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The Relationship Between Major Depression and Nonsuicide Mortality for U.S. Adults: The Importance of Health Behaviors

Jarron M. Saint Onge,[1,2] Patrick M. Krueger,[3] and Richard G. Rogers[4]

[1]Department of Sociology, University of Kansas, Lawrence.
[2]Department of Health Policy and Management, University of Kansas Medical Center, Kansas City.
[3]Department of Health & Behavioral Sciences, University of Colorado at Denver.
[4]Department of Sociology, University of Colorado at Boulder.

Objectives. We aim to elucidate the role of health behaviors and health conditions in the association between depression and mortality. First, we examine the relationship between major depression and nonsuicide mortality among U.S. adults aged 50 and older. Second, we examine the relationship between major depression and cardiovascular disease and cancer, by baseline disease status. Third, we examine the role of health behaviors as potential mediators of the association between major depression and cause-specific mortality.

Methods. We use data from the 1999 National Health Interview Study linked to the 2006 National Death Index ($N = 11{,}369$; M age = 65, deaths = 2,162) and Cox proportional hazards models to describe the relationships among major depression, health behaviors (alcohol use, cigarette smoking, physical activity), and nonsuicide mortality. We examine cause-specific mortality (cardiovascular and cancer) by baseline disease status.

Results. Major depression remains associated with a 43% increase in the risk of death over the follow-up period, after we account for sociodemographic characteristics, health behaviors, and health conditions. Major depression is associated with 2.68 times the risk of cardiovascular disease mortality among those who did not have cardiovascular disease at baseline and 1.82 times for those with baseline cardiovascular disease. Health behaviors reduce the hazard ratio by 17% for all nonsuicide mortality, 3% for cardiovascular disease mortality, and 12% for cancer mortality.

Discussion. Our results provide evidence of the important role of health behaviors and health conditions in the depression–mortality relationship and highlight the importance of identifying risk factors for depression among aging adults.

Key Words: Cancer—Cardiovascular disease—Health behaviors—Major depression—Mortality—NHIS-LMF.

MAJOR depression is a risk factor for all-cause, cardiovascular disease, and cancer mortality among U.S. adults. Major depression remains common in later life and is a major cause of decreased quality of life in older adults (Blazer, 2003; Blazer & Hybels, 2005; Kessler et al., 2010; Wu, Schimmele, & Chappell, 2012). Methodologically, rigorous studies have demonstrated that depression increases the risk of death by 60%–80%, depending on the inclusion of various covariates (Schulz, Drayer, & Rollman, 2002; Wulsin, Vaillant, & Wells, 1999). But questions remain regarding the role of health behaviors and health conditions in the depression–mortality relationship among older adults. We use a large population-based data set of U.S. adults aged 50 and older, with a valid and reliable measure of major depression, to examine relationships among modifiable health behaviors, major depression (a treatable psychological condition), and nonsuicide mortality. We focus on adults aged 50 and older because depression increases among older adults, the risk factors for depression among older adults (e.g., poor health, widowhood, transitions out of the work force) differ from the risk factors among younger adults, and the interventions for depression or health behaviors that work among older adults may differ from those that are most effective among younger adults (Mezuk & Kendler, 2012; Wu et al., 2012).

Our first aim is to examine the relationship between major depression and nonsuicide mortality among U.S. adults aged 50 and older. A review by Wulsin and colleagues (1999) concludes that an understanding of this association is hampered by small, community-based samples, and that future research should use a prospective design with a large enough sample size to examine the association between major depression and mortality while accounting for poor health at baseline. We extend previous research in two ways. First, we use a large, nationally representative, 6-year prospective data set that includes a specific measure of major depression for adults aged 50 and older. Second, our data allow us to adjust for numerous variables that might confound the relationship between major depression and mortality, including age, race/ethnicity, sex, nativity, year of birth, marital status, several indicators of socioeconomic status (SES), and several measures of baseline health

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(Bruce, 2001; Frasure-Smith, Lespérance, & Talajic, 1993; Kessler et al., 2003; Rogers, Hummer, & Nam, 2000).

Our second aim is to examine the relationship between major depression and common causes of death in old age, namely cardiovascular disease and cancer, and to explore the depression–mortality relationship by baseline disease status. In a small community-based sample, Glassman and Shapiro (1998) found that depression was associated with 1.5–2.0 times the risk of cardiovascular disease mortality over the following 6–12 months among those who had cardiovascular disease at baseline. Others have found similar results regardless of baseline disease status, albeit with relatively small samples and short follow-up periods (Penninx et al., 2001; Peters et al., 2010)

Results for other causes of death are less consistent. Studies report no relationship or modest relationships between depression and cancer mortality (see Pinquart & Duberstein, 2010). A meta-analysis of 76 studies found a more robust relationship, with the association between depression and cancer mortality stronger in studies that rely on shorter follow-up periods or samples of older adults (Satin, Linden, & Phillips, 2009). The majority of studies cited in the meta-analysis included postcancer depression screenings and many of the studies were specifically focused on cancer patients, offering limited insight into the association between depression and cancer mortality in the broader population.

Our third aim is to examine the role of health behaviors as potential mediators of the association between major depression and mortality. Although there may be direct links between depression and mortality through biological pathways (e.g., ventricle instability, decreased heart rate variability, platelet reactivity, hypothalamic-pituitary-adrenal axis hyperactivity), depression may also affect mortality indirectly through potentially modifiable health behaviors (Houle, 2013), for three reasons.

First, major depression may result in hopelessness, fatalism, and ultimately more heavily discounting the future costs of unhealthy behaviors (Pulcu et al., 2014). Older adults with major depression may see little value in quitting or reducing smoking, drinking less, exercising more, or otherwise caring for their health if the future seems bleak. For example, even though regular physical activity is associated with reduced depression, depressed adults may be less likely to pursue physical activities if a healthy and happy future seems implausible or unattainable (Elfrey & Ziegelstein, 2009).

Second, adults with major depression may withdraw from social networks and experience decreases in the quality and quantity of social relationships (Allgöwer, Wardle, & Steptoe, 2001). Depression can increase social isolation and loneliness, both of which have been linked to high odds of smoking and physical inactivity (Shankar, McMunn, Banks, & Steptoe, 2011). Further, depressed individuals are less likely to quit smoking if they are exposed to tobacco advertisements, especially for those who had fewer friends or whose friends smoked (Ziedonis et al., 2008).

Finally, depressed individuals may undertake unhealthy behaviors to self-regulate depressive symptoms or to cope with negative feelings and to stimulate affect (Ziedonis et al., 2008). Spring, Pingitore, and McChargue (2003) show that despite knowledge of the risks of smoking, adults with a lifetime history of depression reported greater rewards from smoking and were more likely to choose smoking over other rewarding activities, compared with smokers without psychiatric disorders. To escape or avoid negative emotions, depressed adults routinely use alcohol, which can result in problem drinking (Holahan, Moos, Holahan, Cronkite, and Randall, 2001).

Regardless of the specific pathways that link depression to unhealthy behaviors, those unhealthy behaviors eventually contribute to early mortality (Jackson, Knight, & Rafferty, 2010; Murphy et al., 2008; Win et al., 2011). Because health behaviors are modifiable, and depression is potentially preventable and treatable, the relationships among health behaviors, major depression, and mortality may provide multiple target points for public health and clinical interventions. Understanding the associations between depression and mortality can support efforts to reduce excess mortality risk among older adults.

Method

Data

Data come from the 1999 National Health Interview Survey (NHIS), a nationally representative, publicly available, cross-sectional, face-to-face household survey of noninstitutionalized adults in the United States. We draw our data from the sample adult core, where one adult per family is randomly chosen to respond to detailed health questions including a specific measure of major depression that is not included in subsequent study waves. The 1999 NHIS data are linked to prospective mortality through the National Death Index (NDI) through December of 2006 to create the Linked Mortality File (LMF) (National Center for Health Statistics, 2006). These prospective data measure all covariates, including major depression, only once at baseline; vital status and age are the only variables that vary over time. The NHIS-LMF is of high quality and allows the results to be generalized to the adult civilian, noninstitutionalized population (Lochner, Hummer, Bartee, Wheatcroft, & Cox, 2008). We drop 5.6% of the NHIS records that cannot be linked to the NDI because of missing information on the matching characteristics, as recommended by the NHIS staff (National Center for Health Statistics, 2010). We remove 26 cases where the underlying cause of death was listed as suicide and 88 cases where the underlying cause of death was listed as an accident to remove potential misidentified suicide cases. Our total sample size is 11,369 adult respondents aged 50 and older, of whom 2,162 have died.

Variables

As in several other studies, our measure of all-cause mortality excludes suicide (Schulz et al., 2002). Cause-specific mortality is defined through the International Classification of Diseases-10 (ICD-10) codes. Among primary causes of death, we examine major cardiovascular conditions, excepting essential hypertension and hypertensive renal disease (n = 685; ICD-10 codes I00-I09, I11, and I13-I51), and cancer (n = 466; ICD-10 codes C00-C97).

Our measure of major depression is derived from the World Health Organization Composite International Diagnostic Interview Short-Form (CIDI-SF). The CIDI-SF is a valid and reliable diagnostic instrument and has classification accuracy of 93% for major depressive disorder (Kessler, Andrews, Mroczek, Utsun, & Wittchen, 1997). In accord with the method described by Walters, Kessler, Nelson, and Mroczek (2002), respondents must meet two sets of criteria to be classified as having major depression. First, respondents must affirmatively answer that they have had 2 weeks of either dysphoric mood or anhedonia, with the symptoms lasting at least most of the time, almost every day. Second, respondents must report at least three of the following seven symptoms: losing interest, feeling tired, weight change, difficulty sleeping, trouble concentrating, feeling down, and thoughts about death. Five percent of respondents meet both criteria and are coded as having major depression.

We adjust for various sociodemographic factors that are associated with both depression and mortality. Sex is coded dichotomously with females coded as 1. Race/ethnicity is coded categorically as non-Hispanic white (referent), non-Hispanic black, and Hispanic. Nativity is coded dichotomously, with foreign-born adults coded as 1. We use age to identify the time to death or censoring. Year of birth is continuous and ranges from 1915 to 1949.

We also adjust for marital status and indicators of socioeconomic status. Marital status is coded categorically as currently, previously, or never married. Education, measured continuously as the number of years of school completed, ranges from 0 to 20 years. Employment status is coded categorically as employed (referent), unemployed, or not in the labor force. The NHIS reports total family income in 11 categories. We approximate a continuous variable by assigning the dollar value associated with the midpoint of each category, impute the median value for the open-ended upper category, and present the natural log of the variable (unlogged range: $2,500–$105,000).

Health behaviors include smoking, alcohol use, and physical activity. Smoking is coded as never (referent), former, current light (0–14 cigarettes per day), current moderate (15–24 cigarettes per day), or current heavy (≥25 cigarettes per day). Two variables capture physical activity. The first item, regular physical activity, is dichotomous and indicates whether respondents report undertaking at least 30 min of moderate activity at least five times per week or at least 20 min of vigorous activity at least three times per week (Physical Activity Guidelines Advisory Committee, 2008). The second item, a more stringent measure of physical activity (Schoenborn & Stommel, 2011), is coded as dichotomous and indicates whether a respondent engaged in both regular physical activity (as indicated previously) and strength training of at least two times per week. Alcohol use is measured as abstention, former drinking, current light drinking (referent; <2 drinks per day for men and <1 drink per day for women), or current heavy drinking (average of two drinks per day for men and one drink per day for women). The risk of death is relatively high for both abstainers and former drinkers, low for light-to-moderate drinkers, and highest among heavier drinkers (Himes, 2011). Separate variables indicate abstainers and former drinkers because they reflect distinct reasons for nondrinking (Rogers, Krueger, Miech, Lawrence, & Kemp, 2013).

Our data include several measures of health status at baseline. Body mass is calculated from self-reported height and weight, and is categorized as underweight (body mass index [BMI] < 18.5), normal weight (referent; BMI = 18.5–24.9), overweight (BMI = 25–29.9), or obese (BMI ≥ 30.0). Functional limitation is a dichotomous variable based on any indicated difficulty with walking, climbing, standing, sitting, stooping, reaching, grasping, carrying, pushing, shopping, socializing, or relaxing. Respondents indicated whether they had ever been told by a doctor or other health professional that they had cancer, diabetes (other than during pregnancy), or a stroke. We also coded respondents as having a history of heart disease if they reported ever having been told that they had had a heart attack, coronary disease, angina, or any other heart condition.

Analyses

We use Cox proportional hazards models to examine the risk of death. We include age as the time to death or the end of the follow-up period (i.e., right censoring) (Korn, Graubard, & Midthune, 1997). First, we present descriptive statistics disaggregated by vital status and major depression diagnosis. Second, we present a set of progressive Cox proportional hazards models testing the association between major depression and mortality, controlling for sociodemographic characteristics, socioeconomic status, health behaviors, and health status. Third, we analyze the effect of health behaviors on mortality by baseline disease status (for cardiovascular disease and cancer). We present our results in the form of hazard ratios (HRs; i.e., exponentiated coefficients) and 95% confidence intervals (CIs). HRs above one indicate an increased risk of death, relative to some referent category, and HRs below one indicate a reduced risk of death compared with some referent category. All analyses include appropriate sample weights and adjust for clustering and the complex sample through Taylor-linearized variance estimation design (StataCorp, 2011).

Proportional hazards models require few assumptions when modeling the time to event (i.e., death) or censor (Allison, 1984; Powers & Xie, 2008). Separate tests (data not shown) find that we have satisfied the proportional hazards assumption—the HR comparing any two groups is constant across ages (Hosmer, Lemeshow, & May, 2011). Separate models further used time since survey (rather than age) as the time to event to test whether the effect of major depression (measured cross-sectionally at baseline) on mortality declined over the follow-up period. Those analyses found no evidence that the effect of depression on mortality varied over time; thus, we find no evidence that major depression simply marks impending death at baseline.

Results

Table 1 presents the weighted means and proportions of all of the covariates by vital status and major depression status. Approximately 5% of the population met the CIDI-SF criteria for major depression at baseline. Before adjustment for covariates, those who survived the follow-up period had significantly lower rates of major depression at baseline, higher SES, fewer chronic health conditions, and fewer unhealthy behaviors. Persons with major depression were younger and more often women, and had significantly lower SES, with lower levels of education, employment, and income. They also had worse health at baseline as indicated by higher rates of obesity, functional limitations, heart disease, cancer, stroke, and diabetes; greater prevalence rates of smoking; and higher levels of heavy drinking and physical inactivity.

Table 2 presents HRs from hazards models that examine whether health conditions and health behaviors explain the relationship between major depression and nonsuicide mortality. Model 1 indicates that major depression is associated with 2.6 times the risk of death when adjusting for year of birth, sex, race/ethnicity, and foreign birth. Model 2 shows that the association between major depression and mortality is attenuated (i.e., the HR is slightly closer to 1.0) when adjusting for SES. Adjusting for marital status, education, employment status, and income reduces the association between major depression and mortality by 17% ($[\ln(2.21) - \ln(2.60)]/\ln(2.60) \times 100$). Model 3 adjusts for health behaviors in addition to SES and sociodemographic variables, and demonstrates that major depression remains associated with a 93% increase in the risk of death over the follow-up period. Adjusting for health behaviors closes the HR for major depression by 17% (compare Models 2 and 3; Wald test $p < .001$), although the association between major depression and nonsuicide mortality persists. Notably, drinking statuses, physical activity, and smoking statuses are each associated with mortality as expected.

Model 4 further adjusts for the health status variables. Because Model 4 adjusts for several variables that are closely related to specific causes of death (i.e., self-reported chronic medical conditions) or that may result from health behaviors or major depression (e.g., body mass, functional limitations), it provides a conservative test of the associations among major depression, health behaviors, and mortality. The association between major depression and nonsuicide mortality is reduced by 46% after adjustment for health status at baseline (compare Models 3 and 4; Wald test $p < .001$). The associations between the health behaviors and mortality are only somewhat attenuated after adjusting for health status.

Tables 3 and 4 present the association between major depression and cause-specific mortality from cardiovascular disease and cancer, respectively. First, our baseline model focuses on cause-specific mortality while adjusting for the sociodemographic and SES variables. The next three models build on the baseline model by further adjusting for one of the health behavior variables, and the final model adjusts for all of the health behavior variables simultaneously. We estimate those five models for three groups: (a) a pool containing both those with and those without the condition at baseline (i.e., cardiovascular disease mortality at baseline for models predicting cardiovascular disease mortality, and cancer at baseline for models predicting cancer mortality), (b) those who did not report the given condition at baseline, and (c) those who did report the given condition at baseline. The percentage change in the HR for major depression, shown on the tables, indicates how much of the association between major depression and cause-specific mortality is explained by a given health behavior. Notably, we exclude the health status variables from the models on Tables 3 and 4 to avoid overfitting the data, especially given the small numbers of cause-specific deaths, and because the health status variables may result from health behaviors or major depression.

The baseline model in Table 3 indicates a strong positive association between major depression and cardiovascular disease mortality that persists even when the population is stratified by cardiovascular disease at baseline. Physical activity and smoking each reduce the magnitude of the association between major depression and cardiovascular disease mortality in the pooled sample and for those without cardiovascular disease at baseline, but only physical activity attenuates the association between major depression and cardiovascular disease mortality among those who have cardiovascular disease at baseline. In contrast, adjusting for alcohol consumption increases the magnitude of the relationship between major depression and cardiovascular disease mortality in all three groups. Adjusting for smoking also increases the relationship between major depression and cardiovascular disease mortality among those who had cardiovascular disease at baseline.

Table 4 shows that major depression is associated with a 2.8 times increase in the risk of cancer mortality in the pooled sample. However, that association holds only for those who did not have cancer at baseline. In the sample of

Table 1. Weighted Means and Proportions of Covariates by Vital Statistics and Major Depression, U.S. Adults Aged 50 Years and Older, 1999–2006

		Vital status			Major depression		
	Total	Survived	Died	*p* Value[a]	No	Yes	*p* Value[a]
Major depression	0.05	0.04	0.06	***	—	—	
Sociodemographic characteristics							
Race/ethnicity				***			n.s.
Non-Hispanic white	0.84	0.84	0.86		0.84	0.86	
Non-Hispanic black	0.09	0.09	0.10		0.09	0.07	
Hispanic	0.07	0.07	0.04		0.07	0.07	
Foreign born	0.09	0.09	0.06	***	0.09	0.08	n.s.
Mean year of birth	1933	1935	1925	***	1933	1937	***
Female	0.54	0.55	0.51	***	0.54	0.65	***
Socioeconomic status							
Marital status				***			***
Currently married	0.66	0.69	0.51		0.67	0.56	
Previously married	0.30	0.26	0.45		0.29	0.39	
Never married	0.04	0.04	0.04		0.04	0.05	
Mean education	12.44	12.64	11.46	***	12.46	11.88	***
Employment status				***			***
Employed	0.42	0.47	0.14		0.42	0.33	
Unemployed	0.01	0.01	0.01		0.01	0.01	
Not in labor force	0.58	0.52	0.86		0.58	0.66	
Mean total family income	$33,859	$36,375	$23,015	***	$34,174	$27,835	***
Health status							
BMI (kg/m^2)				***			***
Underweight (<18.5)	0.02	0.01	0.05		0.02	0.04	
Normal weight (18.5–24.9)	0.36	0.34	0.43		0.36	0.32	
Overweight (25.0–29.9)	0.39	0.40	0.32		0.39	0.34	
Obese (≥30.0)	0.24	0.24	0.20		0.23	0.31	
Functional limitation	0.48	0.43	0.72	***	0.46	0.78	***
Self-reported chronic conditions							
Heart disease	0.21	0.18	0.37	***	0.21	0.34	***
Cancer	0.14	0.12	0.25	***	0.14	0.21	***
Stroke	0.05	0.03	0.12	***	0.05	0.08	***
Diabetes	0.11	0.10	0.19	***	0.11	0.16	**
Health behaviors							
Smoking status				***			***
Never smoker	0.45	0.47	0.39		0.46	0.35	
Former smoker	0.38	0.37	0.42		0.38	0.32	
Current light smoker	0.06	0.06	0.07		0.06	0.09	
Current moderate smoker	0.07	0.07	0.08		0.07	0.14	
Current heavy smoker	0.03	0.03	0.04		0.03	0.09	
Physical activity							
Regular physical activity	0.17	0.18	0.10	***	0.17	0.10	***
Regular physical activity and strengthening	0.08	0.09	0.03	***	0.08	0.04	***
Alcohol use				***			***
Abstainer	0.25	0.24	0.32		0.26	0.23	
Former drinker	0.22	0.20	0.32		0.22	0.28	
Current drinker	0.48	0.51	0.33		0.48	0.43	
Current heavy drinker	0.04	0.05	0.03		0.04	0.06	
Survival							
Nonsuicide mortality (died = 1)	0.17	0.00	1.00		0.17	0.24	***
Mean age at death or censor	72.62	71.31	78.21	***	78.63	71.50	***
Mean age at interview	65.67	63.71	74.05	***	65.86	62.07	***
N	11,369	9,207	2,162		10,821	548	

Notes. BMI = body mass index; NHIS = National Health Interview Survey.
[a]All *p* values come from Wald tests that adjust for the complex sampling of the NHIS.
Statistically significant coefficients are indicated as follows: †$p \le .10$. *$p \le .05$. **$p \le .01$. ***$p \le .001$.

adults who did not report cancer at baseline, alcohol consumption explained 13.7% of the association between major depression and mortality, physical activity explained 2% of the association, smoking explained 14.7% of the association, and all of the health behaviors together explained 21.5% of the association.

Table 2. Cox Proportional Hazard Ratios (95% Confidence Intervals) for the Relationships Among Depression, Socioeconomic Status, Health Conditions, Health Behaviors, and the Risk of Nonsuicide Death, U.S. Adults 50 Years and Older, 1999–2006

	Model 1	Model 2	Model 3	Model 4
Major depression	2.60 (2.11–3.21)***	2.21 (1.77–2.75)***	1.93 (1.53–2.44)***	1.43 (1.13–1.82)**
Sociodemographic characteristics				
Year of birth	1.01 (0.98–1.03)	1.03 (1.00–1.05)*	1.03 (1.01–1.06)*	1.06 (1.03–1.08)***
Race/ethnicity (N.H. white)				
Non-Hispanic black	1.27 (1.05–1.52)*	1.12 (0.92–1.35)	1.08 (0.89–1.30)	1.11 (0.89–1.38)
Hispanic	0.82 (0.62–1.08)	0.66 (0.49–0.89)**	0.71 (0.52–0.97)*	0.79 (0.58–1.08)
Female (=1)	0.67 (0.61–0.74)***	0.56 (0.51–0.63)***	0.60 (0.54–0.68)***	0.56 (0.49–0.63)***
Foreign born (=1)	0.74 (0.59–0.92)**	0.67 (0.53–0.84)***	0.70 (0.55–0.89)**	0.66 (0.52–0.84)***
Socioeconomic status				
Marital status (currently married)				
Previously married		1.35 (1.21–1.52)***	1.30 (1.16–1.47)***	1.32 (1.17–1.49)***
Never married		1.09 (0.86–1.39)	1.10 (0.86–1.41)	1.09 (0.84–1.41)
Years of education		0.96 (0.94–0.97)***	0.98 (0.96–0.99)**	0.98 (0.96–0.99)**
Employment status (employed)				
Unemployed		2.07 (0.94–4.56)†	1.66 (0.73–3.77)	2.20 (0.95–5.06)†
Not in labor force		1.93 (1.61–2.31)***	1.86 (1.56–2.23)***	1.62 (1.35–1.96)***
Logged family income		0.93 (0.86–1.00)*	0.96 (0.89–1.04)	0.95 (0.88–1.03)
Health behaviors				
Alcohol use (current drinker)				
Abstainer			1.40 (1.21–1.62)***	1.34 (1.15–1.56)***
Former drinker			1.55 (1.36–1.77)***	1.36 (1.18–1.57)***
Current heavy drinker			1.02 (0.77–1.35)	1.04 (0.77–1.42)
Physical activity (no regular activity)				
Regular physical activity			0.65 (0.55–0.77)***	0.74 (0.62– 0.89)**
Regular physical activity and strengthening			0.53 (0.39–0.71)***	0.54 (0.40–0.73)***
Smoking status (never smoker)				
Former smoker			1.49 (1.31–1.68)***	1.39 (1.22–1.59)***
Current light smoker			1.66 (1.33–2.08)***	1.52 (1.21–1.92)***
Current moderate smoker			2.17 (1.77–2.66)***	2.00 (1.60–2.49)***
Current heavy smoker			3.17 (2.37–4.25)***	2.91 (2.17–3.90)***
Health status				
BMI (kg/m^2; normal weight 18.5–24.9)				
Underweight (<18.5)				3.15 (2.41–4.11)***
Overweight (25.0–29.9)				0.81 (0.72–0.92)***
Obese (≥30.0)				0.78 (0.67–0.91)**
Functional limitation				1.56 (1.36–1.77)***
Self-reported chronic conditions				
Heart disease (=1)				1.26 (1.13–1.42)***
Cancer (=1)				1.55 (1.35–1.77)***
Stroke (=1)				1.32 (1.11–1.58)**
Diabetes (=1)				1.74 (1.50–2.02)***
Observations	11,368	10,530	10,483	9,989
− Log likelihood	−3,381.70	−2,901.83	−2,800.12	−2,488.61
Akaike information criterion	6,775.39	5,827.66	5,642.24	5,035.23
Bayesian information criterion	6,819.42	5,914.81	5,794.64	5,244.29

Notes. Robust 95% confidence intervals in parentheses. Adjusted Wald tests indicate significant model improvement for each subsequent model. BMI = body mass index.

Statistically significant coefficients are indicated as follows: †$p \le .10$. *$p \le .05$. **$p \le .01$. ***$p \le .001$.

Discussion

Our results demonstrate that major depression among older adults in the noninstitutionalized U.S. population is associated with increased risk of nonsuicide mortality during a 6-year follow-up. This finding echoes those of the "most methodologically sound" studies reported by Wulsin and colleagues (1999); our contribution consists in using a nationally representative sample of older adults, a psychometrically validated measure of major depression, and an extensive set of covariates. Research that focuses on older adults has proven particularly challenging because many control variables are associated with depression and mortality (Blazer, Hybels, & Pieper, 2001; Penninx, Geerlings, et al., 1999; Schulz et al., 2000, 2002). Although the association between major depression and mortality is attenuated after we adjust for marital status, education, employment status, family income, alcohol consumption, physical activity, smoking status, body mass, functional limitations, and chronic conditions at baseline, there remains an independent association between major depression and nonsuicide

Table 3. Role of Health Behaviors in Explaining Relationship Between Major Depression and Cardiovascular Disease (CVD) Mortality, by Baseline Heart Disease Status, U.S. Adults 50 Years and Older 1999–2006

	Pooled sample		No CVD at baseline		CVD at baseline	
	Hazard ratio (95% CI)	% Change from baseline	Hazard ratio (95% CI)	% Change from baseline	Hazard ratio (95% CI)	% Change from baseline
Baseline[a]	2.33 (1.51, 3.58)***	—	2.68 (1.25, 5.77)*	—	1.82 (1.01, 3.26)*	—
Baseline + alcohol consumption	2.38 (1.53, 3.71)***	2.77	2.85 (1.28, 6.36)*	6.16	1.89 (1.06, 3.35)*	6.14
Baseline + physical activity	2.27 (1.44, 3.57)***	−3.05	2.64 (1.17, 5.95)*	−1.53	1.71 (0.90, 3.25)†	−9.80
Baseline + smoking	2.26 (1.35, 3.63)***	−3.28	2.53 (1.12, 5.49)*	−5.82	2.03 (1.03, 3.99)*	18.47
Fully adjusted for health behaviors	2.27 (1.40, 3.66)***	−3.13	2.73 (1.08, 6.91)*	1.94	1.91 (0.96, 3.79)†	8.10
Deaths	685		379		306	
N	11,369		8,916		2,453	

Notes. Data derived from the 1999 National Health Interview Survey. CI = confidence interval; CVD = cardiovascular disease.
[a]The baseline model in this table adjusts for year of birth, ethnicity, sex, foreign birth, marital status, education, employment status, logged family income.
Statistically significant coefficients are indicated as follows: †$p \leq .10$. *$p \leq .05$. **$p \leq .01$. ***$p \leq .001$.

Table 4. Role of Health Behaviors in Explaining Relationship Between Major Depression and Cancer Mortality, by Baseline Cancer Status, U.S. Adults Aged 50 Years and Older, 1999–2006

	Pooled sample		No cancer at baseline		Cancer at baseline	
	Hazard ratio (95% CI)	% Change from baseline	Hazard ratio (95% CI)	% Change from baseline	Hazard ratio (95% CI)	% Change from baseline
Baseline[a]	2.83 (1.86, 4.32)***	—	2.05 (1.02, 4.13)*	—	1.24 (0.55, 2.71)	—
Baseline + alcohol consumption	2.74 (1.79, 4.20)***	−3.21	1.86 (0.93, 3.73)†	−13.66	1.25 (0.54, 2.94)	3.81
Baseline + physical activity	2.75 (1.82, 4.16)***	−2.92	2.02 (1.01, 4.06)*	−2.04	1.21 (0.52, 2.84)	−10.71
Baseline + smoking	2.63 (1.70, 4.07)***	−7.24	1.85 (0.93, 3.68)†	−14.72	1.42 (0.45, 4.47)	60.58
Fully adjusted for health behaviors	2.49 (1.64, 3.79)***	−12.29	1.76 (0.89, 3.49)†	−21.46	1.19 (0.32, 4.40)	−20.47
Deaths	466		314		152	
N	11,369		9,786		1,565	

Notes. Data derived from the 1999 National Health Interview Survey. CI = confidence interval.
[a]The baseline model in this table adjusts for year of birth, ethnicity, sex, foreign birth, marital status, education, employment status, logged family income.
Statistically significant coefficients are indicated as follows: †$p \leq .10$. *$p \leq .05$. **$p \leq .01$. ***$p \leq .001$.

mortality (see Table 2, Model 4). The slightly lower risk found in our study compared with others may be due to our conservative exclusion of suicides and inclusion of multiple covariates.

Our second aim was to examine the association between major depression and mortality from cardiovascular disease and cancer. Given the increased rates of depression among those who have been diagnosed with either disease, we estimated models separately by disease status at baseline. Our results are consistent with previous findings that depression is associated with 1.5–2.0 times the risk of death among patients with preexisting cardiovascular disease (Glassman & Shapiro, 1998) and that baseline cardiac disease and depression are additively associated with cardiovascular disease mortality (Penninx et al., 2001). We find that major depression is associated with 2.68 times (95% CI = 1.25–5.77) the risk of cardiovascular disease mortality among those who did not have cardiovascular disease at baseline, compared with 1.82 times (95% CI = 1.01–3.26) among those who did (see Table 3). The persistent association between major depression and cardiovascular disease mortality is consistent with research that links depression to arterial aging among older adults (Scuteri, Modestino, Fedullo, Assisi, & Gianni, 2013).

Our results for cancer mortality were less striking. Although major depression was associated with 2.05 times (95% CI = 1.02–4.13) the risk of cancer mortality among those who did not report cancer at baseline, the association was much smaller and not statistically significant among those who did (HR = 1.24; 95% CI = 0.55–2.71). Reporting cancer at baseline is associated both with higher levels of depression (see Table 1) and higher risks of death (see Table 2). Thus, major depression—which is more common among those who have been diagnosed with cancer—may be weakly associated with the risk of cancer mortality in a subgroup of respondents who already have cancer and who already experience high rates of death. This may in part explain why other slightly older studies have not found significant relationships with cancer mortality (Sun, Schooling, Chan, Ho, & Lam, 2011).

Our third aim was to examine the role of health behaviors as potential mediators of the association between major depression and overall and cause-specific mortality. Adjusting for health behaviors reduce the HR between

major depression and mortality by 17% for all nonsuicide mortality, 3% for cardiovascular disease mortality, and 12% for cancer mortality. The ability of health behaviors to explain the association between major depression and mortality differs by cause of death and baseline disease status. Smoking partially explained the association between major depression and death from cardiovascular disease among those who did not have cardiovascular disease at baseline, and smoking and alcohol consumption partially explained the association between major depression and cancer mortality among those who did not report a cancer diagnosis at baseline.

But smoking and alcohol consumption sometimes increased the association between major depression and cardiovascular disease and cancer mortality among those who reported those conditions at baseline. This suppressor effect may occur because the individuals who have the best survival prospects, such as those who are married, have more socioeconomic resources, or have more treatable conditions, generally give up smoking or alcohol at higher rates than those with poorer survival prospects (Gerber et al., 2011). Higher levels of physical activity attenuated the association between major depression and nonsuicide mortality, cardiovascular disease mortality, and cancer mortality. Promoting physical activity may help reduce the severity and duration of major depression (Strawbridge, Deleger, Roberts, & Kaplan, 2002), and may reduce the risk of death from numerous causes. Early life interventions aimed at reducing rates of smoking and excess alcohol consumption may also reduce mortality, while additional gains in longevity may come from targeting older smokers and drinkers who are not already diagnosed with cancer or cardiovascular disease.

Notably, health behaviors did not completely explain the association between major depression and all-cause or cause-specific mortality in any model. Major depression may be linked to premature death through various mechanisms other than health behaviors. First, depression may affect survival through biological pathways including blood pressure, inflammation, immune function, or the dysregulation of the hypothalamic-pituitary-adrenal axis (Jackson et al., 2010; Shankar, McMunn, Banks, & Steptoe, 2011). Current research suggests that treatment of depression could lower cardiovascular risk factors by reducing arterial aging in older adults (Scuteri et al., 2013). Second, social withdrawal, including the loss of friends or other close social ties, might connect depression to mortality through pathways apart from unhealthy behaviors, such as psychosocial or material support (Kawachi & Berkman, 2000). Finally, the compromised affect typical of depression may result in motivational depletion, vital exhaustion, or a lack of emotional vitality that may result in increased risks of death among older adults. Individuals who have "given up" may have low levels of adherence to physician advice or medical regimens and may disengage from supportive relationships at the same time that they pursue or maintain unhealthy behaviors (Schulz et al., 2000).

Strengths and Limitations

The strengths of this study include detailed measures of health behaviors, the use of a diagnostic screener specific to major depression, the analyses of a large nationally representative sample linked to prospective mortality with a longer follow-up than many clinical or community settings studies, and the incorporation of numerous covariates that are seldom included in a single study (Wulsin et al., 1999).

Several limitations of our study warrant mention. First, because we draw on a nationally representative population-based sample, medical conditions at baseline necessarily come from self-reports. Although self-reports generally have strong prognostic validity (Ferraro & Farmer, 1999), people with major depression may be less likely to get regular health screenings, and may underreport their incidence of cardiovascular disease or cancer. Second, depression may be most strongly linked to mortality in the short term immediately following diagnosis if that diagnosis results in additional negative health behaviors used as coping strategies, or in reduced self-care, functional decline, social withdrawal, or medical noncompliance (DiMatteo, Lepper, & Croghan, 2000; Frasure-Smith et al., 1993; Penninx, Leveille, Ferrucci, van Eijk, & Guralnik, 1999; Roberts, Kaplan, Shema, & Strawbridge, 1997). Although we found no evidence that the relationship between major depression and mortality was strongest early in the follow-up period and then declined as the time from survey increased, we could not directly examine the time since first or most recent depressive episode, because the NHIS does not collect that information.

Conclusion

Our results highlight the need for increased vigilance regarding major depression among older adults. Although depression is not necessarily an inevitable consequence of aging, both depressive symptoms and risk factors for late-life depression generally increase with age (Wu et al., 2012). Depression among the elderly is an ongoing public health concern that is linked to changing work statuses (Ekerdt, 2010), increased rates of widowhood (Sasson & Umberson, 2014), and increased comorbidity (Alexopoulos, 2005; Kessler et al., 2010). Increasing levels of depressive symptoms with age may result in negative health behaviors and health conditions that increase mortality risk (Houle, 2013).

Although depression may respond to treatment, research has consistently shown that approximately 50% of depressed individuals are undiagnosed, few receive effective treatment, and underdiagnoses may be particularly frequent for the elderly (Goldman, Nielsen, & Champion, 1999; Kessler et al., 2003). Indeed, high levels of suicidality and antidepressant use among the elderly, coupled with recent examinations of symptomology suggest that depressive symptomology

may change over the life course and may be increasingly problematic for an aging population (Mezuk & Kendler, 2012; Wu et al., 2012). Even though our study relies on a fairly conservative measure of major depression, we find that 5% of the nationally representative sample indicates major depression, compared with 6.6% in a slightly younger general population (Kessler et al., 2003). Studies have also documented associations between mortality and less severe forms of depression (Penninx, Geerlings, et al., 1999; Wulsin et al., 2005). Depression among adults remains a major psychological problem that limits everyday functioning, increases social withdrawal, lowers quality of life, and, in conjunction with negative health behaviors and conditions, hastens death.

Promoting healthy behaviors may provide one useful way to offset the effects of major depression. People may overeat, abuse alcohol, smoke, or avoid exercise in order to cope with environmental stressors (Jackson et al., 2010; Krueger, Saint Onge, & Chang, 2011). Such unhealthy behaviors may actually decrease the immediate symptoms of depression, and to many individuals, this short-term benefit may outweigh the risk of compromising long-term health (Jackson et al., 2010; Winkleby & Cubbin, 2004). Nonetheless, professionals who treat depression should focus on ways to create immediate payoffs for healthy behaviors, because the depression itself undermines the patient's ability to invest energy in behaviors with only long-term benefits, especially if this means changing established behavioral patterns. As we find, the long-run effects should continue to be of high concern in the treatment of depression over the life course with lasting implications for early mortality.

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Correspondence

Correspondence should be addressed to Jarron M. Saint Onge, PhD, Department of Sociology and Department of Health Policy and Management, University of Kansas, 716 Fraser Hall, 1415 Jayhawk Blvd., Lawrence, KS 66045-7556. E-mail: jsaintonge@ku.edu.

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