Developing a Framework for Patient Input in Medical Device Clinical Trials
Agenda

• MDIC Science of Patient Input Overview
  • Barry Liden, Edwards Lifesciences – SPI Steering Committee Chair

• Patient Preference in Heart Failure
  • Dean Bruhn-Ding, CVRx – Heart Failure Working Group Chair

• Patient-generated Health Data as Real-world Data
  • Bray Patrick-Lake, Evidation Health

• Patient Science & Engagement In Medical Devices
  • Michelle Tarver, CDRH, FDA
MDIC Science of Patient Input
Overview
Barry Liden, Vice President Patient Engagement
Edwards Lifesciences
SPI Steering Committee Chair
MDIC Science of Patient Input

Our Vision:

To advance the science of patient input and the application of patient preference information across the medical device development lifecycle.
MDIC SPI = Increased Access for Patients

MDIC coordinates the development of methods, tools, and resources used in managing the total product life cycle of a medical device to improve patient access to cutting-edge medical technology.
Patient input into product development

Discovery/Development
- Discovery + Ideation
- Invention + Prototyping
- Patient-Informed Needs

Regulatory Evaluation
- Pre-Clinical
- Clinical
- Patient Preference Benefit-Risk Information
- Patient-Informed Clinical Trial Design, Patient Reported Outcomes
- Regulatory Decision

Post-Market Adoption
- Product Launch
- Post-Market Monitoring
- Patient-Centered Outcomes
- Communicating Benefit-Risk Information to Patients

Graphic courtesy of CDRH, the MDIC Patient Preference Framework, and MDIC
Advancing patient preference assessments

Using patient preferences in regulatory benefit-risk assessments - 2015
https://mdic.org/project/patient-centered-benefit-risk-pcbr/

CDRH Patient Preference Guidance - 2016

Using patient preferences in the design of clinical trials – 2017-19
https://mdic.org/resource/patient-centered-outcomes-research-project-overview/
Developing a Framework for Patient Input in Medical Device Clinical Trials – 2018-2020

Deliverables to date:
- Survey Report: Patients and Industry perspective on patient participation in clinical trials
- Literature review / Landscape analysis

Coming soon:
- Draft reports on Patient Participation in Clinical Trials and Lessons Learned from the PCOR workshop (Fall 2019)
- Patient Engagement Forum (November 13, 2019)
- Final Framework – Fall 2020

Completed reports available at:
https://mdic.org/program/science-of-patient-input/
Patient Preference in Heart Failure

Dean Bruhn-Ding, Vice President Regulatory Affairs & Quality Assurance
CVRx
Heart Failure Working Group Chair
Heart Failure Patient Preference Project

- The objective of this project is to advance the science of regulatory patient preference assessment by giving medical device industry sponsors, regulatory agencies, and preference assessment experts another example of a disease-specific patient preference study.

- This study will build on the MDIC Patient-Centered Clinical Trial Design project in Parkinson’s Disease by building a coalition of medical device sponsors, heart failure patients, regulators, and patient preference assessment experts to conduct a preference study across heart failure patients.
Who’s involved in this project?

• Patients
• MDIC staff
• FDA staff (experts in patient preference and heart failure)
• Six medical device companies (Abbott, Abiomed, Boston Scientific, CVRx, Edwards Lifesciences, and Medtronic)
• Duke Clinical Research Institute (DCRI)
  • Researchers from Duke will be responsible for conducting the patient preference study
Key Study Characteristics

• Subjects (Patients) with heart failure stage C – NYHA II-III (ideally)
  • Self-reported & clinically confirmed (100 patients)
  • Should be on guideline directed medical therapy
• Sample size approximately 350 patients
• Discrete choice experiment
  • To assess patient risk preference for a given outcome
Integrating Patient Preference Across the Lifecycle

- Device design – patient preferences into device features
- Trial design – incorporating patient preference metrics
  - Clinically relevant and measurable
  - Developing p-values based on patient preference
- Regulatory market review process
- Marketing – publications & promotional material
- Reimbursement – pay for what is important to patients receiving the treatment!
Recent Key Accomplishments / Decisions

• HF Patient Preference Testing (PPT) Study Attributes and Risks identified March - April 2019

• Draft Survey drafted May 2019
  – Reviewed by Industry and FDA Team May & June 2019
  – Reviewed with Patient Scientists (PS) July 2019

• Contract Signed by MDIC and DCRI 6-12-2019

• DCRI Revised Survey July 2019

• WG minus Patient Scientist reviewed Revised Survey July & August 2019
Planned Activity - Next 2 Months

• Finalize PPT Survey August 2019
• 10-15 Patient Pre-Test in September 2019
• Revise PPT Survey as needed October 2019
  – Obtain final approval from full WG
  – Obtain IRB & Duke Dept. Cardiology Approval
• Implement Web-based Survey to Full Study Participants - October 2019
Patient-generated Health Data as Real-world Data
Helping Generate Real-World Evidence that Matters to Patients

Bray Patrick-Lake, MFS
Director of Strategic Partnerships
Evidation Health

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www.evidation.com
New ways to measure health in everyday life
Patients and their outcomes have historically been characterized using limited, visible-to-the-system data sets. Episodic snapshots rather than continual measure and context of everyday life, true burden of disease, and outcomes with treatments.

Patient-generated health data (PGHD) has the potential to help better understand health and disease and experiences with medical products.
Real-world data (RWD) are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources\(^1\).

Real-world evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD (i.e., RCT, PCT, OS)\(^1\).

- Electronic health records
- Claims data
- Product and disease registries
- Patient-generated data including in home-use settings
- Data gathered from other sources that can inform on health status, such as mobile devices \(^1\)

Patient-generated Health Data can be categorized into 4 groups\(^2\):

**Patient/consumer-reported data**
Responses to questionnaires, symptom and behavior tracking

**Task-based measures**
Objective measurement of a person’s mental and/or physical ability to perform a test consisting of a defined task or set of tasks (6MWT, screen tap)

**Active sensor data**
Measurement of a person’s daily activities, mental state, or physiological status that requires an activation step (e.g., stepping on a scale, glucose self-measurement)

**Passive sensor data**
Measurement of a person’s daily activities, mental state, or physiological status that does not interrupt the person’s normal activities (wearables – HR, steps, sleep)

\(^1\) [https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence](https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence)

Easiest Use of RWD: The Low Hanging “Fruit”

Screening for Clinical Trial Recruitment
- Dr. Robert Temple, Deputy Center Director for Clinical Science, CDER, FDA. Duke Margolis RWE workshop July 2019

1. The presence of the disease or condition being studied
2. Critical patient characteristics
   - Demographics
   - History and potential enrichment characteristics
     - Duration of disease
     - Disease severity
     - History of compliance with treatment
     - Past outcome events such as AMI, stroke, CV surgery
     - Relevant laboratory measures
     - Concomitant illness and concomitant treatments

PATIENT PERSPECTIVE:
Ask what is most important to me and measure it!
What’s my most burdensome symptom? How do I feel and function? How and when am I using a medical device?
What are the benefits, risks, and likely outcomes when someone like me uses the device?
Evidation’s **Behaviorgram** is created with ubiquitous PGHD that is currently inaccessible to the healthcare system.

**Invisible → Visible, Subjective → Objective, Exploratory Measures → Endpoints in Clinical Trials, Clinically Meaningful → Meaningful to Individuals**

### Objective Everyday Data
Collected via sensors and apps
- Heart rate
- Exercise calories
- Steps walked
- Sleep duration
- Calories eaten
- Weight
- Fat percentage

### Phenotypic Labels
Collected via questionnaires
Some values can be verified via traditional data sources (e.g., claims, labs, EHR)
- Age
- Gender
- Ethnicity / race
- Education
- Household
- Zip code
- Employment status
- Employer
- Insurance carrier
- Height / weight
- Medical diagnoses
- Prescription drugs
- Smoking
- Patient-reported outcomes
- Fast food consumption
- Supplements
- Quality of life
- Alcohol use
- Major medical events
- Sleep quality

### Example Digital Assays
Direct assessment
- Functional mobility
- Sleep reliability
- Weight range

Behavioral inference
- Routine/consistency
- Digital utilization
- Responsiveness

Clinical inference
- Exacerbation events
- Treatment utilization
- Disease progression

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**R&D > Trial Design > Product Evidence > Personalized Services > Commercial**
Patient-generated health data has the potential to
• Unlock new insights into disease and how patients feel and function
• Impact clinical trial design and recruitment
• Enhance product knowledge
• Fuel more patient-centered medical device development
PATIENT SCIENCE & ENGAGEMENT IN MEDICAL DEVICES

Michelle Tarver, MD, PhD
Director, Patient Science & Engagement Program
Center for Devices and Radiological Health
Food and Drug Administration
Patients & Medical Device Evaluation

- Patient Engagement
- Clinical Outcome Assessments
- Patient Preference Information
- Patient-Generated Health Data
# CDRH Patient Science & Engagement Program

**Inspired by Patients, Driven by Science**

Understand the patients’ perspectives and proactively incorporate them into all our decisions and regulatory activities where appropriate.

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<th>Consistent Regulatory Review</th>
<th>Patient Engagement</th>
<th>Optimized Research Roadmap</th>
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@MDICAnnualForum
Patient-Focused Regulatory Activities

• Engagement Mechanisms
  • PEAC
  • Patient & Caregiver Connection

• Guidance Documents
  • FY’19 commitment guidance on patient engagement in the design & conduct of medical device clinical investigations
  • MDUFA IV commitment on flexible approaches to developing PRO measures

• Research
  • MDIC Heart Failure PPI study
  • PRO measures modification studies
  • Social media study
Resources

Guidance:
Pre-Submissions: https://go.usa.gov/xmVsh
Patient Preference Information: https://go.usa.gov/xmVHG

FDA Websites:

Outside Sources:
Medical Device Innovation Consortium (MDIC) framework and catalog of methods:
https://mdic.org/project/patient-centered-benefit-risk-pcbr/

Contacts

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