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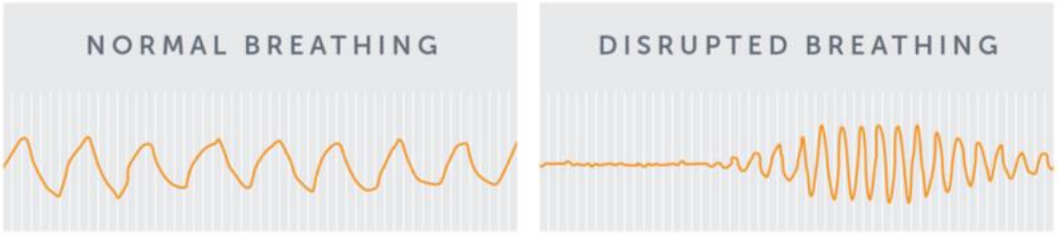
Central Sleep Apnea and Heart Failure Fact Sheet

WHAT IS SLEEP DISORDERED BREATHING? [1,2]

Sleep is a time for body and mind to rest and recuperate, an indispensable time for maintaining or improving health. Many patients with chronic health problems rarely get sufficient, quality, or restful sleep. Sleep Disordered Breathing (SDB), or disrupted breathing is a condition that disturbs the normal breathing pattern during sleep and may have an adverse effect on overall respiratory and cardiovascular health.



WHAT IS CENTRAL SLEEP APNEA? [1,2]

Central Sleep Apnea (CSA) is a serious type of sleep-disordered breathing and occurs when the brain does not send the correct signals to the breathing muscles (the diaphragm). When the diaphragm does not move properly, the lungs do not have a consistent rhythm and breathing becomes irregular. Sleep disordered breathing can be deep and rapid, slow and shallow, or breathing may stop momentarily before restarting.

CSA can lead to excessive daytime sleepiness, fatigue, hypoxia (decrease in blood oxygen level), and irregular or very fast heart rhythms (arrhythmia)[1]. Studies have shown that untreated CSA is a significant contributor to lowered quality of life and contributes to poor cardiovascular outcomes.[1] CSA frequently occurs among people who have other chronic diseases such as chronic heart failure and/or atrial fibrillation.[1]

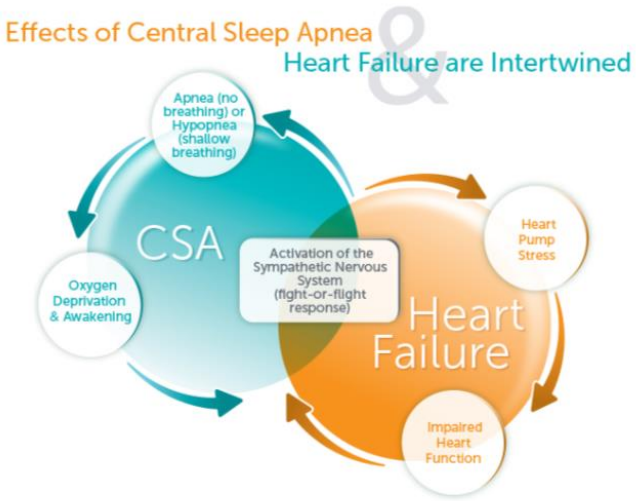
An existing therapy used for CSA, continuous positive airway pressure (CPAP), is a device that delivers positive pressure through a mask worn by the patient while sleeping. This therapy can be effective but is often not well tolerated by patients and can have significant limitations that may negatively impact cardiovascular health. Some patients find it difficult to adhere to this therapy over time.[1] All treatment options should be discussed with a physician to better understand the risks and benefits of each type of

therapy.

CSA and Heart Failure [1,2]

According to the Heart Failure Society of America, heart failure affects over 6.5 million people in the U.S. and over 26 million worldwide.[3,4] Heart failure occurs when the heart is unable to pump enough blood to meet the body's demands, usually due to the heart's inability to contract or relax properly.

CSA is common in cardiac patients, primarily those with heart failure.[1] CSA causes a repeating cycle of disruptive breathing, nighttime wakefulness and increased activation of the body's sympathetic nervous system ("fight or flight response") that contribute to heart failure.[1]



Quick Facts:

- Heart Failure affects nearly 6.5 million people in the United States and over 26 million worldwide [3,4]
- Central Sleep Apnea (CSA) occurs in approximately 1 in 3 HF patients and has shown to be an independent predictor of mortality for this patient population [5,6]
- CSA leads to decreased oxygen and increased sympathetic drive which is associated with worsening HF and death [7]
- 1 in 3 patients hospitalized for heart failure have CSA and 50% are readmitted to the hospital at 6 months [8]
- People with HF or heart rhythm disorders such as atrial fibrillation are at an increased risk of CSA [7]
- ~ 30% of atrial fibrillation patients have CSA [9]

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PROVEN CSA TREATMENT

The **rem**edē® System is an implantable therapy that monitors and stabilizes the breathing pattern to restore sleep throughout the night. The **rem**edē® System stimulates a nerve in the chest (phrenic nerve) that sends signals to the large muscle that controls breathing (the diaphragm). These signals stimulate breathing in the same way that the brain signals breathing. It has been shown to improve sleep, breathing and quality of life for adult patients with moderate to severe CSA.[10]

Quick Facts

In a clinical study, the **rem**edē® System has been shown to significantly reduce the effects of CSA

- 88% of patients had a reduction in the number of sleep apnea events[10]
- 78% of patients had an improvement in quality of life[10]
- 95% of patients reported they would "elect to have the medical procedure again"[10]
- Patients treated with **rem**edē® System demonstrated clinically significant reduction in daytime sleepiness[10]

*The **rem**edē System received U.S. Food and Drug Administration (FDA) approval in October of 2017.*

PIVOTAL TRIAL DATA SUPPORTS SAFETY, EFFECTIVENESS, AND QUALITY OF LIFE IMPROVEMENTS WITH THE remedē® SYSTEM

The **rem**edē® System Pivotal Trial was a prospective, multi-center, randomized (1:1) controlled trial that enrolled patients with moderate to severe CSA based on polysomnographs (in-lab sleep study) scored by a blinded core laboratory. The results of the Pivotal Trial demonstrate the **rem**edē® System therapy was safe and effective with all primary and hierarchically tested secondary endpoints met.[11] Treatment effectiveness and quality of life improvements were sustained at 12 months.[10]

Long term follow-up data out to five years was published in 2021, continuing to show the effectiveness and safety of the therapy.[12]

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Important Safety Information

The **rem**edē® system is indicated for moderate to severe Central Sleep Apnea in adult patients.

Your doctor will need to evaluate your condition to determine if the **rem**edē system is right for you. The **rem**edē system is MR Conditional but conditions apply. Please make sure that your physician knows about the conditions and precautions to ensure safety, which can be found in the **rem**edē system MRI guidelines manual. You should not have the **rem**edē System implanted if you have an infection and you will not be able to have diathermy (special heat therapies) after implantation. The **rem**edē System may be used if you have another stimulation device such as a heart pacemaker or defibrillator; special testing will be needed to ensure the devices are not interacting.

As with any surgically implanted device, there are risks related to the surgical procedure itself which may include, but are not limited to, pain, swelling, and infection.

Once the therapy is turned on, some patients may experience discomfort from stimulation and/or from the presence of the device. The majority of these events are resolved either on their own or by adjusting the therapy settings. The **rem**edē system may not work for everyone. There are additional risks associated with removing your system. If you and your doctor decide to remove the system, another surgery will be required.

Be sure to talk with your doctor so that you thoroughly understand all of the risks and benefits associated with the implantation of the **rem**edē System. Rx only. For further information, please visit remede.zoll.com, call +1-952-540-4470 or email info@remede.zoll.com.

The **rem**edē® System, **rem**edē® EL System, and **rem**edē® EL-X System have received FDA approval. The **rem**edē® System model 1001 has received CE Mark approval.

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