U.S. public may not be aware of important uncertainties about drug benefits and harms

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Many U.S. adults believe that only extremely effective drugs without serious adverse effects are approved, but providing explanations to patients highlighting uncertainties about drug benefits may affect their choices, according to a report in the September issue of Archives of Internal Medicine, one of the *JAMA/Archives* journals. The article is part of the journal's Less Is More series.

Approval from the U.S. Food and Drug Administration (FDA) does not necessarily ensure that a drug has a large or important benefit, or that all serious adverse effects of the drug are known, according to background information in the article. "Uncertainties are greatest in the first few years after approval and for drugs approved solely on the basis of a surrogate outcome," the authors note. They point out that the cholesterol-lowering drugs Zetia and Vytorin reached $1.8 billion in sales in 2007 before a study found no clinical benefit from these drugs, and that the anti-inflammatory medication Vioxx reached $2.4 billion in sales by 2003 before being withdrawn from the market due to its association with myocardial infarctions (heart attacks) and strokes. "The FDA has never required advertisements to acknowledge uncertainties inherent in all new drugs," write the authors. "Enthusiasm for Zetia and Vioxx … might have been dampened had consumers known to look for drugs approved based on patient outcomes or drugs with a longer safety record."

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Clinical Practice, Lebanon, N.H., conducted an Internet-based, randomized, controlled trial of U.S. adults' beliefs and choices regarding prescription drug uncertainties. The 2,944 participants were randomized to three explanations about a pair of cholesterol drugs, one that was approved because of a surrogate outcome (lower cholesterol) and another that was approved because of a patient outcome (reduced myocardial infarctions). Participants in the control group received no explanation, those in the nondirective group were told that surrogate outcomes do not always translate into patient outcomes and those in the directive group received the same explanation as well as advice to "Ask for a drug shown to reduce heart attacks."

In a second randomization, participants received one of three explanations about a pair of heartburn drugs, one that was newly approved and another that was approved eight years earlier. Participants in the control group received no explanation, those in the nondirective group were told "It takes time to establish the safety of new drugs" and those in the directive group were advised to "Ask for a drug with a longer track record."

The primary outcome was choice of the drug for which there was less uncertainty. In the cholesterol drug example, the better choice would be the drug that had a beneficial effect on patient outcome (reducing myocardial infarction) instead of surrogate outcome (lowering cholesterol). In the heartburn drug example, the better choice would be the drug that was approved eight years earlier instead of the recently approved drug. Researchers also asked participants, "What would you do if your doctor recommended the drug with the surrogate outcome? Do you think new—or old—drugs are safer?" and assessed their understanding of FDA approval with four true/false questions.

One-quarter of participants mistakenly believed that the FDA approves only drugs without serious side effects, and more than one-third

mistakenly believed that the FDA approves only "extremely effective" drugs. Equal percentages of participants in the directive and nondirective groups (71 percent in the cholesterol drug example and 53 percent in the heartburn drug example) chose the drug for which there was less uncertainty. In both examples, choice of the drug for which there was less uncertainty was lowest among the control group (59 percent and 34 percent, respectively). When asked what they would do if their physician recommended the drug approved for a surrogate outcome, 61 percent, 58 percent and 49 percent of participants in the directive, nondirective and control groups, respectively, said they would request the drug approved for a patient outcome. When asked which of the heartburn drugs was safer, 46 percent, 45 percent and 31 percent of the directive, nondirective and control groups, respectively, selected the older drug. The proportion of participants who chose the older heartburn drug and said it was safer was 40 percent, 41 percent and 26 percent, respectively. One limitation the authors note is "participants were making hypothetical choices between drugs."

"There are important gaps in what people know about prescription drugs—gaps that undoubtedly contribute to the rapid uptake of drugs despite uncertainty about benefit and harm," write the authors. "Our findings show that simple explanations (ones that are brief enough even for television advertisements) help consumers make better decisions." They recommend that the FDA more effectively communicate what it knows and does not know about how well drugs work.

More information: *Arch Intern Med*. 2011;171[16]:1463-1468.

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