med-ic® Rx FOR THE THIRD MILLENNIUM

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INTERPHEX™

Patient Compliance (Adherence) and Persistence with Prescribed Medication

By Allan Wilson, MD, Ph.D.

Lack of patient compliance with prescribed pharmaceuticals is a huge drain on health-care systems. The most widely cited estimate is that it costs the U.S. system over $100 billion annually, accounts for 100,000 deaths, and 1,000,000 hospitalizations.

Poor patient compliance has been documented in nearly every field of clinical medicine. It affects chronic (eg: diabetes mellitus, hypertension, schizophrenia, HIV) and acute therapy situations (eg: antibiotic treatment of infections).

Patient non-compliance has enormous implications for clinical trials. There are several areas of clinical research where non-compliance has significant negative consequences. Drugs may be erroneously determined to be ineffective and abandoned, at huge cost to the developing company. Non-compliance also affects the signal-to-noise ratio (see below) in clinical trials research, causing the approval process to be drawn out, again at considerable cost to the developer. In approved drugs, optimum dosing schedules may be erroneous due to non-compliance, as evidenced by the large number of drugs whose dosing recommendations are changed after the approval process because clinical experience show them to be faulty. Such changes are almost always in the direction of lowering the recommended dose. If not corrected, erroneous dosing schedules may affect patients and the health care system for the life of the drug (generally many years).

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History of Compliance Monitoring

The standard way of monitoring compliance is to ask the patient. This is known not to work. In clinical trials, medication diaries and pill counts have been the gold standard. For the past decade, electronic compliance monitoring (ECM™) has been available in the form of bottle caps which, when opened, record the time of opening. The new generation of ECM™ is integrated seamlessly into a unit-dose medication format such as a blister package or inhaler, recording when each pill is removed from the package. With the latter technique, it is now possible to monitor patient compliance covertly and without active patient participation.

Compliance Monitoring for Clinical Trials

Clinical pharmacy is an exercise in optimizing a signal-to-noise-ratio (S/N). The signal is the desired clinical effect; the noise is all the factors that conspire to obscure the signal. A widely-known but previous inaccessible source of noise is patient non-compliance.

It is now possible to measure compliance during clinical trials. By removing, via one of several techniques, the noise due to non-compliance, the signal is optimized. This increases the power of the research design, speeding up the decision-making process. This has a large and demonstrable return on investment (ROI) for a pharmaceutical company bringing a new drug to market. See www.med-ic.biz for a detailed discussion.

The Problem of Patient Persistence with Pharamacotherapy

Persistence is relevant to long-term pharamacotherapy, generally for chronic diseases. In general clinical pharmacy (pharamacotherapy with approved medications), persistence is known to be poor. Modest empirical data indicate that about 50 percent of patients discontinue a medication within one year of starting it. They may stop taking it or switch to another medication with the same indication. For some disorders the numbers can be worse.

Pharmaceutical companies spend enormous amounts to induce physicians, patients and pharmacists to use their products. Unfortunately, getting patients to start chronic therapy with a drug is only the beginning. If 50 percent of patients attracted to a new drug

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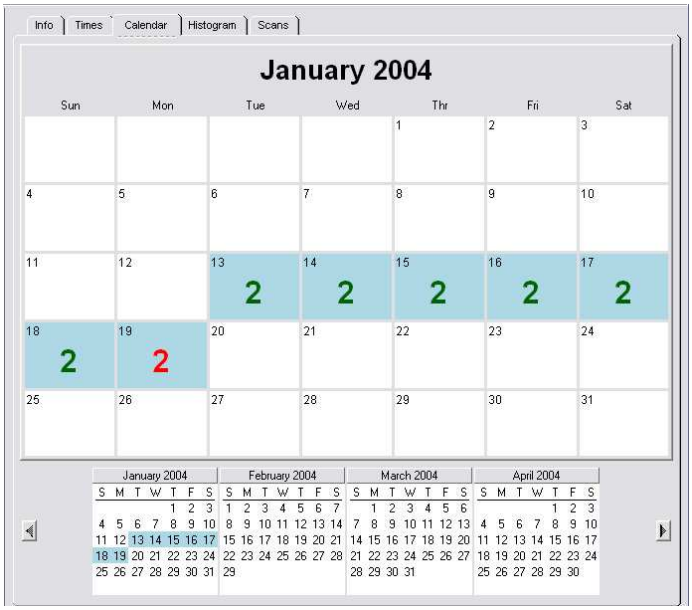
drop out within 12 months, the supply of new patients suitable for that drug will gradually drop off and revenues will start to decline. Typically, within a year or two, a competing "improved" drug is approved for the same indication and starts to make inroads into the market.

Patients stop or switch drug therapy for many reasons. Some are valid. Unavoidable side effects (poor tolerance) and lack of clinical response are the two main reasons for discontinuing or changing therapy. *Per se*, these are valid reasons for changing medication. However, poor compliance is often at the root of both problems. Until the newest generation of ECMs™ became available, little could be done to assess the degree to which side effects or poor clinical response are due to poor compliance, other than asking the patient if he or she was taking their medication as directed (with notoriously unreliable responses).

The business model for including ECM™ in clinical pharamacotherapy is compelling. If 50 percent of the 50 percent changing therapy could be prevented from doing so by ECM™ coupled with targeted education about the need for compliance, significant persistence would be created. What is known is that patients who benefit from a medication and experience no side effects are likely to continue with that medication. They and their physician are unlikely to want to risk losing the benefit by switching to another drug that may not work as well. In addition, it is also known that broad stroke education tends to have little effect on those who need it. Patients who are found to be non-compliant will respond to targeted remediation.



New Generation CertiScan™ ECM™ Software offers a clear "at a glance" view of a patients compliance with their medication regimen based on inputs from ECM™ monitored unit dose packages.

Rather than focusing marketing resources on attracting new patients, pharmaceutical companies would benefit more by combining this process with efforts to retain such patients in therapy over the long run.

Some advantages of ECM™ in clinical pharmacy:

- o Early identification of poorly compliant patients
- o Targeted education at those who need it
- o Improved physician-patient and pharmacist-patient relationships

ECM™ can also have medico-legal benefits. Physicians and pharmacists can demonstrate having done their due diligence in monitoring conditions (eg: epilepsy) where noncompliance may result in legal action (eg: seizures leading to motor vehicle accidents and resulting personal injury). Some examples are:

- o Antibiotic therapy for contagious diseases such as TB
- o Antiandrogen therapy for sexual offenders
- o Opiate antagonists for drug and alcohol dependence where abstinence is court mandated

ECM™ can also detect tampering and prevent counterfeiting of drugs.

ECM™ can be combined with medication reminders.

The new generation of ECM™ devices can be integrated seamlessly in all unit-dose formats including inhalers and strip-packaging formats.