Study Probes 20-Year FDA Practice of Approving Opioids With Little Safety Data

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(CN) — The coronavirus pandemic has been front and center these past six months, but America is still in the midst of another epidemic which never quite subsided: opioid addiction.

Researchers from Johns Hopkins studied the Food and Drug Administration and its record of approving 48 new opioid-based drugs between 1997 and 2018 in a new study published Monday in the journal Annals of Internal Medicine. The team sought to understand the quality, safety and efficacy of the drugs submitted, and what kind of data the FDA required before giving them the green light.

The number of Americans killed by opioid overdoses has more than doubled in recent years, from 21,000 in 2010 to nearly 46,000 in 2018, despite a reduction in the number of prescriptions written. Of those who died in 2018, 15,000 succumbed to prescription opioids — yet the majority began their dark journey under medical supervision.
Americans abuse opioids at rates which far exceed anywhere else on Earth. As well-meaning physicians restrict access to long-term users, many have turned to heroin as a cheaper alternative, which is often laced with an incredibly potent synthetic opioid called fentanyl.

“Despite the scope of America’s ongoing opioid epidemic, little is known regarding the FDA’s approval of new opioid products over the past two decades,” said Caleb Alexander, professor of epidemiology at Johns Hopkins Bloomberg School of Public Health, in an email interview. “Over more than two decades, the FDA approved 48 new opioids, most representing new dosage forms, methods of drug delivery or drug combination. Only one of the 48 approvals was for a new opioid molecule,” he added.

For example, in 1996 the FDA approved Oxycontin, an opioid developed by Purdue Pharma which is among the most sought-after prescription drugs for diversion. In granting its blessing, the agency accepted the claim that addiction arising from opioids when used as directed was “very rare”.

As it turns out, that specious argument has impacted more than a few families. Researchers found the FDA often approved opioids on the basis of short-term, narrowly focused trials which excluded patients who reacted poorly to a drug.

Many of the applications for drugs which were eventually approved turned to data from previously approved opioids for evidence of effectiveness, rather than holding a new trial for each drug. None of the trials for approved drugs extended beyond 84 days, despite most real-world users taking them for far longer periods of time.

According to Alexander, restricting trials to patients known to tolerate a drug well limits their usefulness and risks ignoring a wealth of valuable information on adverse side effects. Ostensibly done to improve the efficiency of drug trials, the result is less data available on those patients at greatest risk.

“Most (17 of 21, 81%) of the products approved for chronic pain with new trials excluded individuals who could not tolerate the drug or who reported few early benefits, limiting the relevance of the results to real world practice,” Alexander said.

When approving a new drug, meaning a previously unapproved molecule, for use among the general public, the FDA requires a minimum of two-phase, three efficacy trials to demonstrate safety and effectiveness. They also allow
for an abbreviated process granting more flexibility for new dosage forms, formulations or combinations of already-approved drugs.

Despite the FDA’s regulatory flexibility in regard to granting market access, researchers found the agency “did not use this to require opioid manufacturers to produce more information about the safety and effectiveness of prescription opioids” prior to a drug going on sale.

They say the agency should be required to produce more detailed and relevant information prior to being allowed to market and sell opioids to the public. The agency should also force drug companies to evaluate known side effects of opioid use, rather than excluding patients who experience problems with the medication.

“The FDA should also improve guidance for manufacturers by explicitly providing information about the populations, duration of therapy, and efficacy and safety outcomes that should be measured in trials going forward,” Alexander said. “The FDA should also relabel chronic opioids so that the labelling for these important products better reflects the conditions under which they have been studied for regulatory approval.”