

# Understanding Medication Compliance and Persistence from an Economics Perspective

Rachel A. Elliott, BPharm, MRPharmS, PhD,<sup>1</sup> Judith A. Shinogle, PhD, MSc,<sup>2</sup> Pamela Peele, PhD,<sup>3</sup> Monali Bhosle, MS, PhD Candidate,<sup>4</sup> Dyfrig A. Hughes, BPharm, MSc, PhD, MRPharmS<sup>5</sup>

<sup>1</sup>School of Pharmacy, The University of Nottingham, University Park, Nottingham, UK; <sup>2</sup>Department of Health Services Administration, University of Maryland, College Park, MD, USA; <sup>3</sup>UPMC Health Plan, Pittsburgh, PA, USA; <sup>4</sup>Division of Pharmacy Practice and Administration, Ohio State University, Columbus, OH, USA; <sup>5</sup>Centre for Economics and Policy in Health, Bangor University, Bangor, UK

## ABSTRACT

**Objectives:** An increased understanding of the reasons for noncompliance and lack of persistence with prescribed medication is an important step to improve treatment effectiveness, and thus patient health. Explanations have been attempted from epidemiological, sociological, and psychological perspectives. Economic models (utility maximization, time preferences, health capital, bilateral bargaining, stated preference, and prospect theory) may contribute to the understanding of medication-taking behavior.

**Methods:** Economic models are applied to medication non-compliance. Traditional consumer choice models under a budget constraint do apply to medication-taking behavior in that increased prices cause decreased utilization. Nevertheless, empiric evidence suggests that budget constraints are not the only factor affecting consumer choice around medicines. Examination of time preference models suggests that the intuitive association between time preference and medication compliance has not been investigated extensively, and has not been proven empirically. The health capital model has theo-

retical relevance, but has not been applied to compliance. Bilateral bargaining may present an alternative model to concordance of the patient-prescriber relationship, taking account of game-playing by either party. Nevertheless, there is limited empiric evidence to test its usefulness. Stated preference methods have been applied most extensively to medicines use.

**Results:** Evidence suggests that patients' preferences are consistently affected by side effects, and that preferences change over time, with age and experience. Prospect theory attempts to explain how new information changes risk perceptions and associated behavior but has not been applied empirically to medication use.

**Conclusions:** Economic models of behavior may contribute to the understanding of medication use, but more empiric work is needed to assess their applicability.

**Keywords:** compliance, economic theory, medication use, patient behavior.

## Introduction

Around a quarter of patients do not take their medicines as prescribed [1,2]. If a medicine has been prescribed appropriately, this represents a lost opportunity to improve or maintain a patient's health status. The potential consequences of noncompliance with an appropriate medicine can be divided into health benefits forgone (human cost and opportunities lost) and productivity costs (personal and social economic burden). Interventions to improve compliance and persistence do not seem to have been very effective in reducing the public health burden of chronic disease [3,4]. Reviews suggest that interventions have largely concentrated on educating patients, with many being multifaceted, but

without evidence for inclusion of each component. They are generally not based on actual reasons for noncompliance [3,5,6]. The most effective interventions are those that promote sustained behavior change [7–9]. Furthermore, linking improved compliance to improved outcomes has proved problematic [3,10]. A recent study by Lee et al. demonstrates that a comprehensive pharmacy care program on medication compliance is associated with a significant increase in compliance and persistence [11]. This study also found a significant decrease in systolic blood pressure among patients treated for hypertension and a significant lowering of low-density lipoprotein cholesterol (LDL-C) among patients treated for hyperlipidemia [11]. Increased understanding of the reasons for noncompliance and lack of persistence is required before interventions can be expected to improve compliance, and thus patient health.

Researchers and practitioners are becoming increasingly aware that compliance with medicines is a

*Address correspondence to:* Judith A. Shinogle, Department of Health Services Administration, University of Maryland, 2324 Health & Human Performance Bldg., College Park, MD 20742, USA. E-mail: [shinogle@umd.edu](mailto:shinogle@umd.edu)  
10.1111/j.1524-4733.2007.00304.x

complex area of human behavior, reflected by the World Health Organization definition of noncompliance as, “a multidimensional phenomenon determined by the interplay of five sets of factors: patient-related, condition-related, therapy-related, health system factors and social/factors” [2].

Explanations of patients’ noncompliance with prescribed treatments have been attempted from epidemiological, sociological, and psychological perspectives. More recently, economists have begun to work with psychologists to examine people’s choice behavior in health-related decision-making more closely [12]. These economic explanatory models may contribute to the understanding of medication-taking behavior. In this article, we summarize existing knowledge around reasons for noncompliance. We then describe relevant economic models and present an argument for their use to further explain medication noncompliance. First, we examine the more traditional economic theories: utility maximization (supply and demand), time preferences, and health capital. Next, we explore extensions to these models including bilateral bargaining, stated preference, and prospect theory. In each section we provide a brief explanation of each model, relate the model to patient medication-taking behavior, and present an example.

#### *Existing Knowledge Around Reasons for Medication Noncompliance*

It is important, when referring to noncompliance, to define the various aspects of noncompliance. “Concordance” refers to a patient-centered process where health-care professionals make a therapeutic alliance with a patient, one result of which may be increased compliance or persistence [13]. Concordance is used in this article as a phrase to capture the “agreement” that needs to take place in the initial doctor–patient consultation. If patients do not agree at this stage, then it stands to reason that they will not fill their initial prescription. Failure to fill the initial prescription is sometimes referred to as “primary noncompliance.” We use “compliance” to refer to the day-to-day medication-taking and as a measure of missed doses, and inaccuracies in timing of doses. “Persistence” describes the duration of continuation with therapy, and is of particular importance in chronic disease management. These concepts are in congruence with ISPOR definitions [14]. Evidence suggests that remembering is a key element in achieving successful compliance to medication [15,16]. One study suggests that 50% of noncompliance may be due to forgetting to take the medicine [17]. This is often referred to as “unintentional noncompliance,” rather than “intentional” noncompliance where people choose not to take a medicine. Poor motivation to take a medicine is thought to increase the likelihood of forgetting, so the

distinction between the two behaviors is not as clear-cut as it might appear [18,19].

Most commonly, an epidemiological approach has looked at identifying “at-risk” groups for (intentional) noncompliance. These studies suggest that compliance with medicines appears to increase with higher income and reduced medication costs, is related to education and social support, and may be affected variably by age, sex, cognitive function, general socioeconomic status, impact of a specific disease, presence of depression, and regimen complexity [1,20–22]. A large body of research examines the effect of information and knowledge on compliance. Nevertheless, these studies do not provide proof of causality because it is not clear how these factors contribute to noncompliance and a consistent link between knowledge and compliance has not yet been demonstrated [3]. Sociological and psychological frameworks have afforded greater understanding of noncompliance with medicines, by suggesting that intentional noncompliance is not a deviant behavior that stems from ignorance or particular “character traits” or sociodemographic characteristics. Compliance is better conceptualized as a variable behavior, rather than a trait characteristic: most people are noncompliant some of the time [23].

The failure of epidemiological models can be attributed to the lack of emphasis given to barriers to compliance and a lack of attention to motivational factors. This in turn can be attributed to the dominance of the health professional’s perspective which assumes that patients passively attempt to comply with providers’ advice and instructions. Psychosocial explanatory frameworks suggest that people often need to understand or evaluate their medicines before deciding whether to take them and may make cost–benefit or risk–benefit choices about treatment options within their own belief and preference framework [23,24]. A substantial amount of qualitative research targeting patients’ perceptions of medicines exists. A meta-synthesis of this body of work provides an explanatory framework that incorporates patients’ perceptions and preferences, and suggests an overall resistance to taking medicines [25]. Quantitative research into factors affecting compliance has been carried out using psychological frameworks, such as social cognition models (health belief model and the theory of planned behavior). This work suggests that compliance can be seen as a volitional act which is, to some extent, the result of a rational decision by the patient [26]. Examining patient decision-making provides a more comprehensive framework for explaining noncompliance. The necessity-concerns framework, in particular, identifies the processes used by patients to balance concerns about the medicine with perceived necessity [27]. Concerns about medicines can be generic, such as concerns about “addiction,” use of “chemicals,” or very specific, such as weight gain with steroid inhalers [28].

Patients may be less likely to take medicines if perceived necessity is outweighed by perceived concerns [26]. It is not yet clear how these decisions change over time.

In addition to the various frameworks surrounding compliance issues, heterogeneity in diseases and treatments add to the complexity. Some conditions present substantial symptoms that may or may not impair function while others are silent diseases without any outward signs or symptoms. The medications used to treat diseases also have variations which in turn affect compliances such as dosing frequency, side effects, effectiveness, and complications to medication-taking (take while standing, no driving, etc.). When researchers examine the proposed models regarding compliance, these factors will need to be incorporated as appropriate to the disease and treatments studied.

### *Traditional Consumer Choice Theory*

Economic theory, supported by empiric evidence, suggests that for a normal good, increased price of a good leads to reduced demand. Within the context of taking medicines, the costs associated with medicines can be complex. Depending on the health system and an individual patient's insurance coverage, a patient may have access to free medicines, pay a fraction of full price such as a copayment, or incur the total market price of the medicine. Prices of medicines are also subject to complex mechanisms, depending on the presence, or not, of a generic preparation. Also, the same medicine may have different prices depending on national, regional, or local contracting or reimbursement arrangements. The effect of "cost-sharing" by patients is twofold: to produce revenue for the payer, and to reduce inappropriate demand ("ex-poste moral hazard"). The full transaction price of medication may also include the cost of the time to purchase and use the health services that has been shown to be significant in some medical services [29].

Cost-sharing mechanisms vary between and within countries. A large body of research in the United States and Canada links patient cost-sharing, such as prescription copayments, to reduced drug use, increased morbidity such as hospitalization, and increased costs. A recent review summarizes the "best" of studies on the effects of cost-sharing mechanisms these [22] and nearly all of the 24 studies show that increases in out-of-pocket payments decreases drug use and affects health outcomes in the chronically ill. Policies that decrease established drug benefit coverage or increase patient cost-sharing, consistently reduce the use of appropriate and essential medicines such as thiazide diuretics and psychotropic agents (e.g., antidepressants), in addition to reducing inappropriate use and drug costs. Patients, forced to reduce medication use because of cost, may choose nonessential medications with symptomatic benefits (e.g., nonsteroidal anti-

inflammatory drugs) while forgoing essential medications that prolong life and prevent morbidity (e.g., antihypertensive agents).

For example, studies found up to 46% reductions in use for both ineffective and effective medicines if drug copayments are introduced [30,31]. Other consequences of price increases are that people who have lower income wait until their condition is more serious before consulting a doctor [32] and they reduce costs by not filling prescriptions, reducing intake, and haggling about price [33]. In Canada, increased cost-sharing by patients led to 15% to 22% reductions in essential drug use among the poor and elderly [31]. There was an increase of 88% to 117% in serious adverse events and 43% to 78% in emergency department visits, associated with decreases in use of essential medicines.

A small amount of equivalent research exists in Europe [34,35]. In Sweden, Lundberg et al. reported that the young, those with poor health status, low educational level, and low income were most likely to decrease use of prescription drugs when user charges were increased [34]. In Germany, poorer insurance coverage has been shown to reduce use of migraine medicines [35].

The copayment on prescriptions in England is currently £6.85, which is almost 30 times higher than the 50 cents reported to reduce compliance in a US study [21]. This is also a higher "fixed" copayment than Austria or Germany [36]. Denmark, Finland, France, Italy, and The Netherlands use graduated charges, depending on pack size or drug cost. In April 2007, prescription copayments were abolished in Wales—the likely impact of this on patient compliance will be significant, particularly as there is some evidence to suggest that medication cost is a barrier that affects compliance in the United Kingdom [37–39]. Research suggests that, in fact, as many as 750,000 people in England and Wales may not be filling prescriptions because of cost [40], and patients' cost reduction strategies are similar to those in the United States [41].

From this evidence, we see that traditional models of consumer choice under a budget constraint do apply to medication-taking behavior in that increased prices cause decreased utilization. Nevertheless, these models do not fully illustrate or explain medication-taking behavior. For example, prescription medicines are free to 85% of the UK population, and yet compliance and persistence rates are no higher than in other countries. This suggests that income budget constraints are not the only factor affecting consumer choice, and thus other aspects of economic models such as time constraints, time preference, and human capital should be considered.

According to consumer choice theory, one would also expect that financial incentives might encourage patients to comply. This is supported by evidence

which suggests that compensating individuals for the time, effort, and cost involved with taking medicines is an effective measure to improve compliance [42]. Financial incentives in the form of cash, vouchers, lottery tickets, or gifts are associated with improvements in the percentage of patients complying. Ten out of the 11 studies identified in the systematic review showed that some form of financial incentive promoted compliance better than any alternative. A reanalysis of their data, assuming a random effects model, suggests that for those given a financial incentive, the pooled risk of being compliant is 1.32 (95% confidence interval 1.17–1.49) of the risk of being compliant with no financial incentive ( $\chi^2 = 19.2$ ,  $df = 1$ ,  $P < 0.0001$ ).

More recent studies have supported these findings; homeless adults with tuberculosis infection living in San Francisco respond favorably to low-cost incentives to improve compliance with preventive therapy [43] among intravenous drug users; monetary incentives are superior to outreach in achieving compliance to the multidose hepatitis B vaccine series [44]; and the use of personalized cues for remembering particular dose times combined with cash reinforcement led to transient improvement in compliance with antiretroviral therapy [45]. Incentives and competitions, however, do not appear to enhance long-term smoking cessation rates, with early success tending to dissipate when the rewards are no longer offered [46].

Theoretical work by Giuffrida and Gravelle [47] supports the use of financial incentives to increase compliance when treatment compliance has a benefit to society beyond the benefit any individual gains. They propose an application of welfare theory to the use of financial incentives for compliance. What their theory finds is that if financial incentives are used to increase compliance (in the form of any type of valued societal resource, money, or other resources), then the optimal level of compliance in a society decreases in direct proportion to the society resources expended on rewarding individual compliance. The authors show that in some, but not all cases, the use of financial incentives to increase compliance will increase social welfare. This is true provided there are sufficient positive benefits from compliance to individuals other than the noncompliance individual. Compliance must be costless or very cheap to verify, and the number of noncompliant members of society must be independent of the financial incentive itself. Besides basing their model on social welfare theory, the Giuffrida and Gravelle model assumes that compliance provides a positive externality. This assumption could be argued for vaccinations; it is more suspect in other diseases.

#### *Time Preference and Medication Compliance*

Time preference refers to the extent to which decision-makers (such as patients) are ready to trade off

between short-term costs and/or gains with long-term costs/gains that are associated with a particular course of action [48,49]. Such decisions are a function of the value placed on future outcomes relative to immediate ones. The concept of time preference is a key factor to understand complex health behavior [50]. Current health behavior models often do not underscore the importance of time in patients' perception of treatment costs, benefits and harms, and their intention to follow the prescribed regimen [51].

The current value of future utility can be computed using the intertemporal discount rates [52]. For example, individuals with lower time preference will have higher value for future utility, are more forward-looking, and discount the future less than those with less value on the future. Thus, for individuals who do not value the future at all, they will totally discount future benefits, indicating no future utility value. Consequently, as time preference increases, one can infer that the person values future utility less now than he/she did earlier. Different mathematical models of time preference exist, e.g., the discounted utility model of Samuelson [53], and the hyperbolic discounting model of Angeletos [54]. Time preference models have been utilized in health-care research to understand peoples' health behavior (e.g., smoking, exercise) in decision-making under uncertainty over time [55].

The concept of time preference can be extended to understand peoples' medication compliance behavior. One would expect an inverse relationship between medication compliance and time preference. Consider a hypothetical example of the use of time preference models in understanding compliance with oral antidiabetic medication for type 2 diabetes. The benefits of complying with the current prescribed regimen are not immediate. Taking medications regularly costs today in terms of person's time (with the associated opportunity costs), efforts, risk of side effect, and maybe monetary investment (costs of medication therapy, traveling to the physicians' office and pharmacy), while potential health benefits such as reduced risk of diabetes-related complications and associated comorbidities are largely in the future. An individual with a lower rate of time preference will be expected to value the future benefits offered by taking medications regularly as prescribed and will have higher medication-related persistence/compliance. According to the time preference model, a person who discounts future outcomes steeply may be less compliant (or less likely to be compliant) as compared to a person who values the future outcomes more than the present outcomes. Thus, a patient's time preference, though associated with factors such as age, sex, race, education, severity of disease, associated comorbidities [56,57], would affect both their compliance and persistence with their medication.



The intuitive association between time preference and medication compliance, however, has not been investigated extensively, and has not been proven empirically [58]. In assessing the decisions of working adults to accept or decline a free influenza vaccination offered at their workplace, Chapman found very little relationship between scenario measures of time preferences and the acceptance of vaccine [58]. They also conducted a separate experiment in patients with hypertension. Compliance with antihypertensive treatments was measured, and correlated with time preference. Although this provided more opportunities for detecting a relationship between scenario measures of time preference and preventive health behavior, no significant correlation was observed. In their third experiment, Chapman assessed time preference and compliance in patients being treated with a cholesterol-lowering medication [58]. The hypothesis that those who preferred the larger, delayed medication effect (demonstrating a high value for future outcomes) would be more compliant, was unconfirmed. No relationship between responses to a time preference scenario and adherence to a cholesterol-lowering medication regimen was observed.

Studies such as these, however, may be limited by the choice of study design. Previous literature examining the association between medication compliance and time preference used measures such as describing hypothetical situations/real-world example to participants and gaining knowledge about their time preference. Measures of compliance used in these studies relied mainly on patient-reported compliance, prescription refill patterns, pill count, and measuring clinical outcomes, e.g., blood pressure or LDL-C measurement. In addition, it is important to take into account an effect of confounders mentioned above. Future studies might consider the use of more sophisticated time preference scenarios that would provide more precise measures of time preference as well as more objective measures of compliance. The effects of time preferences on persistence are not examined and often omitted in research, yet could provide key information regarding why certain individuals are prone to persist with their treatment.

### *Health Capital Models*

Although traditional consumer choice models and time preference models may explain issues in medication-taking behavior, they still lack many factors that may explain noncompliance. Economists have examined how certain commodities have dual uses—consumption as well as production. According to Becker's Human Capital Model [59], increases in a person's stock of knowledge or human capital raise his/her productivity in the market to produce more earnings as well as nonmarket or household commodi-

ties. The application of health to this model was developed by Grossman [60].

In Grossman's health capital model, health is demanded by consumers as 1) a consumption commodity as it directly enters the consumers' preference functions, and 2) an investment commodity as one's health determines the time available for both market (such as labor or household production) and nonmarket activities. The addition of health as an investment commodity expands on traditional models of consumer choice under budget constraints and time constraints. Thus, traditional price effects as well as time preferences apply to this model. In the model, one is born with a stock of health, which depreciates over time. One can affect the depreciation rate through investments in health such as complying or persisting with medication regimens. The effect of this investment or a person's production of health is reflective of the person's characteristics, which may lead to more efficient health production. For example, one may invest in their education and knowledge through higher education. This increase in knowledge could increase the ability of a person to utilize health care more efficiently by complying with medicines, engaging their physician in dialogue regarding their treatment, and recognizing potential side effects or treatment failure.

An example of application of the health capital model for compliance would be the effect of medication compliance on the depreciation rate of health over time. One could imagine that for antidiabetic medication, for instance, treatment compliance would slow the health stock depreciation rate and that noncompliance (or nonpersistence) could cause triggers to increase the depreciation rate. This would affect not only a person's health, but their labor force participation, as well as leisure time. A fully inclusive health capital model would have to include time preference and human capital aspects. This would allow the empiric investigation of the impact of interventions such as education and the unintended consequences of factors such as drug price increases or service delivery changes.

### *Bilateral Bargaining Models*

Other economic models exist that extend beyond traditional models of utility maximization such as health capital, game theory, and prospect theory. Bilateral bargaining models may more appropriately describe the interaction between patients and health-care providers. An important component of disease management is effective communication between patient and health-care provider [61,62]. This two-way social interaction can affect patient compliance with therapy positively, or adversely. Chronic disease management requires some level of agreement between the patient and his/her provider over the type and intensity of

treatment, leading to the development of shared decision-making models that provide a framework for understanding this complex interaction. A large conceptual and empiric literature focused on the components required for a “concordant” consultation or shared decision-making exists, but there is no consideration of “games-playing.” Bargaining models may provide a more global framework for research on factors that determine the success of such consultations.

As an important part of the economic literature since Nash first introduced them in the early 1950s, bargaining models apply to situations where two or more individuals must agree unanimously on a single outcome in order for either person to obtain that outcome [63,64]. In a Nash bargaining model, if two people cannot agree on the same outcome, then neither of them gets that outcome. Hence, when bargainers fail to agree, the only possible outcomes they can get are those that they can get by themselves without the cooperation of the other person.

Consider, for example, a doctor–patient consultation that leads to a prescription being issued. Individuals and their medical providers engage in bargaining each time they agree to a treatment plan. Both parties must agree on the “terms of use” (e.g., Is the diagnosis correct? What are the potential risks and benefits? Is the dosing schedule convenient?), before acceptance of the prescription can take place. Without real agreement to these terms, the patient is not certain that the prescriber understands and can respond to their needs, and the prescriber cannot be certain that the patient will fill their prescription, let alone take any doses. When two parties fail to agree, then neither gets the outcome that was possible through agreement, but they both can still have whatever other outcomes are available to them outside of bargaining. A failed bargaining agreement for the doctor means that the intended therapeutic outcome is unlikely, but the doctor may still issue the prescription (an outcome that is available to the doctor outside of “bargaining” with the patient). For the patients, whatever outcomes they can obtain without bargaining are commonly known as their “outside options.” These may include primary noncompliance, or purchasing of alternative and possibly less efficacious medicines, or not following the treatment plan as prescribed. Also, the patient may not intend to bargain at all, without the prescriber knowing. A patient may go to their consultation as part of their “sick role” to legitimize their illness but with no intention of filling a prescription, such may happen in a system where patients have free consultations but have to pay for medicines. Clearly, when people are interested in engaging in bargaining with each other, there is at least one bargaining outcome that both of them prefer to any of their outside options. If this were not true, then whoever strictly

preferred their outside option would simply take that outcome instead of trying to bargain for an outcome that is less valuable to them. Hence, when an outside option is strictly preferred over anything that can be obtained by bargaining, then no bargaining occurs. This is an intuitively easy concept and a critical element for applying bargaining models to treatment compliance.

Tarrant provides a basic review of several game theory models besides Nash’s prisoner dilemma including the assurance game and centipede game [65]. He also discusses the potential of applying the models to the medical encounter but does not explore their uses empirically [65]. Studies have applied game theory to decision-analytic models to the management of diseases. Specifically, Sonnenberg has developed decision-theoretic models applying the Nash model to the management of reflux as well as to the decision for endoscopy [66,67]. This provides a useful application but does not test if this is the appropriate model. Other researchers have used the game-theoretic model to explore physician behavior, specifically to examine supplier-induced demand [68]. These theoretical models apply the Nash model to physician supply models as another model to explain supplier-induced demand but do not test the models. Researchers have also used game theory to examine contraceptive choice between different types of partners [69]. Applying both the Nash and Stackelberg models, they found that the best fitting model depends on the population studied [70]. This research reflects that the decision-making dynamics between two parties may be applied in medication-taking, but the appropriate model may depend on the parties involved. Each party may have very different factors that affect their utility such as prices, income, tastes, risk aversion, and so on. These studies did not test the predictive power of these models on medication-taking behavior.

#### *Use of Stated Preference Methods to Quantify the Determinants of Medication Noncompliance*

Medication-taking behavior can be conceptualized as the outcome of decisions made about whether taking a medicine will increase utility production. If a person decides that their utility will be increased, because of factors such as symptom control or reduction of future risk, they may decide to comply. If a person decides that their utility will be reduced, because of factors such as side effects, cost, or stigma, they may decide to be noncompliant. Each illness and drug is associated with attributes (symptoms, perceptions of severity, cost, side effects, perceptions of effectiveness, attitudes to present and future risk, convenience) and patients must make their decisions on how to allocate their resources based on these (and other unknown) attributes. This trade-off results in the reported

prescription-filling behavior seen and is actually an expression of revealed preferences.

Revealed preferences demonstrate what consumers actually choose to use in real-life situations, but are not usually considered a practical option for quantifying preferences for health care. Opinion polls and satisfaction surveys provide information about what is important to consumers and their level of satisfaction with the current service as provided, but not information about the potential value of future services. Neither method can be used to identify the factors, and the relative degree of importance of these factors, that drive observed levels of satisfaction. In contrast to revealed preference, “stated preference” provides a measure of what consumers say they will do based on a hypothetical (imaginary) scenario describing the health-care service or intervention in question.

Discrete choice experiments (DCEs) are a stated preference method, rooted in random utility theory, assuming that people have clear preferences for goods or services and are able to choose one good or service in preference to another [71,72]. DCEs are part of a group of stated preference methods called “conjoint analysis” that elicit preferences for scenarios using rating, ranking, or discrete choices and a concise authoritative summary of the method’s application to health care is presented by Ryan and Farrar [73].

There are many examples of DCE being applied to choices between medicines [74–86]. Research suggests that side effects of medicines consistently affect respondents’ stated preferences. Using DCE to investigate treatments for prostate cancer, Sculpher et al. reported that men were prepared to trade life expectancy for reduced incidence of side effects [81]. Side effects can be minor or severe, and have different levels of importance to patients. Watson et al. were able to differentiate between patients’ preferences to avoid specific side effects of drugs used to treat benign prostatic hyperplasia, using DCE [85]. In a cohort of people with osteoarthritis, older people were reported more willing to accept side effects to achieve reduced pain than younger people [86]. This study also suggested that previous experience of side effects led to patients giving those side effects lower priority. This study illustrates the important fact that people’s preferences can alter over time, and with experience of the disease or medicine. Compliance with medicines reduces over time, particularly when the disease is asymptomatic, such as hypercholesterolemia, suggesting that people reassess their preferences over time [87]. DCEs, such as those cited above, provide a static model of medication-taking behavior as it investigates preference at a particular time point [88]. Nevertheless, sequential DCEs could be used to investigate how preferences change over time, and how they, in turn, affect this ongoing decision-making process. DCEs can also examine the effect of different providers [89], the

relationship between patient and provider [90], or the context of a consultation [90], on preferences for medicines, if the experiment is framed appropriately. A DCE of provision of emergency hormonal contraception reported that young women’s medicine preferences were influenced significantly by privacy and judgemental attitudes, whereas older women’s preferences were strongly weighted by speed of access [90]. Methodological limitations of DCEs include lack of consensus about choice set design, cognitive load of questionnaires, and hypothetical nature of the choices [73]. More fundamentally, there are assumptions inherent in this method, about transitivity in choices (ability to rank all choices and attributes), assumptions that people do not use shortcuts to make decisions (“heuristics”) and that preferences for each attribute are additive and independent. The ability of respondents to understand the concept of risk within the choice sets is not proven, and the link between stated and revealed preferences is not clear.

### *Prospect Theory*

While health capital theory [60] is one traditional economic model to examine compliance, a more recent theory, prospect theory [91], is another tractable model. It is congruent with prospect theory that a person may change medication-taking behavior after the arrival of new information (such as an onset of an adverse event, a newly published study on side-effects, or even a friend’s bad experience with the drug). In prospect theory, individuals evaluate costs (in this case, risks) and benefits relative to a reference point and, importantly, this reference point will change after the individual has made the decision in this case to take the drug. Thus, new information about the risks of the drug will be assessed from this new reference point. As prospect theory describes, people are most sensitive to losses near the reference point. This may lead to a more extreme valuation of risk based on new information than had that information been part of a collection of originally assessed risks. With greater sensitivity to this new risk, one may observe much lower rates of use than had all the risk information been available from the beginning.

This hypothesis can be described as analogous to Thaler’s mental accounting behaviors [92]. Thaler argued that monetary costs are perceived as lower if they are integrated or mentally grouped together. This is because of the decreasing sensitivity to loss shown by prospect theory. It could be hypothesized that if risk information is processed in a way similar to monetary units, the process of segregating risks (temporally separating them in the decision-making process) will serve to increase the perception of overall cost or risk. Prospect theory does predict that static risk perceptions will be biased (overweighting high risks while underweighting low risks), but it is silent with respect to how

**Table 1** The relationship of economic models to the various forms of (non)compliance

	Concordance	Initial prescription fill	Compliance	Persistence
Supply and demand		✓	✓	✓
Bilateral bargaining	✓			
Human Capital Model		✓	✓	✓
Prospect theory		✓	✓	✓
Stated preference	✓	✓	✓	✓
Time preference		✓	✓	✓

risk perceptions change in response to new information. Models of prospect theory include a weighting function that overweights low probabilities and underweights moderate to high probabilities. The model also includes a value function for outcomes. One hypothetical study of osteoarthritis patients undergoing total hip arthroplasty did not find any evidence of differential weighting of probabilities [93]. On the other hand, another hypothetical study found that as people's health declines (their point of reference changes), they are more likely to express preferences to live longer in worse health states than currently healthy individuals which conforms to prospect theory [94]. Although previous research has found mixed results on the application of prospect theory, none of these models have examined issues surrounding compliance. In addition, most of the research involves hypothetical situations which are known to be biased.

## Conclusions

This article describes several economic models that could be applied to patient medication-taking behavior. Future research should explore one or more models and derive testable hypotheses from these models. In addition, researchers should examine which models more appropriately describe which aspect of medication-taking behavior. Table 1 begins to place models in the context of certain aspects of medication-taking behavior. This table is a starting place for researchers and should be examined more deeply and refined for various drug-disease combinations.

Application of these models to the various forms of compliance, as shown in Table 1, underlines the distinction between concordance and the other forms of compliance. Concordance is a process which may affect behavior, while initial prescription fill, compliance, and persistence are behaviors that can be described by the models we have discussed. Concordance is best understood using models that assess the process of interaction between patient and provider. Bilateral bargaining can do this directly, and may be more reflective of real life than concordance as gaming is incorporated. Stated preference methods can be used to assess the levels of preference people have for different attributes of a provider [89,90]. It is likely that there are parallels between these models and those

from psychology and sociology. For example, the trade-offs illustrated in stated preference methods can be compared to the necessity-concerns framework in psychology. The advantage of DCE over the necessity-concerns framework is its ability to quantify the direction and magnitude of preferences. Although we have presented these models separately, researchers should note that they could be combined to better describe the behavior being examined.

These models should be applied to the study of medication-taking behavior, and studies should be developed to investigate to what extent these models contribute to the understanding of medication use. While at the present research does not exist that examines the usefulness of each model, future research should examine which model provides the framework for generating hypothesis regarding important covariates as well as hypothesis of direction and unintended effects of covariates. This research should also examine the ability of each theory to predict compliance and the value the theories have in explaining interventions to improve compliance.

The data derived from sociological, psychological, and economic models suggest that compliance and persistence are affected by external modifiable factors, at least as much as, or more than, fixed sociodemographic factors. With a better understanding of how these modifiable factors affect preferences and behavior, which are most important, and how to modify them effectively, we may be able to better support patients in optimal medication-taking behavior.

This article is written by members of the International Society for Pharmacoeconomics & Outcomes Research (ISPOR) Economics of Medication Compliance Working Group; part of the Medication Compliance and Persistence Special Interest Group. The authors are very grateful for discussions with other members of the Working Group.

Source of financial support: No external funding was received for this work.

## References

- DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care* 2004;42:200-9.



- 2 World Health Organization. Adherence to long-term therapies. Evidence for action. 2003. Available from: <http://www.who.int/chp/en/> [Accessed May 7, 2005].
- 3 Haynes RB, McKibbin KA, Kanani R. Systematic review of randomised trials of interventions to assist patients to follow prescriptions for medications. *Lancet* 1996;348:383–6.
- 4 Haynes RB, McDonald H, Garg AX, Montague P. Interventions for helping patients to follow prescriptions for medications. *Cochrane Database Syst Rev* 2002;2:CD000011.
- 5 Bender BG, Milgrom H, Apter AJ. Adherence intervention research: what have we learned and what do we do next? *J Allergy Clin Immunol* 2003;112:489–94.
- 6 Elliott RA, Barber N, Horne R. Cost-effectiveness of adherence-enhancing interventions: a quality assessment of the evidence. *Ann Pharmacother* 2005;39:508–15.
- 7 Bonner S, Zimmerman BJ, Evans D, et al. An individualised intervention to improve asthma management among urban Latino and African-American families. *J Asthma* 2002;39:493–500.
- 8 Gallefoss FR, Bakke PS. How does patient education and self-management among asthmatics and patients with chronic obstructive pulmonary disease affect medication? *Am J Respir Crit Care Med* 1999;160:2000–5.
- 9 Simon GE, Katon WJ, von Korff M, et al. Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. *Am J Psychiatry* 2001;158:1638–44.
- 10 Nichol MB, Venturini F, Sung JCY. A critical evaluation of the methodology of the literature on medication compliance. *Ann Pharmacother* 1999;33:531–40.
- 11 Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA* 2006;296:2563–71.
- 12 Kahneman D, Slovic P, Tversky A. *Judgement under Uncertainty: Heuristics and Biases*. Cambridge: Cambridge University Press, 1982.
- 13 Task Force on Medicines Partnership and the National Collaborative Medicines Management Services Programme. *Room for Review: A Guide to Medication Review—The Agenda for Patients, Practitioners and Managers* (1st ed.). London: Medicines Partnership, 2002.
- 14 Cramer JA, Roy A, Burrell A, et al. Medication Compliance and Persistence: terminology and definitions. 2007. Available from: doi: 10.1111/j.1524-4733.2007.00213x. [Accessed June 25, 2007].
- 15 Vedhara K, Wadsworth E, Norman P, et al. Habitual prospective memory in elderly patients with Type 2 diabetes: implications for medication adherence. *Psychol Health Med* 2004;9:17–28.
- 16 Isaac LM, Tamblin RM. Compliance and cognitive function: a methodological approach to measuring unintentional errors in medication compliance in the elderly. McGill-Calgary Drug Research Team. *Gerontologist* 1993;33:772–81.
- 17 Barber N, Parsons J, Clifford S, et al. Patients' problems with new medication for chronic conditions. *Qual Saf Health Care* 2004;13:172–5.
- 18 Horne R, Weinman J, Barber N, et al. Concordance, Adherence and Compliance in Medicine Taking: A Conceptual Map and Research Priorities. London: National Co-ordinating Centre for NHS Service Delivery and Organisation NCCSDO, 2006.
- 19 Barber N, Safdar A, Franklin BD. Can human error theory explain non-adherence? *Pharm World Sci* 2005;27:300–4.
- 20 DiMatteo MR. Social support and patient adherence to medical treatment: a meta-analysis. *Health Psychol* 2004;23:207–18.
- 21 Soumerai SB. Unintended outcomes of Medicaid drug cost-containment policies on the chronically mentally ill. *J Clin Psychiatry* 2003;64(Suppl. 17):S19–22.
- 22 Lexchin J, Grootendorst P. Effects of prescription drug user fees on drug and health services use and on health status in vulnerable populations: a systematic review of the evidence. *Int J Health Serv* 2004;34:101–22.
- 23 Donovan J, Blake DR. Patient non-compliance: deviance or reasoned decision-making. *Soc Sci Med* 1992;34:507–13.
- 24 Dowell J, Hudson H. A qualitative study of medicine-taking behaviour in primary care. *Fam Pract* 1997;14:369–75.
- 25 Pound P, Britten N, Morgan M, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. *Soc Sci Med* 2005;61:133–55.
- 26 Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999;47:555–67.
- 27 Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development of and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health* 1999;14:1–24.
- 28 Hand CH, Bradley C. Health beliefs of adults with asthma: toward an understanding of the difference between symptomatic and preventive use of inhaler treatment. *J Asthma* 1996;33:331–8.
- 29 Acton JP. Nonmonetary factors in the demand for medical services: some empirical evidence. *J Polit Econ* 1975;83:595–614.
- 30 Soumerai SB, Avorn J, Ross-Degnan D, Gortmaker S. Payment restrictions for prescription drugs under Medicaid. Effects on therapy, cost, and equity. *N Engl J Med* 1987;317:550–6.
- 31 Tamblin R, Laprise R, Hanley JA, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA* 2001;285:421–9.
- 32 Strickland WJ, Hanson CM. Coping with the cost of prescription drugs. *J Health Care Poor Underserved* 1996;7:50–62.
- 33 Cox ER, Henderson RR. Prescription use behaviour among Medicare beneficiaries with capped prescription benefits. *J Manag Care Pharm* 2002;8:360–4.

- 34 Lundberg L, Johannesson M, Isacson DGL, Borgquist L. Effects of user charges on the use of prescription medicines in different socio-economic groups. *Health Policy* 1998;44:123–34.
- 35 Krobot KJ, Miller WC, Kaufman JS, et al. The disparity in access to new medication by type of health insurance. Lessons from Germany. *Med Care* 2004;42:487–91.
- 36 Noyce PR, Huttin C, Atella V, et al. The cost of prescription medicines to patients. *Health Policy* 2000;52:129–45.
- 37 Schafheutle E. Do high prescription charges undermine compliance? *Pharm J* 2003;270:336–7.
- 38 Schafheutle EI, Hassell K, Noyce PR, Weiss MC. Access to medicines: cost as an influence on the views and behaviour of patients. *Health Soc Care Community* 2002;10:187–95.
- 39 Schafheutle E. The prescription charge: a barrier to treatment [editorial]. *Prescriber* 2003;14:10–13.
- 40 Phelps L. Unhealthy Charges. CAB Evidence on the Impact of Health Charges. London: National Association of Citizens Advice Bureaux, 2001.
- 41 Schafheutle EI, Hassell K, Seston EM, Noyce PR. Non-dispensing of NHS prescriptions in community pharmacies. *Int J Pharm Pract* 2002;10:11–15.
- 42 Guiffrida A, Torgerson DJ. Should we pay the patient? Review of financial incentives to enhance patient compliance. *BMJ* 1997;315:703–7.
- 43 Tulskey JP, Hahn JA, Long HL, et al. Can the poor adhere? Incentives for adherence to TB prevention in homeless adults. *Int J Tuberc Lung Dis* 2004;8:83–91.
- 44 Seal KH, Kral AH, Lorvick J, et al. A randomized controlled trial of monetary incentives vs. outreach to enhance adherence to the hepatitis B vaccine series among injection drug users. *Drug Alcohol Depend* 2003;71:127–31.
- 45 Rigsby MO, Rosen MI, Beauvais JE, et al. Cue-dose training with monetary reinforcement: pilot study of an antiretroviral adherence intervention. *J Gen Intern Med* 2000;15:841–7.
- 46 Hey K, Perera R. Competitions and incentives for smoking cessation. *Cochrane Database Syst Rev* 2005;2:CD004307.
- 47 Guiffrida A, Gravelle HSE. Paying patients to comply: an economic analysis. *Health Econ* 1998;7:569–79.
- 48 Critchfield TS, Kollins SH. Temporal discounting: basic research and the analysis of socially important behavior. *J App Behav Anal* 2001;34:101–22.
- 49 Read D, Read NL. Time discounting over the lifespan. *Organ Behav Hum Decis Process* 2004;94:22–32.
- 50 Bleichrodt H, Gafni A. Time preference, the discounted utility model and health. *J Health Econ* 1996;15:49–66.
- 51 Christensen-Szalanski JJ, Northcraft GB. Patient compliance behavior: the effects of time on patients' values of treatment regimens. *Soc Sci Med* 1985;21:263–73.
- 52 Loewenstein G, Prelec D. Anomalies in intertemporal choice: evidence and an interpretation. *Q J Econ* 1992;107:573–97.
- 53 Samuelson PA. A note on measurement of utility. *Rev Econ Stud* 1937;4:155–61.
- 54 Angeletos G, Laibson D, Repetto A, et al. The hyperbolic consumption model: calibration, simulation, and empirical evaluation. *J Economic Perspect* 2001;15:47–68.
- 55 Baker F, Johnson MW, Bickel WK. Delay discounting in current and never-before cigarette smokers: similarities and differences across commodity, sign, and magnitude. *J Abnorm Psychol* 2003;112:382–90.
- 56 Smith PA. Are time preference and body mass index associated? Evidence from the national longitudinal survey of youth. *Econ Hum Biol* 2005;3:259–70.
- 57 Bishai DM. Does time preference change with age? *J Popul Econ* 2006;17:583–602.
- 58 Chapman GB, Brewer NT, Coups EJ, et al. Value for the future and preventive health behavior. *J Exp Psychol* 2001;7:235–50.
- 59 Becker GS. Investment in human capital: a theoretical analysis. *J Polit Econ* 1964;70:9–49.
- 60 Grossman M. The Human Capital Model of the demand for health. In: Newhouse J, Culyer AJ, eds. *Handbook of Health Economics*. Amsterdam: Elsevier Sciences B.V., 2000.
- 61 Ellrodt G, Cook DJ, Lee J, et al. Evidence-based disease management. *JAMA* 1997;278:1687–92.
- 62 Kehoe WA, Katz RC. Health behaviors and pharmacotherapy. *Ann Pharmacother* 1998;32:1076–86.
- 63 Nash J. Two-person cooperative games. *Econometrica* 1953;21:128–40.
- 64 Nash J. The bargaining problem. *Econometrica* 1950;18:155–62.
- 65 Tarrant C, Stokes T, Colman AM. Models of the medical consultation: opportunities and limitations of a game theory perspective. *Qual Saf Health Care* 2004;13:461–6.
- 66 Sonnenberg A. Special article: game theory to analyse management options in gastro-oesophageal disease. *Aliment pharmacol Ther* 2000;14:1411–17.
- 67 Sonnenberg A. Personal view: “don't ask, don't tell”—the undesirable consequences of incidental test results in gastroenterology. *Aliment Pharmacol Ther* 2004;20:381–7.
- 68 De JK, Jegers M. The physician–patient relationship as a game of strategic information transmission. *Health Econ* 2001;10:651–68.
- 69 Chao L-W. A comparison of consensus and nonconsensus approaches to modeling contraceptive choice behavior. *Health Econ* 2002;11:599–622.
- 70 Tirole J. *The Theory of Industrial Organization*. Cambridge, MA: MIT Press, 1990.
- 71 Ryan M, Scott DA, Reeves C, et al. Eliciting public preferences for healthcare: a systematic review of the techniques. *Health Technol Assess* 2001;5:1–186.
- 72 Ryan M, Gerard K. Using discrete choice experiments to value health care programmes: current practice and future research reflections. *App Health Econ Health Policy* 2003;2:55–64.
- 73 Ryan M, Farrar S. Using conjoint analysis to elicit preferences for health care. *BMJ* 2000;320:1530–3.
- 74 Aristides M, Chen J, Williamson E, et al. Conjoint analysis of a new chemotherapy: willingness to pay and preference for the features of Raltitrexed versus

- standard therapy in advanced colorectal cancer. *Pharmacoeconomics* 2002;20:775–84.
- 75 Gan TJ, Lubarsky DA, Flood EM, et al. Patient preferences for acute pain treatment. *Br J Anaesth* 2004;92:681–8.
- 76 Johansson G, Stallberg B, Tornling G, et al. Asthma treatment preference study: a conjoint analysis of preferred drug treatments. *Chest* 2004;125:916–23.
- 77 Kleinman L, McIntosh E, Ryan M, et al. Willingness to pay for complete symptom relief of gastroesophageal reflux disease. *Arch Intern Med* 2002;162:1361–6.
- 78 McKenzie L, Cairns J, Osman L. Symptom-based outcome measures for asthma: the use of discrete choice methods to assess patient preferences. *Health Policy* 2001;57:193–204.
- 79 Osman LM, McKenzie L, Cairns J, et al. Patient weighting of importance of asthma symptoms. *Thorax* 2001;56:138–42.
- 80 Ratcliffe J, Van Haselen R, Buxton M, et al. Assessing patients' preferences for characteristics associated with homeopathic and conventional treatment of asthma: a conjoint analysis study. *Thorax* 2002;57:503–8.
- 81 Sculpher M, Bryan S, Fry P, et al. Patients' preferences for the management of non-metastatic prostate cancer: discrete choice experiment. *BMJ* 2004;328:382–6.
- 82 Taylor S, Armour C. Consumer preference for dinoprostone vaginal gel using stated preference discrete choice modelling. *Pharmacoeconomics* 2003;21:721–35.
- 83 Mark TL, Swait J. Using stated preference modelling to forecast the effect of medication attributes on prescriptions of alcoholism medications. *Value Health* 2003;6:474–82.
- 84 Vick S, Scott A. Agency in health care. Examining patients' preferences for attributes of the doctor-patient relationship. *J Health Econ* 1998;17:587–605.
- 85 Watson V, Ryan M, Brown CT, et al. Eliciting preferences for drug treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia. *J Urol* 2004;172:2321–5.
- 86 Ratcliffe J, Buxton M, McGarry T, et al. Patients' preferences for characteristics associated with treatments for osteoarthritis. *Rheumatology* 2004;43:337–45.
- 87 Mantel-Teeuwisse AK, Goettsch WG, Klungel OH, et al. Long term persistence with statin treatment in daily medical practice. *Heart* 2004;90:1065–6.
- 88 Caro JJ, Salas M, Speckman JL, et al. Persistence with treatment for hypertension in actual practice. *CMAJ* 1999;160:31–7.
- 89 Caldwell J, Bond C, Ryan M, et al. Treatment of minor illness in primary care: a national survey of patient satisfaction, attitudes and preferences regarding a wider nursing role. *Health Expect* 2007;10:30–45.
- 90 Seston EM, Elliott RA, Noyce P, Payne K. Women's Preferences for the Provision of Emergency Hormonal Contraception Services. *Pharmacy World & Science*, 2007. Available from: <http://dx.doi.org/10.1007/s11096-006-9068-9> [Accessed December 15, 2006].
- 91 Kahneman D, Tversky A. Prospect theory: an analysis of decision under risk. *Econometrica* 1979;47:263–92.
- 92 Thaler RH. Mental accounting and consumer choice. *Mark Sci* 1985;4:199–214.
- 93 Feeny D, Eng K. A test of prospect theory. *Int J Technol Assess Health Care* 2005;21:511–16.
- 94 Winter L, Lawton MP, Ruckdeschel G. Preferences for prolonging life: a prospect theory approach. *Inter J Aging Hum Dev* 2003;56:155–70.