Depression—also referred to as major depressive disorder (MDD)—is perhaps the most common mental illness. Nearly one in five people will experience an episode of depression at some point in their lives. For many people, depression will resolve with the first-line treatments of psychotherapy or antidepressant medications. Unfortunately, up to one-half of all people diagnosed with major depressive disorder (MDD) will not respond to their initial choice of treatment.

Treatment resistant depression (TRD) is the clinical term for an episode of major depressive disorder that does not respond to an adequate trial (at least six weeks) of an antidepressant medication. TRD is associated with increased symptoms of depression and more severe impairment in the realms of school, work and social functioning. People with TRD are at greater risk of hospitalization for their psychiatric illness, are more likely to abuse drugs and alcohol, and at increased risk of attempting suicide.

What causes treatment resistant depression?

Treatment resistant depression may represent a type of MDD that is more severe and chronic. People with TRD are more likely to have a family history of depression and other mental illnesses, which suggests that there is a strong biological—or genetic—component to this condition. They are also more likely to be experiencing significant challenges in their lives (e.g., loss of a family member or loved one, divorce, unemployment and financial concerns), which suggests that stress plays a big role in this illness.

Those with TRD are more likely to be diagnosed with other mental illnesses—specifically, anxiety disorders such as posttraumatic stress disorder and personality disorders such as borderline personality disorder. The link between medical illness and TRD has been the subject of significant clinical research, and some medical illnesses such as chronic pain, cardiovascular illness (e.g., heart attacks) and cancer are specifically associated with more severe and challenging forms of depression.

Scientific studies have shown that some people with TRD may not be taking their medications as directed by their physicians. In general, most psychiatric medications need to be taken at least once each day and will not work effectively unless they are taken as prescribed. People who are actively drinking and using substances may also be at risk of developing TRD. This is likely due to the fact that abusing drugs and alcohol can worsen a person’s mood as well as decrease the effectiveness of psychiatric medications.

Other people who do not respond to first-line treatments for depression may have a mental illness that is more complicated than MDD. People with psychotic depression will likely not respond to traditional treatment of depression. People with bipolar depression will also likely need a different, more complex treatment than would be otherwise required.
What treatments are available for treatment resistant depression?

All people with TRD deserve the opportunity to be cared for by trained mental health professionals. Many people with depression will initially be prescribed an antidepressant—e.g., bupropion (Wellbutrin), fluoxetine (Prozac), sertraline (Zoloft), citalopram (Celexa) and other selective serotonin reuptake inhibitors (SSRIs)—by their primary care provider. In general, a person who does not respond to these standard treatments should be seen by a psychiatrist who is more thoroughly trained in the diagnosis and treatment of mental illnesses. Psychiatrists can also be helpful in assessing the role that medical illnesses may be playing in the life of a person with TRD and can work together with other health care providers to comprehensively treat the person as a whole.

People with severe depression will likely also benefit from the combination of psychotherapy and psychiatric medications. Many scientific studies have shown that the combination of psychotherapy and psychiatric medications is more effective than treatment with either on its own. Of the different forms of psychotherapy, cognitive behavioral therapy (CBT) and dialectical behavioral therapy (DBT) may be specifically helpful in cases of severe and treatment resistant depression. Psychotherapy can also be helpful in determining and addressing the role of substance abuse in a person’s depression.

Many people with TRD will require treatment with additional psychiatric medications. The specifics of each individual case should be discussed with one’s mental health providers and loved ones to help make the most well informed treatment decisions. It should further be noted that the US-FDA has specific guidelines for which drugs and treatments are effective in the care of people with TRD.

Some people with TRD may benefit from treatment with a more potent antidepressant from the tricyclic antidepressant class (TCAs) or the monoamine oxidase inhibitor class (MAOIs). Other people may require the use of an adjunctive medication—which is added on to their regular antidepressant—to adequately treat their depression. For some people (i.e., those with psychotic depression or bipolar depression), treatment with an antipsychotic medication—e.g., aripiprazole (Abilify), olanzapine (Zyprexa), quetiapine (Seroquel)—or a mood-stabilizing medication such as lithium may hold the key to their recovery. Other people might elect for treatment with transcranial magnetic stimulation (TMS) or electroconvulsive therapy (ECT) which remains the most effective treatment for TRD.

Families, friends and others can be most helpful in providing empathic and non-judgmental support of their loved ones. With this support, the proper medications and effective psychosocial treatments, many people with TRD disorder will be able to actively participate in their recovery journey.

Reviewed by Ken Duckworth, M.D., and Jacob L. Freedman, M.D., May 2013