

## Depression Is Associated with a Higher Risk of Death among Stroke Survivors

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*Background:* Poststroke depression is common, affecting approximately 1 in 3 stroke survivors. We aimed to evaluate the association between depression and mortality in adults with and without prior stroke. *Methods:* Using the National Health and Nutrition Examination Survey (NHANES) I Epidemiologic Follow-up Study (1982-1992), we investigated the association between depression and all-cause mortality among adults aged 25-74 years with and without prior stroke, and stroke mortality among stroke survivors, adjusting for covariates. *Results:* Among 9919 individuals, 121 (1.2%) reported prior stroke. The adjusted depression prevalence was 37.1% among stroke survivors and 17.3% among individuals without stroke. In persons aged 25-64 years, neither stroke nor depression was associated with all-cause mortality. The combination of depression and stroke was not associated with all-cause mortality (adjusted hazard ratio [HR] 2.83, 95% confidence interval [CI] .67-12.04). Among persons aged 65-74 years, depression alone (adjusted HR 1.24, 95% CI 1.04-1.47), stroke alone (adjusted HR 1.64, 95% CI 1.17-2.32), and the combination of depression and stroke (adjusted HR 2.28, 95% CI 1.79-2.90) were associated with all-cause mortality, consistent with an additive relationship. Among all ages, the combination of depression and stroke was associated with all-cause mortality (adjusted HR 1.93, 95% CI 1.28-2.92). Higher stroke mortality was only observed in those aged 65-74 years (adjusted HR 2.43, 95% CI 1.05-5.60). Compared with stroke survivors without depression, those with depression were ~35 times more likely to die from a stroke (adjusted HR 35.33, 95% CI 7.79-160.32). *Conclusions:* The combination of prior stroke and depression is associated with higher all-cause mortality than either condition alone. The presence of depression after stroke increases stroke mortality 35-fold, highlighting the importance of identifying and treating depression among stroke survivors. **Key Words:** Depression—stroke—mortality—stroke mortality—death—outcome.

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Received February 13, 2017; revision received June 28, 2017; accepted July 10, 2017.

Grant support: This study was supported by the Roxanna Todd Hodges Foundation.

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1052-3057/\$ - see front matter

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<http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2017.07.006>

## Introduction

Depression is a common yet often unrecognized condition in individuals with stroke, affecting approximately one third of stroke survivors.<sup>1-3</sup> Depression is associated with poorer functional outcomes after stroke.<sup>4-7</sup> Individuals with poststroke depression (PSD) appear to have a higher mortality than stroke survivors without depression; however, previous studies are difficult to interpret given the heterogeneity in recruited populations, the sample size, the definition of PSD, covariates, and the duration of follow-up.<sup>4,8-12</sup> In addition, it is unclear whether depression has a stronger effect on mortality in stroke survivors than in individuals without a stroke. Whereas some authors have suggested that PSD may contribute to mortality by affecting behavioral factors such as lifestyle patterns and adherence to secondary stroke prevention medications,<sup>13</sup> others have suggested physiological mechanisms.<sup>14,15</sup> A recent longitudinal cohort study suggested that the association between PSD and mortality was strongest in individuals younger than 65 years of age<sup>9</sup>; however, that finding has not been validated in other studies to date.

In the present study, we aimed to examine the association between depression and all-cause and stroke mortality among individuals with and without a self-reported history of stroke in a large nationwide representative sample of adults, stratified by age (25-64 versus 65-74 years), to determine if depression has a stronger effect on mortality among stroke survivors compared with those without a stroke, and to further characterize the relationship between PSD and mortality.

## Methods

### *Study Design*

The National Health and Nutrition Examination Survey (NHANES) I (National Center for Health Statistics 1973) was used to perform a retrospective, longitudinal study of a population cohort. NHANES I was conducted between 1971 and 1975 using questionnaires of health topics and included 20,729 individuals aged 25-74 years with 14,407 (70%) medically examined. Populations oversampled included individuals living in poverty areas, women of childbearing age, and the elderly ( $\geq 65$  years). The NHANES I Epidemiologic Follow-up Study (NHEFS) is a longitudinal study of participants who were between 25 and 74 years old during 1971-1975.<sup>16,17</sup> The study follow-up began in 1982 and continued in 1986, 1987, and 1992. The 1982 follow-up included data on self-reported medical conditions and a depression assessment using the Center for Epidemiologic Studies Depression (CES-D) scale.<sup>18</sup> In the present study, we examined data on individuals in the NHEFS sample who completed the CES-D in 1982 and who were then followed up until 1992.

We examined the association between the presence of depressive symptoms versus (1) all-cause mortality and

(2) stroke mortality in persons with and without a history of stroke.

### *Depression Scale*

The CES-D is a validated, reliable assessment of depression in population samples.<sup>18-20</sup> The presence of depressive symptoms was determined using the 20-item version of the CES-D scale, with each item rated on a 4-point scale ranging from 0 (rarely or none of the time) to 3 (most or all of the time). Scoring of positive items (4, 8, 12, and 16) was reversed before scores for the 20 items were summed. The total scores ranged 0-60 with 16 or higher as a cutoff for depression, and higher scores indicate more symptoms of depression. A cutoff score of 16 or higher has been used extensively in distinguishing depressed patients.<sup>18-20</sup>

Although the optimal screening tool for PSD is unclear, a meta-analysis of 24 studies through November 2012 showed that the CES-D was 1 of the 3 optimal screening tools for PSD, with a sensitivity of .75 (95% confidence interval [CI] .60-.85) and a specificity of .88 (95% CI .71-.95).<sup>12,21</sup>

### *Study Sample*

From 14,407 individuals eligible for inclusion in NHEFS, 12,220 individuals were interviewed between 1982 and 1984.<sup>16</sup> Of the 12,220 individuals who were interviewed, 2,294 did not have CES-D data and an additional 7 had an unknown stroke status and were excluded, leaving 9919 for the final analysis. Our study sample included all adult participants of NHANES I who were still alive and were interviewed between 1982 and 1984, and who had complete data for the CES-D scale. Individuals who did not have complete CES-D data or had missing stroke history data were excluded. History of stroke and medical comorbidities were determined by self-report. The diagnosis of stroke was based on a "yes" response to the following question: "Did a doctor ever tell you that you had any of the following conditions: Small stroke sometimes known as TIA (transient ischemic attack), stroke (sometimes called a CVA)."<sup>16</sup> A similar approach was utilized to establish a diagnosis of other self-reported medical conditions. The study sample was divided into 4 groups based on the self-reported stroke and depression defined as CES-D score of 16 or higher in 1982-1984 as follows: (1) no stroke, no depression (reference); (2) stroke, no depression; (3) no stroke, depression; and (4) both stroke and depression.

### *Outcome Measures*

The main outcome measures were all-cause mortality and stroke mortality across the 4 groups in the study sample. Follow-up data were collected during the following time periods: 1982-1984, 1986, 1987, and 1992. Follow-up length was calculated from the date of the baseline interview in 1982-1984 to either the date of death

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