**Supplementary Table 1 Population characteristics of the NHANES III sample, stratified by AD case status as of 2011**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All** | **Non-AD** | **AD** | **p-valuea** |
| N | 4994 | 4892 | 102 |  |
| Age (mean (SE)) (years) | 70.4 (0.25) | 70.3 (0.25) | 73.2 (0.85) | 0.003 |
| Urinary cadmium (geometric mean (GSE)) (ng/mL) | 0.60 (1.03) | 0.60 (1.03) | 0.63 (1.11) | 0.58 |
| Urinary creatinine (geometric mean (GSE)) (mg/dL) | 81.7 (1.01) | 81.6 (1.01) | 86.9 (1.11) | 0.55 |
| Follow-up time (mean (SE)) (years) | 13 (0.22) | 13 (0.22) | 12.8 (0.66) | 0.70 |
|  |  |  |  |  |
| Male | 43.5% | 43.6% | 39.3% | 0.46 |
| Female | 56.5% | 56.4% | 60.7% |
|  |  |  |  |  |
| White | 84.7% | 84.6% | 86.1% | 0.62 |
| Black | 8.1% | 8.2% | 5.6% |
| Others | 7.2% | 7.2% | 8.2% |
|  |  |  |  |  |
| Never smoker | 44.8% | 44.7% | 46.7% | 0.87 |
| Past smoker | 40.1% | 40.1% | 40.4% |
| Current smoker | 15.1% | 15.2% | 12.8% |
|  |  |  |  |  |
| Less than high school b | 40.7% | 40.4% | 53.6% | 0.15 |
| High school graduate or some college | 44.7% | 45.0% | 34.0% |
| College graduate or above | 14.5% | 14.6% | 12.4% |

a Comparisons were between AD cases and non-AD subjects. For categorical variables, p-values were obtained from Pearson's Chi-square test with Rao & Scott adjustment. For continuous variables, p-values were obtained from survey-weighted generalized linear models. Urinary cadmium and urinary creatinine were log-transformed in the models.

b 29 missing in education level; all 29 were non-cases.

**Supplementary Table 2 Urinary cadmium levels in population subgroups, NHANES III**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **N** | **Urinary Cadmium****(geometric mean (GSE)) (ng/mL)** | **P-valuea** |
| **Age (years)** |  |  |  |
| 60-64 | 1177 | 0.64 (1.05) | 0.006 |
| 65-69 | 1058 | 0.64 (1.04) |
| 70-75 | 1166 | 0.57 (1.04) |
| 76-90 | 1593 | 0.55 (1.04) |
|  |  |  |  |
| Male | 2467 | 0.62 (1.04) | ref |
| Female | 2527 | 0.58 (1.03) | 0.05 |
|  |  |  |  |
| White | 2876 | 0.59 (1.03) | ref |
| Black | 995 | 0.69 (1.03) | 0.0003 |
| Others | 1123 | 0.64 (1.10) | 0.35 |
|  |  |  |  |
| Never smoker | 2332 | 0.45 (1.03) | ref |
| Past smoker | 1887 | 0.66 (1.03) | <0.0001 |
| Current smoker | 775 | 1.10 (1.05) | <0.0001 |
|  |  |  |  |
| Less than high schoolb | 2780 | 0.65 (1.03) | ref |
| High school graduate or some college | 1677 | 0.61 (1.04) | 0.12 |
| College graduate or above | 508 | 0.45 (1.06) | <0.0001 |

a p-values were obtained through survey-weighted generalized linear regression. Urinary cadmium was log-transformed. The p-values for “Age” were from tests for linear trend over the four age categories.

b 29 missing in education level. All 29 were non-cases.

**Supplementary Table 3 Population characteristics of the NHANES III sample, stratified by AD case status within the first 12.7 years of follow-up**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Non-AD** | **AD** | **p-valuea** |
| N | 4950 | 44 |  |
| Age (mean (SE)) (years) | 70.3 (0.25) | 75.6 (1.39) | .0008 |
| Urinary cadmium (geometric mean (GSE)) (ng/mL) | 0.60 (1.03) | 0.72 (1.12) | .10 |
| Urinary creatinine (geometric mean (GSE)) (mg/dL) | 81.5 (1.01) | 108.2 (1.10) | .005 |
| Follow-up time (mean (SE)) (years) | 10 (0.10) | 8 (0.52) | .00003 |
|  |  |  |  |
| Male | 43.5% | 49.0% | 0.53 |
| Female | 56.5% | 51.0% |
|  |  |  |  |
| White | 84.6% | 93.9% | 0.13 |
| Black | 8.2% | 1.8% |
| Others | 7.2% | 4.2% |
|  |  |  |  |
| Never smoker | 44.8% | 48.7% | 0.71 |
| Past smoker | 40.2% | 41.8% |
| Current smoker | 15.2% | 9.5% |
|  |  |  |  |
| Less than high school b | 40.7% | 46.7% | 0.79 |
| High school graduate or some college | 44.7% | 42.9% |
| College graduate or above | 14.5% | 10.3% |

a Comparisons were between AD cases and non-AD subjects. For categorical variables, p-values were obtained from Pearson's Chi-square test with Rao & Scott adjustment. For continuous variables, p-values were obtained from survey-weighted generalized linear models. Urinary cadmium and urinary creatinine were log-transformed in the models.

b 29 missing in education level; all 29 were non-cases.

**Supplementary Figure 1 Association between cadmium and AD mortality in men and women**

Urinary Cadmium

Blood Cadmium

Urinary Cadmium

(No creatinine in model**)**

 Urinary Cadmium

 (Creatinine in model)

Results came from analyses stratified by sex. Unless otherwise stated, all models were fully-adjusted. Note that a two-category race variable (“white” vs “non-white”) were used in all eight models presented here, and a two-category smoking variable (“ever” vs “never”) were used in the NHANES 99-06 models here because the number of cases in each sex stratum was small. It should be noted that among women in the NHANES 99-06 sample, when one AD case with extremely high urinary cadmium (2.37 ng/mL) and very short follow-up time (1.3 years) was removed, the HR in this stratum became much smaller (HR=1.35, 95% CI: 0.56, 3.21, p-value=0.49), instead of the HR=1.61 (95% CI: 0.81, 3.20, p-value=0.17) shown in the figure. Removing this observation from main analysis (i.e. regression models in Table 3) did not substantially alter results.