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-SD increase in psychological distress was associated with a 1.29-fold elevation (95% CI, 1.12-1.48) in the risk of suicide.
The Figure shows the best-fitting dose-response curve for psychological distress and suicide. Scores of 2 or more on the distress scale were associated with a stepwise elevation in the risk of suicide.

Discussion | We observed a dose-response relationship between a single administration measure of psychological distress symptom severity and suicide risk in the general population up to 17 years later. That this association was apparent after adjustment for a range of confounding factors, including long-standing illness, suggests other mechanisms underlie the association. One possibility is stressful life experiences combine with a predispositional vulnerability involving multiple neurobiological pathways, such as serotonergic and
noradrenergic systems and the ventromedial prefrontal cortex (diathesis-stress model). Our findings raise the question whether health care professionals should pay attention to suicide risk at distress levels lower than current recommendations suggest.

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Author Contributions: Dr Bell had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors reviewed and agreed on the final manuscript as well as the decision to submit the manuscript for publication.

Study concept and design: Batty.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Bell, Batty.

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COMMENT & RESPONSE

Depression and Mood Disorder Among African American and White Women

To the Editor We have critical concerns with the article by Weaver et al. There were very few cases of major depressive disorder and mood disorder among focal subgroups (often <10). Misclassification of depression can thus have a disproportionate impact on estimates. Furthermore, age, education, household income, and marital status adjustment assumes there are, within the joint distributions of factors, at least some white and African American women with depression in all urbanicity subgroups. Mathematically, this is impossible, and basic positivity assumptions are not satisfied.

Regarding the urbanicity comparisons, rural white women had higher prevalence than their urban counterparts for just 2 of 4 outcomes; in the other 2, results were in a similar direction as those of African American women (although of less magnitude), with rural women having slightly lower prevalence. To infer distinct etiologies of mood disorders for white and African American women based on analyses in which half of the results are consistent across demographic groups is puzzling.

Finally, the national sample weights cannot be assumed to be appropriate for approximating regional-specific estimates, especially if weighting factors interact with exposures in association with depression.

The authors speculated that increased risk for depression among rural white women may be owing to labor force pressure, multiple role strain, and traditional sex roles. They implicitly assume that these same causal factors are less operative in African American women. Instead, they suggest that African American women disproportionately benefit from “resources and coping strategies” including religiosity, social ties, and reliance on grandmothers for caregiving. While these coping differences may be operative in some pathways (eg, religiosity is associated with lower depression risk, and the African American population has higher reported religiosity), these conclusions risk minimizing the role of structural, economic, and sex discrimination experienced by African American women, while potentially reifying stereotypes. Attempts to separate depression etiologies based on lived experiences of white and African American individuals are often fraught with problematic assumptions lacking empirical support. For example, the Weaver et al conclusion is consistent with literature suggesting stressors affect African American mental health to a lesser extent than that of white individuals. We have and will continue to refute such hypotheses based on poor conceptualization and contradictory empirical evidence. Existing theories do point to fruitful paths forward; for example, established experimental research on cognitive reappraisal and external attribution in the context of systematic marginalization and discrimination should, perhaps, be given more attention in epidemiology. Off-support analyses and ill-conceived conclusions move us back rather than forward.

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