



A response to medical therapy takes at least 2-3 weeks

Depression – A review

Did you know?

17%

The lifetime prevalence rate of depression in the US and Western Europe

Depression is a common problem in the population and is frequently encountered in the underwriting environment. What makes it difficult to evaluate is the wide range of findings associated with the condition and the significant number of comorbid factors that come into play in assessing the mortality risk associated with it. Thus, more than with many other medical conditions, there is a true “art” to evaluating the risk associated with depression. Underwriters really need to understand and synthesise 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 characterised 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 4 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
- 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 characterised by the presence of the core symptoms but only 3 or fewer of the other findings.

Epidemiology of depression

The median age of onset for major depression is in the early 30's. 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 17%. 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
- 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.

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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 summarised in Table 1.

Table 1: Severity by depression scales¹

	HAM-D-17	BDI	IDS	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	23-30	60-69
Severe	19-22	> 29	31-38	> 69
Very Severe	> 22		> 38	

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.

¹ Please see abbreviations on page 7

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 the DSM-IV (multiaxial assessment - axis V)

Table 3: Practical application of GAF score

Score	Severity
None - Minimal	81 or more
Mild	71-80
Mild - Moderate	61-70
Moderate	51-60
Moderate - Severe	41-50
Severe	40 or lower

Dysthymia

Dysthymia is characterised 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 2 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
- 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.

More than with many other medical conditions, there is a true "art" to evaluating the risk associated with depression.

Treatment of depression

The current feeling is that all depression, including 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), selective serotonin & 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 revolutionised the treatment of depression. Their low side effect profile and tolerance by patients has allowed primary care physicians to now assume the bulk of the care of depressed individuals.

About 60% to 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 maximisation of drug dose and duration, changing to alternative medications, use of combinations of drugs and use of augmentation treatment with mood stabilising agents. Augmentation therapy uses drugs that do not have inherent anti-depressive 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 anti-depressant therapy (an indicator of possible bipolar disorder)
- A concomitant severe anxiety disorder
- Non-compliance with treatment
- Failure to use maintenance therapy despite repeated episodes
- Concurrent severe medical impairments

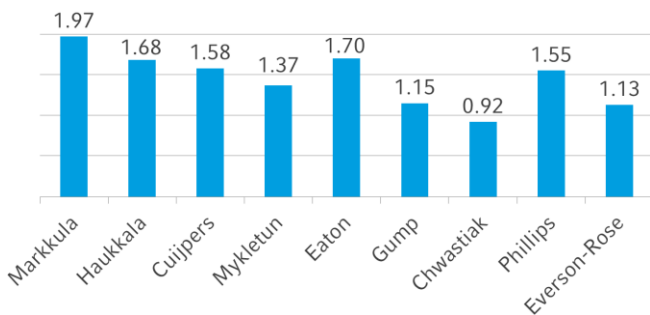
Mortality associated with depression

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 analyse. 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).

Figure 1: Mortality risk with depression

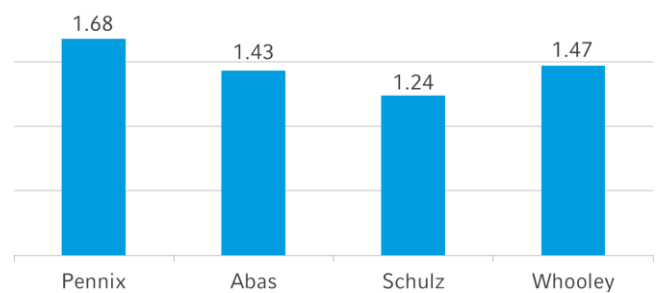
Multiple studies – relative risk



Older individuals are more likely to complete suicide if attempted

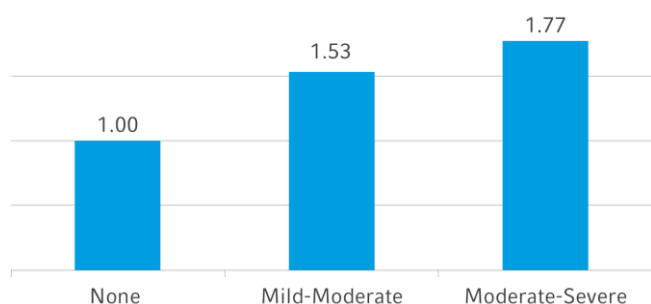
Figure 2: Mortality with depression in the elderly

Relative risk of mortality by various studies – multivariate adjusted



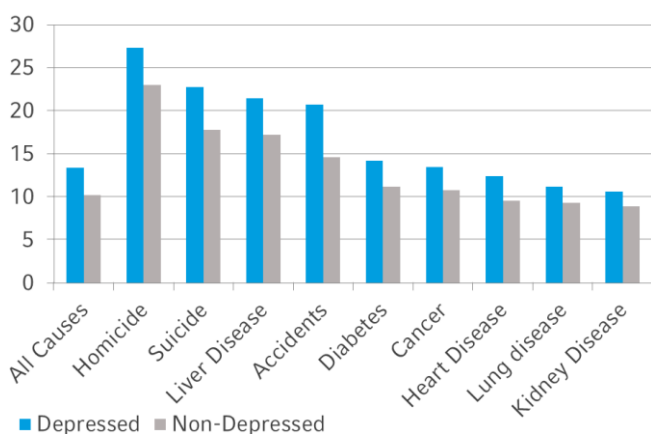
Third, the death rates increase as the severity of depression increases (Figure 3).

Figure 3: Mortality by severity of depression²
Severity gauged by BDI – relative risk



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).

Figure 4: Overall mortality risk with depression – VA Study³
YPLL for depressed vs. non-depressed patients

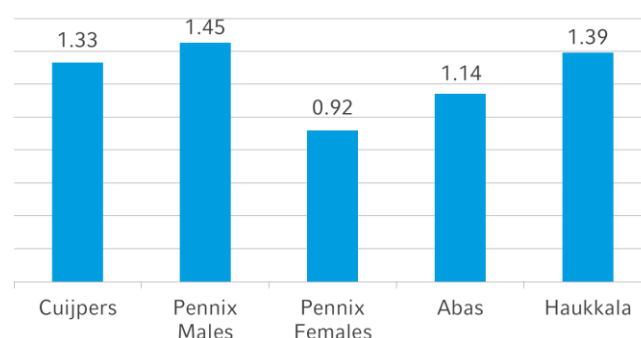


² Markkula N, Br J Psych, 143-149

³ Zivin K, 823-826.

Finally, relative risk in minor depression is increased but at a significantly lower level than that seen with MDD (Figure 5).

Figure 5: Mortality risk with minor depression
Relative risk



Association of depression 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 hospitalisation and in the first month or two after discharge from inpatient care.

Abbreviations

BDI	Beck Depression Inventory
GAF	Global Assessment of Functioning
HAM-D-17	Hamilton Rating Scale
IDS	Inventory of Depressive Symptoms
MAO	Monoamine Oxidase
MDD	Major Depressive Disorder
SSNRI	Selective Serotonin & Noradrenaline Reuptake Inhibitors
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	Tricyclic Antidepressants
VA	Veteran Affairs
YPLL	Years of Potential Life Lost
Zung SDS	Zung Self Rating Depression Scale



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