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Associations between depression and all-cause and cause-specific risk of death: A retrospective cohort study in the Veterans Health Administration

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ABSTRACT

Objective: Depression may be associated with increased mortality risk, but there are substantial limitations to existing studies assessing this relationship. We sought to overcome limitations of existing studies by conducting a large, national, longitudinal study to assess the impact of depression on all-cause and cause-specific risk of death.

Methods: We used Cox regression models to estimate hazard ratios associated with baseline depression diagnosis (N = 849,474) and three-year mortality among 5,078,082 patients treated in Veterans Health Administration (VHA) settings in fiscal year (FY) 2006. Cause of death was obtained from the National Death Index (NDI).

Results: Baseline depression was associated with 17% greater hazard of all-cause three-year mortality (95% CI hazard ratio [HR]: 1.15, 1.18) after adjusting for baseline patient demographic and clinical characteristics and VHA facility characteristics. Depression was associated with a higher hazard of three-year mortality from heart disease, respiratory illness, cerebrovascular disease, accidents, diabetes, nephritis, influenza, Alzheimer's disease, septicemia, suicide, Parkinson's disease, and hypertension. Depression was associated with a lower hazard of death from malignant neoplasm and liver disease. Depression was not associated with mortality due to assault.

Conclusions: In addition to being associated with suicide and injury-related causes of death, depression is associated with increased risk of death from nearly all major medical causes, independent of multiple major risk factors. Findings highlight the need to better understand and prevent mortality seen with multiple medical disorders associated with depression.

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Introduction

Depression is well-known to be a prevalent [1], costly [2], and burdensome disorder [3] leading to substantial disability in the United States [4] and worldwide [5]. Although prior research has reported a relationship between depression and mortality, there have been substantial limitations associated with most existing studies. Many studies that have examined depression and mortality have been limited to specific subgroups of patients with illnesses comorbid with depression (e.g. depressed patients with concurrent coronary artery disease [6], diabetes [7], COPD [8], inpatients [9]). Other studies have examined whether depression is associated with a single cause of death (e.g. stroke [10], cardiac disease [11]). Studies are also frequently restricted to include only older adult populations [12–14]; broader population-based studies have typically been conducted outside the United States [15,16]. Finally, meta-analyses have assessed the relationship between depression and mortality, but include heterogeneous measures of depression, confounders, and approaches to accounting for mortality [17,18].

The present study is unique in several ways. First, it examines how depression influences mortality in a large, US population-based,

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longitudinal study, using analyses that control for a variety of potential confounders. Second, it examines a large range of causes of death in a single population, VA users, who have similar levels of access to medical care. The size of this sample potentially allows the detection of associations that were previously too small to detect, and it allows the examination of different causes of death by age group, which has been infrequently reported in the existing literature.

Prior research by our team has shown unadjusted estimates of age at death and early mortality among Veterans with and without depression, in which we found that depression was associated with earlier

Table 1
Baseline data used in analyses of depression and cause-specific death, according to participants' depression status.

Characteristics	No depression N = 4,228,608 (83.27%)	Depression N = 849,474 (16.73%)	Total N = 5,078,082
Demographic factors			
Age (years) — mean ± SD	63.31 ± 15.62	59.16 ± 13.87	62.62 ± 15.42
Age 18 to <30	169,689 (4.01)	21,922 (2.58)	191,611 (3.77)
Age 30 to <40	209,649 (4.96)	49,194 (5.79)	258,843 (5.10)
Age 40 to <50	411,433 (9.73)	122,487 (14.42)	533,920 (10.51)
Age 50 to <60	920,069 (21.76)	304,538 (35.85)	1,224,607 (24.12)
Age 60 to <70	854,984 (20.22)	155,604 (18.32)	1,010,588 (19.90)
Age 70 to <80	1,034,209 (24.46)	118,509 (13.95)	1,152,718 (22.70)
Ages >80	628,575 (14.86)	77,220 (9.09)	705,795 (13.90)
Gender — n (%)			
Male	3,890,933 (92.01)	767,832 (90.39)	4,658,765 (91.74)
Female	337,675 (7.99)	81,642 (9.61)	419,317 (8.26)
Race			
American Indian	14,797 (0.35)	4659 (0.55)	19,456 (0.38)
Black	509,546 (12.05)	118,941 (14.00)	628,487 (12.38)
Asian	55,880 (1.32)	10,721 (1.26)	66,601 (1.31)
White	2,702,396 (63.91)	620,054 (72.99)	3,322,450 (65.43)
Unknown	929,024 (21.97)	89,717 (10.56)	1,018,741 (20.06)
Multi-racial	16,965 (0.40)	5382 (0.63)	22,347 (0.44)
# of visits/hospitalizations			
Outpatient visits			
0	772,366 (18.27)	40,171 (4.73)	812,537 (16.00)
1	346,860 (8.20)	25,710 (3.03)	372,570 (7.34)
2–5	1,316,698 (31.14)	151,381 (17.82)	1,468,079 (28.91)
≥6	1,792,684 (42.39)	632,212 (74.42)	2,424,896 (47.75)
Psychiatric hospitalizations			
0	4,212,915 (99.63)	806,100 (94.89)	5,019,015 (98.84)
≥1	15,693 (0.37)	43,374 (5.11)	59,067 (1.16)
Non-psychiatric hospitalizations			
0	4,011,494 (94.87)	733,434 (86.34)	4,744,928 (93.44)
1	162,231 (3.84)	80,672 (9.50)	242,903 (4.78)
2–5	53,227 (1.26)	33,934 (3.99)	87,161 (1.72)
≥6	1656 (0.04)	1434 (0.17)	3090 (0.06)
Comorbidities			
Anxiety, PTSD			
Yes	292,697 (6.92)	336,894 (39.66)	585,667 (11.53)
No	3,935,911 (93.08)	512,580 (60.34)	4,492,415 (88.47)
Serious mental illness (bipolar, schizophrenia, other psychoses)			
Yes	149,610 (3.54)	113,279 (13.34)	252,129 (4.97)
No	4,078,998 (96.46)	736,195 (86.66)	4,825,953 (95.03)
Charlson score (CCI14)	0.99 ± 1.48	1.33 ± 1.75	0.98 ± 1.52
Substance use			
Nicotine use			
Yes	528,452 (12.50)	226,933 (26.71)	687,210 (13.53)
No	3,700,156 (87.50)	622,541 (73.29)	4,390,872 (86.47)
Alcohol use disorder			
Yes	183,079 (4.33)	153,952 (18.12)	307,614 (6.06)
No	4,045,529 (95.67)	695,522 (81.88)	4,770,468 (93.94)
Substance use disorder			
Yes	96,873 (2.29)	113,120 (13.32)	193,707 (3.81)
No	4,1317,35 (97.71)	736,354 (86.68)	4,884,375 (96.19)
Facility-level			
Region			
North East	918,474 (21.72)	169,251 (19.92)	1,087,725 (21.42)
Upper Midwest	1,005,310 (23.77)	194,871 (22.94)	1,200,181 (23.63)
West	805,357 (19.05)	172,861 (20.35)	978,218 (19.26)
South	1,499,467 (35.46)	312,491 (36.79)	1,811,958 (35.68)
Academic affiliation			
Yes	2,623,990 (62.05)	529,089 (62.28)	3,153,079 (62.09)
No	1,604,618 (37.95)	320,385 (37.72)	1,925,003 (37.91)
Service connection			
<70%	3,926,165 (92.85)	697,123 (82.07)	4,623,288 (91.04)
≥70%	302,443 (7.15)	152,351 (17.93)	454,794 (8.96)

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