

DEPRESSION AND ANXIETY: A REVIEW



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Depression and anxiety are common problems in the population and are frequently encountered in the underwriting environment. What makes these conditions difficult to evaluate is the wide range of findings associated with the conditions and the significant number of comorbid factors that come into play in assessing the mortality risk associated with them. Thus, more than with many other medical conditions, there is a true “art” to evaluating the risk associated with anxiety and depression. Underwriters really need to understand and synthesize all of the key elements contributing to outcomes and develop a composite picture for each individual to adequately assess the mortality risk.

The Spectrum of Depression

Depression represents a spectrum from dysthymia to major depression. From a mortality perspective, major depressive disorder (MDD) is the most important of these. It is characterized by the presence of the core symptoms of a depressed mood (may be an irritable mood in children and adolescents) and/or reduced interest or pleasure in most things for at least 2 continuous weeks plus the presence of four or more other key symptoms. These symptoms include: insomnia or hypersomnia, reduced interest or pleasure, excessive guilt or feelings of worthlessness, reduced energy or fatigue, diminished ability to concentrate or make decisions, loss or increase of either appetite or weight, psychomotor retardation or agitation, and thoughts of suicide or death or suicidal behavior.

If an individual meets the above criteria for major depression for 2 years or more, the condition is called chronic depression. Minor depression is characterized by the presence of the core symptoms, but only three or fewer of the other findings.

Epidemiology of Depression

The median age of onset for major depression is in

Executive Summary *This article reviews the overall spectrum of depressive and anxiety disorders including major depressive disorder, chronic depression, minor depression, dysthymia and the variety of anxiety disorders, with some special attention to post-traumatic stress disorder (PTSD). It includes a review of the epidemiology and risk factors for each condition. Some of the rating scales that can be used to assess the severity of depression are discussed. The various forms of therapy for depression are reviewed, including the overall therapeutic philosophy, rationale for the choice of different medications, the usual duration of treatment, causes for resistance to therapy, and the alternative approaches that may be employed in those situations where resistance occurs. The overall mortality risks for both depression and anxiety are reviewed, as are the red flags for higher risk situations in each of these conditions. Finally, the basics of suicide are discussed, including its epidemiology and risk factors and how prior suicide attempts influence mortality from a variety of causes. Included in this discussion is the role both depression and anxiety play in the occurrence of suicide.*

the early 30s. Prevalence levels are high in the general population. At any one time 2.3-4.9% of individuals have the disorder. The lifetime prevalence rate is 16%. The condition is more common in the setting of physical illness, reaching levels of 15-20% in nursing home residents and 22-33% in individuals with chronic medical conditions.

Major depression is a chronic disorder. The recurrence rate is 50% after a single episode. This increases to 70% after two episodes and 90% or more after a third episode. Risk factors for recurrence include: an early age of onset, a more severe initial episode,

the presence of dysthymia with MDD, a history of an anxiety disorder, a history of substance abuse, the presence of a bipolar disorder, recurrent life stressors and a poor social support network.

Risk Factors for Depression

There are a number of risk factors for major depressive disorder. It is twice as common in women as in men. It tends to aggregate in families, with the risk 3-4 times higher in first-degree relatives with the disorder. As noted above, a prior episode is a strong predictor for another occurrence. Stressful life events, such as divorce, death of a loved one or abuse, especially if they occur in childhood, are strong precipitants. The presence of substance abuse, other medical conditions and some medications such as beta blockers are associated with development of the condition. Finally, certain personality traits are associated with major depressive disorder, especially being overly dependent and self-critical with a predisposition to emotional upset under stress.

Evaluating the Severity of Depression

A number of rating scales have been developed for assessing the severity of depression. Several of these with their representative scores are summarized in Table 1. However, these scores are rarely seen in the underwriting process. Another approach to gauging severity is offered by use of the Global Assessment of Functioning (GAF) scale seen in Table 2. This score is intended for use with all mental illnesses and is not specific to depression. It allows an assessment of the overall functioning of the individual based on the type of information that can be easily found in an underwriting file. An example of an adaptation of the GAF score as a means to grade the severity of depression is illustrated in Table 3.

Dysthymia

Dysthymia is characterized by a depressed mood (may be an irritable mood in children and adolescents) that is seen most of the day when observed, present more days than not, and that persists continuously for at least 2 years. It is also defined by the presence of at least two of the following symptoms: poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration with difficulty with making decisions, and feelings of hopelessness. The symptoms cannot be due to another medical or psychiatric disease and must cause significant impairment of daily functioning. About 70% of dysthymic patients will eventually go on to at least one episode of major depression. The term “double depression” is applied to these episodes of major depression superimposed on a baseline dysthymic disorder.

Treatment of Depression

The current feeling is that all depression, including

Table 1

Severity by Depression Scales

	Hamilton Rating Scale (HAM-D-17)	Beck Depression Inventory (BDI)	Inventory of Depressive Symptoms (IDS)	Zung Self Rating Depression Scale (Zung SDS)
None-Minimal	0-7	0-9	0-13	0-49
Mild	8-13	10-16	14-22	50-59
Moderate	14-18	17-29	22-30	60-69
Severe	19-22	≥ 29	30-38	≥ 69
Very Severe	≥ 23		≥ 38	

Table 2

Global Assessment of Function Scale (GAF)

Score	Interpretation
91-100	Superior function, no symptoms
81-90	Good function, absent or minimal symptoms
71-80	Symptoms are transient, slight impairment of function
61-70	Mild symptoms, some difficulty, generally functions well
51-60	Moderate symptoms or moderate difficulty in functioning
41-50	Serious symptoms or serious difficulty in functioning
31-40	Impaired reality testing or communication or seriously impaired functioning
21-30	Behavior considerably influenced by psychotic symptoms or inability to function in almost all areas
11-20	Some danger of hurting self or others or occasionally fails to maintain hygiene
1-10	Persistent danger of hurting self or others, serious suicidal act or inability to maintain hygiene
0	Inadequate information

Adapted from DSM-IV, p 22.

Table 3

Practical Application of GAF Score

Score	Severity
None - Minimal	80 or more
Mild	71-80
Mild - Moderate	61-70
Moderate	51-60
Moderate - Severe	41-50
Severe	40 or lower

dysthymia, should be treated aggressively. Both psychotherapy, especially cognitive-behavioral therapy, and medication have been shown to be efficacious. The combination of both of these forms of treatment is better than either used alone.

Medications used to treat depression include the selective serotonin reuptake inhibitors (SSRI), selec-

tive serotonin and noradrenaline reuptake inhibitors (SSNRI), tricyclic antidepressants (TCA), monoamine oxidase (MAO) inhibitors and those drugs that do not fit into one of these classes. The SSRI and SSNRI drugs have revolutionized the treatment of depression. Their low side effect profile and tolerance by patients have allowed primary care physicians to now assume the bulk of the care of depressed individuals.

About 60-70% of individuals respond to first-line therapy. For mild to moderate depression, there is generally no particular advantage to one drug over another for the treatment of the depression itself. The choice of medications is based more on the side effect profile and the symptoms that the individual is experiencing. For example, in a person with a significant problem with insomnia, the choice of a medicine with sedating effects would be better than one that produced agitation. The tricyclic drugs may work somewhat better for severe depression. The MAO inhibitors are generally reserved for severe or resistant depression due to their significant side effects and problems with interactions with drugs, foods and other substances.

A response to medical therapy takes at least 2-3 weeks and may take up to 6-8 weeks or more. The duration of therapy should be at least 6-12 months after remission is achieved, ideally at the higher end of that range. Long-term maintenance therapy is recommended in certain situations, such as when there has been two episodes with the presence of risk factors for recurrence and in the presence of three episodes or more. Thus, cessation of treatment is not necessarily a good thing in all cases. In fact, for individuals with recurrent disease, the cessation of therapy is a major negative from a long-term risk perspective.

Failure to respond to treatment is not unusual. Common reasons for this include failure to use a high enough dosage, failure to stay on the medication for a long enough period of time, skipping doses, intolerance of side effects, and the presence of accompanying medical, psychiatric and substance abuse disorders. Options for treatment of resistant disease include maximization of drug dose and duration, changing to alternative medications, use of combinations of drugs and use of augmentation treatment with mood-stabilizing agents. Augmentation therapy uses drugs that do not have inherent antidepressive effects but, rather, ones that amplify or augment the effects of the established antidepressants. These treatments include lithium, thyroid hormone and the use of the atypical antipsychotic drugs including aripiprazole (Abilify) and risperidone (Risperdal) among others. Another option for severe or resistant disease is use of non-pharmacologic or somatic therapy. The most commonly used of these is electroconvulsive therapy.

This treatment has been used for a number of years and is effective in 50-70% of cases. It tends to be less effective in bipolar disorder, minor disease and depression of long duration. Other, less commonly encountered, but nevertheless effective forms of somatic therapy, at least in some studies, include: deep brain stimulation, repetitive transcranial magnetic stimulation, vagus nerve stimulation and transcranial direct current stimulation.

Red Flags with Depression

Red flags that would indicate more severe depression or a higher risk situation would include: a prior suicide attempt, suicidal ideation (especially if there is intent and a clear plan), psychotic depression with the presence of delusions or hallucinations, use of MAO inhibitor drugs, use of augmentation therapy, use of somatic treatments, worsening symptoms with the initiation of antidepressant therapy (an indicator of possible bipolar disorder), a concomitant severe anxiety disorder, non-compliance with treatment, failure to use maintenance therapy despite repeated episodes and concurrent severe medical impairments.

The Spectrum of Anxiety Disorders

There are a number of different conditions that fall under the designation of anxiety disorders. These include: panic disorder, agoraphobia, social anxiety disorder, obsessive compulsive disorder, post-traumatic stress disorder (PTSD) and generalized anxiety disorder.

Anxiety disorders are the most common mental health conditions encountered in the United States. The prevalence is 18.1% for any given year. The lifetime prevalence is almost 29%.

Anxiety is a normal part of life and is highly functional in many situations, such as preparing for meeting deadlines, avoiding dangerous situations etc. What separates the pathologic anxiety disorders from the functional variety are four characteristics. These include: excessiveness – the anxiety is out of proportion to what would be called for in the given situation; intensity – it occurs at a markedly increased level; duration – it tends to be a chronic, recurrent condition; and impairment – the anxiety interferes with normal daily social and occupational functioning.

Risk Factors for Anxiety Disorders

The risk factors for the anxiety disorders represent a combination of genetic predisposition and environmental triggers. The disease is more common in women. The genetic factors include a family history of anxiety disorder and a personal history of one of these conditions. Other issues that come into play are a history of adverse events in childhood, a recent history of stressful life situations, ineffective emotional

coping strategies, the presence of a chronic pain or other medical conditions, a history of substance abuse and a poor social support network.

Treatment and Red Flags for Anxiety Disorders

As is the case with depression, the combination of psychotherapy, especially cognitive-behavioral therapy, and medication works best. Education about the condition and what triggers it is especially important. The most effective drugs are the SSRIs. However, as with depression, there is a delay in response to this therapy of up to 3 or weeks or more. The benzodiazepines (alprazolam or Xanax, clonazepam or Klonopin, others) are effective and work more rapidly but have significant side effects. These include sedation and respiratory depression. The latter can be a serious problem when the drugs are combined with alcohol or opioid pain medications. Probably the most optimal use of the benzodiazepines is as a bridge from the initiation of SSRI treatment to the onset of the latter's full pharmacologic benefit.

Red flags for the anxiety disorders include: an early age of onset, more severe functional impairment, comorbidity with other mental illnesses, the presence of substance abuse and chronic pain disorders, and comorbidity with other medical illnesses.

One thing to remember about both anxiety and depression is that they are, in general, associated with poor health habits. There is an increased likelihood of smoking and alcohol abuse. The probability of decreased physical activity, poor dietary habits and social isolation is higher. Finally, there tends to be poorer compliance with medical treatment regimens in those with these disorders.

Mortality Associated with Depression

Surprisingly enough, the data on the mortality risk associated with depression has shown mixed results in the past. This is in part due to the fact that the mortality risk is difficult to analyze. The criteria used to define depression vary from study to study. In addition, it is difficult to separate out the effects of comorbid conditions. Medical conditions can lead to depression and depression can influence the outcome with medical conditions. The presence of other mental illnesses, substance abuse and anxiety can significantly affect the prognosis. Finally, the age, sex and health habits of the individuals involved also come into play in the analysis.

In looking more closely at the recent data on the mortality outcomes with depression, several things seem clear. First, there appears to be a consistent increase in mortality in multiple clinical studies (Figure 1). Second, multiple papers show that the mortality is increased in the elderly (Figure 2). Third, the death

rates increase as the severity of depression increases (Figure 3). Fourth, death rates are higher with a reduction in life expectancy in individuals with MDD. The increase in years of potential life lost is seen in all categories of psychiatric and medical illness when depressed individuals are compared to those who are not depressed (Figure 4). Finally, relative risk in minor depression is increased but at a significantly lower level than that seen with MDD (Figure 5).

Mortality Associated with Anxiety Disorders

The mortality information on the anxiety disorders is limited compared to that for major depression and the data is more mixed. Like MDD, comorbidities drive much of the risk but are amplified in the case of anxiety. That having been said, the overall risk with these disorders appears to be clearly lower than with depression (Figure 6). In addition, the same scaling of risk with severity of the condition is not seen with anxiety (Figure 7). Thus, anxiety appears to function more as a modifier of mortality risk. Its effect is to amplify the inherent risk associated with underlying conditions such as depression, substance abuse, chronic pain and chronic medical illness.

Post-traumatic stress disorder (PTSD) has received more attention in recent years in a large part because of the frequency of the finding in veterans of the Iraq and Afghanistan wars. Its occurrence depends heavily on the nature and severity of the inciting event. It is more common in women and young adults, and it is more likely to occur in association with other psychiatric illnesses, especially depression. What is interesting is that PTSD, when other comorbid conditions are controlled for, is not associated with an increase in overall mortality or deaths due to suicide. However, it is associated with a higher risk of opioid abuse and a higher risk of coronary artery disease, including a greater likelihood of higher coronary artery calcium scores.

The Basics of Suicide

It is difficult to discuss depression and anxiety without addressing suicide. Suicide is the 10th leading cause of death in the United States and the 3rd leading cause of death among adolescents. Overall, there are about 8-10 attempts per every completed suicide. Success rates vary with the means chosen, with those with guns being significantly higher than those with drug overdose. It is more likely in certain ethnic groups such as American Indians and Alaskan natives. Age is also a factor. Older individuals are more likely to complete suicide if attempted, with the highest rates in the population occurring in elderly Caucasian men.

Psychiatric illness is present in 90-95% of cases (affective disorders – 50%, substance abuse – 25%, schizophrenia – 10%). Women are more likely to at-

Figure 1
Mortality Risk with Depression

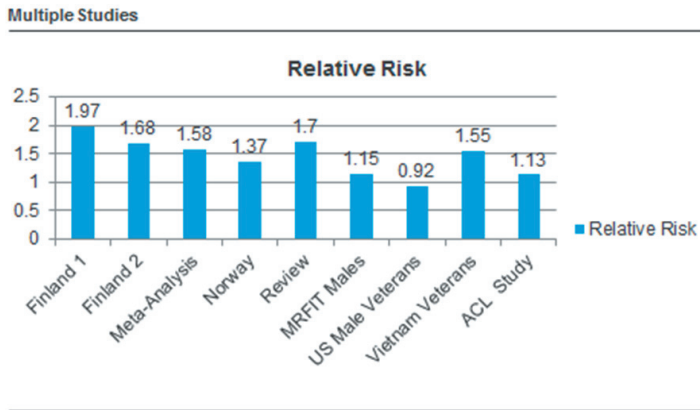


Figure 4
Overall Mortality Risk with Depression – VA Study

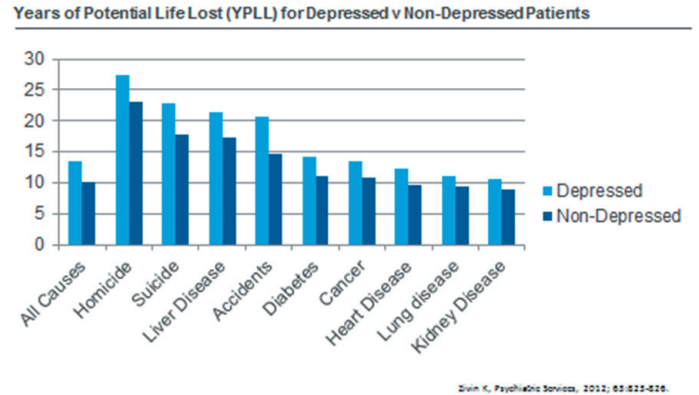


Figure 2
Mortality with Depression in the Elderly

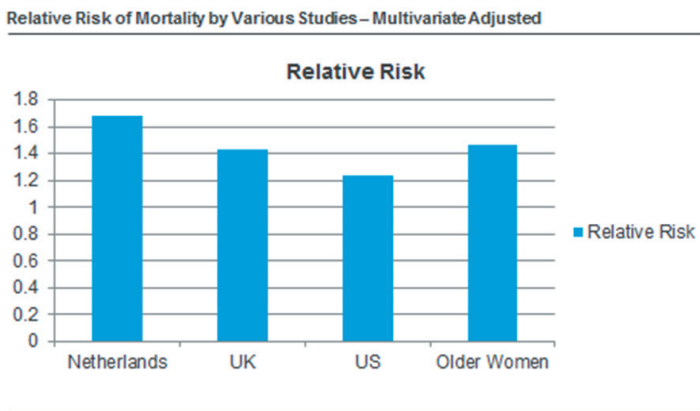


Figure 5
Mortality Risk with Minor Depression

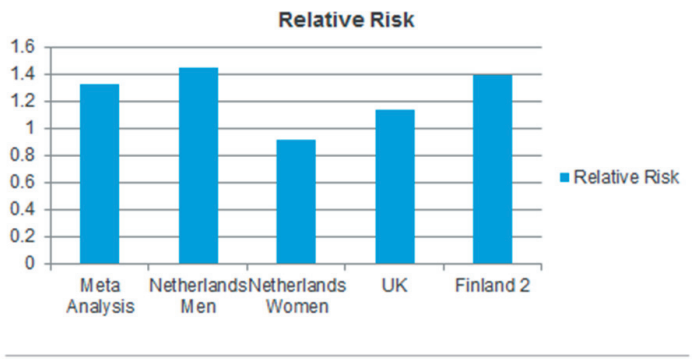


Figure 3
Mortality by Severity of Depression - Finland

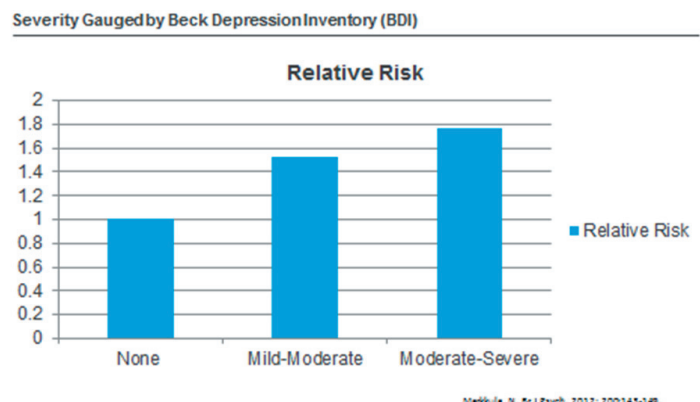


Figure 6
Mortality Risk with Anxiety

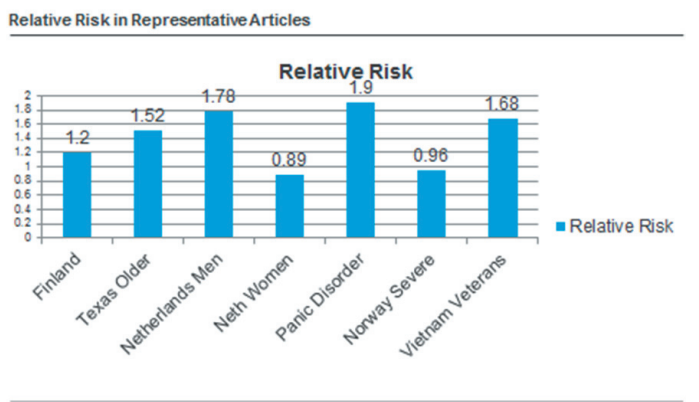


Figure 7

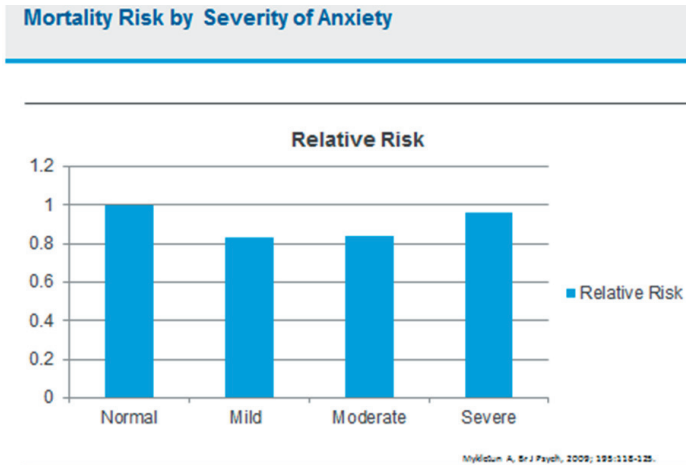


Figure 10

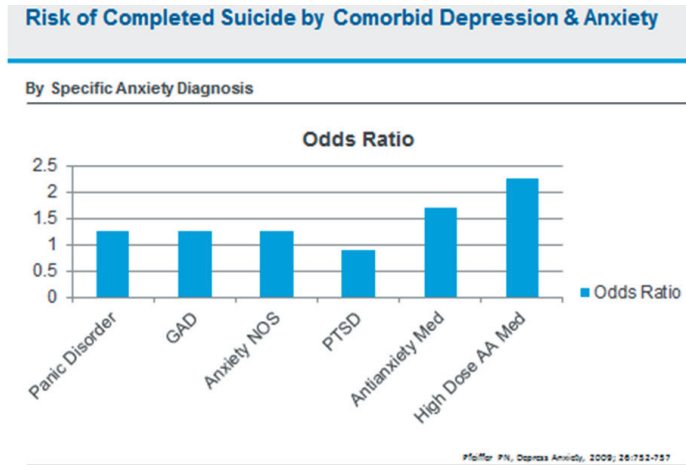


Figure 8

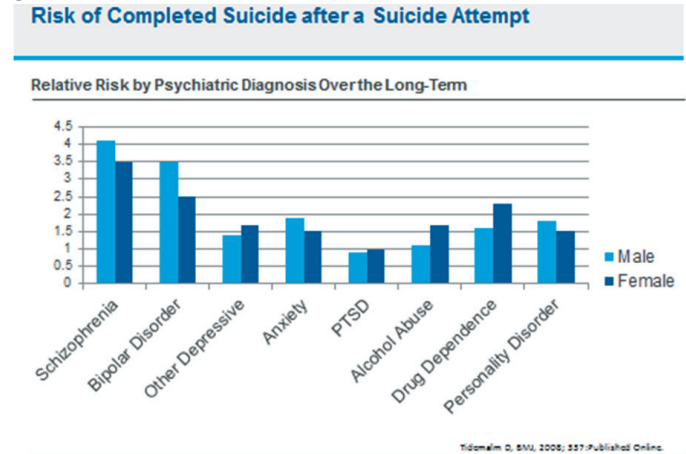
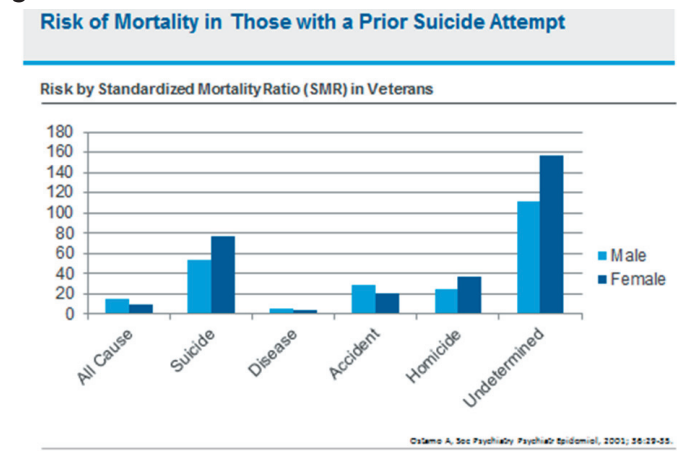


Figure 9



tempt suicide (3-4:1), but men are more likely to complete it (3-4:1). A previous suicide attempt is a strong risk factor and varies somewhat by the underlying psychiatric illness (Figure 8). The death rates after an attempt are increased from a variety of medical and psychiatric illnesses (Figure 9). Other risk factors include: a recent hospitalization for a suicide attempt, a family history of suicide or psychiatric illness, the presence of guns in the house, comorbid medical illness, marital status (higher if widowed, divorced or separated), living alone and recent personal loss, including unemployment and retirement. The importance of financial and legal difficulties is evident in the well-recognized increase in suicide rates and related insurance claims associated with the recent financial crisis.

Association of Depression and Anxiety with Suicide

Suicide is clearly associated with the presence of depression. The feeling of hopelessness appears to be more important than other measures of severity in assessing the risk. Surprisingly, the risk is variable and not consistently substantially elevated in association with psychotic depression. Comorbid anxiety, substance abuse and personality disorders are clearly adverse prognostic indicators. The operative word for risk assessment is “early.” The chances of suicide are increased sooner after the diagnosis of depression, earlier in the lifetime course of the illness, during the first few months after the initiation of therapy, earlier in the course of hospitalization, and in the first month or two after discharge from inpatient care.

The pattern of suicide with anxiety, as with overall mortality, is more mixed. The risk appears to be higher with comorbid depression, with panic disorder and generalized anxiety disorder. A particular red flag is the use of anti-anxiety drugs, especially if they are used in high dose (Figure 10).

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