Industry Perspective on Patient Preference Information

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<table>
<thead>
<tr>
<th>Outcome</th>
<th>Drug A</th>
<th>Drug B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relief of pain</td>
<td><img src="severity.png" alt="Severity Scale" /></td>
<td><img src="severity.png" alt="Severity Scale" /></td>
</tr>
<tr>
<td>Ability to perform work/school and social activities</td>
<td>No limitations</td>
<td>Cannot work, difficulty with chores and shopping</td>
</tr>
<tr>
<td>Annual chance of a heart attack</td>
<td>1 in 10,000</td>
<td>No chance</td>
</tr>
<tr>
<td>Which medicine would you choose if these were the only medicines available?</td>
<td><img src="diagram.png" alt="Diagram" /></td>
<td><img src="diagram.png" alt="Diagram" /></td>
</tr>
<tr>
<td>Outcome</td>
<td>Drug C</td>
<td>Drug B</td>
</tr>
<tr>
<td>---------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>Relief of pain</td>
<td><img src="image" alt="Relief of pain scale" /></td>
<td><img src="image" alt="Relief of pain scale" /></td>
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<td><img src="image" alt="Drug C choice" /></td>
<td><img src="image" alt="Drug B choice" /></td>
</tr>
<tr>
<td>Outcome</td>
<td>Drug D</td>
<td>Drug B</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------</td>
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<td></td>
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<td>No limitations</td>
<td>Cannot work, difficulty with chores and shopping</td>
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<tr>
<td>Annual chance of a heart attack</td>
<td>1 in 100</td>
<td>No chance</td>
</tr>
<tr>
<td>Which medicine would you choose if these were the only medicines available?</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
agree on facts

regulator

may disagree on values

patient
What Did Migraine Patients Say?

Stated choice conjoint preference survey of 200 adult migraine patients

- Relieving all functional limitations was twice as important as relieving all migraine pain

Maximum Acceptable Risk = maximum level of treatment-related 1-year heart attack risk patients would accept for a given improvement in migraine symptoms

- Patients would accept up to a 2/1000 (95% CI 1.6 – 2.4) annual heart attack risk in exchange for restoring their ability to function during migraines

# Three Types of Patient Preference Information

<table>
<thead>
<tr>
<th>Type</th>
<th>What it Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attributes</td>
<td><strong>What Matters</strong></td>
</tr>
<tr>
<td>Relative Importance</td>
<td><strong>How much it matters</strong></td>
</tr>
<tr>
<td>Tradeoffs</td>
<td><strong>What tradeoffs</strong> patients are willing to make between benefits, harms, and other aspects</td>
</tr>
</tbody>
</table>

Adapted from RTI-HS and MDIC
Where Can Patient Preferences Inform the Development Lifecycle?

**Commercial viability / Patient needs**

**Trial design**
- What endpoints do patients care most about?

**TPP**
- What is the relative importance of benefits, risks and other treatment features to patients?

**Approval & reimbursement**
- How do patients vary in these properties (heterogeneity)? Are there distinct subgroups?

**Ph 2a/b**
- What level/rate of endpoints are critical to patients?

**Ph 3**
- Maximum acceptable risk, minimum required benefit, choice share?

**Reg**
- Are there important differences between stakeholders?

**Post-approval**
- Shared decision-making
Identifying Differences Between Key Stakeholders

Preferences for Anticoagulants in Atrial Fibrillation

US Physician

- Death
- Disabling Stroke
- Non-Disabling Stroke
- Major Bleeding
- Heart Attack
- Blood Clot

US Patient

- Death
- Disabling Stroke
- Non-Disabling Stroke
- Major Bleeding
- Heart Attack
- Blood Clot

Levitan, Yuan, González, et al., ISPOR 18th Ann Int Mtg, 2013
### Risk Differences by Clinical Severity/Impact

Atrial Fibrillation Example (mock data)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th># of Events (/10,000 patient-years)</th>
<th>Risk difference /10,000 patient-yrs (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>Study Drug 187, Comparator 221</td>
<td></td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>Study Drug 39, Comparator 51</td>
<td></td>
</tr>
<tr>
<td>Non-CNS systemic embolism</td>
<td>Study Drug 3, Comparator 18</td>
<td></td>
</tr>
<tr>
<td>Non-disabling stroke</td>
<td>Study Drug 80, Comparator 78</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Study Drug 90, Comparator 111</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>Study Drug 361, Comparator 346</td>
<td></td>
</tr>
<tr>
<td>Non-major clinically-relevant bleeding</td>
<td>Study Drug 1179, Comparator 1135</td>
<td></td>
</tr>
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</table>
Maximum Acceptable Risk of treatment-related death or permanent severe disability due to stroke

Patient Preference Studies Can Inform Target Product Profiles

- Consider TPP a point on a continuum of B-R tradeoffs
- Preference studies given many acceptable tradeoffs
- Can generate a family of viable TPPs
- Provides much greater proactive flexibility for alignment between compound and TPP goals
What Sponsors Worry About When Considering A Patient Preference Study

- Do we really need it?
- Who is involved?
- Can we publish?
- How rigorous?
- What method?
- When should we do it?
- Will regulators pay attention?
- How much does it cost?
- Whose preferences?
- How do we design it?
- Work with a patient group?
- What can we do with it?
- How long will it take?
- Can we trust the results?
- Who can help us?
### Many Methods for Assessing Preferences

<table>
<thead>
<tr>
<th>Group</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structured-weighting</td>
<td>• Simple direct weighting&lt;br&gt;• Ranking exercises&lt;br&gt;• Swing weighting&lt;br&gt;• Point allocation&lt;br&gt;• Analytic hierarchy process&lt;br&gt;• Outranking methods</td>
</tr>
<tr>
<td>Health-state utility</td>
<td>• Time tradeoff&lt;br&gt;• Standard gamble</td>
</tr>
<tr>
<td>Stated-preference</td>
<td>• Direct-assessment questions&lt;br&gt;• Threshold technique&lt;br&gt;• Conjoint analysis and discrete-choice experiments&lt;br&gt;• Best-worst scaling exercises</td>
</tr>
<tr>
<td>Revealed-preference</td>
<td>• Patient-preference trials&lt;br&gt;• Direct questions in clinical trials</td>
</tr>
</tbody>
</table>

Factors Influencing Whether Patient Preference Information May Be Valuable for Regulatory Review

- **Patient’s perspective**
  - Important differences in preferences of patients and other stakeholders
  - Important differences in preferences of subgroups of patients
  - Understanding the patient experience requires considerable familiarity with the disease (e.g. very subjective endpoints, lifestyle indication, rare disease)

- **Benefit-risk tradeoffs (preference sensitive)**
  - Clear benefit with rare serious risks compared to alternatives
  - Harms occur early/benefits occur later (e.g. secondary prevention)
  - Considerable uncertainty whether a patient will realize the benefit or risks

- **Novelty**
  - New mechanism of action or type of device
  - Lack of precedent

What do you want to know? Two basic approaches to patient-preference studies

• **Product-evaluation (top-down) approach**
  - Assess patient preferences for known features of treatment options to make decisions
  - Applies to existing products or services or those in development
  - Example: CDRH weight-loss preference study *(Ho et al., 2015)*

• **Issues-identification (bottom-up) approach**
  - Patients define relevant features, priorities, or needs
  - Preference methods used to quantify the relative importance of features
  - Not necessarily specific to the features of an existing product
  - Example: PPMD Duchenne Muscular Dystrophy Studies *(Hollin et al., 2015; Peay et al.,)*

Survey pretest similar to cognitive debriefing

Survey development similar to concept elicitation

Based on slide from Brett Hauber
Many Open Questions on Preference Work

- **Technical / methodological questions**
  - Methods, population, bias, internal validity, external validity, …
  - E.g. MDIC framework gap analysis

- **Regulatory standards in development**
  - Design requirements
  - Sample requirements
  - Internal validity

- **Avenues for regulatory communication**
  - ICH update to common technical document – place for pref studies
  - Label - Limited opportunity for benefit-risk or patient preferences

* Levitan, Hauber, Damiano, Jaffe and Christopher, “The Ball is in your Court: Agenda for Research to Advance the Science of Patient Preferences in the Regulatory Review of Medical Devices in the United States,” Patient, August, 2017 (online)
Huge Growth of Initiatives on Methodology, Policy and Application of Patient Preference Studies

Regulatory/Govt  Trade Orgs  Pub Private/Prof  Patient Groups

[Logos of various organizations and initiatives]
Future Direction: Consortium Approach to Preference Studies

- Multiple stakeholders (e.g. industry, patient group, academia, regulatory) collaborate on a preference study

- Pool resources and expertise
- Lessen covert bias
- Larger sample size
- Greater acceptance
Goal

agree on facts

Understand values