FDA Regulatory Decision Making: Obesity Study as a Potential Tool

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Patients are at the Heart of What We Do

CDRH Vision: Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.
Where can patient perspectives inform the medical device TPLC?

- Patient-Informed Needs
- Patient-Informed Clinical Trial Design
- Patient Preference Benefit-Risk Information
- Communicating Benefit-Risk Information to Patients
- Patient-Centered Outcomes
**Study on devices to treat obesity**

- Explore how to elicit and incorporate patient preferences into regulatory decision-making
  - Treatments involve difficult benefit-risks tradeoffs
  - Decisions are preference sensitive
  - Gastric band was the only approved device in US at the time
  - Broad array of potential devices with diverse benefit-risk profiles
- Used discrete-choice experiment
- Published in *Surgical Endoscopy* April 2015.

# Treatments for Obesity

## Hard Choices, Wide Range of Benefit-Risk Tradeoffs

<table>
<thead>
<tr>
<th>Wt. Loss: 1-5%</th>
<th>Wt. Loss: 7-9%*</th>
<th>Wt. Loss: 17-20%</th>
<th>Wt. Loss: ≈ 30%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Very mild risk:</strong> exercise related injuries; Yo-Yo diet</td>
<td><strong>Mild-mod. risk:</strong> fetal toxicity; increase in HR; suicidal thoughts; glaucoma, etc.</td>
<td><strong>Mod.-high risk:</strong> band erosion &amp; explant; laparoscopic surgery related mortality and risks; etc.</td>
<td><strong>High risk:</strong> Blood clot; excessive bleeding; heart attack; leaks in GI system; death, malnutrition, etc.</td>
</tr>
</tbody>
</table>

**Indication:** For almost every one

- BMI ≥ 30 kg/m²
- BMI ≥ 27 + Weight-related comorbidity

- BMI ≥ 35 kg/m²
- BMI ≥ 30 + Weight-related comorbidity

Medical judgment; med. societies' guidelines vary

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*Plus Diet & Exercise; unlikely to work if weight loss < 3% by Week 12*
Which is a Favorable Benefit-Risk Tradeoff?

Risks

↓ Benefit

↓ Risk

Weight Loss

New Device

Diet
Exercise

Gastric Banding

Gastropasty
Sample: obese subjects willing to lose weight

- Jointly developed by CDRH and RTI-Health Solutions
- ~650 subjects with BMI $\geq 30$ kg/m$^2$
- Administered via the Internet
- Subjects evaluate choices between pairs of hypothetical weight-loss devices defined by attributes and levels
- Only weight-loss devices are considered
- Subjects assume that insurance covers all costs
Attributes and Levels

- **Type of operation** (Laparoscopic, Endoscopic, Open)
- **Average Weight Loss** (0% to 30%)
- **Weight loss duration** (0 to 5 years)
- **Comorbidity improvement** (none to 100%)
- **Duration of side effects** (0 to 5 years)
- **Chance of re-hospitalization** (0 to 20%)
- **Mortality** (0 to 5%)
- **Dietary restrictions**
  - Eat ¼ cup at a time
  - Wait 4 hours between meals
  - Can’t eat sweets or hard to digest foods
<table>
<thead>
<tr>
<th>Attribute</th>
<th>Device A</th>
<th>Device B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of operation</td>
<td>Endoscopic surgery</td>
<td></td>
</tr>
<tr>
<td>Recommended diet restriction</td>
<td>Wait 4 hours between meals</td>
<td></td>
</tr>
<tr>
<td>On average, how much weight is lost</td>
<td>30 lbs.</td>
<td>60 lbs.</td>
</tr>
<tr>
<td>On average, how long the weight loss lasts</td>
<td>Weight loss lasts 5 years</td>
<td>Weight loss lasts 1 year</td>
</tr>
<tr>
<td>Average reduction in dose of prescription drugs for diabetes at the lower weight</td>
<td>Eliminates the need for prescription drug</td>
<td></td>
</tr>
<tr>
<td>On average, how long side effects last</td>
<td>Last 1 month</td>
<td>Last 1 year</td>
</tr>
<tr>
<td>Chance of dying from getting the weight loss device</td>
<td>![10%](10 out of 100)</td>
<td>![1%](1 out of 100)</td>
</tr>
<tr>
<td>Which weight-loss device do you think is better for people like you?</td>
<td><img src="image" alt="Device A" /></td>
<td><img src="image" alt="Device B" /></td>
</tr>
</tbody>
</table>
Decision Aid Tool

**Device outcomes and features**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Weight loss (TBWL%)</td>
<td>14.3%</td>
</tr>
<tr>
<td>Side effect duration (months)</td>
<td>60</td>
</tr>
<tr>
<td>Chance of side effects requiring hospitalization</td>
<td>5%, surgery</td>
</tr>
<tr>
<td>Recommended diet restrictions</td>
<td>Can’t eat sweets</td>
</tr>
<tr>
<td>Expected duration of weight loss (months)</td>
<td>60</td>
</tr>
<tr>
<td>Comorbidities: Reduce treatment dose / chance</td>
<td>No change</td>
</tr>
<tr>
<td>Type of operation</td>
<td>Laparoscopic surgery</td>
</tr>
</tbody>
</table>

**Maximum Acceptable Risk for Selected Group**

0.08% (95% CI 0.03 to 0.21)

**Relative contributions of device attributes**

- Average utility of not getting a weight-loss device
- Type of operation
- Comorbidities: Reduce treatment dose / chance
- Expected Duration of weight loss (months)
- Recommended diet restrictions
- Chance of side effects requiring hospitalization
- Side effect duration (months)
- Total Body Weight loss (TBWL%)
Decision Aid Tool

- Calculates the minimum benefit patients would require for a treatment with a given mortality risk and other attributes
- Calculates the maximum risk patients would accept for a treatment with given weight-loss benefit and other attributes
- Results reported for various levels of risk tolerance
- The estimated values inform clinicians in the determination of the "**minimum clinically meaningful benefit**" used by CDRH to size, design and evaluate clinical trials for weigh-loss devices.
Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling
Objectives of Draft Guidance

1. Voluntary submission of patient preference information
2. Recommended qualities of patient preference studies which may be valid scientific evidence
3. Recommendations for collecting patient preference information
4. Recommendations for including patient preference information in labeling for patients and health care professionals
Voluntary Submission

- Submission of patient preference information (PPI) to FDA is voluntary.

- May consider PPI as part of the totality of evidence from clinical and nonclinical testing for premarket review and benefit-risk determination for devices.

- Draft guidance does not change any review standards for safety or effectiveness, or create any extra burden on sponsors of premarket submissions.
Recommended Qualities of Patient Preference Studies

- Including:
  - Representativeness
  - Heterogeneity
  - Minimal cognitive bias
  - Effective Communication
  - Robustness of analysis of results
Sponsors should include a plan for how they intend to communicate the patient preference information to patients and health care professionals.

Labeling should describe the patient preference study data including:
  • range of patient preferences
  • characteristics of patients who considered the device’s probable benefits to outweigh its probable risks

Patient labeling should use terminology and numerical data that is easily recognized and understood.
How to Get Involved

- Encourage you to have early interactions with FDA if you are considering collecting patient preference information for regulatory purposes
- Patients and patient groups can inform or even perform patient preference studies

- Patient Labeling Workshop – Sept. 29 and 30

- This has been done before, and we hope to see more:
  - Obesity study
  - Parent Project Muscular Dystrophy
  - More groups are in progress
Thank You

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