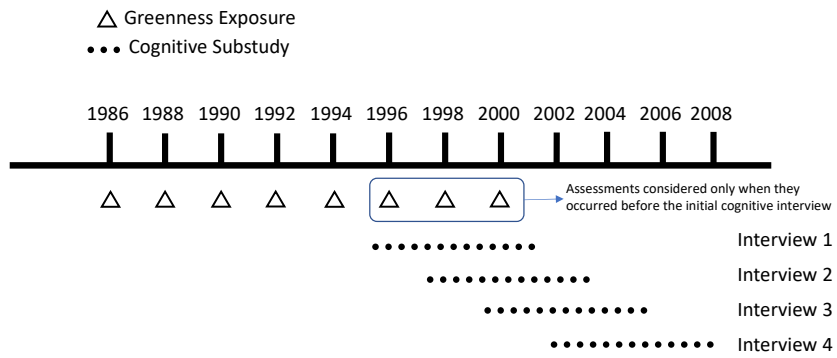
Table S14. Association of midlife exposure to greenness (NDVI, 1986-1994) with baseline cognitive function and cognitive decline of global cognition (1995-2008), stratified by: apolipoprotein E ϵ 4 (apoE ϵ 4) carriers, restricted to women without any APOE- ϵ 2 allele, the Nurses' Health Study (n=15,709).^{a,b}

	Mean difference in baseline cognitive function per interquartile range [IQR] increase in NDVI (95%CI)	Mean difference in slope of cognitive decline per interquartile range [IQR] increase in NDVI (95%CI)
ApoE ϵ 4 carriers		
Non-carriers (N=14,601)	0.03 (0.02, 0.04)	0.004 (0.001, 0.01)
Carriers (N=1,108)	0.03 (-0.02, 0.08)	0.01 (-0.002, 0.02)
Interaction p-value	0.91	<0.001

^a NDVI – Normalized Difference Vegetation Index

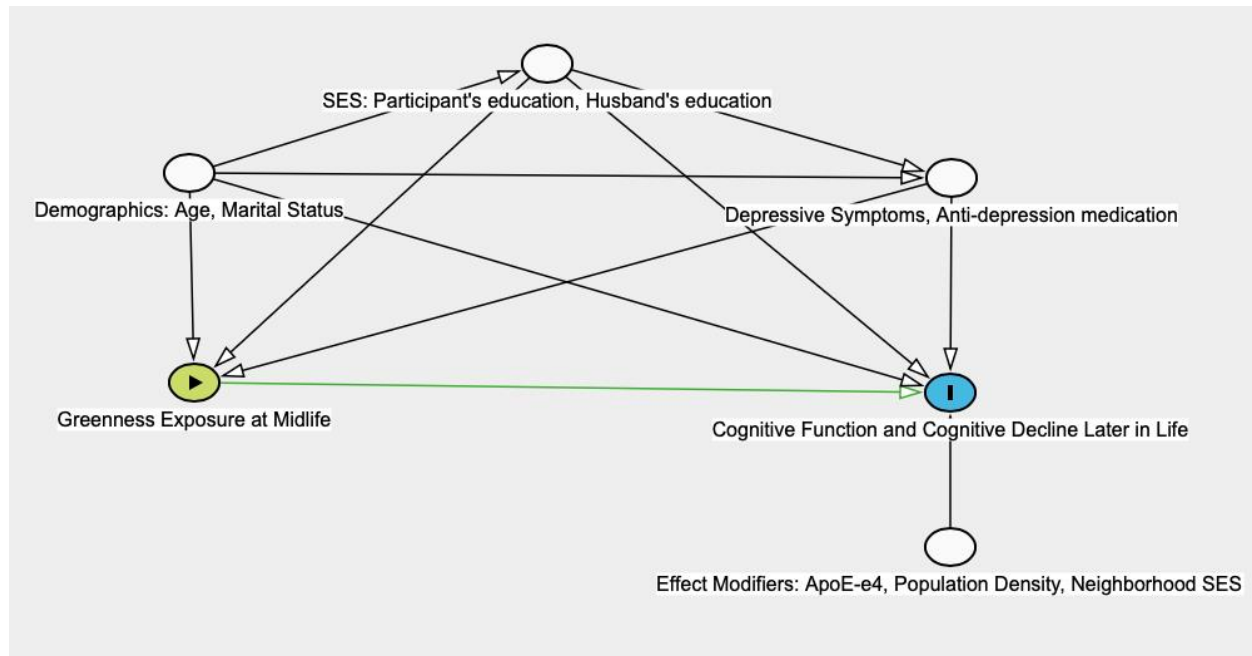
^b Linear mixed models were used, including an intercept that represents the mean cognitive level at baseline and a slope parameter that represents the mean annual rate of cognitive decline over time.

Figure S1. Study timeline^a



^aAdapted from Wagner et al. "Long-term trajectories of body weight, diet, and physical activity from midlife through late life and subsequent cognitive decline in women". *AJE*. 2019; 4(189),305-313.

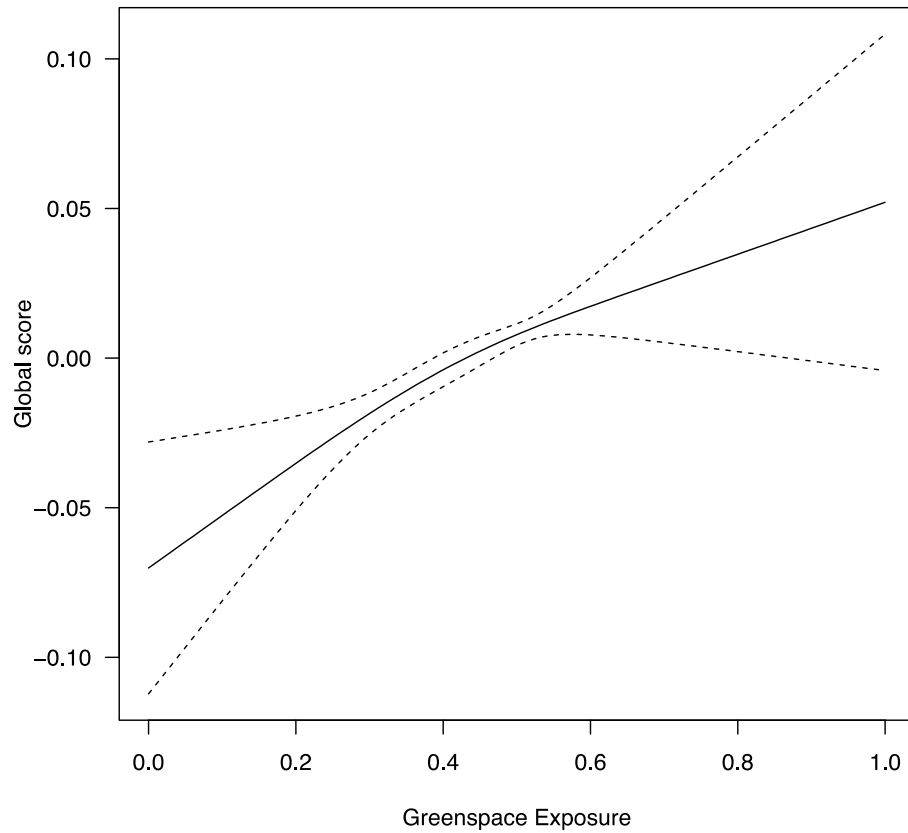
Figure S2. Directed Acyclic Graph of the hypothesized association^{1,2}



¹Green node indicates exposure, blue node indicates outcome, white nodes indicate adjusted variables.

²Textor J, van der Zander B, Gilthorpe MS, Liskiewicz M, Ellison GT. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol.* 2016 Dec 1;45(6):1887-1894. doi: 10.1093/ije/dyw341. PMID: 28089956.

Figure S3. Non-linear associations between midlife exposure to greenness (NDVI, 1986-1994) and baseline cognitive function (1995-2001) among women in the Nurses' Health Study, at a 270m buffer.^{a,b,c}

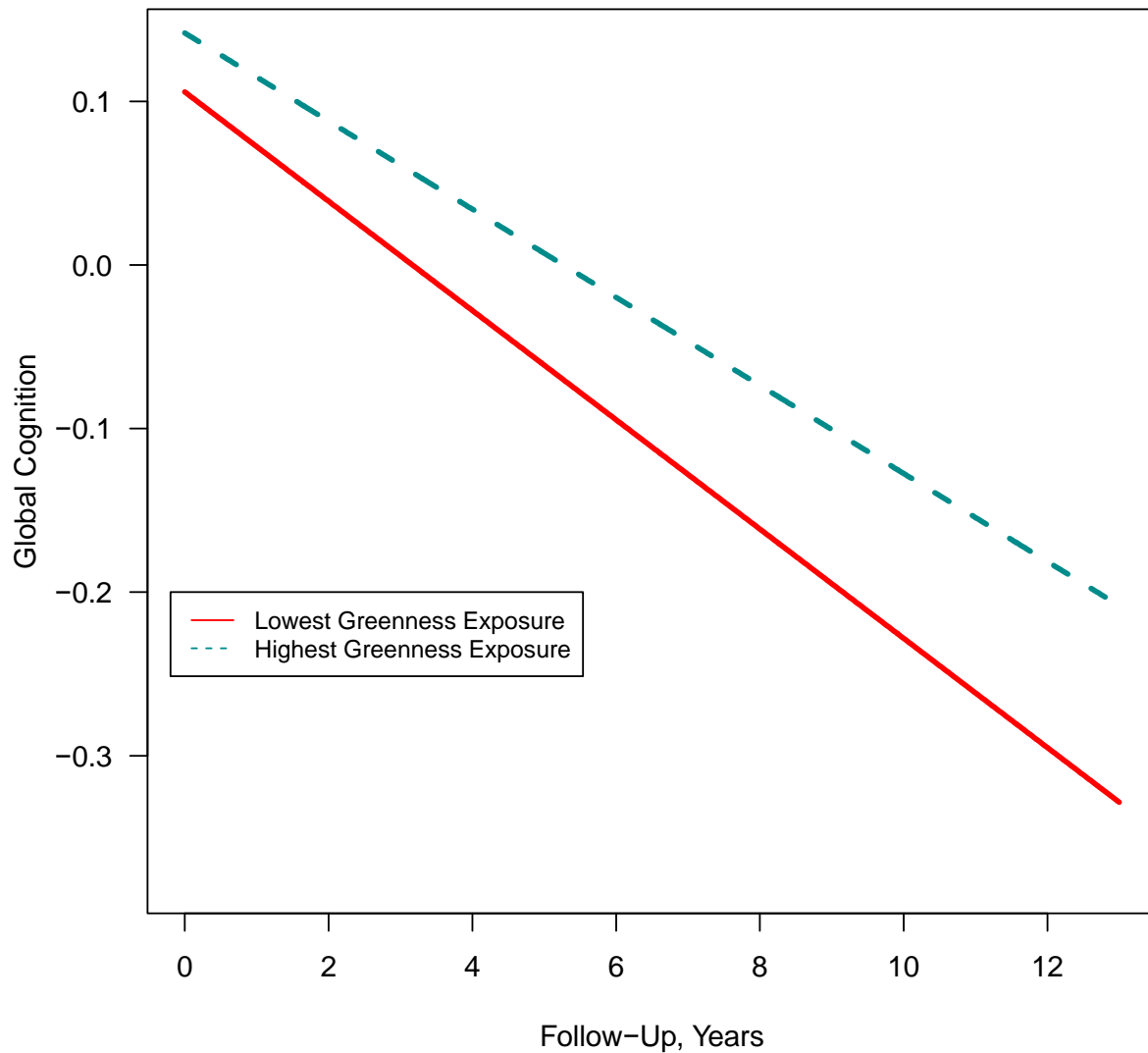


^a NDVI- Normalized Difference Vegetation Index

^b The multivariable model 1 (n= 57,256 observations from n=16,962 participants) adjusted for age, individual SES, and neighborhood SES, depression and antidepressant use. The y-axis represents the time-varying association between Global cognition score and an interquartile (IQR) increase in NDVI; the x-axis depicts NDVI exposure. P-value for spline term was <0.001. Adjusted R-squared = 0.0489.

^c Numeric data available at Excel Table S1

Figure S4. Estimated trajectories of global cognition over time for the lowest and highest midlife exposure to greenness (NDVI, 1986-1994) among women in the Nurses' Health Study (n=16,962)^{a,b,c}



^a NDVI- Normalized Difference Vegetation Index

^b Mean trajectories of global cognition according to lowest (solid red line) and highest (blue dotted line) greenness exposure at midlife with 95% pointwise confidence intervals (in lighter red and blue respectively) were estimated using a linear mixed model adjusted for average greenness exposure at midlife (per interquartile range, IQR), age, educational level, husband's education, marital status, neighborhood median household income, neighborhood median home value, mental health and antidepressant use, and the interaction of greenness (IQR) with the linear function of time; correlated random effects were considered on both the intercept and the slope. Trajectories were plotted for the most common profile of covariates in the study sample (i.e., participant's education level as Bachelor's degree, husband's education level as high school graduate, married, not taking antidepressants)

^cThe multivariable model 1 (n= 57,256 observations from n=16,962 participants) adjusted for adjusted for age, individual SES, and neighborhood SES, depression and antidepressant use. The slope for lowest greenness exposure (percentile 10 = 1.5499) was 0.037; and the slope for highest greenness exposure (percentile 90 = 3.3487) was 0.079. Numeric data for predictions for percentile 90 available at Excel Supplemental Table S2, and for percentile 10 available at Excel Supplemental Table S3.