Approaches for Utilizing Patient Preference Information to Inform Clinical Trial Design

Medical Device Innovation Consortium (MDIC)
MDIC’s mission is to leverage its unique position as the only public-private partnership of its kind to transform health care into human care. Collaborating with our partners to advance science, we enable transformational medical technology to shape the world we want to live in and make that world possible by shortening the path from innovation to safety to access.
Today’s Panel Presentation

Objective: Learn how Patient Preferences can inform study design

Barry Liden, JD (Facilitator)  Intro/Overview  5 min
MDIC Science of Patient Input

Shelby Reed, PhD  Case Study: Heart Failure Patient Preferences  10 min
Duke University

Barry Liden  Overview of MDIC Framework  20 min

Michelle Tarver, MD, PhD  The Regulator’s Perspective  10 min
FDA-CDRH

All & Audience  Discussion; Q&A  15 min
Case Study:
Heart Failure Patient Preferences

Shelby Reed, PhD - Duke University
Background and motivation

- Applications for utilizing patient preference information in designing clinical trials
  - Prioritizing study endpoints
  - Weights for composite endpoints
  - Preference-weighted PROs
  - Meaningful effect sizes
  - Statistical criteria and power calculations
Collaborative Effort

Patient representatives

Six Industry Partners

MDIC

DCRI PrefER Group

FDA CDRH
Study Objectives

• To apply best-practice stated-preference methods to quantify heart-failure patients’ willingness to accept therapeutic risks in exchange for improved efficacy.

• Engage patients, providers, device industry representatives and preference-research experts in a collaborative effort.

Inform clinical-trial designs for studying heart-failure devices.
Selecting attributes and choice context

Potential Attributes
- Functional capacity
- Quality of life improvement
- Number of hospitalizations
- Risk of adverse events associated with device
- Uncertainty about benefit
- Mortality
- Device features

Decision Context
- Motivation for a change in HF management
- Severity of disease
- Device vs. device vs. medication
## Attributes and Levels

### Attributes

<table>
<thead>
<tr>
<th>Category</th>
<th>Attribute</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning and survival</td>
<td>Years in NYHA class II/III/IV</td>
<td>0 out of 100 (0%) (&quot;no device&quot;)</td>
</tr>
<tr>
<td>Risk of mortality</td>
<td>How many people died within 30 days</td>
<td>2 out of 100 (2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 out of 100 (5%)</td>
</tr>
<tr>
<td>Risk of device-associated complications</td>
<td>Low-risk arm: 10 out of 100 (10%)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High-risk arm: 15 out of 100 (15%)*</td>
<td></td>
</tr>
<tr>
<td>Remote device programming</td>
<td>Risk of complications leading to additional 2 days in hospital</td>
<td>0 out of 100 (0%) (&quot;no device&quot;)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 out of 100 (5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 out of 100 (15%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40 out of 100 (40%)</td>
</tr>
</tbody>
</table>

### Remote device programming

<table>
<thead>
<tr>
<th>Device feature</th>
<th>Remote programming</th>
<th>Yes</th>
</tr>
</thead>
</table>
Level '3' represents people who get out of breath and must stop to rest when climbing a flight of stairs. Also, when doing light housework like doing the dishes or running the vacuum, they must stop to catch their breath. They feel comfortable when they are sitting watching television or reading.

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Climbing stairs:</td>
<td>Climb at regular speed</td>
<td>Climb slowly</td>
<td>Must stop to rest</td>
</tr>
<tr>
<td>Housework:</td>
<td>Can do</td>
<td>Can do</td>
<td>Must stop to rest</td>
</tr>
<tr>
<td>Resting:</td>
<td>Comfortable</td>
<td>Comfortable</td>
<td>Comfortable</td>
</tr>
</tbody>
</table>

This picture shows by the end of 3 years, their symptoms would get noticeably worse, so that after the 3^{rd} year they aren't able to climb stairs or do housework. Even when resting, they feel tired and out of breath (Level 4).

They would live that way for 2 more years and then die at 5 years.

In the last three months of life, they feel increasingly tired and out of breath.
Example Choice Question

Which of the 3 options shown below would you choose?

<table>
<thead>
<tr>
<th></th>
<th>Ability to Do Daily Activities</th>
<th>Additional risk of death in 30 days</th>
<th>Risk of complications with 2 extra days in the hospital</th>
<th>Remote Adjustment of Settings</th>
<th>Which would you choose?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No Device</strong></td>
<td><img src="image1.png" alt="Diagram" /></td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>☑</td>
</tr>
<tr>
<td><strong>Device A</strong></td>
<td><img src="image2.png" alt="Diagram" /></td>
<td>2% (2 out of 100)</td>
<td>None</td>
<td>None</td>
<td>☑</td>
</tr>
<tr>
<td><strong>Device B</strong></td>
<td><img src="image3.png" alt="Diagram" /></td>
<td>5% (5 out of 100)</td>
<td>5% (5 out of 100)</td>
<td>None</td>
<td>☑</td>
</tr>
</tbody>
</table>
Pretesting the survey instrument

- Patients with heart failure from Duke University Health System

- Examples of changes to survey instrument:
  - Added 3 health literacy questions
  - Devised logic-notification experiment
  - Days with NYHA 1-IV symptoms rather than selecting a class
  - Added training for NYHA trajectories, modified graphics, and added comprehension questions
  - Explained potential harms with remote monitoring; not useful in an emergency
Validity Testing

• Study included several validity tests and safeguards
  – Respondent comprehension questions
    • Activity levels/duration and graphics
    • Risks and definitions
  – Randomized logic-notification experiment
  – Straight-lining (response non-variance)
  – Dominance patterns
  – Time to completion
  – Within-set and cross-set monotonicity tests
  – Scope tests
Patients with physician-confirmed heart failure

Web-based panel of participants reporting a diagnosis of heart failure

500 Total responses
-11 Straight-liners
489 Final sample size

126 Total responses
-2 Straight-liners
124 Final sample size
# Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NHANES* (HF)</th>
<th>Web Panel (N = 500)</th>
<th>DUHS (N = 126)</th>
<th>P-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>48%</td>
<td>52%</td>
<td>47%</td>
<td>0.10</td>
</tr>
<tr>
<td>Age in years, mean (SD)</td>
<td>66</td>
<td>64 (12)</td>
<td>66 (11)</td>
<td>0.06</td>
</tr>
<tr>
<td>Hispanic or Latino, %</td>
<td>5%</td>
<td>2%</td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>89%</td>
<td>66%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>24%</td>
<td>8%</td>
<td>32%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>American Indian/Alaskan native</td>
<td>3%</td>
<td>3%</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2%</td>
<td>0</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>Native Hawaiian/other Pacific islander</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
<td>0</td>
<td>0.59</td>
<td></td>
</tr>
<tr>
<td>Education, %*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school or less</td>
<td>28%</td>
<td>19%</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>Some college but no degree</td>
<td>28%</td>
<td>19%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associate degree/tech school</td>
<td>16%</td>
<td>19%</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>4-year degree (+/- some grad studies)</td>
<td>23%</td>
<td>20%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduate or professional degree</td>
<td>14%</td>
<td>19%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Disease characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Web Panel (N = 500)</th>
<th>DUHS (N = 126)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days over the past 7 days with... ,mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA I</td>
<td>3.1 (2.9)</td>
<td>3.5 (2.8)</td>
<td>0.22</td>
</tr>
<tr>
<td>NYHA II</td>
<td>3.4 (2.6)</td>
<td>3.8 (2.6)</td>
<td>0.21</td>
</tr>
<tr>
<td>NYHA III</td>
<td>3.0 (2.8)</td>
<td>3.0 (2.6)</td>
<td>0.80</td>
</tr>
<tr>
<td>NYHA IV</td>
<td>0.9 (2.0)</td>
<td>0.9 (1.7)</td>
<td>0.86</td>
</tr>
<tr>
<td>Heart failure management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Take Rx meds</td>
<td>95%</td>
<td>92%</td>
<td>0.13</td>
</tr>
<tr>
<td>Changed diet</td>
<td>59%</td>
<td>68%</td>
<td>0.05</td>
</tr>
<tr>
<td>Heart valve device</td>
<td>3%</td>
<td>2%</td>
<td>0.78</td>
</tr>
<tr>
<td>Heart valve repair/replacement</td>
<td>7%</td>
<td>7%</td>
<td>0.92</td>
</tr>
<tr>
<td>ICD</td>
<td>24%</td>
<td>31%</td>
<td>0.13</td>
</tr>
<tr>
<td>Cardiac resynch device</td>
<td>2%</td>
<td>2%</td>
<td>1.0</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>20%</td>
<td>23%</td>
<td>0.52</td>
</tr>
<tr>
<td>Stents</td>
<td>29%</td>
<td>27%</td>
<td>0.69</td>
</tr>
</tbody>
</table>

* p-values correspond to web panel vs. DUHS
<table>
<thead>
<tr>
<th>Question description</th>
<th>Web Panel (N = 500)</th>
<th>DUHS (N = 126)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>How easy is stair climbing for Level 3?</td>
<td>82%</td>
<td>91%</td>
<td>0.04</td>
</tr>
<tr>
<td>How easy is stair climbing for Level 4?</td>
<td>84%</td>
<td>91%</td>
<td>0.07</td>
</tr>
<tr>
<td>Path 2, die at what year?</td>
<td>58%</td>
<td>66%</td>
<td>0.38</td>
</tr>
<tr>
<td>Years in level 3?</td>
<td>60%</td>
<td>63%</td>
<td>0.49</td>
</tr>
<tr>
<td>Which path shows 2 yrs in level 4?</td>
<td>57%</td>
<td>60%</td>
<td>0.19</td>
</tr>
<tr>
<td>How many more died?</td>
<td>84%</td>
<td>92%</td>
<td>0.12</td>
</tr>
<tr>
<td>Which showed improvement in activities?</td>
<td>81%</td>
<td>86%</td>
<td>0.17</td>
</tr>
<tr>
<td>True/False- problems after hospital stay</td>
<td>56%</td>
<td>65%</td>
<td>0.19</td>
</tr>
</tbody>
</table>
Random-parameters logit model with effect-coded variables for all levels in each attribute

Expectations:

- More positive preferences for longer periods in NYHA III and NYHA II
- Positive preferences time in NYHA II vs. NYHA III
- More positive preferences for lower risk of death and complications
- More negative preferences for the risk of death compared to risk of complications for overlapping levels (i.e. 5% and 15% [high-risk arm])
Results

No differences in scale or preferences
Maximum-Acceptable Risk

30-Day Mortality

- All Respondents (N=613)
  - 1 year in NYHA II: 6%
  - 1 year in NYHA III: 5%
  - 1 year in NYHA II & 1 year in NYHA III: 11%

In-hospital complication

- All Respondents (N=613)
  - 1 year in NYHA II: 27%
  - 1 year in NYHA III: 20%
  - 1 year in NYHA II & 1 year in NYHA III: 46%
Summary

• Patients agreed that functional status corresponding to NYHA Class and survival represented important heart failure outcomes.

• Overall preference weights were similar between online panel and DUHS participants.

• On average, participants with heart failure preferred a device and were willing to accept a 5-6% risk of mortality for 1-year gains in survival with NYHA II or III functioning.
MDIC’s Framework:
Using Patient Preference Information in the Design of Clinical Trials

Barry Liden, JD – USC Schaeffer Center for Health Policy & Economics
(Formerly VP, Patient Engagement, Edwards Lifesciences – Chair of MDIC’s Science of Patient Input Working Group)
A patient-centered approach to clinical trial design has many important benefits, including the potential to:

- Improve patient experience in clinical trials
- Accelerate enrollment
- Improve retention and long-term follow-up
- Improve data quality
- Assure that trials are focused on outcomes that matter most to patients
- Support regulatory decision-making activities
- Assist in payer evaluations of value of new medical devices
- Help ensure new technological innovation is focused on bringing the most benefit to patients
Science of Patient Input Steering Committee Members

- Marc Boutin, JD, NHC*
- Dean Bruhn-Ding, RAC, CVRx
- Katie (O’Callaghan) Capanna, FDA CDRH
- Katherine Chowdhury, MA, FDA CDRH****
- Kelly Close, MBA, The diaTribe Foundation
- Heather Colvin, Johnson & Johnson
- Paul Coplan, ScD, MBA, Johnson & Johnson
- Tara Federici, AdvaMed
- Emily Fitts, The diaTribe Foundation
- Jessica Foley, PhD, Focused Ultrasound Foundation
- Pamela Gavin, MBA, NORD
- Scott Goates, PhD, Abbott Laboratories
- Alissa Hanna, Edwards Lifesciences
- Brett Hauber, PhD, RTI***
- Ross Jaffe, MD, MBA, Versant Ventures
- Julia Kenney, The diaTribe Foundation
- Barry Liden, JD, Edwards Lifesciences††
- Franchesca Liao, MS, Illumina
- Alexandra Massoud, Exact Sciences
- Mimi Nguyen, MS, FDA CDRH
- Mike Otlewski, MS, MED Institute Inc.
- Eric Relkin, LivaNova*****
- Liliana Rincon-Gonzalez, PhD, MDIC†
- Anindita Saha, FDA CDRH
- Diana Salditt, FRAPS, Medtronic******
- Peter Saltonstall, NORD
- Melissa Schooley, JD, Abiomed
- Dan Stephens, PhD, Boston Scientific
- Michelle Tarver, MD, PhD, FDA CDRH
- Karena Yan, The diaTribe Foundation
Goals of Framework:
1. Improve patient-centricity
2. Discover new approaches
3. Provide a useful resource
Highlights of Framework Today

PPI for Clinical Trial Design – Key Steps and Checklist for Sponsors

A. Decide to Generate PPI to Inform Clinical Trial Design
- ✔ Determine the Purpose and Define the Question
- ☐ Select an Appropriate Disease State and Patient Population
- ✔ Engage Expertise
- ✔ Engage Regulators
- ☐ Engage Patient Advocacy Organizations and Patient Advisors

B. Lay the Groundwork
- ☐ Establish Budgets and Timelines
- ☐ Engage Patients

C. Develop PPI to Inform Clinical Trial Design
- ✔ Select Attributes for the Patient Preference Study
- ☐ Recruit Representative Patients for the Patient Preference Study
- ☐ Address Diversity
- ☐ Work With Patient Advocacy Organizations
- ☐ Engage Clinical Sites and Online Platforms
- ☐ Recruit via Confirmed Diagnosis and/or Self-Report
- ✔ Leverage a Bayesian Decision Analysis Framework
- ☐ Choose Between Fixed or Preference-Based Statistical Significance and P Values

D. Communicate the Effort
Determine the Purpose & Define the Question

**PPI USE IN CLINICAL TRIAL DESIGN**

1. Define primary and secondary endpoints
2. Design composite endpoints
3. Determine endpoint weighting
4. Evaluate statistical components
5. Identify subpopulations
Engage the Right Expertise

Find experts who have:

• Appropriate rigor and technical expertise to generate data acceptable for use in clinical trial design
• Experience conducting patient preference studies and ability to recruit study participants
• Statistical design capabilities and familiarity with the BDA model
• Patient perspective
Engage Regulators EARLY AND OFTEN

• Guidance documents
• Early discussions
• Q-sub process

Lessons Learned from Case Studies:

✓ PPI Study design needs to be fit for purpose
✓ Review staff familiarity with PPI is still developing
✓ Patient experts’ input can be helpful to regulators’ flexibility
✓ Endpoint selection may have practical challenges
Wait, what are “Preferences” again?

“Qualitative or quantitative statements of the relative desirability or acceptability of attributes that differ among alternative interventions.”

Evidence representative of a group

Often obtained from surveys

Defined by what people are willing to give up

Characteristics or features

or

- health states
- care processes
- health policies
- other

Source: CDRH

Relative weight of high-level factors on decision to undergo a procedure to repair / replace mitral valve

- Level of invasiveness
- Risk of disabling stroke (within 30 days of procedure)
- Recovery time / intensity
- Risk of new onset atrial fibrillation (within 30 days of procedure)
- Risk of re-intervention (within 2 years of procedure)
- Risk of re-appearing / new MVR symptoms (within 2 years of procedure)

Attribute Selection Considerations

- Some study designs limit number of attributes
- Tools to reliably measure what matters most to patients might not be available
- PPI study attributes need to align with clinical trial endpoints
  - Comparing new devices to status quo may require using “traditional” endpoints
  - Conversely, patient priorities can move clinicians and FDA
  - Regardless, regulators need a clear, agreed-upon “crosswalk” from PPI attributes to clinical trial endpoints
Leveraging Bayesian Decision Analysis

Traditional Clinical Trial Design

\[ P = 0.05 \]

Fixed \( P \) value does not incorporate patient risk tolerance and preferences

VS.

Bayesian Decision Analysis Clinical Trial Design

\( P < 0.05 \) or \( P = 0.05 \) or \( P > 0.05 \)

Flexible \( P \) value incorporates patient risk tolerance and preferences
Highlights of Framework Today

PPI for Clinical Trial Design – Key Steps and Checklist for Sponsors

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   - Select an Appropriate Disease State and Patient Population

B. Lay the Groundwork
   - Establish Budgets and Timelines
   - Engage Expertise
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   - Choose Between Fixed or Preference-Based Statistical Significance and P Values

D. Communicate the Effort
Patient Preference Information & Medical Devices: Guidances and Learnings from the Center for Devices and Radiological Health (CDRH)

Michelle Tarver, MD, PhD
Deputy Director, Office of Strategic Partnerships and Technology Innovation
Center for Devices and Radiological Health
U.S. Food and Drug Administration
michelle.tarver@fda.hhs.gov
Patients are at the Heart of All We Do

*Inspired by Patients, Driven by Science*
Medical Device Regulatory Impact of Patient Experience Data

25 Industry-sponsored regulatory PPI studies completed or in pipeline

Over 50% of PMAs, HDEs, and de Novos have PROs
Patients & Medical Product Evaluation

- Patient Engagement
- Clinical Outcome Assessments
- Patient Preference Information
- Patient-Generated Health Data
Final Guidance: Principles for Selecting, Developing, Modifying, & Adapting of PRO Instruments for Use in Medical Device Evaluation

- Measure concepts important to patients
- Ensure PRO instruments are understandable to patients
- Be clear about the role of PRO instrument in the clinical study protocol and statistical analysis plan
- Leverage existing PRO instrument and validity evidence
- Consider alternative platforms and parallel development for generating validity evidence for PRO instruments
- Collaborate with others in the pre-competitive space

### Topics of PEAC Meetings

<table>
<thead>
<tr>
<th></th>
<th>Patient Engagement in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Patient-Generated Health Data &amp; Medical Device Safety</td>
</tr>
<tr>
<td>3</td>
<td>Communicating Cybersecurity Vulnerabilities</td>
</tr>
<tr>
<td>4</td>
<td>Artificial Intelligence &amp; Machine Learning</td>
</tr>
<tr>
<td>5</td>
<td>Medical Device Recalls</td>
</tr>
<tr>
<td>6</td>
<td>July 12-13, 2022: Augmented and Virtual Reality Devices</td>
</tr>
</tbody>
</table>

CDRH Encourages Patient Engagement Through Guidance

Patient Engagement in the Design and Conduct of Medical Device Clinical Studies

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders


The draft of this document was issued on September 24, 2019.

For questions about this document regarding CDRH-regulated devices, contact Michelle Tarver in the Office of Strategic Partnerships and Technology Innovation (OSTI) at (301) 796-6884 or by email CDRH_PatientEngagement@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-833-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov.

MDUFA 5 Draft Recommendations: Patient Science and Engagement

Continue engaging patients and incorporating their perspectives in the regulatory process:
• Facilitate patient engagement through patient-friendly educational content
• Explore ways to advance health equity by incorporating data and perspectives from diverse patients
• Expand patient science review expertise and capacity
• Improve the regulatory predictability and impact of patient science, including shared examples
• Hold public meeting on patient-generated health data (PGHD) for collecting COA data and for remote clinical trials
• Issue draft guidance on incorporating clinical outcome assessments (COA) into premarket studies and update patient preference information (PPI) guidance
Core Principle: Structured Data Collection

Structured approach to collecting information on patient’s lived experience with condition

- Allows aggregation of data from multiple people facilitating quantitative assessments
- Facilitates consistent assessment of concept of interest (measures what we intend to measure)
- Can be used to show treatment benefits as well as natural history of disease
- Facilitates healthcare provider and patient discussions
- Minimizes noise in clinical investigations if well-defined and characterized
Patient Preference Information Meets a Need

- Opportunity to integrate real-world perspectives into decisional frameworks
- Puts healthcare providers’ and regulators’ perspectives in context with patients’ perspectives
- Informs patients’ priorities in a list of many outcomes
- Illuminates patients’ tolerance for adverse events in exchange for:
  - Quality of life benefits
  - Earlier access to potentially effective treatments
  - Convenience
## Use of Patient Preference Information

<table>
<thead>
<tr>
<th>Device Development</th>
<th>Clinical Trial Design</th>
<th>Benefit-risk Assessment</th>
<th>Post-Market Decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify unmet medical need</td>
<td>Inform endpoint selection</td>
<td>Clarify what matters most to patients about their disease or treatment</td>
<td>Post-market benefit-risk re-assessment for compliance</td>
</tr>
<tr>
<td>Understand what matters most to patients about their disease or treatment</td>
<td>Inform performance goal</td>
<td>Illuminate patient benefit-risk tradeoffs</td>
<td>Inform studies of new or expanded use populations</td>
</tr>
<tr>
<td></td>
<td>Inform uncertainty (alpha error) and sample size</td>
<td>Identification of subgroup preferences</td>
<td></td>
</tr>
</tbody>
</table>
Device Benefit-Risk Guidances
Recommended Qualities of Patient Preference Studies

Well-designed and conducted patient preference studies can provide valid scientific evidence regarding patients’ risk tolerance and perspective on benefit. This may inform FDA’s evaluation of a device’s benefit-risk profile during the PMA, HDE application, and de novo request review processes.

A. All about Patients
   • Patient Centeredness
   • Sample Representativeness
   • Capturing Heterogeneous Patient Preferences
   • Comprehension by Study Participants

B. Good Study Design
   • Established Good Research Practices
   • Effective Benefit-Risk Communication
   • Minimal Cognitive Bias
   • Relevance

C. Good Study Conduct and Analysis
   • Study Conduct
   • Logical Soundness
   • Robustness of Analysis of Results
PPI Reviews: Lessons Learned

- Be clear about the research question (PPI) and the applicability to the clinical trial
- Consult regulatory bodies early and often
- Develop a thoughtful plan for recruiting patients to align with indications for use
  - Ensuring heterogeneity and generalizability of the study sample
  - Including under-represented populations
- Involve patients in the development process
- Assure patient comprehension of attributes and levels used in the survey
- Ensure PPI attributes align with outcomes of interest in clinical studies
- Pre-specify analysis plan and potential subgroup analyses
- Determine all the ways in which the PPI study will be used (e.g., BDA)
- Provide sufficient information for regulatory bodies to assess the quality of the study and the evidence
Solid qualitative work grounds a patient-centric quantitative preference study

- Informs attribute selection
- Ensures patient comprehension of attributes and levels

Consult FDA early when designing PPI studies for a regulatory context

- Ask for the Patient Science & Engagement Team Members to be consulted
- Be clear about the regulatory question you want your study to answer

Develop a plan for recruiting patients

- Ensure heterogeneity & generalizability of sample
- Include under-represented populations
- Determine criteria for disease validation

Take Home Points

Ensure PPI benefit and risk attributes align with outcomes of interest in clinical studies to inform benefit-risk decision
Journey from Concept to Care

Supporting a Paradigm Shift

- CDRH has made significant progress in advancing the science of patient input, integrating that science into medical device evaluation, and making interactions with patients part of our daily business culture.

Understand the Value Proposition for Patients

- Understanding the patients’ perspectives and proactively incorporating them into medical device evaluation will help promote and protect public health.

Explore Novel Applications of Patient Input

- Emerging methods and technologies afford more opportunities to integrate patient perspectives seamlessly into the evaluation of medical technologies.

Journey Together in Pre-competitive Space

- Working collaboratively across the healthcare ecosystem will help broaden the inclusion of the patients and their diverse voices in all aspects of health and wellness.
Resources

FDA CDRH Websites:


Contacts for Medical Devices

• For Patient-Reported Outcome Questions: CDRH-PRO@fda.hhs.gov

• For Patient Preference Information Questions: CDRH-PPI@fda.hhs.gov

• For Patient Engagement Questions: CDRH_PatientEngagement@fda.hhs.gov

• For Collaborative Community Questions: CDRHCollabCommunities@fda.hhs.gov
Today’s Panel Presentation

Objective: Learn how Patient Preferences can inform study design

Barry Liden, JD (Facilitator)
MDIC Science of Patient Input

Intro/Overview 5 min

Shelby Reed, PhD
Duke University

Case Study: Heart Failure Patient Preferences 10 min

Barry Liden

Overview of MDIC Framework 20 min

Michelle Tarver, MD, PhD
FDA-CDRH

The Regulator’s Perspective 10 min

All & Audience

Discussion; Q&A 15 min

MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM