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2. Institute for Rational Pharmacotherapy Web site. 2004. Available at: <http://www.irf.dk>. Accessed September 1, 2004.

In Reply: We strongly endorse the use of direct generic substitution and “rational prescribing” when they are based on rigorous scientific information, because these are important ways to help people manage their drug expenditures. This is based on our own finding that seniors who exceeded their drug benefit caps decreased their use of essential medications, as well as on estimates from others that 1 in 4 Medicare beneficiaries will face the “donut hole” in the new Medicare drug benefit.¹ This “donut hole” represents the gap in coverage when beneficiaries’ annual drug expenditures exceed their benefit cap but are not yet high enough to qualify for catastrophic coverage. Better mechanisms to help people manage their drug costs must be found. We thank Drs Bjarnason and Kampmann for highlighting these programs in Denmark.

Currently, all 50 states in the United States allow pharmacists to make direct generic substitutions unless directly prohibited by clinicians on the prescription.² We support the additional development of evidence-based guidelines that take into account cost as well as safety and effectiveness to help clinicians and patients choose medications. However, transparency to both the patient and the clinician regarding potential cost-effectiveness trade-offs is essential. In the United States, health plans, insurers, and pharmacy benefit managers often send information to clinicians and patients to increase their awareness of drug costs and effectiveness. Other sources such as the treatment guidelines from *The Medical Letter on Drugs and Therapeutics*³ and from the State of Oregon⁴ have also added cost information to independent comparisons of drug effectiveness and safety. Further work is needed to ensure consistency among these guides and to help patients and clinicians use these tools in daily practice so that a patient’s health is optimized at the price that he or she is willing to pay.

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Surgical Mortality, Hospital Quality, and Small Sample Size

To the Editor: Dr Dimick and colleagues¹ recently emphasized the challenge of measuring surgical performance in the face of the pervasive problem of small sample size. We additionally note that classic statistics, developed to test differences between random samples, do not apply to hospital populations. The 95% confidence interval (CI), a frequent measure of precision that reflects variability among samples, is the range within which means are expected to fall 95 times if sampling is repeated 100 times. However, there is never a way of repeating a 1-year experience for an operation 100 times without changing conditions, population, and physicians. The CI for the specific operative mortality of an individual hospital is usually wide because of small numbers, so that even in a recognized example of poor performance (the Bristol case for pediatric cardiac surgery, based on a careful analysis of data from many years²), the CI for a specific operation at the problematic unit would often cross the mean mortality rate in other hospitals. Used as such, the CI can actually give the false confidence of adequate performance.

We propose that a reference range including 95% of individual data be derived from the largest pool of populations studied. When a hospital has a mortality higher than the upper limit of this range, the following possibilities could then be raised. (1) This is a “chance” finding, expected by definition less than 5% of the time, and therefore unlikely to be found again on the next year’s record. (2) Local performance may be substandard and this should be examined by other parameters such as review of processes or complications. (3) Local case-mix of patients may differ from the reference population, perhaps because of a neglected parameter in risk adjustment such as socioeconomic status.³ (4) Selection or reporting bias may have occurred in the reference population leading to apparent lower mortality for the procedure.

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This letter was shown to Dr Dimick, who declined to reply on behalf of the authors.—Ed.