
FROST & SULLIVAN
PATIENT NONADHERENCE:
TOOLS FOR COMBATING
PERSISTENCE AND
COMPLIANCE ISSUES
A Frost & Sullivan White Paper

INTRODUCTION

Adherence is the extent to which patients follow the recommendations on medication, diet and lifestyle modifications

Patient adherence (or the lack thereof) to prescribed medications has been one of the more extensively discussed topics in recent times. Nonadherence can constitute many forms, including not having a prescription filled, taking an incorrect dose, taking medications at incorrect times, forgetting to take doses, or stopping therapy before the recommended time.

Adherence is interchangeably used with the term compliance in describing the extent to which patients follow the recommendations of their healthcare provider on medication, diet and lifestyle modifications to ensure favorable clinical outcomes. The use of the term adherence is generally favored over compliance because the latter connotes a more passive patient-physician relationship. Adherence endeavors to transform the relationship from what is currently perceived by many as subservient, where the physician 'instructs' a patient what needs to be done, to one based on a physician-patient partnership which involves an interactive dialogue, leading to a mutually acceptable therapeutic course of action.

The problem of nonadherence to medications is serious, but not insurmountable. With each passing day, tremendous progress is being made to understand the core reasons for nonadherence and design programs that will address these issues. Also, there has been a realization by all concerned stakeholders that they need to stop viewing nonadherence as either 'my problem' or 'their problem' and treat it as 'our problem'.

The purpose of this discussion is to understand the causes and consequences of nonadherence and the types of adherence programs and the barriers affecting them. We will also address some of the current adherence initiatives and analyze emerging trends such as drug discount cards and patient loyalty programs.

CONSEQUENCES OF NONADHERENCE

Nonadherence affects three major constituents- patients, pharmaceutical manufacturers and the healthcare system. Patients have a reduced quality of life, shorter life spans and higher long-term health costs. Pharmaceutical companies forego potential revenues worth billions of dollars, especially for medications used in chronic diseases. The entire health care system is burdened by increased healthcare costs, including increased hospitalization rates and physician consultation.

The adverse consequences of nonadherence with medications have been well documented by a multitude of studies. In the United States, patient adherence with chronic medications averages only 50 percent.[1] It has been estimated that nonadherence to prescribed medications causes nearly 125,000 deaths annually.[2] 10 percent of hospital and 23 percent of nursing-home admissions are due to medication nonadherence.[3] One-third of all prescriptions are never filled, and over half of prescriptions that are filled are associated with incorrect administration. Nonadherence contributes to direct annual costs of $100 billion to the U.S. health care system. Indirect costs exceed $1.5 billion annually in lost patient earnings and $50 billion in lost productivity.[4] The seriousness of this problem has prompted the National Council on Patient Information and Education (NCPIE) to term nonadherence as "America's other drug problem".

"America's other drug problem".

- NCPIE

Besides impacting patients and the health care system, nonadherence has grim financial implications for other stakeholders, such as pharmaceutical manufacturers, insurance companies and employers. Corporate health insurance premiums are showing annual double digit growth rates and an estimated 20 to 25 percent of employers' healthcare expenses are a direct consequence of nonadherence to medications, according to the benefits consulting firm Watson Wyatt Worldwide[5].

Pharmaceutical manufacturers lose potential revenues worth billions of dollars, especially for chronic diseases such as hypertension, hyperlipidemia, osteoporosis and mental disorders due to patients not filling their prescriptions. It has been estimated that pharmacies lose nearly $8 billion yearly from non-refilled prescriptions.[6]

Patient adherence with chronic medications averages only 50 percent

Several clinical studies have illustrated that nonadherence to prescription medications is extensive. In a study of 240,604 patients who were given a new prescription for an antidepressant and who had not been taking an antidepressant for at least the previous six months, fewer than 30 percent continued to take their medication for a full six months.[7] Adherence with concomitant antihypertensive and lipid-lowering therapy is poor, with only 1 in 3 patients adherent with both medications at six months.[8] Only 26 percent of elderly patients who initiated statin treatment to reduce the risk of coronary heart disease maintained a high level of use five years later and that the greatest decline occurred during the first six months of treatment.[9]

1 Haynes RB. Interventions for helping patients to follow prescriptions for medications: Cochrane Database of Systematic Review, 2001 Issue 1.
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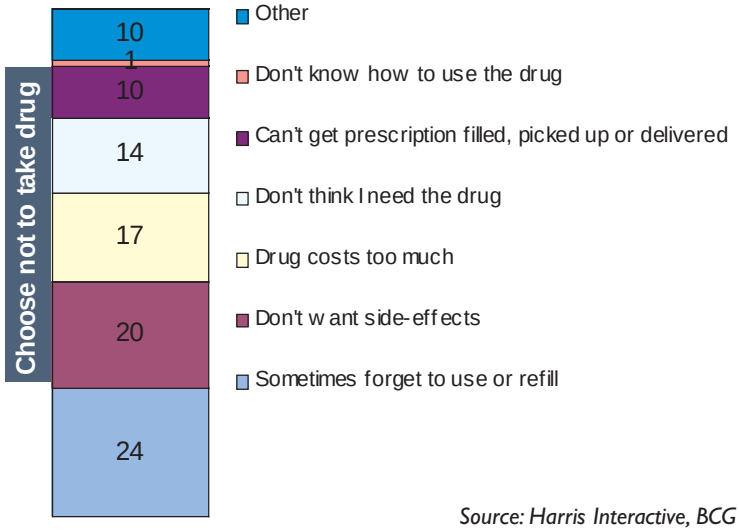
3 Noncompliance with medication regimens. An economic tragedy. Emerging issues in pharmaceutical cost containing. Washington, DC: National Pharmaceutical Council; 1992:1-16.
4 Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence: American Journal of Health System Pharmacists; 60(7):657-665, 2003
5 10th Annual survey of large employers: Watson Wyatt Worldwide and National Business Group on Health, March 2005.
6 Jackson RA, Worthen DB, Barnett CW. The financial aspects of improved refill management. Practice Opportunities. Cincinnati,Ohio: Proctor & Gamble Health Care; 1998:1-15
7 Tierney R, Melfi CA, Signa W, Croghan TW. Antidepressant use and use patterns in naturalistic settings. Drug Benefit Trends. 2000;12(6):7BH-12BH
8 Chapman, R. H., Benner, J. S., Petrilla, A. A., Tierce, J. C., Collins, S. R., Battleman, D. S., Schwartz, J. S. (2005). Predictors of Adherence With Antihypertensive and Lipid-Lowering Therapy. Arch Intern Med 165: 1147-1152
9 Benner JS, Glynn RJ, Mogun H et al. Long-term persistence in use of statin therapy in elderly patients. JAMA. 2002; 288:455-61.

REASONS FOR NONADHERENCE

The common perception is that patients are generally nonadherent because they forget to take their medications. While this is an important factor, the reasons for nonadherence to medications are multi-dimensional. A survey of 10,0000 patients conducted by Harris Interactive and the Boston Consulting Group (BCG) in 2002, revealed multiple reasons for nonadherence. (See Exhibit 1)

Exhibit 1 : Reasons for nonadherence

Percentage of patients stating each reason



Source: Harris Interactive, BCG

Percentages do not total to 100 due to multiple and no responses

Majority of nonadherent patients choose to disregard treatment guidelines

As evident, only 24 percent of respondents ascribed nonadherence to forgetfulness. As many as 20 percent of the respondents did not take medications due to perceived side effects, 17 percent felt that drug costs were too high and 14 percent of respondents did not feel that they had to take the prescription, as it would have little or no effect on their disease.

An active disregard for treatment guidelines by the majority of nonadherent patients is ominous for healthcare practitioners and the pharmaceutical industry. Such patients will not participate in conventional adherence programs, which rely heavily on reminding patients to take their prescribed medications on time. Unless the core issues of nonadherence are addressed, "one size fits all" types of programs do not have a high probability of making an impact.

The core reasons for nonadherence need to be addressed to ensure patient participation in programs

Once the reasons for nonadherence have been identified for a brand, it becomes easier to offer a tailor-made approach based on three areas- reminders, education and offsetting costs.

For instance, forgetfulness is best tackled by reminders through directly mailed letters, telephone, emails, text messages to cellular phones and alarms. The fear of side-effects can be overcome by information on what patients can expect when they start therapy, and more importantly, if they can do anything to relieve those side-effects. Inability to pay for medications can be alleviated through a variety of programs including rebates, checks and discount loyalty cards. Similarly, solutions for other reasons for nonadherence can be obtained, provided the causes are identified correctly.

TYPES OF ADHERENCE PROGRAMS

Traditionally, adherence programs have been focused on the following areas - simplifying dosage regimens and delivery, patient education and communication and modifying patient behavior.

Simplifying dosage regimens and delivery is the most commonly used strategy for increasing adherence. Adherence improves exceptionally when a patient is prescribed medication that can be taken once a day. Longer acting medications that reduce the frequency of dosing, such as the weekly transdermal contraceptive patch have also been introduced. The route of delivery is also an important factor in ensuring adherence. Patients prefer taking medications orally, rather than suffer the pain of injections. Some programs have also used aids to help patients organize medications such as pillboxes, alarms and other microelectronic devices. Lastly, the use of compliance packaging has increased in recent years. This includes blister cards with pill specific calendars and directions for use and patient-friendly inhalers that record the number of doses taken.

Patient education and communication is an integral part of most adherence programs

Patient education and communication has been an integral part of most adherence programs and involves the dissemination of information on the drug, disease and other relevant aspects of therapy. This takes the form of direct mail, brochures or cards, CD-ROM, media promotion (television, radio, print, and internet); contact centers and online communities and forums. These programs may also include nurse and pharmacist outreach programs, patient peer group support and family counseling. Patients can also be sent reminders to take their medication at the appropriate time through telephone, pager, e-mail and text messaging on cellular phones.

Adherence programs that focus on modifying patient behavior are the most complicated, because they endeavor to address beliefs, intentions, and values to encourage behavioral and lifestyle changes. This involves ensuring that patients understand the severity of their condition and the risks involved if they become nonadherent. After this, patients are educated about the benefits of their prescribed medication and anxieties concerning adverse effects are dealt with. Finally, patients are given positive reinforcement regarding their ability to stay on course with the treatment program.

IMPACT OF ADHERENCE PROGRAMS

Do adherence programs work? The answer is 'yes'. A meta-analysis of trials designed to enhance medication adherence that included 18,922 patients, where 9,604 patients had received an intervention to improve adherence and 9,318 patients served as controls, revealed an increase in adherence of 4-11 percent.[10]

A combination of several different types of interventions is needed in an adherence program

Another meta-analysis to determine the effectiveness of interventions aiming to increase adherence to blood pressure lowering medication, examined 38 studies testing 58 different adherence interventions on 15,519 patients. The studies were conducted in nine countries between 1975 and 2000. Simplifying dosing regimens increased adherence in seven out of nine studies, with a relative increase in adherence of 8 percent to 19.6 percent. Motivational strategies were successful in 10 out of 24 studies with generally small increases in adherence up to a maximum of 23 percent.[11]

10 Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence: American Journal of Health System Pharmacists; 60(7):657-665, 2003

11 Schroeder K. Interventions for improving adherence to treatment in patients with high blood pressure in ambulatory settings: Cochrane Database of Systematic Review; Oct 2005

Thus, no single strategy appears to be the best, due to the multitude of factors that affect a patient's decision to adhere to the prescribed medications. Direct mail, pillboxes, and self-help materials are inexpensive strategies and will produce better adherence rates than standard care alone. However, programs that involve personal contact or counseling with a healthcare provider are generally more effective than programs that rely purely on non-personal intervention such as efficient packaging or automatic reminders.

A combination of several different types of adherence interventions under a single platform is most likely to produce optimal results.

Reliable data, consistency in adherence assessment and longer duration of patient follow-up needed in adherence programs

BARRIERS TO ADHERENCE PROGRAMS

Some of the common barriers to adherence programs are as follows -

Sub-optimal organizational adoption - The frequent changes in marketing and product management within pharmaceutical organizations can create a short-sighted branding approach to the detriment of adherence programs which need to be measured for a minimum of six months to determine effectiveness. Consequently, many adherence programs are not able to survive the tenure of a brand manager. Pharmaceutical companies may also have internal divisions, such as professional and consumer marketing teams who may have differing objectives.

No standard ROI measurement - There can be significant variability among pharmaceutical brands and their implementing organizations regarding ROI measures. Thus, it becomes very difficult to compare programs for different brands or even different programs for the same brand. This lack of consistency in determining ROI margins makes it tough to publicize and replicate adherence program successes within the organization.

*The **why** of nonadherence needs to be addressed*

Concern over privacy issues - Many companies perceive adherence programs as another avenue that could lead to potential violations of patient privacy. This results in a cautious approach towards adherence programs that collect, use and store patient data.

Lack of adherence measurement gold standard - There are various methods for measuring adherence such as patient self-report, physician judgment, pill count calculation, pharmacy records and microelectronic monitoring devices. The lack of a gold standard method of measuring adherence has been cited as a major barrier in adherence research. To increase the veracity of adherence programs, what is needed is more reliable data, more consistency in adherence assessment and longer duration of patient follow-up.

Lack of qualitative insights - Most prescription tracking methodologies, merely deal with the problem of nonadherence on a quantitative basis by counting the number of prescriptions filled. They do not provide insights into why nonadherence takes place based on the attitudes, beliefs and values of the patients. Programs that endeavor to address the why of nonadherence will be more effective.

CURRENT ADHERENCE INITIATIVES

There are several adherence programs being conducted by various stakeholders - pharmaceutical manufacturers, managed care companies, drug distributors, retail pharmacy chains, medical researchers and health care providers. Most of these programs involve multiple stakeholders that increase synergy for optimal results.

Involvement of multiple stakeholders required for the success of adherence programs

One of the largest, controlled intervention studies to assess the effectiveness of adherence programs is currently ongoing. The primary aim of this Open Label Primary Care Study: Rosuvastatin Based Compliance Initiatives To Achievements of LDL Goals (ORBITAL) study is to determine the long-term cost-effectiveness of a compliance-enhancing intervention in a total of 7598 patients with hypercholesterolemia (HC).[12] The study comprises of a one-year intervention period for administering the adherence program and a two-year follow-up period.

As a part of the adherence program, patients were sent a starter pack that included a videotape and an educational brochure with information on HC and other risk factors contributing to cardiovascular disease, information on a help line and website, and labels for treatment reminders. Further components of the adherence program are applied in two parts: the first throughout the initial 6 months and the second (booster) throughout the last 3 months (months 10 to 12) of the intervention phase. These include - (i) standardized telephone calls from a call center at weeks 4, 11, 18, 24, 43, and 52 to emphasize the initial education; (ii) standardized letters delivered in weeks 6, 9, 13,16, 20, 22, 41, 46, and 49 forming a pattern of repeated instruction and provide additional information; (iii) a toll-free help line to answer questions and discuss worries; and (iv) a website with information about HC, its treatment, and other important links.

The sequential study design which includes an initial intervention and subsequent observation phase combines the benefit of a controlled trial, focusing on the efficacy of compliance-enhancing tools, with that of outcomes research, focusing on long-term effectiveness in the setting of general medical care. The study also includes a detailed primary health economic evaluation and a cost versus benefit comparison of the adherence program which may justify the potential cost of establishing such a program into general medical practice.

12 Willich SN, Muller-Nordhorn J, Sonntag F, Voller H, Meyer-Sabellek W, Wegscheider K, Windler E, Katus H. Economic evaluation of a compliance-enhancing intervention in patients with hypercholesterolemia: design and baseline results of the Open Label Primary Care Study: Rosuvastatin Based Compliance Initiatives To Achievements of LDL Goals (ORBITAL) study: Am Heart J. 2004 Dec;148(6):1060-7.

DRUG DISCOUNT LOYALTY CARD PROGRAMS

Pharmaceutical companies have attempted to enhance adherence by providing patients with price discounts in the form of debit cards, checks, rebates and pharmacy loyalty cards. The use of financial incentives resulting in increased adherence was affirmed by 10 of 11 research studies.[13] The primary drawback of this scheme is the potential for fraud and abuse (for example, a patient using the funds for a transaction other than the prescription), which motivated stakeholders to develop newer programs that could directly tie a discount to a patient's prescription.

Drug discount card based adherence programs go beyond providing only financial incentives.

The next generation programs require a national network of retail pharmacies and provide a variety of adherence tools, including co-payment discounts at the point-of-sale. These discounts can be adjusted based on the patient's insurance benefit structure resulting in real-time, customized discounts that can be tied directly to the prescription.

Pharmacy loyalty card programs go beyond providing only financial incentives. These programs incorporate many of the traditional patient communication initiatives, offering them across a multitude of channels such as telephone, the Internet, interactive voice response systems and direct mail. But, because newer discount card programs offer visibility into prescription fulfillment behavior, communication interventions can be delivered according to patient fulfillment behavior, resulting in more timely and effective interventions.

In addition, next generation pharmacy loyalty card programs provide patient-level prescription, pharmacy and physician data that can be combined with third party data sources to produce comprehensive analyses of adherence rates, return on investment, and other metrics to provide brand teams actionable data. Over time, as the program's database becomes more robust, program elements can be modified based on their ROI. For instance, if mail or telephone based interventions fail to produce an ROI for a specific patient segment, email based interventions could be adopted for this segment. Furthermore, the data and ROI metrics that these programs are able to generate may provide an important benefit for pharmaceutical marketers seeking to bolster internal support and credibility.

Patient-level data can provide a comprehensive analysis of adherence rates, return on investment, and other metrics.

Thus, next generation pharmacy loyalty card programs provide a viable platform that brings multiple adherence initiatives under one umbrella and address the common barriers, discussed earlier. A multi-pronged approach has been found to be more effective in ensuring adherence and persistence. More importantly, patient-level prescription data answers the 'why' of adherence, allowing customization of initiatives and avoiding the 'one size fits all' trap. Lastly, by providing standardized ROI metrics, they enable pharmaceutical companies to promote the success of adherence programs and overcome organizational barriers.

13 Giuffrida A, Torgerson DJ. Should we pay the patient? Review of financial incentives to enhance patient compliance: BMJ 1997;315:703-707

PRESCRIPTION FOR FUTURE SUCCESS

Some of the common failings of adherence programs have been to rely heavily on busy physicians for implementation; a one size fits all approach; one-way communication with patients; and sole dependence on non-personal elements such as direct mail. A new approach is needed to ensure the success of future programs. While earlier programs have been limited to patient acquisition, the next generation programs are focused on patient retention and loyalty.

Key elements of successful adherence programs are tailored interventions by patient profiles and disease segment, addressing multiple barriers to adherence instead of only one or two and designing and delivering messages that will allow patients to stay on therapy, such as how to overcome medication side effects.

Pharmaceutical companies and other stakeholders should start benchmarking and propagating the successes of adherence programs across therapeutic classes. An ideal adherence program team should include members from professional and consumer marketing, managed care, clinical affairs and trade relations, within the pharmaceutical company. On the outside, key opinion leaders, patient advocacy groups, managed care organizations, payors, drug distributors, nurses and pharmacists should be actively involved. It will require the concerted effort of all stakeholders, to ensure the success of adherence programs and a win-win for all involved.

This is the first in a series of two white papers on patient adherence developed in co-operation with McKesson Specialty. In the second white paper to be published in early 2006, we will profile and analyze some of the key adherence programs that have resulted in measurable success for stakeholders.

Start benchmarking and propagating the successes of adherence programs across therapeutic classes

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