The science of measuring patient preferences

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Transparency

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• LUNGevity (supported by Celgene)
Overview

There are three broad aims of the presentation today:

1. To review the context of (regulatory) benefit-risk analysis and introduce why incorporating patient preferences might be important.

2. To overview the science of measuring preferences to inform benefit-risk analysis.

3. To present a case study to demonstrate how we quantified preferences of patients with idiopathic pulmonary fibrosis.
1. Benefit-risk decision analysis
The need to study benefit-risk

• Regulators, clinicians, and patients routinely make decisions that require trading safety for desired clinical benefits in the absence of directly comparable metrics.

• Economists and epidemiologists recently have developed quantitative methods for systematically evaluating the risks and benefits of new or existing medical interventions.

• When comparing unweighted risk and benefit incidence rates, one needs to assess the decision makers’ willingness-to-trade risks for benefits.
agreed on facts

disagree on values

physician

patient
Preferences for Anticoagulants in Atrial Fibrillation

Levitan, Yuan, González, et al., ISPOR 18th Ann Int Mtg, 2013
Patient-focused drug development

- The **U.S. Food and Drug Administration** (FDA) has received a mandate to account for the perspectives of patients and caregivers in decision making.
- In response to **PDUFA V requirements**, FDA has focused primarily on inviting patients, caregivers and advocacy groups to provide testimony.
- The role of qualitative and quantitative data on **patient preferences** will play in drug development and in regulatory benefit-risk evaluations is yet to be determined.
Patient-focused drug development

- Under the patient-centered drug development programs, the FDA has formalized a series of 20 meeting with patients and patient groups to foster patient-centered drug development in certain disease areas.

- “We’d like to take those resources and really develop a process whereby we can robustly elicit this information in a broad range of diseases and have a much better understanding of patient tolerance for risks and desire for benefits.”

  Janet Woodcock, Director, CDER
  Patient Network Annual Meeting, May 2012
Why preferences matter
2. How can we measure patient-preferences?
Evaluating multiple endpoints

**Identification**
- What criteria should the technology/ies be evaluated?
- Have all stakeholders contributed to this process?

**Assessment**
- How does the technology/ies perform on the criteria?
- Do all stakeholders endorse/accept this assessment?

**Valuation**
- How should each of the criteria be weighted?
- Have the criteria been weighted fairly?

**Deliberation**
- What is the final decision?
- Have all stakeholders contributed to the decision?
Engaging patients and the public

- Two schools of thought have emerged to engage patients and the public in decision making:
  - Direct engagement via representation, consultation and/or testimony.
  - Formal study of the priorities and preferences of patients and the public.

- “When asking the public to assist in determining health priorities, we should use techniques that allow people to reveal their true preferences. If not, why bother asking them at all?” Gafni, 1995
Improving the science

- ISPOR conjoint analysis working group (2006-11)
- Conjoint Analysis & Health Conference (2007-12)
- The Patient journal launched (2008)
- ISPOR conjoint analysis taskforce (2008-10)
- ISPOR experimental design taskforce (2010-12)
- International Academy of Health Preference Research (www.IAHPR.org) (2014)
- FasterCures Benefit-Risk Advisory Council (2014)
- ISPOR Stated-Preference Methods SIG (2015)
- ISPOR Patient-focused Benefit-Risk Analysis working group (2015)
Stated-preference methods

- Stated-preference methods are **grounded in the choice theories** of economics and psychology.
- They use a range of **qualitative and quantitative** survey methods to identify what patients prefer.
- Common **stated-preference methods** include:
  - Conjoint analysis
  - Discrete choice experiments
  - Best-worst scaling
Discrete-choice experiment (DCE)

- A DCE aims to value the levels for each of the attributes to assess tradeoffs.
- For two (or more) given profiles, respondents indicate the profile they prefer.

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Drug 1</th>
<th>Drug 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c levels go down</td>
<td>1%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Stable blood sugar</td>
<td>2 days/week</td>
<td>4 days/week</td>
</tr>
<tr>
<td>Low blood sugar</td>
<td>2/month</td>
<td>None</td>
</tr>
<tr>
<td>Nausea</td>
<td>None</td>
<td>4 hours/day</td>
</tr>
<tr>
<td>Treatment burden</td>
<td>2 pills/day</td>
<td>1 pill/day</td>
</tr>
<tr>
<td>Costs</td>
<td>$50/month</td>
<td>$30/month</td>
</tr>
</tbody>
</table>

Which drug do you prefer?
BWS Case 1 (object case)

- BWS Case 1 (the object case) aims to measure a respondents priorities across a set of statements that define attributes/objects.
- These are presented in subsets, and the respondent is asked to select the best and worst.

<table>
<thead>
<tr>
<th>Objects</th>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td>The medication reduces A1c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The medication needs to be taken every day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The medication causes low blood sugar events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The medication makes me nauseous</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
BWS Case 2 (Profile case)

• BWS Case 2 (profile case) aims to weigh multiple levels for each of the attributes.
• For a given profile, respondents indicate the best and worst levels.

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Drug A</th>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c levels go down</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable blood sugar</td>
<td>4 days/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low blood sugar events</td>
<td>2/month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment burden</td>
<td>2 pills/day</td>
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</tr>
<tr>
<td>Costs</td>
<td>$50/month</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
BWS Case 3 (multiple profile)

- BWS case 3 (multiple profile) is like a traditional choice experiment, but with 3 or more profiles.

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Drug 1</th>
<th>Drug 2</th>
<th>Drug 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c levels go down</td>
<td>1%</td>
<td>0.5%</td>
<td>0%</td>
</tr>
<tr>
<td>Stable blood sugar</td>
<td>4 days/week</td>
<td>4 days/week</td>
<td>2 days/week</td>
</tr>
<tr>
<td>Low blood sugar</td>
<td>2/ month</td>
<td>None</td>
<td>1/ month</td>
</tr>
<tr>
<td>Nausea</td>
<td>None</td>
<td>4 hours/day</td>
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<tr>
<td>Costs</td>
<td>$50/month</td>
<td>$30/month</td>
<td>$10/month</td>
</tr>
</tbody>
</table>

**Best**

**Worst**
3. Case study: Idiopathic pulmonary fibrosis
Idiopathic pulmonary fibrosis (IPF)

- Idiopathic pulmonary fibrosis (IPF) is a rare, fatal lung disease of unknown origin affecting an estimated 14-43 per 100,000 people in the US.
- IPF affects mostly older adult males.
- IPF is highly variable and causes scarring of the lungs, resulting in a progressive decline in lung function as well as shortness of breath and involuntary cough.
- The prognosis of patients with IPF is poor and median survival ranges from 2.5 to 3.5 years.
Development of survey instrument

- Based on the themes identified through interviews with diverse stakeholders, a preliminary survey was developed to assess the benefit and risk tradeoffs IPF patients are willing to make.
- Researchers sought to refine the survey by conducting one-on-one cognitive interviews.
- The 15 participants were patients of the Johns Hopkins Interstitial Lung Disease Clinic.
- Participants were engaged in the research and provided valuable feedback that helped to refine the instrument for a pilot study.
Example BWS choice task

For each treatment, choose the one best and the one worst thing. Please answer based on your experience with IPF and your current stage of the disease. Even if you don’t like the treatment, tell us what is the one best and the one worst aspect of it. Some may not seem realistic; some may even sound bad. Even though this may feel wrong, it is important to make the study work.

<table>
<thead>
<tr>
<th>Benefits and Risks</th>
<th>Best</th>
<th>Worst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant slowing in decline in lung function</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>No effect on shortness of breath</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Potential slowing in the worsening of persistent cough</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>No gastrointestinal problems</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Mild skin problems</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>1 in 1,000 patients show signs of liver toxicity</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

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Results – Treatment Preferences

Effect on slowing of decline in lung function
Effect on slowing of worsening of shortness of breath
Effect on slowing of worsening of cough
Gastrointestinal problems
Skin Problems
Liver toxicity

Relative Best-Worst Score

<table>
<thead>
<tr>
<th>Signif</th>
<th>Mod</th>
<th>None</th>
<th>Signif</th>
<th>Poten</th>
<th>None</th>
<th>Signif</th>
<th>Poten</th>
<th>None</th>
<th>Mod</th>
<th>Mild</th>
<th>None</th>
<th>Mod</th>
<th>Mild</th>
<th>None</th>
<th>0.10%</th>
<th>0.01%</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.774</td>
<td>0.774</td>
<td>-0.32</td>
<td>0.524</td>
<td>0.143</td>
<td>-0.29</td>
<td>0.095</td>
<td>-0.06</td>
<td>-0.13</td>
<td>-0.45</td>
<td>-0.45</td>
<td>0.024</td>
<td>-0.13</td>
<td>-0.06</td>
<td>0.024</td>
<td>-0.34</td>
<td>-0.15</td>
<td>0.036</td>
</tr>
</tbody>
</table>