Dear Editor:
The publication of "Analyzing Variations in Medication Compliance Related to Individual Drug, Drug Class, and Prescribing Physician" in JMCP's January/February 1999 issue raises serious concerns both about the journal's editorial policies and about the outcomes research field.

First, the methodological descriptions are inconsistent with the work actually performed. To cite two particularly troubling examples: (1) The authors state that they included only participants "who were eligible for pharmacy benefits throughout the study period." In reality, no eligibility data were used. Instead, continuous eligibility was defined as filling at least one prescription in the first and last three months of the study period. In a study that measures compliance using prescription claims, this approach is problematic at best. (2) The authors describe the Drug Enforcement Agency (DEA) number analysis as representing an assessment of "prescribing physician." In reality, "out of the top 10 most frequent DEA numbers, only three were associated with physicians. The remaining were numbers assigned to hospitals, pharmacies, or no entity, or they were 'dummy' numbers." Despite this serious problem, the authors go on to say that they "feel confident that important differences exist among physicians with regard to patient compliance." In the face of data problems of this magnitude, it is inappropriate to make such conclusions. Developing an accurate provider database is often difficult and expensive, but is essential to useful analyses of prescriber practice patterns. At a minimum, information that is essentially missing ("dummy" or group-provider numbers) should be treated as missing values, not included in analyses and attributed to "physicians." Moreover, a multivariate analysis could have provided useful information about practice patterns controlling for therapy class and patient demographics. Although the data were available for such an analysis, the authors say that explaining compliance differences among "physicians" was beyond study scope.

Second, the value of the information provided by this study is questionable. As the authors point out, patients who terminated treatment very early in therapy—a serious compliance problem—were not included in the analysis, limiting the study population to "a small subset" of the population of medication consumers. Since much of the most seriously noncompliant behavior had essentially been weeded out in sample selection, it is not surprising that the medication possession ratio (MPR) showed little variation. For example, out of 190 drug-specific comparisons only 14 were significant, and 11 of these were attributable to data artifact.

Analyses of patient compliance using prescription refill records have been a part of outcomes research for about five years. The authors' major conclusion—that "prescription claims can be useful... for detecting differences in patient compliance"—has been demonstrated previously. At this stage of development in the use of claims databases in outcomes research, cursory exploratory analyses are not enough. We as outcomes researchers must dig a little deeper—identify appropriate databases, redesign a study when we determine that our initial design is inappropriate, and use multivariate techniques when descriptive analyses lead to substantial unanswered questions. Yes, these efforts are sometimes time-consuming and expensive—but they will give the outcomes research field its best possible chance to inform the important policy debates taking place in our health care system today.

—Kathleen A. Fairman, Outcomes Research Manager, Express Scripts, Inc., Tempe, Arizona

Authors' Response:
We commend Ms. Fairman on her call for outcomes researchers to "dig a little deeper" and give their best efforts to help shape health care policy. At the time our research was first presented, May 1996, the use of prescription refill records to analyze patient compliance was just starting to gather momentum. Progress continues to be made in identifying the appropriate databases, obtaining critical information, and applying appropriate analyses for prescription refill records.

To further this progress, we feel obligated to address Ms. Fairman's concerns regarding methodological descriptions and the value of the information. Because continuous eligibility data were not available for this study, we used a proxy measure for eligibility throughout the study period. Although we listed this as a limitation, we did not believe this imperfection was enough to discontinue the study. Since then, however, we have progressed to using continuous eligibility data for compliance studies and initiatives.

We should clarify the methodology used for assessing the impact of physicians on medication compliance. As Ms. Fairman correctly points out, those DEA numbers associated with nonphysicians should not be included in analyses. Nonphysicians actually were removed and the top 25 physicians by DEA number were included. Our analyses did control for specific drug and therapeutic class and found statistical differences between physicians.

In addition to those factors that have been previously demonstrated to impact medication compliance, our findings showed that physicians themselves may have an independent effect on compliance as well. Admittedly, patients who become
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noncompliant before they receive their third fill are a problem. However, we feel that patients who become noncompliant after three fills are also a serious problem. As we stated, including those with fewer than three fills invited confounding factors such as discontinuation due to tolerability, certainly a limitation of higher magnitude. Still, with these limitations, our methods detected differences in patient compliance by medication, therapeutic class, and prescribing physician. Moreover, we noted these limitations and that the findings may not be widely generalizable and certainly should be confirmed.

We look forward to the progress that the outcomes research field will make regarding medication compliance and its impact on the health care system. Although prescription records are not perfect instruments for measuring compliance, researchers cannot let these imperfections stand in the way of progress.

—Larry Blandford, Pharm.D., Senior Director, Clinical PBM Products; Peter E. Dans, M.D., F.A.C.P., Medical Consultant, Advance Paradigm, Inc., Hunt Valley, Maryland