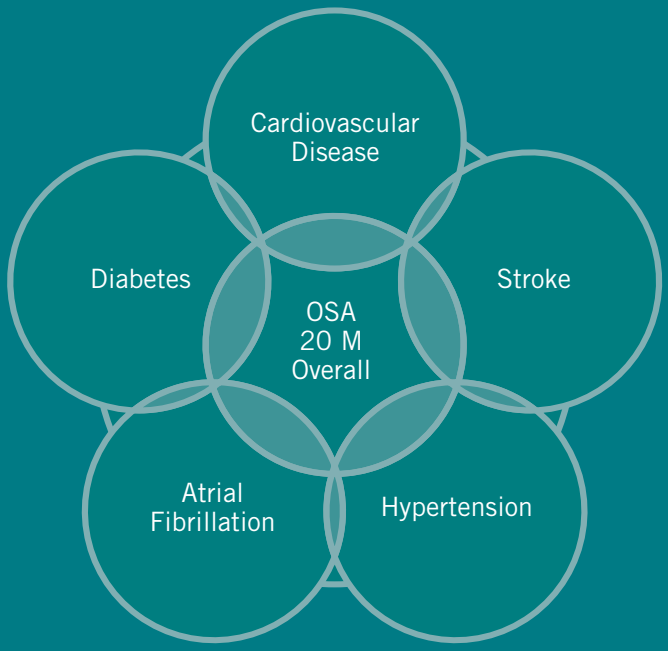
RESPIRONICS®

SLEEP APNEA: THE HEART OF THE MATTER.

Obstructive Sleep Apnea (OSA) is a common breathing disorder that has been associated with an increased risk of **hypertension, heart failure, stroke, atrial fibrillation, diabetes** and other conditions. For these reasons, it is important to properly **identify** and successfully **treat patients** with obstructive sleep apnea.

PREVALENCE OF OSA

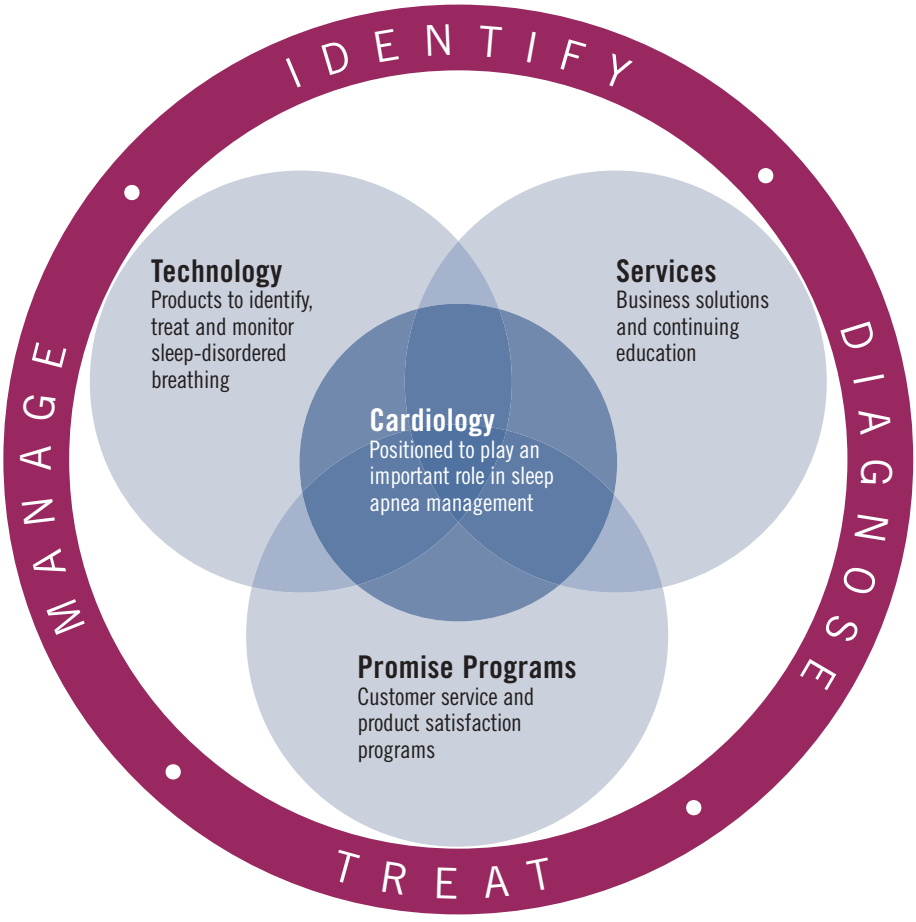
- As many as 5 to 10 percent of adults in the U.S. have OSA, approximating 20 million people.[1, 2]
  - 9 percent of men and 4 percent of women have an AHI >15.
  - 4 percent of middle-aged men and 2 percent of middle-aged women have an AHI >5 and daytime sleepiness.
- Prevalence of OSA is higher in the following ethnic groups[3]:
  - Asian
  - Hispanic Women
  - African-American
- 85 to 90 percent of patients have not been identified.[1]
- 1 in 4 patients is at risk for OSA.[2, 4]



Many of the 20 million people in the U.S. suspected of having OSA may have an increased risk for other serious health conditions.

THE CARDIOLOGIST'S ROLE

A patient with sleep apnea may have an increased risk of developing potentially life-threatening conditions. Early screening and identification of sleep apnea may help to prevent the development of these other conditions. Once your patients have been diagnosed with sleep apnea and have begun therapy for their sleep apnea, close follow-up is important in order to ensure that they are receiving appropriate treatment for their sleep apnea. Effective treatment of sleep apnea not only results in better sleep, but also may decrease the risk of developing other potentially life-threatening conditions.



RESULTS OF EFFECTIVE TREATMENT OF OSA

Cardiovascular Outcomes in Patients Treated for OSA vs. Patients with Untreated OSA

- Patients with untreated OSA were 2.68 times more likely to suffer a non-fatal CV event compared to those whose OSA was effectively treated with CPAP[15]
- Patients with untreated OSA were 2.5 times more likely to suffer a fatal CV event compared to those whose OSA was effectively treated[15]

Treatment of OSA Can Positively Impact Hypertension

- Reduced daytime blood pressure in patients whose OSA is effectively treated[17, 18, 19, 20]
- Effective treatment of OSA resulted in reduced systolic blood pressure in refractory hypertension patients with OSA (avg. BP sys from 138.3mm Hg to 126.0 mm Hg)[21]
- Normalized nocturnal blood pressure pattern (restored dipper status) in a non-dipper OSA population whose OSA was effectively treated[22]

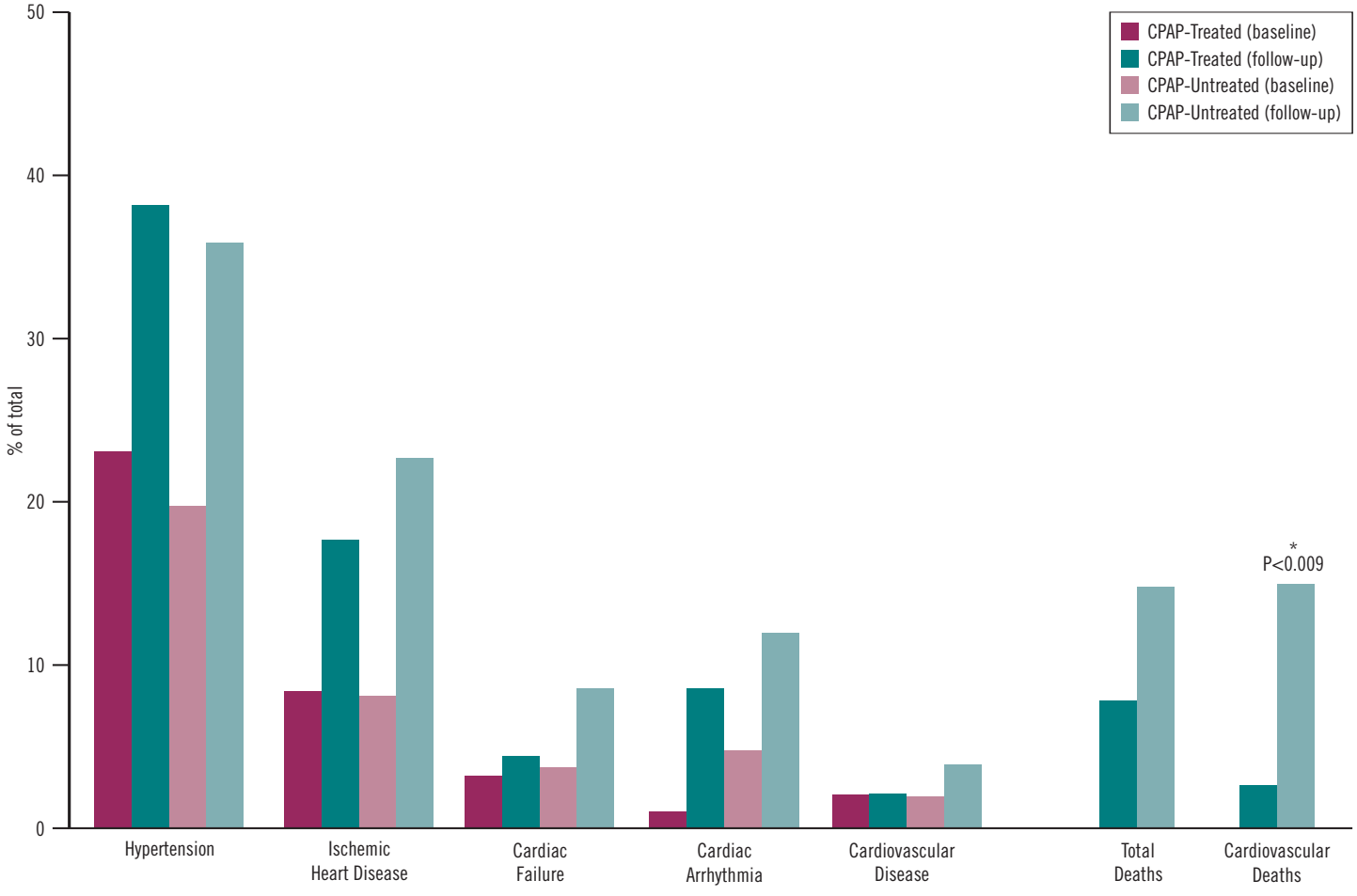
Treatment of OSA Can Positively Impact Heart Failure (HF)

- Effective treatment of OSA resulted in improved Left Ventricular Ejection Fraction percent (from 25% to 34%), Left Ventricular End Systolic Diameter (from 55 mm to 52 mm), and systolic blood pressure (from 126 to 116 mm Hg) in HF patients with OSA[23]
- Significantly improved quality of life for HF patients whose OSA was effectively treated[24]

Treatment of OSA Can Positively Impact Arrhythmias

- Appropriate treatment of OSA was associated with a reduction in atrial fibrillation recurrence after cardioversion[25]
- Untreated OSA is associated with an increased rate of recurrence of atrial fibrillation and severity of nocturnal oxygen desaturation[25]

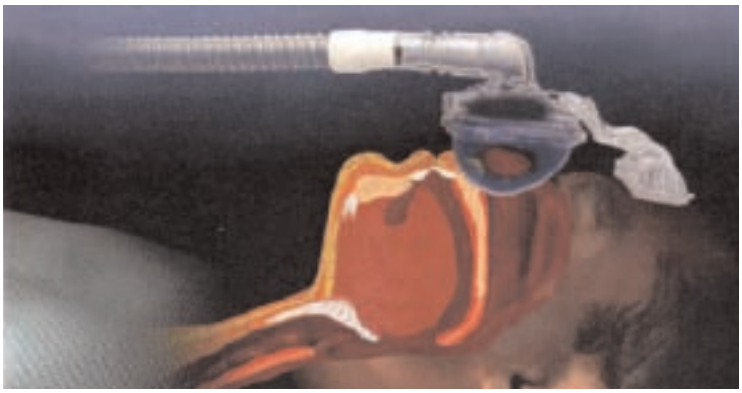
CARDIOVASCULAR OUTCOMES WITH TREATED VS. UNTREATED OSA



[16] Reprinted with permission.

TREATMENT OF OSA WITH CPAP THERAPY

CPAP provides a pneumatic splint to keep the OSA patient's airway open to treat OSA.



Treatment of OSA with positive airway pressure (PAP) therapy improves sleep-related breathing. Adequately treated OSA also has been associated with improved cardiovascular outcomes.

COMORBIDITY – SLEEP APNEA AND CARDIAC DISEASE

Obstructive Sleep Apnea has been independently associated with an increased risk of cardiac arrhythmias, hypertension, heart failure, stroke, Type 2 diabetes, and coronary artery disease. A large percentage of patients with OSA remain undiagnosed.

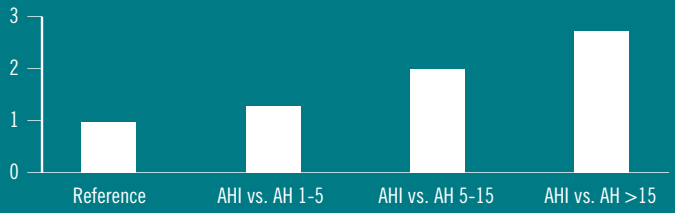
Sleep-disordered breathing (SDB) has been associated with various forms of cardiovascular (CV) disease.

- Individuals with severe SDB are two- to four-times more likely to develop complex arrhythmias than those without SDB.[5]
- Individuals with diagnosed OSA are between two and three times more likely to develop hypertension.[6]
- The prevalence of OSA in patients with heart failure is estimated at 40 to 70 percent.[7, 8]
- Individuals with diagnosed OSA are more likely to suffer a stroke than those without OSA.[9, 10]
- Type 2 diabetes is more prevalent in patients with SDB independent of other risk factors.[11]

Hypertension

- Sleep apnea has been associated with the development of hypertension in a dose response relationship.[6]

Relative Risks for HTN (dx,BP) — Adjusted, P<.002[6]



- NIH/NHLBI JNC7 recognizes OSA as an identifiable cause of hypertension and recommends screening newly identified hypertensive patients or patients who develop refractory hypertension for OSA.[12]

Heart Failure

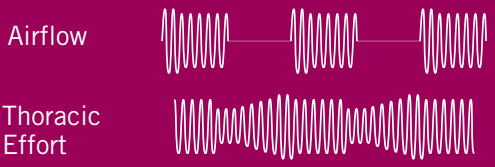
- ACC/AHA Heart Failure Guidelines recognize OSA as a possible cause of heart failure and recommend screening newly identified heart failure patients for OSA.[13]

Arrhythmias

- OSA is associated with a significant risk of atrial fibrillation even after controlling for known confounding parameters.[14]
- 49 percent of patients with atrial fibrillation have OSA while 32 percent of the general cardiology practice have OSA.[14]

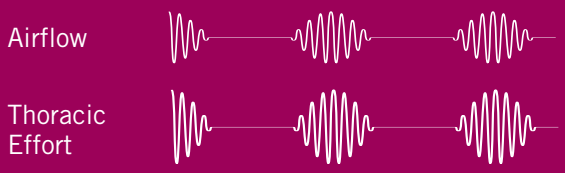
SLEEP APNEA

Obstructive Sleep Apnea (OSA)



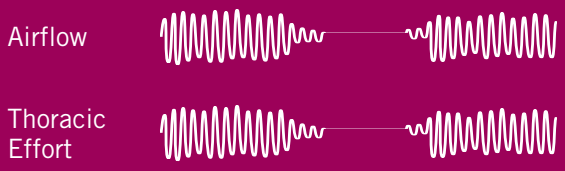
OSA is the absence of airflow due to an occlusion in the upper airway that lasts at least 10 seconds in spite of continual effort to breathe. Severity is measured by the Apnea/Hypopnea Index (AHI) – the number of episodes per hour of sleep.

Periodic Breathing



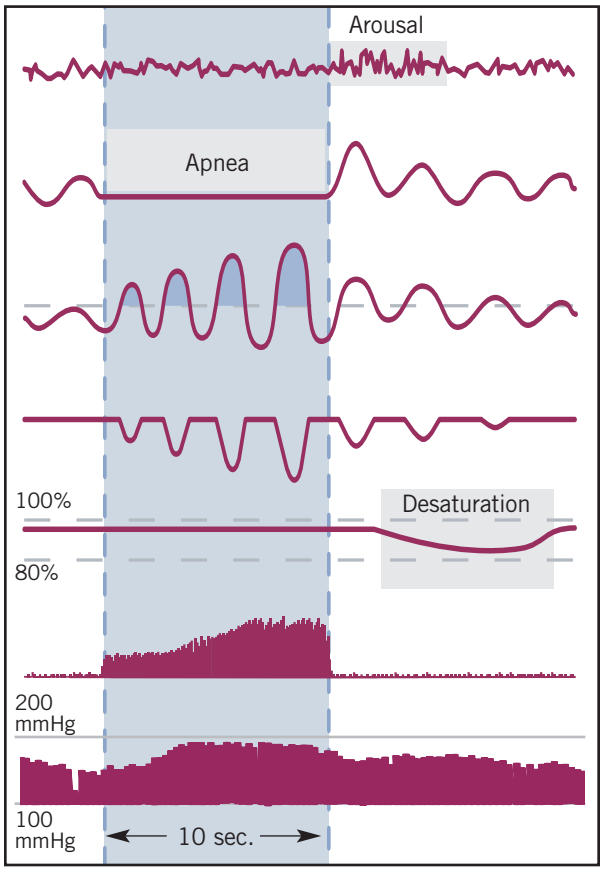
Periodic breathing is defined as alternating periods of hyperventilation with waxing/waning tidal volume and periods of central hypopneas or apneas. There are many forms of periodic breathing, one of which is Cheyne-Stokes Respiration (CSR).

Complex Sleep Apnea



Complex Sleep Apnea is a condition that occurs when a patient is identified as having OSA, but with the application of Continuous Positive Airway Pressure (CPAP) to eliminate the OSA, the patient develops Central Sleep Apnea. The cause of Complex Sleep Apnea is not known at this time.

CONSEQUENCES OF AN APNEA EVENT



EEG — Arousal from Sleep

Airflow

Thoracic Effort — Exaggerated Negative Intrathoracic Pressures

Intrathoracic Pressure

Oxygen Saturation SpO_2 — Hypoxemia/Hypercapnia

Sympathetic Nerve Activity — Sympathetic Activation

Blood Pressure — Hemodynamic Swing

Respironics' goal is to provide the most up-to-date information on clinical research with respect to the relationship between OSA and other disease states. While research has established a comorbidity relationship between OSA and the disease states discussed in the literature below, research is ongoing to identify potential causative relationships between OSA and other disease states.

[1]Young, T., et al., *NEJM* 1993;328:1230-1235
[2]Young, T., et al., *AJRCCM* 2002;165:1217-1239
[3]O'Connor, et al., *Sleep* 2003;26(1):74-79
[4]Hiestand, D.M., et al., *Chest* 2006;130:780-786
[5]Mehra, R., et al., *AJRCCM* 2006;173:910-916
[6]Peppard, P., et al., *NEJM* 2000;342:1378-1384
[7]Javahari, S., *Cur Treat Options in CV Med* 2005;7:295-306
[8]Sin, D., et al., *AJRCCM* 1999;160:1101-1106
[9]Yaggi, H.K., et al., *NEJM* 2005;353:2034-2041
[10]Arzt, M., et al., *AJRCCM* 2005;172:1447-1451
[11]Reichmuth, K.J., et al., *AJCRRCM* 2005;172:1590-1595
[12]Chobanian, A.V., et al., *JAMA* 2003;289:2560-2571
[13]Hunt, S.A., et al., *Circulation* 2005;112:1825-1852
[14]Gami, A.S., et al., *Circulation* 2004;110:364-367
[15]Marin, J.M., et al., *Lancet* 2005;365:1046-1053
[16]Doherty, L.S., et al., *Chest* 2005;127:2076-2084
[17]Hla, K.M., et al., *Chest* 2002;122:1125-1132
[18]Faccenda, J.F., *AJRCCM* 2001;163-344-348
[19]Pepperell, J.C., *Lancet* 2002;359:204-210
[20]Heinrich, F., et al., *Circulation* 2002;107:68-73
[21]Logan, A.G., et al., *Eur Respir J* 2003;21:241-247
[22]Akashiba, et al., *Sleep* 1999;22(7):849-853
[23]Bradley, T.D., et al., *NEJM* 2003;348:1233-1241
[24]Naughton, M.T., et al., *AJRCCM* 2004;169:361-366
[25]Kenaglala, R., et al., *Circulation* 2003;107:2589-2594

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