

Unique treatment for chronic or recurrent depression

**A clear advance
to help you reconnect**





*Karmen, diagnosed with depression in 1989,
VNS Therapy™ since 1999*

Time to consider a unique approach to treatment?

If you have tried different medications but still not had the long-term results you want, don't get discouraged. There are other options.

Many people experiencing **chronic** or **recurrent treatment-resistant** depression do not get the results they want even after trying several different medications.

- **Chronic depression:** continuous depression lasting 2 years or more
- **Recurrent depression:** 2 or more episodes of depression over time
- **Treatment-Resistant depression:** occurs when 4 or more adequate antidepressant treatments have not provided desired improvement

Don't give up hope! A unique approach to treating chronic or recurrent treatment-resistant depression is now available.

Reference: American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry*. April 2000;157(suppl):1-45.

Effective long-term treatment can give lasting improvement to your quality of life

Many people with chronic or recurrent treatment-resistant depression experience compromised quality of life due to:

- Treatments not adequately reducing symptoms of depression
- Undesirable side effects of treatments
- Treatments that work initially, but then seem to stop working

Fortunately, there is a unique treatment approach—called VNS Therapy™—that is helping many people experience a renewed quality of life.



Karmen, VNS Therapy since 1999,
with daughter Claire, born 2003

When other treatments have not worked or have stopped working, adding VNS Therapy may be your next step

VNS Therapy has been shown to provide:

- Effectiveness that improves over time and lasts long term
- Significant and lasting improvement in vitality, social functioning, emotional well-being, and mental health
- Side effects that are mild to moderate and typically decrease over time
- A unique safety profile

VNS Therapy has been studied since 1988 and has been used in clinical studies since 1998 for the treatment of depression



Reference: Rush AJ, Sackeim HA, Marangell LB, et al. Effects of 12 months of vagus nerve stimulation in treatment-resistant depression: a naturalistic study. *Biol Psychiatry*. 2005;58:355-363
Depression Physician's Manual. VNS Therapy™ Pulse Model 102 Generator and VNS Therapy™ Pulse Duo Model 102R Generator. Houston, Tex: Cyberonics Inc.; 2005.

VNS Therapy™ provides improvements in mood that last long term

- Adding VNS Therapy has been shown to succeed where other treatments have not
- Clinical studies confirm that the effectiveness of VNS Therapy improves over time and is sustained long term
 - About 6 out of 10 people experienced a meaningful clinical benefit from VNS Therapy
 - After one year, 1 in 3 people receiving VNS Therapy experienced significant mood improvements and 1 in 6 had few or no remaining symptoms of depression
 - People who receive VNS Therapy in addition to other treatments are 2 - 4 times more likely to show mood improvements than those on other treatments alone.
- Some people experienced mood improvements within the first few weeks; for others, the benefits developed gradually over time
- Many people who did not respond immediately to VNS Therapy did experience improvement over time
- Most people who responded to VNS Therapy maintained improvement long term
- For some people, VNS Therapy reduces the need for antidepressant medications over time



Improving your quality of life—every day

In addition to experiencing improvements in mood, many people receiving VNS Therapy™ and their psychiatrists also report significant and lasting improvements in:

- Vitality - increased energy
- Social functioning - increased interaction with family and/or friends
- Emotional well-being - better function at work and in daily activities
- Mental health - more positive feelings



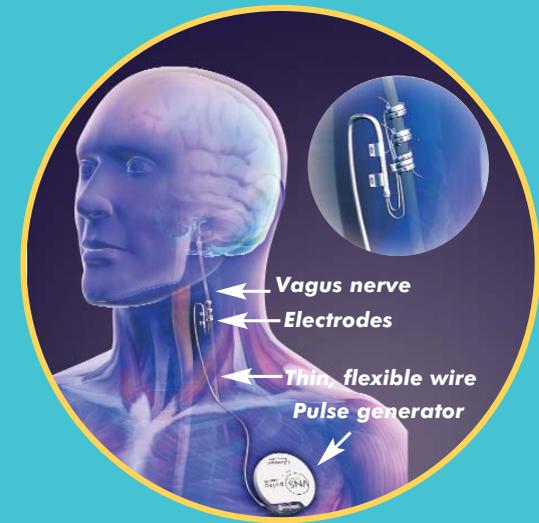
“I am very optimistic about my future, and my life is just starting in many ways.”

Lauri, VNS Therapy since 1999

Reference: Depression Physician’s Manual. VNS Therapy™ Pulse Model 102 Generator and VNS Therapy™ Pulse Duo Model 102R Generator. Houston, Tex: Cyberonics, Inc.; 2005.

How VNS Therapy™ works

- VNS stands for vagus nerve stimulation
- The vagus nerve is one of the primary communication pathways from the major organs of the body to the brain
- VNS Therapy is delivered by a pulse generator and a thin, flexible wire that send mild pulses to the left vagus nerve
- The vagus nerve delivers these pulses to the areas of the brain that are involved in the regulation of mood
- VNS Therapy is typically painless, because the vagus nerve does not contain pain fibers
- VNS Therapy stimulation is regular, automatic, and typically unnoticeable
- VNS Therapy is added to your current antidepressant medications

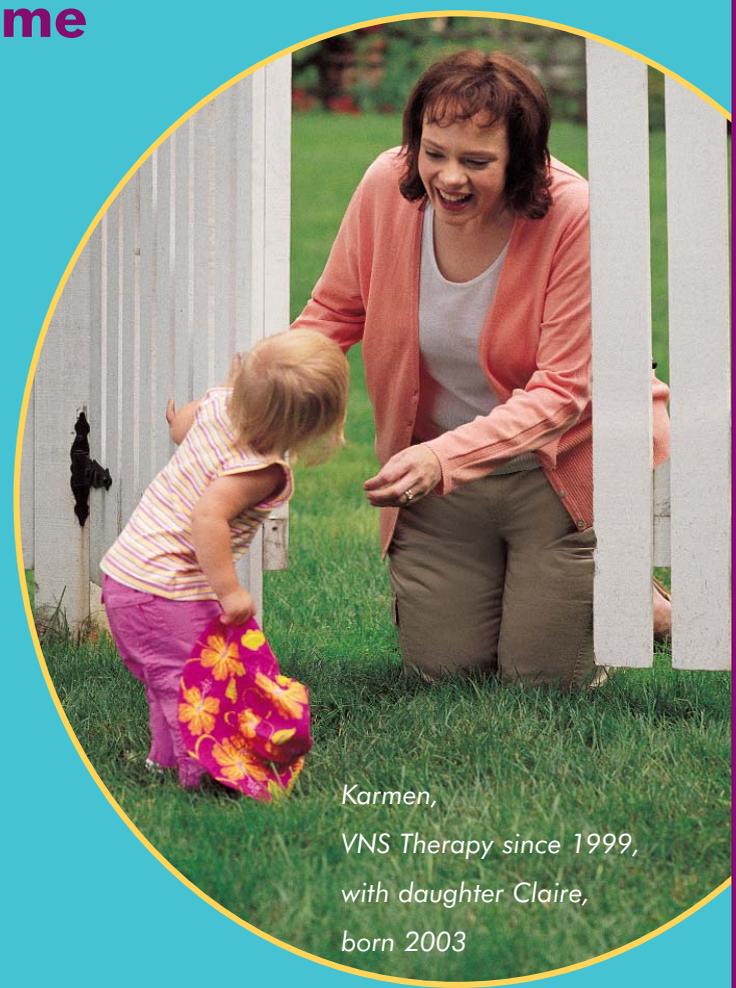


Side effects of VNS Therapy™ are mild to moderate and typically decrease over time

Side effects:

- Typically occur only during stimulation and may include:
 - Temporary hoarseness/changes in voice tone
 - Cough
 - Tickling in the throat
 - Feeling of shortness of breath during exertion
- Can be minimized through dose adjustments
- Typically decrease over time

VNS Therapy works with your other treatments without undesired interactions. VNS Therapy is not associated with sexual dysfunction or memory impairment, common side effects of other antidepressant treatments. The incidence of weight gain and sleep disturbance (also commonly reported side effects of other antidepressant treatments) is less than 2%.



*Karmen,
VNS Therapy since 1999,
with daughter Claire,
born 2003*

References: Depression Physician's Manual. VNS Therapy™ Pulse Model 102 Generator and VNS Therapy™ Pulse Duo Model 102R Generator. Houston, Tex: Cyberonics, Inc.; 2005. Data on file. Cyberonics, Inc.; Houston, Tex.

If necessary, you can control VNS Therapy™ side effects

The VNS Therapy System includes a small magnet. This may be useful if you experience any side effects that need to be temporarily controlled.

You can hold or place the magnet over your VNS Therapy pulse generator to temporarily stop stimulation during certain situations or activities when even mild side effects are troublesome, for example:

- Public speaking
- Singing
- Exercising or other strenuous activity

If you experience troublesome side effects for an extended period of time, contact your psychiatrist.



*Karmen,
VNS Therapy since 1999*

VNS Therapy™ — adjusting the dose

- Your psychiatrist adjusts the VNS Therapy pulse generator to deliver the appropriate stimulation for you, and can easily provide dose adjustments if the need arises
- VNS Therapy stimulation typically lasts for 30 seconds every 5 minutes
- Once the dose is adjusted, stimulation is regular, automatic, and typically unnoticeable
- You do not have to worry about undesired interactions with other treatments
- The dose 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*



Lauri, VNS Therapy since 1999

*For the full range of settings in relationship to battery life, see physician's Manual or ask your psychiatrist

The VNS Therapy™ procedure is straightforward

- Actual implant procedure takes about 1 hour
- Usually performed under general anesthesia and is an outpatient procedure
- Two small incisions are made—one in a natural crease on the left side of the neck and one in the left chest area, below the collarbone
- The pulse generator is placed just under the skin in the left chest area. A thin, flexible wire connects the pulse generator to the left vagus nerve in the neck
- The two incisions heal in about a week
- The small scars typically fade over time and become minimally noticeable for many people



Connections™: the VNS Therapy™ patient program

Resources to help you through your decision-making process

- A wide range of educational activities and resources
- Newsletters and brochures that provide specific information to help you at each step of the decision-making process
- VNS Therapy nurse case managers can help you with medical insurance coverage
- Participate in VNS Therapy Phone Facts Sessions in which you can talk with people receiving VNS Therapy
- Enroll in the Connections program now!



VNS Therapy™ is a unique approach specifically for chronic or recurrent treatment-resistant depression

- Effectiveness that improves over time and lasts long term
- Significant and lasting improvement in vitality, social functioning, emotional well-being, and mental health
- VNS Therapy is not associated with sexual dysfunction or memory impairment, common side effects of other antidepressant treatments.² Incidence of weight gain and sleep disturbance (also commonly reported side effects of other antidepressant treatments) is less than 2%
- VNS Therapy procedure is straightforward
- Adding VNS Therapy may succeed where other treatments have not, and VNS Therapy does not interact with other antidepressant treatments
- For some people, VNS Therapy may reduce the need for antidepressant medications over time
- If you think it's time to review your treatment options, talk with your doctor about VNS Therapy

SAFETY INFORMATION FOR THE VNS THERAPY SYSTEM*

INTENDED USE/INDICATIONS - UNITED STATES

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 short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with the VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

WARNINGS

This device is a permanent implant. It is only to be used in patients with severe depression who are unresponsive to standard psychiatric management. It should only be prescribed and monitored by physicians who have specific training and expertise in the management of treatment-resistant depression and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System Physician's Manual, including information that VNS Therapy has not been determined to be a cure for depression. 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 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 or any part of the VNS Therapy System implanted should not have full body MRI.

ADVERSE EVENTS

The most commonly reported (≥10%) side effects from stimulation included hoarseness, increased cough, neck pain, dyspnea (shortness of breath), dysphagia (difficulty swallowing), paresthesia (prickling feeling in the skin), and laryngismus (sore throat). The most commonly reported (≥10%) side effects from the implant procedure included incision pain, hoarseness, incision site reaction, device site pain, device site reaction, pharyngitis (sore throat), dysphagia, and hypesthesia (numbness).

*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. (CAUTION: U.S. FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.)



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