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White Paper

Practical Solutions to Adherence

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Introduction

To quote C. Everett Koop, M.D., the former U.S. Surgeon General, "Drugs don't work in patients who don't take them."

The high level of non-adherence in the U.S. today poses a major obstacle to achieving optimal health outcomes for patients and a major challenge for the pharmaceutical industry. While it is clear that the pharmaceutical industry does care about non-adherence and is spending money to address it, the sad fact is that this investment may be at best ineffective and might even be counterproductive.

The scope of the problem is well documented.

- 33% of prescriptions are never filled
- 50% of patients with chronic conditions are non-adherent
- $1.5 billion is lost in earnings; $50 billion is lost in productivity
- 36% losses in sales for the average drug due to non-adherence
- $30 billion shortfall in sales for the pharmaceutical industry as a whole

The Human Cost

The National Council on Patient Information and Education (NCPIE) report (the source for the figures cited above), "Enhancing Prescription Medicine Adherence: A National Action Plan," pegs the costs for poor medical adherence at approximately $177 billion annually. Included in the report:

"In the United States non-adherence affects Americans of all ages, both genders, and is just as likely to involve higher-income, well-educated people as those at lower socioeconomic levels. Furthermore, since lack of medication adherence leads to unnecessary disease progression, disease complications, reduced functional abilities, a lower quality of life, and even premature death, poor adherence has been estimated to cost approximately $177 billion annually in total direct and indirect health care costs."

Of the $177B cited, hospital admissions represented $121.5 billion (69%) per year, and long-term care admissions represented $32.8 billion (18%). Physician visits accounted for another $13.8 billion (8%), and emergency department visits and additional treatment cost more than $5.8 billion (3%) and $3.5 billion (2%), respectively.[1]

Challenges Facing the Industry

Early attempts by the industry to tackle non-adherence have focused on patient education, prescription reminders, and incentives. While these have had some short-term successes, they have done little to address the deeper issues of non-adherence. One reason is that people who sign up for a non-adherence program are more than likely reasonably adherent to begin with. These "hand raisers" are quite definitely not the major problem. With minimal support and encouragement, their continued high level of adherence is likely assured. The major problem lays with the "non-hand raisers" and the reasons why they do not initiate or why they quickly fall off medication regimens.

Generally speaking, about 20% of patients will effectively comply with a medication regimen if their physician asks them to and another 20% will not, no matter what steps are taken. It is extremely hard to move these two

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White Paper

groups away from their core behaviors – nor would we want to discourage the former group for that matter. However, the other 60% of patients present an opportunity to pursue individual causes of non-adherence and to find solutions that effectively change the behavior of potential non-adherents. Changing behavior is no trivial task; one has only to look at the classically unsuccessful health campaigns geared to smoking cessation or obesity prevention.

A compounding factor may likely be a result of the considerable investment in DTC (Direct to Consumer) advertising, designed to urge patients to ask their physician about a pharmaceutical brand. Some of these more aggressive marketing practices have backfired, however, and have caused the public to develop a distrust of the industry and to view any efforts that it may make to provide patient education as self-serving. The advent of health-related social networking sites and burgeoning information resources available online have only served to increase patient concern. Social networking sites, while offering a rich array of patientlevel comments and advice can be alarming places for those people still undecided or uninformed about a particular course of therapy. In many cases, the negative feedback from fellow patients far outweighs the positive. Pharmaceutical companies have been trying to find a way to engage with patients in this new social media world, but have found themselves compromised by the overwhelming number of potential adverse events which, once identified to the manufacturer, must be reported and acted upon appropriately.

For a long time, the goals for pharmaceutical sales growth were met by development and marketing of new drugs. Budgets were structured around heavy promotion of new products while programs addressing nonadherence took second place. To use the analogy of a leaky bucket, with the holes representing nonadherence, if water is poured quickly enough into the bucket, it remains full despite the fact it is losing water. This strategy has worked for years. However, the industry's pipeline of blockbuster drugs is not as robust as it once was and the traditional sales model is under attack on many fronts.

The shrinking pipeline of new blockbuster drugs and the changing world of pharmaceutical marketing have turned the attention of the industry. The new paradigm is "patient centric" and the new target of opportunity is non-adherence.

Taking Positive Steps

Today, adherence has become a frequent topic of discussion in the pharmaceutical industry, and many companies are exploring or implementing new techniques to address it. Nursing hotlines are being expanded to accommodate adherence programs and new technologies have been developed and are under examination. Recent product developments include combo packaging for multi-course regimens, E-pill prescription reminders to keep patients on track, and telephone reminder systems.

Below are two very different examples of how technology can help improve adherence:

- In South Africa (where 80 percent of the population has mobile phones), 300 individuals with tuberculosis were enrolled in a text message-based support program. The patients had fairly complex medication regimens which involved taking four tablets, five times a week for six months. The poor adherence associated with this treatment regimen resulted in low cure rates and increased the incidence of multi-drug resistant strains. To improve adherence, SAS messages containing tips, jokes, and pearls of wisdom were relayed to patients. Despite the fact that many patients came from disadvantaged socio-economic backgrounds which presented multiple challenges to their adherence, 295 of the 300 enrolled were adherent as a result of the program. This case was so successful that the World Health Organization designated it as "best practice."[2, 3]

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- A recent Allergy & Asthma Network Mothers of Asthmatics study of 500 families showed that 25% found their metered dose inhalers empty when they needed to use them. To resolve this lifethreatening problem, a single-increment dose counter was used to improve dose tracking, forgetfulness, and communication with health professionals.[4]

While these solutions are interesting, they may not be adaptable and scalable to all medication regimens and treatment challenges. For an adherence program to be successful it must accommodate each patient's particular barrier to each medication and be capable of addressing (and to some degree, anticipating) common medication challenges.

Following is a guideline of the essential elements of a successful adherence program.

Creating a Comprehensive Program

A comprehensive adherence program needs to accommodate a variety of easy access "on-ramps," or points at which a patient might be engaged to enroll in a program to support their initial and ongoing decisions about their condition and treatment plan. Given the multiple channels and tools available and the variety of consumer interests, motivational levels, and behavioral challenges, no single on-ramp is sufficient; every program should include multiple approaches. Four basic rules for success are:

1. Engage patients on a variety of fronts · Physician's office: For the physician to encourage participation if he/she suspects that the patient is struggling with adherence
    - Pharmacy: Loyalty card fulfillment shows which patients are refilling their prescription
    - Websites: Both product sites and condition websites can catch patients when they are gathering information or making decisions about whether to start or refill a prescription.
    - Advertising: Engage patients at all stages and venues of their treatment lifecycle
    - Waiting room: Brochures or video messages designed to reach patients at that "teachable moment"
    - CRM programs: Offer patients condition and medication education and/or loyalty incentives
2. Analyze the demographics of the likely patient population for each specific drug. Identify possible "on-ramps", where it might be possible to engage patients, and bring them into the program.
3. Interact with patients using diverse technology-based frameworks. While older methods – having nurses call individual patients, for example – are not cost effective for large populations, Web-based and IVR (interactive voice) programs are increasingly sophisticated in accommodating personalization and can support high volume at modest costs.
4. Interact with each patient several times over four to six months and preferably longer. Every drug has a "cooling off" period when non-adherence becomes an issue. Some drugs, such as anti-depressants, may cause side effects before patients experience benefits. To counteract this, plan for relevant interactions/interventions scheduled around that critical falling-off period. For example, if a medication is known to have a major drop in use around month three, then structure the program to engage the patient intensively around that period of time.

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Map and Monitor Patient Experience

Three factors can be analyzed to provide an expected adherence profile for each patient.

- Patient's previous history in managing various treatment regimens
- Level of motivation to undertake this particular treatment regimen
- Level of confidence in their ability to manage this treatment regimen

When designing an adherence program, it is important to work with patients to identify and overcome barriers which may arise during the medication regimen. By continually checking motivation and confidence levels, as well as understanding about the medication, potential barriers can be identified and circumvented. At specific times throughout treatment, offer plain language, useful support mechanisms that allow patients to achieve adherence and get over any hurdles they encounter during their treatment. It is equally important to let patients know how successful they have been and to "graduate" them from the program once adherent behavior has been achieved.

Each medicine presents its own unique set of characteristics, which can in some cases be problematic and pose a barrier to adherence. For example, one pharmaceutical manufacturer launched a cholesterol medication which caused some patients to experience significant flushing (becoming markedly red in the face and often other areas of the skin). The symptom appeared suddenly and resulted in a significant dropoff in medication adherence. What patients did not realize was that the symptom was transient, quite harmless and could be tolerated with a few coping skills. In this case the manufacturer introduced a treatment education program which specifically addressed the flushing issue with the patient prior to the usual time frame in which the side effect occurred. The result was a dramatic improvement in adherence to the prescribed medication regimen.

Pharmaceutical companies are in the best position of any stakeholder to supply accurate and reliable health information about the medicines they develop, manufacture, and market. Data gained from preclinical research and regulatory documentation can serve physicians well as they help patients to understand the optimum use of drugs, how to manage side effects, minimize risks and maximize benefits by adhering to medication regimens.[12]

Managing patient expectations includes communicating the concept of risks versus benefits. The National Council on Information and Education (NCPIE) has been trying to educate patients about just that. Several years ago, NCPIE, the FDA, and about a dozen other organizations (including the trade association PhRMA) came together to draft a common message to consumers:

"The benefits of medicines are the helpful effects you get when you use them, such as lowering blood pressure, curing infection, or relieving pain. The risks of medicines are the chances that something unwanted or unexpected could happen to you when you use them. Risks could be less serious things, such as an upset stomach, or more serious things, such as liver damage. When a medicine's benefits outweigh its known risks, the U.S. Food and Drug Administration (FDA) considers it safe enough to approve. But before using any medicine-as with many things that you do every day, you should think through the benefits and the risks in order to make the best choice for you."

"And that depends on your particular situation. You must decide what risks you can and will accept in order to get the benefits you want. For example, if facing a life-threatening illness, you might choose to accept more risk in the hope of getting the benefits of a cure or living a longer life. On the other hand, if you are facing a minor illness, you might decide that you want to take very little risk. In many situations, the expert advice of your physician, pharmacist, or other health care professionals can help you make the decision."

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One Size Doesn't Fit All

Because patients differ so markedly in individual behavior, it is important to segment them effectively before designing an adherence program for any particular product. Some assumptions have to be made in order to focus energies and budget dollars where they can be the most effective: The top 20 percent who are already treatment-adherent and will remain so do not need an adherence program; the bottom 20 percent who are stolid non-adherents will probably not respond no matter what steps are taken. It is the large middle group, the 60 percent who desire to be on their medication, but who are experiencing challenges, which will yield the most positive results in an adherence program.

By carefully structuring early patient dialogue, patients can be divided into subgroups according to tendencies centered on adherence, each with a separate pathway through the program. Weak adherence programs typically focus on only one barrier, such as tools to combat forgetfulness with blanket reminders, and so are not applicable to all patient subgroups. For example, if emotional factors are largely responsible for non-adherence, reminder programs will be completely ineffective.[5]

By tailoring the adherence strategy's approach to each patient segment, the program is more likely to be effective when complex sets of behaviors exist over extended periods of time, particularly in situations where patients have chronic conditions – for example, asthma, hypertension, diabetes and osteoporosis – that require significant lifestyle changes and long-term commitments. Tailored strategies allow intelligent allocation of resources to patient segments that are more likely to respond more positively.[6]

Understanding and Removing Barriers – both Revealed and Derived.

The National Council for Patient Information and Education (NCPIE)[7] has laid out a recommended framework for a comprehensive adherence solution which combines education, motivation, and monitoring. The Council also identified the existence of multiple barriers which need to be tackled independently in order for the program to succeed.

Each intervention should start by looking at adherence history: namely, whether patients have taken their previous medications all of the time, some of the time, or none of the time. This is an important predictor of future behavior. Then patients should be asked about specific barriers known to be problematic in the disease category or with a specific medication. These are known as revealed barriers because each barrier is presented to the patient, who then determines if it has been a problem. The following are some common revealed barriers:

- Concern about side effects
- Poor communication with physician
- Health conditions, such as cognitive problems, that affect adherence
- Doubts about and/or not valuing medication
- Cost of medication
- Forgetfulness
- Difficulty refilling the medication
- Keeping track of a complicated regimen

Then it is important to consider motivation and confidence. If a patient has poor motivation or low confidence in her/his ability to take medications regularly, the risk for non-adherence or relapse increases. Low confidence in being able to adhere can be a result of practical roadblocks such as high co-pays, inability to acquire medication if housebound, or cognitive impairments. Low motivation usually results from barriers such as concern about side effects, physician communication problems, denial about the

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condition, or questions about the value of the medication. By assessing motivation and confidence, one can indirectly determine which barriers might be problematic, even if the patient would not admit to the barrier. These are therefore called derived barriers. Each patient is unique and many individuals are often trapped in life situations that make adherence difficult. Understanding and then addressing these barriers has the potential make a profound difference in treatment outcomes for these patients.

Patient-Physician Communications

The quality of the relationship between the physician and the patient plays a key role in patient medication adherence. This relationship starts with the effectiveness of communication and the resulting degree of comprehension concerning the prescribed treatment regimen and is underpinned by the level of trust that the patient has in the physician. In today's busy world the time that physicians get to spend directly with each patient has often been shown to be continually diminishing. Authority plays a key role as well. Older patients tend to accept unconditionally what the physician says and are often more inclined to take their medication if the physician tells them it is important. Younger patients, on the other hand, who rely on the vast information resources (both accurate and suspect) that the Internet provides, may uncover opinions that compromise the physician's advice.

Trust issues aside, treatment communication between physician and patient are not always ideal. According to an Archives of Internal Medicine study in 2006, patients who are given more information and who discuss their medication regimen with their physician are more likely to be adherent.[8] Five different variables were measured: name of the medication, purpose, duration, dosage (amount/frequency), and adverse events. The study concluded that thirty-eight percent of essential elements were not communicated. This is an overwhelming hurdle at the initiation of the patient journey that only serves to exacerbate the patient-specific challenges that each new medication regimen brings.

In comments to the FDA, the AMA (American Medical Association) advocated ways in which the pharmaceutical industry could improve the communication of risk and side effects information, from prescriber to patient.

"Pharmaceutical companies should be obliged to train and send their sales forces to physicians to educate them on important new risk information about company products. The company should provide incentives to sales representatives to do this because the highest priority of any company should be to prevent harm to patients who use their products. The effectiveness of the 80,000 pharmaceutical sales representatives in the United States in promoting the benefits of their companies' products is well documented, and they could have similar success in educating physicians about important product risks."

Proactive Education for Patients Sets the Stage for Adherence

Pharmaceutical companies struggle with effective ways to communicate a balance of information about a medication's benefits and risks. When helpful and complete information is clearly outlined to patients up front, they are able to anticipate, identify, and react appropriately. Armed with this information, they are able to understand changes in symptoms and anticipate side effects, either dismissing the symptoms (because they understand they will subside) or calling their physician when needed. As indicated earlier when discussing a program that educated patients proactively on a common side effect (flushing) when using a particular cholesterol medication, this approach reduces patient anxiety and increases adherence. Getting information that is balanced also increases patient trust in their medication, something the industry desperately needs to restore.

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The Consumer Health Information Corporation feels strongly that information provided in patient inserts, DTC ads, and collateral must be written in a style that makes sense to patients. If symptoms are described in ways that are not meaningful from a patient's experience, then the warnings are not helpful. For example, instead of simply listing "liver dysfunction" as a potential side effect, The Corporation suggests being quite specific to the patient about what warning signs to look for and recommends that the educational materials provided help patients understand when and how they should manage side effects themselves or when it is advisable to call the prescribing physician.[9]

Map and Monitor Patient Experience

In addition to educating patients, for any program to be successful it is imperative to keep the physician informed and in the loop. Very few adherence programs today fully address this critical need, dealing exclusively with the patient despite the physician's demonstrable influence on patient behavior. Physicians for the most part are appreciative of the receipt of net new information about their patients and are usually happy to incorporate interim reports into each patient's medical record. The content of the reports which are fed back can radically accelerate physician understanding of the product and thereby increase confidence in subsequent prescribing and support.

Return on Investment (ROI) - Program Design

While much investment has been made in adherence support for patients, a nagging doubt lingers about the ROI that such programs yield, compared to other marketing initiatives.

If we accept the 20-20-60 rule (20% of patient will fall off therapy no matter what, 20% will stay on therapy no matter what, and 60% are open to persuasion one way or another), then clearly the ROI is only as good as the program's ability to reach the 60% before they take a non-adherent turn. Most programs attract the hand-raisers (20%) who are already compliant and will stay that way. Few programs effectively capture the 60% and fewer still have a customized response to the different challenges experienced by this group.

Unless a program can identify and respond to individual barriers, a huge percentage of patients will be excluded from successful participation and results will be garnered from the few barriers or single barrier that are addressed. Herein lays the problem with many adherence programs: isolating and addressing only a small subset of adherence issues significantly impacts ROI.

Patient feedback programs have proven remarkably effective at improving adherence and they offer the capability for customization for the brand and individualization for the patient. Results from adherence deployment of patient feedback programs indicate a capability for radically accelerating and amplifying ROI. A recent adherence program designed to educate and support patients with their cholesterol medication successfully increased adherence 17-26% over matched controls. When physicians participate in these programs and see the benefit of the additional education, support and its positive effect on their patients, it elevates the profile of that medication in the office. This improved "medication profile" means that the physician, nursing and office staff are stimulated with positive treatment messages through ongoing and credible information from their own patients about their experience starting and staying on the prescribed treatment. The physician receives reinforcement of his/her prescribing decision and feels confident prescribing the medication and recommending the program to other patients as well. This will likely result in a second source of ROI - increased new prescription writing. In the adherence program mentioned above, there was

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a 17% increase in new prescriptions written by doctors participating in the program compared to matched controls, generating estimated incremental revenue of $7.4 million.

Conclusion

"Everyone in the health care system has a significant role to play in improving prescription medicine adherence. Thus, an agenda that removes the barriers and advances education and information sharing is a critical step to improving the health status of all Americans. Clearly, the time for action is now."[10]

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NCPIE remains a leading organization in helping to support improved medication adherence and safe use. NCPIE is a coalition of over 100 diverse organizations whose mission is to stimulate and improve communication of information on appropriate medicine use to consumers and healthcare professionals.

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