

## Improving the Quality of Medications Use: The Case for Medication Management Systems

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The quality of drug therapy is a major contributor to overall quality of health care. Drug therapy can increase quality, as when it stops a life-threatening infection. Medication use, however, also can cause toxicity, side effects or other adverse events. These are, in effect, new medical problems. They may lower quality of life and require additional expense to correct. Common examples include digoxin overdose or bleeding from warfarin or non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen or aspirin.

Medication use can also fail to achieve the intended therapeutic effect, allowing a disease to continue or worsen. Finally, medications may not be ordered or many not be taken when needed. This has the same effect as treatment failure, as when a patient with asthma misuses his medications until he has a life-threatening crisis.

Expenditures for prescription drugs outside hospitals represent about 12% of total expenditures for personal health care goods and services. This is substantial, but the quality of medications use can greatly affect expenditures for many other goods and services, the “other 88%”.

The need for more effective management of medications use is clear. The usual, very unsystematic, ambulatory care medications use processes found in North America and Western Europe do not provide consistently acceptable quality of drug therapy. Drug therapy in hospitals is not much better.

This is evidenced by many research studies showing that *preventable* drug-related patient injury is prevalent in many health care organizations. The corresponding cost of correcting such patient injuries is staggering. The causes and preventives of many drug-related patient injuries are known. The money spent on correcting injuries (or compensating victims when injuries cannot be corrected) could be better spent on systems that would prevent them.

The case for constructing well-functioning medications use systems is also clear. First, little evidence supports the effectiveness of intuitively appealing interventions like prescribing improvement or adherence improvement programs. On the contrary, some well-meant prescribing restrictions have been associated with lower overall quality of medications use.<sup>a</sup> Increasing patient adherence as an end in itself is illogical and may occasionally exacerbate some adverse drug effects. There is substantial evidence, however, that systematizing medications use improves outcomes, often at lower total cost of care.

Despite the evidence of a problem and a possible solution, the road to medications management has turned out to be rough and long. In the past 20 years, systematic medications management has not become a *de facto* standard for the safe and effective use of medicines. Passage of Medicare Part D and the requirement for Medication Therapy Management (MTM) certainly was a step toward that goal. The MTM requirement officially recognized the need for

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<sup>a</sup>See, for example, discussion below of studies by Soumerai, et al.,<sup>1,2</sup>Horn, et al.<sup>3,4</sup>, and the review by Kozma et al.<sup>5</sup>

improved systems of drug therapy for selected Medicare recipients. Unfortunately, Centers for Medicare and Medicaid Services (CMS) did not mandate which services must be provided under MTM or the qualifications of the providers.

Likewise, professional standards for the quality of medications use remain minimal, compared to what the professions could accomplish if they worked cooperatively. Despite occasional flurries of anxiety, the public remains poorly informed about the dangers of medications use while preventable injuries continue, apparently undiminished.

Even though the transition is not complete, pharmaceutical care has influenced thousands of practices and saved tens of thousands of people from adverse outcomes or treatment failure. Medications management systems need more and stronger advocates from many disciplines.

This paper will present a synthesis and interpretation of research and scholarship related to the quality of medications use systems and the outcomes of drug therapy. It is, to that extent, personal opinion. To paraphrase the late Senator Daniel Patrick Moynihan, we are each entitled to our own opinions, but we are not entitled to our own facts. Therefore, I will begin by reviewing the facts as they are revealed by research.

**Problem Statements**

Studies from many nations over many years have shown the need for better management of drug therapy. This first became clear from “process” studies showing inappropriate prescribing, inadequate monitoring and advice by pharmacists, and patient non-adherence. Other, more convincing, studies have shown adverse outcomes of drug therapy. Preventable patient injury from medications mis-use is frequent and costly. We have reviewed published studies reporting preventable drug related morbidity (PDRM) as a cause of hospital admission.<sup>b</sup> All of the studies we reviewed used expert review of patient medical records. (Fig. 1)

Typically, more than half of all drug-related hospital admissions were preventable in the opinion of the respective investigators. The median rate of hospital admissions from PDRM was 4.3%.<sup>6</sup>

In the US, in 1996, the most recent year for which we had comparable data, this would have ranked adverse outcomes of drug therapy about equal to cancer as a cause of hospital admissions, ahead of coronary heart disease, diabetes

Data on DRM

Type	Ambulatory Care (DRA)*	Inpatient Care*
Total DRA/DRM prevalence	7.1 %	6.5%
Preventable DRM prevalence	4.3 % (1.4% - 15%).	1.5% (.32% to 3.9%)
Preventability (PDRM/DRM)	58.9 % (32-86 %)	41% (20% to 56%,)

\* % is per 100 admissions; DRA = drug related admission from ambulatory care; Meta-analysis of 15 ambulatory & 6 inpatient studies.

**Figure 1.** Prevalence of Drug-Related Patient Injury. The ranges shown in parentheses are the extreme ranges among studies.

<sup>b</sup> Please see the Glossary in the Appendix. DRM is much broader than adverse drug reactions (ADR) and somewhat broader than adverse drug event (ADE). Like ADE, DRM include errors and other problems in drug use. In addition, DRM include injuries caused by the ineffective use or non-use of indicated drugs.

mellitus and asthma. The rate of adverse outcomes among inpatients typically was 1.5%.

The studies we reviewed had a very wide range of PDRM prevalence rates. This is probably attributable in part to differences in the populations sampled, sampling and measurement methods, and definitions. It may also, however, reflect major differences in quality of medications use between systems. In other words, some medications use systems may be much safer than others. The now-famous Harvard Medical Practice Study found that, “adverse events and negligence do not appear to be randomly distributed.”<sup>7</sup> This is a rather reserved way of suggesting that safety is a system property. Some systems are safer than others.

In our own studies using PDRM indicators, one study of elderly patients in Florida had a period prevalence of about 6 PDRM events per 100 patient-years, roughly comparable to the results of the 15 studies that used medical record review.

A 2005 retrospective study by Field et al estimated the cost consequences of adverse drug events (ADE) within a cohort of Medicare enrollees in a large multispecialty group practice. They identified 1210 older adults with an ADE, and randomly selected a matched comparison group from enrollees with recent healthcare encounters, for whom medications had been dispensed but who had not had an ADE.

The average increase in costs after the ADE was \$1310 (95% CI=\$625-\$1995) greater for those experiencing *any* ADE, compared with the control group, after adjusting for age, sex, comorbidity, number of scheduled medications, and hospitalization during the pre-ADE period. For *preventable* ADE, the adjusted increase was \$1983 (\$193-\$3773) greater than for controls. Based on ADE rates and these cost estimates, 1000 older adults would have annual costs related to ADE in the ambulatory setting of \$65,631 with \$27,365 of this associated with preventable events. The authors concluded that ADE in the ambulatory setting substantially increase the healthcare costs of elderly persons. They noted that their methods would be unlikely to detect untreated indications and that their cost estimates were “conservative.”<sup>8</sup>

Gurwitz et al carried out a cohort study of all long-stay residents of two academic long-term care facilities over a period of up to 9 months during 2000 to 2001. They assessed the number, severity and preventability of ADE. They found 815 ADE, of which 42% were judged preventable. The overall rate of adverse drug events was 9.8 per 100 resident-months, with a rate of 4.1 preventable ADE per 100 resident-months. Errors associated with preventable events occurred most often at the stages of ordering and monitoring. Residents at increased risk of a preventable ADE were those taking medications in several drug categories and those taking antipsychotic agents, anticoagulants, diuretics, or antiepileptics. The authors concluded, “Our findings reinforce the need for a special focus on the ordering and monitoring stages of pharmaceutical care for preventing adverse drug events in the long-term care setting.”<sup>9</sup>

Forster, et al. determined post-hospital outcomes approximately 24 days following discharge by performing a chart review and telephone interview in 400 patients discharged to home from the general medical service of an urban academic health center hospital. Using telephone interviews, they identified new or worsening symptoms, the patient's use of health services, and patient recollection of processes of care. Post-hospital outcomes were independently judged by 2 internists. Of the 400 patients, 45 developed an ADE. Of these, 27% were preventable and 33% were ameliorable. Injuries were significant in 32 patients, serious in

6, and life threatening in 7. The risk of ADE per prescription was highest for corticosteroids, anticoagulants, antibiotics, analgesics, and cardiovascular medications. Risk increased with the number of prescriptions. Failure to monitor was an especially common cause of preventable and ameliorable ADEs. The authors recommended that side effects of medications should be discussed with patients. Patients receiving specific drug classes or multiple medications should include better monitoring after hospital discharge.<sup>10</sup>

PDRM wastes money. Ernst and Grizzle estimated the total amount of money spent in the US for additional medical services to correct DRM was US\$177 billion in the year 2000.<sup>11</sup> Based on a US population of 275 million, the average annual per capita expenditure in 2000 would have been \$644. If about half of DRM are preventable (Figure 1) the US expenditure to correct PDRM was about \$322 in the year 2000.

Using another approach, I estimated that the cost is somewhat lower, \$84-\$128 per capita in 1997, equivalent to about \$90-\$135 in 2007 dollars.<sup>12</sup> (See Fig. 2). Note that these expenditure estimates are not averages per patient-year for people receiving therapy. They refer to average expenditures for every man woman and child in the US.

Compare these estimates with \$390, the amount spent per capita annually on prescription medications in 1997 (roughly equivalent to \$410 in 2007 dollars). We could say that ambulatory care medications use in the US creates additional costs of from 33-83%, just for correcting PDRM.

### Causes of PDRM

Given that PDRM events are common and expensive, the next question should be, "What causes the problem?" The authors of 10 of the 15 outpatient studies we reviewed listed the drug therapy problems associated with the hospital admissions. (See Figure 3.) Inadequate follow-up (drug therapy monitoring) was the leading cause of preventable drug related hospital admissions in these studies, followed by prescribing problems.

As many as 70% of drug-related hospital admissions involved inadequate followup of ongoing drug therapy. Inadequate follow-up included not

### How Much Does This Problem Cost?

- Total annual *per capita* cost estimate: \$84 - \$128**
- Based on 15 reviewed PDRA studies , and 1997 data, at \$1000 per day PDR Admissions cost . . . \$25
  - Based on two studies, PDR ED visits cost. . . \$42 - \$86
  - Based on 1 study (Bates) inpatient PDRM cost \$17
    - increase in LOS of 4.6 days
    - increased cost of \$5857/ admission
    - Given 114 hospital admissions/1000 population, & prevalence of 2.6% of stays, i.e. about 3 inpatient PDRM per 1000 population.

**Figure 2.** Cost of PDRM (Estimates based on 1997 Data)

Prescribing %		Drug Distrib. %	Follow-up %	
Choice	Dosage		ADR, SE, DI	Tx Fail
6.3	10		56	14
<b>16.3</b>		<b>13.4</b>	<b>70</b>	

Ten of 15 reviewed studies gave a % breakdown of the node at which the DTP had occurred

**Figure 3.** Ambulatory Care Failure Nodes (Step from which preventable drug related admissions originated. SE=side effects; DI=drug interaction; TX Fail=treatment failure). Numbers do not total 100% because of rounding.

responding to ADRs while they could still be mitigated, allowing them to become so severe that they required hospital admission; lack of monitoring for progress and problems; and laboratory tests not being done or not being acted upon.

It is not clear from these studies how many adverse drug reactions (ADR) could have been mitigated before they caused a hospital admission. Perhaps many could have been caught and corrected. Figure 3 shows that, even if we assume that no admissions caused by ADR were preventable, hospital admissions due to side effects (SE) and drug interactions (DI) would still constitute the majority of severe PDRM in ambulatory care.

Problems with prescribing, including drug choice, dosage, and route accounted for about 16% of drug related admissions. Drug distribution and administration, including dispensing errors and patient nonadherence, accounted for about 13%. Among inpatients, the situation was roughly the opposite: most problems involved prescribing and the fewest involved follow up.

These data suggest that the main opportunity for improving outcomes in ambulatory care will involve improving follow-up and management of on-going therapy. This implies a medications management system. In a well-functioning system, follow-up and management can detect problems from earlier system nodes, e.g., prescribing and, often compliance.

DTP/ STEP	Ambulatory Care	Inpatient Care
Prescribing (drug, dose, route)	16.3 %	55.3 %
Drug Distribution	13.4	29.6
Follow-up	70.1	10.3

Approximate average % of PDRM with cause at given step in medications use

Figure 4. Comparison of Inpatient and Ambulatory Care Failure Nodes

### Finding a New Way

Albert Einstein famously said, “We can't solve problems by using the same kind of thinking we used when we created them.” Will Rogers said, “If you find yourself in a hole, stop digging.” Many people who are responsible for the quality of medications use in organizations will need a new way to think about medications use before they can stop digging the hole even deeper.

We all have a *weltanschauung*, a “theory of the world,” a set of assumptions, mental habits, and beliefs that we use to make sense of the world. We must have such a theory of the world to guide what we pay attention to and how we interpret our experiences. In particular, a health care manager’s *weltanschauung* inevitably influences what information he or she considers important and how it is interpreted. Understanding this, and taking one’s own *weltanschauung* into account, is a mark of an educated person.

Three pieces of conventional thinking seem to interfere with efforts to improve the quality of medications use. These concern:

1. Concepts of health care quality
2. The Iron Triangle relationship between cost, access and quality
3. The model of medications use.

Disagreements about how to improve quality of medications use, whether we can afford to do

that, and which drug-related morbidities should be preventable can be traced to different definitions, assumptions and models. We should examine our implicit views and assumptions. Then, when they are clear and explicit, we can validate (test) them and, if necessary, modify them to correspond to the facts.

### **A Useful Conception of Health Care Quality**

Health care quality is a complex topic. Certainly it is multi-dimensional. Most people in the health care enterprise are familiar with Avedis Donabedian's notions of structure, process, and outcome.<sup>13</sup> But what is quality? This has been a topic of confusion, frustration and rancor. In the last decade, however, the Institute of Medicine's (IOM) definition of quality has become widely accepted.

According to the IOM, health care quality is "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge."<sup>14</sup> It is based on the following statement of purpose: "The purpose of the health care system is to reduce continually the burden of illness, injury, and disability, and to improve the health status and function of the people of the United States."<sup>15</sup>

Furthermore, quality consists of six elements, abbreviated STEEEP: all health care should be safe, timely, effective, efficient, equitable, and patient-centered:

- care which is intended to help patients should not harm them (safe);
- care should be based on sound scientific knowledge (effective);
- care should be responsive to individual preferences, needs, and values (patient-centered);
- unnecessary waits and harmful delays should be reduced (timely);
- care should be efficient (not wasteful);
- quality of care should not depend on patient characteristics (equitable).

From those six elements, the IOM authors created ten basic "New Rules" of health care. Each rule reflects a STEEEP element:

- care is based on continuous healing relationships.
- care is customized based on patient needs and values.
- the patient is the source of control.
- knowledge is shared freely among providers and among providers and patients.
- decision-making is based on evidence.
- safety is a property of a system.
- transparency is necessary, secrecy is harmful.
- care anticipates patient needs rather than waiting to react.
- waste is continuously decreased.
- clinicians cooperate in providing care.

According to Donald Berwick, implementing this concept of quality requires changes in American health care at four different levels:<sup>15</sup>

- the experience of patients (Level A);
- the functioning of small units of care delivery (“Microsystems”) (Level B);
- the functioning of the organizations that house or otherwise support Microsystems (Level C);
- the environment of policy, payment, regulation, accreditation, and other such factors (Level D), which shape the behavior, interests, and opportunities of the organizations at Level C.

This model is hierarchical. The quality of actions at Levels B, C, and D should be defined only with reference to the effects of those actions at Level A. Berwick calls level A “true north.”

One commentator has called the IOM’s conception of health care quality a way back from the other side of the looking glass. He means that the American health care enterprise has been lost and confused in a fantastic landscape where *quality* was nearly anything one wanted it to be. Many definitions of quality were too much about frills, flash and provider convenience. We had lost the connection to patient outcomes as the true north to steer by.

### Breaking the Iron Triangle

According to a popular assumption, cost, access, and quality are locked in an “iron triangle.” According to this idea, we cannot improve the quality of health care unless we either decrease access to health care or increase total expenditures. (The same argument is often made for other service industries, e.g., higher education.)

The validity of the Iron Triangle depends mainly on how quality is defined. The Iron Triangle could perhaps be true if quality were defined in terms of structure or process without a valid basis in patient outcomes. For example, some ideas of quality are framed in terms of more expensive facilities, equipment, qualifications of personnel, drug products, etc. without regard to evidence connecting these elements to patient outcomes.

According to the IOM definition, increasing quality is equivalent to increasing STEEEP. Reducing or eliminating PDRM would increase quality by that definition and reduce or eliminate the cost of correcting the patient injury they cause. Economically, PDRM is pure waste, the drug therapy equivalent of a mis-adjusted industrial machine or an out-of-control process. PDRM almost always have to be corrected, if possible, often at considerable additional expense.

If that money could be spent on prevention instead of correction, quality could be increased at no additional cost. Useful health care analogies are cholesterol reduction, immunizations, other cost-effective preventive measures. In those examples, external factors like

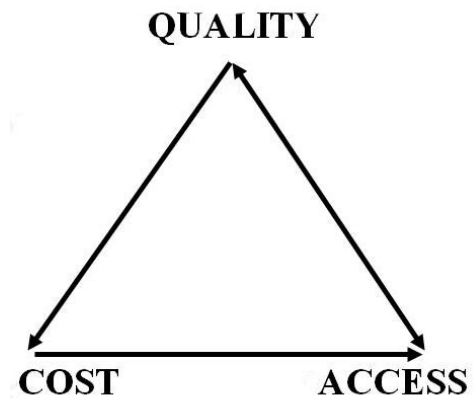


Figure 5. The “Iron Triangle”

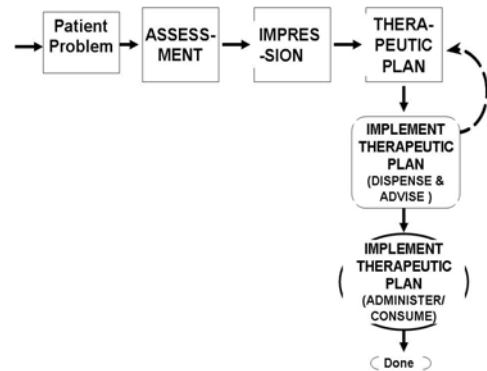
diet or viruses are causing the burden of disease. In the case of drug therapy, much of the burden is caused internally, by the programs we operate.

Other industries, e.g., automobiles, have greatly lowered their costs by reducing defective parts and re-work, and have increased value by producing a more reliable product<sup>16</sup>. This is a very different kind of quality improvement than adding a bigger engine, leather seats, cupholders and chrome. The objective of higher-quality medications use is to do therapy correctly the first time, i.e., safely, effectively, etc. Theoretically, avoiding the expensive "re-work" caused by PDRM should more than pay for the cost of operating a high-quality (safe, effective, etc.) medications use system.

### A Theory of Medications Use

System structure and process including communications (information flow) are vitally important. This is shown by the following analysis. Suppose that a medications use process comprises three steps:

- physician services (assessment, clinical impression and therapeutic plan) involving an indication for drug therapy;
- pharmaceutical services (dispensing and advising the patient); and
- patient or lay care giver care (consuming or administering the medicine).



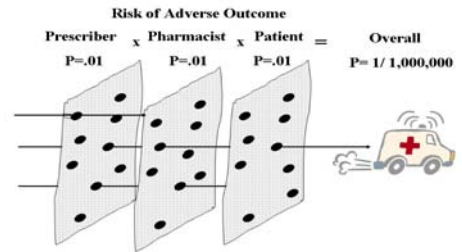
(See Figure 6.) The physician assesses the patient’s problem, forms a clinical impression or diagnosis, makes a therapeutic plan, and writes one or more prescriptions. The patient takes the prescription to the pharmacist who fills it. Then the patient takes it home and consumes it according to his interpretation of the label instructions and what he recalls of other directions for use. (I believe that this more or less describes the medications use process in ambulatory care for most people.)

**Figure 6.** Flow Diagram of Ambulatory Care Medications Use Process

Now, suppose for the moment that there is very little communication between the steps in the process. If each person carries out his or her step independently of the others (which is typically how we do it today) errors at each step can accumulate. For example, if the total risk of “error” (actually, error or unfortunate happenstance) at each step is 1%, the maximum risk after one pass through the system is 3%. If some errors can recur over time, e.g., if the risk of a dispensing error or patient non-compliance recurs with each repeat prescription, the overall risk can increase with time.



If, in contrast, the people at each stage are aware of the purpose of therapy, of what should happen, and of what could go wrong, the risk that an error will harm a patient can be much less. To appreciate the significance of this, consider James Reason’s “Swiss Cheese” analogy of injury prevention. (See Figure 7.) In this model, an error at one point in a process may be stopped at a subsequent step.

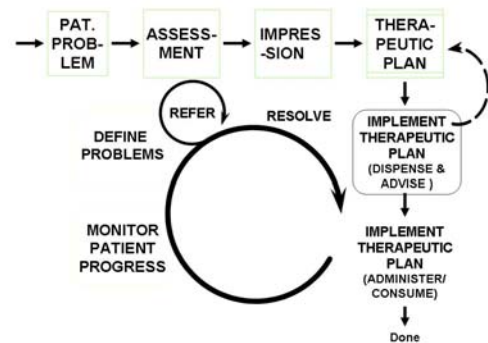


**Figure 7.** Depiction of Reason’s Swiss Cheese Analogy

Before it could affect a patient, an error would have to escape detection and resolution at all subsequent steps. If the pharmacists and the patient are adequately informed and provide independent checks on the progress of therapy, the risk of an error actually reaching the patient is the *product*, not the sum, of the three error probabilities. In this example, the risk of injury would *fall* to one chance in a million.

The difference between 3 chances in 100 and 1 chance in a million illustrates part of the argument for a cooperative process such as that shown in Fig. 6, *with* adequate information flow. Each step provides an independent check on progress toward the therapeutic objectives. That would require that people at each step have the information necessary to judge the correctness of the process up to that point. It would also require that the person performing each step take a critical attitude toward the work up to that point, and not assume that it is correct.

Now, suppose further that the system includes monitoring and feedback, as shown in Figure 8. As the system continues to operate, the risk that an error will adversely affect a patient theoretically should fall, from the same mechanism of independent assessments.



**Figure 8.** Diagram of a MTM/Pharmaceutical Care System.

Simulation is a technique for representing the real world by means of mathematical models, usually application of numerical methods to represent a dynamic process.

I constructed a simulation model to demonstrate and test the idea of a multi-pass “Swiss Cheese” model.<sup>12</sup> The simulation was a representation of the diagram in Fig 8. It has three stages, corresponding to diagnosing and prescribing (physician), dispensing and advising (pharmacist) and consumption or administration (patient).<sup>c</sup> The logic of the simulation model is straightforward.

1. A patient enters care with one drug therapy problem (DTP). That would represent his reason for visiting the doctor, i.e., an untreated indication.
2. During the simulated physician visit, the DTP may be resolved (or not) and an additional

<sup>c</sup>For a more detailed description of the simulation model, see Hepler & Segal, pp. 246-253.

- DTP may be created (or not).
- Each simulated patient then enters the “pharmacist” stage and then the “patient” stage with his number of accumulated drug therapy problems. A new DTP can be created (or not) and an existing DTP can be resolved (or not) at each stage.
  - The simulation then “recycles” from the patient stage back to a professional followup stage, as in the circular loop in Figure 8.
  - Again, each existing DTP may or may not be corrected (with probability pcd) and another may or may not be created.

The range of probabilities that a DTP would occur bracketed data in the literature. The probabilities of having a PDRM based on the number of DTP’s was based on my educated guess. They ranged from zero for a patient with no current DTP to one for a patient with four DTP.

I then simulated drug therapy for 1000 hypothetical patients over six months. I partially validated the simulation by comparing the outcomes (frequency distribution of DRM) to data reported in the literature. The prevalence of PDRM per six months (8-10%) is somewhat higher than usual literature reports, but within the realm of reality.

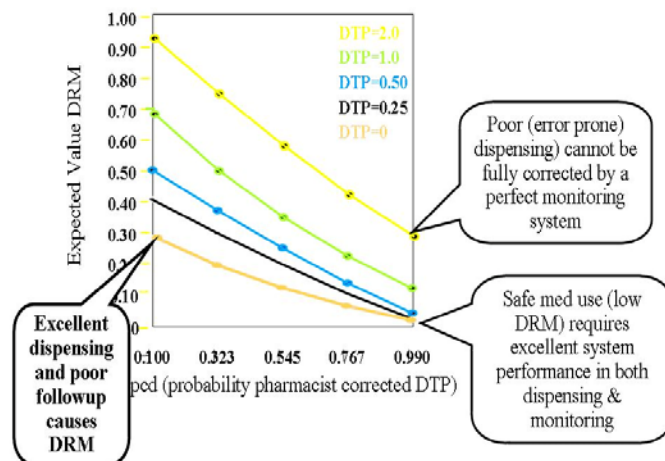
The simulation model precisely elaborates the theory of pharmaceutical care. It illustrates the dynamics of a medications management system and allows us to test hypotheses about it.

Quality of care is represented as the two probabilities (a) that a DTP would occur and (b) that a DTP would be resolved. I varied those probabilities over wide ranges.

In Figure 9, the expected number of DRM (i.e., risk) is plotted on the “y” axis, while the effectiveness (pcd) of monitoring is plotted on the “x” axis. The five colored curves each represent the quality of the initial pass through the system, e.g., prescribing and dispensing.

For example, the bottom (orange) curve represents patients who leave their first “visit” (steps 1-3) with no DTP. The physician and pharmacist, in other words, did a perfect job of detecting and correcting the DTP that the patients had when they entered. Nonetheless, these patients still have about a 30% chance of developing a DRM within six months if they receive poor followup monitoring.

In contrast, the top curve represents



**Figure 9** Mean Number of DRM by Starting Conditions (DTP) and Intensity of Follow-up (pcd)

The simulation confirmed the theoretical proposition that all four steps in a medications use system must be carried out properly to prevent DRM.

patients who emerge from their first visit with two DTPs, as if their initial problem was not recognized and an unnecessary or inappropriate therapy had been prescribed and dispensed. For such patients, even very intense monitoring cannot eliminate DRM.

This analysis shows that monitoring can gradually reduce the risk of developing a DRM, even if a patient initially has a DTP. More intense monitoring (simulated as increasing the probability that DTP would be detected and resolved) resulted in a decreasing rate of DRM.

It confirmed the theoretical proposition that all four steps must be carried out properly to prevent DRM. Within the six-month period of the simulation, even very intensive monitoring cannot overcome failure to detect and resolve DTP when therapy was initiated.

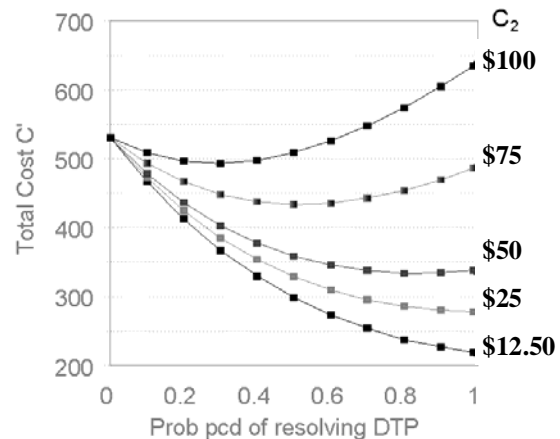
Figure 10 shows total cost curves that include five alternative costs of medications monitoring to detect and resolve DTP and the cost of correcting a DRM event, e.g., extra doctor visits, ER visits, hospitalizations. The cost function is

$$C' = C_1(\text{pcd}) + C_2(\text{pcd})$$

where  $C'$  is the total incremental cost of drug therapy.  $C_1(\text{pcd})$  is the average cost of correcting a DRM.  $C_1(\text{pcd})$  is a function of pcd. Its value decreases as pcd increases.  $C_2(\text{pcd})$  is the cost of monitoring. It also is a function of pcd and increases as pcd increases. Pcd is the probability that a DTP will be resolved. (Drug product cost and dispensing services are not functions of pcd and are excluded. Including them would just change the scale of the Y axis.)

The scenario modeled in Figure 10 is that the intensity of monitoring may vary, from no DTP being resolved (pcd=0) to all DTPs being resolved (pcd=1). The cost of monitoring varies proportionally to the number of DTP being resolved, as if a payment were made for each individual monitoring event (e.g., drug therapy review). The values of  $C_2$  (from \$12.50 to \$100 per patient per month) represent the cost per month if every DTP were resolved. The simulations illustrate that detecting and resolving some DTP may be cost-effective even when monitoring is very expensive compared with the cost of correcting a DRM.

This simulation refines and extends the theory of medications use. It supports the theoretical argument for a pharmaceutical care system (PCS). Obviously, every simulation depends on its inputs and other assumptions. I do not claim that this simulation proves that paying for pharmaceutical care or medications therapy management would be cost effective. In some ways, the simulation model is an over-simplification. For example, it assumes that all DTP are equally



**Figure 10.** Total Cost Curves from Med Use System Simulation.

The average cost of correcting a DRM was arbitrarily set at \$1000. The scenario modeled is that monitoring intensity in the patient group may vary from 0% to 100% of DTP's being resolved and that the cost of monitoring varies proportionally. The values of  $C_2$  (from \$12.50 to \$100 per patient per month) represent the cost per month for resolving all DTPs.

likely to lead to DRM.

It does suggest, however, that the optimal amount of monitoring provided might not be zero. A cost-minimizing “service level” may exist in a given medications use system, even when monitoring is expensive compared with the cost of correcting DRM. For example, it appears that  $C'$  would be minimized by resolving all DTP when  $C_2$  (cost of monitoring) is less than \$50.00 per patient per month.

## Solutions

Prescribing improvement programs have little research support for improving patient outcomes or lowering total costs in ambulatory care. This is not really surprising, given the research showing that prescribing is not a leading cause of PDRM in ambulatory care. On the contrary, some studies show that prescribing restrictions (as they are carried out in America) have “unintended consequences”: they may actually worsen outcomes and increase total costs of care.<sup>3-5</sup> More about this later.

In contrast, the research evidence in support of *systems change* is quite encouraging, the more so if it is interpreted because of the theory described above. Many studies suggest that cooperative medications use systems are associated with improved outcomes and reduced total costs of care. Perez, et al carried out a review intended to “summarize and evaluate studies that measured the economic impact of clinical pharmacy services . . . published between 2001 and 2005.”<sup>17</sup> Their review included studies performed in hospitals, ambulatory care clinics, physician’s offices, and community pharmacies. The quality of studies varied widely, with fewer than one-half considered good to fair.

The most frequent types of clinical services evaluated were general pharmacotherapeutic monitoring services, as well as target drug and disease management programs. Among the 45 studies reporting full economic evaluations, a positive economic benefit associated with clinical pharmacy services was noted in 31 (69%). Fifteen studies reported data necessary to calculate a benefit-to-cost ratio (BCR). Among these studies, the BCR ranged from 1 to 34.6, with a median of 4.81 and a mean of 8. In other words, each dollar spent on clinical pharmacy services returned from \$1 to \$34.60, on average \$4.81.

This return was not achieved through drug cost savings. (Even a 1:1 BCR would seem impossible to achieve from reductions in drug expenditures alone.) Rather, these returns were achieved through reductions in total costs of care.

Results like these are not new. Some older examples are summarized in Appendix Tables 1 and 2. These studies suggest that even modest improvements in the customary, disjointed, medications use process may be cost-effective. All of the “successful” studies in Tables 1 and 2 increased pharmacists' responsibilities for medications use, and all involved other team members as well. These studies do not prove that pharmacists are the only health professionals who can contribute in this way, or even that pharmacists are the best for this purpose.

Some studies have shown little improvement in outcomes associated with pharmaceutical care systems, or that they increased total costs of care. Two studies are particularly instructive.

In a study of asthma disease management led by Weinberger, as few as one-quarter of eligible asthma patients actually received care, as documented in their records.<sup>18</sup> In another study by Stergachis et al, the authors concluded, “The intervention may not have been powerful enough to significantly affect pharmacists' behaviors and asthma patients' outcomes in community pharmacy settings.” In addition, only patients with mild asthma were included in the study, so there may have been too little scope for clinical improvement.<sup>19</sup> Neither of these “negative” studies was completely implemented.

In other words, a decision to implement medications management may not result in care actually being provided to the patients who need it. Obviously, it is important (a) to manage the implementation of a new medication management program to be sure that it is implemented as planned, and (b) to offer medication management services to patients who are likely to benefit from them.

None of the studies cited in the Appendix met the “gold standard” of randomized, blinded, controlled clinical trials. The scientifically pure position, of course, would be to reject them all as poorly designed, and to suspend judgement until better evidence becomes available. Some people advocate this position.<sup>20</sup>

In the meantime, however, patients may continue to experience preventable injury from drug therapy and treatment failures, while their health care program incurs avoidable expense to correct them and spends on projects based on conventional wisdom, with much less evidence than is provided by these “imperfect” studies.

This is where the values of scientists and professionals diverge somewhat. Health services *managers* and *professionals* need to take timely and specific actions, because not doing something is as much of a decision as any other. They are accustomed to choosing from among available alternatives, under conditions of uncertainty. They make decisions every day that researchers might feel are unsupported by enough adequate studies. Perhaps part of the slow progress in implementing medications management is just resistance to change.

## **Pharmaceutical Care and the Adoption of Innovation**

The objective argument in favor of implementing pharmaceutical care systems (PCSs) justifies – at the very least – further demonstration projects, pilot programs or research programs. And these are surely going on. The question remains, however, what might accelerate the spread of medications management systems?

According to the theory of Diffusion of Innovation (DoI) the most fundamental issue in adoption of an innovation is recognition of an unsatisfied need or unresolved problem. The obvious problems in medications use were described above. The fundamental obstacle in the adoption of pharmaceutical care is that PDRM remain largely invisible to most stakeholders. Possibly, the people responsible for health systems are unaware of the research reviewed above. Some may be aware of the problem as it is described in the literature, but think of it as “out there,” not in their specific populations, programs or practices.

Managers rely on their information systems or on clinicians to identify problems like this. If

a clinical database does not include many reports of PDRM, then a manager may assume that *his* program does not have a PDRM problem. Perhaps he can believe that he is doing a better job than the managers of the programs studied for the published reports.

A clinician may admit a patient to a hospital in asthmatic crisis, for example. This is very *unlikely* to be coded as a drug treatment failure. In one study, only 18% of drug related admissions (determined by medical audit) had been coded as such in hospital records by the admitting physicians.<sup>21</sup>

In a more recent study, about a third of ER visits for adverse drug events were not recognized as such by the ER physician. The authors of that study concluded, “A significant proportion of drug-related visits are not deemed medication related by emergency physicians. Drug-related visits not attributed to medication-related problems by emergency physicians may be missed in ongoing outpatient adverse drug event surveillance programs intended to develop strategies to enhance drug safety.”<sup>22</sup> So, the prevalence of PDRM may not be visible in medical records. Routine hospital and managed care epidemiology would miss it, even though specific research projects would find it.

Furthermore, a database has to be searched properly to find PDRM events. For example, a database might show high emergency department utilization by people with asthma. It might also show low utilization of inhaled steroids by people with asthma. But the two might never be linked in a report unless a search routine had been written to uncover the connection.

A second issue in adoption theory concerns the advantages of the new idea over the old, i.e., of a medications management system over the status quo. We have seen that many published studies show that a PCS can improve quality at equal or lower cost. Perhaps many decision makers do not know about these studies, or doubt their applicability to their specific circumstances. Some skepticism may be explained simply by the fact that actual pharmaceutical care practices are not common or easy to find.

A third issue in adoption is the perceived risk of change. This is related to problem awareness, mentioned above. If one does not accept the prevalence of costly and injurious PDRM, it would be difficult to see how a program to improve quality of drug therapy could receive high priority. If there is no problem, why risk implementing a new service?

A fourth issue is the compatibility of the innovation with current practices, norms, and beliefs. Pharmaceutical care is an official goal of many pharmaceutical societies worldwide, and has been adopted as policy in the Medicare program under the name of Medication Therapy Management (MTM). It is totally consistent with the stated values of pharmacy, nursing and medicine.

Some physicians and pharmacists, however, are accustomed to isolated practice. They may have developed negative stereotypes, may not value interprofessional cooperation, or may not believe that it is possible. Some professional organizations may be preoccupied with maintaining or expanding professional power and boundaries. They would need to see the benefits to patients and ultimately to all professions that could result from interprofessional cooperation.

The belief (actually, assumption) that money saved in the “pharmacy benefit” would be

reflected in total expenditures is incompatible with pharmaceutical care. This belief, however, is institutionalized in the organization and management of many third party payers and hospitals. It is virtually cast in concrete when a firm contracts with an outside pharmacy benefit management company, and evaluates the performance of the pharmacy director or contractor based on drug expenditures.

This belief has little or no research support, and does not make sense from a patient-oriented view of drug therapy, let alone a systems view. The safety and effectiveness of drug therapy may greatly affect other expenditures, e.g., for doctors, emergency departments and hospitalizations. An inappropriate or clumsy attempt to save \$50 in pharmacy expenditures can easily result in a \$10,000 hospital admission or even a death. Conversely, spending an extra \$50 can easily avert the admission.

Implementing pharmaceutical care may actually increase drug expenditures slightly, and surely would increase pharmacy and nursing payrolls, while greatly reducing expenditures for physician services, hospital costs, etc. that are spent today on correcting PDRM. Unless this is recognized by top management, it is easy to imagine that a pharmacy service could go over budget or otherwise fail to meet corporate expectations, while saving lots of money for other departments. Such perverse incentives might demand too much of a pharmacy manager.

If the financial significance and performance of pharmacy in an organization is mainly measured by drug expenditures, it should not surprise anyone that pharmaceutical services tend to be preoccupied with drug expenditures. For example, the process called drug use evaluation (DUE) seldom, if ever, actually evaluates drug use. It is primarily concerned with issues like formulary adherence within a therapeutic class.

Drug use review is usually blind to such common drug therapy problems as no drug therapy for a valid indication, continuing an ineffective drug product or dosage, and prescribing the “right” drug even though it is not actually most appropriate for a particular patient. Problems like these, however, may ultimately cost the organization as much as the drug budget itself. The connection between inappropriate drug use and adverse outcomes must be made clear to top-level managed care decision makers.

Pharmaceutical care is fundamentally incompatible with a typical dispensing-oriented pharmacy practice. To mention only two examples, the fee structure for pharmaceutical care would be based on continuous patient relationships, rather than dispensing physical products. Pharmacists are not accustomed to documenting care and do not typically keep patient oriented records (as distinct from documenting dispensing and prescription profiles). In short, many independent pharmacists may not understand a professional business model for a pharmaceutical care practice, and many corporate pharmacies may not feel comfortable managing such practices.

Application of DoI theory to medications use uncovers an important additional complication. Usually, a supply of an innovation already exists. In other words, adoption theory presumes a “push” strategy by the innovators. For example, enough photocopiers, personal computers, cell phones, electric cars, etc. were produced (in anticipation of demand) to allow consumers to try them.

For medications use systems, however, diffusion and adoption by both potential suppliers and purchasers have to go on concurrently. Otherwise, the demand side (patients or managed care organizations) may not believe that a supply of pharmaceutical care providers exists, while the supply side (pharmacies and cooperating physicians) may believe that there is no demand. Furthermore, although the basic issues may be similar for all groups, the same arguments will not persuade pharmacists, patients, physicians, and payers.

In conclusion, resistance to pharmaceutical care, by pharmacists, physicians, patients, or payers is not unique. People often resist change, for a variety of reasons. Some resistance to change may be irrational, or rational but based on one or more mistaken premises. Other reasons for resistance may involve fear of the unknown, psychological defenses, ineffective thinking styles, and a narrow perspective. In his book, *The Fifth Discipline*, Peter Senge described some everyday patterns of resistance to needed change and other inappropriate responses to complex problems. Denial is a common and very effective initial defense against change.

So, perhaps pharmacy managers in health care programs stay busy with other, more obvious and less intimidating problems. This might seem safer than changing their way of thinking about drug therapy and their basic structures for providing it.

Pharmaceutical care has many theoretical obstacles to adoption. Each of them can be overcome, if they are addressed directly. Since health care managers are intelligent, responsible and well-meaning people, the obvious way forward is to give them a means of assessing the prevalence of PDRM in their programs. The most powerful means of overcoming most of these obstacles is to monitor the quality of individual systems. Performance indicators can provide an inexpensive and useful means for doing that.

### **Medications Management Systems**

A managed care organization (MCO) has the capacity to influence the care provided by the microsystems within it and ultimately the quality of care. To do that, a MCO needs a medication management system (MMS). A MMS is a system on an organizational level whose purpose is to manage pharmaceutical care activities on the microsystem level. It is a way to measure the effect of policy on the care actually provided and, possibly, patient outcomes. We can think of an MMS as the organizational-level counterpart to a microsystem-level PCS.

Pharmaceutical care refers to the care of patients as individuals. The purpose of a MMS is not to manage care of individual patients, but instead to manage the quality of pharmaceutical care systems. Just as pharmaceutical care may employ *clinical indicators*, which are specific observations used to evaluate the progress of therapy in one patient, medications management should employ *performance indicators*, which are specific observations used to evaluate the



overall performance of PCSs. (See Figure 11.)

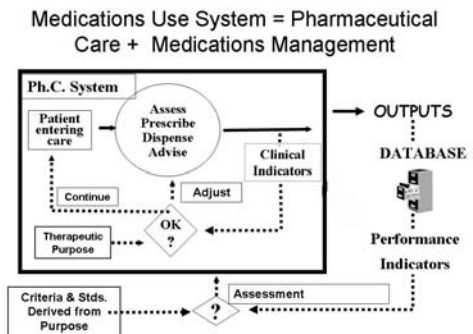
### *Performance Indicators*

A performance indicator is a measurement used to monitor and evaluate important processes that affect patient outcomes, or the outcomes themselves. These measurements can be compared with benchmarks or other expectations, and can be tracked over time. They can be analyzed statistically to differentiate basic shifts in system performance from random variation. If the analysis suggests that system performance is not acceptable or changing in the wrong direction, indicators can form the basis of root cause analysis to identify specific problems, guide problem solving, and monitor the effectiveness of remedial action. Indicators are available from the National Quality Measures Clearinghouse, NCQA, and JCAHO.<sup>d</sup>

By providing timely and specific information about a particular system, performance indicators can also encourage adoption of necessary innovations and help to overcome irrational defenses against change. For example, adoption depends on recognition that the “old way” is not satisfactory. Denial of a problem is more difficult when objective data show that a problem is indeed present. Also, performance indicators can guide problem solving toward useful solutions. For example, blaming individuals becomes less tenable when indicators suggest that a significant problem is widespread and involves many people.

Drug use evaluation (DUE) is a well-known procedure in health care organizations, especially managed care organizations. DUE is an audit procedure that may be used to evaluate the quality of prescribing or simply to measure adherence to a restrictive formulary. For example, an MCO may favor one lipid-lowering agent over all others. It can search its database to find out how often the preferred agent is being prescribed (and by which prescribers).

Despite its name, DUE does not evaluate drug use, only prescribing. It uses simple, highly specific indicators, often just the identity of the drug, sometimes drug identity and dose, and rarely, concurrent therapies. More sophisticated prescribing indicators have been developed by Beers and his co-workers and by Hanlon and his co-workers.<sup>23,24</sup> Hanlon’s Medication Appropriateness Index (MAI) reflects ten drug regimen criteria. Despite its narrow scope, DUE may serve as a helpful starting point for understanding how to use indicators to manage quality in a MMS.



**Figure 11.** Pharmaceutical Care System Nested within Medications Management System (Diagram does not show a prescribing improvement system, which would also be part of a MMS.)

<sup>d</sup> For examples, see the National Quality Measures Clearinghouse at <http://www.qualitymeasures.ahrq.gov/> especially <http://www.qualitymeasures.ahrq.gov/browse/measureindex.aspx> and MacGlynn (reference 6).

The indicators needed for a MMS go far beyond prescribing. Medication use process indicators can also reflect such aspects as duplicate therapies, length of therapy, patient compliance (refill patterns, doses received as a proxy for doses consumed), monitoring, lab tests, and other kinds of followup. Other indicators reflect aspects of medication use *outcome*, for example, adverse drug reactions or adverse drug events.

Here is an example of a medications use *process* indicator:

The proportion of asthma patients using SABA metered dose inhalers who receive two consecutive early refills.<sup>e</sup>

A well-defined indicator has a clear definition of a measurable numerator, denominator (if rate-based), rationale, data source, and intended scope. Furthermore, the rationale should be based on evidence and consensus guidelines.

- *Numerator*: Number of asthma patients using SABA metered dose inhalers who receive two consecutive early refills.
- *Denominator*: Number of asthma patients using SABA metered dose inhalers
- *Data source*: MCO payment records or pharmacy computer
- *Scope*: issues in asthma control that are sensitive to drug use management and patient education;
- *Rationale*: Frequent use of SABA rescue inhalers by asthmatic patients may
  - indicate a worsening or lack of control of underlying disease.
  - may also mask the worsening or lack of control of underlying disease
  - may predict asthmatic crisis, ER visit, hospitalization, or death.
- *Guideline*: patients requesting early refill of rescue inhalers should be interviewed and assessed. If their disease is worsening they should be referred to medical attention. If their inhaler use is incorrect, the training should be repeated.

The numerator and denominator would be operationalized using the coding system of the database, e.g., ICD disease codes, CPT and drug product billing codes. Also, mechanical details would have to be worked out. For example, the designation of an early refill would depend on the maximum recommended number of doses in each SABA drug product.

*Interpretation of indicators.* The value of an indicator depends on its interpretability (e.g., its rationale, measurement validity and reliability.) As the rationale says, a positive for this indicator implies poor quality of asthma management.

A rate-based indicator like the example above is seldom a direct measure of quality. It is interpreted differently than a sentinel indicator (see below). Rate-based indicators are interpreted historically in the context of the system they were collected from. In the present example, one early refill is meaningless, but repeated early refills may indicate over-use of rescue medications. If this occurs for many patients, it may suggest low quality of asthma therapy in a patient group

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<sup>e</sup>SABA – short term beta agonists – are often used as “rescue” medications for patients with asthma and other diseases that constrict airways.

and deficient monitoring. If those patients also have a high rate of ER visits for asthma, a pattern of low quality drug management of asthma becomes apparent.

If management decides that an improvement in quality is necessary, then it may be followed up by root cause analysis and selection of a corrective intervention. A Shewhart Cycle (FOCUS-PDCA) is an example of such a problem solving procedure.<sup>12</sup>

To offer a quick (perhaps oversimplified) example, suppose that a health care organization decided that community pharmacies were key points in managing chronic asthma. Suppose it inserted an alert in its pharmacy computers. When an asthmatic patient requests an early refill or renewal of a SABA, the computer reminds the pharmacist to review medications use, to interview the patient about the status of his asthma control, and to check the patient's inhaler technique. Then, the indicator would be very useful in tracking the effect of that intervention. If some pharmacies tended to ignore the alerts, they could be targeted to solve the problem.<sup>f</sup>

*Indicators as Medication Alerts.* Piontek, et al described the prospective application of medications use process indicators (which they called an “adverse-drug-event (ADE) alert system”) in a group of seven community hospitals. For example, an alert triggers whenever a patient over 65 years of age receives an order for a drug with significant sedative effects or for amitriptyline.

Using administrative data, the investigators evaluated costs and outcomes for all inpatients admitted to the participating hospitals after, and one year, before the deployment of the alert system. Inpatients in two network hospitals that did not use the alert system constituted a control group. Mean differences in outcome measures across all four groups were compared using analysis of variance.

Analysis showed significant decreases in mean pharmacy department costs per patient between pre-implementation and post-implementation observations ( $p < 0.001$ ), while pharmacy department costs increased significantly in the control group ( $p = 0.029$ ). Drug costs decreased significantly from baseline ( $p < 0.001$ ) in the post-implementation group, compared to a significant increase in drug costs in the control group ( $p = 0.029$ ). Severity-adjusted mortality rates and length of stay (LOS) decreased significantly in the post-implementation group. Total patient hospitalization costs, both crude and severity adjusted, significantly increased in both groups. The authors concluded that the ADE alert system was associated with significant decreases in pharmacy department costs, variable drug costs, and severity-adjusted mortality rates.<sup>25</sup>

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My use of a single indicator example does not suggest that one or two indicators would be sufficient to operate a MMS, or that improved management of a single disease is sufficient to improve the quality of medications use. On the contrary. A variety of indicators representing the drug therapy of many diseases and patient types would be necessary to prevent gaming the system (“cherry picking”), to improve patients' HRQoL, and to reduce overall utilization.

A *sentinel indicator* (also called a sentinel event or a “never” event) is considered a direct measure of quality. A sentinel event has no denominator, because a single occurrence indicates low quality and should be followed up. Examples would include such things as inpatient falls out of bed, a mis-matched blood transfusion, surgery on the wrong patient, or amputation of the wrong limb. Usually, sentinel events are not monitored from databases, but are reported at once as untoward incidents.

*PDRM Outcome-Process Indicators.* Most medication use indicators refer either to process or outcome, but not both. Sometimes, a process indicator may be associated with an outcome so frequently that it is used as a proxy for the outcome. That may be the case with overuse of SABA inhalers without concomitant use of steroid preventer medications. Such a strong association with an outcome would greatly strengthen the rationale of the process indicator. Nonetheless, it would still be a proxy outcome measure.

Performance indicators, however, can include both process and outcome elements. Such indicators may be more useful than process indicators for routine management of medications use systems.<sup>26,2728</sup>

Process-outcome indicators are based on the definition of preventable drug related morbidity first given by Hepler and Strand in 1989.<sup>29</sup> A preventable DRM is one that was preceded by a *recognizable* drug therapy problem (DTP). Further, that DTP must have the following three characteristics that constitute a *correctable* problem:

- The possibility of the DRM must have been reasonably *foreseeable*
- The cause of the DTP and DRM must have been *identifiable*
- The cause must have been *controllable* within the scope of the therapeutic objective.

The format of each indicator is *patient outcome + process of drug therapy*. For example, a process + outcome indicator for monitoring the management of asthma was written as follows:

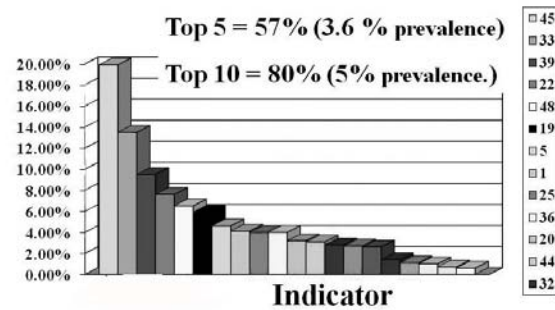
An event of asthma exacerbation or status asthmaticus or emergency department (ED) visit/hospitalization due to asthma in a patient with (1) a diagnosis of moderate to severe asthma; (2) use of a bronchodilator as shown by pharmacy records; and (3) no evident use of maintenance corticosteroids.

The following example was the most frequently-found PDRM in a recent study by Richard Faris:

A patient admitted to a hospital or emergency department (ED) with decompensated congestive heart failure (CHF) when he had a history of CHF and no record of ACE inhibitor use.

Note that, in these indicators, an attempt is made to directly identify the outcome, e.g., hospital admission for a specific cause. Since the outcomes used in the indicators are adverse outcomes or treatment failures, these are PDRM indicators.

In one study, an automated search of a managed care claims database using about 50 process-outcome indicators showed an overall period prevalence of 6.25 per 100 patients per year. The five most frequently occurring indicators accounted for 57% of all occurrences of PDRM. The “top 10” indicators accounted for 80%. (Figure 12) Many indicators were not associated with any events. The point is that substantial improvement in the performance of that medications management system could be achieved if relatively few recurring problems could be corrected.<sup>27</sup>



**Figure 12.** Distribution of Indicator Frequencies in the Faris Study (Each bar shows the number of positives from one indicator.)

Faris also studied the association of process and outcome within the indicators. For example, 75% of the patients with CHF who did not receive ACE inhibitors decompensated during the observation period. All asthmatic patients receiving frequent SABAs but not inhaled steroids had at least one asthmatic crisis.

*Pharmaceutical care and medications use management.* Performance indicators may accelerate adoption of pharmaceutical care and medications management systems by providing feedback on quality of medications use. Furthermore, the information they provide may facilitate implementation. Performance indicators would . . .

- allow a hospital, provider network, or third-party payer to assess the quality of medications use among its patients or members and to identify any quality deficiencies in medications use. From a DoI perspective, this would increase problem awareness.
- help to prioritize problem solving. (See Figure 12.)
- facilitate root cause analysis. Process failures are included in the indicators. (For example, the process element in the CHF indicator mentioned above was non-treatment of a valid indication). This would help to identify specific process problems through system analysis and would avoid simplistic explanations such as blaming individuals or bad luck. A recurring association between questionable process and adverse outcome shows that the outcome results from system failures and not from occasional bad luck.
- provide data that would help to identify corrective actions, including gradual construction of improved medications use systems
- be useful in monitoring and assessing the effectiveness of corrective action
- provide a basis for incentives, bonuses, etc. Managers could use the process component of the indicators to assess whether providers are actually providing appropriate care, overall. This could, if necessary, be a basis for payment for services.

- Competition or regulations could require each MCO to operate a performance review program based on drug therapy problems and process indicators.<sup>30</sup>

The statistical association of process and outcome elements suggests a direct connection to pharmaceutical care. Many indicators may have a strong association between their process elements and outcome elements. Pharmacists (or others) can seek to identify patients who are receiving processes of care that have been associated with undesired outcomes in a particular MCO or patient cohort, for example patients with heart failure who are not receiving an ACE inhibitor; or asthmatics who are not well controlled on inhaled SABA but who are not receiving inhaled steroids (either because none was prescribed or because they have chosen not to use it.)

Avery, et al. used this strategy to identify about 60,000 patients at high risk of specific, defined PDRM in 72 UK general practices with a combined list size of 480 942 patients.

Practices were randomly assigned to an experimental, multifaceted pharmaceutical care intervention (PINCER) or simple feedback. At 6 months' follow-up, patients in the PINCER group were significantly less likely to have experienced one of the following PDRM:

- to have been prescribed a non-selective NSAID if they had a history of peptic ulcer without gastroprotection (OR 0.58, 95% CI 0.38–0.89)
- to have been prescribed a  $\beta$  blocker if they had asthma (0.73, 0.58–0.91)
- to have been prescribed an ACE inhibitor or loop diuretic without appropriate monitoring (0.51, 0.34–0.78).

Improved quality of medications use was also seen in 9 other “secondary” PDRM categories.

The authors concluded that the pharmacist intervention (PINCER) is an effective method for reducing a range of medication errors in general practices with computerised clinical records.

Cost of avoiding serious PDRM in ambulatory care was £75 (at 6 month followup or £85 (12 months) per error avoided.

(Avery, AJ, et al. A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis *Lancet* 2012; 379: 1310–19)

The key strategic coup in the PINCER study was the identification of “at risk” patients (i.e., patients receiving inappropriate drug therapy prescribing or monitoring) through the use of computerized searches. This identified patients most in need of intervention and made the study much more efficient by reducing the amount of “noise” variance. The same strategy would make medications use quality improvement program more efficient by targeting at risk patients.

*A Caveat – Don't Try to Fly The Plane from the Tower.* Although medications management is important for improving outcomes on a population level, the importance of the pharmaceutical care component must also be stressed. General problems shown by indicators should not lead to the imposition of one-size-fits-all guidelines on a whole population. Individual patient assessment is still needed, and these indicators facilitate that.

Continuing with the previous example of ACE inhibitors in CHF, the positive predictive value of the *process* (no ACE inhibitor) for the *outcome* (cardiac decompensation) was about 75%. Not all heart failure patients without ACE inhibitors decompensated. Probably, not all decompensations could have been prevented by ACE inhibitors. So, on a population level, the indicator data tell us that many patients with heart failure did not receive a needed ACE inhibitor. They tell us that pharmacists or physicians should be more careful in their patient assessments.

If used in real time, the indicator would show which patients with heart failure are not presently receiving an ACE inhibitor, but they would not show who should receive one, or in what dose, how the patient can be convinced to take the medicine, or how side effects can be ameliorated while the therapeutic effect is optimized. Population data do not address the possibility that other diseases, drugs or patient problems may affect the decision to add an ACE inhibitor. That is why we need both a macro-level MMS and a patient-level PCS.

The relationship between pharmaceutical care on the microsystem level and a medication management system on the organizational levels is shown in Figure 11. Note that pharmaceutical care and medications management are analogous and complementary. Clinical process indicators on a patient level correspond to performance indicators on a population level, as shown by the wide, blue arrow. In fact, some process indicators in a PCS can be the process part of a PDRM indicator, for example ACE inhibitor usage in patients with CHF. Just as patient care is controlled according to therapeutic purpose, the system is controlled according to performance criteria and standards.

### **Ethical Responsibility**

To summarize to this point:

1. Our society has a significant problem with medications use
2. It needs pharmaceutical care and a MMS to improve the quality of medications use, especially performance indicators to manage the system.
3. Pharmacists are strategic in solving this problem.
4. Performance indicators are a major tool for assessing the quality of medications use in a system, i.e., the prevalence of PDRM in a population. Specific data might be essential to overcome resistance to change.

Patients, members of managed care organizations, and for that matter members of society expect health professionals to do more to protect them from the dangers of drug therapy. If people do not demand better quality, perhaps it is because they assume (trust) that their providers already provide high quality.

Many professionals and managers see PDRM as a business problem. Perhaps it is, but it is also an ethical problem that raises questions about professional values and character. If we know (or could easily discover) that a medications use system allows preventable injury, we are obliged to correct it as best we can. To spend money on amenities (valet parking, so to speak)

instead of improving quality and increasing efficiency is unethical.

Evaluating and improving the quality of medications use, in the face of conventional wisdom, inertia and career timidity is difficult. But health professionals, program managers, and insurance executives have a duty to make our systems safer, more effective and more efficient. When both the difficulty and the significance of an endeavor are high, strength of character becomes crucially important.

Many virtues are needed in today's business oriented climate. I have written elsewhere about these, but here I'll just discuss two: honesty and courage.<sup>31</sup> When I look at the world of health care management I see a double standard for evidence. Managers in private industry and government seem to demand impossible levels of proof for ideas that contradict the conventional wisdom, or that might change the status quo, even while they operate useless or even harmful programs in the name of quality. Let me provide two examples.

Susan Horn and her colleagues published a paper evaluating the effect of formularies on costs of care, as they were used by five managed care programs nationwide. This elaborate, large scale study suggested that formularies, as used by those managed care programs, *did not* result in lower costs of care. Use of formularies was associated not only with higher drug costs but also higher costs for physician office visits, emergency room visits, etc.<sup>3</sup> A storm of criticism followed this study. Most of it concerned details of the study's methodology. Some of it was personal and vicious. Some of the methodological criticisms might have been valid, but all of them begged the question of "Where is the evidence for formulary effectiveness?"<sup>32</sup>

The critics seemed to assume that an abundance of rigorous scientific evidence exists to show that formularies do control costs in managed ambulatory care. However, the truth was that no such evidence existed, certainly none that would meet the rigorous research standards demanded by Horn's critics. In fact, earlier reviews had been consistent with Horn's results.<sup>5</sup>

For another example, Steven Soumerai and colleagues at Harvard showed that a prescription cap imposed on Medicaid recipients in New Hampshire backfired in a particularly nasty way. Although the cap (a limit of five active prescriptions) reduced prescription numbers and prescription expenditures, it increased nursing home and hospital admissions. Therefore, it increased total expenditures per patient-year many times more than the prescription cost savings. In addition, the policy dislocated many poor elderly people who were not able to return home after the cap was abolished. The effect among schizophrenic patients was even worse. One would think that this caused a nationwide movement away from prescription caps, but that did not happen.<sup>1,2</sup>

At least six state Medicaid programs ignored these studies for years. (I don't know how many private insurance programs also continued prescription limits.) A man died in Mississippi long after the deficiencies of prescription caps should have been widely known, in part because an antibiotic prescription for pneumonia exceeded his insurance program's five- prescription limit.

In contrast, studies have been appearing regularly for years that show the cost effectiveness of cooperative drug therapy management systems. However, some pharmacists and managers seem to miss the thrust of these studies, preoccupied instead with the



imperfections in each study.

So, what is honesty? Must it rest on proof beyond any doubt? What about type II error, the error of rejecting a research hypothesis that is actually true? Perhaps the root cause of resistance to pharmaceutical care is a lack of education in systems, lack of willingness to make a decision based on “imperfect” evidence, and a wish to avoid responsibility. Perhaps we require another virtue — the courage to advocate what we believe in, even if we cannot absolutely prove we are right. One of William Blake’s “proverbs from hell” says, “if you lack the courage to be a hammer you will get the role of the anvil.”

## Summary and Conclusions

(1) The most commonly accepted definition of health care quality (IOM) is in terms of safety, effectiveness, etc.(STEEEP) as delivered to the patient, not frills and flash and cool stuff for providers and suppliers. That's what the "true North" analogy is all about: patient outcomes.

(2) Therefore, increasing quality of medications use is equivalent to increasing STEEEP by reducing or eliminating PDRM.

(3) Economically, PDRM is pure waste. PDRM is the drug therapy equivalent of a mis-adjusted industrial machine. PDRM almost always has to be corrected, if possible, at considerable additional expense. Even if correctable, PDRM lowers HRQoL, worsens clinical outcomes, etc.

(4) The objective of medications use is to do therapy correctly the first time, i.e., safely, effectively, etc. Theoretically, avoiding the expensive "re-work" caused by PDRM should more than pay for the cost of operating a high-quality (safe, effective, etc.) medications use system.

Other industries have greatly lowered their costs by improving quality in the same way. Reducing PDRM is essentially preventive action, similar in spirit to cholesterol reduction, immunizations, etc., preventive measures that are clearly cost-effective. In those examples, however, we are attempting to avoid the burden of disease caused by external factors like diet or viruses. In the case of drug therapy, much of the burden is caused internally, by suboptimal organization of medications use into financial “silos” and ineffective programs.

(5) As matters stand today, there's no proof that we can achieve the theoretical objective of safe and effective medications use. Many studies suggest that we can, some suggest that we can't. We still have a lot to learn. But it's obvious that we won't know unless we see the possibilities enough to give it a fair trial.

(6) Changing the status quo always creates winners and losers. Some corporate pharmacy executives are happy with the status quo, and do not want to be in the patient care business. Also, the economic incentives are perverse. It is an ugly fact that providers are paid to correct injury caused by poor quality of care. Improving the quality of medications use without increasing total expenditures for care will require that expenditures shift from the providers who are currently paid to *correct* PDRM to providers who will be paid to *prevent* it. Some will surely find a rationale for resisting change that may reduce demand for their services.

(7) The problem of PDRM has existed for years, and public and political appreciation of

it has resulted in adoption of the concepts, at least, in the Medication Therapy Management (MTM) requirements under Medicare. Pharmaceutical care and MTM have empirical support that is stronger than the evidence supporting other approaches to improving drug therapy, yet they have been taken up very slowly. The lack of standards means that MTM providers have wide latitude to provide effective care or to game the program.

(8) The spread of pharmaceutical care requires inter-dependent “adoption” decisions by pharmacists, patients physicians and payers. It confronts many defenses against change and will require stronger advocacy from more people.

(9) The science is clear, the technology to address it is feasible, and the personnel are potentially available. This is now a problem of politics, marketing, and ethical will. Market forces have failed to produce the necessary change. In many countries, an initiative by government or private health care payers may be necessary to initiate the needed system reforms. Indicators may play an essential part both in creating demand and in making supply more effective and efficient. Pharmacists should work with payers to create and implement pharmaceutical care and medications management systems.

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Please see also the *Bibliography on PDRM Indicators*

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**Appendix Table 1. Examples of Community Practice and Ambulatory Care Outcomes Studies**

Authors	Setting	Design	Sample	Intervention	Results
<b>Feedback on Medications Use</b>					
Sleath, et al 1997 <sup>33</sup>	Community Practice	CT	35 I 45 C	Mailed information about patient drug use I=pharmacist and physician C=physician only	In I, total cost of care/pt/month reduced by \$30, including asthma drug cost reduced by \$21. In C, total cost of care/pt/month increased by \$123 in C group while asthma drug cost was reduced by \$19.
<b>Referral</b>					
Lipton et al. 1992 <sup>34</sup>		RCT	n=236	"I" - pharmacy consultations "C" - no consultations	Patients of physicians receiving pharmacy consultations had improved prescribing and significantly fewer drug related problems.
Borgsdorf et al. 1994 <sup>35</sup>	Clinic	BA	n=836 patients	Referral of patient to pharmacy clinic for medication consultation	Average cost savings of \$644/patient-year after patients were referred to pharmacy for assessment of therapy. Savings mostly through reductions in physician visits, emergency room use and hospitalization.
<b>Cooperative Drug Therapy Management</b>					
Wilt et al. 1995 <sup>36</sup>	family practice clinic	Cohort control	n=112 pt. receiving oral anticoagulants	"I" - pharmacist and physician cooperation "C" - physician only management	"I" patients had 1/20 risk of adverse events from oral anticoagulants. Cost savings \$4073/patient-year. .
Malone, et al. <sup>37,38</sup>	9 VA Med. Centers	RCT	n=523 "I" 531 "C" high risk patients	"I" - pharmacist and physician cooperation "C" - usual care	No. of clinic visits increased in the "I" group (p=0.003), with no difference in clinic costs. Total health care costs increased on average \$1,020 for "I" group and \$1,313 for "C" group (p=0.06). CONCLUSION: Including the cost of pharmacist interventions, overall health care expenditures were similar for patients randomized to see a clinical pharmacist versus usual medical care

**Appendix Table 1. Examples of Community Practice and Ambulatory Care Outcomes Studies**

Herborg et al. <sup>39,40</sup>	Community Practice	CT	n=413 asthmatic patients attending 16 "I" and 15 "C" Danish pharmacies	"I" - Cooperative pharmaceutical care (Therapeutic Outcome Monitoring) "C"- usual ambulatory care in Danish community practice	Asthma patients receiving pharmaceutical care had fewer MD visits, higher drug costs, fewer sick days, higher symptom control improved quality of life, asthma prescribing closer to guidelines.
Isets, et al 2001-2002 <sup>41</sup>	Community Practice	CT	285"I", 252"C" in 6 ambulatory care clinics	"I" - Collaborative face-to-face MTM services from pharmacists & prescribers "C" usual care	Total health expenditures \$11,965 per person ("C") vs \$8,197 ("I"). Savings exceeded the cost of MTM services by > 12 to 1. Patients receiving "I" improved clinical outcomes & lowered total health expenditures. Results support inclusion of MTM services in health plan design
Designs: BA: before-after; RCT: randomized controlled trial; CT nonrandom controlled trial; I-intervention group; C- Control group, n - sample size					

**Appendix Table 2. Examples of Inpatient Care Outcomes Studies**

Authors	Setting	Design	Sample	Intervention	Results, Design
Cooper, 1985 <sup>42</sup>	LTCF	Time Series	72-beds, 5 observations over 3 years	Consultant pharmacist reviewed medication orders	Pharmaceutical consultations reduce numbers of prescriptions and costs of drugs.
Clapham et al. <sup>43</sup>	Hosp	CT	n=168 admissions of medical-surgical inpatients admitted over 5 mo.	I-Rounding team included pharmacist C - team without pharmacist.	Patients on I teams had average length of stay (ALOS) 1.5 days less (cost savings \$1200 per admission) after correcting for diagnostic and age differences

**Appendix Table 2. Examples of Inpatient Care Outcomes Studies**

Authors	Setting	Design	Sample	Intervention	Results, Design
Bjornson DC et al, 1993 <sup>44</sup>	Hosp	CT	n= 3081 general med-surg patients admitted over a 1 yr period	I - clinical pharmacist participation in health care teams (2 / 5 med., 1 / 2 surg) C - team without pharmacist	Patients on I teams had a shorter ALOS than C. The average cost savings for I teams was \$377 per inpatient admission, and the benefit-to-cost ratio was 6.03:1.
Leape, et al., 1999 <sup>45</sup>	Hosp ICU	Mixed	n=120	I-Rounding team included pharmacist C - team without pharmacist	Preventable prescribing ADEs decreased from 10.4/1000 pt.-days <i>before</i> to 3.5 <i>after</i> (66% reduction). In C, the rate was essentially unchanged 362/366 (99%) pharmacist recommendations related to drug ordering were accepted by physicians.

### Glossary

#### Adverse Drug Reaction (ADR)

Any noxious and unintended effect caused by the drug itself. By far, ADRs are the most widely recognized adverse outcomes from drug therapy.

#### Drug Related Morbidity (DRM)

An unintended patient injury with a scientifically plausible relationship to either (a) drug therapy or (b) an untreated indication for drug therapy. See *injury*. DRM include significant adverse or toxic effects of drugs, treatment failures, and occasions when a valid indication was not treated. DRM do not include DTP or minor (technical) ADR. For example, oozing of blood after brushing teeth is technically an ADR but is not a DRM; however it is a DTP because it may indicate the drug therapy is not progressing toward the therapeutic objective.

#### Drug Related Problem (DRP)

This term is ambiguous. It is used by some authors to denote a drug therapy problem, and by others to denote an adverse drug event or drug-related morbidity. This ambiguity blurs an important distinction between DTP (part of the process of drug therapy) and DRM (an outcome of drug therapy)



Drug Therapy Problem (DTP)	Any circumstance that a competent professional would judge to be inconsistent with achieving a therapeutic objective, but which does not itself constitute injury (p.41); an observable latent injury <i>before</i> it has become a manifest injury (p. 33). A <i>potential</i> or <i>theoretical</i> DTP is a discrepancy between a patient's actual drug regimen and a treatment guideline, usual dose, or other therapeutic generalization. An <i>actual</i> DTP requires a theoretical DTP and a corresponding physical manifestation, e.g., symptom or laboratory test.
Drug Use Evaluation (DUE)	(1) an evaluation of prescribing appropriateness according to explicit criteria; (2) A structured, ongoing, authorized quality assurance process designed to promote safe, appropriate and effective drug use. (American Society of Health-System Pharmacists)
Injury	In the context of a drug-related injury: a severe, dangerous or disabling clinical outcome that was not correctable or which required significant additional resources to correct, e.g., emergency treatment, hospitalization.
Managed Care Organization (MCO)	A method of organizing the finance and provision of care delivery so that payers and insurers can influence providers and suppliers. A MCO may contract with purchasers (e.g., employers; labor unions; business coalitions; federal, state and provincial governments; and individuals) to provide health care to people ("members") in defined populations. Although it is widely regarded as an American model, the health care systems of many countries use various forms of managed care.
Medications Management System (MMS)	A system on an organizational level whose purpose is to manage pharmaceutical care activities on the microsystem level
Medications Therapy Management	See Pharmaceutical Care
Pharmaceutical Care	Pharmaceutical Care is responsible, cooperative provision of drug therapy for the purpose of achieving definite outcomes intended to improve a patient's quality of life. Many practical aspects of pharmaceutical care are embodied in federal regulations as Medication Therapy Management.

Pharmaceutical Care System (PCS)	A interdependent group of patients and providers people who cooperate to provide pharmaceutical care. (See <i>system, pharmaceutical care</i> , and Fig. 8 in the body of this paper.
Preventable Drug Related Morbidity, Adverse Drug Event, Etc	<i>A preventable drug related morbidity or preventable adverse drug event, etc.</i> is one that followed a recognizably significant premonitory event, e.g., a DTP, that should have revealed the underlying cause of eventual injury, when the cause could have been controlled without sacrificing the therapeutic objective. The formal elements for preventability are (1) a recognizable DTP; (2) the foreseeability of the DRM, given the occurrence of the DTP; (3) an identifiable cause of the DTP and DRM; and (4) the ability to control that cause without foregoing the therapeutic objective.
System	<ol style="list-style-type: none"><li>1. A set of interdependent human or material elements interacting to achieve a common aim. (Institute of Medicine)</li><li>2. An organized collection of potentially interacting elements capable of self control toward common purposes.</li></ol> <p>A specific system is defined by its environment, purpose, inputs, outputs, transformations (processes), and control subsystem (command signal, comparator and feedback.)</p>
Therapeutic Objective	The intended culmination of a therapeutic plan, e.g., cure, control of disease, relief of symptoms, improvement of quality of life.