

Measuring Stated Preferences for Pharmaceutical Risk Management: A Brief Introduction

F. Reed Johnson
Principal Economist and RTI Fellow
RTI Health Solutions

PO Box 12194
Research Triangle Park, NC 27709
(919) 541-5958
frjohnson@rti.org

Rev. 5/12/05

INTRODUCTION

Many pharmaceuticals and medical devices add value to treatments in addition to clinical efficacy. Understanding various dimensions of patient preferences requires a valid and reliable measurement method. Stated-preference (SP) or conjoint-analysis methods are the most valid and reliable techniques available for quantifying patient and physician preferences. SP estimates can provide both relative utility weights and monetary value-to-patient or willingness-to-pay measures.

SP methods recognize that products have value because of their characteristics or attributes. People have preferences for each attribute and are willing to accept tradeoffs among them. SP analysis examines these tradeoffs to assess the weight people assign to various treatment attributes. Analysts have used SP to quantify preferences for a variety of market and nonmarket goods and services. These include medical interventions, pharmaceutical treatments, and environmental health risks (Bryan et al. 1988; Johnson et al. 2000; Johnson et al. 1998; Johnson and Desvousges 1997; Ryan and Hughes 1997; Viscusi, Magat, and Huber 1991; Wittink and Cattin 1989).

An important advantage of SP is that it can provide a values for the individual features of the treatment, as well as for the treatment as a whole. Thus SP unbundles treatment characteristics to explain *why* patients and physicians prefer some treatments over others. Methods such as concept testing or quality-of-life surveys may provide little insight into the relative perceived importance of specific attributes.

SP studies can provide useful information for several areas of product development and marketing.¹

- *Risk management.* Risk managers often must weigh the potential risks of medical interventions to a small number of patients against the potential benefits of the same interventions to a large number of patients. In addition, interventions designed to minimize the risk to patients requires understanding behavior that can lead to adverse events. Prescription drug off-label use and adherence problems can occur when there are systematic differences between physicians' and patients' perceptions, and regulators' explicit or implicit judgments regarding relative risks and benefits. SP

¹ See Johnson and Manjunath (2002) for a recent review of SP studies relating to the value of reduced morbidity.

methods can quantify such differences and help structure effective risk-management programs.

- *Development strategies for new pharmaceuticals.* If the SP study is undertaken early in the development process, researchers can identify the relative importance that consumers place on particular drug attribute levels. Balancing expected cost with SP satisfaction measures can lead to improved product designs.
- *Formulary approval.* SP estimates can predict patient satisfaction for a study drug relative to actual and potential competing drugs.
- *Marketing applications.* The information from SP surveys can identify attributes that should be emphasized in promotional campaigns and identify preference-based market segments for more focused direct-to-consumer advertising. Combined with information on the market environment, value-to-patients estimates may be directly helpful for pharmaceutical pricing decisions.

SP encourages subjects to explore their preferences for various attribute combinations through a series of judgment tasks. This process of explicitly trading off attributes encourages subject introspection. Because each subject provides answers to multiple tradeoff questions, SP allows analysts to devise internal checks for attentiveness and consistency.

Implementing a valid and reliable SP study requires accurate treatment definition (attributes and levels),¹ attention to format selection (ratings, rankings, or choice), efficient experimental design, and careful statistical analysis. The remainder of this document considers each of these study requirements.²

TREATMENT DEFINITIONS

Measuring stated preferences for medical interventions requires a systematic framework to characterize relevant treatments. Demand for such interventions arises directly from preferences for treatment attributes and indirectly from preferences for the health states realized by their use. Thus, attributes and levels must incorporate the most important health outcomes and treatment attributes associated with medical treatments.

¹ An attribute is a qualitative characteristic of the treatment, while a level is one of several values the attribute may have. Color and price are attributes. Blue and \$25 are levels.

² A discussion of statistical analysis is beyond the scope of this brief paper.

While many pharmaceuticals and medical devices have demonstrated clinical value in alleviating symptoms of disease, such benefits often are accompanied by risks of adverse events. These undesirable outcomes can range from mild symptoms such as transitory drowsiness to potentially life-threatening conditions. Tolerance for adverse-event risks may vary among patients and physicians. Thus including such risks is important in situations where therapeutic decisions require determining what level of risk is acceptable for a particular patient or group of patients.

Once identified, outcomes associated with treatments must be defined in sufficient detail such that subjects can distinguish among them. In addition, these outcome definitions must be consistent with the ways that people think about their health. For instance, people often do not think of their health in terms of clinical outcome measures. Rather, they may consider how the severity of symptoms associated with clinical outcomes limit or affect physical, social, and emotional functions. It is the task of survey developers to determine how subjects think about health outcomes for the intervention of interest and to identify salient attributes and levels. Focus groups and survey pre-testing are a vital part of this process. Table 1 illustrates a possible list of outcome attributes and levels for hepatitis B virus (HBV) treatments.

Table 1. Example of Possible Attributes for HBV Treatments

ATTRIBUTE	LEVELS	DESCRIPTION
Treatment Duration	Short	6 months
	Medium	One year
	Long	Two years
Efficacy	Higher potency and lower resistance	High viral potency Low viral resistance
	Lower resistance	Moderate viral potency Low viral resistance
	Moderate	Moderate viral potency Moderate viral resistance.
Mild to Moderate Side Effect Risk: (Headache, rhinitis, fatigue, abdominal pain)	40 20 Fewer than 1	Number of patients out of 100 who experience at least one side effect
Side-Effect Limitations on Daily Activities	Restrictive	Requires a doctor's intervention and bed rest for 7 days a month for the duration of treatment
	Some	Requires a doctor's intervention and bed rest for 3 days
	No	Brief discomfort that does not significantly limit daily activities
Severe Side Effect Risk (Liver cancer)	5 2 0	Number of patients out of 10,000
Treatment Cost¹	\$15,000 \$5,000 \$1,000	Personal treatment cost that is <u>not</u> covered by insurance.

¹ Including cost as a treatment attribute is not necessary, but allows deriving the value of an intervention to patients in equivalent monetary terms. Value to patient is useful for comparing the relative importance of outcomes with different features and for cost-benefit analysis.

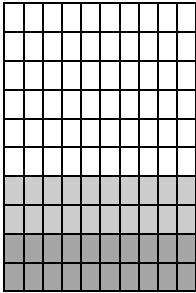
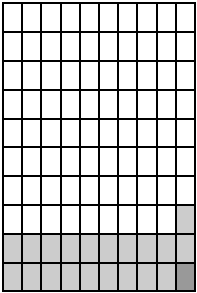
ALTERNATIVE STATED-PREFERENCE FORMATS

Once attributes and levels are determined, they can be combined into treatment profiles that subjects evaluate in a series of SP tasks.¹ Choosing an SP task format is an important step in developing an SP survey. Ranking, rating, and discrete-choice formats have been used in SP surveys. In a ranking study, subjects may be given cards, each showing a treatment profile. Subjects are asked to order these cards from most preferred to least preferred. In a graded-pair comparison rating, the subjects are presented with two treatment profiles and asked to indicate how strongly they prefer one to the other. Viscusi, Magat, and Huber (1991) used this approach to measure the value of avoiding an increase in the risk of contracting chronic bronchitis. Alternatively, discrete choice provides subjects with several different treatments simultaneously and simply asks them to identify the most-preferred option in each choice set. Ryan and Hughes (1997) used the discrete-choice format to value women's preferences for miscarriage management. Johnson and colleagues (2000) used both formats to value avoiding cardiovascular and respiratory symptoms.

Although the various SP task formats appear similar, studies have shown that subjects often use different decision heuristics for different formats. These decision strategies can produce somewhat different results for different SP formats. Therefore, the SP elicitation method should be context specific, and study objectives should play a role in format selection (Huber, 1997). Figure 1 illustrates a graded-pair task based on the HBV-treatment attributes in Table 1. We have combined the risk probability and severity attributes into a single combined attribute.

¹ A profile is a list of attribute levels describing a particular real or hypothetical treatment.

Figure 1. Example of Graded-Pair Stated-Preference Task for HBV Treatments

Feature	Treatment A	Treatment B
Treatment Duration	Long	Short
Efficacy	Higher potency Lower resistance	Moderate potency Moderate resistance
Mild to Moderate Side Effects	Out of 100 patients:  <div style="border: 1px solid black; padding: 2px; margin: 5px;">40 experience <u>some</u> limitations</div> <div style="border: 1px solid black; padding: 2px; margin: 5px;">20 experience <u>restrictive</u> limitations.</div>	Out of 100 patients:  <div style="border: 1px solid black; padding: 2px; margin: 5px;">20 experience <u>some</u> limitations</div> <div style="border: 1px solid black; padding: 2px; margin: 5px;">Fewer than one experiences <u>restrictive</u> limitations.</div>
Severe Side Effect Risk	0 in 10,000 patients	2 in 10,000 patients
Treatment Cost	\$15,000	\$1,000

Please mark one box:

A is much better

A is somewhat better

A and B are about the same

B is somewhat better

B is much better

EXPERIMENTAL DESIGN

Full-factorial experiments generate data based on all possible combinations of attribute levels. Such designs typically are impractical for SP surveys because subjects' cognitive and time limitations do not allow consideration of a large number of profiles. For example, a full factorial design of the treatment attributes

in Table 1 contains five attributes, four with three levels and one with four levels leading to 729 (3^6) possible combinations. In addition, subjects do not rate these options individually. Rather, subjects compare two or more options at a time. Considered in pairs, the number of possible combinations is over 250,000, clearly an impossible task.

Most current SP applications use a D-optimal design to reduce the number of paired comparisons to the smallest number necessary for efficient estimation of preference weights (Dey, 1985; Huber and Zwerina, 1996; Kuhfeld, Tobias, and Garratt, 1994). Such efficient designs can be produced using an iterative computer algorithm (Zwerina, Huber, and Kuhfeld, 1997).

A NUMERICAL EXAMPLE

The SP experimental design determines a sequence of profile evaluations for each subject. Responses to these choices form the data necessary for estimating the relative importance of each attribute level. Our earlier example considered a set of 6 attributes that described HBV-treatment profiles. For simplicity, we now assume that the only relevant attributes and levels are treatment duration (short or long), efficacy (good or moderate), and risk of severe side effect (low or none). In this case, the following eight (2^3) possibilities describe all the possible profiles. Thus, the eight alternatives in Table 2 represent the full-factorial design. In a graded-pairs or two-alternative choice format, there are 28 possible profile pairs. These could be divided into four blocks or survey versions so that each subject would evaluate seven pairs. Subsequent statistical analysis of the SP data produces estimates of the relative importance of each of attribute level.

Table 2. HBV Treatment Profiles

Profile	Treatment Duration	Efficacy	Risk
1	Short	Good	None
2	Long	Good	None
3	Short	Good	Low
4	Long	Good	Low
5	Short	Moderate	None
6	Long	Moderate	None
7	Short	Moderate	Low
8	Long	Moderate	Low

Again in the interest of simplicity, suppose we estimate a linear function with three attributes, D, E, and R, each with two levels, 1 and 2. Here D₁ is short response time and D₂ is long duration. E₁, E₂, R₁, and R₂ are defined similarly.

$$U_{ijk} = \alpha_i D_i + \beta_j E_j + \delta R_k$$

U_{ijk} is the utility of some combination of D, E, and R, weighted by the preference weights α_{long} , α_{short} , β_{moderate} , β_{good} , δ_{none} , and δ_{low} associated with the attribute levels.¹ Assume the value of no treatment is zero and preference-weight estimates are:

$$\begin{aligned} \alpha_{\text{long}} &= 0.2 & \alpha_{\text{short}} &= 0.4 \\ \beta_{\text{moderate}} &= 0.2 & \beta_{\text{good}} &= 0.6 \\ \delta &= -0.2 \end{aligned}$$

Table 3 shows the combined utility weights for four possible benefit profiles. For example, the utility corresponding to combination (D₁, E₁) is $\alpha_{\text{long}} + \beta_{\text{moderate}} = 0.2 + 0.2 = 0.4$.

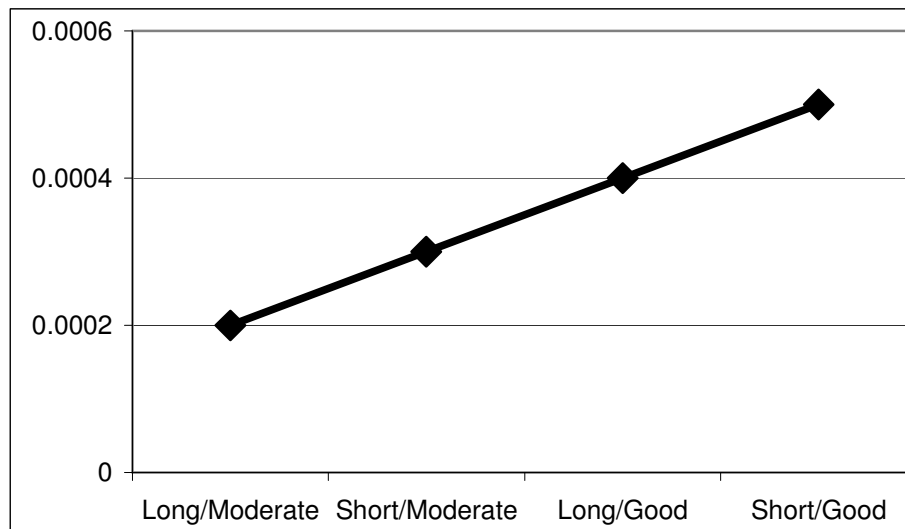
¹ We use the term “utility” here in the conventional economic sense, not the specialized sense of standard-gamble utility that ranges between zero for death and one for perfect health.

Table 3. HBV Treatment Benefits

	Efficacy = Moderate	Efficacy = Good
Duration = Long	0.4	0.8
Duration = Short	0.6	1.0

Finally, suppose that the preference weight for a 1/10,000 increase in risk -0.2 . Thus a risk of 2 in 10,000 has a preference value of -0.4 . People generally will accept a given level of risk if the corresponding benefits are large enough. Consequently, patients would be willing to accept any risk less than 2/10,000 to obtain treatment benefits of $\alpha_{\text{long}} + \beta_{\text{moderate}} = 0.4$ because the positive value of the treatment benefits is at least as great as the negative value of the treatment risks. Thus, we can calculate the maximum acceptable risks for each treatment profile in Table 3 by dividing each cell in Table 3 by $.2$, as shown in Figure 1.

Figure 1. HBV Treatment Maximum Acceptable Risks



USING STATED PREFERENCES TO INFORM RISK MANAGEMENT

Understanding patient and physician perceptions, preferences, and choices is important for reducing the incidence of adverse outcomes while making treatment benefits available to the largest possible number of patients. A carefully designed and skillfully implemented SP survey can produce valid estimates of patients' or physicians' perceived treatment risks and benefits. These estimates are useful for predicting behavior that can influence the incidence of adverse outcomes. For example, if patients are willing to accept higher levels of risk than physicians or regulators, we may observe adherence problems that require intervention.

In addition, SP surveys can help identify the factors that influence patients and physicians' perceived maximum acceptable risk levels. If those perceptions are based on inadequate information about treatment benefits and adverse outcomes, then information programs may help correct the misperceptions that could lead to risky behavior. SP studies also can help identify patient groups for which perceived risk-benefit relations are most favorable. In some circumstances, treatment benefits may be large enough to justify elevated risks, assuming patients are fully informed about both treatment benefits and risks.

Finally, when attributes and levels are carefully selected, the SP estimates can provide useful answers to a variety of "what if" questions. For example, understanding what kinds of side-effect risks are of greatest concern to patients may help identify appropriate strategies for modifying drug formulations, designing more useful labels, or helping physicians communicate more effectively with their patients. SP researchers can then predict how such changes would affect patient and physician choices based on the original preference estimates.

SP methods offer a powerful and flexible tool to risk managers. Combined with clinical and epidemiological data, SP surveys provide a behavioral link necessary for designing effective risk-management interventions.

REFERENCES

- Bryan, Stirling, Martin Buxton, Robert Sheldon, and Alison Grant. 1998. "Magnetic Resonance Imaging for the Investigation of Knee Injuries: An Investigation of Preferences." *Health Economics* 7:595-603.
- Dey, Aloke. 1985. *Orthogonal Fractional Factorial Designs*. New York: Halstead Press.
- Glickman, Theodore S. and Michael Gough, eds. 1990. *Readings in Risk*. Resources for the Future: Washington, D.C.
- Huber, Joel. 1997. What We Have Learned from 20 Years of Conjoint Research: When to Use Self-Explicated, Graded Pairs, Full Profiles or Choice Experiments. Sawtooth Software Annual Conference:1-16. (<http://www.sawtoothsoftware.com/download/techpap/WhatweMS.zip>)
- Huber, Joel, and Klaus B. Zwerina. 1996. "The Importance of Utility Balance in Efficient Choice Designs," *Journal of Marketing Research*, 33 (August 1996): 307-317.
- Johnson, F. Reed, William H. Desvousges, Melissa C. Ruby, David Stieb, and Paul De Civita. 1998. "Eliciting Stated Preferences: An Application to Willingness to Pay for Longevity." *Medical Decision Making* 18 (Suppl):S57-S67.
- Johnson, F. Reed, and W.H. Desvousges. 1997. "Estimating Stated Preferences With Rated-Pair Data: Environmental, Health, and Employment Effects of Energy Programs." *Journal of Environmental Economics and Management* 34:79-99.
- Johnson, F. Reed, Erin Fries, and H. Spencer Banzhaf. 1997. "Valuing Morbidity: An Integration of the Willingness-to-Pay and Health-Status Index Literatures." *Journal of Health Economics* 16:641-665.
- Johnson, F. Reed, Melissa Ruby Banzhaf, and William H. Desvousges. 2000. "Willingness to Pay for Improved Respiratory and Cardiovascular Health: A Multiple-Format Stated-Preference Approach." *Health Economics* 9:295-317.

- Kahneman, Daniel, and Amos Tversky, eds. 2000. *Choices, Values, and Frames*. Russell Sage Foundation, Cambridge University Press: Cambridge.
- Kuhfeld, Warren F., Randall D. Tobias, and Mark Garratt. 1994. "Efficient Experimental Design with Marketing Research Applications." *Journal of Marketing Research* 31:545-557.
- Ryan, Mandy, and Jenny Hughes. 1997. "Using Conjoint Analysis to Assess Women's Preferences for Miscarriage Management." *Health Economics* 6:261-273.
- Ryan, Mandy, and Jenny Hughes. 1997. "Using Conjoint Analysis to Value Alternative Models of Antenatal Care." *Soc. Sci. Med.* 44(3):371-380.
- Viscusi, W. Kip, Wesley A. Magat, and Joel Huber. 1991. "Pricing Environmental Health Risks: Survey Assessments of Risk-Risk and Risk-Dollar Trade-offs for Chronic Bronchitis." *Journal of Environmental Economics and Management* 21:32-51.
- Wittink, Dick R., and Philippe Cattin. 1989. "Commercial Use of Conjoint Analysis: An Update." *Journal of Marketing* 53:91-96.
- Zwerina, Klaus, Joel Huber, and Warren F. Kuhfeld. 1996. "A General Method for Constructing Efficient Choice Designs." SAS Technical Document TS-694E. <http://support.sas.com/techsup/technote/ts694e.pdf>.