Association Between Alzheimer Dementia Mortality Rate and Altitude in California Counties

Environmental risk factors for Alzheimer dementia are not well understood. Air pollution may have a causative role. In light of findings about lower incidence of psychiatric conditions, such as attention-deficit/hyperactivity disorder, at higher altitudes, we sought to determine whether rates of dementia were associated with average altitude of residence.

Methods | In an effort to minimize differential reporting by location and time, we analyzed the county-specific deaths attributed to Alzheimer dementia reported within a single statewide public health system during 1 year. The California Department of Public Health published deaths attributed to Alzheimer disease in 2005, based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision code G30, categorized by county of residence (not of death). Sociodemographic information by county was obtained from 2010 US Census data. Mean altitudes of inhabited areas in each county were computed using US Board on Geographical Names data. Given nonlinear effects of altitude on gas physiology, we used the logarithm of altitude in meters as our main predictor, using base 2 to simplify interpretation (each 1-point increase being a doubling in rate).

To account for sociodemographic confounders, we analyzed the association of log₂(altitude) with (1) crude mortality rates, (2) age-adjusted rates, and (3) age-adjusted rates, controlling for each county’s age, sex, race/ethnicity, education, and average income. There may be inconsistencies in reporting of dementia-related mortality, so we also examined (4) a model incorporating total county population and (5) adjusted models including only counties that had more than 15 dementia deaths (which were considered statistically reliable).

We estimated crude mortality rates as the number of deaths attributed to Alzheimer disease per 100,000 inhabitants aged 65 years and older in each county. Age-adjusted rates were published for each county in the Department of Public Health report. We used linear regression to estimate associations. Analyses were performed in Stata (StataCorp). Institutional review board approval was not sought because the epidemiologic data used had already been published in a government report.

Results | The Figure shows log₂(altitude) plotted against age-adjusted dementia mortality rates. A similar trend was seen for the crude mortality rate.

The Table shows the coefficients for log₂(altitude) from the regression models. In age-adjusted models, each doubling in altitude was associated with a roughly 2-point decline in the age-adjusted mortality rate for dementia. The predicted rate at the highest county (1800 m) was 14 points lower than at the lowest county (15 m), or about half. The results were similar in the counties that had more than 15 dementia deaths.

Table. Association Between Altitude and Dementia Mortality Rate in 58 California Counties

<table>
<thead>
<tr>
<th>Coefficient for Log₂(Altitude)</th>
<th>Unadjusted*</th>
<th>P Value</th>
<th>Age-Adjusted*</th>
<th>P Value</th>
<th>Adjusted for Age and Sociodemographic Variables*</th>
<th>P Value</th>
<th>Adjusted for Age, Sociodemographic Variables, and County Population*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All counties (N = 58)</td>
<td>-1.51</td>
<td>.001</td>
<td>-1.73</td>
<td>.002</td>
<td>-1.97</td>
<td>.009</td>
<td>-2.01</td>
<td>.01</td>
</tr>
<tr>
<td>Counties with &gt;15 dementia deaths (n = 36)</td>
<td>-1.46</td>
<td>.02</td>
<td>-1.30</td>
<td>.13</td>
<td>-2.17</td>
<td>.02</td>
<td>-2.21</td>
<td>.03</td>
</tr>
</tbody>
</table>

* The coefficient represents the change in the dementia-related death rate (per 100,000) for each doubling in altitude. A negative coefficient indicates lower rates at higher altitudes.

* Sociodemographic variables are percentage female, percentage with college education, average income, and percentage white, black, Hispanic, and Asian.
Discussion | This analysis suggests that altitude of residence may impact the risk for dying of Alzheimer dementia. Ecologic studies of this type must be interpreted cautiously. Unexamined factors may account for differential reporting of cases across counties, including miscategorization of other forms of dementia. For instance, 1 high-altitude county (Alpine) reported no cases in 2005. We were not able to reliably assess many confounders, including comorbidities and air pollution. None of the sociodemographic factors we controlled for mitigated the estimated association, and the same results were found among the larger counties that had more reliable rate estimates.

Altitude of residence might be associated with environmental, lifestyle, or health-related factors, which influence dementia rates. Oxygen levels might have direct long-term effects on brain physiology. Oxidative abnormalities have been long proposed to be central to the pathogenesis of dementia. One group of researchers previously found that hypoxia prevents neurodegeneration in rats in experimental Alzheimer disease and hypothesized that adaptation to induced hypoxia may prevent dementia. To our knowledge, our work is the first to find epidemiological evidence for such effects. Additional work is needed to determine whether this relationship holds in other populations.

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Dose-Response Association Between Psychological Distress and Risk of Completed Suicide in the General Population

Elevated suicide rates in people with clinical depression, as indexed by hospitalizations or use of psychiatric outpatient services, are well documented. However, the association between depression across the full range of severity and subsequent suicide risk is unknown. With single-cohort studies insufficiently powered to examine this relation, to our knowledge, we provide the first pooling of individual-level data from a series of large general population-based cohort studies.

Methods | Described in detail elsewhere, independent, geographically representative surveys conducted between 1994 and 2008 of individuals living in private households were used in the present analyses: the Health Survey for England (N = 13) and the Scottish Health Surveys (N = 3). Combining these studies resulted in a total of 193 873 participants, 166 606 (86%) of whom had data on age, sex, and psychological distress. Study members were linked to the UK National Health Service register for primary and contributing causes of death. Ethical approval was given by the London Research Ethics Council, and informed consent was obtained from all participants.

Psychological distress was measured using the 12-item General Health Questionnaire, which contains items principally concerned with symptoms of depression and anxiety. The sensitivity (0.70) and specificity (0.80) against standardized psychiatric interviews are acceptably high. In the present analyses, participants were classified according to standard thresholds: asymptomatic (score of 0), subclinically symptomatic (1-3), symptomatic (4-6), and highly symptomatic (7-12). We used any mention of suicide on the death certificate as our outcome (associations were very similar in analyses using suicide as the underlying cause).

We computed 2 sets of analyses. First, having used Schoenfeld residuals to ascertain that the proportional hazards assumption had not been violated, we calculated hazard ratios (HRs) and accompanying 95% CIs for the association between the categories of psychological distress and suicide using Cox proportional hazard models. Having found no evidence of effect modification by sex (P for interaction = .81), data for men and women were combined. We adjusted HRs for several covariates, the selection of which was based on empirical evidence—in the present data set, the existing literature, or both—that they are associated with both suicide and psychological distress: socioeconomic position, marital status, frequency of alcohol consumption, smoking status, and presence of a somatic long-standing illness. We accounted for between-study variation using a shared frailty parameter. Additionally, to allow us to explore inflections in the distress-suicide relation, we used fractional polynomials to estimate the best-fitting dose-response curve for the full distress scale and suicide.

Results | There were 108 deaths ascribed to suicide during a mean duration of 9.5 years of follow-up (1 581 805 person-years). Compared with the asymptomatic group, adjusted HRs (aHRs) for suicide were raised for participants in the symptomatic (aHR, 1.83; 95% CI, 0.99-3.39) and highly symptomatic (aHR, 2.43; 95% CI, 1.38-4.27) groups (P for trend <.001; Table). A 1.5D increase in psychological distress was associated with a 1.29-fold elevation (95% CI, 1.12-1.48) in the risk of suicide.