

# Using Stated-Preference Methods to Inform Pharmaceutical Risk Management

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## Abstract

**Background:** Understanding physicians' and patients' willingness to accept the risk of adverse events in exchange for therapeutic benefits can help inform more effective risk-management strategies.

**Objectives:** To adapt and validate stated-preference methods developed in other settings to quantify risk-benefit trade-offs.

**Methods:** **Design:** Review evidence on adapting stated-preference methods to risk-benefit trade-offs, including cognitive burden, relevant trade-off domains, and risk attitudes and perceptions unrelated to probability. Apply methodology to two case studies: physician risk-benefit trade-offs for insulin therapy, risk-benefit trade-offs for interventions to reduce at-risk patients' likelihood of contracting diabetes. **Settings:** Endocrinologists and general-practice physicians in the US (N=200), UK (N=100), France (N=100), Germany (N=100), and Spain (N=100) were recruited through a web-based physician network. At-risk patients were screened on the basis of age, ethnicity, and body-mass index from a web-based patient panel (N=600). **Interventions:** Physicians selected preferred treatment alternatives for specified patient types. Patients selected preferred risk-reduction interventions. **Outcome measures:** Utility weights and marginal rates of substitution among treatment attributes. **Statistical analysis:** Conditional logit analysis of the probability of selecting a given alternative.

**Results:** Physicians' mean willingness to accept an increase in the HbA1c measure of glucose control to avoid one mild-to-moderate hypoglycemic event per month was 0.00 for young type 1 patients, 0.34 for middle-aged type 2 patients, and 0.93 for elderly type 2 patients. All differences are significant at the 5% level. The probability of enrolling in a risk-reduction program was less than 0.5 even for an unrealistically attractive set of intervention features.

**Conclusions:** Physicians' willingness to accept higher hypoglycemia risks varies significantly by patient type. Therapeutic guidelines for managing such risks should account for systematic differences in treatment benefits by patient type. Patients at risk for contracting diabetes perceive the burden of diet and exercise to be large relative to the perceived benefits of reducing long-term diabetes risks. In this patient group, risk management based simply on information interventions is likely to be unsuccessful.

## Acknowledgment

This research was funded by Aventis Pharmaceuticals and the Centers for Disease Control and Prevention (CDC).

## Presenter

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Presented at: 20th International Conference on Pharmacoepidemiology and Therapeutic Risk Management  
August 2004  
Bordeaux, France

## Physicians' Willingness to Trade Glucose Control for Lower Hypoglycemia Risks

### Study Design

#### Respondents

- 600 physicians in five countries
  - France (N=100)
  - Germany (N=100)
  - Spain (N=100)
  - UK (N=100)
  - US (N=200)
- Physician specialties
  - Primary care physicians (55%)
  - Endocrinologists (29%)
  - Internal medicine specialists (16%)

Physicians evaluated three hypothetical patient profiles, as shown.

#### Hypothetical Patient Profiles

Characteristic	Patient 1	Patient 2	Patient 3
Diabetes	Type 1	Type 2	Type 2
Sex	Male	Female	Male
Age (years)	20	50	75
Treatment regimen	Four insulin injections (basal-bolus)	Two insulin injections plus oral agents	Two insulin injections plus oral agents
Co-morbidities	None	Elevated cholesterol and hypertension	Cardiovascular disease, circulatory problems, amputation risk
Other comments	Nonobese, physically active, lives with partner	Clinically obese, sedentary, lives alone	Overweight but not clinically obese, lives alone

#### Stated-Preference Survey

Physicians evaluated 15 stated-preference tasks, five for each of the three patient types.

#### Example Trade-off Task

Treatment Outcome	Outcome A	Outcome B	Outcome C
A1c	8.5%	6.5%	7.5%
Daytime hypos in the last month	Mild to moderate	10	25
	Severe	0	2
Nighttime hypos in the last month	Mild to moderate	5	1
	Severe	1	0

Which case do you think represents the most acceptable clinical outcome for this patient?  
(Please check only one box.)

#### Outcome Attributes and Levels Used in Trade-Off Tasks

Attributes	Levels
A1c	6.5% 7.5% 8.5% 10.0%
Daytime hypoglycemic events in the last month	Mild-to-moderate (MD)
	Severe (SD)
Nighttime hypos in the last month	Mild-to-moderate (MN)
	Severe (SN)

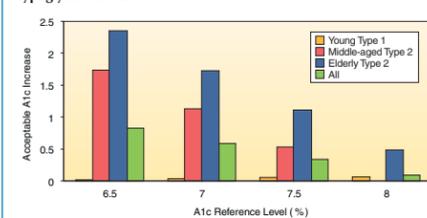
#### Statistical Methods

- Conditional logit estimate of preference weights
  - The probability that alternative B will be selected between alternatives A and B is
- $$\text{Prob}(\text{Chosen} = B) = \frac{\exp[U(X_B)]}{\exp[U(X_A)] + \exp[U(X_B)]}$$
- $$U(X_i) = \beta_1 X_{i1} + \beta_2 X_{i2} + K + \beta_K X_{iK}, \quad i = A, B$$
- where  $X_{ij}$  is a program attribute level, and  $\beta_j$  is an estimated preference weight.

## Results

- Physicians were less willing to trade increased A1c for reduced MN hypoglycemic events as reference A1c increased.
- Physicians were extremely unwilling to trade an increase in A1c for reduced MN hypoglycemia in young Type 1 patients at any A1c reference level.
- In contrast, physicians were willing to trade relatively high increases in A1c for reduced MN hypoglycemic events in Type 2 patients, particularly the elderly, at all A1c reference levels up to 7.5%.
- At A1c reference of 8%, physicians were only willing to accept increased A1c for reduced MN hypoglycemic events in elderly Type 2 patients.

#### Willingness to Adjust A1c to Avoid One Mild-to-Moderate Nocturnal Hypoglycemic Event



## Risk Management Implications

Physicians' risk-benefit trade-offs imply greater willingness to sacrifice glucose control benefits to reduce short-term hypoglycemia risks for older patients than for younger patients. Therapeutic guidelines for managing risks should account for perceived and actual differences in risks and benefits among different patient populations.

## High-Risk Patients' Willingness to Trade Glucose Control for Lower Hypoglycemia Risks

### Study Design

#### Respondents

- 400 subjects identified as high risk
  - Obese
  - Over age 45
  - 25% minorities
- 200 subjects identified as lower risk
  - Not obese
  - Over age 45
  - 25% minorities

#### Stated-Preference Survey

Subjects evaluated nine stated-preference tasks comparing two hypothetical risk-reduction programs and a status quo/no participation alternative.

#### Example Trade-off Task

	Program A	Program B	Neither
Program Features	Restricted diet 3 hours of exercise per week No counseling No medication Goal: Lose 20 lbs in 1 year \$25 per month for 3 years	Flexible, low-calorie diet 6 hours of exercise per week 16 sessions of counseling Medication Goal: Lose 40 lbs in 1 year \$200 per month for 3 years	I will not enroll in either of these programs.
Program Benefits	I will reduce my risk of getting diabetes in the next 3 years from 30% to 21%. 	I will reduce my risk of getting diabetes in the next 3 years from 30% to 15%. 	I will maintain my current 30% risk of getting diabetes in the next 3 years. 
Which program do you prefer? (Please check one box.)	Prefer A <input type="checkbox"/>	Prefer B <input type="checkbox"/>	Prefer Neither <input type="checkbox"/>

How likely is it that you actually would follow the diet, exercise, and counseling requirements for the program you chose above?  
(Please check one box.)

Very likely   
Fairly likely   
Not very likely

#### Outcome Attributes and Levels Used in Trade-Off Tasks

Diet	No diet restrictions Flexible, low-calorie diet Restricted diet
Exercise	No exercise per week 3 hrs of exercise per week 6 hrs of exercise per week
Counseling	No counseling 8 sessions of counseling 16 sessions of counseling
Medication	No medication Medication: a pill that can reduce the risk of developing diabetes with mild side effects
Weight Loss Goal	No weight loss in a year Lose 20 pounds in a year Lose 40 pounds in a year
Personal Cost for 3 Years	\$25 per month for 3 years \$50 per month for 3 years \$100 per month for 3 years \$200 per month for 3 years
3-Year Reduction in Risk of Diabetes	30% risk reduction in the next 3 years 50% risk reduction in the next 3 years

#### Statistical Methods

- Conditional logit estimate of preference weights
- The probability that alternative B will be selected from among three alternatives—A, B, and Neither (N)—is

$$\text{Prob}(\text{Chosen} = B) = \frac{\exp[U(X_B)]}{\exp[U(X_A)] + \exp[U(X_B)] + \exp[U(X_N)]}$$

$$U(X_i) = \beta_1 X_{i1} + \beta_2 X_{i2} + K + \beta_K X_{iK}, \quad i = A, B$$

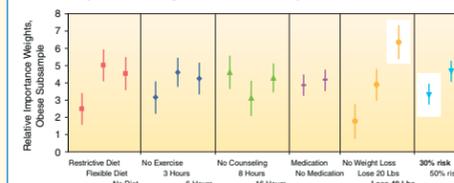
$$U(X_N) = \gamma_1 Z_1 + \gamma_2 Z_2 + \dots + \gamma_m Z_m$$

where  $X_{ij}$  is a program attribute level,  $\beta_j$  is an estimated utility weight,  $Z_n$  is a personal characteristic, and  $\gamma_n$  is a parameter.

## Results

For the obese subsample, the 40-lb weight-loss feature is about twice as important as a 30% reduction in three-year risks. Other features were about equally as important as risk reduction.

#### Relative Importance Weights, Obese Subsample



Respondents who always chose a risk-reduction program alternative were more likely to

- Perceive risk to be high
- Be obese or nonobese minority
- Know someone with diabetes
- Have been diagnosed with high blood pressure
- Have been advised by doctor to change diet or exercise
- Be interested in counseling
- Have attempted weight loss
- Have weight loss goals.

The "most preferred" diabetes risk-reduction program includes an unrealistic combination of features:

- Diet: Flexible, low-calorie
- Exercise: 3 hours a week
- Medication: None
- Counseling: None
- Weight loss goal: 40 pounds
- 3-year diabetes risk reduction: 50%

The probability of choosing either the most preferred or a realistic risk-reduction program is only about 0.5 for obese subjects and 0.6 for subjects who perceive their risk is high.

## Risk Management Implications

Perceived health benefits generally are not sufficient to overcome perceived cost and inconvenience. These stated preferences may indicate a role for improved risk-communication programs and innovative interventions that reduce physical and financial impediments to risk-reduction activities.