RECOVER
A VNS Therapy® Clinical Trial

VNS Therapy®

Answers to Frequently Asked Questions

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DEPRESSION

What is treatment-resistant depression?

Treatment-resistant depression (TRD) is sometimes referred to as difficult-to-treat depression (DTD).[1] This means that someone with depression has tried several treatments without success.

How many adults have treatment-resistant depression?

You are not alone. More than 2.7 million American adults suffer from the burden of treatment-resistant depression (TRD).[2,3]

VNS Therapy®

What is VNS Therapy?

VNS Therapy is not a drug; it uses the natural pathways in your body. VNS Therapy is a device that works by stimulating the vagus nerve. The vagus nerve is connected to areas of the brain associated with controlling mood.[4]

How does VNS Therapy work?

VNS Therapy is a device that stimulates the vagus nerve in your neck, which is connected to areas of the brain associated with controlling mood. VNS Therapy works by regularly sending mild pulses to the vagus nerve in the neck, which has been shown to improve depression symptoms.[4]

How many people have had VNS Therapy?

VNS Therapy is a proven technology with more than 25 years of patient experience and over 100,000 patients implanted worldwide across multiple health conditions.[5]

How effective is VNS Therapy in people with depression?

Nearly 7 in 10 people significantly improved and more than 4 in 10 people fully or almost fully recovered.[6] Results with VNS Therapy get stronger over time. In a 5-year study of 795 patients with depression that is difficult-to-treat, results were superior with VNS Therapy + traditional treatment compared with traditional treatment alone.*

Will VNS Therapy work for me?

When the device was tested in the clinical trials, depressive symptoms decreased for most patients. Some patients had no change in depressive symptoms, and some got worse while receiving VNS Therapy. Among those patients who did improve while receiving VNS Therapy, some did not improve until they had been receiving VNS Therapy for 6 months or longer.[6]

Your doctor or psychiatrist will help you determine whether VNS Therapy is right for you.*

* Individual results may vary

Is VNS Therapy® FDA-approved?

VNS Therapy has been FDA-approved for the treatment of depression since 2005.[7]

Will I still need to take medication with VNS Therapy?

Yes. VNS Therapy is an add-on treatment. Most patients treated with VNS Therapy in past clinical studies also continued to take antidepressant medications.[7]

Does VNS Therapy involve surgery?

VNS Therapy begins with a one-time outpatient procedure that takes approximately 1-2 hours. The procedure is typically done under general anesthesia, and most people go home the same day.[7]

RECOVER
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What is the RECOVER study?

The RECOVER study is for people who have depression or bipolar depression that has been difficult-to-treat. The study was designed in partnership with many of the nation's top experts in treatment-resistant depression and approved by Medicare, in order to provide additional evidence of the benefit of VNS Therapy®.

If I am interested in participating in the RECOVER study, what are my next steps?

If you appear to be eligible for the RECOVER study, you will be referred to a study site near you. The site staff will contact you within a few days to talk with you about your history of depression, and they may ask you to attend an appointment to learn more about the study and to help determine if the RECOVER study is right for you.

Does everyone in the study get VNS Therapy?

Although everyone joining the study will have VNS Therapy implanted, the device will be turned on in only half the participants (Group A) during the first 12 months of the study. The other half (Group B) will have their device turned on after 12 months of participation. All participants in the study will receive active VNS Therapy for the remaining four years of the study.

Could I qualify for the RECOVER study even after electroconvulsive therapy (ECT)?

Yes. Having ECT does not disqualify you from the study. If you are 18 years of age or older, are experiencing a major depressive episode, and have not had an adequate response to four or more adequate antidepressant treatments, you may be eligible for the RECOVER study. Having had ECT does not disqualify you from the study. The study doctor will help you determine if the RECOVER study is right for you.

I'm bipolar. Do I qualify for the RECOVER study?

Having bipolar disorder does not disqualify you from the study. The study doctor will help you determine if the RECOVER study is right for you.

What are the benefits and things to consider with participation in the RECOVER study?

BENEFITS	THINGS TO CONSIDER
• By joining the RECOVER study, you have a chance of benefiting from an FDA-approved treatment for your depression that is not generally available unless you pay for it yourself. • By joining the study, there is a possibility that your depressive symptoms will improve or even resolve. You may also experience an improved quality of life. • Once your VNS Therapy® device is activated, you will receive a continuous antidepressant therapy that's always with you. • By taking part in the study, you might also be helping other people like you to access this treatment in the future. • If you are in Group A of the study, your VNS device will be turned on from the start. After 12 months, patients in both groups will have their VNS device turned on for the remaining four years of the study. • Being in a research study may mean you will get more healthcare attention than you would get outside of a study. For some people, this increased attention can be beneficial.[8] • Whichever group you are in, you can continue to use your usual medication or therapies.	• Whichever group you are in, you'll need a short outpatient surgical procedure to place the device.[7] • There is a 50/50 chance you will be in Group B. This means that, although you will receive a VNS device, treatment may be delayed for the first 12 months of the study. • The surgical procedure and stimulation from the device may sometimes cause side effects (unwanted changes in your health). Side effects are a risk with all medical treatments.[7] The most common side effects from stimulation include voice changes (hoarseness), prickling or tingling in the skin, sore throat, and breathlessness. These tend to improve over time. The most commonly reported side effect from the implant procedure is infection (1.6%).[9] The study team will discuss the possible side effects with you but won't be able to predict what side effects you may get and how troublesome these may be.

PROCEDURE

What is the VNS Therapy® implantation procedure like?

Implanting the device is done in a short outpatient procedure that takes approximately 1 to 2 hours. The procedure is typically done under general anesthesia, which means you will be put to sleep for a short while.[7]

During the procedure, a small device is implanted underneath the skin just below the collarbone and a thin wire (the lead) connects the device to the vagus nerve in the neck. No part of the device is connected to your brain itself.[7]

There can sometimes be side effects related to the procedure such as headache, nausea, and soreness or skin reactions in the area where the device was implanted and at the incision sites.

The most commonly reported side effect from the implantation procedure is infection (1.6%).[9] Your surgeon and medical team will give you more information about the procedure and how to prepare for it.

Where under the skin is the device implanted?

The generator is placed under the skin of the upper chest. The lead is attached to the vagus nerve on the left side of the neck and runs under the skin to connect to the generator.[7]

Does the lead (wire) go into the brain?

No. The lead (wire) does not go into the brain. The lead is attached to the vagus nerve on the left side of the neck. The vagus nerve is connected to areas of the brain associated with controlling mood.[7]

Are there risks linked with the surgery?

Any surgery has some type of risk. There can sometimes be side effects related to the VNS Therapy® procedure such as headache, nausea, and soreness, or skin reactions in the area where the device was implanted and at the incision sites.[7]

Complete healing can take a month or more, and you may experience some numbness or tingling during the healing process. The most commonly reported side effect from the implantation procedure is infection, which occurs in 1.6% of cases.[9]

It is important that you discuss this question with your surgeon or the RECOVER study team.

Will my psychiatrist perform the procedure?

No. A surgeon who has been trained to perform VNS Therapy implants will perform the procedure. The procedure is usually performed in an outpatient setting.[7]

What if I want the device removed?

Even if you join the study, you are free to leave at any time without giving a reason. If you leave the study, you can choose to have your device removed (explanted).

If you ever feel you need to stop the stimulation from the device—either because it is causing uncomfortable side effects, seems not to be working properly, or you want to ensure your voice will be unaffected by it for a particular period of time—please contact your study doctor.

If you and your psychiatrist or the study doctor make the decision to remove VNS Therapy, the device can be removed during another short outpatient procedure. The risks related to having the device removed are similar to those related to the implant procedure. When a device is removed, the surgeon may leave part of the lead behind. This may pose certain risks.[7]

POST-PROCEDURE

What should I expect after the procedure?

After implantation of the device, you'll need to attend a few clinic visits to have the device turned on and to adjust the device settings.

RECOVER study participants:

The study has two groups. Although everyone joining the study will have VNS Therapy® implanted, the device will be turned on in only half the participants (Group A) during the first 12 months of the study. The other half (Group B) will have their device turned on after 12 months of participation.

There is an equal chance of being in Group A or Group B, and neither you nor your doctor will know which group you are in. Your group will be chosen by random, like flipping a coin. The reason for having Group B is to allow the research team to directly compare Group A results with Group B results.

Even if you are in Group B—which means your device won't actually be turned on for the first 12 months—you will still need to attend these visits, because it's important that neither you nor your doctor knows which group you are in.

Does the device start to work immediately?

The effect of VNS Therapy is not immediate, but over the course of weeks and months, you may notice a significant improvement of your symptoms. Based on past clinical studies, results with VNS Therapy get stronger over time. In addition, studies have shown that people who benefit from VNS Therapy tend to go on benefiting.[6,7]

Will I have a noticeable scar?

Each person has different healing and scarring results. You should expect some scarring from surgery. Most people do not think the scarring after surgery is a major concern. If this is a special concern for you, please discuss it with your surgeon.

Will people be able to see the implanted device through my skin?

The lead is attached to the vagus nerve and not visible. The generator is shaped like a disk and is up to approximately 2 inches (5 cm) in diameter, depending on the model. If you have a small frame or are very thin, the device may be visible below your left collarbone.[7] Please talk to your surgeon if you have concerns.

Will electronic equipment interfere with VNS Therapy®?

Electric and electronic equipment generally will not affect the pulse generator.

Will I be able to go through airport security?

At the airport, we recommend that you provide TSA personnel with your VNS Therapy ID card, which explains you have an implanted medical device. You can choose to request a pat-down check instead.

SAFETY

What are the side effects of VNS Therapy®?

The most commonly reported side effects from stimulation include hoarseness or changes in voice, prickling or tingling in the skin, sore throat, and shortness of breath.[7] These side effects generally only occur during stimulation, are well tolerated, and are less noticeable over time. The most commonly reported side effect from the implant procedure is infection (1.6%).[9]

Is the hoarseness permanent?

In general, most side effects become less noticeable over time. Side effects, including hoarseness, generally only occur during stimulation and are less noticeable over time.[7] The safety and efficacy of VNS Therapy have not been shown for people with a history of preexisting hoarseness. As with all types of treatment for depression, VNS Therapy carries some risks. Please talk to your psychiatrist if you experience hoarseness.

What is the infection rate?

All procedures carry some risk of infection. The most commonly reported side effect from the implantation procedure is infection, which occurs in 1.6% of cases.[9]

Can I have VNS Therapy if I have asthma?

Shortness of breath may occur with active VNS Therapy, especially if you have chronic obstructive pulmonary disease (COPD) or asthma.[7] The safety and efficacy of VNS Therapy have not been shown for people with a history of lung diseases or disorders, including shortness of breath and asthma. As with all types of treatment for depression, VNS Therapy carries some risks. Please talk to your psychiatrist if you experience shortness of breath. Your doctor or psychiatrist or the study doctor will help you to determine if VNS Therapy and the RECOVER study are right for you.

Can I have VNS Therapy if I have anxiety?

Yes. If you have difficult-to-treat depression or bipolar depression along with generalized anxiety disorder you could be a candidate for VNS Therapy.[6]

Can I have VNS Therapy® if I have heart problems?

The safety and efficacy of VNS Therapy have not been shown for people with irregular heartbeats (heart arrhythmias) or other heart abnormalities.[7] As with all types of treatment for depression, VNS Therapy carries some risks. Your doctor or psychiatrist or the study doctor will help you to determine if VNS Therapy and the RECOVER study are right for you.

Does the device get in the way if I have a pacemaker?

The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers. Please talk to your surgeon if you have concerns.

Is it safe for me to get an MRI with the VNS Therapy System?

If you have a VNS Therapy System implanted, you can have certain types of MRI scans but not others. In many cases, an MRI can be performed safely under certain conditions. However, for a few other cases, surgery may be required to remove the VNS Therapy System prior to an MRI.[7]

Call your study doctor if you have questions about having an MRI scan before you have any MRI performed.

MAGNET

What does the magnet do?

You will be given two special magnets (one is a spare) after your implantation procedure. The magnet is used to stop stimulation (the pulses from the device) when it is placed over the generator, and it stops the pulses for as long as the magnet is there.

When should I use the magnet?

Use the magnet to stop stimulation temporarily or to turn OFF the generator when you plan to sing or speak in public (if stimulation bothers you when you do this), when you are eating (if you have swallowing problems), or if stimulation becomes uncomfortable. If you need to use the magnet for any other reason, inform your psychiatrist. If you do ever use the magnet, it's important to let the study team know so that a visit can be arranged to check the device settings.

Is it possible to stop all stimulation using the magnet?

Yes. To stop stimulation, hold the magnet over the generator and keep it there. If you stopped stimulation because it felt unusual or painful, call your psychiatrist right away. The magnet will stop all stimulation while it is in place. The stimulation cycle begins again when the magnet is removed. You may need to secure the magnet by taping it to your chest over the implanted device.

Can any magnet be used?

Only the VNS Therapy® magnet should be used with your VNS Therapy system. If you lose your magnet or need extra magnets, contact your doctor. In an emergency, you may try other strong magnets. The use of other magnets will not harm the VNS Therapy System, but there is no way to know in advance whether a magnet other than the VNS Therapy magnet will work.

Who should carry the magnet?

You should carry the magnet with you at all times. You may also want your family members or caregivers to carry a VNS Therapy magnet.

BATTERY

How long does the battery last?

The battery in the generator can last from 1 to 16 years. The device settings impact how long the battery will last. For example, the battery may last for 3 years at a higher setting, compared with 8 years at a lower setting.[7] Talk to the study team if you have any questions about VNS Therapy® battery life.

Do I have to have surgery again to have the battery replaced?

When the battery in your generator runs out, the generator must be replaced in order for you to continue to receive VNS Therapy. This requires an additional surgical procedure. The operation involves anesthesia and generally takes less than an hour to complete. The risks related to having the device replaced are similar to those related to the implant procedure.[7] Replacement or removal of the lead is not required for routine replacement of the generator.

Can the battery be recharged without having surgery?

At this time, the battery cannot be recharged. When the battery in your generator runs out, the generator must be replaced in order for you to continue to receive VNS Therapy. This requires an additional surgical procedure. The procedure requires anesthesia and generally takes less than an hour to complete.
The risks related to having the device replaced are similar to those related to the implant procedure.[7]

IMPORTANT SAFETY INFORMATION

VNS THERAPY FOR DEPRESSION INDICATIONS FOR USE (US)
The VNS Therapy System is indicated for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments.

CONTRAINDICATIONS
The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy. Do not use shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with the VNS Therapy System.

WARNINGS
All potential risks and adverse events are discussed in the VNS Therapy System physician's manuals. VNS Therapy may not be a cure for depression. Individual results will likely vary. Beneficial results might not become evident for months. Most patients will continue to require antidepressant medications and/or electroconvulsive therapy (ECT) in addition to VNS Therapy. Patients being treated with adjunctive VNS Therapy should be observed closely for clinical worsening and suicidality, especially at the time of VNS Therapy stimulation parameter changes or drug dose changes. Patients who have pre-existing swallowing, cardiac, or respiratory difficulties (including, but not limited to, obstructive sleep apnea and chronic pulmonary disease) should discuss with their physicians whether VNS Therapy is appropriate for them, since there is the possibility that stimulation might worsen their condition. Patients with the VNS Therapy System implanted should have MRI procedures performed only as described in the MRI Chapter of the Physician Manual.

ADVERSE EVENTS
The most commonly reported side effects from stimulation include hoarseness (voice alteration), paresthesia (prickling feeling in the skin), dyspnea (shortness of breath), sore throat and increased coughing. Other adverse events reported during clinical studies as statistically significant are ataxia (loss of the ability to coordinate muscular movement); dyspepsia (indigestion); hypesthesia (impaired sense of touch); insomnia (inability to sleep); laryngismus (throat, larynx spasms); nausea; pain; pharyngitis (inflammation of the pharynx, throat); and vomiting. These typically occur only during stimulation, and are well tolerated and noticed less as time goes on. The most commonly reported side effect from the implant procedure is infection.

*THE INFORMATION CONTAINED IN THIS SUMMARY REPRESENTS PARTIAL EXCERPTS OF IMPORTANT PRESCRIBING INFORMATION TAKEN FROM THE PRODUCT LABELING. THE INFORMATION IS NOT INTENDED TO SERVE AS A SUBSTITUTE FOR A COMPLETE AND THOROUGH UNDERSTANDING OF THE VNS THERAPY SYSTEM NOR DOES THIS INFORMATION REPRESENT FULL DISCLOSURE OF ALL PERTINENT INFORMATION CONCERNING THE USE OF THIS PRODUCT. PATIENTS SHOULD DISCUSS THE RISKS AND BENEFITS OF VNS THERAPY WITH THEIR HEALTHCARE PROVIDER. PRESCRIPTION ONLY - DEVICE RESTRICTED TO USE BY OR ON THE ORDER OF A PHYSICIAN.

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