Diabetes and sleep problems often go hand in hand. It has been known for some time that diabetes-associated factors such as neuropathy and nighttime hypoglycemia can contribute to sleep problems in patients. Research is now providing growing evidence that insufficient sleep can also contribute to diabetes risk. The most recent studies reveal some of the potential mechanisms behind this link.

“Sleep can affect diabetes, and diabetes can affect sleep,” said Elizabeth Bashoff, MD, of the Joslin Diabetes Center in Boston. “For everyone, but especially for patients with chronic conditions such as diabetes, it’s important to take care of your health overall to improve sleep, and to take steps to get a good night’s sleep to restore the body.”

How diabetes affects sleep
Fluctuations in blood glucose can be particularly disruptive to sleep for many individuals with diabetes. “It’s not uncommon for people to experience hypoglycemia in the middle of the night, which can cause headaches, sweating, and nightmares,” Bashoff said. “Blood glucose that is too high can also be a problem because it may cause people to wake up repeatedly to use the bathroom.”

Sleep apnea is also a major cause of sleep problems, and it is more common in individuals with diabetes than in the general population. Sleep apnea is linked to obesity, and weight loss is by far the most effective treatment for individuals with sleep apnea who have high BMIs.

Leg pain due to neuropathy can also keep diabetics up at night. Controlling blood sugar levels can help. Also, there are many medications to treat the condition, some of which also have a beneficial sedative effect at bedtime.

How sleep affects diabetes
While diabetes and its associated comorbid conditions are well understood, the impact of sleep on diabetes is less well studied. Research has shown that sleep deprivation can lead to increased blood glucose levels, which can exacerbate diabetes.

Elevated phosphate levels in the blood—even when levels are in the high normal range—carry increased heart-related risks, but taking a phosphate binder did not improve cardiovascular measures in patients with mild kidney disease in a recent study published in the Journal of the American Society of Nephrology. "It would appear that for now it would be better to lower the amount of phosphate in the diet rather than rely on pharmacological interventions," said senior author Charles Ferro, MBChB, MD, of the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham, in England.

Because adherence to the study medication was low, though, additional studies are warranted to test the true potential of phosphate binders for protecting the heart health of patients with mild kidney disease. Chronic kidney disease (CKD) is the most common condition associated with deranged phosphate homeostasis. Ferro and his colleague Colin Clue, MBChB, led a research team that conducted a double-blind, randomized, placebo-controlled trial of 120 patients with stage 3 CKD to test the effects of the phosphate binder sevelamer carbonate, which is approved only for patients with kidney failure. Sevelamer carbonate holds promise for improving cardiovascular health because high blood levels of phosphate promote calcification and stiffening of blood vessels and can cause structural changes in the heart, such as increased wall thickness.
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Applications can have clear impacts on sleep quality, sleep quality may also impact dia-

betes and diabetes risk.

The first clue to this connection came from a 1999 study published in The Lancet. The study found that restricting healthy young people’s sleep to just four hours for six nights in a row produced striking changes in glucose tolerance and endocrine function (Spiegel K et al. Lan-

Since then, studies have generated additional evidence that disrupted sleep affects insulin resistance, and that indi-

viduals with diabetes who keep regular sleep schedules seem to maintain better blood sugar control, perhaps in part due to circadian rhythms connected to glu-

cose metabolism. Also, research suggests that people who get less sleep tend to be heavier than those who sleep well, which

puts them at increased risk for developing type 2 diabetes.

Research is starting to tease out the mechanisms by which sleep affects dia-

betes risk. A new Journal of the American Medical Association study found that indi-

viduals who secrete low levels of mela-

tonin at night have about twice the risk of developing type 2 diabetes as individ-

uals who secrete high levels of the hor-
mone (McMullan CJ et al. JAMA 2013; 309:1388–1389). The study included

370 women who developed diabetes and 370 controls. Melatonin secretion was measured at the start of the study, when

none of the participants had diabetes. Women in the highest category of mela-

tonin secretion had an estimated diabetes incidence rate of 4.27 cases/1000 person-

years compared with 9.27 cases/1000 person-years in the lowest category.

“This is the first time that an inde-

pendent association has been established between nocturnal melatonin secretion and type 2 diabetes risk,” said first au-

thor Ciaran McMullan, MD, a nephrolo-

gist at Brigham and Women’s Hospital in Boston. “Hopefully this study will

prompt future research to examine what influences a person’s melatonin secretion and what is melatonin’s role in altering a person’s glucose metabolism and risk of diabetes.”

New evidence presented at SLEEP 2012, the 26th annual meeting of the Associated Professional Sleep Societies, links sleep apnea with carbohydrate crav-

ings. Researchers screened 55 individuals (more than half of whom had diabetes) for sleep apnea and carbohydrate crav-

ings. They found that among the diabetic patients, the prevalence of sleep apnea was 82 percent, and they had almost twice the risk of carbohydrate craving than nondia-

betics. In addition, patients with sleep apnea were almost twice as likely to have high carbohydrate craving than were pa-

tients without sleep apnea.

“Previous studies have shown that sleep deprivation may lead to changes in hormones that regulate appetite and hunger. These hormonal changes can lead to significant craving for high-calorie car-

bohydrates,” said study co-investigator

Mahmood Siddique, DO, of the depart-

ment of medicine at the Robert Wood

Johnson Medical School in New Brun-

swick, NJ. “This study supports previous findings by validating this in a commu-

nity sample of diabetics.”

Getting a good night’s sleep
While some aspects of sleep may be out of one’s control, experts agree that certain measures can help improve sleep for most people, leading to considerably better health.

“Maintaining a regular schedule, get-

ting exercise, avoiding alcohol at night—

and for people with diabetes, testing

blood sugar at bedtime—can lead to a better night’s sleep,” said Bashoff. “I of-

ten see patients who are so busy that they don’t think of these simple steps.”

Individuals who sleep poorly are sus-

ceptible to depression and other mood

disorders, changes in eating, decreases in physical activity—and as indicated by the latest evidence, perhaps an in-

creased risk of developing diabetes.

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After a 4-week open label run-in period, during which all patients received sevelam-

er carbonate, 109 patients were randomly assigned to sevelamer or placebo for an additional 56 weeks. The investigators as-

sessed left ventricular mass and systolic and diastolic function with cardiovascular mag-

netic resonance imaging and echocardiogra-

phy, and they assessed arterial stiffness by carotid–femoral pulse wave velocity.

“We hoped that by asking a very mo-

tivated group of patients with early stage

chronic kidney disease to take phosphate binders with every meal, we would be able to reduce the amount of phosphate absorbed from the diet,” Ferro said. How-

ever, at the end of the study, the investi-
gators found no differences in any of the measures of cardiovascular structure and function between the groups.

Yet despite repeated reminders and sug-
gested methods to maximize compliance, adherence to treatment was low, with only 56 percent of patients taking more than 80 percent of the study medication. Also, several patients withdrew from the study because of difficulty with the frequency (two tablets taken three times daily) and tolerability of the study agents. When the subgroup of patients with more than 80 percent compliance was analyzed sepa-

rately, the group taking sevelamer excreted significantly smaller amounts of phos-

phate in their urine compared with those taking placebo. The sevelamer group also had reduced levels of the hormone fibro-

blast growth factor 23, which is critical for maintaining phosphate balance but is also toxic to the cardiovascular system. No changes were noted in any of the measures of cardiovascular structure nor in serum levels of phosphate, klotho, and vitamin D, though.

“Although only 56 percent of patients took 80 percent or more of the prescribed medications in this controlled study, which

is a legitimate limitation to the results, this level of adherence is very commonly seen in clinical practice, which makes the find-

ings of this study translatable to the real clinical setting,” said Jeannie Kim Lee, PharmD, BCPS, CGP, of the University

of Arizona College of Pharmacy. Lee, who was not involved with the study, has con-

ducted extensive research addressing pa-

tients’ medication adherence.

More research needed
In an accompanying editorial, Rajiv Agar-

wal, MD, of the Indiana University School of Medicine, noted that the study “should not serve as a death knell to investigations on phosphorus in progressive CKD, but should instead serve as a crèche for future investigations on the value of phosphorus reduction in preventing cardiovascular dis-

ease and CKD progression.”

He noted that it is unlikely that seve-
lamer is ineffective because the drug is ap-

proved with adequate trial data to support

its use in people with hyperphosphatemia.

He added that while the drug in the doses used in this trial was not effective in reducing an already normal level of phos-

phorus concentration, perhaps the partici-

pants increased their dietary phosphorus intake, which would prevent an overall de-

cline in serum phosphorus.

Until more information is available about the potential heart-related benefits of phosphate binders for individuals with mild CKD, these patients should focus on dietary changes to reduce their phos-

phate levels. Foods with large amounts of added phosphate are processed meat, ham, sausages, canned fish, baked goods, cola drinks, and other soft drinks.

“Fast food and ready-to-eat processed foods are the main contributors to today’s rising dietary consumption of phosphate,” Ferro noted. He suggested that a com-

prehensive public education effort that explains the harmful effects of high phos-

phate intake and provides clear labeling of the phosphate content of food could help limit the damage done by this cardiovascu-

lar risk factor.