

## Depression and Mortality in the Elderly

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### Abstract

It is well known that depression can be a consequence of medical illness and disability, but a growing literature suggests also that depression can cause biological changes linked to morbidity and mortality. Depression is strongly implicated as a contributor to cardiovascular disease and mortality. Using the cascade-to-death model as a conceptual framework, we explore the complex relations among behavior, affect, motivation, and pathophysiology that might

account for the association between depression and premature death. Our model suggests that some individuals become entrapped in a downward spiral in which behavior, medical illness, and depressive affect feed on each other to undermine the biological integrity of the organism. In addition to specifying behavioral and biological mechanisms linking depression to mortality, future research needs to more closely examine phenomenological aspects of depression in order to determine

what aspects of depression and related constructs such as hopelessness, vital exhaustion, and motivational depletion account for the link between depression and mortality.

### Keywords

depression; death; elderly; motivation; hopelessness

Scientists have long been interested in the underlying causes of death, and in the past two centuries have identified a wide array of behavioral and biological factors linked to mortality. For example, scientists now have a good understanding of how a behavior such as smoking undermines the functioning of multiple physiological systems, which in turn leads to disease and, ultimately, death. Much less is known about psychological processes such as depression and hopelessness and their role in causing death, although it is widely be-

lieved that they are important contributing factors to mortality. The role of depression in mortality is clearly illustrated in the act of a depressed person who commits suicide; however, this role is less apparent when the primary cause of death is a medical illness. It is suspected that depression may cause or exacerbate medical illness, or interact with other biological vulnerabilities brought about by medical illness.

This article explores the relation between depression and mortality in the elderly. We focus on the elderly because both disease and death are highly prevalent in late life, and symptoms characteristic of depression, although not necessarily clinical depression, are relatively common among individuals of advanced age. Thus, from a scientific perspective, the convergence of depression, illness, and mortality in the elderly provides an ideal platform for studying the relation among these variables.

### IS DEPRESSION RELATED TO MORTALITY?

Before answering this question, it is useful to describe how investigators test hypotheses concerning the relation between depression and mortality. A frequently used approach in large population studies is to identify a group of individuals, assess their levels of depression, and identify those who die within a fixed follow-up period. The depression-mortality hypothesis predicts that people who are more depressed are more likely to die or will die sooner than individuals who are less depressed. Of course, this simple test of the depression-mortality link is open to a major criticism: People who are ill are more likely both to be depressed (Dew, 1998) and to die,

something that has been known for a long time. To address this methodological problem, researchers have typically controlled for the known associates of mortality, including demographic factors (e.g., gender, age), behavioral risk factors (e.g., smoking), biological risk factors (e.g., being overweight), and subclinical and prevalent disease. (Subclinical disease is a condition in which a disease is detected by special tests but does not reveal itself by overt symptoms, e.g., blockage of the coronary artery indicating atherosclerosis but without the presence of chest pain or shortness of breath. Prevalent disease refers to conditions, such as cancer or heart disease, with overt symptoms.)

To the extent that depression is associated with mortality after known causes of death are controlled for, one might conclude that depression is a unique contributor to mortality. For example, in a recent study of 5,201 persons aged 65 and older (Schulz et al., 2000), we showed that those who had high levels of depressive symptoms were 25% more likely to die within 6 years than those who had low levels of depressive symptoms, after we controlled for a large number of sociodemographic, disease, and biological and behavioral risk factors. Even larger effects of depression on mortality have been found in studies examining the relation between depression and cardiovascular disease and mortality. Depression is a risk factor for the onset of ischemic heart disease (i.e., significant blockage of blood flow to the heart) among individuals initially free of disease. In addition, individuals who already have heart disease and are depressed are more likely to die than individuals who have heart disease and are not depressed (Glassman & Shapiro, 1998). Attempts to link depression and other causes of mortality such as cancer have yielded less consis-

tent results, and, more generally, the literature includes numerous studies that have failed to find an association between depression and mortality (Wulsin, Vaillant, & Wells, 1999).

Whether or not a study finds that depression has an effect on mortality depends on a number of factors, including the choice of control variables, the manner in which they are measured, the completeness of follow-up, and whether the sample size is large enough to detect statistically significant differences given the mortality rate in the population studied. In general, the chances of finding that depression is associated with mortality diminish to the extent that studies have small samples with relatively few deaths or include large numbers of control variables, particularly if the control variables include other subjective self-assessments that conceptually overlap with depression. Our own work and recent reviews of this literature suggest that depression substantially increases the risk of death (Glassman & Shapiro, 1998; Musselman, Evans, & Nemeroff, 1998; Wulsin et al., 1999). This effect has been observed in diverse populations, including patients needing psychiatric care, patients in long-term-care facilities, persons who have diverse medical illnesses and are in acute-care hospitals, post-heart attack and cancer patients, and persons who reside in the community and are not medically ill.

### HOW DOES DEPRESSION INCREASE THE RISK OF MORTALITY?

Whether or not one agrees with the proposition that depression affects mortality depends to some extent on the plausibility of specific mechanisms that might account for

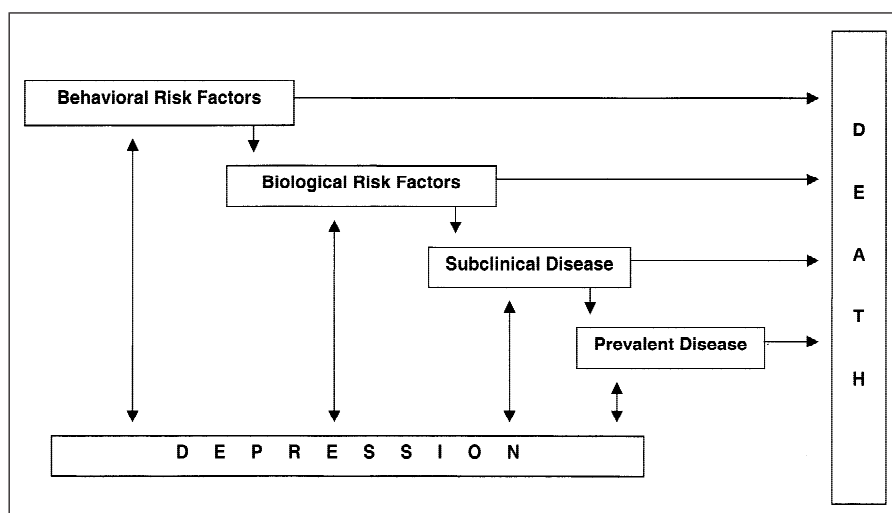


Fig. 1. Depression and the cascade to death.

this relation. To address this issue, investigators have searched for linkages between depression and known behavioral and pathophysiological causes of death.

Figure 1 illustrates our cascade model of mortality and shows how four major categories of health-related variables might cause an individual to die. Although variables within each category can directly cause death, less proximal causes (i.e., causes that are typically farther removed from death) such as behavioral risk factors are thought to have their impact on mortality primarily through more proximal downstream causes (i.e., more immediate causes of death) such as biological risk factors, subclinical disease, and, finally, prevalent disease. For example, depression can lead to inactivity, increased alcohol consumption, eating and sleeping problems, and lack of adherence to treatment for medical problems. Each of these factors may directly or indirectly, through other factors downstream, lead to mortality. Similarly, depression has been linked to activation of the hypothalamic-pituitary-adrenal (HPA) axis and compromised immune function, which in turn may predispose individuals to infectious disease, cancer, or the exacerbation of exist-

ing medical illness. (The HPA axis is involved in the body's stress response. Neurons within the hypothalamus send a signal to the pituitary gland, which in turn secretes a hormone that causes the adrenal glands to secrete the stress hormone cortisol into the bloodstream.)

One of the most robust findings in the literature is the relation between depression and cardiovascular disease and mortality, suggesting that the pathophysiologies of heart disease and depression are closely intertwined. Compared with nondepressed persons, depressed individuals have been found to have both functional and structural changes in the brain that may result in pathophysiological changes such as reduced heart rate variability or ventricular arrhythmias, which are known to be risk factors for cardiovascular disease and mortality (Musselman et al., 1998). It is tempting to conclude that depression can cause cardiovascular disease and mortality, but it is also possible that another factor, perhaps genetic, causes both depression and cardiovascular disease (Lesperance & Frasura-Smith, 1999).

Although our discussion thus far implies a causal direction from

depression to behavioral and health mediators to death, Figure 1 also suggests reciprocal causation between the mediators and depression. This is most apparent with subclinical and clinical disease (e.g., cardiovascular disease), which may affect brain chemistry to cause depression or result in depression because of the functional consequences of medical illness (e.g., disability). Thus, our model of depression and mortality is a complex interactive system involving affect, behavior, and physiology with multiple feedback loops. One can easily envision a downward spiral leading to death that is instigated and perpetuated by any one of the mechanisms involved in depression and mortality.

The search for mechanisms of the association between depression and mortality will likely yield both behavioral-affective and biological answers. In addition, researchers in this area have paid little attention to the underlying motivational states that are considered part of the depressive syndrome and may be directly linked to health-related behaviors. For example, analysis of scales used to assess depression in the elderly has shown that the link with mortality is strongest for items reflecting motivational depletion (e.g., "I could not get going," "Everything I did was an effort"; Schulz et al., 2000). It has also been suggested that states such as vital exhaustion, which is characterized by lack of energy, increased irritability, and feelings of demoralization, are key factors contributing to death (Kop, Appels, Mendes de Leon, de Swart, & Bar, 1994), as are related constructs such as hopelessness or pessimism (Scheier & Carver, in press). Studying these motivational states and their behavioral, affective, and health-related consequences may help researchers better understand the link between depression and mortality.

### WHAT CAN INTERVENTION STUDIES TELL US ABOUT DEPRESSION AND MORTALITY?

A number of studies comparing individuals given an antidepressant (nortriptyline or fluoxetine) or a placebo have shown greater improvement in physical functioning in the active-treatment group compared with the placebo group. Psychotherapy interventions for depression have also been shown to increase people's ratings of their own health. Conversely, successful treatment of many medical illnesses results in the reduction of depressive symptoms. These findings are consistent with those of descriptive studies, but add little new information to this puzzle. One of the limitations of most depression treatment studies is that they are typically not powered to detect changes in medical morbidity or mortality. One exception to this is the ongoing SADHART (Sertraline Antidepressant Heart Randomized Trial) study, a large, multicenter trial in which post-heart attack patients who also have major depression are randomly assigned to treatment groups that receive either the antidepressant sertraline or a placebo. Another study currently under way (Enhancing Recovery in Coronary Heart Disease, or ENRICHD) is comparing rates of heart attack and mortality among depressed post-heart attack patients who receive psychosocial treatment (e.g., counseling and group sessions) and those who receive standard medical care. These studies have the potential to provide important information about the effectiveness and safety of treating post-heart attack patients for depression, as well as about the mechanisms linking depression to cardiovascular disease and mortality.

### FUTURE DIRECTIONS

Clearly, researchers are only just beginning to unravel the mystery of why depression might lead to mortality. To better understand the mechanisms that might link depression and mortality, one would want to simultaneously assess depression, behavioral and pathophysiological mediators, and their relation over time. An underlying assumption of the cascade-to-death model is that individuals can become entrapped in a downward spiral in which behavior, medical illness, and depressive affect feed on each other to undermine the biological integrity of the organism. An important clinical implication of this view is that the downward spiral can be broken through multiple treatment approaches. One could treat the depression, the behavioral problems, the medical illness and its functional consequences, or some combination of these factors. Achieving desired effects in any one of these domains will likely have a positive impact on the remaining factors as well. Because depression is often not recognized or treated in the elderly, its diagnosis and treatment should receive high priority among health professionals. The successful treatment of depression not only will improve the quality of life of older persons, but may also enhance their physical health and survival, as well as reduce health care costs and enhance productivity.

Conceptual and empirical work is also needed to help determine what aspect of depression accounts for the depression-mortality link. Depression is a complex syndrome, involving affective, somatic, cognitive, and motivational elements, each of which may have unique relations to the behavioral and biological factors identified in our model. Researchers also need to explore in this context the relation be-

tween depression and related constructs such as hopelessness, pessimism, and vital exhaustion, which also have been linked to mortality. Is there a critical underlying feature of these constructs that needs to be identified and assessed with new measurement tools? Possible candidates for this underlying construct might include motivational depletion, giving up on life, or disengagement from life and health-related goals. The stakes for unraveling this mystery are clearly high. But the payoffs may be equally high, when viewed in the context of the enhanced quality and duration of life that would ensue should underlying mechanisms be accurately identified and effective interventions devised to counteract their effects.

### Recommended Reading

Schulz, R., Beach, S.R., Ives, D.G., Martire, L.M., Ariyo, A.A., & Kop, W.J. (2000). (See References)  
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### Note

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