

# In higher doses, over longer periods, painkillers for chronic pain raise overdose risk

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It's been seven years since actor Heath Ledger, only 28, was found dead in his Manhattan apartment. The New York medical examiner ruled that Ledger died of "acute intoxication" from six kinds of painkillers, sleeping pills and anti-anxiety drugs.

Most drug overdoses are unintentional, said Barbara J. Turner, M.D., M.S.Ed., MACP, professor of medicine at The University of Texas Health Science Center at San Antonio and director of the Center for Research to Advance Community Health (ReACH). "People with [chronic pain](#) don't mean to end their lives," she said. "But they're taking a lot of drugs with substantial risks."

These painkillers include prescription opioids such as hydrocodone that are often prescribed along with sedative-hypnotics, such as alprazolam (Xanax) and zolpidem (Ambien). Many patients are prescribed antidepressants, as well, to treat their pain and mood disorders.

## Risk over time

Two new studies authored by Dr. Turner and Yuanyuan Liang, Ph.D., of the School of Medicine at the UT Health Science Center San Antonio, bring fresh insights about the risks faced by patients taking cocktails of medications for non-cancer chronic pain. Ultimately, Drs. Turner and Liang advocate placing more emphasis on common-sense, non-medication approaches to alleviate patients' chronic pain.

Drs. Turner and Liang developed a database to analyze health care delivery, medications and comorbid conditions for more than 200,000 HMO-enrolled patients who filled at least two prescriptions for opioids for non-cancer pain between 2009 and 2012. In this national study, they found that a morphine equivalent dose of 100 milligrams or more a day significantly increased the risk of drug overdose, but they also found that even lower doses of opioids, from 50 to 99 milligrams a day, were dangerous if the patient filled prescriptions totaling the equivalent of at least 1,830 milligrams of morphine over a six-month period. Patients prescribed more than four to six weeks of even moderate doses of opioids often reach this risky level.

"If you take moderately high daily doses of opioids and exceed a total dose of about 1,800 milligrams, you are almost at the same risk of drug overdose as somebody who is taking a very high daily dose," Dr. Turner said.

Physicians should take into account how much opioid a person has been prescribed over a period of time, in addition to the daily dose, she said. Those findings are in a recent issue of *The Journal of Pain*.

## Combination risk

A second study, published Feb. 4 in *The Journal of General Internal Medicine*, examined the increase in drug overdose risk for patients with mental health disorders who are taking opioids, hypnotic-sedatives and antidepressants in combination—the type of cocktail that killed Ledger.

"We found that if a patient is taking benzodiazepines (one class of hypnotic-sedative) on top of the narcotics, the risk is multiplicative," Dr. Turner said. "If you are at fourfold greater risk of overdose from higher-dose [opioids](#), and then there is more than a twofold greater risk from being on benzodiazepines for 90 days or more, the risk of drug overdose using both together becomes eight times greater."

### Catch-22

The antidepressant part of the story is more complicated, she said. Because antidepressants have benefits for pain management independent of their ability to regulate mood, physicians increasingly are prescribing them for people in chronic pain.

"What we found is, if you have a diagnosis of depression and are on 90 or more days of antidepressants, you are significantly less likely to have a drug overdose, so it is protective and a good thing," Dr. Turner said. "But there is a Catch-22: If you don't have a diagnosis of depression, you are more likely to have a drug overdose."

"It isn't clear why we are finding these two contradictory effects of antidepressants," Dr. Turner continued. "Overall, our study finds that people are on a boatload of potentially risky drugs when they have chronic pain. The longer they are on these drugs, the more risk they have, except there seems to be a glimmer of hope for people with depression for whom long-term use of antidepressants may be beneficial. Otherwise, doctors really have to limit the long-term use of these drugs."

Among more than 200,000 HMO enrollees, the researchers found about 1,400 overdoses. "It's not like these are happening every day, but these drug overdoses are dangerous events," Dr. Turner said.

### Access to services that improve function, reduce pain

Dr. Turner is also an adjunct professor in The University of Texas School of Public Health. The ReACH Center she directs is working to reduce health disparities for vulnerable populations. She is working with rural communities in southern Bexar County to develop ways to help low-income, predominantly Hispanic residents with chronic pain on a project funded by a federal agency, the Patient-Centered Outcomes Research Institute (PCORI). Potentially beneficial services to help people improve function and reduce pain are weight loss, stretching, walking, low-level exercises, yoga and massage. However, access to these services is poor currently, so she is working with the communities to improve this situation, along with Paula Winkler, M.Ed., director of the South Central Area Health Education Center, and regional Texas A&M AgriLife Extension agents.

"The increasing rate of [drug overdose](#) in the U.S. is partly a consequence of our reliance on medicines for managing chronic pain, and not taking advantage of all the other things we can do to help people manage it," Dr. Turner said. "Chronic pain is a common problem that isn't being dealt with well because people often lack access to alternative approaches to address pain."

Provided by University of Texas Health Science Center at San Antonio

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