

## PROFESSION

### FDA drug warnings often ineffective, study says

A 20-year review finds that the agency's actions frequently fail to make an impact on prescribing and clinical monitoring.

By **KEVIN B. O'REILLY**, *amednews* staff. *Posted Jan. 30, 2012.*

The Food and Drug Administration's communications to physicians and patients about the newly discovered dangers of approved medications often miss the mark, said a systematic review of 49 studies covering 16 medicines.

Researchers examined cases from 1990 to 2010 in which the FDA added warnings to labels, issued public health advisories or wrote letters to physicians and other prescribers to inform them of unanticipated drug risks. But these actions often did not achieve their aim or resulted in unintended consequences, said the review published online in January in the journal *Medical Care*.

For example, the FDA recommended that patients taking atypical antipsychotics be monitored for diabetes, yet rates of glucose testing did not rise. When the agency advised doctors of drug-drug interactions such as those involving the gastroesophageal reflux disease medication cisapride and the antihypertensive drug candesartan, prescribing of the medicines persisted despite repeated warnings and did not fall notably until 18 months later.

"I think the agency works quite hard to try to identify and assess and communicate prescription drug risks that it deems are the most important," said G. Caleb Alexander, MD, who co-wrote the study. "One of our findings is just how complex the task at hand is for the Food and Drug Administration."

Researchers could not offer an average effect of FDA actions on prescribing because of methodological differences in the dozens of studies included in the systematic review.

#### When warnings backfire

Sometimes, FDA warnings against prescribing drugs among certain patients can reduce use of the medications in other patients, the review found. In April 2005, the FDA added a black-box warning to atypical antipsychotics warning against their use in patients with dementia. Although physicians curbed such prescribing, they also quit ordering the drugs as frequently for their FDA-approved uses and for patients without dementia.

Well-intentioned advisories may have unintended consequences, the review said. Warnings about antidepressant use in children and teens in 2003 and 2004 resulted in big drops in prescribing for younger depressed patients. Later research found a spike in youth suicides after that decline in antidepressant prescribing.

"It's a tough call to know when to sound the alarm," said Dr. Alexander, associate professor of medicine at the University of Chicago Pritzker School of Medicine. "This is all done in the context of uncertainty. The agency has to consider a combination of facts and judgment."

The FDA said it is trying to upgrade its drug risk-communications system.

"We remain committed to improving our capacity to provide the public with timely, accurate, evidence-based safety information," said agency spokeswoman Erica V. Jefferson. "We acknowledge it is difficult to change medical practice patterns once they are established. Additionally, practice patterns may not change substantially, because in many cases we are communicating about risks that may not apply to all patients, and different prescribers and patients vary in their approaches to considering risk and applying those considerations to their benefit-risk analysis."

The FDA has had the most success when sending clear messages on risks and consistently repeating those messages over time, the review found. Dr. Alexander suggested that the government actively monitor physician prescribing to target warnings.

"The agency might learn a thing or two from the pharmaceutical firms that it regulates with respect to risk communication," he said. "They should be using principles of market segmentation to identify high-volume prescribers and then disseminating or conducting messaging of drug risks to those specific physicians."

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#### WEBLINK

"Impact of FDA Drug Risk Communications on Health Care Utilization and Health Behaviors: A Systematic Review," *Medical Care*, Jan. 18 ([www.ncbi.nlm.nih.gov/pubmed/22266704](http://www.ncbi.nlm.nih.gov/pubmed/22266704))

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