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**Online-Only Material:** The eTable is available at <http://www.archinternmed.com>.

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## Psychological Distress as a Risk Factor for Dementia Death

Current estimates suggest that neuropsychiatric disorders account for 28% of the global burden of disease.<sup>1</sup> While depression and anxiety (commonly referred to as psychological distress) have been shown to be a consequence of dementia, the converse is less clear. The possibility that psychological distress might be a risk factor for dementia has major public health implications. However longitudinal studies—which are best placed to examine this relationship—have, with some exceptions,<sup>2,3</sup> been small in scale (affecting study precision), excluded individuals younger than 65 years (limiting insights into the pre-older age origins of dementia), or have used clinical samples (reducing generalizability). Accordingly, we examined the role of psychological distress as a risk factor for and dementia death by pooling 10 large community-based cohort studies.

**Methods.** Participants were recruited from the Health Survey for England,<sup>4</sup> an annual general population-based cross-sectional study (with a longitudinal component) representative of household-dwelling individuals in England. Results from 1994 through 2004 were pooled. Participants gave informed consent; ethical approval was obtained from the London Research Ethics Council.

Psychological distress was measured during a household visit using the 12-item General Health Questionnaire (GHQ-12), a widely used measure of psychological distress in population studies comprising items rating

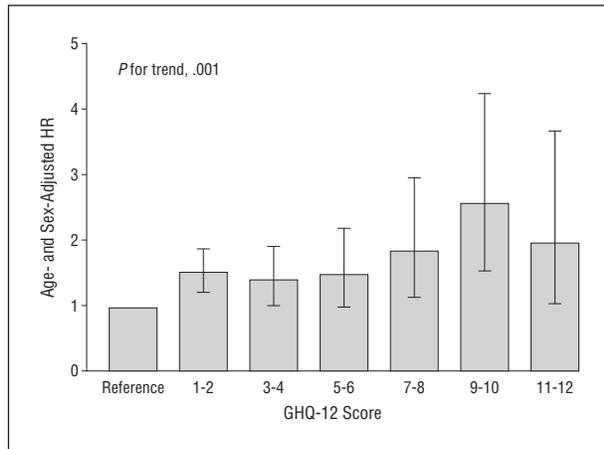
anxiety, depression, social dysfunction, and loss of confidence. Higher scores indicate greater distress. We used a cut off score of 4 or greater to denote psychological distress as validated against standardized psychiatric interviews.<sup>5</sup> Dementia was identified from death certification and coded according to the *International Classification of Diseases, Ninth Revision (ICD-9)* codes 290.0 through 290.4 and 294.9 and *International Statistical Classification of Diseases, 10th Revision (ICD-10)* codes F01, F03, F09, and G30. Follow-up was until date of death or February 15, 2008, whichever came first.

We used Cox proportional hazards models to compute hazard ratios with accompanying 95% confidence intervals for GHQ-12 score in relation to dementia-related deaths. Study members scoring zero (no apparent distress) denoted the reference group. Models were adjusted for age, sex, occupational social class (OSC),<sup>6</sup> parental OSC, age at leaving full-time education, current smoking (yes/no), alcohol consumption (units per week), and existing cardiovascular disease (CVD) (yes/no), and diabetes (yes/no). Statistical analyses were conducted using PASW statistics, version 18.0 (SPSS, Chicago, Illinois), and R for Max OS X, version R-2.13.0.

**Results.** The initial sample included 85 261 adults (in 1996 the GHQ-12 was not used). After removing individuals who declined linkage to mortality records (n=9325) and those with missing GHQ-12 data (n=2865), the analytic sample comprised 73 071 individuals (54.8% women) with a mean (SD) age of 55.9 (14.3) years (range, 35-102 years). Data were missing for 1 or more variables in 21% (n=15 355) of the sample. Individuals with missing data were more likely to be older, be female, belong to a manual OSC, leave school later, be a nonsmoker, drink alcohol moderately, and have CVD and diabetes.

Of the 10 170 deaths during follow-up, 455 had dementia coding. A higher GHQ-12 score was associated with increased risk of dementia death in an age-adjusted model (GHQ-12 score of 1-3: HR, 1.44 [95% CI, 1.17-1.78]; GHQ-12 score of 4-12: HR, 1.74 [95% CI, 1.36-2.22]; *P* value for trend, <.001). Adding all remaining covariates (sex, OSC, parental OSC, age at leaving full-time education, current smoking, alcohol consumption, and existing CVD and diabetes) led to some attenuation of effect but statistical significance at conventional levels was retained (GHQ-12 score of 1-3: HR, 1.27 [95% CI, 1.00-1.61]; GHQ-12 score of 4-12: HR, 1.56 [95% CI, 1.17-2.07]; *P* value for trend, .005). In the **Figure** we relate 7 categories of GHQ score to dementia death to provide more detailed insight into the shape of the relationship. There was evidence of a dose-response effect (*P* value for trend, .001). Excluding individuals with any missing data (sample n=57 716; 361 dementia deaths) or dementia deaths within 5 years (sample n=72 926; 310 dementia deaths)—the latter to explore reverse causality—did not affect our results.

**Comment.** We found an association between elevated psychological distress and an increased risk of dementia death in a large general population sample of apparently dementia-free adults, which remained after adjustment for age, sex, OSC, education, alcohol use, smoking, and existing CVD and diabetes. Cardiovascular risk factors have been linked



**Figure.** Age- and sex-adjusted hazard ratios (HRs) with 95% confidence intervals for psychological distress in relation to the risk of dementia death: the Health Surveys for England. Reference=zero score on the 12-item General Health Questionnaire (GHQ-12). Higher score indicates greater distress.

with dementia,<sup>7</sup> but the association found in our study remained after controlling for them, thus implicating other explanations for the gradient seen. One possibility is a toxic effect of hypercortisolemia in depression on the hippocampus.<sup>8</sup> Further research is required to investigate whether appropriate treatment of depression reduces dementia risk.

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## COMMENTS AND OPINIONS

### More Is Less

I read with great interest the article by Sipahi et al<sup>1</sup> and the thoughtful accompanying editorial by Warner Stevenson<sup>2</sup> on the impact of QRS duration on outcomes with resynchronization therapy. I wholeheartedly endorse Redberg's acknowledgment of the merit of the article.<sup>3</sup> However, considering the data showed that far more costly and invasive procedures were being done than the evidence justified with far less benefit than anticipated, would not the designation "More Is Less" be more appropriate, as is true for many treatments and procedures that fall in the "Less Is More" category?

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### QRS Morphology Rather Than QRS Duration for Predicting CRT Response

Sipahi et al reported in their meta-analysis of 5 cardiac resynchronization therapy (CRT) trials that QRS duration was an important predictor of response to CRT.<sup>1</sup> They concluded that patients with a QRS of 150 milliseconds (ms) or greater had a reduction in heart failure events, whereas those with a QRS less than