Rates and Predictors of Mortality in an Aging, Rural, Community-Based Cohort

The Role of Depression

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Context: Depression, functional disability, cognitive impairment, and self-rated health all predict mortality in the elderly population. There is no consensus on their relative contributions when examined together.

Objectives: To measure rates and identify predictors of mortality in an aging community-based cohort.

Design: Ten-year prospective epidemiological study. Predictor variables examined in Cox proportional hazards models were self-rated health, ability to perform instrumental activities of daily living (IADLs), depressive symptoms, and cognitive functioning, controlling for age, sex, education, and number of prescription drugs.

Setting: A largely blue-collar rural community in southwestern Pennsylvania.

Participants: A population-based cohort of 1064 adults, 67 years or older at the beginning of follow-up.

Main Outcome Measures: Mortality at 3, 5, and 10 years (133, 218, and 482 deaths, respectively).

Results: Mortality rates were similar to those of the 1990 US population. Older age, male sex, IADL disability, and number of prescription drugs measured at baseline were significant predictors of mortality at all 3 follow-up end points. Depression at baseline predicted earlier (3- and 5-year) mortality but not later (10-year) mortality. The interaction between self-rated health and depression independently and strongly predicted mortality at all end points. Cognitive functioning predicted mortality only when IADL disability was excluded from the model.

Conclusions: Age, sex, depression, and functional disability are strong and consistent independent predictors of mortality in older adults in the community, in addition to objective medical burden (prescription drugs). Depression alone predicts mortality in the shorter rather than longer term, but in combination with poor self-rating of health, it strongly predicts mortality at all end points.

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A substantial but surprisingly inconclusive body of literature has focused on the prediction of mortality in older members of the population at large. There is little debate about the importance of functional disability, particularly the inability to independently perform instrumental activities of daily living (IADLs), as a predictor of mortality.1-18 A separate, less consistent, corpus of work demonstrates that depressive illness or depressive symptoms also predict mortality.18,19,25 Another group of studies has shown that self-perceptions or self-ratings of health predict mortality.3,4,6,11,13,14,16,17,22,26,27,28,30,31 While still others have found cognitive impairment to predict mortality.2,5,6,10,11,12,18,21,26-32 Furthermore, self-rated health, functional disability, and cognitive impairment themselves have been shown to be associated with depression.3,4 All measure different but related, broad aspects of ill health in individuals. Their combined effects on mortality in a representative population sample would shed light on their relative contributions.

In an aging, population-based cohort in southwestern Pennsylvania, we conducted a prospective epidemiological study with 10 years of follow-up. We first determined whether overall, age-specific, and sex-specific mortality rates in our cohort were similar to the corresponding national rates, confirming the representativeness of our cohort with respect to mortality. We then considered the key variables mentioned herein: depression, IADL disability, self-rated health, and cognitive impairment, examining them jointly to understand how they may operate together to predict mortality in our cohort.
METHODS

STUDY SITE AND POPULATION

Originally designed as a population-based dementia registry, the study was conducted within the mid-Monongahela Valley area of Washington and Westmoreland Counties in southwestern Pennsylvania. The 23 communities served by the Mon Valley Community Health Center were selected for the study. The population was largely blue-collar, of low income and education levels, and of European descent. Sampling and recruitment of the study cohort have previously been described in detail.35 The sampling frame for the survey was the voter registration list for 2 counties; given the stability of the local population, the electoral rolls were the most comprehensive lists available for our use. They include all individuals who have ever voted in the area, thus reducing systematic bias resulting from the aged and infirm not having voted in recent elections. From the master sampling frame, a 1:13 random sample was drawn within each of the 65 to 74 years and 75 years and older age strata. The study was named the Monongahela Valley Independent Elders Survey (MoVIES). Study procedures were approved annually by the University of Pittsburgh Institutional Review Board.

ENTRY CRITERIA

Eligibility criteria for entry into the study cohort, between 1987 and 1989, have been described and justified earlier.35 Briefly, they included community residence (ie, not already being in long-term care), 65 years or older, fluency in English, and at least sixth grade education; the latter 2 criteria were intended to facilitate interpretation of the neuropsychological (cognitive) tests we administered. A total of 1422 randomly selected participants met eligibility criteria and consented to participate at study entry (wave 1, 1987-1989).35 Subsequently, at approximately 2-year intervals, subjects were rescreened in a series of data collection “waves.” Mortality rates were calculated using data from wave 1 through wave 6, with deaths occurring from study entry until the end of 1999. Duration of follow-up ranged from 0.93 years to 10.77 years (mean, 7.67 years) until death or the end of 1999. Wave 2, at which time the cohort numbered 1101, was selected as the starting point for the risk factor analyses because several of the key variables were first measured at wave 2. Attrition between wave 1 and wave 2 occurred in 321 individuals (143 who died, 111 who skipped wave 2 but returned to the cohort subsequently, 65 who relocated or dropped out, and 2 excluded for other reasons).

SCREENING

After providing written informed consent, each participant underwent an in-home screening interview including the Mini-Mental State examination (MMSE),40 a brief general mental status test on which scores range from 0 to 30, with lower scores suggesting poorer cognitive functioning. Screening also included a modified, interviewer-administered version of the Center for Epidemiological Studies–Depression Scale (mCES-D).41 on which scores range from 0 to 20, with higher scores representing a greater number of depressive symptoms. The original CES-D is a screening tool for depressive symptoms in the general population. It is a self-rated questionnaire consisting of 20 items (symptoms), each scored on a 4-point scale ranging from 0 to 3, depending on whether the patient experienced the symptom on 0 to 1, 2 to 3, 4 to 5, or 6 to 7 days of the previous week. Thus, the maximum possible score is 60 points. Several different groups have modified the original CES-D in different ways for different populations. Our modification, the mCES-D,43 differs from the original in that it is interviewer-administered rather than self-rated and that participants are asked whether the symptom was present “most of the time” (defined as 3 or more days) during the preceding week; the symptom is then rated as either present (score, 1) or absent (score, 0), for a maximum possible total of 20 points. We selected a score of 5 as the cutoff point on the 20-point scale because this score was at the upper tenth percentile of our cohort (ie, it defined the 10% of the cohort with the largest number of depressive symptoms). It is a population-based approach based on the distribution of symptoms within the sample and does not identify persons meeting criteria for any specific diagnostic entity.

Ability to perform IADLs was assessed using the Older Americans Resources and Services48 scale on which higher scores represent disability in a greater number of daily tasks. Self-rated health was determined by a single question asking the participant to describe his or her own state of health: excellent, good, fair, or poor.34 Prescription medications reported by the participant as being taken regularly were also examined during the interview. The total number of current prescription medications was used in the present analyses as an overall objective measure of morbidity, to control for medical burden.49 Of the 1101 participants who participated in wave 2, 37 were eliminated from these analyses because they had missing data on 1 or more of the variables of interest. The total cohort included in the risk factor analyses therefore numbered 1064.

MORTALITY DATA

The small towns and rural communities of the Monongahela Valley are known for their low rates of in- and out-migration. Family and neighborhood networks are close-knit. Regular tracking of participants allowed us to become aware of deaths within the MoVIES cohort. Obituaries of area residents and former residents are published in local newspapers even if the decedent has moved away from the area; a “daily death index” was compiled from obituaries in 6 local newspapers. Almost all deaths (95.4%) occurred in Pennsylvania, most of them within the study area or in contiguous counties. Annually, with clearance from the Commonwealth of Pennsylvania Department of Health, death certificates issued during the previous year within Pennsylvania were reviewed and abstracted; copies of death certificates from other states were obtained to the extent possible. As reported previously,40 we have been able to obtain complete ascertainment of the vital status of our cohort members.

Mortality data are reported as of December 31, 1999. As of that date, among the 1064 participants in the cohort at the beginning of wave 2, 133 participants had died within 3 years, an additional 85 by 9 years, and another 264 by 10 years, for a total of 482 deaths. These figures are consistent with expected mortality rates for this age group according to the US Decennial Life Tables for 1990.41

STATISTICAL ANALYSES

Mortality rates were calculated by dividing the number of deaths in each age group by the number of person-years of follow-up in that age group. Person-years were calculated from the time of study entry for each individual until the time of death or December 31, 1999, whichever came first. For comparison, we calculated person-year mortality rates for the white population of the United States based on the US Decennial Life Tables for 1990.41

The following 9 variables were examined as potential predictors. (1) age at baseline (wave 2); (2) sex; (3) education (high school and greater vs less than high school); (4) MMSE score dichotomized at the conventional clinical cutoff point (≤23 vs ≥24).
Using Cox proportional hazards models, predictors of mortality were examined one at a time, and those that were statistically significant were included in the final models. Cox proportional hazard models are a type of multiple regression analysis commonly used to model survival data as a function of multiple covariates (in this case, depression, IADL disability, self-rated health, and cognitive impairment, controlling for age, sex, education, and prescription drugs). This method takes into account not only vital status but also the actual duration of survival. These models are based on the assumption of “proportionality” (ie, that the hazard ratios between each pair of subgroups being compared [eg, men and women, depressed and nondepressed] are constant over time). The proportionality assumption for our Cox models was examined or not documented on the death certificates. We calculated the total expected numbers of suicide deaths in our cohort during the follow-up period, according to age- and sex-specific US national suicide rates from the Centers for Disease Control and Prevention for the year 1992, which was approximately the middle of the study period. The expected numbers were 1.3 suicides among men and 0.3 among women, for a total of 1.6 (95% confidence interval, 0.99-2.35). Thus, it is possible that our cohort experienced zero (<1) suicides during this period; it is of course also possible that 1 or 2 suicides were not recognized or not documented on the death certificates.

RISK FACTOR ANALYSES

Sample Characteristics

The 1064 participants included in the risk factor (mortality predictor) analyses had a mean (SD) age of 74.9 (5.5) years at wave 2, which served as the baseline for the risk factor analyses. Women comprised 57.5% of the cohort, and 58.4% of cohort members had high school or greater education.

Distribution of Risk Factors

Among the cohort of 1064 participants at baseline, 7.9% of the cohort obtained MMSE scores at the conventional clinical cutoff point of 23 or less (operationally defined as “cognitive impairment”). With respect to functional disability, 23.8% had IADL disability scores between 1 and 3 (ie, were unable to perform 1 to 3 IADLs independently), while 3.7% had IADL disability scores of 4 or greater. Self-rated health was described as “poor” by 2.1% of the cohort. The number of prescription medications regularly taken by cohort members ranged from 0 to 11, with a median of 1 and a mean (SD) of 2.09 (2.11).

Five or more depressive symptoms (mCES-D scores ≥5) were reported by 10.2% of participants. Antidepressant use was reported by 24 persons (2.3%). Those taking antidepressant drugs were significantly (Fisher exact test, 1 df, P<.001) more likely to be “depressed” by

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Table 1. Mortality Rates per 100 Person-years (MoVIES Cohort vs United States, 1990)*

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Male Rate (95% CI)</th>
<th>Female Rate (95% CI)</th>
<th>All Rate (95% CI)</th>
<th>Male Rate</th>
<th>Female Rate</th>
<th>All Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-69</td>
<td>2.17 (1.21-3.89)</td>
<td>1.42 (0.72-2.80)</td>
<td>1.77 (1.14-2.77)</td>
<td>2.68</td>
<td>1.53</td>
<td>2.07</td>
</tr>
<tr>
<td>70-74</td>
<td>4.40 (3.45-5.62)</td>
<td>2.22 (1.62-3.03)</td>
<td>3.20 (2.64-3.89)</td>
<td>4.29</td>
<td>2.42</td>
<td>3.22</td>
</tr>
<tr>
<td>75-79</td>
<td>5.77 (4.73-7.03)</td>
<td>3.36 (2.69-4.20)</td>
<td>4.39 (3.78-5.09)</td>
<td>6.56</td>
<td>3.81</td>
<td>4.89</td>
</tr>
<tr>
<td>80-84</td>
<td>10.44 (8.64-12.62)</td>
<td>6.03 (4.65-7.34)</td>
<td>7.73 (6.74-8.87)</td>
<td>10.22</td>
<td>6.39</td>
<td>8.04</td>
</tr>
<tr>
<td>95-104</td>
<td>48.84 (27.94-85.38)</td>
<td>45.41 (22.00-93.74)</td>
<td>47.52 (30.42-74.22)</td>
<td>34.52</td>
<td>29.31</td>
<td>30.39</td>
</tr>
<tr>
<td>Overall</td>
<td>7.18 (6.50-7.95)</td>
<td>4.96 (4.47-5.50)</td>
<td>5.90 (5.49-6.34)</td>
<td>6.56</td>
<td>5.21</td>
<td>5.74</td>
</tr>
</tbody>
</table>

*MoVIES indicates Monongahela Valley Independent Elders Survey; CI, confidence interval.

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Mortality rates in person-years of follow-up for the MoVIES study cohort from study entry (1987-1999) until the end of 1999 were similar to those of the US population (white) according to the 1990 US Life Tables (Table 1). The US rates were well within the confidence intervals around our study cohort’s rates, except in the oldest age group, for which we had insufficient numbers of participants to produce stable rates.

No deaths in our cohort were attributed to suicide, according to the death certificates. We calculated the total expected number of suicide deaths in our cohort during the follow-up period, according to age- and sex-specific US national suicide rates from the Centers for Disease Control and Prevention for the year 1992, which was approximately the middle of the study period. The expected numbers were 1.3 suicides among men and 0.3 among women, for a total of 1.6 (95% confidence interval, 0.99-2.35).

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RESULTS

MORTALITY RATES

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Predictors of Mortality

Cox proportional hazards models identified predictors of mortality as measured at wave 2 (Table 2). As the interaction term of poor self-rated health with depression (≥5 mCES-D depressive symptoms) was significant when added to the main effect models, it was included in the final models. The interactions of time with 4 or more IADL disabilities and of time with 5 or more mCES-D depressive symptoms were significant in the main effect models and were therefore included in the final models to adjust for these deviations from the proportionality assumptions (data not shown).

Older age and male sex were significant predictors of mortality, but education was not. In all models, objective morbidity (number of prescription medications) significantly predicted mortality, with a relative risk of approximately 1.2 (ie, a 20% increase in risk for each additional prescription drug).

After adjusting for the effects of these variables, baseline IADL disability significantly predicted mortality at all 3 follow-up points. Baseline depression, as measured by a score of 5 or more on the mCES-D, was a significant predictor of earlier (3- and 5-year) mortality but not of later (10-year) mortality. Self-rated health by itself did not predict mortality at any of the 3 end points. However, the interaction between depression and self-rated health was a significant predictor of mortality in all 3 models, even after adjusting for prescription drug frequency. In post hoc analyses, when depression alone was excluded from the model, the model did not change; only when both depression and number of prescription drugs were removed from the model did poor self-rated health become a significant predictor at all 3 follow-up points:

<table>
<thead>
<tr>
<th>Potential Predictors</th>
<th>Relative Risk (RR) for Mortality† at Progressively Longer Intervals From Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-Year Mortality (133 Deaths), RR</td>
</tr>
<tr>
<td></td>
<td>P Value</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.04  .02</td>
</tr>
<tr>
<td>Sex (male vs female)</td>
<td>2.00  &lt;.001</td>
</tr>
<tr>
<td>Education (≥high school vs &lt;high school)</td>
<td>1.22   .28</td>
</tr>
<tr>
<td>Cognitive functioning (MMSE score ≤23 vs &gt;24)</td>
<td>1.43   .16</td>
</tr>
<tr>
<td>Functional disability (IADL) (1-3 disabilities vs none)</td>
<td>1.54   .05</td>
</tr>
<tr>
<td>Functional disability (IADL) (≥4 disabilities vs none)</td>
<td>2.49   .02</td>
</tr>
<tr>
<td>Self-rated health (poor vs excellent, good, fair)</td>
<td>1.55   .24</td>
</tr>
<tr>
<td>Depression (≥5 symptoms vs ≤4 symptoms)</td>
<td>1.40   .03</td>
</tr>
<tr>
<td>Number of prescription drugs taken (per drug)</td>
<td>1.22   &lt;.001</td>
</tr>
<tr>
<td>Depression and poor self-rated health (interaction)</td>
<td>7.83   .02</td>
</tr>
</tbody>
</table>

Overall, 10-year age-specific and sex-specific mortality rates in our cohort were almost identical to those of the US census for the same period. As expected, older age and male sex were strong predictors of mortality. Thus, the MoVIES cohort’s mortality experience is probably representative of, and our findings most likely generalizable to, other similar populations.

Depressive symptoms, functional disability, and cognitive impairment are all common and fairly specific parameters of morbidity that increase with age and are often associated with one another. Self-rated health is a global and remarkably sound measure of health status, which itself has been found to be related to depression and disability. However, the literature is mixed on the relationship of these 4 health parameters to survival. Essentially, all 4 have been shown in some studies, but not in others, to predict mortality. Most previous studies have examined 1 or 2 of them together, as discussed herein. By examining all 4 variables simultaneously, we were able to examine their relative contributions to mortality in an aging, representative, population-based cohort followed over approximately 10 years. Furthermore, we were able to examine predictors of both shorter term (3 and 5 years) and longer term (10 year) mortality.

In our cohort, depressive symptoms and functional (IADL) disability were strong and consistent independent predictors of mortality. However, disability predicted mortality at all 3 end points, while depression
predicted mortality only at the earlier (3- and 5-year) end points. Cognitive impairment became a significant predictor only when functional disability was removed, implying that the relationship between cognition and mortality occurs primarily in the context of disability. Similarly, self-rated health by itself was a significant predictor only when the effects of both depression and an objective measure of health (number of prescription drugs) were removed. However, the interaction between poor self-rated health and depression was strongly predictive of mortality at all 3 follow-up points, even after adjusting for number of prescription drugs taken.

The literature is mixed, as exemplified by the following summary review of depression and mortality. Earlier studies examining this relationship have used varying measures of depressive symptoms or diagnoses and varying lengths of follow-up in a variety of population types (medical inpatients, primary care outpatients, rehabilitation patients, community samples) and sizes (ranging from 805 201 participants). Six of these 12 studies found that depression significantly predicted mortality. Of the 6, functional disability was also examined in 4 of which 3 found that disability predicted mortality along with depression. Of the 6 positive studies, 3 also included self-rated health; 2 found independent positive associations with mortality; 1 did not. One did not assess disability or self-rated health but did include several specific objective measures of physical health. Of the same 6 studies, 2 also examined cognitive functioning, and 1 examined dementia; both predicted mortality independently of depression. Blazer et al used a study design fairly similar to our own, including the original CES-D. They found that depression predicted 3-year mortality but with decreasing relative odds as other variables were added into the model, and that did not interact with other predictors. However, they did not examine the interaction of depression and self-rated health and used logistic regression rather than proportionate hazards models. In another study, the lack of independent association between depression and 6-month mortality was attributed to the short duration of follow-up. A separate group of studies has shown consistently that depression strongly predicts mortality in patients with heart disease.

Depressive symptoms are heterogeneous in origin. They can represent a primary, major depressive illness, or a depressive illness secondary to other medical conditions; they can also reflect a psychological reaction to the individual’s burden of comorbid disease and disability, or to other stressful situations. Furthermore, symptoms may be transient, persistent, or recurrent; these distinctions cannot be captured by screening alone. Our data on depressive symptoms are restricted to those present during the preceding week, as in the original and widely used CES-D; we cannot comment on their total duration. Approximately one third of those depressed at each wave, if still alive at the next wave, again reported depression at the next wave.

Objectively, an individual’s level of medical burden may be measured in number and severity of conditions (or affected organ systems) or reflected by number of prescription medications taken or amount of health services used in a given period. Subjectively, the individual’s perceived or self-rated health depends in part on the burden of objectively measurable disease but may be also strongly influenced by associated levels of disability and depression. In an authoritative review, Idler and Benyamini showed that global self-rated health independently predicted mortality even after accounting for known health risk factors in 23 of 27 previous studies. They suggest several possible interpretations. For example, self-rated health may be a more inclusive and accurate measure of health status and health risk than the covariates that were examined in those studies and may better capture the full array of both diagnosed and undiagnosed (preclinical) diseases than an individual might have. Self-ratings of health represent “complex human judgments” regarding the severity of a person’s current illnesses, may reflect family history, and may represent not just assessment of current health but also health trajectory over time. Self-rated health may also be a self-fulfilling prophecy in that it influences behaviors that affect subsequent health status. Alternatively, it may reflect the presence or absence of internal and external resources needed to maintain health. Our own review shows that self-rated health has been found to predict mortality in several studies but not in others. Only a few of these studies controlled for depression.

In our cohort, while self-rated health did not predict mortality after controlling for depression, the interaction between the two was a powerful predictor even after adjusting for objectively measured ill health (prescription drugs). Thus, it is unlikely that depression and poor self-rated health simply predict death together more often than can be explained by chance, making it hard to disentangle cause from effect. It may be that those who rate their own health poorly and are also depressed are in fact the sickest and closest to death, or that depression itself is the lethal ingredient. The issue here is more whether these conditions are useful markers of impending mortality and less whether they “cause” or directly increase the risk of death. Ruberman has remarked, “It is well to remember that not every important public health development is preceded by complete understanding of its mode of action.” For example, some debate exists as to whether the depression that seems to increase the risk of mortality can be treated, thus postponing death, or whether it is an epiphenomenon (“terminal drop”) of various other conditions that are the actual causes of impending death. Blazer et al examining 3-year mortality, concluded that depression, unlike other known predictors, was associated with mortality “through a number of independent mechanisms, perhaps through complex feedback loops.”

Another approach to assessing cumulative medical burden is to examine the overall degree of functional disability experienced by the individual. Disability and depression are consistently associated with each other and clinically may become part of a vicious cycle of increasing debilitation as the individual approaches death, or even hasten death. Each could also be the result of underlying conditions that lead to death. In our sample, depression and disability predicted mortality independently of each other, with depression by itself being more...
likely to predict mortality in the shorter term than in the longer term. In part this may reflect the relative stability of disability compared with depression. The persistence of depression in our cohort stands in contrast to those of a greater than 20-year follow-up study in Denmark. That study found depression to be stable over time and to have a long-lasting effect on risk of myocardial infarction and mortality, suggesting that it was a “chronic psychological characteristic rather than a discrete and episodic psychiatric condition” (ie, a trait rather than a state).

Functional disability has been measured more consistently than depression across studies, although some have examined basic (self-care) activities of daily living, some have focused on higher-order IADL and some have measured both. The results of these studies are also more consistent than those on depression. Of 19 studies reviewed, all except one found that functional disability predicted mortality. Among the studies reporting associations of disability with mortality, depression was also examined by only 4 groups of which three found, as we did, that both disability and depression independently predicted mortality. In our models, as in those of Blazer et al, we detected no interaction between depression and disability (ie, the 2 variables acting together did not have an effect on mortality over and above the effect that each of them had separately).

Cognitive impairment could be the result of conditions such as stroke or Alzheimer disease, which can cause disability followed by death. In our data, the effect of cognitive impairment on mortality seemed to be explained by functional disability; we found no significant interaction between the two. All but one of several previous studies found a positive association between cognitive impairment and mortality. However, only 6 of these studies simultaneously examined functional disability and cognitive impairment. Five of them found that disability predicted mortality, but the sixth found that mortality was predicted by cognitive impairment but not by functional disability. Cognitive impairment can also be the result of depression, delirium, and other medical conditions foreshadowing death. In our cohort there was no significant interaction between cognitive impairment and depression. In 2 previous studies, both cognitive impairment and depression predicted mortality; in a third, neither of them was a predictor. In another study, diagnosed syndromes of both major depression and dementia (rather than depressive symptoms and cognitive functioning) had negative impacts on survival.

In addition to identifying predictors of mortality over 10 years in a representative community-based cohort, our data reinforce the need for the systematic assessment of older patients for cognitive impairment, functional disability, and depression. Detecting these problems should help identify high-risk patients and at least in some cases prevent premature mortality. Some therapeutic nihilism has been engendered by the finding that successful treatment of depression did not necessarily improve cardiac event-free survival in patients recovering from acute myocardial infarction. However, it has also been found that depression predicted both rehospitalization and nursing home admission in the short term (6 months) in elderly medical inpatients. The remediation of depression, functional impairment, and cognitive impairment may be of greatest value in the reduction of morbidity and excess disability, even when it does not extend life.

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