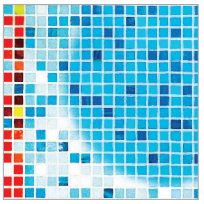


Understanding and Improving Adherence for Specialty Products

An English expression dating back over 800 years perfectly captures the challenge of non-adherence to drug therapy: you can lead a horse to water, but you can't make him drink. Physicians can prescribe treatment, but there is no guarantee that patients will follow "doctor's orders." Indeed, the statistics are sobering:

- In chronic therapy areas, about 50 percent of patients do not take their medication as directed
- Close to a third (31 percent) of patients never fill their original prescriptions[1]
- Non-adherence results in 125,000 deaths in the U.S. per year[2]
- Poor adherence accounts for $177 billion in direct and indirect healthcare costs[3]

In short, America has "*another* drug problem" as suggested by the National Council on Patient Information and Education. And it is clearly a problem that affects all stakeholders up and down the line; from the patients themselves to practitioners, manufacturers, payers, and

1 "Take as Directed: A Prescription Not Followed," Press Release, National Community Pharmacists Association, December 15, 2006.

2 Wertheimer, Albert I., PhD, MBA, Santella, Thomas M., "Medication Compliance Research: Still So Far to Go," *The Journal of Applied Research*, Vol. 3, Issue 3, 2005.

3 "NEHI Launches First-of-Its Kind Initiative to Improve Patient Adherence to Medication," Press Release, The New England Healthcare Institute, June 22, 2009

4 Cramer, Joyce A., BS et al., "Medication Compliance and Persistence: Terminology and Definitions," *Value in Health*, 11(1):44-7, 2008.

5 "Adherence to Long-term Therapies: Policy for Action," Meeting Report, World Health Organization, June 4-5, 2001.

YOU SAY "COMPLIANCE," I SAY "ADHERENCE"

The terms "adherence" and "compliance" are often used interchangeably even by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), which regards them as synonyms.[4] We, however, consider them to have precise and somewhat different meanings, along with the term "persistence." We've made the distinction in this report, using the following definitions:

COMPLIANCE: Following a treatment regimen as prescribed—in other words following the correct medication timing, dosing, and frequency.

PERSISTENCE: Remaining on therapy for the prescribed duration of time.

ADHERENCE: A more general term that combines the notions of compliance and persistence and represents "the extent to which a patient follows medical instructions."[5]

DRUG HOLIDAY: A lapse in therapy, after which it is resumed. Any number of reasons can prompt a drug holiday including: therapy failure, side effects, cost factors (including a change in co-pay), physician-directed switches, and the subsiding of symptoms (ironically because the therapy is working).

DISCONTINUATION: A lasting termination of a given therapy.

MEDICATION POSSESSION RATION (MPR): The ratio of the number of days supply dispensed to a patient, divided by the number of days in the cohort period, typically a year.

society in general, everyone loses when a medication is not taken as directed for as long as needed. Given that specialty products treat serious conditions and are often expensive treatments, the issue of non-adherence is intensified in specialty disease areas.

It is not, however, a newly recognized problem. Between 1975 and 2005, nearly 31,000 articles were published on the subject. This research has covered every conceivable angle of the issue including: identifying causes and exploring possible solutions, analyzing adherence by condition, and exploring the role of various stakeholders.

And today's adherence rates are essentially unchanged from those mentioned by the World Health Organization in 2001. So little has changed in the magnitude of the problem and in the attention given to the issue over the past 35 years, we seem to be caught in a "Groundhog Day" scenario in which we're destined to continually repeat the same experience. Why have we made so little progress? Why does non-adherence persist?

The following presents a brief overview of the issue and explains how IMS helped one company measure the return on investment it was receiving for one adherence program in the specialty marketplace.

REASONS FOR POOR COMPLIANCE AND PERSISTENCE

An individual's reason(s) for not conforming to a prescribed treatment can be just that—individual reasons. However, the most common reasons fall into several broad categories:

- **Lack of efficacy.** A drug may not be meeting the patient's or prescriber's expectations, or not meeting them quickly enough. Patients for whom a diagnosis was difficult and delayed, such as is often the case with rheumatoid arthritis for example, may be over eager for results given the length of time they have already suffered.
- **Characteristics of the therapy itself.** Many specialty drugs have side-effect profiles that patients find hard to tolerate, and many cannot be self-administered, presenting a delivery inconvenience.
- **Cost factors.** As a rule, specialty products are expensive, and can range from approximately $12,000 to $750,000 in a given year. A change in health insurance coverage (for example, a patient reaching the Medicare "donut hole" or being subjected to a change in a plan's co-pay structure) could push a patient to alter his or her therapy routine to save costs. Sometimes, to stretch a prescription, patients will take the therapy less frequently or cut their dosage in half.
- **Cessation of symptoms.** Many patients become complacent about continuing treatment if their condition is asymptomatic, if their disease enters remission, or if symptoms ease because, ironically, the treatment is working. A patient with multiple sclerosis might be tempted to halt treatment when the disease is in remission, but this would be detrimental with treatment meant to slow disease progression.
- **Co-morbidity.** Some co-morbid conditions, such as depression for example, can greatly contribute to a patient's ability to follow a treatment regimen. Depressed people are, in fact, three times more likely to be non-adherent with their drug therapy.[6]

THE TOLL OF NON-ADHERENCE

The unfortunate consequences of patients reducing, skipping, or discontinuing their medication are many, and include:

- Sub-optimal health outcomes with the exacerbation of symptoms, relapse of disease states, and increased morbidity
- Greater resistance to drug therapy in some disease states such as HIV and tuberculosis, for instance
- Patients' care being escalated to more potent, more expensive medications based on the assumption that the first line of therapy was ineffective
- Increased costs in the form of additional physician visits, hospitalizations, and lost productivity from absenteeism
- Loss of revenue for pharmacists and drug manufacturers. For manufacturers, the loss may extend beyond the patient in question to new patients because physicians may attribute the lack of therapeutic benefit to the drug itself, rather than to a patient's non-adherence

6 DiMatteo, Robin M., PhD; Lepper, Heidi S., PhD; Croghan, Thomas W., MD, "Meta-Analysis of the Effects of Anxiety and Depression on Patient Adherence," *Arch Intern Med.* 2000;160:2101-2107.

Estimates vary, but the New England Health Institute estimates that in 2009, direct and indirect healthcare costs related to non-adherence were $177 billion a year.[7]

MEASURING ADHERENCE FOR SPECIALTY PRODUCTS

For the past several years, it's been possible to measure adherence (in terms of both compliance and persistence) with anonymized, patient-level data (APLD). This information, however, has had limited applicability to complex chronic therapies that rely in varying degrees on specialty pharmacy providers (SPPs) for product distribution. However, with the availability of robust longitudinal specialty prescription data gathered from multiple SPPs, we can now:

- Measure levels of adherence, monitor improvement, and calculate the value of each support program
- Compare a product's adherence rates to industry benchmarks and competitive performance
- Compare adherence rates across distribution channels
- Analyze the types of patients that take drug holidays by channel, by indication, and demographically, and determine which portion of them are recoverable
- Analyze the time between refills for products to be taken as needed

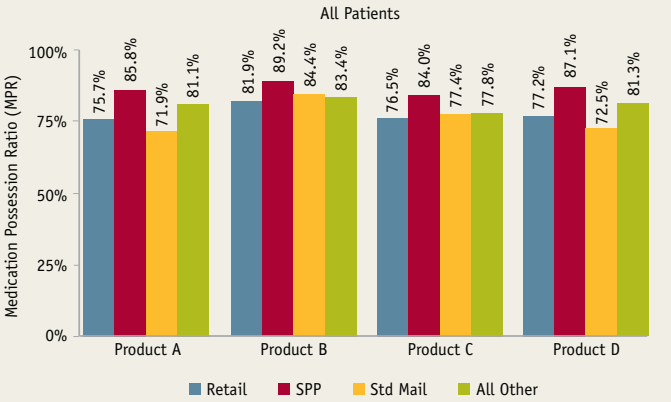
The overall goal in understanding the magnitude and cause of non-adherence is, of course, to find ways to improve patients' compliance with the treatment regimen and to retain them on therapy (or, failing that, to return them to therapy).

CASE STUDY: MEASURING THE RETURN ON INVESTMENT OF SPP ADHERENCE EFFORTS

The following case study reveals how one leading company used insights gleaned from SPP and retail longitudinal prescription data to calculate the value of its adherence program and guide its future investment.

One tactic that manufacturers of injectables and difficult-to-manage therapies use to improve compliance and persistence is to distribute their products through SPPs. SPPs offer patient counseling and follow-up services with the promise of improving patient outcomes. One client engaged IMS to learn if these patient-centered services were actually improving patient adherence to the point of delivering a positive return on its investment (ROI).

FIGURE 1: 360-DAY COMPLIANCE BY PRODUCT AND CHANNEL



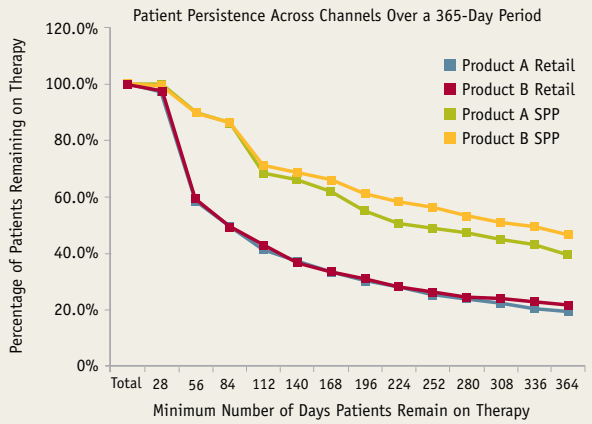
To answer that question, we compared compliance and persistence results between all products in the class across the retail and SPP channels.

Compliance was measured for over a 360-day period using the industry standard Medication Possession Ratio. For all products, the SPP compliance ratios were significantly higher (by 7-10 percentage points) than those of the retail channel for the drugs studies. (See Fig. 1)

For persistence (based on an allowable gap of less than 60 days), the results were also starkly different between the SPP and retail channels. For two products, the percentage of patients still on therapy after a year was more than 20 percentage points higher in the SPP channel (approximately 50-60 percent for the SPP channel and 30-40 percent for the retail channel). (See Fig. 2) Obviously, there are a number of factors that could account for this, but given that the compared drugs (and dosage forms) were identical between the channels, it is reasonable to infer that the difference is attributable to some aspect of the SPPs' service. For example, it could relate to the convenience that the SPPs offer in handling renewal prescriptions for

7 "NEHI Launches First-of-Its Kind Initiative to Improve Patient Adherence to Medication," Press Release, The New England Healthcare Institute, June 22, 2009.

FIGURE 2: NEW-TO-BRAND PATIENTS BY PRODUCT FOR RETAIL AND SPECIALTY PHARMACY CHANNELS



patients, or it could relate to the patient education and support that SPP nursing staff provide. Clearly more research will need to be done to determine exactly what aspects of these services are the most influential.

What are the financial implications for the brand franchise? Knowing that the average treatment cost to the payer is about $2,700 a month, the annual incremental difference in revenue per patient between the specialty and retail channels would be $8,717 for one example product and $9,055 for another. Replicate such amounts by thousands of patients, and the resulting difference is substantial.

The issue of non-adherence will never be completely solved, even with the commitment and participation of all stakeholders. Some product volume and some patients will simply be lost. However, manufacturers can make significant inroads by:

- Measuring the extent to which non-compliance and lack of persistence is affecting their business
- Understanding the reasons that patients are not adhering to treatment as prescribed
- Monitoring the effectiveness of their support initiatives
- Allocating resources across the channels that provide the best return

And now, with the availability of longitudinal data gathered from SPPs and retail pharmacies, manufacturers can approach the problem with specialty pharmaceuticals with the same rigor that they apply to large molecules. As in the case illustrated above, it is possible to test approaches to improving adherence to specialty products and to calculate the return that they deliver with great precision. With such insight, manufacturers can devote their resources toward those efforts that deliver the greatest return and thus improve the situation with the greatest number of patients.

This is an important breakthrough for manufacturers of specialty pharmaceuticals, given the heightened costs (both in revenue impact and health outcomes) associated with every specialty medication not taken as directed.

To learn more about IMS Specialty Solutions™, our recently launched specialty portfolio, and our therapeutic expertise, call us at **1.800.523.5333, x5590** or contact your local IMS representative.

IMS SPECIALTY SOLUTIONS

IMS Specialty Solutions is a portfolio of next-generation market intelligence all focused exclusivelyon specialty markets. With a full continuum ofinformation assets, analytics and consulting services, IMS Specialty Solutions empowers clients to make more confident, evidence-based commercial decisions, faster and with greater efficiency.