Therapeutic Substitution—Should It Be Systematic or Automatic?

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Generic drugs are substantially less expensive than brand-name drugs but equally effective. The surest path to generic medication use is for physicians (or other clinicians) to use generic drug names when prescribing. However, many physicians still write prescriptions using brand names, sometimes for no other reason than the brand name is easier to remember or to spell.

However, state laws and Medicaid insurance plans generally mandate generic substitution when there is a US Food and Drug Administration (FDA)-approved generic, unless the physician specifically checks the “dispense as written” box. As an example, if a physician writes a prescription for the brand-name drug Zocor, pharmacists can automatically substitute the FDA-approved generic version of simvastatin. When a generic version of a drug is available, use exceeds 85%, with brand-name drug use less than 15%.

Where generic substitution becomes more complicated is when a prescription names a brand-name drug for which there is no FDA-approved generic, but there is an approved generic version of another drug within the same class. Using the prior example: the physician writes a prescription for the brand-name drug Crestor, for which no FDA-approved generic drug is available, although the within-class generic drug simvastatin is available. State laws vary on whether pharmacists can substitute within therapeutic classes—also known as therapeutic substitution or interchange— but generally require specific protocols and explicit requests for physician approval.

In this issue of *JAMA Internal Medicine*, Johansen and Richardson demonstrate the substantial potential savings that could be achieved if therapeutic substitution were implemented systematically. Using nationally representative data and examining the most commonly prescribed classes of medications, they estimate that $73 billion in excess costs was spent on brand-name drugs for which there was no FDA-approved generic, but there was available a within-class generic. Of this, nearly $25 billion was in out-of-pocket costs spent by patients. The medication classes that accounted for the largest amounts of excess costs included proton pump inhibitors, statins, atypical antipsychotics, and selective serotonin reuptake inhibitors.

It is important to understand what benefits, if any, are achieved through these additional expenditures incurred by patients and health plans. Medications within a class are not necessarily equally effective and may have slightly different potencies and safety profiles. For example, the efficacies of the different selective serotonin reuptake inhibitors for the initial treatment of depression are similar, but the adverse effect profiles differ substantially, with the result that within-class substitutions may not be appropriate. On the other hand, drug companies often market their new brand-name medications as having special benefits over existing competitors, even when these benefits have not been substantiated in randomized clinical trials. To achieve the benefits of within-class substitution, we need wider adoption of systematic protocols, aligned with physician judgment, as to when such substitutions are beneficial and when not. This work is not easy; it requires close collaboration between physicians and pharmacists, but the financial savings will be large.

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