Medication, Quality of Life, and the Role of the Pharmacist

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INTRODUCTION

As the reader certainly knows, quality of life is becoming an important discussion topic among health care policymakers, pharmaceutical companies, and, inevitably, pharmacists. Pharmacists should be interested because their patients are beginning to expect them to evaluate the effects of the drugs they are dispensing on the patients' quality of life. This means that pharmacists must think about how the drugs affect patients in ways that go beyond therapeutic effectiveness. Consideration of these issues can help pharmacists answer questions such as what exactly quality of life *is* and how it can best be measured.

The interaction between quality of life issues and medication compliance is vital to patient and pharmacist alike. Compliance problems and their solutions are a well-recognized subject of study in pharmacy. Not so with quality of life. A literature search of research publications on quality of life using the MUST Database found more than 360 citations (1). Only 17 of these appeared in pharmacy publications.

It is not that quality of life (QOL) is a new concept. Certainly social scientists have used the term in common parlance for a quarter century or more. Neither is measurement of a person's ability to perform the activities of daily living a recently developed technique. Systematic ways of measuring a patient's ability to function

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have been used by clinical researchers for more than 50 years. These older instruments of evaluation were developed by clinicians to systematize the information that they thought would be relevant for diagnosis and treatment. Forty years ago, the medical literature described a quantifiable system of measuring mobility in the arthritic patient. Today, the mobility of arthritis patients remains a quality of life issue.

Work such as that by Patrick and Erickson on the concepts involved in QOL shows how, thanks to more sophisticated research, assessing quality of life is becoming increasingly complex (2). These investigators define QOL as "the value assigned to the duration of life as modified by the social opportunities, perceptions, functional states, and impairments that are influenced by disease, injuries, treatments, or policy" (2).

Quality of life is measurable, even though the process of finding a way to measure it is complex, difficult, and at times controversial. However controversial its definition and measurement, quality of life does have meaning for patients, even if they do not always know its exact definition. It has value for physicians and other health professionals as an indirect goal for their efforts. And increasingly, it helps policymakers, in government and elsewhere, to choose among therapeutic alternatives.

Pharmacists are realizing that the patients themselves can be interested in how medicines affect their quality of life. Although patients' current level of awareness tends to be low, drug companies seem keen to educate them through drug product advertising about the issue. After these companies and the Food and Drug Administration come to an agreement about the appropriate use of direct-to-consumer advertising, patients are likely to become much more aware of quality of life issues.

SOME DIMENSIONS OF THE COMPLIANCE PROBLEM

The effectiveness of a medication is at best only as good as the degree to which it is properly taken. Failure to take medication properly may result in billions of dollars spent in direct and indirect health care costs. Successful efforts to improve compliance

have been shown to result in reductions in costs that exceed the expense of the interventions. Thus, it would appear that a substantial investment potential is available for efforts to improve compliance.

It seems hardly necessary to point out, again, that cost is becoming an intensive way of life in the health care system. It *may* be worthwhile, however, to remember that there is more to cost control than cost cutting. It is *certainly* worthwhile to continue to call attention to the *outcomes* component of the health care cost equation; i.e., What are we getting for our money?

Major reports on the cost-effectiveness of medication have appeared, and cost-effectiveness comparisons have a place as a standard criterion for drug selection. Overlooked by many cost-effectiveness studies, however, is the role of the drug-taking patient. Such studies tend to show that if Drug A is taken according to directions, it is more effective and less costly, overall, than taking no drug, having surgery, or perhaps taking Drug B. This is all well and good, but what if the drug is *not* taken according to directions?

This issue was raised in an important paper by Worthen, who described the construct of a "usefulness product" in a study of the use of timolol in glaucoma patients (3). Worthen's premise is simple but basic and can be shown by his example: ". . . if the drug's effectiveness is 90% (i.e., works 90% of the time) but the patient's compliance is only 50%, we can say that the 'usefulness product' of that medication is 45%" (3). Worthen's procedure can be valuable in drug comparisons. In his own experience, for example, epinephrine was 70% effective, but over time, compliance may be as low as 30%, for a usefulness product of 20-30%. Timolol, while only 10% more effective, had a compliance rate of about 95%, for a usefulness product of more than 75%, or 3.5 times that of the less expensive drug (Table 1). Studies such as Worthen's, performed carefully and extensively, promise to usher in a second generation of drug cost-effectiveness studies, with compliance factors being the important added dimension.

One of the possible consequences of noncompliance is underutilization of cost-effective pharmaceutical products (4). Underutilization of pharmaceutical products and services also undermines the economic viability of the pharmacy profession, perhaps more so than most pharmacists realize.

TABLE 1. Examples of Worthen's Usefulness Product

Drug	Effectiveness	X	Compliance	=	Usefulness Product
Epinephrine	70%		30%	=	21%
Timolol	80%		95%	=	76%

Source: Ref. 3

Schulz and Gagnon analyzed more than 1,000 refillable prescriptions in an effort to determine the degree to which authorized refills were obtained by patients (5). They found that only just over half the authorized medication was ever dispensed. And this is certainly a conservative finding, given the careful controls in their research methodology. Although Schulz and Gagnon did not report the actual number of refills dispensed and authorized, it is possible to project revenues lost as a result of the documented failure to refill prescriptions in their study. Assuming an average of three authorized refills for each of the 1,000 prescriptions, we reach a total authorization of 4,000 prescriptions. At the refill rate found by the researchers, we calculate a total number of 1,840 prescriptions authorized but not dispensed. At a relatively modest $10 (U.S.) average prescription charge, this amounts to more than $18,000 in lost business for the 1,000 refillable prescriptions.

It is important to point out that these projections are hypothetical, and surely some of these prescriptions need *not* have been refilled. Schulz and Gagnon note the possibility that "physicians are overindulgent in refill authorizations" (5). Nevertheless, the data suggest that both a financial loss to pharmacists *and* the potential of inappropriately abbreviated therapy result from necessary but unfilled prescriptions.

For the pharmacy, poor compliance means more than simply lost refill revenues. Fewer refills mean fewer visits to the pharmacy and loss of sales of nonprescription items. A lack of faith in the efficacy of medication has been shown to be associated with poor compliance (6). That, in turn, may cause less effective therapy–a self-fulfilling prophecy for the patient. The pharmacist who successfully enhances compliance in such a patient is likely to be building long-term benefits. Such benefits can only be realized if *patient* behavior is changed.

Patients are concerned about how treatment may interfere with their life-styles and social relationships. The benefits of drug therapy that works generally are understood as reduced or eliminated problems. A patient's evaluation of the effectiveness of a medication is based on how well the treatment minimizes the interference of the disease in his or her life. But as all pharmacists know, drug therapy frequently presents its own form of interference in terms of side effects and dosage and administration problems. Ultimately, it is the patient who judges the balance between the positive and negative effects of drug therapy. A judgment that the drug is doing more harm than good, or simply is not doing any good, is likely to result in poor compliance.

Pharmacists can be alert for patient complaints that may go unrecognized by the patient as medication-induced problems. Pharmacists can explain what the patient can expect from therapy and explore whether that therapy is likely to interfere to an unacceptable degree with important aspects of the patient's life-style. Furthermore, pharmacists can help patients weigh the positive benefits of a therapy against the negative effects to determine whether the net effect of treatment, as perceived by the patient, is functionally beneficial.

When compliance is poor, the medical as well as the economic consequences can be serious. The list in Table 2 provides a few examples, but a much longer list could be generated with little difficulty. Perhaps the most dramatic evidence of the costs of malcompliance is the estimate that noncompliance "appears to contribute to approximately 10% of all adolescent females becoming pregnant each year" (8). It has been estimated that it costs about a quarter of a million dollars to raise a middle-class child to age 18 (9). And, of course, that is only *one* of the costs. Consider interrupted education for the mother or the father, or both. Consider yet another child on the welfare rolls, if that is the case. All in all, a *single* missed pill can have astounding fiscal results.

What has compliance to do with quality of life issues, and vice versa?

EFFECTS OF MEDICATIONS ON QUALITY OF LIFE

The assessment of quality of life changes appears particularly useful as an outcome measure in the following instances:

TABLE 2. Possible Results of Poor Compliance with Some Major Drug Classes

Drug Type	Possible Impact of Poor Compliance
Antiepileptics	Seizures/?rebound decrease in seizure threshold
Antiarrhythmics	Arrhythmias/?rebound decrease in arrhythmia threshold
Diuretics	Fluid retention/pulmonary congestion
Cardiotonics/inotropics	Fluid retention/pulmonary congestion
Oral contraceptives	Pregnancy
Systemic ß-blockers	Rebound risk of myocardial infarction
Central α-blockers	Rebound hypertension/tachycardia
Calcium channel blockers	Reflex tachycardia on restart
H_2 antagonists	Failure to heal/relapse
Antibiotics	Relapse/resistant organisms
Antidepressants	Relapse/?rebound phenomena
Major tranquilizers	Relapse/?rebound phenomena
Anticoagulants	Thrombosis/?rebound hypercoagulation

Source: Ref. 7

- When mortality or morbidity outcomes in clinical trials of therapies are not the best indicators of the effectiveness of an intervention, such as when there are marginal differences in survival between the treatments being compared
- In diseases with a generally favorable prognosis, where standard mortality/morbidity indexes are insensitive indexes
- In conditions with a generally poor prognosis, where the goal of therapy is comfort and maintenance of function rather than improvement in survival
- When treatment is highly efficacious in lessening mortality but is fairly toxic and results in significant morbidity
- When patients are asymptomatic or only mildly symptomatic and the disease complication rate is low but the therapy is lifelong and may even produce symptoms.

The range of results of QOL assessment is shown in Table 3.

In choosing a drug to prescribe, the physician's concerns are, in

TABLE 3. Possible Effects of Disease, Drug Therapy, and Their Interaction on Quality of Life

Effect of Disease on QOL	Added to →	Effect of Drug Therapy on QOL	Results in →	Net QOL Effect from Patient's Viewpoint
Negative		Strongly positive		Positive
Negative		Positive		Neutral
Strongly negative		Positive		Negative
Negative		Neutral		Negative
Negative		Negative		Strongly negative
Neutral		Positive		Positive
Neutral		Neutral		Neutral
Neutral		Negative		Negative

principle, the same as those of regulatory agencies: to obtain a satisfactory therapeutic response while increasing as little as possible the risk to the patient. For the prescribing physician, however, each decision involves an *individual* patient, whereas regulatory decisions are based on an aggregate of patients. Furthermore, that individual patient is usually known by and is in one-on-one communication with the prescribing physician. Quality of life concerns can become a valuable aid to decisions on therapy when individual psychological, educational, and social characteristics are known to the prescriber.

For the patient, QOL considerations seem to be a logical step in yet another progression. In his well-known analysis, psychologist Abraham Maslow noted that people typically try to fulfill some needs only after other, more primary needs have been satisfied. He identified five different need categories that can be arranged into a vertical hierarchy, with the most primary listed first:

- Physical or biological needs
- Safety and security needs
- Love and affiliation needs
- Prestige and esteem needs
- Self-fulfillment needs.

As the concept of quality of life is explored and definitions are offered, it should become clear that the highest level, self-fulfillment, is a goal toward which this work is striving.

A more practical QOL consideration for the patient is that of compliance with the prescribed regimen. If compliance declines

because of side effects, inconvenience, or other factors–some of which are QOL variables–the *benefits* of the drug are also likely to decline and the costs to increase. Thus, reducing the QOL-related negative effects of drugs that affect compliance will have at least three positive results:

- Better compliance
- Better health benefits
- Reduced costs of malcompliance.

When a patient takes medication for a medical problem, there are four possible quality of life outcomes: (1) QOL is improved, (2) QOL is actively maintained at the present level, (3) QOL decreases, or (4) QOL is unchanged. It is possible, however, that the patient or the physician, or both, may perceive an outcome different from what actually occurs. For example, suppose that an anti-inflammatory product is effective in reducing joint inflammation and swelling in an arthritic patient, but the overall effect is not sufficient to have a perceptible impact on the patient's ability to perform common daily tasks or to engage in other activities important to the patient. In addition, suppose the medication has the side effects of stomach irritation and nausea. From the patient's perspective, not only did the medication fail to provide significant functional benefit, but it also made him or her feel worse, and the patient would be likely to consider this therapy to be a failure.

In contrast, if the physician judged the therapy to be successful on the bases of laboratory findings and the clinically observable positive outcome (reduction of swelling and inflammation) but overlooked the *patient's* criteria for success, it is easy to see how miscommunication between the physician and patient could arise. This, in turn, could lead to patient dissatisfaction, noncompliance, and a potential aggravation of the course of the disease and its symptoms.

Antihypertensive drug therapy is a classic example of a medication-related quality of life problem. Often the patient with high blood pressure is asymptomatic, but the medication needed to control the disease causes unpleasant side effects so that the patient feels worse than he or she did without the therapy. The patient's perceived quality of life is reduced even though he is better off physiologically. Such dissatisfaction and related noncompliance

with the treatment can lead to a host of medical problems as well as to a lack of confidence in the physician.

Meyerowitz, Watkins, and Sparks interviewed cancer patients treated with cyclophosphamide, methotrexate, and fluorouracil (10). The results dramatically illustrate the negative effects that medication can have on quality of life, despite any positive benefits in mortality. Some of the results were:

Effects of Chemotherapy	*% Experiencing*
Fatigue	96
Nausea	88
Reduction in social activity	88
Decrease in work-related activity	74
Nervousness, irritability	62
Major disruptive factor in life	60
Change in appetite and weight	38
Great distress on receiving treatment	28
Change for worse in family and relationships	23

A patient's judgment that the drug is doing more harm than good, or simply not doing any good, is likely to result in poor compliance.

ROLE OF THE PHARMACIST

Many pharmacists are already experienced at helping patients maintain or improve their quality of life within the context of their medical treatment. They are in an excellent position to use that skill to do even more for patients in a confusing era of high-cost/high-tech drugs, generic medications, and increasing direct-to-patient drug advertising.

Every pharmacist has patients who have medication-related quality of life problems. These patients are either adhering to treatment regimens and enduring the inconveniences and undesirable effects of those regimens or attempting to minimize the negative effects of their therapy through unsupervised adjustments in dosage and administration. Identification of these patients can be difficult

and will depend on making them aware that something can be done to minimize or eliminate their problems without compromising the therapeutic efforts of their physicians.

Pharmacists can use the concept of quality of life in communications with patients and physicians to help improve medication compliance and to give patients a better understanding of the value of their therapy and its limitations.

There are specific actions that can and should be taken by pharmacists if they are to fulfill their role as mediators in the effects of medications on their patients' health-related quality of life. Among these are:

- Educate themselves and the entire pharmacy staff about the concept of medication-related quality of life and its importance
- Translate the concept into terms that are meaningful to patients and physicians and educate them through newsletters, talks at local civic group meetings, senior citizen centers, and the like
- Be alert for medication-induced patient complaints that may go unrecognized by the patient
- Communicate medication-related patient complaints to the physician and suggest alternatives
- Encourage patients to discuss any perceived negative effects of therapy with the pharmacist or the physician
- Explain to patients what they can and cannot expect from their therapy and help them weigh the benefits against any negative effects
- When a patient receives a new medication, explore whether the therapy is likely to interfere with important aspects of his or her life-style
- Offer suggestions for minimizing the impact of negative effects of therapy on the patient's quality of life
- Include important life-style characteristics, such as hobbies and occupation, in patients' medication profiles
- Alert the physician to potential and perceived conflicts between patient life-style and medication effects.

CONCLUSION

There is a critical relationship between clinical practice and personal patient outcome. At the clinical level, a disease process may be understood in molecular detail, and a treatment may have been developed. However, the treatment will not succeed unless three new and essential criteria are met:

- It must be possible to deliver the treatment to the patient in the real world.
- Measures of outcome must be comprehensible and relevant to the patient, whose perspective is emotional and personal, in contradistinction to that of the scientist.
- The net effect of a treatment must be perceived by the patient to be of functional benefit. In other words, patients are unlikely to accept a treatment, whatever its scientific merit, if they see nothing in it for themselves.

Pharmacists have both an opportunity and a duty to understand that quality of life issues play a significant part in patient compliance and to use that understanding in the patient's best interests. Fortunately, those patient interests are virtually identical with those of the pharmacist.

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