

Patient compliance is vital in clinical trials. Of 23 sites in the National Lung Screening Trial, which is comparing x-rays with spiral CT scans, DHMC has one of the highest compliance rates.

On the record about off-label drug use

When a doctor says “take two and call me in the morning,” patients tend to assume there’s sound evidence backing up the recommendation. But that may not be the case, according to a study led by David Radley, M.P.H., a Ph.D. student at DMS’s Center for the Evaluative Clinical Sciences.

Uses: Using a national database, Radley and colleagues analyzed 725 million prescriptions written in 2001. They found that 79% were for uses approved by the Food and Drug Administration (FDA), while 21% were “off-label”—for uses not approved by the FDA.

Off-label prescribing is not necessarily cause for alarm, notes a DMS pharmacologist. “A lot of the time, using a drug in a way that’s not FDA-approved is very good treatment,” says David Nierenberg, M.D., who was not involved in the study. But there must be “good papers in the peer-reviewed journals that are unbiased that show that the drug is safe and effective” for the off-label use. Herein lies the most disconcerting finding of Radley’s study.

Of the 725 million prescriptions he analyzed, 15% were written without evidence of safety or effectiveness. In other words, these drugs were not approved by

the FDA for the condition they were prescribed for *and* there were few or no reports in the scientific literature supporting the use. Psychiatric and allergy drugs were the most common ones in this category. “This issue of sneaking off of FDA approval into another area can be very dangerous,” observes Nierenberg.

“By definition, off-label uses receive less scrutiny than labeled ones do,” Radley says. “This doesn’t mean that all of them are bad. This doesn’t mean that they are not carefully considered by the physician prescribing the drug. But it does imply that off-label uses may carry greater unknown risks compared to approved uses.”

Concerns about patient safety are what first inspired Radley to begin researching prescribing patterns, when he was an M.P.H. student at Yale. Although his study—published in *Archives of Internal Medicine*—does not assess patient safety, it provides a foundation for further inquiry. “Our study was innovative in that it was the first” to comprehensively examine off-label prescribing, says Radley.

He is also concerned about the wastefulness of prescribing practices with little or no scientific evidence. “The efficiency with which we provide care,” says Radley, “is something that everybody should be thinking a lot about.”

To address both concerns, he and his coauthors call for “more extensive post-marketing surveillance to identify non-evidence-based prescribing practices that lack FDA approval.”

Evidence: And at the individual level, Radley encourages patients to ask their doctors about the evidence behind prescriptions they write. “Patients should be asking their doctors, ‘Is this going to work for me? Is it going to put me at risk?’” Radley advises. “That holds not just for off-label medication use, but for all medication use.”

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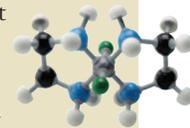


MARK WASHBURN

A recent study found that 15% of U.S. prescriptions do not have sound evidence behind them.

A mast-er regulator

Mast cells—the cells responsible for making allergy sufferers miserable—have important, beneficial roles to play in tissue transplants, DMS immunologists recently reported in *Nature*. Lead researcher Randolph Noelle, Ph.D., and his team found that mast cells regulate specific T-cells



that are “essential to establish and sustain self-tolerance” of a transplant. “Even though recent studies have underscored the plasticity of mast cells in regulating acquired immune responses,” Noelle and colleagues wrote, the finding “that mast cells may be instrumental in orchestrating T_{Reg}-cell-mediated peripheral tolerance is unprecedented.”

Talk therapy

Just three phone calls a year from a nurse-educator can significantly improve emotional and physical functioning in patients with chronic pain and psychosocial problems. That was the primary finding of a controlled

trial by researchers in DMS’s psychiatry department. The nurse-educators assessed patients’ pain, psychosocial problems, and treatment preferences; reviewed self-management strategies with them; provided problem-solving approaches; and gave rapid feedback to the patients’ primary-care physicians. The paper was published in *Annals of Family Medicine*.

