

Prescribing Evidence: The Effectiveness and Safety of New Drugs

ADRIANE FUGH-BERMAN, MD, *Georgetown University Medical Center, Washington, DC*

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In this issue of *American Family Physician (AFP)*, Mr. Pegler and Mr. Underhill expose the myth that new drugs are better than old drugs, and lay out a practical guide for assessing therapeutics.¹ Our society values brand-name products, and drugs are no exception. However, only rudimentary safety information is available for new drugs. Required safety studies are short-term and may involve only 100 to 300 patients. Randomized controlled trials, the gold standard for testing effectiveness, may also be short-term.

As noted in the *AFP* article, a study of more than 30,000 persons is needed to detect an adverse event that occurs in one in 10,000 patients¹; such megatrials are rare. Additionally, safety in older persons, young children, or the chronically ill is not usually assessed before the drug is marketed. Because of these reasons, most adverse effects are detected only after a drug is released. Novel drugs are associated with increased risk of adverse effects.² One half of drug withdrawals or U.S. Food and Drug Administration boxed warnings occur within two years of new drug approval.³

Many “new” drugs are new only in formulation; sustained-release and long-acting preparations are patent-extending measures. Renamed drugs with new indications are considered “new” drugs, and using a new brand name means that a generic equivalent cannot be provided. For example, fluoxetine, which was first released as Prozac, was renamed Sarafem. Both are fluoxetine; however, a prescription written for Prozac can be filled with generic fluoxetine, whereas a prescription written for Sarafem cannot. Other renamed drugs include sildenafil (Viagra and Revatio), zoledronic acid (Zometa and Reclast), finasteride (Proscar and Propecia), and bupropion (Wellbutrin and Zyban).

Drug combinations are also considered “new” drugs; recent examples include atorvastatin/amlodipine (Caduet) and omeprazole/sodium bicarbonate (Zegerid). Promoting metabolites or precursors of existing drugs as new drugs may cost patients money without conferring benefit. For example, esomeprazole (Nexium), the S-isomer of omeprazole (Prilosec), confers no clinical advantage; the same may be true for escitalopram (Lexapro), an isomer of citalopram (Celexa), and desloratadine (Clarinet), the main metabolite of loratadine (Claritin).

Family physicians are well positioned to counsel

patients that classic, time-tested drugs are generally preferable to whatever is currently being promoted on television. The risks and benefits of generic drugs are better delineated because they have been around longer. To be approved, generic drugs must prove bioequivalence (similar blood levels) to brand-name drugs. In fact, the allowable variability between brand-name and generic drugs is exactly the same as the variability allowed between different batches of a brand-name drug.

A meta-analysis of 38 randomized controlled trials comparing brand-name with generic cardiovascular drugs found no evidence that branded preparations were superior to generic, even in drugs with narrow therapeutic indices.⁴ The meta-analysis also examined 43 editorials and commentaries; only 28 percent encouraged the use of generic drugs, whereas 53 percent took a negative view of the interchangeability of brand-name and generic drugs. Although this meta-analysis did not examine the effect of funding on opinion, prescribers should be aware that pharmaceutical companies devote considerable resources to countering generic drugs. In spite of this evidence, physician bias against generic drugs persists.⁵ Although about three fourths of U.S. drugs are available as generics, generic drugs comprise about 63 percent of prescriptions dispensed.⁶

Physicians could avoid a great deal of iatrogenic harm by routinely asking the simple question that Mr. Pegler and Mr. Underhill suggest: “Is there good evidence that this new drug is likely to make my patient live longer or better compared with the available alternatives?”¹ Family physicians are ideally situated to practice—and preach—evidence-based prescribing.

Address correspondence to Adriane Fugh-Berman, MD, at ajf29@georgetown.edu. Reprints are not available from the author.

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