

Depressive Symptoms and Nine-Year Survival of 1,001 Male Veterans Hospitalized With Medical Illness

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Authors examined effects of depressive symptoms on after-discharge survival of hospitalized medically ill male veterans. Psychosocial and physical health evaluations were performed on a consecutive sample of 1,001 patients ages 20-39 (16%) and 65-102 years (84%). Subjects or surviving family members were later contacted by telephone, and Cox proportional-hazards regression modeled the effects of depressive symptoms on time-to-death, controlling for demographics and social, psychiatric, and physical health. Follow-up was obtained on all 1,001 patients (average observation time, 9 years), during which 667 patients died (67%). Patients with depressive symptoms were significantly less likely to survive. For every 1-point increase on the 12-item Brief Carroll Depression Rating Scale (BCDRS), the hazard of dying increased by 10% ($P < 0.0001$). Age did not significantly affect the association between depressive symptoms and mortality. Depressive symptoms during acute hospitalization are a predictor of shortened survival. (Am J Geriatr Psychiatry 1999; 7:124-131)

The impact of depression on all-cause mortality is controversial, and may vary depending on the particular population studied and the way that depression is measured. Most of these studies involve older adults, because death rates are high enough in this population to examine predictors of mortality with some degree of statistical power. When psychiatric patients are examined, investigators report an association between depression and shortened survival in both older patients¹⁻³ and mixed-age patients.⁴ The majority of these studies, however, compare psychiatric patients with "community" control subjects. Lack of an association between depression and survival, on the other hand,

has been particularly evident in community studies;⁵⁻¹⁰ as length of follow-up increases, however, findings may begin to emerge,^{11,12} although not always.⁶

Studies most likely to report an impact of depression on natural mortality are those involving clinical samples with medical illness. Frasure-Smith and colleagues¹³ reported an increased death rate within the first 6 months after myocardial infarction (MI) in 35 patients with major depression compared with 187 nondepressed post-MI patients. Morris and colleagues¹⁴ likewise reported a three- to fourfold greater mortality among 37 stroke patients with major or minor depression, compared with 54 nondepressed stroke patients;

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over 90% of depressed patients with few social contacts died. In a 1-month follow-up study of 211 patients with life-threatening physical illness, Silverstone¹⁵ reported increased mortality among the 34% of patients identified as being depressed by use of an observer-rated depression scale (the Montgomery-Asberg Scale); whereas age and sex were reported as similar between depressed and nondepressed subjects, severity of medical illness and other health factors were not controlled. Finally, Rovner and colleagues¹⁶ found that depressive disorder, but not depressive symptoms, increased 12-month mortality by 59% (adjusting for health factors) in a group of 454 newly admitted nursing home patients (57 with depressive disorder).

In contrast, some studies that have carefully controlled for physical health factors in medically ill patients have not found an association between depression and mortality. Parmelee and colleagues¹⁷ examined 30-month mortality in a sample of 898 nursing home and congregate-apartment residents, finding no association between depressive disorder ($n = 387$) and mortality once functional disability and other health factors were controlled. Likewise, Koenig and colleagues¹⁸ found no difference in 5-month mortality after hospital discharge in 41 elderly medical inpatients with major depression compared with control patients matched by age, functional status, and medical diagnosis.

Depressed medical inpatients may be particularly vulnerable to the effects of depression on survival. First, depression can interfere with the medical patient's motivation toward recovery because of reduced energy, interest, and concentration necessary for active participation in rehabilitation programs.¹⁹ Second, depression may adversely affect compliance in elderly medical patients, who may be taking multiple medications at different times of the day, or who may be seeing several different specialists for their medical problems.²⁰ Third, depression may interfere with immune system functioning so that vulnerability to disease is greater and biological capacity to recover from illness is reduced.^{21,22}

To our knowledge, no study has yet examined the association between self-rated depressive symptoms and mortality in a clinical population of medical patients, controlling for multiple demographic, physical health, social, behavioral, and psychiatric predictors of survival. Brief self-rated depression scales may be useful in screening medical patients for both depression and increased mortality risk, while avoiding the cost and time of administering a structured psychiatric interview.

In the present study, we examined the association between depressive symptoms assessed by two self-rated depression scales and mortality in a relatively large sample of medically ill hospitalized patients followed for 9 years. We hypothesized that depressive symptoms during hospitalization would predict shortened survival after hospital discharge, an association that would persist after we controlled for demographic, psychosocial, psychiatric, and physical health factors.

METHODS

Between September 1, 1987, and January 1, 1989, men under age 40 and over age 65 consecutively admitted to the general medicine or neurology inpatient services at the VA Medical Center in Durham, North Carolina, were recruited into the study. The primary purpose of the study was to examine age differences in rates and predictors of depression in this population.^{23,24} Patients were excluded if they were women, were admitted to intensive care settings, were transferred from other services to the medical ward, scored less than 15 on the Mini-Mental State Exam (MMSE),²⁵ or had severe medical illness or communication problems preventing evaluation. Evaluations were obtained on 1,010 subjects (92% of eligible participants); 1,001 of these completed one or both of the two depression scales and comprise the sample for this report.

Patients were generally seen within 48 hours of admission by a master's degree-level social worker and/or by a physician. Demographic information and data on social support, religious coping, self-rated depression, past psychiatric history, alcohol use, ability to perform ADLs, and primary medical diagnosis were collected.

Measures

Depression. Depressive symptoms were measured with the 12-item Brief Carroll Depression Rating Scale (BCDRS) and the 30-item Geriatric Depression Scale (GDS).²⁶ These instruments have been validated for use in detecting major depression in older populations.²⁷ Scores range from 0-12 for the BCDRS and 0-30 for the GDS. At a cutoff of 6, the BCDRS has a sensitivity of 100% and specificity of 93% for detecting major depression; at a cutoff of 8, the GDS has a sensitivity of 92% and specificity of 70% for major depression.²⁷

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Social support. Social support was measured by means of a three-item index that assessed frequency of interaction, size of support network, and satisfaction with support.^{7,28} Response options ranged from 1-5 for each item, with a total scale range of 3-15 (Cronbach alpha=0.57). Living situation (living with others vs. alone) and marital status (married vs. not) were also assessed.

Religious coping. Religious coping was assessed with a three-item index.²⁹ Each item measured the extent to which the patient relied upon religion to help him manage or cope with the stress in his life. Summing responses to the three items resulted in a scale ranging from 0 to 30. Internal reliability (Cronbach's alpha=0.82) and interrater reliability (Pearson $r=0.81$) were high.

Psychiatric history. Patients were asked about personal psychiatric history, family psychiatric history, and use of alcohol; single items with Yes-No response categories were used to collect this information.

Physical functioning. Both physical and instrumental activities of daily living (ADLs) were measured. Ability to independently perform six physical ADLs³⁰ (0-2 scale) and five instrumental ADLs³¹ (0-1 scale) was assessed. For analysis purposes, patients were dichotomized into those with (impaired ADLs>0) or without (impaired ADLs=0) physical disability.

Admitting medical diagnosis. Admitting medical diagnosis was categorized into seven major diagnostic categories: cancer or malignancy, cardiovascular disease, neurological illness, respiratory disorder, gastrointestinal disorder, renal or genitourinary disease, and other disorders. For example, patients with a diagnosis of cancer were assigned a value of 1 and those without a diagnosis of cancer, a value of 0. This "cancer" variable was then included in the regression models; the same procedure was followed for the other disorders listed.

Determination of Survival Status

Between July 1996 and April 1997, 1,010 subjects or their families were called on the telephone (survival status data for the 1,001 subjects with data on depressive symptoms are relevant to this report). After informed consent was obtained and witnessed by a sec-

ond interviewer, the survival status of the patient was determined. For patients still alive and interviewed by telephone, the date of interviewer contact was recorded (censoring date). If the family was interviewed, and the patient was reported to be alive, then the date of last contact between the patient and family member was recorded (censoring date). Family members of patients who had died were asked to give the approximate date of the patient's death.

The Beneficiary Identification and Records Locator Subsystem (BIRLS) is maintained by the United States Department of Veterans Affairs as a record of all claims and benefits paid to veterans and their beneficiaries.³² This database is often used as a tool for survival-status follow-up activities and, in fact, is one of the three national sources of survival status ascertainment for veterans (the other two being the National Death Index of the National Center for Health Statistics and the Master Beneficiary Record of the Social Security Administration).

Date of death for patients in the present study was verified in one of three ways: 1) confirmation by BIRLS (92%); 2) confirmation by obtaining death certificate (8%); or 3) confirmation by the National Death Index (<1%). Eighty-five percent of deaths were confirmed by two or more sources (BIRLS, death certificate, National Death Index, phone contact with kin, or Durham VA computer). If there was conflict about the date of death between any of these sources, the death certificate was used as the "gold standard."

Statistical Analyses

Bivariate analyses of differences between subjects who survived and those who died were examined with chi-square tests for all categorical variables. Survival time was calculated from the first day of the hospital admission when initial evaluation took place to either the date of death (event) or the date when the patient was last known to be alive (censored). A Cox proportional-hazards model was used to determine the effect of depression on survival. Cox models were used to examine BCDRS scores and then GDS scores as predictors of time-to-death. Demographic, social, psychiatric, and physical health variables were successively added to each model containing either the BCDRS or GDS. Because the subjects were either below age 40 or over age 65, the final models were examined for the significance of the interaction between these two age-

groups and depression. Estimated hazard ratios (HR) along with 95% confidence intervals (CI) are reported from the Cox models. Kaplan-Meier survival curves were used to compare time-to-death in patients scoring in the depressed range of the BCDRS with those scoring in the nondepressed range. Statistical Application Software (SAS) was used to analyze the data.³³

RESULTS

The characteristics of the sample during the index hospitalization are presented in Table 1. The vast majority (84%) of patients were age 65 or older ($n = 843$), and a smaller proportion (16%) were age 20–39 years ($n = 158$). Two-thirds of the sample (68%) were white, and one-third black (32%). The majority had less than a high school education (64.3%) and had a total yearly family income of less than \$15,000 (82%). Over 80% were living with at least one other person, and two-thirds were married. Disability was prevalent in this hospitalized sample, 50% of whom required assistance with at least one ADL. The most common admitting diagno-

TABLE 1. Baseline characteristics of the sample in 1987–89, % (n) or mean \pm SD (range), (N = 1,001)

Demographic	
Age, 65 or over	84.2 (843)
Sex, male	100.0
Race, black	32.1 (321)
Education, high school graduate or more	35.6 (356)
Income, \$15,000/year or more	17.3 (173)
Social Characteristics	
Marital status, married	64.7 (647)
Living situation, alone	18.0 (180)
Social support, mean	10.6 \pm 1.8 (5–15)
Religious coping index	14.0 \pm 8.7 (0–30)
Psychiatric Characteristics	
Past psychiatric history	28.2 (282)
Family psychiatric history	10.9 (109)
Alcohol use	22.6 (226)
Physical Health Characteristics	
Physical functioning, number of unimpaired ADLs	14.5 \pm 3.8 (0–17)
Medical Diagnoses	
Cancer	20.0 (200)
Gastrointestinal disease	14.6 (146)
Neurological disease	16.8 (168)
Respiratory disease	9.9 (99)
Renal or genitourinary disease	5.3 (53)
Cardiovascular disease	24.1 (241)
Depressive Symptoms	
Brief Carroll Depression Rating Scale (BCDRS)	3.6 \pm 2.4 (0–12)
Geriatric Depression Scale (GDS)	7.4 \pm 5.7 (0–28)

ses were cardiovascular disease (24.1%), cancer (20.0%), neurological disease (16.8%), and gastrointestinal disease (14.6%). Average scores on the BCDRS and the GDS, respectively, for patients with these diagnoses were the following: cardiovascular disease (3.0 and 6.7), cancer (3.7 and 7.2), neurological disease (3.5 and 7.8), and gastrointestinal disease (3.6 and 7.5).

Depressive Symptoms and Mortality Rate

Two-thirds of the sample (66.7%) died during the average 9-year follow-up period ($3,285.2 \pm 137.7$ days). Supporting our first hypothesis, bivariate analyses revealed that depressive symptoms were significantly related to mortality (Table 2). Among those scoring at or above 6 on the BCDRS, 77.7% died, vs. 63.7% of those scoring less than 6 ($\chi^2_{(1)} = 14.3$; $P < 0.001$). Among

TABLE 2. Mortality by patient characteristic at baseline (bivariate analyses)

		Deceased, % (n)
Age	20–39 years	24.1 (38)
	65 years or over	74.6 (629)***
Race	White	69.1 (470)
	Black	61.4 (197)*
Education	Less than high school graduate	74.3 (479)
	High school graduate or more	52.8 (188)***
Annual income	Less than \$15,000	69.3 (574)
	\$15,000 or more	53.8 (93)***
Alcohol use	No	69.7 (540)
	Yes	56.2 (127)***
Impaired ADLs	None	54.3 (273)
	1 or more	79.1 (394)***
Medical diagnoses (each diagnosis compared to all others)		
Cancer		90.5 (181)***
Gastrointestinal disease		58.9 (86)*
Neurological disease		50.0 (84)***
Respiratory disease		79.8 (79)**
Renal or genitourinary disease		64.2 (34)
Cardiovascular disease		57.9 (140)***
BCDRS	Less than 6	63.7 (504)
	6 or greater	77.7 (160)***
GDS	Less than 8	63.8 (381)
	8 or greater	70.7 (285)*

Note: BCDRS = Brief Carroll Depression Rating Scale; GDS = Geriatric Depression Scale.

Unrelated to vital status and not shown were marital status, living situation, social support, religious coping, past psychiatric history, and family psychiatric history.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ ($\chi^2_{(1)}$).

those scoring at or above 8 on the GDS, 70.7% died, vs. 63.8% scoring below 8 ($\chi^2_{[1]} = 5.2$; $P = 0.02$); using a higher cutoff on the GDS (i.e., 11 or 14) did not increase the mortality differences observed between depressed and nondepressed patients.

Depressive Symptoms and Time-to-Death

Results from the Cox proportional-hazards regression analysis (Table 3) revealed that when depressive symptoms (as continuous variables) were added to the model without other predictor variables, they significantly predicted time-to-death whether symptoms were measured by the BCDRS (HR: 1.10; 95% CI: 1.07-1.13; $P < 0.0001$) or by the GDS (HR: 1.02; 95% CI: 1.00-1.03; $P < 0.01$). When demographic, social, psychiatric, and physical health variables were added successively to the models containing the BCDRS, the association between survival and BCDRS persisted (HR: 1.08; 95% CI: 1.05-1.12; $P < 0.0001$). The association between GDS and survival also persisted after adding demographic, social, and psychiatric covariates, but weakened when physical health variables were entered into the model (HR: 1.01; 95% CI: 1.00-1.03; $P = 0.07$). Stratifying analyses by age-group (20-39 years vs. 65 years or over) demonstrated few differences in overall magnitude of effect, although the larger sample size for older adults resulted in statistical significance in that age-group only. Interaction terms involving age and the BCDRS and age and the GDS were included in the final models; in neither case was the interaction term significant (HR: 0.84,

$P = 0.23$, for BCDRS \times Age; HR: 1.06, $P = 0.63$, for GDS \times Age). Kaplan-Meier survival curves for depressed and nondepressed patients by BCDRS in the overall sample are displayed in Figure 1. The probability of survival of the nondepressed subjects is larger than that for depressed subjects.

DISCUSSION

In this large clinical sample of medically ill hospitalized male veterans, depressive symptoms measured by the BCDRS were significantly related to time-to-death. A similar association was seen for depressive symptoms measured by the GDS, although that association weakened when physical health covariates were controlled. The BCDRS is a 12-item, self-rated depression scale that is easy to understand and respond to (with a dichotomous "Yes-No" response format). Even older medical inpatients with severe physical health problems had no difficulty completing this scale. Because it takes less than 1 minute to complete and is self-rated, the BCDRS does not overly burden the patient nor waste precious personnel time in busy medical settings. This screening instrument has both relatively high sensitivity (73%-100%) and specificity (79%-93%) for identifying major depression,^{27,34} and now has been shown to significantly predict mortality, even after multiple demographic, psychosocial, and physical health factors are controlled. We found that for every 1-point increase on the BCDRS, the likelihood of dying within 9 years after hospital discharge increased by almost 10%.

TABLE 3. Depressive symptoms and 9-year survival, unstandardized β (standard error)

	Overall Sample	Younger (20-39)	Older (65+)
BCDRS alone	0.097 (0.015)**	0.072 (0.051)	0.126 (0.016)**
BCDRS + demographics	0.120 (0.016)**	0.041 (0.054)	0.128 (0.017)**
BCDRS + demographics + social variables	0.123 (0.016)**	0.042 (0.057)	0.130 (0.017)**
BCDRS + demographics + social + psychiatric variables	0.129 (0.017)**	0.094 (0.064)	0.134 (0.018)**
BCDRS + demographics + social + psychiatric + physical health variables	0.080 (0.017)**	0.087 (0.075) ^c	0.080 (0.018) ^{c**}
GDS alone	0.016 (0.006)*	0.021 (0.021)	0.027 (0.007)**
GDS + demographics	0.026 (0.007)**	0.014 (0.022)	0.028 (0.007)**
GDS + demographics + social variables	0.027 (0.007)**	0.011 (0.023)	0.028 (0.007)**
GDS + demographics + social + psychiatric variables	0.029 (0.007)**	0.032 (0.026)	0.029 (0.008)**
GDS + demographics + social + psychiatric + physical health variables	0.014 (0.008) ^b	0.040 (0.030) ^d	0.011 (0.008) ^f

* $P < 0.01$, ** $P < 0.001$.

^aModel $\chi^2_{[19]} = 383.5$; $P < 0.0001$; $n = 997$; deaths = 664.

^bModel $\chi^2_{[19]} = 365.6$; $P < 0.0001$; $n = 1,000$; deaths = 666.

^cModel $\chi^2_{[19]} = 52.7$; $P < 0.0001$; $n = 158$; deaths = 38.

^dModel $\chi^2_{[19]} = 53.1$; $P < 0.0001$; $n = 158$; deaths = 38.

^eModel $\chi^2_{[19]} = 222.2$; $P < 0.0001$; $n = 839$; deaths = 626.

^fModel $\chi^2_{[19]} = 205.0$; $P < 0.0001$; $n = 842$; deaths = 628.

Mortality may be higher among depressed patients with medical illness, particularly older adults, for a number of reasons. First, certain factors may increase vulnerability to both depression and mortality, such as more chronic diseases, bereavement, increased isolation and loneliness, and reduced economic resources.^{35,36} Depression itself, on the other hand, may negatively affect survival by causing impaired immune functioning and greater susceptibility to life-threatening diseases.^{21,22,37}

Whereas the BCDRS continued to predict mortality after covariates were controlled, the GDS weakened as a predictor when physical health variables were adjusted for: Why this apparent discrepancy between depression scales? The GDS was originally designed in order to avoid any confounding with medical illness;²⁶ for this reason, many of the biological symptoms of depression (insomnia, weight loss, fatigue, etc.) were eliminated from the scale. The BCDRS, on the other hand, is a shortened version of the Carroll Depression Rating Scale, which was designed to identify patients with symptoms of biological or endogenous major depression;³⁸ these include

symptoms like weight loss, reduced concentration, insomnia, and fatigue.

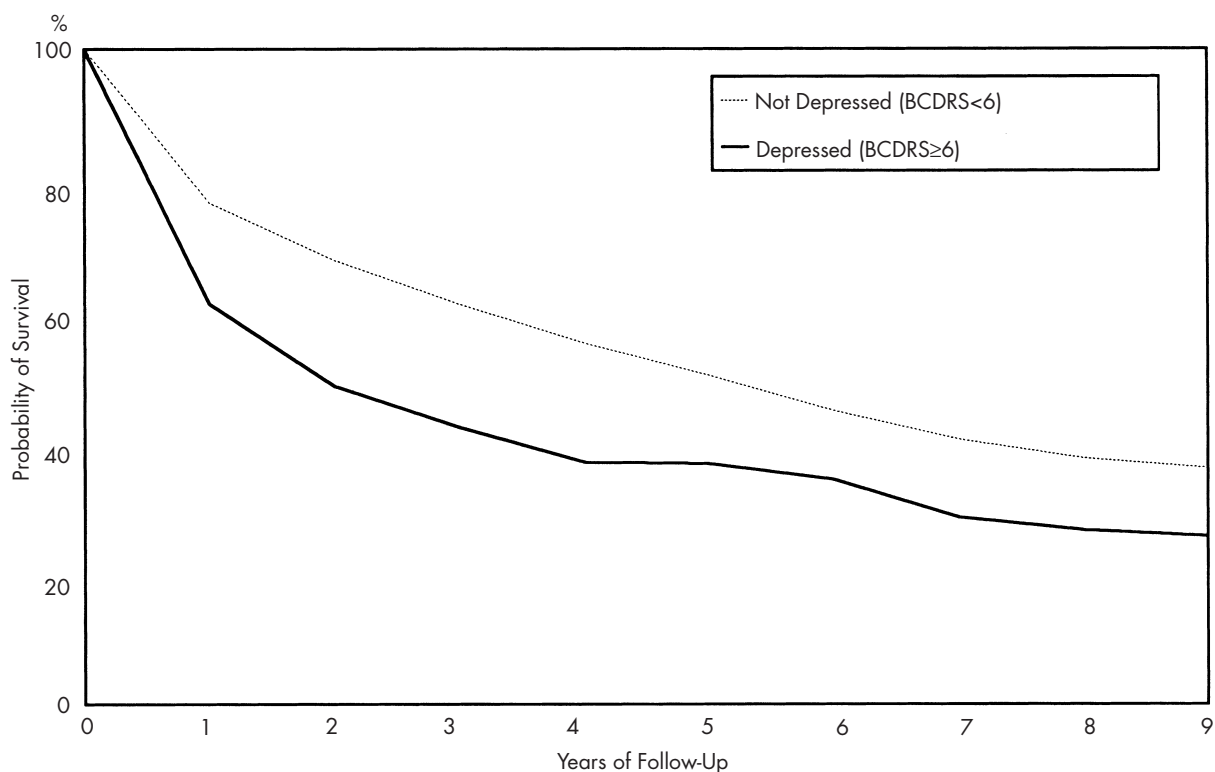
Thus, either the BCDRS is confounded by symptoms of medical illness (that could not be adequately controlled for using the covariates measured in this study) or the BCDRS more accurately measures symptoms of endogenous major depressive disorder (which, as noted above, has been shown to have an impact on mortality in multiple populations and settings). The GDS, in turn, may be more likely to assess symptoms reflective of milder, non-endogenous depressive syndromes that are less likely to adversely affect survival.

Limitations

Given our all-male, veteran, primarily elderly sample, the results of this study should be generalized with caution to non-VA settings, to women, and to younger adults. Many patients were from lower socioeconomic classes, with relatively low education and reduced family income, factors that may relate to depression and affect mortality in subtle ways difficult to measure.

Finally, variables assessing aspects of physical health status are important moderators (if not mediators) of the

FIGURE 1. Kaplan-Meier survival curves after hospital discharge for depressed vs. nondepressed patients (unadjusted)



depression-mortality relationship. Patients with specific medical disorders (e.g., recurrent malignancies, cardiac events) may be depressed in response to, rather than as a cause of, their medical prognosis. A more sophisticated analysis of interactions between types of medical illness and specific depressive symptoms would be necessary to derive a model assessing depressive symptoms and medical illness as independent and interactive predictors of mortality. Furthermore, the present study did not include a measure of medical illness severity that had been independently validated as a predictor of mortality. We did, however, control for both level of physical functioning and the specific medical diagnosis, both of which were strong predictors of mortality in this sample.

Clinical Implications

To our knowledge, this is the first study to identify a short, self-rated depression scale capable of predicting shortened survival among medical inpatients after hospital discharge. Such an instrument may be useful as a

brief screening tool for identifying patients at risk for both depression and early mortality. Compared with a patient scoring 0 on the BCDRS, we found that a patient with a BCDRS of 5 has a 40%–50% increased risk of dying within 9 years after discharge. Because this instrument was devised for use in patient populations of all ages, it may be applicable to geriatric and non-geriatric patients alike.

Despite the wide prevalence of depression among medical inpatients (up to 50% in some settings),³⁹ this treatable mental disorder is only infrequently identified or managed appropriately by medical providers during hospitalization or after discharge.^{40,41} The present study suggests that patients found by the BCDRS to be at risk for depression should have their depressive symptoms carefully evaluated and managed both during their inpatient stay and after hospital discharge.

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