MOTIVATING MEDICATION-ADHERENCE VIA WELLNESS
One of health-care's most neglected and underestimated opportunities?
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John, a 50-year-old, hard-working manager, finally visits his physician, 'Dr. Smith,' for a long-delayed check-up. Blood tests show John has elevated cholesterol. Dr. Smith tells him to diet and exercise and prescribes a cholesterol-lowering statin. John is a bit shocked at the idea of serious medication. Dr. Smith warns John that his condition can lead to heart disease.

John finds the news rather depressing, but starts taking the statin, frequently irritated that he may be 'ill.' As the months go by, he increasingly avoids and forgets his pill, and by 12 months stops taking it. For two years, he occasionally worries, but dreads hearing more about disease, so he procrastinates. Then he suffers a mild heart attack; Dr. Smith is disappointed, but feels he could hardly have done more; John's medical bills rise dramatically, while his job-performance and quality-of-life suffer. At least his employer's ever-more-expensive insurance plan covers the bills.

In our strategy consulting for the pharmaceutical industry, we have encountered an amazing phenomenon. Undermining the healthcare system is a huge problem, medication non-adherence (or 'non-compliance') – the extent to which patients do not take medications as prescribed. John's scenario is only one variation. Incredibly, in *more than half* of US prescriptions for long-term chronic conditions patients simply discontinue, or cut back dosage to ineffective levels, within a year. This non-adherence leads inevitably to serious medical consequences including an estimated 125,000 premature deaths per year, with total-system annual costs estimated at $150-300 Billion.

A real solution would benefit the healthcare system - payers, insurers, physicians, manufacturers, pharmacists, technology solution-providers, and the government - with no losers or real tradeoffs (unlike so many contentious health-care issues). Nonetheless, little is done to address the problem, while the US health-care debate has given it only minor attention. Yet, we believe that medication adherence can actually be improved dramatically, on a practical, timely basis.

We have reviewed the existing research and conducted extensive in-depth interviews of patients, physicians, pharmacists, and pharmaceutical-firm managers. Non-adherence is clearly multi-faceted, partly reflecting cost, regimen-complexity, real side effects, patient misunderstanding and genuine forgetfulness. Clearly, sustained communications that explain, remind, and encourage can cost-effectively reduce non-adherence. However, our work also indicates that much of it is driven by less-obvious negative attitudes, including many patients' profound discomfort with accepting illness and surrendering their autonomy to physicians' orders.

For this difficult aspect of the problem, our work also points to a non-obvious solution – that these patients can best be motivated by the positive long-term wellness benefits of successfully managing their condition. Thus, much more effort is required, but also a paradigm shift: from striving for *compliance* by convincing patients of their *sickness* (often experienced as a depressing personal failure), to *motivating adherence* by helping them achieve and sustain *wellness* (experienced more as a self-reinforcing, personal triumph).

More research is needed, but our interviews and the literature on communications-intensive efforts indicate that positively motivating adherence via wellness can be a feasible solution. It requires more focus on positive communication, with better coordination among stakeholders, all at substantial costs - though less than the total system pays now for non-adherence. While not the largest healthcare issue, it is a neglected, underestimated opportunity to dramatically and rapidly improve outcomes, yet save enormous costs, to everyone's benefit. Improving medication adherence, including the solutions proposed here, deserve high priority in health-care reform.

WHY OUR APPROACH YIELDED NEW INSIGHTS

Our work produced insights into medication adherence that are realistically actionable and quite different from much conventional thinking in healthcare. Our strategy-development approach is more profoundly patient-focused and total-system oriented than what is typically practiced.

Our approach to a long, complex chain of participants, such as the healthcare system, first seeks to identify the ultimate customer, whom the entire system exists to serve, and who of these is most important to deeply understand. In this case, while recognizing physicians' importance, we believe the ultimate customer is the chronic-condition patient. To study them and non-adherence, we conducted extensive, in-depth (e.g. 90-120 minute) individual interviews with patients and others, and reviewed existing research. We did not rely on conventional assumptions, nor expect patients to articulate explanations or solutions. We probed as deeply as we could into the actual experiences and attitudes of patients, as recounted by them and also physicians, pharmacists, caregivers, and family. We thus attempted to identify the most important *end-results* for these patients, to discover or creatively infer what they *really want,* plus *why* they may not adhere, and what might cost-effectively stimulate healthier behavior. In exploring all these issues, we considered the entire healthcare system and its relevant participants, asking how new kinds of interaction among the players could help better achieve adherence and thus the right end-results.

Across the healthcare system (including industry and providers), typical approaches to strategy development are different in two respects. First, while most healthcare managers and providers would insist that they are *of course* patient-focused, their approach falls short of being truly patient-focused, on three counts:

1. Much of the system puts physicians, not patients, at the center of attention. Instead of asking who the ultimate customer is, many strategy approaches ask, "Who wields the purchasing decision-making power?" which in healthcare leads to physicians; but in our view, for adherence, patients are the *real* deciders.
2. The system does not adequately seek deep understanding of what these patients actually experience, their attitudes, and how other players interact with them. For example, non-adherence explanations and solutions often place too much weight on product-based obstacles (cost, dosage complexity, side-effects), or assume non-adherent patients are simply irrationally ignoring the professionals' instructions. Viewing the phenomenon through patients' eyes revealed a path to much better solutions
3. The system concentrates mostly on the *product* (medication), without enough attention to what the patient must do with that product to realize the intended *end-results*. Thus, the system develops, promotes, packages, distributes, and prescribes medications that are proven effective *if* taken exactly as prescribed. But this is insufficient; most patients do *not* achieve the key end-results – to actually get better, contain their condition, and control their symptoms over time - because they do not use medications as prescribed. There is thus a disconnect between the healthcare system and the patients, for treating chronic conditions.

Second, healthcare strategies are mostly developed for companies, sectors, or professions, rather than leveraging the power of multi-functional or whole-system solutions. This parochial approach overlooks opportunities to enhance adherence via better physician-pharmacist teamwork, for example. However, even greater benefits and savings can best be realized through coordinated, complementary system-wide changes in practices, incentives, and investment priorities.

A PROBLEM OF ENORMOUS MAGNITUDE…

Americans spend about $2.5 Trillion per year on healthcare, including about $300 Billion for prescribed medication, a large portion for chronic conditions (e.g. diabetes, high cholesterol, hypertension, asthma, gastro-intestinal, oncology, or psychiatric). These medications have been proven in clinical trials to provide real benefits that outweigh the side effects, in comparison to taking no medication. Astoundingly, however, while adherence for acute conditions is generally better, not just some but *most* prescriptions for long-term chronic conditions are not actually followed sufficiently to provide *any* benefit.

Consider statins, proven effective in lowering cholesterol. Numerous studies show that only about 50% of US patients continue taking the statin after 6 months, 30-40% after a year, and less than 30% after two years. Similar rates are found in the UK, Canada, and Australia. Hypertension has comparable results. Within a year of being prescribed medication, over 50% of US patients drop out of care and one-third of remaining ones cut back dosage to ineffective levels. Thus, over 67% of patients are getting no benefit within a year of starting therapy. WHO data shows a similar global picture, with over 75% getting no effective therapy within a year.

A common assumption throughout the healthcare system is that non-adherence is mostly a problem for asymptomatic conditions e.g., high cholesterol or hypertension. However, rates for symptomatic conditions such as asthma and GI disorders are even worse, and rates for many psychiatric conditions worse still. Even rates for cancer medication are astoundingly poor.

Very little non-adherence reflects a medication *change*, or physician's decision that a medication is ineffective or no longer needed. Many patients simply do not follow their prescriptions.

…WHICH IF SOLVED WOULD BENEFIT ALL STAKEHOLDERS

Most fundamentally important, patients would benefit from better adherence. While medical progress seems impressive based on the over 300 new medications approved by the FDA in the past 15 years, most patients with long-term chronic conditions are typically not actually experiencing the benefits of this technology. As a result, their disease progresses unnecessarily, causing complications, reducing quality of life, and sometimes leading to premature death. Studies in the past 10 years have estimated total direct and indirect costs (from medical expenses to productivity losses, all avoidable had patients adhered) at $177-to-300 Billion per year.

These disappointing outcomes and huge costs are clearly poor results not only for patients but also for healthcare payers, both private and public. The problem keeps insurers' costs high, since many chronic patients who discontinue or underuse medication eventually make much more expensive claims. Physicians, while typically seeing little they can do about it, generally know they are not achieving the results that should be possible if patients followed their instructions.

Meanwhile, pharmaceutical companies are not only failing to deliver the full benefits of these medications, but are also losing major revenue and profit opportunities. On a base of some $300 Billion per year in current US sales, with at least half of new chronic-condition patients dropping out of care or using severely reduced dosages, pharmaceuticals would clearly stand to gain enormous new revenues if non-adherence were significantly reduced. If at least two-thirds of sales are for chronic conditions and over half the target population has been prescribed, but uses little-to-no medication, there may be as much as $200 Billion in lost revenues per year at stake.

The profitability implications are even more noteworthy, since incremental sales of a pharmaceutical product enjoy exceptionally high profit margins. Moreover, average developmental costs and risks of failure for new compounds are very high. With pipelines distressingly empty in the pharma industry, and marketing costs so high for a new prescription, it would seem that large increases in the sale of established products would be highly attractive. Similarly, pharmacies are losing their share of profits from these same lost sales.

Thus, all stakeholders in healthcare – patients, families and employers, payers, insurers, providers, manufacturers, and pharmacists – stand to gain from better adherence.

NONETHELESS, LITTLE IS CURRENTLY DONE

Payers and insurers rarely demand, reward, or invest in higher adherence; in fact, increased employee cost-sharing may lower adherence. Manufacturers focus on discovering new compounds, and convincing physicians to prescribe their drugs, devoting little to improved adherence. Regulators and manufacturers together produce packaging with massive quantities of unread fine print, but which rarely does anything to encourage adherence.

Many physicians believe that they have done all they can, since they told the patient what to do (and see it as the patient's responsibility to comply), but in reality most patients only partially hear and understand these instructions, and remember less. Some excellent counseling programs involving pharmacists, teaming with physicians, have been pioneered on a limited basis; and some pharmacy chains provide refill reminder services for patients requesting them (e.g. automatic refills and a reminder phone call or email); however, pharmacists typically dispense drugs and ensure patients are aware of side effects, but do little more to encourage the patient's longer-term adherence. In fairness, both physicians and pharmacists have limited time with each patient and generally are not directly compensated for educating and counseling, whereas they are well compensated for providing medical services or dispensing medication.

The government has likewise done far too little. The NIH, for example, with a total budget of $2 Billion per year, spends only $3 Million on medication-adherence research. Meanwhile, the current national debate has mostly focused on issues plagued by difficult tradeoffs, such as how to pay for healthcare, or cost containment via restrictions on healthcare access, rather than the tradeoff-free issue of adherence, although the Congressional bill has an encouraging provision supporting counseling efforts that promote adherence. Much more can be done to encourage total-system-wide collaboration to solve this problem.

Increasing medication adherence can be seen in context of an even larger opportunity, often discussed, to improve health outcomes and save costs by influencing behavior generally. Screening for cancers after age 50, or quitting smoking are examples where progress has been made, and more seems possible. Much attention has been paid to the potential for diet and exercise. However, these behaviors have proven highly resistant and slow to change. Medication-adherence may be different - while largely neglected up to now, major progress seems possible, at net cost savings, if approached with serious resources, some persistence, and the right attitude.

EVIDENCE SHOWS THAT NON-ADHERENCE CAN LARGELY BE SOLVED

Causes of non-adherence

Some patients fully accept their physician's diagnoses, and follow instructions well. Among the many that do not, there are multiple causes, though these are not understood well enough and much more research is needed. Some factors are clearly difficult to eliminate. Cost is an important factor for some patients, and likely to remain so. The complexity of regimen (e.g., 33% of patients over 65 take 8 or more medications per day) can be an obstacle to adherence. Real and severe side effects can also inhibit adherence. However, non-adherence is very high even when these factors are not at play. Some non-adherent patients misunderstand or underestimate the seriousness of their illness, do not fully understand how to use their medication, or may genuinely forget to take it. For many, however, the problem is quite different and cannot be adequately solved by better explaining, reminding, or reemphasizing the serious risks of not sticking with the prescribed medications.

In fact, much of the traditional, wholly inadequate efforts to improve adherence seem misguided by flawed assumptions long held by physicians, pharma firms, pharmacists, and others, about the underlying reasons for poor adherence: non-adherent patients must not understand the severity of their illness or the dangers of non-compliance; they should be reminded of their sickness and its risks, admonished to follow physicians' instructions, and sternly warned of dire consequences.

Thus the common mistaken assumption that non-adherence is particular to asymptomatic diseases. And in the classic media campaign to frighten hypertensive patients into taking their meds, the voice-over announcer asks, 'if you won't take it for yourself, what about for them?' as we see the patient with family; i.e. you don't want to die and leave them alone, do you?

However, our in-depth interviews, backed by a growing body of clinical research, convince us that this attitude misunderstands much of the problem. Rather, we believe that much of non-adherence is driven by a set of negative attitudes about illness and medication, which patients can overcome if given the right kind of support. Among these attitudes are:

- An unwillingness to accept an illness (i.e. denial), and equating medications with illness
- Low awareness and understanding of the benefits of medication and adherence over time
- Fear (often exaggerated) of the medication itself – i.e., potential side effects or risks
- Overestimating the healing power of life-style changes in place of medication[1]
- Perceived social stigma of having an illness and using medications

These cognitive barriers to adherence are not trivial. It seems clear that many patients resist seeing themselves as 'sick,' and want to fight against their disease, and ultimately to win. They find it a depressing surrender to accept a chronic condition requiring long-term disease containment, and they associate their medication, and adherence, with the disease and with this surrender. As part of resisting surrender to the disease, many have a strong instinct to maintain their autonomy, not compliantly follow orders, so they respond poorly to control and fear.

Faced with the initial fear of the disease and their physician's strong urging, most patients start by taking the medication as directed. But without follow-up support to help them fully accept, in positive terms, the use of medication as an integral part of their lives, they typically lose motivation and discontinue or severely cut back dosage within six months or a year.

Seeing these patients as flawed and at fault, the traditional instinct is to repeat the instructions and warnings, and when that fails, to give up on them as irrational. However, the problem is not an inability to understand the dangers of high cholesterol, diabetes or asthma; it is that being sick and following instructions are not nearly as motivating for many people as following an autonomous, self-directed path to gain and sustain wellness – including on-going medication.

Consider, in contrast, that many consumers who do not adhere to medication prescriptions are enthusiastic users of vitamins or some other health-promoting product. About half of adults take a daily multivitamin, and most of those we interviewed feel that they are doing something smart and proactive to maintain their health, not paying the price for being ill. Positive reinforcement is more effective than fear and punishment.

In our in-depth interviews, we repeatedly found a pattern where not only does the initial communication between physician and patient fail to positively motivate the patient (as illustrated by the scenario above with John), but what happens next is also not helpful. After leaving the physician, the patient fills the script but the pharmacist, who has limited resources for interacting with the patient, rarely fills the gap in understanding and motivation. The package in which the

[1] That is, patients may overestimate their ability to change life-style enough to improve their condition; and some conditions may not respond adequately anyway, to life-style changes alone

patient receives the medication also does nothing further to fill this information and attitude gap. Both package and pharmacist tend to highlight risks and side effects, not benefits of the medication. Moreover, carrying the pills in the patient's pocket or purse may be awkward, reinforcing the sterile, clinical symbols of 'sickness.'

For many, the medication experience becomes generally negative and depressing. And when the patient finally cuts back on dosage or discontinues entirely, they are told they are now 'non-compliant' – yet another negative epithet.

Much more effective patient-communications - key to addressing these obstacles

However, the good news is that the evidence shows that these substantial obstacles of understanding and attitude can be successfully addressed, via better, more extensive communications with patients, both initially and then reinforced over time. Such communications inform, educate, discuss with, and persuade the patient to better understand their condition, medication, and the benefits of long-term adherence. These communications, when effective, are also persistent, following up to remind, reward, and reinforce the patient's positive understanding and healthy, adherent behavior.

Communication efforts (or 'interventions') have been shown effective in various forms. Payers (e.g. employers) or insurers can offer incentives for adherence. Physicians and pharmacists can much more fully explain and discuss the benefits of adherence with patients when prescribing or dispensing medications. Packaging can also help convey and reinforce the same adherence messages, and overtly remind patients when to take their medication.

Among the most effective are interventions that include on-going education and counseling - what some call 'Medication Therapy Management' (MTM) or 'pharmacy care' - with personal contact between healthcare professionals and patient, sometimes involving family or community members. The most effective efforts treat the patient respectfully, as an autonomous partner in the pursuit of wellness, rather than as a subject to be given instructions. When professionals regularly speak with the patient (e.g. every two months), and listen to and discuss the patient's concerns and perceptions, the results are highly encouraging and apparently can be sustained long term.

Research and real-world programs increasingly show that all these kinds of interventions can be effective, and that combinations of them are the most effective. Moreover, the cost of such interventions is significant but the evidence indicates that the savings in total system costs, due to better adherence, consistently outweigh these costs.

How strong is evidence that communication-intensive intervention works?

Although the literature on adherence-interventions (hundreds of studies, of uneven scientific validity) is thin versus the many thousands of rigorous clinical trials for single medications, it still provides convincing evidence that various interventions work.

Meta analyses have been conducted on hundreds of published studies of adherence-related interventions. A 1995 meta-analysis of 21 studies showed that the quality of physician-patient communications significantly affects adherence. A 1998 analysis of 153 studies showed that interventions combining education and behavioral counseling were more effective than one-dimensional efforts. A 2001 analysis covering 44 studies published since 1970 showed that most intervention methods work, across the range of disease areas, with impacts of +15-25% on adherence; the strongest techniques were behavioral or cognitive counseling, family-oriented approaches, and adherence-oriented packaging; combinations of techniques were most effective.

Many individual studies in more recent years strongly reinforce these conclusions. For example, Osterberg and Blaschke in 2005 showed a strong impact of physician-patient communications on adherence. Bull et al in 2002 showed that adherence with antidepressant medication was 60% higher for patients who had three or more visits to the physician in the first three months, vs 1-2 visits; and patients who fully discussed side effects with their physician were 51% less likely to discontinue. Brogan in 2002 showed that cardiac medication (ACE I or II) adherence after 9 months was 50-60% with no 'Compliance Program' but 85-90% with such a program of education and support. In 2006, one pharmaceutical manufacturer's support program for statin adherence, with education and personal contact by a healthcare professional, showed 12-month adherence levels of about 28% without this program, but about 65% with it.

COULD EVEN *TEENAGERS* BE CONVINCED TO ACT IN THEIR OWN INTEREST?

Consider teenagers - a group notoriously prone to abysmal adherence. As all parents discover, it is very difficult to communicate effectively with teens, who can often be maddeningly and irrationally self-destructive. Adherence with asthma medication is a major problem with teenaged patients. Our research indicated that many of these young patients associate medication strongly with illness and some embarrassment, and resent being forced to 'comply,' so they may simply refuse to use their medication often enough. Interventions that are cognizant of these strong emotions, including packaging solutions that reinforce the positive adherence story for a teenager, while deemphasizing the clinical and 'dorky' appearance of the inhaler, seemed promising.

In another example from this difficult group, over 50% of teenaged organ-transplant patients, whose survival utterly depends on medication, become non-adherent once they hit puberty. As reported recently by the New York Times, they are four times more likely than adults to forget their medication or take it at the wrong time, a major cause of organ rejection. Applying the traditional paradigm for non-adherence, one solution has been for physicians to increase the frequency of clinic visits for apparently non-adherent teen patients, and then lecture them on the dangers. This has not worked well, as would surprise no teenager. ('Duh!' as they might say).

Amazingly, however, a recent study in *Pediatrics* magazine found that *texting* – automatically sending alerts as text messages - can actually improve adherence among these patients. Clinicians entered the appropriate medications and dosages in the text-messaging program, but the teens were allowed to determine the frequency and timing of the alerts.

As the study's lead author commented, "Teenagers can have very busy or obscure lifestyles…so we thought it was important that they choose whatever time they wanted to get their reminders …This system was a way for parents to give their children a sense of autonomy…but it also allowed them to follow behind a screen, so to speak." After getting the text alert, the teen confirms within an hour, by text, that they took their meds, or a parent or caregiver is sent an alert. The system also allows the physician to more accurately track adherence.

The study showed that adherence improved significantly; as a result, while 12 of the 41 patients in the study had experienced an organ-rejection episode in the previous year, only two did so during the 12 months of the study. Saving one patient from needing a new transplant can save a life, and at least $500K. Yet, almost a third of patients had to drop out because of losing their phone privileges or no longer being able to afford a cell phone. Maybe teens are irrational, but who will save us from adults who make so many penny-wise and pound-foolish decisions?

ACTIONS THAT CAN IMPROVE ADHERENCE

Smarter incentives by payers and insurers

Growing experience supports the rationale for employer programs that reward adherence. Grocer Safeway Inc's Healthy Measures program, for example, allows employees to reduce what they

pay for the company's health plan by up to 20% if they better control certain key health measures, including weight, smoking, blood pressure, and cholesterol levels. Safeway believes this program, which resembles auto insurance, has yielded significant increases in employees' healthy behavior. And at least one health insurer, United Health Care, is experimenting with discounts on co-pays for customers who refill certain medications within 30 days of their last refill, thus rewarding adherence.

Most employer health plans have increased co-payments for medications, cutting their drug spending, but not stopping the relentless increases in their total healthcare spending (over 7% per year, according to the Kaiser Foundation). So a few companies are simply eliminating medication co-pays, including Marriott, Pitney Bowes, the University of Michigan, the state of Maine, and Mohawk Industries. Smart corporations should watch these experiments closely. Cost sharing has a logical rationale - to encourage consumers to make smart economic choices about medical services. However (to be economically rational for the payer) the goal regarding medication must be focused heavily on long-term adherence.

Physicians – opportunities to change tune and learn a little more harmony

Despite real obstacles, many physicians must focus more attention on medical adherence, and change the terms of their dialogue with many chronic-condition patients.

An early, crucial moment of truth is when the physician first gives the patient a diagnosis of chronic disease. Our research found that many patients are somewhat shocked by this bad news, and are slow to accept that they actually have a serious illness. They often do not fully hear or absorb what the physician says next, about treatment. Physicians must be better attuned to this initial state of shock, and work harder to help the patient understand the nature of the illness, and that in most cases the patient can achieve and maintain their wellness if they positively embrace a self-directed program of treatment, typically including long-term use of appropriate medication.

The physician must then ensure that patients really understand how and when to use their medication, plus what side effects if any to realistically expect, and how best to manage them. In some cases it will be possible and beneficial on balance to simplify regimens (e.g. combining multiple medications into a single dose) or prescribe more 'forgiving' medications (e.g. ones still effective even if not taken on a precise schedule; or time-release, or transdermal medications).

Physicians must then work harder to identify non-adherence, including tracking refills and response to medication, and asking their patients – non-judgmentally – about their adherence behaviors and attitudes. Physicians should also more overtly communicate, then reinforce, the benefits of long-term adherence, helping the patient connect it with life-long wellness.

Fundamental to making these communications work is both accepting the physician's own accountability and yet recognizing the patient as the ultimate decider of adherence. Many physicians believe that adherence is the patient's responsibility, but clearly the patient cannot get well if not continuing the medication prescribed. So, ensuring adherence is as important – to effective therapy - as making the right diagnosis and prescription in the first place. However, the physician must also accept that the patient will do what they want to do. Some patients want to do whatever the physician says, but as discussed above, our work indicates that long-term adherence is miserably low in part because many patients resist being 'sick' and surrendering autonomy to a physician's orders. Therefore, the physician must listen carefully to patients, discovering their attitudes about the disease, the medication, and their ability to adhere. Physicians may need to accept some compromises, but by treating patients more as co-equal partners who have some control over treatment, much better long-term adherence can result.

Physicians should also do more to collaborate. Many do little to work with pharmacists, yet research shows the effectiveness of teamwork between physician and pharmacist to better educate and adjust therapy for patients, and for pharmacists then to follow up with reinforcing counseling. Physicians should also reach out to pharma manufacturers who could provide useful packaging and various materials that can help communicate the adherence story. Physicians can also take steps to involve patients' families more fully in the effort to sustain adherence, and (again with help from manufacturers and pharmacies) to connect patients with community support organizations, on-line resources, and other sources of reinforcement for good adherence.

Of course, to be realistic much of the above also calls for changes in how physicians and pharmacists are reimbursed. The payer/insurer community clearly needs to support changes that pay physicians for health outcomes and healthy behaviors like medication adherence.

Packaging - a powerful but mostly ignored tool for enhancing adherence

Our work also convinced us that packaging can help simplify adherence and remind patients when to take their medications; especially in combination with on-going education and counseling by trained healthcare professionals, packaging is clearly able to help improve adherence significantly. Examples include blister packs, unit-dose calendar packs, and color coded bottles. However, again reflecting the very low priority that the pharma industry and the whole system actually give to adherence, packaging is generally not even used; instead, in the manufacturers' penny-wise, pound-foolish approach, it is largely ignored.

The vast bulk of US prescription medication is distributed to pharmacies in bulk, and then dispensed in the pharmacist's standard plastic bottle. A small label shows some basic information, sometimes including a warning or two about drug interactions or side effects. This bottle is given to the patient in the pharmacist's bag, along with the required package insert (a page or more of dense, regulatory jargon that conveys little to patients except for a long list of side effects which sometimes frighten patients into not taking the medication).

This approach saves supply chain costs, and apparently satisfies the regulators, but wastes important opportunities to at least facilitate adherence, and potentially to also convey and reinforce the positive reasons for adherence. It is clear from our analysis that packaging could and should be used much more extensively to influence adherence, starting with message content.

Reminding the patient of the end-result health benefits of using the medication, and then overtly and persuasively encouraging them to keep using their med as prescribed, would be a major improvement. In addition, while side effects must and should be fully disclosed to patients, current packaging typically does little or nothing to help patients keep side effects info in balanced context. The odds of getting most side effects are low and the physician can help the patient manage or avoid most side effects – and packaging should make this story clear. Most pharma packaging can also do more to give patients easy-to-use links to additional information and programs that may be available to support continued adherence.

Packaging should be fundamentally redesigned to facilitate communication of these adherence-oriented messages. As a start, for example: more space for communication (e.g. bigger boxes with more panel space, 5th panels, large unfolding inserts, etc.); better layouts to emphasize the message; readable text (large enough, using headlines and other obvious techniques to communicate effectively); and greatly expanded use of visualization – icons, color, graphics, story-telling (think about older, younger, and no-so-literate patients).

Recently, an innovative concept was introduced, illustrating the potential for technology to enhance packaging for adherence. The GlowCap® signals the patient with changes in color, automatically reminds them by phone if they miss a dose, and can provide adherence information to a caregiver or physician. The maker claims that adherence for chronic hypertension and diabetes increase from a typical 50% to 86% with use of GlowCap, at a total cost of about $20 per month. Given the high cost of non-adherence, such technology could actually be cost effective.

Much more beneficial packaging carries some cost for the pharmaceutical manufacturers and/or pharmacies. However, while some solutions such as GlowCap can be expensive, most of these packaging improvements have potential to improve adherence at relatively low cost.

Advertising to promote adherence, anyone?

Turn on a TV in the US and you will soon be bombarded with prescription pharmaceutical advertising. Viewers are urged to recognize one illness or another, and are told how well the medication in question works. Yet virtually none of that advertising speaks to the specific issue of medication adherence. Given the money manufacturers, due to non-adherence, leave on the table, advertising seems an obvious candidate for real investment in this important message. Perhaps the story should be told by the whole industry, for all chronic conditions, but it should be told.

Pharmaceutical manufacturers – now is the time to make adherence a *real* priority

To effectively collaborate with physicians and pharmacists, to develop and deploy much more helpful packaging, and to devote significant advertising dollars, all in pursuit of dramatically higher, sustained adherence rates, pharma companies must change their mindset. As noted earlier, the potential return on investment is clearly there. However, the commitment is not – beyond lip service, pharmas are still not making a serious effort to improve adherence, commensurate with its importance to the wellness of patients and to the companies' bottom lines. How can this be?

Based on our work, we believe that one important reason is that pharmas are overly fixated on the physician as customer, with inadequate focus on the end-user, the patient. True, these companies' products are designed to affect the patient, and many hundreds of millions are spent on direct-to-consumer advertising. But the object remains to get the next prescription (or a higher share of all scripts in a given therapy area) from the doctor. Marketing is almost entirely devoted to either directly convincing physicians to prescribe the company's brand, or to convincing patients to ask their physician to prescribe that brand. What gets far too little attention by the manufacturers is influencing what happens next – what the patient actually understands, feels, and does, importantly including how long they take the medication as prescribed.

At the same time, research budgets are still single-mindedly focused on discovering the next blockbuster drug. Huge investments are poured into understanding and optimizing the pharmacological impact a compound may have, under controlled conditions of a clinical trial. Of greatest interest is showing that the drug, if used correctly over time by the patient, is more beneficial than a placebo, and represents no unacceptable safety risk in tradeoff. Meanwhile, precious little is known or understood about why patients behave as they actually do, and how to influence their understanding and outlook so as to optimize adherence, which is totally crucial to the efficacy (in the real world, outside the clinical trial) of any medication for a chronic condition.

Partly this odd myopia may reflect the distorted time horizons typical of so many industries. Even though pharmaceutical firms must regularly manage in long time frames, including many years to develop and bring a product to market, it seems that short-term financial pressures still drive much behavior, at least in sales and marketing. A pharma brand manager, who may only be in

place for a year or two, can get higher returns over the next 6-12 months by investing in more sales calls on physicians, and running more advertising, in the effort to win the next prescription. Investment in adherence will likely pay off only over a longer time period. As one senior Sales Manager told us, "Adherence is great; but I guarantee you we can produce more revenue this year by increasing our detailing budget to win more scripts, than by talking about adherence!"

Moreover, the physician-centric perspective means that marketing focuses on brand image and reputation, share of scripts by physician and therapy area, and brand loyalty (do physicians keep prescribing our brand, or switch away to competitors?). These issues are important, but they apparently crowd out any serious attention to adherence. Exacerbating this low interest seems to be an inaccurate perception that not much can be done to influence the patient anyway. Of course, there are limits to what a rep can achieve in a 5 minute detailing call. However, in addition to yet again repeating the product benefits of each brand, reps might periodically tell a useful adherence story. They could raise physicians' awareness of non-adherence in each relevant therapeutic area, and emphasize any available evidence for the effectiveness of certain adherence messages to patients. If backed up by effective packaging and other patient-communication materials that could be given to the physician to use with patients, plus possibly some support programs sponsored by the rep's company, such a marketing effort might have a productive impact.

As far as we can determine, most pharma executives would agree that "medication adherence is an important priority!" However, they do not seem to manage their companies as if it were. With perhaps $200 Billion in additional US revenues at stake (not to mention the well being of their *real* customer), pharmas should make a major adjustment in their mindset and priorities, to (really) include adherence.

Education, Counseling, and Multi-Functional Teamwork

Education and counseling of patients by healthcare professionals to improve adherence sounds to many like an exotic and prohibitively expensive strategy. While needing more research, the available evidence indicates that such interventions can be highly successful and cost effective.

The Asheville Project is a pharmacist-directed program of education and supportive counseling, called MTM (Medication Therapy Management), conducted in Asheville, N.C. Trained pharmacists, working with physicians, provided MTM to three groups totaling over 800 patients for over 5 years, through 2008. Co-pay costs were also lowered or eliminated. Success of this project has spawned similar efforts by a handful of employers, and should generate more.

In the Asheville diabetes study, medication adherence improved from 27% at baseline, to 65% at the end. The portion of patients with lab values in optimal range for a key diabetes metric jumped from 40% at baseline, to over 60%. Despite employers' higher costs for MTM and medications (due to higher adherence and reduced cost-sharing), total net direct medical costs went down over $3350 per patient per year (PPPY), because emergency, inpatient, and physician costs declined by over $6500. And, lost productivity costs declined as sick days PPPY went from 12.6 to under 7.

Asthma non-adherence is seen in underuse of appropriate medication. Ashville clearly improved adherence, since patients using a standard adherence aid (an Action Plan) increased from 63% at baseline, to 99%, while medication usage (costs PPPY) more than doubled. The percent of patients classified with 'severe or moderate-persistent' asthma declined from 82% at baseline, to 49% at one year, 42% at five years. Despite higher costs of MTM and medication, net direct costs declined $725 PPPY. Since lost productivity is quite high (absenteeism and reduced productivity at work), indirect costs savings were estimated as even higher, at another $1230 PPPY.

In the cardio vascular (CV) study, medication usage PPPY nearly tripled. Patients at goal increased (from baseline to end of study) from 40% to 67% for blood pressure, and from 50% to 75% for LDL cholesterol. The number of CV 'events' declined by 53%. Medication cost increased $559 PPPY. Direct medical costs, net of MTM, declined by $629 PPPY; applying the American Heart Association's cited estimates for indirect CV costs implies another $327 indirect savings, for a total estimated net savings of $397 PPPY.

Counseling plus packaging to help adherence in the elderly – a study that should be Famous

A key demographic group for medication adherence is the over-65 population, since so many patients in this age bracket use multiple medications, which complicates adherence further. One study indicates that about a third of patients over 65 uses 8 or more medications. A relatively recent and rigorous study published in JAMA, the Journal of the AMA, yielded compelling evidence for the combined effects of MTM and customized packaging, to help this group.

In the FAME study (Federal Study of Adherence to Medications in the Elderly) 200 patients over 65 (mean age 78), with at least 4 chronic conditions, were studied over two years (2004-06). After measuring baseline adherence and levels of blood pressure (BP) and cholesterol (LDL-C), all participants were subjected to the same Phase 1 intervention, over 6-8 months. They were given medication-education to discuss and address underlying obstacles to adherence. Then they were given their medications in blister packs, which laid out each multiple-medication dose needed, by day and time of day. And then trained pharmacists provided regular follow-up every two months (one hour in the initial session, then 30 minutes each session).

At the end of 6-8 months, a second 6-8 month phase began. Half the group was randomly assigned to continued MTM care and time-specific blister packs; the other half were returned to conventional ('usual') care – no MTM and no blister packs.

Among all participants, after Phase 1, medication adherence went from 61% at baseline, to 96%. The portion of patients for whom medication adherence was at least 80% for all their chronic conditions rose from 5% at baseline to 99%. At the end of Phase 2 (14 months), the 'Usual Care' group had reverted most of the way back to their baseline behavior. Adherence was 68%, and 22% were at least 80% adherent for all their chronic conditions. In the MTM Group, however, adherence stayed at 96%, and 97% were at least 80% adherent for all chronic conditions.

Education and follow-up counseling that address misunderstanding and reinforce the benefits of adherence, supported by much easier to use packaging, works. Admittedly, this study does not include an analysis of its cost effectiveness. However, the three Asheville studies showed direct medical cost savings (net of increased medication and MTM services) averaging about $1800 PPPY, implying that savings can probably pay for packaging such as that used in FAME.

Possible help from community groups, families, and social networks

Consumers increasingly want control over their own health, to achieve self-determined wellness. They want to find information from the media, the Internet and other sources, rather than relying only on the authority of their doctors. Physicians and pharmacists clearly can play a major role in motivating good adherence. However, for some groups of patients, other sources of support may be important, and possibly more effective than the traditional healthcare professionals.

Research is again lacking, but it seems plausible that community support services and the involvement of patients' families may provide useful alternative or supplemental resources. There are many organizations, with physical and/or on-line presence, available to provide health information and support to consumers, but they need to include much more focus on adherence.

Similarly, it may be possible to leverage the use of social networking to create on-line communities that could help reinforce patients' motivation to adhere. With physician, pharmaceutical, or pharmacy-industry support, some of these resources could possibly be shaped to provide strong community and peer support for adherence. Physicians, pharmacists, advertising, packaging, etc., could then possibly direct patients to these additional resources.

Role of Government

The health bill, and the debates surrounding it, have focused much energy on extending coverage and trying to cut costs, partly by reducing wasteful or 'unnecessary' healthcare expenditures. Naturally, people will debate what is 'unnecessary' (ask people about the need for breast cancer screening before age 50, for example.) The Administration should now embrace a chance to save billions while actually increasing care and improving outcomes. Few issues fit these criteria better than adherence. Whether within the framework of the health bill, or independently, the government should aggressively move to better fund pro-adherence initiatives, and increase national appreciation of the need and benefits of adherence. Such policy would be very good for the nation's health, and much closer to win-win politics than most issues prominent today.

Meanwhile, the FDA, while acknowledging (in its public positions) the importance of adherence, could do much more to spur product development and packaging that actually improve adherence. The FDA rightly focuses on ensuring that drugs have proven efficacy, safety, and tolerability; it should add a strong emphasis on making sure patients actually use those drugs. Finally, the NIH and other governmental bodies should dramatically increase the currently negligible budget for rigorous clinical research on adherence and how to improve it.

CONCLUSION

We admittedly come at the medication-adherence problem as strategy-generalists, not healthcare specialists. However, we have used a more deeply patient-centric, and total-system-focused approach than is common in healthcare (and elsewhere). We believe that our findings show that the healthcare system would benefit greatly from much wider adoption of the methodology we used. And understanding how different, and inherently more insightful, it is, system participants should better appreciate the potential of solutions such as those proposed in this article.

Physicians, pharmacists, manufacturers, insurers, employers, the government, and the public all have an enormous shared stake in seeing medication adherence improve dramatically. Of course, to make money, and to save money, sometimes one has to spend some money. Surely the payoff – saving many thousands of lives, improving the quality of many millions more, and largely eliminating $300 Billion per year of avoidable costs – more than justifies the effort. In fact, for once, here is an issue with benefits to go around for all, and virtually no real tradeoffs for anyone. And there is even a realistic path for getting it done, reasonably quickly.

The key challenge is getting people across the system to recognize this huge opportunity, and to adopt a new paradigm for addressing it, one more truly focused on the patient. Generally, it does not work well to either ignore this rather large elephant in the room, or to rely on scaring the non-adherent patient with their 'sickness.' What does work is intensive, adequately funded communications, usually involving collaboration among various players, and often supported by well-designed packaging, all aimed at positively motivating adherence as part of patients' pursuit of wellness. With such help, patients can discover and understand the benefits of long-term adherence, and then can autonomously and permanently integrate this healthy behavior into their lives, with great benefit for all.