

Sleeping pills linked to higher risk of cancer, death, study says

By Melissa Healy, Los Angeles Times/For the Booster Shots Blog

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[Video link](#)

A new study suggests that the 6% to 10% of Americans who use prescription sleep medications such as zolpidem (Ambien), temazepam (Restoril), eszopiclone (Lunesta) and zaleplon (Sonata) are more likely to develop cancer, and far more likely to die prematurely, than those who take no sleep aids.

The increased rates kick in at really low levels too, the study says. For those prescribed as few as one to 18 sleeping pills in a year, deaths during the period of the new study were more than three and a half times greater than for those who got no such prescriptions, the study says. And for patients who took home the largest number of prescriptions for sleep aids--for more than 132 pills per year--the risk of death was five times greater than among those who appeared to take no sleep aids, according to the study.

Studies such as this one do not establish whether sleep drugs are a cause of the increased cancers and deaths or whether, perhaps, those who are at greater risk of dying or developing cancer are simply more likely to seek a prescription for sleep problems. To establish such cause-and-effect relationships, clinical trials, which would compare subjects taking sleep medications against those taking a sham drug, would be necessary, said study coauthor Dr. Daniel F. Kripke, a professor of psychiatry emeritus at UC San Diego now affiliated with the Scripps Clinic in La Jolla.

In addition, the "all-cause mortality" used in the study is a crude measure of a drug's risk, because the measure aggregates a wide range of seemingly unrelated health crises: automobile accidents, injuries, suicides, infectious diseases such as influenza, and chronic conditions, including asthma, diabetes and cancer.

The study, released this week by the British medical publication BMJ Open, found an increase in cancer incidence among those taking sleep medications that was modest but statistically significant. Compared with patients with no record of taking prescription sleeping pills, the study says, those who were the heaviest users of prescription sleep aids were 35% more likely to be diagnosed with cancer during the study period.

The use of sedative medications was a better predictor than a participant's current smoking habit of whether he or she would develop lymphoma or cancer of the lung, colon or prostate during the study period, according to the research.

Conducted by researchers from Scripps and the Jackson Hole Center for Preventive Medicine in Jackson, Wy., the study tracked 10,531 patients given prescriptions for hypnotic sedatives for at least three months and for as long as four years. For comparison, researchers matched each patient prescribed with a sleep aid with at least two patients of similar age, gender and health status who had no record of having had sleep aids prescribed.

Zolpidem--sold as Ambien--was the most widely used prescription sleep medication used by study participants, followed by Restoril, the research says. But 4,117 of the participants got prescriptions for other sleep aids, including Lunesta, Sonata, benzodiazepines, barbituates and sedative antihistamines.

Given the millions of Americans for whom prescription sleep medication is a routine habit, the authors estimate that in 2010 alone, 320,000 to 507,000 deaths in the United States may have been associated with prescription sleep-aid use. Despite evidence that they may not add much to a night's sleep, Americans in 2010 filled some 66 million prescriptions for "hypnotics and sedatives," according to IMS Health, which tracks drug trends. That makes sleep aids the 20th most used class of prescription therapies.

Kripke acknowledged he was "very shocked" by the higher cancer levels he found in this large population. "I suspect people who work for the manufacturers of these drugs might be shocked too."

Sanofi-Aventis, the maker of Ambien, said Tuesday in a statement that the BMJ Open study had limitations beyond those acknowledged by its authors. The company called the study's conclusions "highly questionable," and cited its average follow-up of 2.5 years as insufficient to detect whether cancers were new, and might be the result of sleep aids, or whether they had already taken hold at the time a patient got a prescription for sleep problems.

Kripke agreed that cause and effect had not been established but underscored that a litany of studies have stirred concern about the safety of sleep medications, including research that was submitted to the Food and Drug Administration when some of these drugs were approved.

Kripke said that beyond their common role in fatal medication overdoses, there's evidence that widely used sleep medications raise risks for many ills: "hangover" effects dull alertness and cognitive performance, which may lead to accidents and injuries; studies (including this one) have found that gastroesophageal regurgitation and peptic ulcers are more common among those taking sleep aids, which could drive up rates of infection and of cancer; other studies

have linked sleep aids' use with depression and sleep apnea, which in turn raise risks of suicide, diabetes and heart disease.

As for how sleep medicine could be linked to cancer, that is harder to discern. A 2008 study by Kripke on rodents found hypnotics to have a carcinogenic effect, and suggested they can cause chromosomal damage. But human studies have been more mixed.

For those who rely on prescription sleep drugs to get to sleep and stay asleep, Kripke, a specialist in sleep disorders and their treatment, said that changes in "sleep hygiene" can make a difference, as can cognitive-behavioral therapy. But he added that many--especially older patients-- who lean on sleep aids should know that they may function perfectly well with a little less sleep, and that medications do not add large chunks of sleep-time to a night's rest anyway.

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