

Persistence With Drug Therapy: A Practical Approach Using Administrative Claims Data

CHRISTOPHER M. DEZII, R.N., M.B.A.

Senior Manager, Outcomes Research, Bristol-Myers Squibb

Since Hippocrates, physicians have been perpetually plagued by concerns over whether patients continue to take medication as prescribed—or at all.¹ Many methods attempt to identify adherent behaviors, methods that range from patient and physician surveys to microprocessor-chip technologies on medicine containers.²

Most, if not all, of these approaches provide only a modicum of understanding about specific aspects of adherence, such as how long a patient persists with a prescribed therapy.

Inefficacy or lack of compliance?

From the perspective of the practicing physician as well as the managed care organization, therapeutic goals focus on bringing about a curative or, at least, palliative effect. Yet physicians frequently find patients are responding inadequately to the drug therapy they prescribe.

Because patient testimony is often a primary indicator of therapeutic effect, the physician is immediately faced with the question as to whether this is an issue of efficacy or adherence. To assume inefficacy is the true cause, without a clear basis for this decision, brings the physician to contemplate titration at the risk of overdose. The underlying assumption here—an assumption that could further jeopardize the patient's health—is that the patient would comply with these new orders. All this merely underscores the need for a methodology that can effectively identify patients who are not persisting with therapy, in the effort to target such patients for interventions that will promote adherence.

For the purposes of this paper, compliance refers to how well a patient follows physician orders within a designated timeframe (number of days supplied/observable period) while persistence addresses how long a patient remains on therapy. Persistence introduces chronology into the assessment while compliance does not. Both compliance and persistence are viewed here as components of overall adherence.

The Estimated Level of Persistence with Therapy (ELPT) approach that will be discussed here makes efficient use of valuable information that is already available within administrative pharmaceutical-claims databases. The ELPT provides an inexpensive, unobtrusive way to determine the extent to which patients are filling their prescriptions for long-term therapies or treatments for chronic disease on a regular basis. While the analysis of this information does not reveal whether a pill is actually being ingested, it can be reasonably assumed that patients would not continue to refill a prescription without the intention to adhere.

While some might argue that failure to validate ingestion is a severe limitation within a methodology designed to determine persistence with therapy, the use of patient testimony alone as the basis for such a determination is fraught with risk.

The power of influence

Several influences are important considerations for predicting patient behavior with respect to therapeutic adherence. To the extent that the prescribing physician has gained a pa-

tient's trust, he or she is in a unique position to improve behavior by effectively communicating the importance of prescription adherence in the recovery process.

The Health Belief Model, by Rosenstock et al, strongly suggests that if patients believe the seriousness of their condition, they will follow a physician's direction.³ This model hypothesizes that health-related action depends on a patient being motivated to make health issues relevant. Sufficient motivation is defined here as the belief that one is susceptible to a serious health problem and, further, that actually following a particular health recommendation would be beneficial in reducing the perceived threat at a cost that is viewed as acceptable.

Prescription-refill analysis

Analyses of prescription refills can provide crucial insights into patient willingness to comply. This can be a valuable adjunct to decision making, in that physicians often have difficulty appraising the adherent behaviors of their patients.^{4,5}

To derive the most benefit from the ELPT approach, certain reasonable assumptions come into play. First, as already noted, it is important to recognize that prescription-refill data do not verify administration. Such data do, however, directly address the question of drug availability. Clearly, patients cannot comply with a drug therapy if they have

This paper has been peer reviewed by appropriate members of MANAGED CARE's Editorial Advisory Board.

not obtained the prescribed drug, so adherence is secondary to availability. Additionally, at the outset of using this assessment approach, each physician or group must make a clear determination as to his or her working definition of persistence with therapy. If, for example, a patient fills a 30-day prescription in January, then July, and again in December, would this patient be viewed as persisting with therapy?

Maximizing the usefulness of this approach also necessitates that the provider define the parameters for what is to be considered tolerable within the bounds of therapeutic adherence. A somewhat restrictive threshold of tolerability was established by McCombs et al as two weeks beyond the exhaustion of a 30-day supply [$1.5 \times$ number of days supplied].⁶ This tolerability threshold, in effect, defines a less-than-66% compliance rate (30 days/45 days) as "termination of therapy." The most rigid threshold could be derived using the half-life of the examined agent as its basis.

In prior studies,^{7,8} our investigators have applied a threshold of tolerability of 3×30 -day supply. The rationale we have used as the basis for establishing an extended threshold has been to include those patients with lower levels of compliance who make an effort to persist with therapy, e.g., patients who consistently take their medication every other day, although it is prescribed for daily ingestion. We also extend the threshold to account for the impact of hospitalizations: prescription-refill data are lost when a patient enters the hospital because pharmacy-claims data systems do not capture intra-hospital drug use.

In other words, in attempting to reasonably assess whether a patient is adhering to a prescribed therapy, we allow (perhaps generously) 90 days from the filling of a 30-day prescription for the patient to refill. If this level of adherence is not met, such

patients are considered "not persistent with therapy" and would be targeted for more intensive counseling and education.

Monitoring the level of adherence in patients with 90-day (mail-order) prescriptions necessitates a slightly different method. In this case, the treble approach would provide a far-too-generous grace period of 270 days ($90 \text{ days} \times 3$). Since we have committed to a 60-day range of tolerance for a 30-day supply that is obtained from a regular retail pharmacy, we have established that for patients using mail orders this period would include the initial 90 days plus a 60-day grace period. It is also worth considering that a patient who makes the effort to establish a mail-order account would intend to comply with the prescribed therapy. Further, Sherbourne et al have examined the effects of variables such as patient-provider relationship, health perceptions, past behaviors, and individual characteristics on adherence, with past compliance and satisfaction being strong predictors of compliance.⁹

Minimizing data distortion

As mentioned, the provider's degree of tolerance shapes the specific design of the ELPT model. Grace periods can be defined by the user's comfort level. A tighter period of tolerability yields results that demonstrate less persistence; a longer period will yield evidence of more persistence. Once the baseline tolerance level has been established, the user can construct individual patient-persistence curves.

A key point is to identify those patients who are likely to benefit from this methodology through the establishment of an observation period. First, it is important to establish a patient's continuing participation in the health plan through the presence of any claim beyond the observation period. This averts the potential misinterpretation of data from individ-

uals who switch plans. Since, to the clinician, it would become apparent that these patients did not have claims in the extended observation period, "switchers" would become ineligible for inclusion in the analysis. This evaluation at the outset can assist in minimizing false positives that arise due to fatalities or exits from the plan.

A typical study using the ELPT method would last from 6 to 12 months. This approach is most useful when identifying patients new to therapy, since observing prevalent patients (new and current users) will introduce the selection bias of assessing persistence in a persistent population. In our use of the ELPT methodology, we establish "new to therapy" by insistence on a drug-free period of 6 months prior to the index period.

Patient-persistence curves

Using the methods being described, nonadherent behavior becomes readily apparent to the careful observer. Patient-persistence curves for patients new to a particular therapy can be constructed based on a diagnosis (if available) followed by a particular therapy (index). Such categorizations allow for comparisons as to the degree of persistence associated with different therapies. When using pharmaceutical-claims-only databases, a 6-, 9-, or 12-month period that is study-drug (or -class) free would be established to approximate a new user. This would, of course, necessitate extending the study horizon to include this eligibility period — and the extension would be determined relative to the length of the observation period, i.e., 180 days prior to index + 360-day observation period = 540 days required eligibility.

Once the desired parameters are defined, the cohorts are evaluated on a patient-by-patient basis. Patients failing to meet the persistency threshold that has been established are identified as "not persistent with therapy" at the point that is the last day on which the evaluated script was sup-

plied that was not within the determined threshold.

The curves start at 100% and decay over the succeeding months of the observation period. For example, one study addressing differences in persistence between a one-pill combination-drug therapy and a two-pill polytherapy shows a persistency benefit with combination products.⁷ In terms of the analysis of these data, of equal importance are the specific endpoints in persistence with therapy (the point of patient discontinuation with therapy) and the differences that are detected between therapies. Regimens with less complexity and fewer side effects tend to yield higher persistency rates. A comparison of persistency with different therapies within a patient population provides valuable information about what works best in a population. The figure below depicts patient-persistence curves indicating that at 12 months, 60% of patients are persistent with therapy on one agent vs 40% on another.

Such data can form the basis for establishing more aggressive patient-education, compliance, and/or monitoring programs for specific patient populations. The data also can serve to alert the physician to possible causes of nonpersistence, in determining if it is due to adverse effects of therapy, regimen complexity, or cost, through more directed patient/provider interaction.

Towards a practical approach

The ELPT methodology lends itself to a practical view of assessing persistence. The Medication Possession Ratio (MPR) is a formula used to determine compliance that is measured from the first to the last prescription, with the denominator being the duration from index to the exhaustion of the last prescription and the numerator being the days supplied over that period from first to last prescription.¹⁰

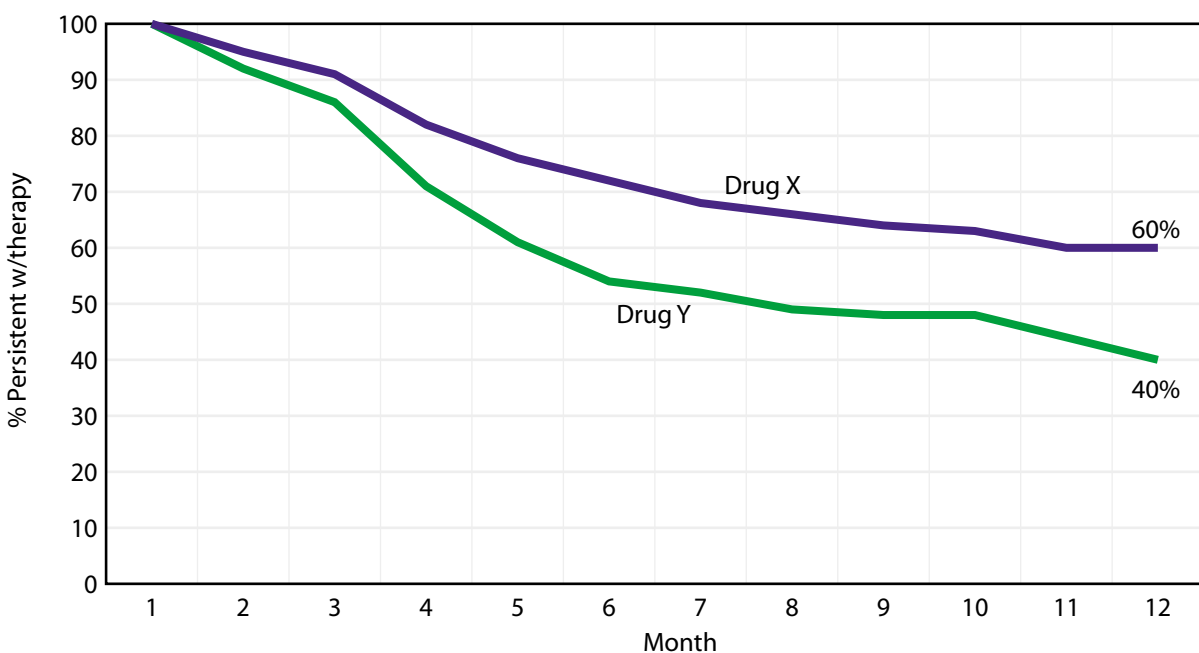
To demonstrate the practical limitations associated with the application of this approach, consider initi-

ating a therapy and assessing the patient 6 months later. If the patient had a first prescription filled, and then followed that initial prescription with one refill, while not getting that prescription refilled in any of the 4 months prior to his or her visit, a calculation based on the MPR ratio would indicate 100% patient compliance with therapy. That is, the period beyond the patient's last filled prescription may well be a vacuum of noncompliance that has not been accounted for.

This method alone would be useful if the physician could determine with some degree of certainty that these patients were "churners." This is a term that is often used to describe patients who take their medications regularly, only to stop for a while and then again make a behavioral shift that demonstrates a willingness to adhere to therapy.

The ELPT approach to determining persistence accounts for those patients who "churn" as well as those discontinuing therapy in a sequen-

Tracking persistence in a patient population — characteristic curves



tial manner, because it has an extended threshold of tolerability. The ELPT method also has a limited tolerance for the gap between prescriptions since it clearly defines the tolerable level of a gap. The MPR method, by contrast, will tolerate gaps of every level.

Advancing the quality of care

The ELPT approach provides opportunities for managed care organizations, physicians, and providers of prescription drug benefits to collaboratively advance the quality of care being offered to patients. This improvement could be accomplished through the implementation of adherence programs, such as patient-reminder calls or focused patient-education efforts that target those demonstrating such a need.

To a great extent, the practice of medicine is a practical art. Creative efforts to improve the quality of care are not fostered within an environment of limited resources and data overload. Yet much needed information can be seen to be available by recognizing the connection between what is wanted and what can be

found. Sometimes, what is obvious is harder to see.

The goal of this methodology is to glean information from available data, necessitating the investment of minimal time and expenditure, thereby providing a more comprehensive plan of care that effectively addresses the important area of patient compliance. Without patient persistence with therapy, the success of even the most carefully designed therapeutic plan is limited to the best of intentions.

References

1. Haynes RB. Introduction. In: Haynes RB, Taylor DW, Sackett DL, eds. *Compliance in Health Care*. Baltimore, Md: The Johns Hopkins University Press;1979:1-3.
2. Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette. VL. How often is medication taken as prescribed? A novel assessment technique. *JAMA*. 1989;261:3273-3277.
3. Rosenstock IM, Strecher VJ, Becker MH. Social learning theory and the Health Belief Model. *Health Educ Q*. 1988;15(2):175-183.
4. Roth HP, Caron HS. Accuracy of doctor's estimates and patients' statements on adherence to a drug regimen. *Clin Pharmacol Ther*. 1978;23:361-370.
5. Goldberg AI, Cohen G, Rubin A-H. Physician assessments of patient compliance with medical treatment. *Soc Sci Med*. 1998;47(11):1873-1876.
6. McCombs JS, Nichol MB, Newman CM, Sclar DA. The costs of interrupting antihypertensive drug therapy in a Medicaid population. *Med Care*. 1994;32(3):214-226.
7. Dezii CM. A retrospective study of persistence with single-pill combination therapy vs concurrent two-pill therapy in patients with hypertension. *Managed Care*. 2000;9(9):S2-S6.
8. Dezii CM, Kawabata H, Tran M. Compliance and persistency benefits achieved utilizing a once daily extended release medication vs a twice daily regimen [poster]. Presentation at the Fifth Annual Meeting of the International Society for Pharmacoeconomics and Outcomes Research (PDH 14), May 21-24, 2000. Arlington, Va.
9. Sherbourne CD, Hays RD, Ordway L, DiMatteo MR, Kravitz RL. Antecedents of adherence to medical recommendations: results from the Medical Outcomes Study. *J Behav Med*. 1992;15(5):447-468.
10. Blanford L, Dans PE, Ober JD, Wheelock C. Analyzing variations in medication compliance related to individual drug, drug class, and prescribing physician. *J Managed Care Pharm*. 1999;47-51.