Survey on Patient Risk Tolerance

Background

Patients, physicians, and the FDA may have similar goals of maximizing treatment benefit while minimizing risk. However, they may have different perspectives on tradeoffs among benefits and risks of a treatment. As a consequence, the Center for Devices and Radiological Health is currently exploring ways to incorporate patient's preferences in the decision making process that leads to approval of new medical devices.

In order to pursue this idea, CDRH decided to survey obese patients to assess how much risk they would tolerate in order to lose weight. To capture patients' preferences in a systematic and scientifically valid way and to conduct a nationally representative survey, CDRH commissioned the Research Triangle Institute Health Solutions (RTI-HS) to carry out a benefit-risk preference study that will provide information on patient risk tolerance.

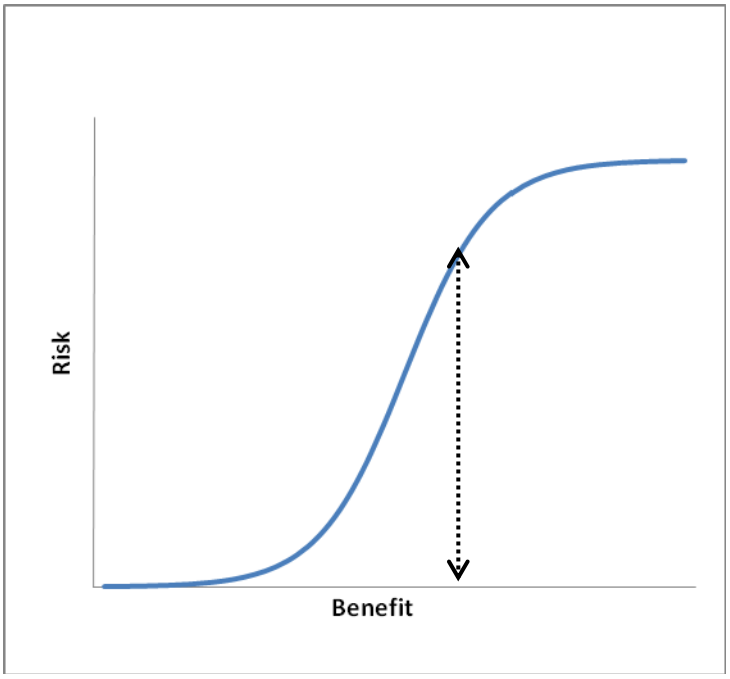
The acceptable level of risk tolerated by a patient depends not only on the benefit provided by the device but also on the seriousness and severity of the disease, the availability of other treatments to the patient population, and other factors described on the Guidance for Industry and FDA Staff entitled "Factors to Consider When Making Benefit Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications." http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf

CDRH considered several indications and types of medical devices to conduct its first ever patient risk tolerance survey. Weight reduction was chosen because of the increasing prevalence of obesity and its impact on public health. Moreover, the potential diversity of benefit-risk profiles of weight reduction devices allows CDRH to evaluate the general applicability of a patient risk tolerance survey as a tool in assisting the Center's decision making process.

Quantitative Approach to Assessing Patients' Benefit-Risk Preferences

Patient preferences will be quantitatively captured by a benefit risk tradeoff curve, as illustrated in Figure 1 below. For a specified amount of treatment benefit (in this case, for a specified weight loss), the Maximum Acceptable Risk (MAR) is defined as the highest level of risk (for example, probability of death) that and average subject would accept in return for the benefit.

Figure 1. Benefit-risk tradeoff curve and maximum acceptable risk



In this survey, we will use a ***choice-format conjoint analysis survey instrument*** to elicit patient preferences for generic medical devices to reduce weight. Choice-format conjoint analysis studies, sometimes called discrete-choice experiments, are designed specifically to provide information about individuals' willingness to accept tradeoffs among features of treatments with different characteristics.

Conjoint analysis (CA) assumes that the value of a treatment stems from its attributes. Users have preferences for each attribute and are willing to accept tradeoffs among them. Analysts use CA to quantify preferences for a variety of products, including medical interventions and pharmaceutical treatments.

In this study, the CA will elicit individual preferences through a sequence of systematically structured tradeoff questions. Subjects evaluate a series of pairs of hypothetical treatment options, and the resulting pattern of choices reveals the underlying preferences associated with various treatment outcomes. For example, patients may be willing to tolerate more treatment side effect to achieve greater weight loss. Patients may also prefer to comply with a more stringent diet restriction in exchange for a lower mortality risk associated with the device or the device placing procedure, if other attributes including weight loss are equal.

The weight reduction risk tolerance survey will be administered over the Internet to 450 respondents with self-reported BMI greater than 30 kg/m^2. These respondents will be recruited from a panel of nationally representative subjects. Among these 450 respondents, the study will target 100 to 150 respondents who underwent prior weight reduction procedures such as gastric bypass or gastric banding procedures in order to capture the different preferences of patients who have or have not had a weight reduction procedure.

The survey instrument was jointly developed by the FDA and RTI-HS. The study has three phases: (1) study design and survey instrument development (accomplished), (2) pre-testing of survey instrument in face-to-face interviews of 9 subjects for instrument improvement and validation (accomplished), and (3) administration and analysis of web-based survey of 450 respondents (in process).

The Center and RTI-HS identified a set of important attributes and levels that will define the benefits (effectiveness outcomes) and risks (safety outcomes) associated with each hypothetical treatment in the tradeoff questions. Each attribute will have a set of pre-specified meaningful values, or levels. The survey instrument will ask respondents to evaluate a series of choices between pairs of hypothetical weight reduction device treatments. Each hypothetical treatment will be defined by effectiveness outcomes and safety outcomes. The survey will also include other attributes such as the surgical procedures to place the hypothetical medical device, e.g., endoscopic, laparoscopic, or open surgery. The survey was designed to collect data for the following:

- Estimating log-odds relative preference weights for safety and effectiveness outcomes.
- Conducting odds-ratio tests of whether selected treatment-profile preferences are significantly different from patients who already underwent weight reduction procedures such as gastric bypass or gastric banding.
- Calculating the MAR for specific improvements in effectiveness outcomes. Other possible measures of risk tolerance include minimum acceptable effectiveness for a given adverse-event risk and incremental net benefits.

Pre-testing of the draft survey instrument has been conducted to ensure understandability and relevance of the range of benefits and risks offered. The pre-test employed in-person cognitive interviews with 9 subjects with BMI greater than 35 kg/m^2. Among them, 3 had undergone gastric bypass procedures. Analysis of the pre-testing is in progress. The final set of attributes and levels was carefully defined in the survey instrument and will be clearly presented to respondents. The following attributes will be included in the survey:

- Type of operation
- Recommended diet restriction
- On average, how much weight is lost
- On average, how long the weight loss lasts
- Average reduction in dose of prescription drugs for, or future risk of [diabetes/high blood pressure/high cholesterol] at the lower weight
- On average, how long side effects last
- Chance of a side effect requiring hospitalization
- Chance of dying from getting the weight loss device

Survey subjects will first go through a short training section to help them understand the meaning of each device attribute and its levels in the survey. Then they will be asked to evaluate a series of choices between pairs of hypothetical medical devices. Each

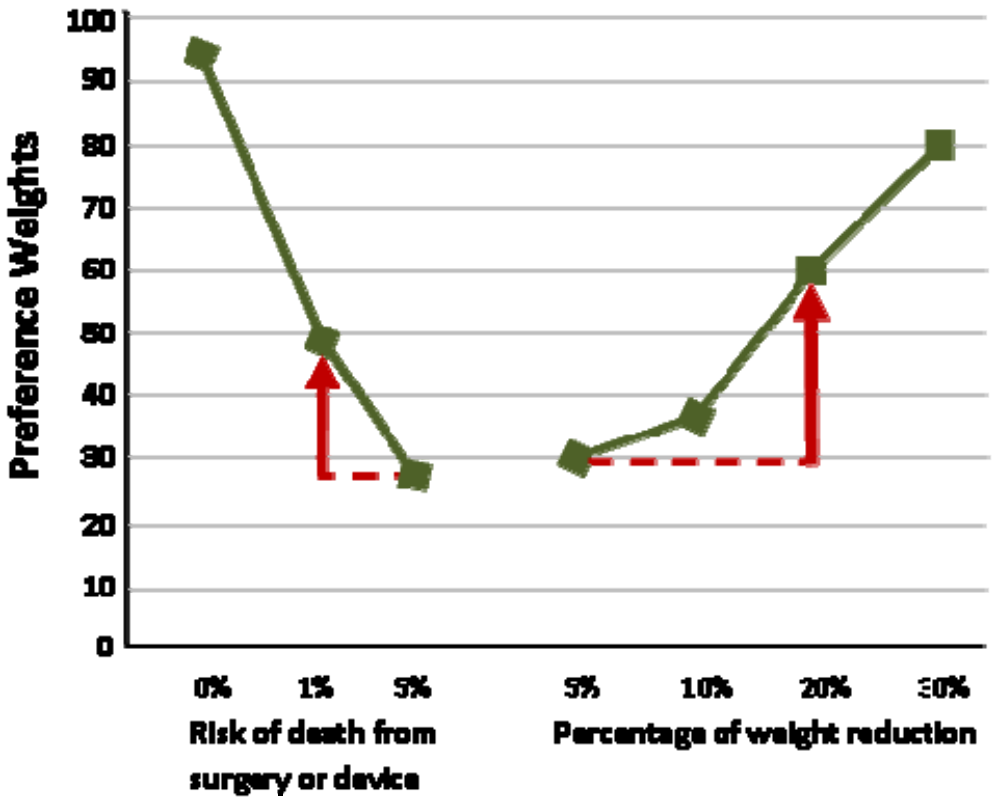
hypothetical device will be defined by treatment attributes such as the amount and duration of weight loss, side effects, risks associated with hypothetical weight-loss devices, and the effect of the device on weight-related co-morbidities. Different combinations of medical device features are created by permuting levels of attributes. Table 1 provides an example of the question format.

Table 1. An example of choice-format question

Feature	Device A	Device B
Type of operation	Laparoscopic surgery	
Recommended diet restriction	Wait 4 hours between meals	Eat ¼ cup of food at a time
On average, how much weight is lost	30 lbs.	90 lbs.
On average, how long the weight loss lasts	Weight loss lasts 1 month	Weight loss lasts 6 months
Average reduction in dose of prescription drugs for [diabetes/high blood pressure/high cholesterol] at the lower weight	Reduces number of pills by half	Eliminates the need for prescription drug
On average, how long side effects last (Remember that side effects will limit your ability to do daily activities several times a month.)	Last 1 month	Rest of life
Chance of a side effect requiring hospitalization	None	5% chance of needing visit to the hospital with no surgery
Chance of dying from getting the weight loss device	 **1%** **(1 out of 100)**	
Which weight-loss device do you think is better for people like you?	☐ Device A	☒ Device B

Final results will provide an estimate of the maximum levels of various treatment-related risks that obese patients would be willing to accept to achieve specific levels of weight loss or improvements in weight-related diseases. These results will be used to estimate the effect of each attribute level on subjects choosing between devices with different profiles. For illustration purpose, Figure 2 below shows the hypothetical results of a weight reduction device survey that includes only 2 attributes, risk of death from surgery or device and percentage of body weight reduction. The weights indicate the relative strength of preference for each level and attribute. Better outcomes carry higher weights than worse outcomes. For example, 0% risk of death is preferred to 5%, which reflected by the higher preference weight of the former compared to latter (95 vs. 25).

Figure 2. Sample preference weights for risk of death from surgery or device and weight reduction



The vertical distances between preference weights indicate the relative importance of moving from one level to another. In this example, the relative importance of an improvement from 5% to 1% risk of death is about 20 units. Likewise, for the percentage of

weight loss, an improvement from 5% to 20% is worth 30 units. This suggests that, in this hypothetical survey, a gain in benefit (weight loss) from 5% to 20% is about 1.5 times as valuable to respondents as a reduction in risk of death from 5% to 1% (30 units / 20 units). In other words, respondents would tolerate increasing risk of death by 4% (from 1% to 5%) in exchange for increasing weight loss from 5% to 20%.