CLAIMS DATA AND DRAWING APPROPRIATE CONCLUSIONS

Health care and prescription drug claims databases are becoming a major source of data for health care outcomes and economic research. The use of these secondary data sets saves time and costs, and gives researchers vast amounts of data. Some claims database studies would be too costly if researchers were to collect primary data. Also, the large databases give researchers the numbers necessary to insure reliable estimates. Given these advantages, one needs to keep in mind that claims databases were not established for research purposes, but for reimbursement purposes. Therefore, a major weakness of claims databases is the compatibility of the data with the research questions. Often, available data within a claims database are not ideally suited to the purpose of the research. This weakness is the focus of our discussion.

Using a Medicaid prescription drug claims database, Malkin et al. found that the mean amount of dispensed opioid analgesic was greater than expected given the manufacturers' recommended dosing guidelines. Specifically for fentanyl transdermal system claims, the mean number of patches per day was 0.43, while the manufacturer recommends 0.33 patches per day, or one patch every three days. For oxycodone hydrochloride (HCl) controlled-release (CR) claims, the mean number of tablets per day was 3.4. Based on the assumption that patients took one tablet per dose, the authors concluded that the average patient took oxycodone HCl CR tablets more often than twice daily (the recommended dosing guidelines). The researchers clearly stated and discussed the limitations of their one-tablet-per-dose assumption and conducted a sensitivity analysis to test the effect of this assumption. Their overall conclusion was that "consumption of both medications exceeded the dose administration guidelines recommended in manufacturers' prescribing information."

When drawing conclusions from claims (reimbursement) database analyses, researchers need to be cautious that they do not present conclusions that are not supported by the data variables. Malkin et al. concluded that patients use fentanyl patches and oxycodone HCl CR tablets more often than the manufacturers recommend. The authors made a conclusion about patient consumption patterns of opioid analgesics, when in fact it would be more appropriate to draw a conclusion about the prescribing patterns of dispensed opioid analgesics. This distinction is important because claims databases reflect inferred prescribing directions, not patient consumption patterns. Furthermore, many times actual consumption is inconsistent with prescribing directions.

When researchers explain their findings, it is important for them to address all the reasonable explanations. A clear question raised by this study's results is: Why were more fentanyl patches and oxycodone HCl CR tablets dispensed than would be needed to meet the manufacturers' dosing guidelines? Though Malkin et al. state that their study was designed to describe and not explain

pharmacy claims, they do list one possible explanation for their findings: "We speculate that the recommended dosing schedules for both products provide inadequate pain control for many patients." Based on the data variables used to derive their conclusion, there is not enough evidence to make this statement without considering alternative explanations.

Certainly some patients require opioid analgesic dosing more often than the manufacturers' guidelines, and their physicians write prescriptions with dosing schedules to meet these patients' pain control needs. In the case of these patients, perhaps the manufacturers' standard dosing guidelines are inadequate to control pain. On the other hand, some physicians prescribe opioid analgesics more often than necessary, and the recommended dosing guidelines would have resulted in adequate pain control for the patient. The database variables in this study do not provide information on the inadequacy of manufacturers' guidelines for pain control.

Because claims databases are believed to be reliable and analyses often provide generalizable results, decision makers look to these studies to provide useful information. Since study conclusions could impact crucial patient care decisions, it is especially important that researchers stay within the limitations of the data variable measurements when drawing their conclusions.

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DETERMINING THE VALUE OF PHARMACY SERVICES—THE SEARCH FOR RIGOROUS RESEARCH DESIGNS

Determining the Value of Pharmacy

In this issue of *JMCP*, Bieszk et al. report on the impact of clinical pharmacist interventions for a group of Medicare + Choice recipients within a health maintenance organization (HMO).¹ In this study a group of 80 persons 65 years of age or older and taking more than five chronic medications were evaluated for appropriateness of care relative to national guidelines by clinical pharmacists. These same pharmacists recommended changes they deemed appropriate to the patient's primary care physician. Comparisons were made between 6 months prior to the pharmacist intervention and 6 months after. The authors reported that prescriptions and prescription costs significantly declined from the pre- to the post- period, but no change was observed in the number of medical encounters. Adherence to national guidelines was reported to increase by 10.2%. Both patients and physicians

reported being highly satisfied with the pharmacist interventions. No significant change was observed in total medical costs.

The findings of this study are similar to other studies involving clinical pharmacy services. Comprehensive reviews have been conducted by Carter and Helling.^{2,3} A brief review of this literature is provided here.

Within community pharmacy, Rupp et al. described an intervention for patients with asthma and found a 77% decrease in hospitalizations, a 78% decrease in emergency room visits, a 25% decrease in urgent care visits, and an improvement in asthma-specific quality of life.⁴ In another study, interim data from a lipid management program in community pharmacies found that patients had significant reductions in total cholesterol and low-density lipoproteins.⁵

Several evaluations have been conducted that demonstrate the value of clinical pharmacists within anticoagulation clinics.⁶⁻⁸ All of these studies found that clinical pharmacist monitoring of anticoagulation improves outcomes of care, including reducing bleeding events, averting thromboembolic complications, and lower costs for the health care system.

Similar to the study reported in this issue of *JMCP*, Hanlon et al. evaluated the impact of a clinical pharmacist on inappropriate prescribing for 208 persons aged 65 years of age and older who were receiving five or more medications.⁹ Inappropriate prescribing scores were reduced by 24% for patients randomized to see a clinical pharmacist, compared to 6% reduction in the control group ($p=0.0006$). However, there was no difference in medication compliance, SF-36 scores, or patient satisfaction.

The IMPROVE study enrolled 1,054 patients from nine VA medical centers and randomized 523 subjects to ambulatory clinical pharmacy services plus usual medical care and 531 to only usual medical care. No differences were observed in terms of SF-36 scores or overall resource utilization.^{10,11} The economic analysis took into account the cost of pharmacist services, which averaged slightly over three visits per subject. Thus, it was encouraging that adding additional visits to pharmacists did not increase overall costs. In addition, a subset of patients with hyperlipidemia had statistically significant improvement in lower total cholesterol and low-density lipoprotein in the intervention group as compared to those randomized to the control group.¹²

Another study conducted in a VA population found better blood pressure control and increased compliance.¹³⁻¹⁵ Erickson et al. also found that hypertension was reduced to a greater extent in 40 patients who were seen by pharmacists compared to a control group ($N=40$).¹⁶ Favorable outcomes of care have been noted from studies evaluating pharmacist interventions for patients with diabetes,^{17,18} heart failure,¹⁹ hyperlipidemia,²⁰ and *Helicobacter pylori*.²¹

These studies are but a few of the reports in the literature that measured the value of pharmacists in various health care settings. Upon closer inspection of these studies, the observer will note that the quality of studies varies tremendously. Poor study designs can undermine the value of the profession of pharmacy, and especially managed care pharmacy. One example of how others may view

pharmacy activities is provided by Soumerai et al.²² It is important to keep in mind that administrators, payers, government officials, and employers may use a given study to support or deny the pharmacy profession from performing pharmaceutical care and drug therapy management. Below are several suggestions to improve the quality of research associated with pharmacy services.

Conducting Rigorous Research of Pharmacy Practice

Because we refuse to accept poorly conducted clinical trials as evidence that a medication works, it is just as important not to overstate the value of pharmacy services based upon studies with poor research designs. Common study design problems consist of not including a control group, poor measurement of the principal outcome(s), selecting cases based upon extreme scores, and inadequate follow-up periods.

The lack of a control group is a common occurrence in many studies of pharmacy services. Without a control group, it is impossible to rule out alternative explanations for the observed findings. Most non-controlled studies are subject to many threats to internal validity, including history, maturation, selection, and experimental mortality.²³ Without a control group, it is impossible to rule out alternative theories for why change was observed in the study population. For example, in the IMPROVE study we evaluated patients who had a diagnosis of hyperlipidemia and found that both the control and the intervention groups had a decline in lipid levels during the study.¹² Patients in the intervention group had a greater decrease in total and lower density cholesterol than the control group. However, in addition to the interventions by pharmacists in this study, the entire VA health care system initiated a program to improve treatment of hyperlipidemia during the time the IMPROVE study was being conducted. Thus, without a control group it would have been impossible to separate the effect of the pharmacist intervention from the effects of the influence of physicians and other health care providers.

Selection bias is particularly problematic in retrospective studies. For example, patients who are using a particular medication are likely to be different from persons not on that medication. Patients on inhaled corticosteroids for the treatment of asthma are likely to be different from those who have only obtained a short-acting beta-agonist. The patients on inhaled corticosteroids are likely to have more severe disease than those only receiving an occasional beta-agonist. It is important for researchers to have groups that are comparable. Because many administrative databases do not contain specific measures of disease severity, the researcher should attempt to identify a surrogate for disease severity. This might include other medications that would reflect more severe disease. With retrospective studies it is difficult to find identical control groups so the analyst must use regression techniques that attempt to control for differences in the population. The most common methods include using multiple regression with independent variables that are proxies for disease severity. Clinic visits, hospitalizations, and various medication use in a pre-intervention period may be useful variables to include in a regres-

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sion model that analyzes post-period cost, hospitalization, or other outcomes.

Another common flaw in pharmacy service studies involves the selection of patients based upon extreme values, such as patients with high total cholesterol, hemoglobin A1c, or total costs. If patients are selected on the basis of extreme values, then the natural tendency is for these extreme cases to “regress to the mean” of the population of interest. Similarly, a group of patients with high total cost in one period is likely to have lower costs in the next period regardless of the pharmacy intervention. In the study by Coast-Senior et al., patients were referred to ambulatory clinical pharmacists for management of chronic diseases.¹⁸ It is likely that these patients were referred based upon the lack of disease control and hence represented statistical outliers. Figure 1 in the article displays a classic regression to mean phenomena, whereby patients had high hemoglobin A1c at baseline but had significantly lower values at the end of the study. Bluml et al. reported on a collaborative practice of pharmacists managing hyperlipidemia for patients who were already receiving therapy but who were “poorly controlled.”⁵ After a mean follow-up time of 14 months, lipid values were found to significantly decline in 454 patients enrolled in the study. Results from both of these studies may have been due to the pharmacist intervention. However, without a control group, it is impossible to rule out the possibility that these patients would have “regressed to the mean” regardless of the intervention. This is because they were selected for participation due to poor control of their disease. The natural tendency for out-of-normal range subjects is to regress back to the population mean. In addition, there may be other coincident interventions that influence the result. The threat from regression to the mean can be minimized if a control group is selected based upon the same criteria.

Because many evaluative studies of pharmacy services use existing clinical services or programs, it can be difficult to identify a control group. One option is to seek a control group in a separate but similar setting, such as another clinic or pharmacy in the same area.^{7,8,16,24} It is important to use the same criteria to select control and intervention patients. Historical controls are a distant second choice because treatment practices are constantly changing. A good study will measure the same attributes in both control and intervention patients. Subject evaluations should not be made by the same pharmacist who is providing the service because of the opportunity to introduce bias. Ideally, the observer or evaluator should be blinded to the treatment group. However, this may not be possible. The strongest study designs randomize subjects to control or intervention groups. Few reported evaluations of pharmacy services include randomization.^{9,13,17,25,26} The major benefit of randomization is to remove selection bias and any other unseen systematic differences between the two groups. Thus, the researchers should always consider if it is feasible to randomize subjects to treatments.

Determining what to measure is another important consideration that is often an afterthought or poorly developed. For novice researchers the best approach is to find a measurement tool that

has already been developed and validated. Keep in mind that just because a tool has been published doesn't necessarily mean it has been validated. Look for evidence that the tool measures what it purports to measure. For example, an asthma quality of life instrument should correlate well with an objective measure of lung function.^{27,28} Also, make sure the instrument is sensitive enough to measure meaningful changes when they occur. Alternatively, the instrument should report nearly identical values when the subjects do not change (test-retest reliability).

Be aware of self-selection bias. For example, patients who agree to participate in a study measuring patient satisfaction with pharmacy services are probably more likely to report a higher satisfaction with the pharmacist than those who do not, especially if the intervention group is told they will be receiving “special” attention. Even if you have a control group, they will not be exposed to the pharmacy service you are evaluating, so it may be difficult to provide a relevant reference from which to make comparisons.

Another critical issue in pharmacy-based studies is the follow-up period. All too often the follow-up period is insufficient. This is especially true when end-point outcomes, such as mortality or rare events, are studied. Because of the pressure to complete a project within a short time frame, many researchers are tempted to conduct a study with 3- to 6-month pre- and post-intervention measurement periods. Changes in chronic disease control are likely to take months to manifest, especially for conditions like hyperlipidemia and diabetes. The same holds true for episodic and seasonal conditions such as asthma. It is may often be unrealistic to expect clinically and statistically meaningful changes due to pharmacist interventions for many health status measures in three to six months. Researchers who are considering evaluation of a pharmacy service should plan to collect data for 12 months retrospectively and 12 months prospectively when possible. Thus, before implementing a new service, collect baseline measurements for the outcomes of interest. It is also important to address organizational factors that might affect the delivery of care.²⁹ It may be difficult to control for these other factors that may affect the study outcome, but data can be collected to permit statistical control of these factors in the study analysis.

Numerous other study design considerations exist and extend beyond the scope of this review. Pharmacists who are interested in evaluating their programs are encouraged to contact their local college or school of pharmacy. Often, pharmacy school faculty are interested in assisting the pharmacy community in conducting such research. Another source of expertise can be found in graduate programs within schools of public health, educational psychology, and education. Appropriate study design will improve the credibility of study results and increase the likelihood that the study will be published.

A few well-designed studies will better define the value of pharmacist interventions than the conduct of 100 poorly designed and executed studies. Constraints of time and funds affect all studies. It is important to estimate the available resources required to conduct a rigorous study and evaluation of the results. Although it

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may be tempting to overlook or ignore the components of good study design, it is time well spent for making an impact with decision makers, payers, governmental agencies and legislative bodies.

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