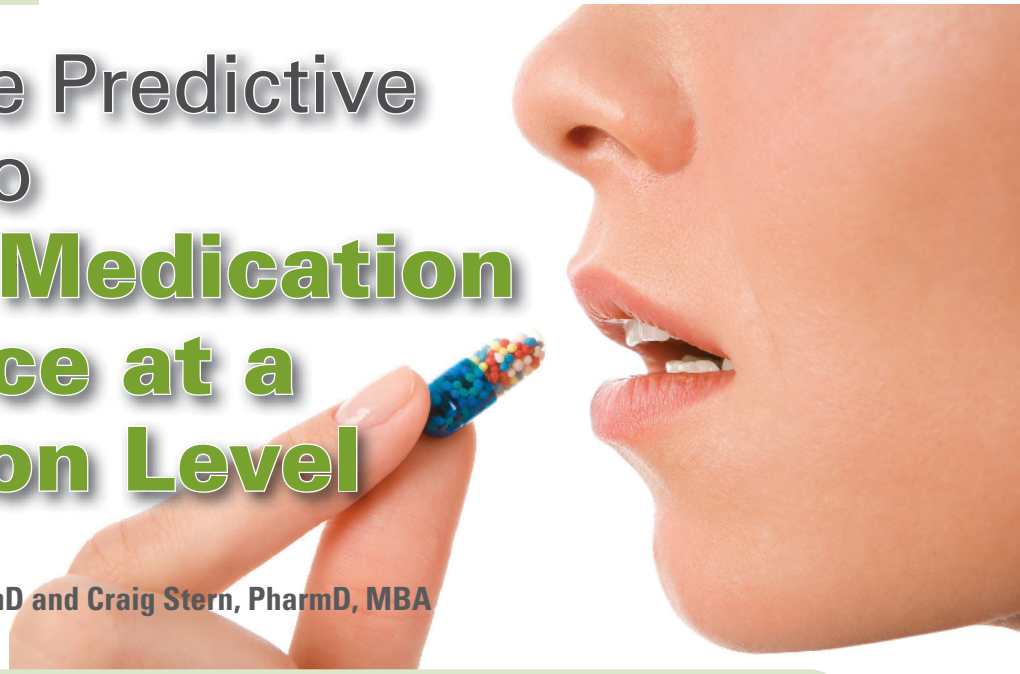
How to Use Predictive Analytics to Improve Medication Adherence at a Population Level



By Michael Pazirandeh, PharmD and Craig Stern, PharmD, MBA

Analytics is a term frequently used, but what does it mean? How is it used? How can the results of analytics be used by managed care professionals and pharmacists to make better decisions about patient care? This article attempts to place analytics in the context of its use for evaluating data. The goal is to quantify the performance of selected metrics for compliance and persistence (also commonly referred to as "adherence") and in so doing make analytics more understandable for the professionals who use it.

Introduction

Analytics is the discovery and communication of meaningful patterns in data. "Especially valuable in areas rich with recorded information, analytics relies on the simultaneous application of statistics, computer programming and operations research to quantify performance. Analytics often favors data visualization to communicate insight."[1] Often analytics is used to find answers to specific problems; for example, how many patients who experienced a myocardial infarction use antidepressants? Of particular import is that analytics is composed of two parts – analysis and communication. Analysis is the deep dive into data that describes patterns, associations and potentially causation; and sometimes, forecasting or making predictions of the impact of particular trends in the future. Communication takes the role of imparting the results of analysis to individuals who can use the information to make change or actionable decisions.

However, the use of any method to review data must be used judiciously to ensure that false information is not imparted through interesting patterns or associations that are anomalies, or worse, used as causation when only an association exists. In addition, statistics imparts a need to review data under defined mathematical rules. The impact of large data sets, like pharmacy claims, tests the limitations of statistics and associated pattern recognition. Large data sets often include poor data elements due to input errors, missing data elements, and data outliers. For example, pharmacy claims data may contain invalid physician identifiers, retired or invalid NDC numbers, absent bases of cost, pricing anomalies due to allocation between various payers, etc.

This article uses medication compliance and persistence as an example of analytics in pharmacy practice. While we do not provide examples of actual data analysis in this paper, we do impart the approach and process that should be considered for any valuable analytics.

Analytics is anchored by clear definitions. So, first, what is compliance and persistence? *Compliance* is the act of taking medication as prescribed according to a specific schedule, while *persistence* is the act of filling and refilling medications on time. For simplicity, compliance for chronic medications is following the prescribed directions (e.g., QD, BID, TID, etc.), and persistence is refilling a prescription every month.

Approach

While analytics can be a very large topic, this article approaches the subject of using analytics to describe and communicate the compliance and persistence of patients and populations of patients. If the focus is on

Objectives

At the end of this article, one will be able to:

- explain the differences between compliance and persistence;
- identify the metrics used to measure compliance and persistence; and
- identify how one can use predictive analytics in a patient population.

one patient, then traditional methods like tablet counts, brown bag programs where patients bring their medications to a health care professional for review, refill reminders, etc., are easily achievable.

However, if the focus is on a population of patients, then the prescription data must be analyzed for fills, refills, and continuity of care. Analytical decisions must separate acute from unscheduled, i.e., as needed, and chronic medications. Further decisions must review fill patterns for an adequate number of original fills and refills, e.g., 90 days of continuous therapy, to have enough information to identify patterns. Other decisions must be made about which data is evaluable, e.g., fills indicating dosage titration, drug switching within a category, outlier anomalies, etc. These decisions lead to how much data will be needed to analyze and which data should be removed from analysis.

Methodology

The use of analytics to address a problem requires several pre-analysis steps. First, review the available metrics that have been validated by multiple studies. (A cardinal problem exists for many analyses that use methods that have not been validated or are new, but not sufficiently validated, leading to analyses that do not provide useful information.) Second, make sure that the data will support the metrics such that sufficient data is available to supply an adequate result. Third, review the data using statistical tests to ensure that the population studied will provide mathematical veracity. From this testing, data outliers (as described in the Approach above) may need to be removed to ensure accurate results. Fourth, after the analysis and review of the results, it is crucial that a complete review of confounding variables and circumstances that could lead to different conclusions is conducted. Fifth, communicate the results of the analysis in a way that is understandable to the intended user and with sufficient information to allow for the intended actions to be accomplished.

In line with the prescribed methodology, a review of the literature was undertaken with the results summarized in Appendix A. The review indicates that there are a variety of measurements for compliance and persistence based on diagnostics obtained from surveys, scales used in surveys, and metrics used to quantify the level of compliance in a population. For analysis purposes, two metrics – medication possession ratio (MPR) and proportion of days covered (PDC) – were most commonly used and verified by multiple sources.

Metrics

In managed care organizations, MPR and PDC are the two most common metrics utilized to measure adherence. Both metrics use retrospective claims data to properly assess how often a patient is taking the prescribed medication(s). The values are expressed from 0% to 100%, where 100% is defined as perfect adherence or persistence. For example, if a patient is supposed to be on therapy for 180 days, but only picked up three 30-day prescriptions (90 days), the patient would have a value of 50% (90 days of therapy / 180 days of total therapy). The goal for managed care organizations is to achieve an MPR or PDC of 80% for most disease states. If a patient achieves the 80% threshold, then he or she is deemed to be optimally adherent, or alternatively, persistent. However, one study does question whether the 80% threshold may be low and should be increased to 90%.[2] In fact, the Centers for Medicare & Medicaid Services (CMS) has specifically called out a PDC threshold of 90% for Medicare Part D patients on antiretroviral medications for the treatment of HIV/AIDS. There are a handful of other metrics that one can use, such as refill compliance rate, compliance ratio and continuous measure of medication gaps.[3] These additional metrics, however, are not used as they have lower predictive capabilities compared to MPR and PDC.

Historically, MPR was used in most analytical reports to assess adherence; however, PDC has become more popular, especially with organizations such as CMS. One of the main benefits of PDC is that it can better assess multiple drug regimens. A day is only counted in the numerator if all medications are available on that day. For example, imagine a patient is prescribed to take Drug A and Drug B for 60 days. The patient picks up Drug A and Drug B in the first month, but in the second month, the patient only picks up Drug A. An MPR calculation would calculate the following:

90 days of total therapy (60 days for Drug A + 30 days for Drug B) / 2 drugs
60 days' supply
Or
45/60 = 75%

A PDC calculation would calculate the following:

30 days of complete therapy (e.g., Taking Drugs A and B together)
60 days' supply
Or
30/60 = 50%

Another area of predictive analytics that is developing traction is the use of questionnaires to predict which characteristics correlate with nonadherence. Polypharmacy (i.e., taking multiple medications) has traditionally been the primary characteristic associated with nonadherence, but there are potentially other correlating factors. There are several studies that use different questionnaires to assess adherence, such as the Beck Depression Inventory, the Morisky–Green questionnaire, the Hospital Anxiety and Depression Scale, and the Millon Behavioral Medicine Diagnostic (Appendix A). The overall conclusions of the studies indicate that patients at risk of nonadherence have the following characteristics: taking many medications, depressed, comorbid disease states, a high level of independence at an old age, and low psychological well-being. More research in this area is needed to create a formal and widely accepted method to properly predict which patients are truly at risk for nonadherence.

Limitations

Using retrospective claims data to measure MPR and PDC has a couple of limitations. First, even though a patient picks up a prescribed medication from a pharmacy does not mean

the patient is truly taking the prescription. In fact, as with the case of mail-order pharmacies, a prescription can be automatically delivered to a patient's house month after month without the patient ever taking one pill. The MPR and PDC metrics will be inflated and not reflect the true adherence values for the member. Another limitation of using retrospective claims data is that managed care organization can only measure data that the pharmacy adjudicates through the insurance plan. If the member decides not to use the insurance plan and instead uses the pharmacy's prescription discount program (e.g., Walmart's $4 list), the claim will not be captured by the managed care organization. This will result in a lower MPR or PDC.

Using prospective questionnaires to predict nonadherence also has a couple of limitations. First, the administrative burden to carry out these questionnaires in any setting is very impractical. The current work stream would need to change in order to incorporate these questionnaires into everyday practice. Additionally, another limitation is that these studies analyzed specific patient populations who may not necessarily correlate with one's customers.

How Can This Information Be Used by Practicing Pharmacists in Any Setting?

As indicated, analytics is also composed of communication of the results. This means that before analysis is performed, there should be a clear understanding of the intended use. It does not mean that we structure analyses to achieve a particular result. That is not science. What it does mean is that a number of analyses can be performed, but we must choose those that are easily communicable and actionable.

Managed care professionals can use the analysis of compliance and persistence to determine if there are quality gaps between providers, medications and groups of providers. The results of analyses are frequently included in quality "report cards" to identify areas for improvement and programs that should be undertaken to improve compliance in a population. For example, a group of providers may score low in adherence for inhaled corticosteroids in asthma. If the analysis also identified a correlation with low numbers of office visits, then corrective actions may drive toward pharmacist-directed interventions as the patients visit the pharmacy more often than they do physicians.

Practicing pharmacists in ambulatory practice may use compliance analysis to identify specific patients requiring further education and training to comply with their anti-hypertensive medications. The value of the analyses is that the pharmacists can be highly productive by focusing on specific patients, or groups of patients that display adherence problems, rather than hit-and-miss or a shotgun approach to all patients. Further, the pharmacists may request specific analyses to determine if they should place emphasis on certain target medications so that they do not use scarce pharmacist resources and time on medications for which compliance may not be affected easily, e.g., opiates and other analgesics. Analyses may also provide specific target patients and conditions that allow the pharmacist to be more successful in creating change, e.g., patients on chronic short-term opiates with varying dosages, history of tapering, multiple changes of medications indicating a problem with pain control that could be accomplished with a multimodality approach, including, but not limited to, medications.

Conclusion

Analytics has arrived as an exciting option for pharmacists as both a profession and a tool. Those with an interest in mathematics, computer programming, and pattern recognition will find this area of practice engaging, consuming, and fulfilling. The need for high ethical values and objectivity are paramount. The approach and communication of results must be scientific and easily understandable. Compliance and persistence provide a crucial opportunity for improvement. All pharmacists will be subject to the results of analytical studies. Why not find out how to get involved? As an analyst or user of the results, everybody wins!

About the Authors

Michael Pazirandeh, PharmD, is a Senior Clinical Pharmacist at Blue Shield of California in the Outcomes & Analytics department. He received his PharmD at the University of Southern California and his B.S. Biology at the University of Notre Dame.

Craig Stern, PharmD, MBA, is President of Pro Pharma Pharmaceutical Consultants, Inc. and serves as the Chairperson of the CPhA Editorial Review Committee. Dr. Stern and Dr. Pazirandeh have no bias or conflict of interest to disclose.

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Appendix B: Metric Formulas[3]

Adherence Metric	Formula
Proportion of Days Covered (PDC)	[Number of days' supply/number of days in the study period] * 100
Medication Possession Ratio (MPR)	[Number of days' supply/(last rx date - first rx date + last rx days supply)] * 100
Refill Compliance Rate (RCR)	[Number of days' supply/(last claim date - index date)] * 100
Compliance Ratio (CR)	Number of days' supply in the index period - last days supply/last claim date - index date
Continuous Measure of Medication Gaps (CMG)	Total days of treatment gaps/total days to next fill or end of observation period

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Appendix A: Literature Review

Author (Year)	Title	Sample Size	Study Design	Demographics	Questionnaires/Metrics	Factors Associated with Nonadherence
Atzori (2009)	Predictive Factors for Persistent Use and Compliance of Immediate-Release Methylphenidate	N = 134	Retrospective evaluation	Children ages 4-16 91% Male	Conners' Teacher and Conners' Parent Rating Scales–Revised, the Parent Interview for Children Symptoms the Wechsler Intelligence Scales for Children, the Multidimensional Anxiety Scale for Children, and the Children Depression Inventory.	Absence of associated disorders, older age, and male
Couzi (2013)	Factors Predictive of Medication Nonadherence After Renal Transplantation	N = 312	Prospective, non-interventional cohort study	Ages 18-79 68.3% Male	Hospital Anxiety and Depression Scale	Young age, failure to use the Organ Transplant Information System software package and patient reports of adverse events
Cruess (2007)	Utility of the Millon Behavioral Medicine Diagnostic to predict adherence to highly active antiretroviral therapy medication regimens among HIV-positive men and women	N = 117	Prospective, non-interventional cohort study	Mean age: 42.75 63% Male Black 63%, White 20%, Hispanic 9%, Other 8%	The Millon Behavioral Medicine Diagnostic	Depression
Gelb (2010)	Predicting medication adherence and employment status following kidney transplant	N = 108	Prospective, non-interventional cohort study	Mean age: 50.07 52.4% Male 72.8% White, 16.5% Asian, 10.7% Other	The Instrumental Activities of Daily Living questionnaire and the Center for Epidemiological Studies-Depression Scale.	Poorer performance on the everyday problem-solving test and a higher number of depressive symptoms
Glazer (2002)	Psychological predictors of adherence and outcomes among patients in cardiac rehabilitation	N = 46	12 week prospective study	Mean age: 58 73.9% Male 74% White, 22% Black, 2% Hispanic, 2% Other	The Life Orientation Test, the Beck Depression Inventory and the State-Trait Anxiety Inventory.	Depression
Insel (2006)	The negative association of independent personality and medication adherence	N = 58	Descriptive, retrospective study	Mean age: 77 (Ages 67-93) 21% Male 72% White, 22% Hispanic, 6% Black	Six-Factor Personality Questionnaire	Higher levels of independence in an older population
Jansa (2010)	Multidimensional analysis of treatment adherence in patients with multiple chronic conditions. A cross-sectional study in a tertiary hospital	N = 301	Cross-sectional, prospective, comparative study	Mean age: 62 (Ages 15->65) 59% Male 98% White, 2% Other	Morisky–Green questionnaire	Older age, more chronic conditions, a higher frequency of hypertension, ischemic heart diseases, hyperlipidaemia and more pills/day
Karve (2008)	An empirical basis for standardizing adherence measures derived from administrative claims data among diabetic patients	N = 4,943	Retrospective Analysis	Mean age: 60.9 24.3% Male 52.8% White, 34.3% Black, 12.9% Other	Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC)	Low MPR and PDC
Karve (2009)	Prospective validation of eight different adherence measures for use with administrative claims data among patients with schizophrenia	N = 3,395	Retrospective Analysis	Mean age: 42.9 47.5% Male 52.8% White, 39.1% Black 8.1% Other	Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC)	Low MPR and PDC
Mateus-Solarte (2008)	Factors predictive of adherence to TB treatment	N = 300	Prospective fixed cohort study	Median age: 34.5 56.7% Male 14.3% White, 36.3% Black, 45% Mestizo, 4.3% Indigenous	Face-to-face questionnaire	Living away from the family, overcrowding at home (2 persons per bedroom), lack of family support, living 10 min away from the treatment facility and not having used the services of the treatment facility before
Liu (2012)	Factors associated with adherence to treatment with olanzapine and other atypical antipsychotic medications in patients with schizophrenia	N= 1,103 (Olanzapine) N=1,090 (Other atypical)	Post-hoc analysis of pooled data from 5 randomized, double-blind trials	Mean age: 36.4-40.4 62.2-66.7% Male	Positive and Negative Syndrome Scale	Lack of significant improvement in positive, hostility and depressive symptoms
O'Carroll (2010)	Predictors of adherence to secondary preventive medication in stroke patients	N = 180	Longitudinal observational study	Mean age: 69 54% Male	The Medication Adherence Report Scale	Younger age, increased specific concerns about medications, reduced cognitive functioning and low perceived benefit of medication
Penkower (2003)	Psychological distress and adherence to the medical regimen among adolescent renal transplant recipients	N = 22	Longitudinal observational study	Adolescent ages 13-18 50% Male 86.4% White	The Beck Depression Inventory and the Spielberger State-Trait Anxiety Scale	Adolescents with excessive anger
Poulet (2009)	Psychological variables as predictors of adherence to treatment by continuous positive airway pressure (CPAP)	N = 122	Observational pre-post intervention study	Mean age: 56 81.1% Male	The Nottingham Health Profile, the Hospital Anxiety and Depression Scale, the Apnea Knowledge Test and the Apnea Beliefs Scale.	Low psychological well-being and subjective health status
Santos (2008)	Predictors of adherence to treatment in patients with severe asthma	N= 160	Prospective cohort study	Mean age: 49 25% Male	Basic demographic questionnaire, the Asthma Control Questionnaire and the Beck Depression Inventory	Adverse effects, living far from the referral center, limited resources to pay for transportation and dose schedule.

Limitations:
1. Several studies have a small sample size.
2. Several studies were not double-blind, placebo-controlled trials.

CONTINUING EDUCATION QUIZ

How to Use Predictive Analytics to Improve Medication Adherence at a Population Level

1. **What is the definition of compliance?**
   a. Conforming to the recommendations made by the provider with respect to timing, dosage, and frequency of medication taking.
   b. The duration of time a patient is on the medication from initiation to discontinuation of therapy.
   c. Both A and B.
   d. None of the above.

2. **What is the definition of persistence?**
   a. Conforming to the recommendations made by the provider with respect to timing, dosage, and frequency of medication taking.
   b. The duration of time a patient is on the medication from initiation to discontinuation of therapy.
   c. Both A and B.
   d. None of the above.

3. **What does MPR stand for?**
   a. Medication Possession Ratio
   b. Medication Possession Rate
   c. More Possession Ratio
   d. Medication Pressure Ratio

4. **What does PDC stand for?**
   a. Proportion of Days Complied
   b. Positive Days Covered
   c. Proportion of Dimensions Covered
   d. Proportion of Days Covered

5. **Which metric best measures adherence for multiple drug therapies (e.g., HIV regimens)?**
   a. Refill Compliance Rate
   b. Compliance Ratio
   c. Proportion of Days Covered
   d. Medication Possession Ratio

6. **What is one limitation of using claim data for adherence measurement?**
   a. Picking up a medication doesn't mean the patient is actually taking it.
   b. Claims data have poor predictive capabilities.
   c. Retrospective analyses are difficult to perform.
   d. None of the above.

7. **For most medication classes, what is the MPR/PDC threshold for optimal adherence?**
   a. 70%
   b. 80%
   c. 85%
   d. 90%

8. **For Medicare Part D patients on antiretroviral medications, what is the PDC threshold for optimal adherence?**
   a. 70%
   b. 80%
   c. 85%
   d. 90%

9. **Health plans and PBMs are able to obtain claim data, even if a patient goes through a pharmacy's prescription discount plan (e.g., $4 drug plans).**
   a. True
   b. False

10. **Higher depression scores are associated with higher nonadherence scores.**
    a. True
    b. False

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