Front & Center

Global Forum Focuses on Medication Adherence Framework

Medication adherence is a widely recognized problem of striking magnitude. The World Health Organization notes that, on average, 50 percent of patients do not take medications as prescribed.

It is less often recognized that adherence is not an issue of yes or no, nor a continuum that extends from perfect adherence to perfect nonadherence. Adherence has three distinct phases, each of which presents distinct barriers to adherence and provides opportunities for interventions to improve adherence.

The World Health Organization addressed adherence during a Global Forum on Innovation for Aging Populations held in Kobe, Japan held during October, 2015. Bernard Vrijens, PhD, Chief Science Officer at WestRock Healthcare and Associate Professor of Biostatistics at the University of Liège, Belgium, led a discussion that highlighted the three phases of adherence and the steps the pharmaceutical industry can, and must, take to improve adherence.

Key industry changes include improving the use of adherence measures in clinical trials, improving access to medications, improving the packaging of medications and improving communications between healthcare providers and patients in order to boost adherence.

Defining Adherence

Defining adherence is easy. It is the process by which patients take medications as prescribed.

Achieving adherence is somewhere between difficult and impossible. Taking a medication is a new behavior, a novel habit that must be accepted, adapted and followed on a routine basis.

Research using electronic monitoring devices across multiple drugs and multiple patient populations in multiple countries has found that adherence is composed of three distinct phases. In order to achieve adherence, patients must first initiate treatment. Once they have begun treatment, they must implement the dosing regimen on a regular basis. And they must convert their regimen into a habit and persist with the new habit for the duration of treatment.

Each of these three phases, initiation, implementation and persistence, presents unique barriers and unique opportunities for intervention.

Initiating Treatment

The traditional view of adherence assumes that once a healthcare provider prescribes a medication, patients obtain the medication from a pharmacy and begin taking it as prescribed. In reality, 30% of patients in developed economies never even pick up their initial prescription.

Some patients simply cannot afford medications. Cost can be a major barrier to initiating treatment in conditions such as hepatitis C, HIV and oncology. Health insurance may help, but many health plans deliberately impede access to higher-cost medications.

Cost is a common barrier in less developed economies where many people may not be able to afford adequate nutrition, much less medications. Patients who cannot afford medications cannot initiate treatment and will never develop the behaviors that contribute to adherence.

Lack of physical access can also be a barrier. Patients who must travel for injections, infusions or directly observed medication administration may find the trip too long, too expensive or too bothersome, especially if the journey must be repeated at regular intervals. Uncertain supply chains, lack of refrigeration or other storage conditions, shortages of trained healthcare providers can also impede access. Even with the best of intentions, patients who cannot access medications cannot initiate treatment and can never become adherent.

Lack of engagement with treatment is another key barrier. Patients may be told that they should begin medication for hypertension, type 2 diabetes, hyperlipidemia or some other condition, but they do not always accept the need for the prescribed medication.

Implementing Treatment

Once patients have initiated treatment, they must implement dosing on a regular basis. For some medications, all it takes is remembering to take a single tablet at about the same time every day or every week.

For other medications, implementation can be complex. Some medications must be taken with food, others without. Some must be taken precisely every four hours, six hours, or some other strict interval without regard to sleep, family, work or other considerations. The complexity multiplies with every additional medication, especially if different medications have different, possibly conflicting, schedules. The more complex the regimen, the less likely the patient is to implement dosing on a regular basis.

Medication formulation can also hinder implementation. Inhaled asthma medications are notoriously difficult to take correctly. Many inhaled medications can cause significant irritation to the mouth and throat, which can discourage regular use.

Medication timing is another barrier. Many traditional medications such as metformin for type 2 diabetes or statins for hyperlipidemia are quite forgiving in terms of timing. Taking a dose a few hours early or a few hours late, or even missing a single dose, rarely has significant clinical effects.

A growing number of highly effective medications have very narrow therapeutic

windows. Timing can be critical for many oral oncolytic agents, oral anticoagulants and oral hepatitis C agents. Narrow or precise dosing windows complicates the regimen and makes it more difficult to implement treatment.

Persisting with Treatment

Once patients implement treatment, they must persist with the regimen and make it a habit. The longer the duration of treatment, the more difficult it can be to continue. Persistence of treatment is a particular problem in chronic conditions with lifetime regimens.

Persistence is also a problem in conditions such as hyperlipidemia or hypertension where adherence brings clinical benefits but the patient feels no better. Lack of adherence can lead to significant long term health consequences, morbidity or even premature death, but continuing treatment brings no obvious benefit.

Overcoming Barriers to Adherence

Biopharma manufactures can significantly reduce barriers in all three phases of adherence. A key first step is to implement adherence measures in clinical trials. Repeated studies using electronic monitoring devices have shown that actual adherence in clinical trials is far lower than reported adherence.

This unacknowledged and largely undocumented adherence gap can significantly alter trials. Adherence directly affects participants' actual exposure to the agent being trialed, which affects both the clinical and statistical outcomes of the trial. Analyzing and stratifying outcomes by adherence in addition to other variables could improve the success rate of clinical trials that would otherwise be obscured by varying levels of adherence. It is only when adherence is measured and documented that the optimal dosing regimen can be identified and the relevant deviations can be recognized and managed.

Once medications are approved, implementing automated adherence monitoring for select products or populations could be appropriate. The current cost of electronic monitoring is minimal and will fall rapidly as the technology is scaled up.

Medications in which precise adherence is critical to clinical effect could be good candidates for electronic monitoring. A recent study at the University of Alabama Birmingham found that 40 percent of children with acute leukemia failed to achieve levels of adherence sufficient to cure their disease. Children who were less adherent had higher relapse rates. Systematic monitoring in populations in which precise adherence is critical could improve treatment outcomes and potentially improve payer coverage.

Industry can also improve implementation and adherence by improving access to medications. In some locations, that could mean bolstering the healthcare infrastructure and supply chain. In other locations, it could mean making medications affordable to all.

Improving access also means improving delivery devices and making medication easier to open. The calendar-type packages that have been so successful in improving adherence for oral contraceptives could be expanded to other medications. Smartphone apps and other electronic devices to remind patients of doses are available, but not widely studied or implemented. Industry routinely spends hundreds of millions of dollars to improve candidate molecules and virtually nothing to improve delivery devices that could enhance adherence, thus improving outcomes and boosting sales.

Key Roles for Non-Physician Providers

Many of the barriers to adherence can be surmounted with improved communication. Communication can help patients who are not engaged with treatment initiate that first prescription. Communication can help patients who have trouble implementing regular dosing or begin to doubt the need for persistence.

Physicians rarely have the time to engage patients on a regular basis, but pharmacists and nurses have both the training and the time to deal with adherence issues. Industry can not only take the lead in advancing adherence-informed clinical trials and adherence-improving packaging, but also in promoting adherence-improving professional services.

Improving adherence offers direct and measurable advantages for patients, healthcare providers, product manufacturers, regulators, patient advocacy groups, payers and other stakeholders. There are clearly costs involved, but there are even greater savings to be achieved.

When a hyperlipidemia patient on statins fails to show improvement, for example, current treatment algorithms call for increased dosing or a new, usually more expensive agent. For most patients in this situation, poor adherence is the root problem. A more clinically effective and cost effective strategy could be adherence monitoring, possibly using pharmacy dispensing records or electronic monitoring.

Randomized trials and longitudinal studies in clinics for hyperlipidemia, hypertension, asthma, type 2 diabetes and other chronic conditions have repeatedly showed that improved communication and coaching from a pharmacist or nurse, based on reliable and precise adherence data, is more effective and less costly than increased dosing. Industry can take the lead in turning these largely academic studies in improving adherence into practical healthcare policy that improves clinical outcomes and reduces overall spending by improving the three stages of adherence.

A combination of discrete steps discussed at the WHO forum: improving the use of adherence measures in clinical trials, improving access to medications, improving the packaging of medications and improving communications between healthcare providers and patients, will work to improve all three stages of adherence. The ultimate goal of improved adherence is to improve clinical outcomes and reduce overall spending on health care.