

Legally prescribed opioid use may increase mortality in chronic pain patients

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Associations between opioid-related overdoses and increased prescription of opioids for chronic noncancer pain are well known. But some suggest that overdose occurs predominately in individuals who obtain opioids from nonmedical sources. In a new study published in the November issue of the journal *Pain*, researchers in Denmark found an increased risk of death associated with chronic pain without opioid treatment, as well as an even higher risk among those prescribed opioids for long-term use and a somewhat lower risk associated with short-term use.

"Our study provides the first evidence that directly links legally prescribed opioids to risk of deaths related to short- and long-term opioid use in patients with chronic noncancer pain," notes lead investigator Ola Ekholm, a senior advisor in the National Institute of Public Health, University of Southern Denmark in Copenhagen.

In the United States and Denmark, about 3% to 5% of the populations are using opioids regularly for treatment of chronic pain. In the U.S. from 1999 to 2010, the number of dispensed opioid prescriptions doubled (120 million to 210 million), and during the same period annual deaths related to opioid overdoses quadrupled from 4,030 to 16,651.

Using data from two Danish Health and Morbidity surveys from 2000 and 2005, combined with information from official Danish health-care statistics and socioeconomic registers, researchers from the University of Southern Denmark and the Rigshospitalet Copenhagen University

Hospital in Copenhagen found that the risk of all-cause mortality was 1.72 times higher among long-term opioid users and 1.39 times higher among non-opioid-using chronic pain patients than among individuals without chronic pain. Although the study showed no statistically significant association between long-term opioid use and cardiovascular and cancer mortality, the results indicated that risk of death due to other causes was almost 2.4 times higher among long-term opioid users than among individuals without chronic pain.

Investigators also determined that long-term opioid users had four times higher risk of toxicity/poisoning by drugs, medications, and biological substances than individuals without chronic pain. Non-[opioid users](#) with chronic pain also had a higher mortality risk but did not present with higher risk for poisoning by drugs, medications, and biological substances. They did, however, have a slightly higher risk for injury, poisoning, and certain other consequences of external causes when compared with individuals without chronic pain.

In an accompanying commentary, Harald Breivik, MD, DMSc, and Audun Stubhaug, MD, DMSc, from the Department of Pain Management and Research, University of Oslo and Oslo University Hospital, Oslo, Norway, pose a number of important questions about opioid treatment of chronic pain.

Dr. Breivik and Dr. Stubhaug comment that the most robust finding in the Danish study is the higher mortality rate in chronic pain patients not using opioids compared with persons without pain. They note that opioids may aggravate this burden of disease in chronic-pain patients, but it remains to determine whether this higher mortality rate is caused by the opioid treatment or the seriousness of the pain problem. They discuss how the relatively liberal attitude toward prescribing opioids in Denmark contrasts with the more restrictive policies in neighboring Nordic countries and assert that striking a balance poses a major

challenge in pain medicine.

The final question they propose is whether the primary culprit is opioids per se or the way in which patients are treated with opioids. They write: "Safe and effective treatment of [opioid](#)-sensitive pain is possible but continues to be a double-edged sword that is difficult to handle. It requires deep pharmacological knowledge, experience, resources, considerable patience, and mental energy from a group of helpers who are able to take care of the whole bio-psycho-social conundrum of the [chronic pain](#) patient."

More information: "Chronic pain, opioid prescriptions, and mortality in Denmark: A population-based cohort study," by Ola Ekholm, Geana Paula Kurita, Jette Højsted, Knud Juel, and Per Sjøgren ([dx.doi.org/10.1016/j.pain.2014.07.006](https://doi.org/10.1016/j.pain.2014.07.006)).

"Burden of disease is often aggravated by opioid treatment of chronic pain patients: Etiology and prevention," by Harald Breivik and Audun Stubhaug ([dx.doi.org/10.1016/j.pain.2014.07.006](https://doi.org/10.1016/j.pain.2014.07.006)).

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