**SUPPLEMENTAL MATERIAL**

**Long-term effects of latitude, ambient temperature, and ultraviolet radiation on the incidence of multiple sclerosis in two cohorts of US women**

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| **Table S1.** Hazard ratios (95% CI) for the association of multiple sclerosis with continuous cumulative average annual temperature and cumulative average July UV among women in the NHS (1984-2004) and NHS II (1989-2011). | | | | | |
|  |  | **Basic1** | **Multivariable2** | **Full3** | **Two Exposure4** |
| **Cumulative Average Exposure** | cases/PY | HR (95%CI) | HR (95%CI) | HR (95%CI) | HR (95%CI) |
| **July UV (IQR=28.49 mW/m2)** |  |  |  |  |  |
| NHS | 153/1,858,955 | 0.90 (0.75, 1.08) | 0.93 (0.77, 1.13) | 1.00 (0.81, 1.22) | 1.05 (0.78, 1.40) |
| NHSII | 425/2,266,493 | 0.86 (0.78, 0.96) | 0.90 (0.80, 1.01) | 0.93 (0.82, 1.05) | 1.00 (0.86, 1.17) |
| NHS & NHSII4 | 578/4,125,448 | 0.87 (0.80, 0.96) | 0.91 (0.82, 1.00) | 0.95 (0.85, 1.05) | 1.01 (0.88, 1.16) |
| P for heterogeneity |  | 0.71 | 0.74 | 0.58 | 0.80 |
|  |  |  |  |  |  |
| **Annual Temperature (IQR=4.81°)** |  |  |  |  |  |
| NHS | 153/1,858,955 | 0.80 (0.63, 1.02) | 0.84 (0.66, 1.08) | 0.95 (0.72, 1.25) | 0.91 (0.62, 1.34) |
| NHSII | 425/2,266,493 | 0.78 (0.68, 0.90) | 0.83 (0.72, 0.95) | 0.86 (0.74, 1.00) | 0.86 (0.71, 1.03) |
| NHS & NHSII5 | 578/4,125,448 | 0.78 (0.69, 0.89) | 0.83 (0.73, 0.94) | 0.88 (0.77,1.00) | 0.87 (0.73, 1.02) |
| P for heterogeneity |  | 0.86 | 0.88 | 0.52 | 0.78 |
| 1 Adjusted for current age, calendar period, and ancestry.  2 Additionally adjusted for pack-years of smoking, BMI at age 18, vitamin D intake at baseline, population density, and individual- and area-level socioeconomic status.  3 Additionally adjusted for latitude of residence at age 15  4 Additionally adjusted for either cumulative average annual temperature or cumulative average July UV exposure,  5 NHS & NHSII HRs calculated via meta-analysis, using Cochran’s Q to examine heterogeneity | | | | | |

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| **Table S2.** Hazard ratios (95% CI) for the association of multiple sclerosis with continuous cumulative average annual temperature, cumulative average July temperature, and cumulative average July UV among women in the NHS (1984-2004) and NHS II (1989-2011). Person time is calculated based on doctor recorded date of first symptoms. | | | | |
|  |  | **Basic1** | **Multivariable2** | **Full3** |
| **Cumulative Average Exposure** | cases/PY | HR (95%CI) | HR (95%CI) | HR (95%CI) |
| **July UV (IQR=28.49 mW/m2)** |  |  |  |  |
| NHS | 64/1,858,139 | 0.77 (0.56, 1.05) | 0.76 (0.54, 1.06) | 0.69 (0.47, 1.01) |
| NHSII | 275/2,264,716 | 0.88 (0.77, 1.00) | 0.90 (0.79, 1.04) | 0.93 (0.80, 1.08) |
| NHS & NHSII4 | 339/4,122,855 | 0.86 (0.76, 0.97) | 0.88 (0.78, 1.00) | 0.84 (0.64, 1.11) |
| P for heterogeneity |  | 0.44 | 0.34 | 0.15 |
|  |  |  |  |  |
| **Annual Temperature (IQR=4.81°)** |  |  |  |  |
| NHS | 64/1,858,139 | 0.69 (0.46, 1.02) | 0.67 (0.43, 1.04) | 0.62 (0.37, 1.03) |
| NHSII | 275/2,264,716 | 0.81 (0.68, 0.96) | 0.85 (0.71, 1.01) | 0.88 (0.73, 1.06) |
| NHS & NHSII4 | 339/4,122,855 | 0.79 (0.67, 0.92) | 0.82 (0.70, 0.97) | 0.80 (0.59, 1.09) |
| P for heterogeneity |  | 0.47 | 0.32 | 0.20 |
|  |  |  |  |  |
| **July Temperature (IQR=3.91°)** |  |  |  |  |
| NHS | 64/1,858,139 | 0.70 (0.47, 1.03) | 0.69 (0.45, 1.06) | 0.67 (0.42, 1.06) |
| NHSII | 275/2,264,716 | 0.79 (0.67, 0.93) | 0.82 (0.70, 0.97) | 0.84 (0.71, 1.00) |
| NHS & NHSII4 | 339/4,122,855 | 0.77 (0.66, 0.90) | 0.80 (0.69, 0.93) | 0.82 (0.70, 0.96) |
| P for heterogeneity |  | 0.58 | 0.48 | 0.35 |
| 1 Adjusted for current age, calendar period, and ancestry.  2 Additionally adjusted for pack-years of smoking, BMI at age 18, vitamin D intake at baseline, population density, and individual- and area-level socioeconomic status.  3 Additionally adjusted for latitude of residence at age 15  4 NHS & NHSII HRs calculated via meta-analysis, using Cochran’s Q to examine heterogeneity | | | | |

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| **Table S3.** Pearson correlations between the examined exposures for NHS (top) and NHSII (bottom) participants throughout follow-up | | | | | |
|  | Latitude | UV | Annual average temperature | July average temperature |
| Latitude | 1 | -0.67 | -0.86 | -0.84 |
| UV | -0.62 | 1 | 0.70 | 0.64 |
| Annual average temperature | -0.86 | 0.65 | 1 | 0.94 |
| July average temperature | -0.77 | 0.51 | 0.86 | 1 |
| Note that all p-values <0.0001 | | | | | |