This report emanates from The Apnea Positive Pressure Long-Term Efficacy Study (APPLES). The APPLES website reports that APPLES is “...a randomized, double-blinded, sham-controlled, multicenter study sponsored by the National Heart, Lung and Blood Institute (NHLBI) to assess the long-term effectiveness of nasal continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea (OSA). This study is critical because sleep disordered breathing is increasingly recognized within the general population, yet the therapeutic effectiveness of the first-line therapy, CPAP, on neurocognitive function, mood, sleepiness, and quality of life has not been tested in a systematic, scientifically valid way.” The study is funded by a $14.1 million dollar grant from the NHLBI. APPLES has already been over a decade in the making and is just now starting to bear fruit (pun intended).

The current report investigates a clinical sample of individuals from the Tucson and Walla Walla APPLES centers, comparing varying levels of sleep disordered breathing with regard to dietary intake and energy expenditure. The investigation reports that those with the highest RDIs ate more cholesterol, protein, and fat, especially in women, and tended to expend fewer calories in recreation. What is new here is that the increased caloric intake in these individuals was primarily in fat and protein rather than carbohydrates. The authors speculate that individuals with higher levels of sleep disordered breathing are more likely to consume a heart-unhealthy diet, and that diet may be a factor contributing to the excess cardiovascular morbidity and mortality in those with severe sleep disordered breathing.

This is an important point, and one that the APPLES trial may be able to address. If those randomized to CPAP have improved or normalized cardiovascular morbidity and mortality (in the absence of diet change), it weakens the argument that diet is a primary culprit. Although APPLES is not specifically designed to address the cardiovascular benefits of CPAP (its primary endpoints are related to neurocognitive function), the data collected in this randomized treatment trial is rare and valuable, and will at least include blood pressure and mortality. We have several observational studies demonstrating that those who use CPAP are less likely to die than those who do not, but the “healthy adherer” effect is a powerful uncontrolled factor in those studies. APPLES does not suffer from this flaw because the subjects are randomized. I hope the APPLES investigators (or somebody!) exploits the data set to address this tantalizing issue about cardiovascular disease, diet, and SDB that they have raised.

Which brings us to the issue of data mining, defined as the extraction of useful, often previously unknown information from large databases or data sets. Sleep Medicine is a relatively new field, and we have so much to learn! The National Center on Sleep Disorders Research, a branch of the Division of Lung Diseases of the National Institutes of Health, maintains a national research plan. Among the research needs identified in the current plan are:

- Investigate and advance our understanding of the genetic, neurobiologic and physiologic mechanisms that are pathophysiologically important in the development, potentiation, and maintenance of SDB. Studies are also needed to access the interaction between cardiac dysfunction and the ventilatory control system in the pathogenesis of Cheyne-Stokes respiration.
- Conduct adequately powered clinical trials, particularly in high-risk populations, to assess the impact of therapy of SDB on functional status, psychiatric disorders, neurocognitive function, and other disease processes (hypertension, cardiovascular disease, metabolic syndromes, etc). Studies assessing the impact of successful therapy of Cheyne-Stokes respiration on cardiac dysfunction, quality of life, and survival are needed as well.
- Design new and improved modalities for the treatment of SDB, including pharmacologic, surgical, oral appliance, behavioral, muscle stimulation, positive airway pressure (including CPAP compliance), and other novel approaches. Methods to
individualize these therapies to the different SDB phenotypes are also needed, for example improved upper airway imaging approaches to define site of collapse.

• Develop novel noninvasive screening / diagnostic methodologies that are less expensive and more widely applicable than standard full polysomnography. This might include biomarkers as indicators of the presence of SDB, of its severity, or of its consequences.

Waiting for studies specifically designed to address these critical issues will leave us in the dark for a very long time. We need to exploit the wealth of data already available to begin to address the many mysteries of sleep. Where to start?

In addition to the large studies that focus specifically on sleep such as APPLES, the Sleep Heart Health Study (SHHS), the CPAP Apnea Trial North American Program (CATNAP), The Wisconsin Sleep Cohort, and the Cleveland Family Study, there is a wealth of data about sleep and sleep disorders in national survey databases such as National Health and Nutrition Examination Survey (NHANES) and the Behavioral Risk Factor Surveillance Study (BRFSS), and as part of ancillary studies in ongoing cohorts such as the Study of Osteoporotic Fractures (SOF) in women and the Osteoporotic Fractures in Men Study (MrOS), and Coronary Artery Disease Risk Development in Young Adults (CARDIA). The NHANES and BRFSS datasets are particularly suited to addresses the “healthy adherer” effect, since they routinely assess healthy activities. The aforementioned studies are merely examples of the potential wealth of data available to the curious, intrepid investigator. In fact, there are dozens of untapped studies world-wide where sleep quality or duration effects have not been fully analyzed and reported against other measures such as cognition, metabolism, and disease. A list of relevant databases, last completed and updated in 2006 by Dr Michael Twery, Director, National Center on Sleep Disorders Research (NCSDR) Branch and Acting Program Director, Sleep and Neurobiology Program Division of Lung Diseases, NHLBI, can be found at: http://www.nhlbi.nih.gov/about/ncsdr/research/sleep-datasets-july-06.pdf.

Dr Twery notes, “Dozens of potential analyses using existing sleep datasets are possible but may not be done for years (if ever).” Sleep and circadian researchers are urged to contact their NIH program office or Dr Michael Twery (Twery@nih.gov) at the NCSDR to discuss their plans for applications and mining existing datasets. We have a wealth of data—let the mining begin!

DISCLOSURE STATEMENT

Dr. Phillips has indicated no financial conflicts of interest.

REFERENCES

7. Personal communication, August 4, 2008.