NONCOMPLIANCE WITH MEDICATIONS

AN ECONOMIC TRAGEDY WITH IMPORTANT IMPLICATIONS FOR HEALTH CARE REFORM

Although pharmaceutical therapy accounts for only about five percent of our total national health care expenditures, better use of medications by patients can realistically result in clinical savings that amount to more than the original cost of the drugs.

Accordingly, a major focus of health care reform proposals should be improving quality control in the prescribing, dispensing and taking of medicines. Mobilizing patients' responsibility for their own pharmaceutical care is key to improving compliance with medication regimens and managing costs systemwide.

A REPORT BY THE TASK FORCE FOR COMPLIANCE

November 1993 Revised April 1994
Executive Summary

Patients’ failure to take prescribed medications correctly is pervasive and often results in any of three negative effects on their health status. Patients may fail to improve, worsen, or relapse, and each effect has a negative economic impact on the entire healthcare system. Recent surveys on the issue of noncompliance have found that patients often fail to have their prescriptions filled and often discontinue their medication too soon. The consequence of these behaviors is a multi-billion dollar burden on the American economy. Costs of hospitalization and physician visits caused by relapse from noncompliance account for $8.5 billion in otherwise unnecessary spending. Research on other effects of noncompliance, such as lost work days, also reveals huge, but largely hidden, costs to multiple systems—including manufacturing costs.

Although pharmaceutical therapy accounts for five percent of the $900 billion spent on U.S. healthcare, noncompliance accounts for up to $100 billion in health care and productivity costs. A concerted effort to increase patient compliance can result in significant savings to the U.S. economy. From this economic perspective, it is important that health care reform proposals include programs designed to improve patient compliance with medications.

Recent research indicates that healthcare delivery and reimbursement systems will benefit when patients receive information on the rationale and importance of drug therapy and effective instruction on its use. As changes in healthcare policy are considered, the patient's responsibility for taking medication appropriately and for treatment outcomes should be addressed.
The March 25, 1992 edition of the Wall Street Journal reported the efforts of two pharmaceutical companies (ICI Pharmaceuticals and Searle) to improve the compliance rate of patients taking some of the companies’ leading prescription products. These efforts, which include such tactics as regular phone calls to remind patients about refills, newsletters to users, and a toll-free number for patients’ inquiries, are costly, but the investment has an enormous potential to improve health care and reduce overall costs. The costs of noncompliance with medication regimens are tremendous and affect all players in the health care system—manufacturers, pharmacies, employers, third-party/managed care programs, society as a whole, and, of course, patients and their families.

Failure to take prescribed medications correctly is pervasive, and may have any of at least three negative medical (and attendant economic) effects. The patient may fail to improve, worsen, or (especially in long-term therapy) relapse. In a recent comprehensive review, for example, Turk and Rudy (1991) found a clear relationship between noncompliance with medications and relapse in patients with arthritis, various types of pain, and severe headache.

A Case in Point

An advertisement appearing in the spring of 1992 shows a physician observing, “When my patients don’t return, I assume the therapy is working.” On the facing page, one of those patients says: “I couldn’t tell my doctor his migraine therapy didn’t work.” The text of the ad cites data indicating that nearly half of all migraine sufferers have given up on their physicians either because of failure to improve or because of side effects of the medication prescribed. This example illustrates the complexity, subtlety, and importance of the compliance problem. The potential consequences of this particular situation with migraine include:

- Physician misjudgment of the effectiveness of his/her therapy, in this case probably resulting in repeats of this scenario with the next medication prescribed for this patient;

- Loss of confidence by the patient in the effectiveness of medications and perhaps in the skill of the physician;

- Continued migraine attacks with continued erosion of the quality of life of the patient;
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- Loss of patient productivity (One estimate, cited in the ad, found that annual lost productivity from migraine attacks fell in the $6 to $17 billion range);
- Cost of other therapies, including over-the-counter medicines, used by the patient to “try to cope,” but to no avail.

This report provides some background on the economics of noncompliance with medication regimens and strategies that can be used to improve compliance.

The Problem

Although medicines comprise only about five percent of our total national health care expenditures, their appropriate use by patients can result in substantial savings by reducing the need for more expensive medical treatment. Unfortunately, medications are not generally taken properly. Patients miss doses, stop taking medication prematurely, misunderstand instructions, and swap medications with friends and relatives. The five most common types of noncompliance are:

1. not having the prescription filled;
2. taking an incorrect dose;
3. taking the medicine at the wrong times;
4. forgetting to take one or more doses; and
5. stopping the medication too soon (Burrell & Levy, 1985).

This behavior has important therapeutic consequences and often results in the failure to control the symptoms and progress of the disease. Noncompliance with medications is especially problematic in chronic diseases that are not associated with any symptoms and in diseases in which the symptoms occur erratically (e.g., mental disorders, cardiovascular diseases, asthma, glaucoma, osteoporosis, and epilepsy).

Noncompliance is common in patients of all ages and across a wide range of diseases. There is generally no correlation with age, sex, socioeconomic status, or level of education.

A recent study of “The Forgetful Patient” by Schering Laboratories (The Schering Report IX, 1987) revealed the following patterns of noncompliance:

- Seven percent of patients did not have their prescriptions filled.
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- Fifteen percent of patients admitted to discontinuing their medication too soon.
- Thirty-two percent of patients, told by their doctors to have their prescriptions refilled, failed to do so.

Even those patients who fill and refill their prescriptions appropriately may have lapses in the continuity of their dosing pattern. Many patients take what has been termed “drug holidays”—two-to four-day interruptions in dosing. These holidays are responsible for breakthrough seizures in epileptic patients and for unwanted conception in patients using oral contraceptives (Dirks and Kinsman, 1982).

One in five patients who receives a prescription medication cannot read the label. Some 20 million American adults are illiterate and another 20 million are functionally illiterate to the extent that they cannot comprehend the information. The elderly are particularly likely to have difficulty in reading, in that they tend to have impaired vision and often cannot distinguish the print and certain colors on prescription labels. The elderly are also more likely to have more serious illnesses and must often take multiple medications.

The problem of noncompliance will escalate as the number of elderly persons increases. Currently, one out of every four prescriptions written is for a person who is 65 years of age or older. Diseases of the elderly tend to be chronic, and noncompliance with treatment regimens is more of a problem in chronic as opposed to acute conditions.

Failure to Fill Prescriptions

One important aspect of noncompliance is the failure to fill or refill prescriptions. Nearly 30 years ago, Hammel and Williams (1964) reported that 3.3% of patients never filled newly issued prescriptions. In 1975, Taubman et al., using triplicate prescription forms to track filling behavior, found that approximately 6% of new prescriptions issued were never filled.

The refilling of prescriptions for chronic diseases (e.g., heart conditions, arthritis, asthma) is also a problem. Refilling prescriptions is especially important for the elderly, who, since their diseases tend to be chronic, receive refill authorizations at more than twice the rate of younger persons. Refill noncompliance is also important for other (nonelderly) patients needing chronic medications.
For example, Elixhauser et al. (1990) found, for patients with depression, that less than 70% of authorized lithium prescription refills were obtained between the first and second office visits. The dropoff rate for refilling prescriptions for chronic diseases may reach 75% after one year. Typically, hypertensive patients refill only about 60% of their yearly prescriptions.

A 1988 study of pharmacy services conducted by the Upjohn Company reported that nearly one out of five (19%) consumers interviewed said that at least once in the previous 12 months they had received a prescription and had not filled it. Figure 1 shows the reasons they gave for not filling the prescription. Three-fourths of the time, they either felt they did not need the medicine or did not want it. Similar reasons for not filling prescriptions were given by respondents in a survey by the American Association of Retired Persons (AARP, 1992, Figure 1).

Logic suggests that the cost of the medication might be a factor in failure to fill prescriptions. But in the Upjohn survey only 10.5% of the respondents mentioned cost as a factor in their failure to have a prescription filled. Similarly, in the AARP survey only 14% of elderly respondents who did not fill a prescription cited cost as a reason. Among those who reported that they stopped taking the drug before it ran out or consumed less than the prescribed dose, only 2-4% cited cost as a factor (AARP, 1992). Overall, among the four types of noncompliance reported (failure to fill, failure to take after filling, stopping medication before it ran out, taking less than prescribed dose), cost was given as a reason by only 7% of respondents (AARP, 1992).

Studies of the effect of patient cost sharing have shed some light on the degree to which cost is a deterrent to prescription filling. In these studies patients were required to "copay" out-of-pocket part of the cost of the medication. In one study (Harris et al., 1990), prescriptions filled by employed HMO patients were subjected to two successive, small copayments of $1.50 and $3.00 over a three-year period. This resulted in a 21% reduction in prescription fills, but mostly for drugs used for symptomatic relief (e.g., pain killers, cough and cold preparations, muscle relaxants). Prescription filling rates for drugs with important effects on health status (e.g., for high blood pressure, heart conditions, diabetes) were reduced to a far lesser extent.

Cost sharing is likely to represent a greater disincentive to fill a prescription for economically disadvantaged persons. Imposition of a small copay ($0.50) on South Carolina Medicaid patients reduced prescription filling rates for important medications, such as cardiovascular and psychotherapeutic drugs (Reeder and Nelson, 1985). But in New Hampshire, a $1.00 copay caused only a minimal reduction in prescription filling by Medicaid patients (Soumerai et al., 1987). These studies suggest that cost may be a significant deterrent to filling prescriptions by our poorest populations.
Note: Multiple responses allowed.

AARP Survey

Noncompliance With Medications: An Economic Tragedy

Upjohn Survey

Figure 1.

Why Prescriptions Are Not Filled
Important areas for future research on prescription filling behavior include efforts to determine:

- Relationships between prescription filling and cost for different diseases, severity of disease, and socioeconomic status;
- The extent to which different levels of patient copayment for prescriptions (cost sharing) in third-party programs influences filling rates;
- The effect of triplicate prescription forms for benzodiazepines (tranquilizers) on prescription-filling behavior.

**Underuse and Overuse of Medicines**

There are literally hundreds of reports describing poor compliance among patients with various medical conditions. Both overmedication and undermedication are common results of poor compliance. Overmedication may lead to increased adverse effects and increased hospitalization (Schernitzki et al., 1980). Undermedication may lead to inadequate treatment of the disease, resulting in complications, an increase in the severity of the disease, and hospitalization or rehospitalization. The data in Table 1 indicate the relative frequency of overmedication compared to undermedication, collected in several studies. The differences in relative frequencies of over- and undermedication among the three studies cited in Table 1 may reflect differences in sample populations and methodologies. Nevertheless, the data suggest that both overcompliance and undercompliance are common.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Overuse/Underuse</td>
<td>1.7</td>
<td>0.36</td>
<td>0.75</td>
</tr>
<tr>
<td>Ages 65+ Ages 0-64</td>
<td></td>
<td></td>
<td>0.45</td>
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Values over 1.0 indicate overuse exceeds underuse; values under 1.0 indicate underuse exceeds overuse. The data of Latiolas & Barry and Malahy is from outpatient populations; the data of Leroy & Morse is from drug-related hospital admissions of Medicaid patients.
A sampling of medication compliance rates for chronic conditions is shown in Table 2. In all of these studies, the noncompliance behavior studied was *under*compliance, i.e., the process of taking a medication at a level or for a duration less than that intended by the prescriber. *Overuse* of prescription medications (sometimes called hypercompliance) has a cost as well. This can take the form of expenditures for prescription medication not really needed or an increased incidence of side effects and adverse reactions. It is equally important to correct both underuse and overuse of medications; best use is the goal.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate of Noncompliance</th>
<th>Possible Consequences</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Epilepsy</td>
<td>30-50%</td>
<td>Relapse</td>
<td>Leppik (1990)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>55-71%</td>
<td>Condition worsens</td>
<td>Bloom (1988)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>40%</td>
<td>Hospitalization</td>
<td>Clark (1991)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>40-50%</td>
<td>Loss of control</td>
<td>Nagasawa et al. (1989)</td>
</tr>
<tr>
<td>Contraception (Pill)</td>
<td>8%</td>
<td>Unwanted pregnancy</td>
<td>Jones &amp; Forrest (1992)</td>
</tr>
<tr>
<td>Asthma</td>
<td>20%</td>
<td>Attacks, hospitalization (?)</td>
<td>Bauman et al. (1989)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>48-56%</td>
<td>Relapse, hospitalization</td>
<td>Powell et al. (1986)</td>
</tr>
<tr>
<td>Organ Transplant</td>
<td>18%</td>
<td>Rejection, death</td>
<td>Rovelli et al. (1989)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>30%</td>
<td>Bleeding, hospitalization</td>
<td>Joglekar et al. (1988)</td>
</tr>
<tr>
<td>Estrogen deficiency</td>
<td>57%</td>
<td>Symptoms, osteoporosis</td>
<td>Hemminki et al. (1991)</td>
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</table>

**Economics of Noncompliance**

There is no shortage of opinion on the economic effects of failure to fill or to refill prescriptions. The *Wall Street Journal* article cited above noted a cost of $8.5 billion for increased hospital admissions and physician visits. The problem exists in other countries as well. Lauper (1988), for example, imputes a DM $2-3 billion economic loss due to drugs not taken in the Federal Republic of Germany. The *exact* costs, direct and indirect, of compliance failures cannot be calculated. Some components of the total, however, have been estimated.
The economic value of a medicine is closely related to the ease with which patients can comply with the dosing regimen. A more expensive drug can be more useful than a cheaper drug if compliance is better. Worthen (1979) described the construct of a “usefulness product” in a study of the use of timolol in glaucoma patients. Worthen’s premise is simple but basic and can be shown by his example: “...if the drug’s effectiveness is 90% (i.e., works 90% of the time) but the patient’s compliance is only 50%, we can say that the ‘usefulness product’ of that medication is 45%.”

Worthen’s procedure can be valuable in drug comparisons. In his own experience, for example, inexpensive epinephrine is 70% effective, but over time, compliance may be as low as 30%, for a usefulness product of 20-30%. Timolol is more expensive and is only 10% more effective than epinephrine, but it had a compliance rate of about 95%. This results in a usefulness product of more than 75%, or 3.5 times that of the less expensive drug.

Economic Effects of Failure to Fill or Refill Prescriptions

The number of prescriptions dispensed annually in the United States is likely to exceed 2 billion by the year 2,000, although that number would be much higher but for the phenomenon of unfilled/unclaimed prescriptions. Recent statistics suggest that sales consist of about an equal number of new versus refill prescriptions, although these proportions vary significantly by therapeutic class. As the population continues to age and chronic diseases become more prevalent, refills will predominate. Thus, failure to refill will become an increasingly important health and economic problem.

Economic Impact on Retail Pharmacy and Pharmaceutical Manufacturers

If only 20% of all written prescriptions were never filled or refilled, the resulting economic effect would be a loss of more than 400 million prescriptions. The economic impact on the retail pharmacy business is considerable:

- At a $20 average prescription charge, the gross revenues lost to pharmacy would be $8 billion.

- Using only a $4 dispensing fee, pharmacies would still be missing $1.6 billion in revenues with no associated cost of goods sold. That is more than $30,000 in fees per pharmacy per year.
Fedder (1990) studied the fate of some 120,000 prescriptions in just five pharmacies. He found that 77% of authorized refills were never activated—a projected annual loss of $1.5 million!

The Schering Report (1992), based on 2,000 consumer interviews, estimated that failure to fill prescriptions results in “a shortfall at the pharmacy counter of about 140 million prescriptions worth $2.8 billion.” These estimates are based on reports by 8.7% of those interviewed that they failed to have initial prescriptions filled.

All of the losses cited above for pharmacy (aside from the dispensing fee) are also felt by pharmaceutical companies.

Economic Effects of Noncompliance in Clinical Trials

The effects of noncompliance during clinical trials of a drug in development have only recently begun to receive appropriate attention. Noncompliance in this situation has long-range consequences far beyond the few hundred patients who might be involved in the trial. To the degree that noncompliance occurs without a correction factor, it may have effects ranging from failure to gain FDA approval at all to the necessity to increase the recommended dose beyond that which would be required of a fully compliant population. Ironically, an elevated dose may cause a higher incidence of side effects, which may lead to noncompliance.

Urquhart and Chevalley note that “drug trials rarely show the effects of poor compliance, and so reveal average-compliance efficacy.” They describe the phenomenon of “patient-initiated drug holidays” of three or more days during chronic therapy. These holidays, which the authors suggest also occur during clinical trials, are believed to result in added medical costs equal to or greater than the procurement costs of the drugs themselves. Of special interest in this paper is the description of the case of cholestyramine (for high cholesterol), which, because of careful planning in clinical trials, was allowed to be relabeled to reflect the efficacy of the drug in cases of full compliance.

Noncompliance Results in Excess Hospital Admissions

Nonfederal hospital costs in the United States now exceed $225 billion. If only 10% of hospital admissions could be traced to noncompliance, the cost would be $22.5 billion. The following studies provide evidence that the impact of noncompliance on hospital costs is at least this great.

- McEvoy et al. (1984) compared groups of noncompliant and compliant relapsed—and therefore hospitalized—schizophrenic patients. The noncompliant patients
were found to have had a gradual onset of the determinant episode, to have been committed involuntarily, and to remain in the hospital longer.

- In an Israeli study, Levy et al. (1982) identified 2.9% of nearly 1,200 hospital admissions as having been principally caused by noncompliance.

- Kelly and Scott (1990) described a project to improve medication compliance among a group of outpatients with chronic mental disorders. Compliance did improve, and at the end of six months, 33% of the better compliers were in the hospital compared with 45% of a control group whose compliance did not improve.

- Col et al. (1990) reviewed the records of and interviewed 315 consecutive elderly patients admitted to an acute-care hospital. They determined that 11.4% of the admissions could be traced directly to some form of noncompliance. Total cost of these admissions was $77,000 ($2,150 each).

- Green (1988) used a retrospective chart review to compare community mental health center patients having three or more hospitalizations in an 18-month period with a matched group of patients without such hospitalizations. Noncompliance with medications was associated with frequent hospitalization in 92% of the patients.

- Maronde et al. (1989) evaluated the association of underutilization of drugs prescribed for the treatment of hypertension and acute-care hospital readmissions. Controlling for demographic factors and blood pressure, the authors concluded that underutilization of antihypertensive drugs may be associated with hospitalization.

- Sullivan et al. (1990) reviewed several studies and estimated that nearly 2 million admissions annually can be traced to noncompliance.

*Noncompliance Increases Nursing Home Costs*

Some of the most dramatic data on the costs of noncompliance among the elderly come from Oregon. In this study by Strandberg (1984), functional assessment profiles (ability to take care of oneself) of nursing home residents and of people successfully living at home were compared. The single characteristic that best distinguished individuals who were in a nursing home from those who were not was found to be the inability to manage medications. It was more important than the actual health condition. Indeed, 60% of those placed at extreme risk of nursing home
placement had no equally serious impairment other than their inability to manage their own medication. A more conservative view, removing other impairments that were lower on the risk scale, still left nearly 23% who had no high-risk problem other than the inability to manage medications.

Much more research on this issue is urgently needed, but if even 10% of nursing home admissions are related to compliance problems, this represents an annual cost of at least $5 billion (based on a national figure of $50 billion annually for nursing home care).

Table 3.
The Economics of Noncompliance

**Negative Economic Effects of Compliance Behaviors**

- Morbidity costs associated with noncompliance
- Additional medical treatment
- Need/use of additional medications
- Hospital/nursing home admissions or readmissions
- Absenteeism or reduced productivity at work
- Mortality costs - including direct costs and indirect costs associated with lost earnings
- Overcompliance leading to overspending
- Lost revenues to drug companies and pharmacies

**Positive Economic Effects**

- Savings associated with undercompliance with overprescribed medications
- Failure to fill or refill third-party prescriptions resulting in savings to payers

**Summary of Economic Losses**

Some of the economic effects of noncompliance are listed in Table 3. Most of these economic effects are negative, i.e., they add costs to the health care system. An approximation of the overall economic effects of noncompliance is presented in Table 4. There can only be an approximation
at this point because the pharmacoconomics of noncompliance is as yet poorly developed. Even with these limitations, the results are compelling.

<table>
<thead>
<tr>
<th>Table 4.</th>
<th>Annual Economic Costs of Noncompliance</th>
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<tbody>
<tr>
<td>Revenues from unfilled new and refill prescriptions (Retail)</td>
<td>$ Billion</td>
</tr>
<tr>
<td>Hospital admissions linked to noncompliance</td>
<td>8</td>
</tr>
<tr>
<td>Nursing home admissions linked to noncompliance</td>
<td>25</td>
</tr>
<tr>
<td>Lost productivity caused by noncompliance</td>
<td>5</td>
</tr>
<tr>
<td>Premature deaths caused by noncompliance</td>
<td>&gt; 50</td>
</tr>
<tr>
<td>Health costs in ambulatory patients linked to noncompliance</td>
<td>?</td>
</tr>
<tr>
<td>Total Costs</td>
<td>$100 billion plus</td>
</tr>
</tbody>
</table>

Source: Berg et al., 1993

Detecting and Improving Poor Compliance

Despite the enormity and complexity of the noncompliance problem, numerous studies have suggested remedies that may be actionable in the real world. Additionally, the high cost of noncompliance is beginning to attract the attention of various stakeholders who wish to improve compliance rates. The following sections describe methods for predicting which patients will be poor compliers, and efforts to improve medication compliance on the part of pharmaceutical companies, health professionals, and managed care organizations.

Diagnosis and treatment of noncompliance must be based on sound basic research delineating the characteristics and causes of this condition, and on demonstrations of effective interventions. The situation is analogous to the process of developing medicines to treat diseases; basic science knowledge in physiology, chemistry, and molecular biology of the disease forms a solid platform of information from which drug development proceeds.

The existing basic science in compliance comes from many disciplines—behavioral sciences, pharmacy, social sciences, community health, public health, psychiatry, specialty medicine, and others. Among all these disciplines, thousands of research articles have been written about
medication compliance. But all of this activity has not resulted in the emergence of a coherent basic knowledge platform. Much of the available research on compliance is poorly done and, more importantly, usually does not address the key clinical and economic issues. Essential research questions for determining the value of specific compliance enhancement programs should include:

- Does the intervention result in improved compliance and also in improved clinical outcomes?
- What are the direct and indirect savings resulting from improved compliance?
- Do the overall savings resulting from the compliance-enhancing program exceed the costs of the program?

Noncompliance as a Behavioral Disease

It is useful to conceptualize noncompliance as a behavioral disease. This disease model may be useful in helping to develop effective interventions. When all illnesses and treatments impacted by noncompliance are considered, noncompliance is arguably one of our society's most expensive diseases, with yearly costs totaling over $100 billion (see Table 4).

Noncompliance with medications has many features of a disease, including:

- Various risk factors have been demonstrated;
- Depending on numerous patient- and disease-related variables, noncompliance is associated with important variations in severity, morbidity, and mortality;
- Triage is necessary to identify those patients in greatest need of treatment for noncompliance;
- Iatrogenic (doctor-caused) noncompliance is an important aspect of this “disease,” and validated screens are available to identify physicians who need to improve their communication skills;
- Some cases of noncompliance are “curable,” but some are probably not;
- Noncompliance is a public health problem and, accordingly, prevention is a goal.
The noncompliance “disease” can be detected by general screening, using validated demographic, sociographic, and psychographic predictors and questionnaires. The behavior of noncompliant patients and iatrogenic physicians, as identified by these means, can be subjected to detailed examination. Differential diagnosis of noncompliant behavior in patients can be performed by computerized monitoring of refill patterns, and more specifically by analysis of daily pill-taking behavior using microelectronic monitoring devices.

Interventions to treat the “disease” of noncompliance, like that of any other illness, must be tailored to the needs and circumstances of the individual patient, and should be based on underlying causes. Specific interventions with validated effectiveness can be selected. Noncompliance with treatment for chronic disease is itself a chronic disease, and needs sustained or periodic attention.

Importantly, interventions to improve compliance must be subjected to cost-benefit analysis to determine whether, and to what extent, the cost savings resulting from improved compliance exceed the costs of the program. Outcomes studies are required to assess the effect of interventions not only on improving compliance behavior, but also on the overall health of the patient and overall treatment costs.

A scientific approach to the noncompliance “disease” will require well-developed information on each of the dimensions discussed above: risk factors and predictors; differential diagnosis in the individual patient and doctor; effective and specific interventions to improve compliance; and cost benefit analysis and outcomes studies.

Logic suggests that the most efficient approach to the compliance problem is to accurately predict those patients at highest risk and then to use the most specific and effective means to intervene. Choice of intervention should be matched to the type of illness and personality type and social circumstances of the patient.

**Predicting Noncompliance**

At present a great deal is known about some predictors of noncompliant behavior, but very little is known about others. Many studies have been published, but no consensus has been achieved. As a consequence, interventions have resulted in mixed success. Nevertheless, some general risk factors for noncompliance have emerged.

More than 250 social, economic, medical, and behavioral factors have been found to affect compliance (Fincham and Wertheimer, 1985). Studies to date on determinants of noncompliance have
addressed the following types of variables:

- Demographic, such as gender, age, and income;
- Sociographic, such as family stability, support, and size;
- Psychographic, such as attitudes, self-image, and locus of control.

Some of these patient characteristics may be disease-specific (e.g., those affecting cognitive ability), and some are subject to change through professional interventions. But all have value in alerting the concerned health professional to the potential for noncompliance. It is not far-fetched to suggest that a “compliance profile” should be a part of every patient’s medical and pharmacy record. Before that step is taken, however, much more progress in integrating our knowledge of compliance science and patient behavior will be necessary.

A diversity of factors may be predictive of good or poor compliance. Both patient-related and physician-related predictors of compliance are reported in the literature. One approach to synthesizing the existing research on predictors of noncompliance is to use the technique of “meta-analysis” to reduce the multitude of research results to a usable form. Meta-analysis is defined by one of its primary developers as “the statistical analysis of a large collection of results from individual studies for the purpose of integrating the findings.” The following example illustrates the potential of this procedure in pulling together and making some sense of the compliance literature.

Nagasawa et al. (1991) performed a meta-analysis of 26 studies of compliance among diabetic patients. More than 180 different factors correlated with compliance behavior were reduced to the following collective findings:

- Factors related to good compliance: emotional stability, internal and external motivations, perceived benefit of therapy, supportive social and family structure.
- Factors related to poor compliance: perceived barriers to therapy, negative social environment.

Additional meta-analyses are required to assess compliance risk factors for other diseases, for special groups of patients (i.e., elderly, severely ill, ethnic groups, etc.), and for various intervention strategies (see below).
The most important predictor of noncompliance appears to be the interpersonal skills of the physician (Consoli and Safar, 1988; Morse et al., 1991; Manson, 1988). Debra Roter and her colleagues at the School of Hygiene and Public Health of the Johns Hopkins University have developed and tested a tool for assessing doctors' communication styles. The Roter Interaction Analysis System (RIAS) provides physicians with direct feedback and analysis of their individual communication skills based on analysis of audiotapes of actual patient interviews (Inui et al., 1982).

Through the use of the RIAS, strong evidence has been gathered which confirms that a physician's interpersonal skills correlate strongly with, and are predictive of, patient adherence, satisfaction, and recall of information about treatment plans. The RIAS has been found to be highly reliable in predicting both quality of care and patient satisfaction (Inui et al., 1982).

Health Belief Model

A frequently used, intuitively attractive, and validated framework for understanding and predicting compliance behavior has been the Health Belief Model. This simple but powerful concept proposes that being compliant is a function of:

- How serious and how likely are the consequences of noncompliance as perceived by the patient?
- How likely is it that something bad will happen and how bad would it be?
- How beneficial will compliance be and what real or perceived barriers to compliance exist?
- How much better will the patient be if he or she takes the medication and is that worth the cost or risk?

In addition, the model acknowledges the importance of social, psychological, economic, and structural factors in determining compliance. It is, of course, the interaction of all of these variables that results in the behavior of an individual patient.

Using the Health Belief Model, Fincham and Wertheimer (1985) studied the reasons why HMO patients did not pick up their prescriptions. They analyzed factors predictive of compliance and found more than a dozen to be significant. The two most important, however, were 1) the patient's
lack of belief in the benefits of care and 2) lack of information on how to take the medicine. The authors suggest that some measure of potential for non-compliance be included in initial contacts with patients. A short questionnaire, such as the one used in this study, that takes only a few minutes to complete in the physician’s office or pharmacy, would enable health professionals to take the steps necessary to encourage compliance.

Predicting Compliance by Asking the Patient

General factors associated with poor compliance that are discovered through research or incorporated into models, have only limited utility in identifying the noncompliant patient (e.g., a patient with a complex medication regimen probably warrants special attention). But if efficiency is to be built into programs to improve compliance, some means of predicting the likelihood of compliance in an individual patient is necessary. Fortunately, some progress has been made in that direction. And, as sometimes happens, the solution may be surprisingly simple — ask the patient whether she or he is a compliant patient.

For example, Morisky et al. (1986) have reported success in the use of a four-item scale as a predictor of future medication compliance as well as a measure of current compliance. The scale was shown to be reliable and a valid predictor of compliance and blood pressure control. The four questions in the scale could be quickly posed to most patients:

1. Do you ever forget to take your medicine?
2. Are you careless at times about taking your medicine?
3. When you feel better do you sometimes stop taking your medicine?
4. Sometimes if you feel worse when you take the medicine, do you stop taking it?

Hogan et al. (1983) developed a reliable 30-item scale which accurately assigned 89% of a sample of 150 schizophrenic patients to compliant and noncompliant groupings. The authors believe that compliers and noncompliers may differ in their awareness of internal bodily sensations, attitudes, feelings, and emotions. Thus, strategies designed merely to inform may be ineffective with patients who are unaware of these internal cues. The authors felt that the general lack of positive results in promoting compliance may reflect the growing belief among researchers that information which people generate themselves is a more important determinant of behavior than is information provided by others.

Litt (1985) found that adolescent patients’ self-assessment of their compliance with contraceptive pills accurately predicted compliance in 75% of the cases. Similar success was achieved using
short vignettes in which patients compared their own behavior with that of hypothetical patients their own age.

Cromer et al. (1989) studied adolescents and their iron therapy, finding only 67% compliant. Among the factors predicting compliance were:

- Patients prediction of his/her own compliance at first visit
- Patient belief in his/her own control of health
- Reminders from family members

In a study of inner-city blacks’ compliance with an insulin regimen, Uzoma and Feldman (1989) measured individuals’ belief in their own ability to comply and used this measurement to successfully predict compliance. This, in turn, suggested that a program to increase the belief in their own performance would enhance performance.

Interventions to Improve Compliance

For those people who simply forget, telephone, postal, or electronic reminders are likely to be helpful. But given the multiplicity of factors shown to contribute to noncompliance, there must be a correspondingly broad range of interventions. Indeed, many types of intervention have been tried. They range from electronic reminder systems to training sessions aimed at modification of the behavior of physicians and patients. Some successes have been reported, but no ‘gold standard’ or universally accepted program of compliance enhancement has emerged. It is unlikely that a cure for noncompliance among all patients will be found. Rather, a range of options is needed, each suited to the individual needs of patients with specific risk factors, disease manifestations, and social circumstances.

Compliance Packaging

Various types of compliance packaging have been designed for patient use to facilitate remembering when to take a dose and whether the dose has already been taken. Compliance packaging could become a key tactic in forging a physician-pharmacist-patient communication loop (Smith, 1989). Compliance packaging enables the product to reach the patient with several “built in” compliance features. A compliance package is a prepackaged, ready-to-dispense system that contains one treatment cycle of a medication, compliance aids and patient education materials to help motivate and remind the patient to take the medication correctly.
The Ortho-Novum Dialpak for oral contraceptives was the earliest type of compliance packaging. The complicated dosage schedule of Medrol later led Upjohn to develop the unit-of-use Medrol Dosepak which simplified the dosage schedule. Lilly's Axid Convenience Pak helps remind ulcer patients to take the medication every evening and not to stop therapy when symptoms abate. Allergan's C Cap Compliance Cap can be attached to any of their glaucoma products, to remind patients about the frequency of administration.

The macrodantoin MACPAC (Procter & Gamble) is an integrated system containing seven daily blister-pack cards that can be carried to work, a reminder card between the third and fourth dose cards to encourage the patient not to stop the medication although the symptoms may be disappearing, an information booklet on urinary tract infections, and two dispensing stickers for the pharmacist.

To be maximally effective, a complete compliance package must be developed according to patient education guidelines. Once a quality package is produced, health professionals must support it through counseling and reinforcement (Smith, 1989). The utility and economic viability of compliance packaging systems, however, must ultimately depend on demonstrations of their efficacy and cost effectiveness.

**Devices**

Several marketplace trends and technical developments are converging to set the stage for the appearance in the near future of a plethora of compliance-improving devices. The first trend is the burgeoning popularity of consumer electronic products. The second trend is the explosive growth in home healthcare devices. These include: home glucose monitoring, now the standard for diabetes management; home blood pressure cuffs for self-monitoring, allowing hypertensive patients increased control over their illness; hand-held smoking cessation computers which allow for programmed withdrawal from smoking; and electronic devices to monitor cholesterol and triglycerides through simple home testing.

These devices are appearing at a time when patients increasingly want to assume greater control over their health care, and when managed care companies are increasingly demanding that patients be treated at home rather than in hospitals. The confluence of these trends, plus growing awareness of the extraordinary costs of noncompliance with medications, is driving the rapid development of compliance device technologies.

Compliance devices are already marketed through specialty catalogues, gift shops, electronics retailers, pharmacies, and direct mail channels. At present, these versions are limited to portable
devices that signal the patient to take medication, and require an elapsed timer being set and reset, or the individual entry of each medication taking time. Bedside versions for nursing homes or invalids are also available, although these instruments are often expensive, and may be difficult to operate. However, clinical trials have shown these devices to have a significant impact on improving compliance and reducing morbidity (McKenney et al., 1992).

A new generation of compliance technologies now under development will utilize “off the shelf” microelectronic technology now widely used in hand-held computers and calculators. These devices will be portable, offer interactivity with the patient, accommodate multiple medications, and provide a record of patient behavior. Their cost/benefit ratios will have to be demonstrated, but are likely to be favorable. An example is CompuMed, an automated medication dispenser (CompuMed Inc., Meeteetse, WY). The Wyoming Medicaid Agency believes the dispenser is effective, since it is covering the device as a reimbursable expense at over $450, or a rental fee of $46 monthly. At least three other state Medicaid programs cover this device.

Integrated Approaches

Patients for whom the situation is more complicated will require more than just prompting or reminding, and for these patients an integrated approach, featuring multiple interventions, will be needed. An example of such an integrated approach is the program described by Sclar et al. (1992), which has evolved into the Wellspring program of ICI Pharmaceuticals. The program, which includes telephone contact, postal reminders, an educational newsletter, and various samples of health-related items, resulted in a significant increase in the number of days supply of medication acquired by both new and experienced hypertensives (Figure 2).

Windsor et al. (1990) demonstrated the effectiveness of a multi-strategy intervention program in asthmatic adults. The interventions included: one-to-one instruction, a self-help guide, a support group session, and two reinforcement phone calls. The program, which costs about $32 per patient, was associated with a compliance rate increase of more than 40% in inhaler use.
Figure 2. Education Improves Compliance with Antihypertensive Medicines, Reduces Utilization of HMO Services, and Lowers Overall Costs.
Cost Effectiveness of Compliance-Improving Strategies

Comprehensive, integrated programs, like those described by Sclar and Windsor, are the exception rather than the rule. Many more demonstrations of intervention programs in specific diseases, patient populations, and health care settings must be done to convince stakeholders that compliance intervention is worth doing.

What is most needed are demonstrations that compliance enhancement programs save money for healthcare payers. Sclar's study, for example, showed that although the Wellspring program resulted in higher use and costs of medicines, overall costs were lowered due to reduced utilization of other, generally more expensive services such as lab tests, hospital stays, and office visits. Net treatment costs declined by about $100 per patient (Figure 2).

Other studies which calculate the dollar savings or cost effectiveness of educational programs and other compliance-enhancing strategies are shown in Table 5. These studies generally show cost savings resulting from fewer hospitalizations, office and emergency room visits, lab tests, and other services.

These studies vary in size, patient characteristics, methodological rigor, type of intervention, and other important parameters. The magnitude of demonstrated cost savings varies widely among these studies, but all show that money was saved. Some have calculated that more was saved than was spent on program costs. None of the studies report net losses resulting from compliance-enhancing programs.

These findings are encouraging, but further information is required. Additional analysis of these and other cost benefit studies of compliance are required to identify and confirm the most cost effective interventions. The results would also help to design convincing, large-scale demonstrations of cost savings associated with improved compliance.
**TABLE 5.**
COST SAVINGS OF COMPLIANCE PROGRAMS

<table>
<thead>
<tr>
<th>Program</th>
<th>Patients</th>
<th>Savings</th>
<th>Benefit/Cost</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy-based compliance clinic</td>
<td>25</td>
<td>$43,000 in 33 months</td>
<td>12/1</td>
<td>1</td>
</tr>
<tr>
<td>Medication-monitoring service for geriatric patients</td>
<td>14</td>
<td>$265-565/patient/month</td>
<td>7/1-4/1</td>
<td>2</td>
</tr>
<tr>
<td>Compliance education for hypertension</td>
<td>--</td>
<td>$100/patient/year</td>
<td>2.5/1</td>
<td>3</td>
</tr>
<tr>
<td>Asthma self-management</td>
<td>683</td>
<td>--</td>
<td>111/1</td>
<td>4</td>
</tr>
<tr>
<td>Education of schizophrenics at a day treatment center</td>
<td>18</td>
<td>$10,000</td>
<td>--</td>
<td>5</td>
</tr>
<tr>
<td>Asthma self-management in inner city*</td>
<td>58</td>
<td>--</td>
<td>5.9/1</td>
<td>6</td>
</tr>
<tr>
<td>Education for congestive heart failure</td>
<td>50</td>
<td>452 hospital patient-days</td>
<td>--</td>
<td>7</td>
</tr>
<tr>
<td>Telephone hotline service for diabetics*</td>
<td>6,000</td>
<td>$1.7-3.5 mil hospital emergency and hospital hospital admissions, and office visits for medications</td>
<td>--</td>
<td>8</td>
</tr>
<tr>
<td>Computer-assisted telephone refill reminders in a community pharmacy</td>
<td>450</td>
<td>--</td>
<td>1.26/1-1.67/1</td>
<td>9</td>
</tr>
<tr>
<td>Hospital-based clinical pharmacy program</td>
<td>355</td>
<td>$208,000</td>
<td>--</td>
<td>10</td>
</tr>
</tbody>
</table>

* Medication management was part of an overall education effort, involving life-style, diet, and general health measures.

Partners in Identifying Noncompliant Patients and Improving Compliance

Programs with a focus on interventions directed at health care professionals are especially likely to show positive results. There is considerable literature indicating that good compliance is associated with good communication between health professionals and the patient and with a high level of patient satisfaction with the provider and the care received.

Physicians

Considerable research has shown a relationship between compliance and the quality of the doctor-patient relationship. The importance of the doctor-patient interaction as a determinant of good compliance may vary for different illnesses and types of patients, but one component of any effective compliance-enhancing plan is almost certain to involve the physician.

Kaplan et al. (1989) found that specific aspects of physician-patient communication were consistently related to compliance and also to overall health as assessed physiologically (blood pressure, blood sugar), behaviorally (functional status), and subjectively. Uhlmann et al. (1988) concluded that patients whose physicians responded to specific requests over time had fewer insulin reactions and greater compliance with insulin injection regimens.

The evidence is compelling that some improvement in compliance is achieved through improvement in the physician-patient encounter. Inui et al. (1976) found that patients of physicians who were tutored in techniques of communication and education were more compliant with drug regimens and had better control of their blood pressure than patients of untutored physicians. This landmark study concluded that physicians who are provided with strategies for identifying the noncompliant patient and for intervening in that behavior, can improve both compliance and control of hypertension (Inui et al., 1976).

Educational programs and other assistance for physicians to help them better manage the compliance problem can take at least three forms: instruction in the general factors involved in noncompliance; instruction in interpersonal behaviors shown to promote compliance; and assistance in identifying those patients most at risk for noncompliance. This may be as simple as supplying copies of one of the short questionnaires described above.

Since information alone is insufficient to effect a change in compliance behavior, the mere distribution of educational materials to patients, without a meaningful emotional link between patient and
physician, is unlikely to be effective.

Physicians need to be advised that some proportion of their patients are noncompliant and that the medical consequences may be accompanied by a loss of confidence in the physician or dissatisfaction with care.

Pharmacists

The retail pharmacist has significant potential, both as a source of compliance information and as a partner in enhancing compliance. It is essential, however, to demonstrate to pharmacists that increased compliance makes good business sense as well as contributes to better pharmaceutical care. Providing economic incentives is one approach. Development of computer software to assist in identifying noncompliers is another.

A special opportunity is available in the U.S., where some pharmacists are now required to "counsel" Medicaid patients when a prescription is dispensed. Even basic assistance by the pharmacist is likely to be effective. According to the Schering Report XIV (1992), the simple act of the pharmacist, rather than the clerk, handing the medication to the customer improved compliance by 25%!

Managed Care

Because of its strong economic interest in enhanced outcomes, the managed care industry has the potential to become a highly motivated player in efforts to improve medication compliance. Managed care organizations compete in the areas of efficiency and quality, and improving compliance will enhance both.

However, compliance enhancement programs are likely to increase drug utilization (see Sclar et al., 1992); managed care pharmacy directors responsible for line item drug budgets are understandably reluctant to implement programs that will increase their expenses. The challenge is to bring the compliance message to those managed care executives responsible for overall operating costs. Ways must be found to involve chief executives and chief financial officers of these organizations. And to convince these individuals to adopt a given compliance program, studies will be required to show the added value and overall cost savings of the proposed intervention.
The Bottom Line - Patient Responsibility

It is clear that to improve compliance we need to improve the relationship between providers and patients and between patients and pharmaceutical products. Yet it is important to remember that in two studies discussed above—one by the American Association of Retired Persons and one by The Upjohn Company—the primary cause of failure to fill prescriptions was the patients' belief that they had no need for the medication. This finding leads many researchers to the conclusion that we must direct our efforts toward educating patients and assisting them in accepting responsibility for their own treatment.

Leading researchers Debra Roter and Judith Hall conclude that “the most important contribution to patient compliance with drug prescriptions appears to be the patients’ understanding of the illness, the rationale and importance of the drug therapy, and the instructions for its use” (Roter and Hall, 1992). This information must be conveyed within the context of a relationship between the doctor and patient characterized by shared responsibility for the patient’s health.

In the end, the patient makes the ultimate decision to have a prescription filled, to take the medicine as prescribed, and to refill it as instructed. In their landmark book *Facilitating Treatment Adherence*, authors Donald Meichenbaum and Dennis Turk assure providers that the time and effort spent on helping patients take responsibility for their treatment “will pay handsome rewards.” Most importantly, they conclude, “Health care providers can share the responsibility for treatment adherence with patients and significant others in their lives. The teaching of self-management skills to patients represents a major challenge for the health care professions.”

Patient choice is emerging as an important theme in the healthcare reform agenda, but patient responsibility has not yet been emphasized. Patient responsibility, especially in taking medications properly, needs to assume its proper place next to patient choice of providers and health plans. The dual engines of choice and responsibility must be harnessed for effective management of health care costs.
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