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# Examining the Role of Patient Preferences to Inform Regulatory Decisions

Third Plenary Session

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## THIRD PLENARY:
## Examining the Role of Patient Preferences to Inform Regulatory Decisions

**Jeff Shuren, MD, JD**
U.S. Food and Drug Administration
Silver Spring, MD, USA

**Matt Reaney, FRSPH, MSc**
Sanofi
Guildford, Surrey, UK

**Bennett Levitan, MD, PhD**
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**Jeff Shuren, MD, JD**
U.S. Food and Drug Administration (FDA)
Silver Spring, MD, USA

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FDA U.S. FOOD & DRUG ADMINISTRATION

# The Role of Patient Preferences to Inform Regulatory Decisions

**Jeff Shuren, MD, JD**
Director
Center for the Devices and Radiological Health
U.S. Food and Drug Administration

www.fda.gov

## 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**

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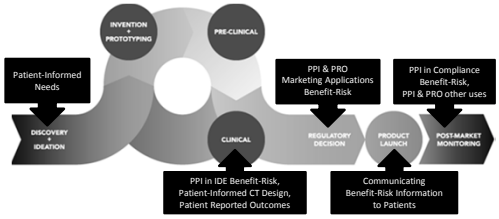
## Medical Device Total Product Life Cycle

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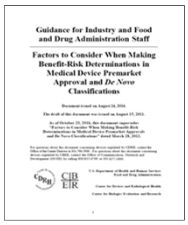
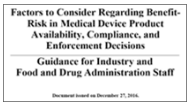
## Device Benefit-Risk Frameworks


Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions

Guidance for Investigational Device Exemption Sponsors, Sponsor-Investigators and Food and Drug Administration Staff


Guidance for Industry and Food and Drug Administration Staff

Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications


Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 27, 2016.

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## Medical Device Benefit-Risk Guidance

***Factors to Consider for Benefit – Risk Determinations Medical Device Premarket Approval and De Novo Classifications***

Patient perspective on risk and perspective on benefit:

*"if risks are identifiable and definable, **risk tolerance will vary among patients**, and this will affect individual patient decisions as to whether the risks are acceptable in exchange for a probable benefit. … FDA recognizes that patient perspectives on benefits and risks **may reveal reasonable patients who are willing to tolerate a very high level of risk to achieve a probable benefit**, especially if that benefit results in an improvement in quality of life."*

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## Patient Perspectives

- Information relating to patients' experiences with a disease or condition and its management
- May be useful for:
  - better understanding the disease or condition and its impact on patients
  - identifying outcomes most important to patients
  - understanding benefit-risk tradeoffs for treatment

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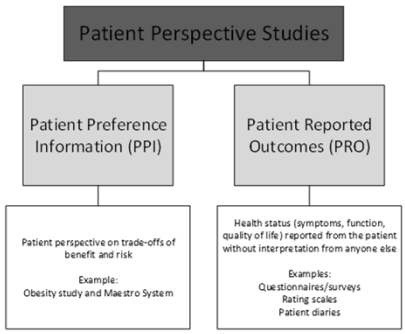
## Patient Perspective Studies

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## What is Patient Preference Information?

- Patient Preference Information (PPI) is defined as:
  ***qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions***
- Relevant preferences of care-partners (e.g., parents) and health care professionals may also be considered

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## Patient Preference Information (PPI)

- Qualitative PPI may be used to:
  - identify which outcomes, endpoints or other attributes are valued most by patients
  - understand which factors affect patients' perspectives on risk and benefit
- Quantitative PPI may be used to:
  - provide estimates of how much different outcomes, endpoints or other attributes are valued by patients
  - understand tradeoffs that patients state or demonstrate they are willing to make

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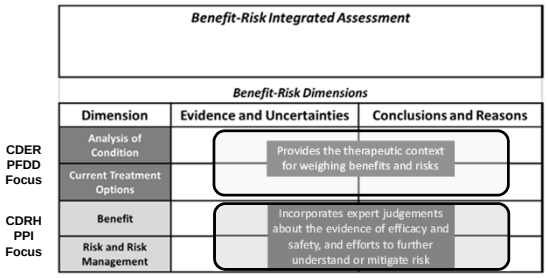
## Complementary Efforts

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## PPI in Medical Product Development

| Development | Clinical Trial Design | Pre-Market Benefit-Risk Assessment | Post-Market |
|---|---|---|---|
| 1. Identify unmet medical need<br>2. Understand what matters most to patients about their disease or treatment | 1. Inform endpoint selection<br>2. Inform performance goal<br>3. Inform effect size | 1. Analysis of condition<br>2. Current treatment options<br>3. Patient perspective on benefit-risk tradeoffs<br>4. Population subgroup considerations | 1. Inform interpretation of new data affecting benefit-risk assessment<br>2. Inform studies of new/expanded use populations<br>3. Communicate benefit-risk information to patients |

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## Medical Device Patient Preference Initiative


www.fda.gov

## Patient Preference Guidance

***Patient Preference Information – Voluntary Submission, Review in PMAs, HDE Applications, and De Novo Requests and Inclusion in Decision Summaries and Device Labeling***

Objectives

1. To encourage submission of PPI, if available, by sponsors or other stakeholders to FDA and to aid in FDA decision-making
2. To outline recommended qualities of patient preference studies, which may result in valid scientific evidence
3. To provide recommendations for collecting and submitting PPI to FDA
4. To discuss FDA's inclusion of PPI in its decision summaries and provide recommendations for the inclusion of such information in device labeling

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## PPI as Valid Scientific Evidence

- FDA may consider submitted PPI along with other evidence from clinical and nonclinical testing when making benefit-risk determinations
- This guidance does not change any review standards for safety or effectiveness
- It provides recommendations relating to the voluntary collection of PPI that may be submitted for consideration as valid scientific evidence as part of FDA's benefit-risk assessment

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## PPI Submission to FDA is Voluntary

- PPI may not be relevant or appropriate for all device types
- May be useful for sponsors to collect and submit such information where usage decisions by patients and health care professionals are preference-sensitive
- Devices that could benefit from PPI include those with the following characteristics:
  - A direct patient interface
  - Intended to yield significant health and appearance benefits
  - Intended to directly affect health-related quality of life
  - Certain life-saving but high-risk devices
  - Developed to fill an unmet medical need or treat a rare disease or condition
  - Offer alternative benefits to those already marketed
  - A novel technology

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## 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

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## Regulatory Impact

FDA News Release

**FDA approves first-of-kind device to treat obesity**

For Immediate Release

January 14, 2015

Release

The U.S. Food and Drug Administration today approved the Maestro Rechargeable System for certain obese adults, the first weight loss treatment device that targets the nerve pathway between the brain and the stomach that controls feelings of hunger and fullness.

The Maestro Rechargeable System, the first FDA-approved obesity device since 2007, is approved to treat patients aged 18 and older who have not been able to lose weight with a weight loss program, and who have a body mass index of 35 to 45 with at least one other obesity-related condition, such as type 2 diabetes.

BMI, which measures body fat based on an individual's weight and height, is used to

NxSTAGE

Aug 28, 2017
Previous Release

NxStage Medical Announces FDA Clearance for Solo Home Hemodialysis Using NxStage® System One™

**First clearance of its kind gives trained NxStage patients freedom to dialyze without a care partner**

LAWRENCE, Mass., Aug. 28, 2017 /PRNewswire/ -- NxStage Medical, Inc. (**Nasdaq**: NXTM), a leading medical technology company focused on advancing renal care, today announced that the U.S. Food and Drug Administration (FDA) has cleared its System One for solo home hemodialysis, without a care partner, during waking hours.

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## Lessons Learned from PPI Reviews

- Consult FDA early in designing PPI studies for a regulatory context
- Ensure PPI benefit and risk attributes match to outcomes of interest in clinical studies
- Pre-test instrument to ensure patient comprehension of benefit, harm, and uncertainty
- Develop a plan for recruiting patients
  - Ensure there is heterogeneity and generalizability of the study sample
  - Take into account recruiting for underserved populations
- Pre-specify analysis plan and potential subgroups

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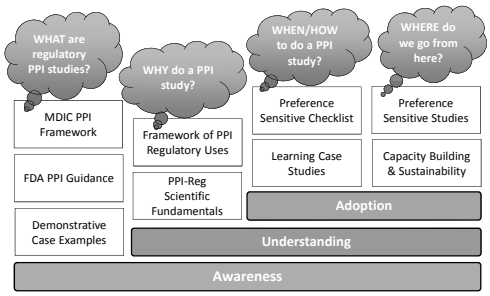
**Dec. 2017 CERSI-FDA Workshop:**
**Advancing Use of PPI as Scientific Evidence for Medical Product Evaluation**

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## Advancing the Science

- Understand which methods are fit-for-purpose for the following types of questions:
  - Regulatory benefit-risk tradeoffs
  - Endpoint identification and/or prioritization
  - Identifying outcomes to guide patient-reported outcomes development
  - Informing clinical trial size

- Develop and refine approaches for:
  - Cognitive bias minimization
  - Effective communication of benefit-risk information to patients
  - Qualitative research best practices
  - Evaluation of study and data quality

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## Advancing the Science (Continued)

- Need to build capacity
  - Develop and establish training programs
  - Research resources and tools
  - Establish the value proposition for various regulatory uses

- Should include:
  - Sharing findings publicly
  - Establishing good work and good data collection tools for others to use or build on
  - Contributing to establishing standards regarding study quality and validity

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## Final Considerations

- FDA is invested in including the patient perspective in regulatory decision making
- ISPOR and other professional organizations can help advance the science of patient input by addressing existing scientific questions about robust and reliable preference studies, through:
  - Building capacity for conducting and assessing PPI studies
  - Methodology research to overcome current barriers to conducting and incorporating PPI studies to inform regulatory decision-making
- We are all working to do more research to strengthen the approaches for greater quality, trust, cost efficiency, and respect for patients' views and time

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**Thank You**

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ISPOR www.ispor.org

## THIRD PLENARY: Examining the Role of Patient Preferences to Inform Regulatory Decisions

**Matt Reaney, FRSPH, MSc**
Sanofi
Guildford, Surrey, UK

## Examining the Role of Patient Preferences to Inform Regulatory Decisions

### My views on stated preference methods via a tour of my music collection

Matt Reaney, Global Head of Clinical Outcomes
May 23 2018

SANOFI

## Disclaimer

The views expressed in this presentation are my own and do not necessarily reflect those of Sanofi

SANOFI


*"You can't always get what you want; but if you try sometimes you might just find you get what you need"*

- Patient Preference Information (PPI) can be extremely relevant
  - **Identifying what is important, desirable or valuable to patients can be important for sponsors**
    - TPP
    - Trial design
  - **Particularly relevant where benefit-risk trade-off is not clear, or where a novel route/mode/frequency of administration is under consideration**
  - **Also very relevant in a choice-based healthcare system**

## My issues with stated preference methods to allow regulatory judgement about benefit-risk of a drug, device or biologic

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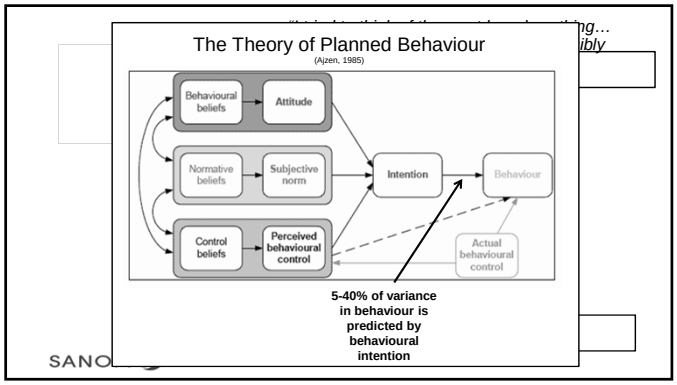
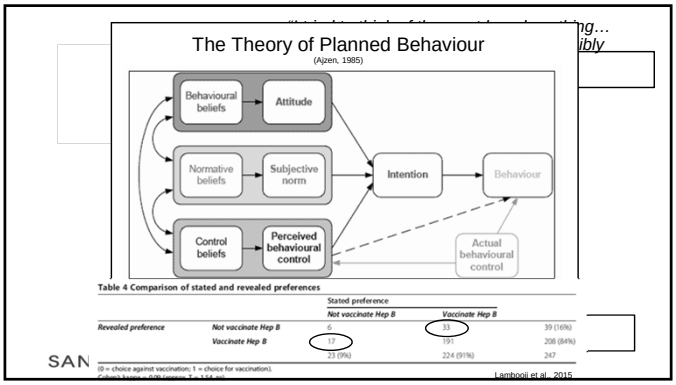
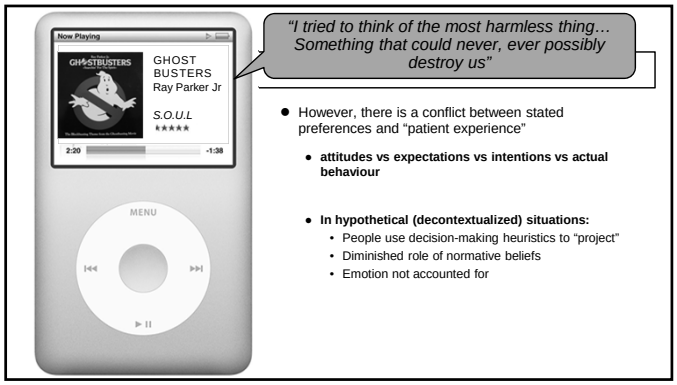
*"I tried to think of the most harmless thing… Something that could never, ever possibly destroy us"*

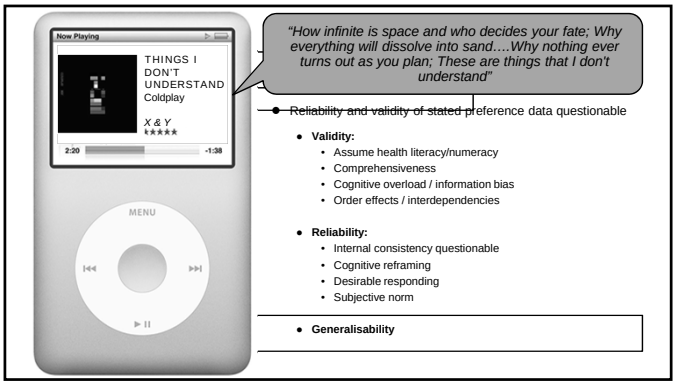


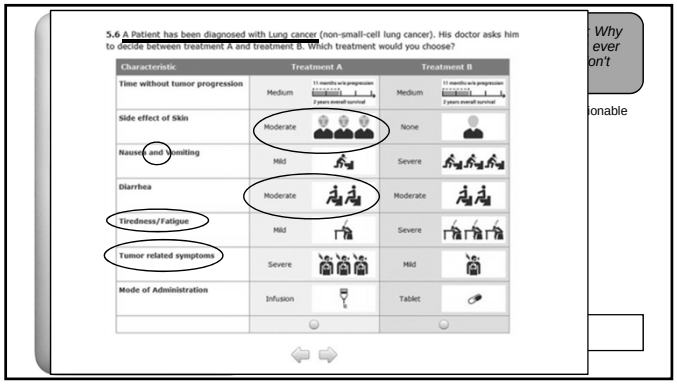

*"I tried to think of the most harmless thing… Something that could never, ever possibly destroy us"*

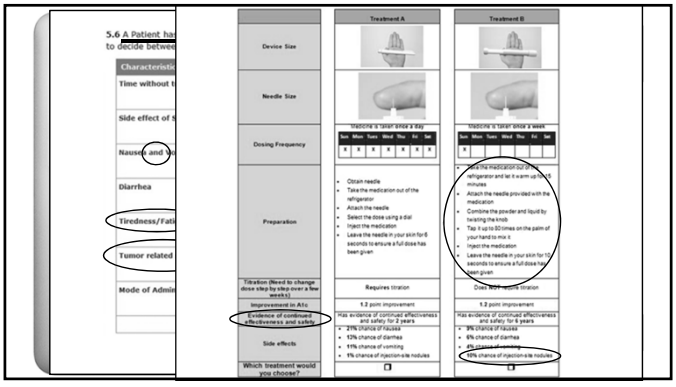
- However, there is a conflict between stated preferences and "patient experience"
  - **attitudes vs expectations vs intentions vs actual behaviour**
  - **In hypothetical (decontextualized) situations:**
    - People use decision-making heuristics to "project"
    - Diminished role of normative beliefs
    - Emotion not accounted for

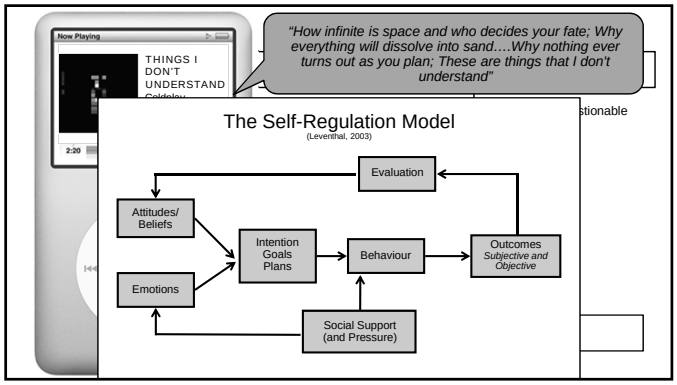


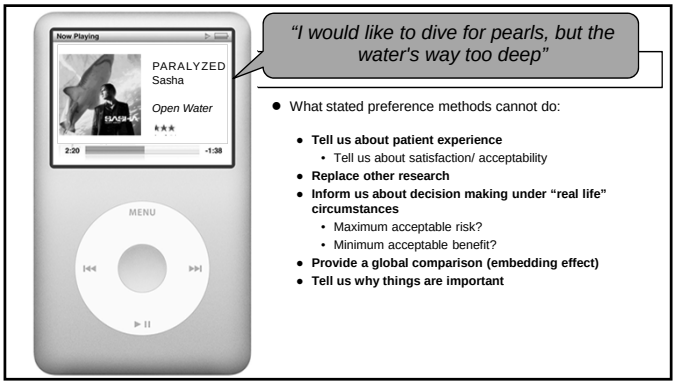

*"How infinite is space and who decides your fate; Why everything will dissolve into sand….Why nothing ever turns out as you plan; These are things that I don't understand"*

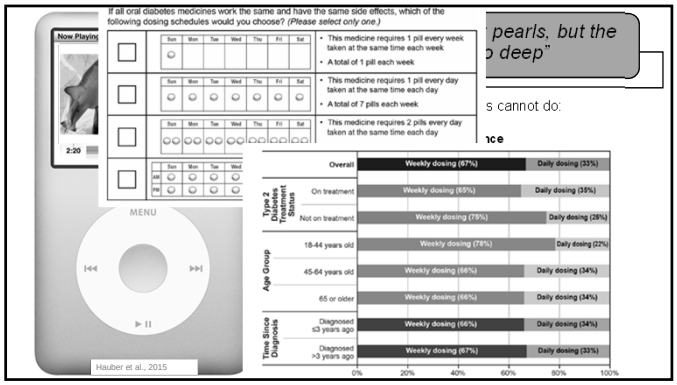
- ~~Reliability and validity of stated~~ preference data questionable
  - **Validity:**
    - Assume health literacy/numeracy
    - Comprehensiveness
    - Cognitive overload / information bias
    - Order effects / interdependencies
  - **Reliability:**
    - Internal consistency questionable
    - Cognitive reframing
    - Desirable responding
    - Subjective norm
  - **Generalisability**

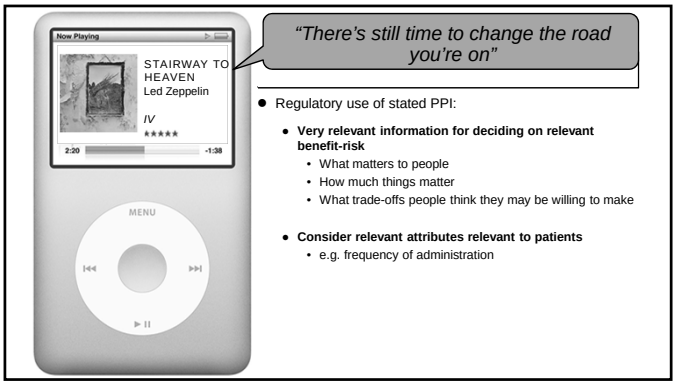


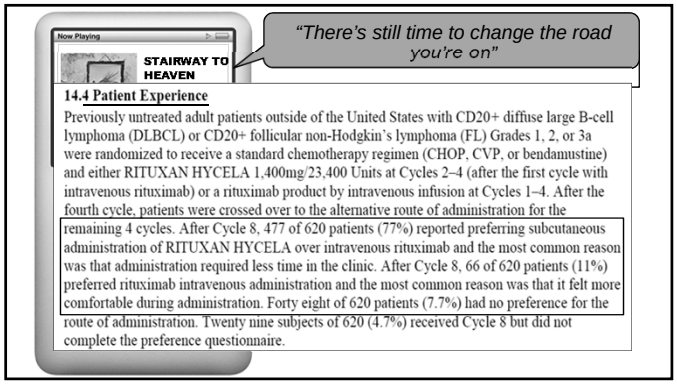



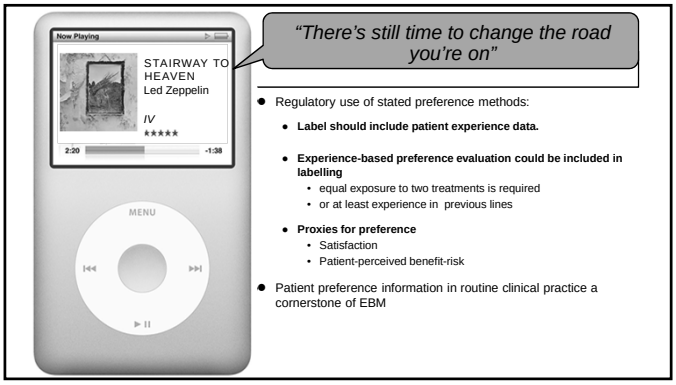

Now Playing
THINGS I DON'T UNDERSTAND
2:20
"How infinite is space and who decides your fate; Why everything will dissolve into sand….Why nothing ever turns out as you plan; These are things that I don't understand"
The Self-Regulation Model
(Leventhal, 2003)
Evaluation
Attitudes/ Beliefs
Intention Goals Plans
Behaviour
Outcomes Subjective and Objective
Emotions
Social Support (and Pressure)


Now Playing
PARALYZED
Sasha
Open Water
2:20
-1:38
MENU
"I would like to dive for pearls, but the water's way too deep"
What stated preference methods cannot do:
Tell us about patient experience
Tell us about satisfaction/ acceptability
Replace other research
Inform us about decision making under "real life" circumstances
Maximum acceptable risk?
Minimum acceptable benefit?
Provide a global comparison (embedding effect)
Tell us why things are important


If all oral diabetes medicines work the same and have the same side effects, which of the following dosing schedules would you choose? (Please select only one.)
This medicine requires 1 pill every week taken at the same time each week
A total of 1 pill each week
This medicine requires 1 pill every day taken at the same time each day
A total of 7 pills each week
This medicine requires 2 pills every day taken at the same time each day
Overall
Type 2 Diabetes Treatment Status
On treatment
Not on treatment
Age Group
18-44 years old
45-64 years old
65 or older
Time Since Diagnosis
Diagnosed ≤3 years ago
Diagnosed >3 years ago
Weekly dosing (67%)
Daily dosing (33%)
Weekly dosing (65%)
Daily dosing (35%)
Weekly dosing (75%)
Daily dosing (25%)
Weekly dosing (78%)
Daily dosing (22%)
Weekly dosing (66%)
Daily dosing (34%)
0%
20%
40%
60%
80%
100%
Hauber et al., 2015


Now Playing
STAIRWAY TO HEAVEN
Led Zeppelin
IV
2:20
-1:38
MENU
"There's still time to change the road you're on"
Regulatory use of stated PPI:
Very relevant information for deciding on relevant benefit-risk
What matters to people
How much things matter
What trade-offs people think they may be willing to make
Consider relevant attributes relevant to patients
e.g. frequency of administration


Now Playing
STAIRWAY TO HEAVEN
"There's still time to change the road you're on"
14.4 Patient Experience
Previously untreated adult patients outside of the United States with CD20+ diffuse large B-cell lymphoma (DLBCL) or CD20+ follicular non-Hodgkin's lymphoma (FL) Grades 1, 2, or 3a were randomized to receive a standard chemotherapy regimen (CHOP, CVP, or bendamustine) and either RITUXAN HYCELA 1,400mg/23,400 Units at Cycles 2–4 (after the first cycle with intravenous rituximab) or a rituximab product by intravenous infusion at Cycles 1–4. After the fourth cycle, patients were crossed over to the alternative route of administration for the remaining 4 cycles. After Cycle 8, 477 of 620 patients (77%) reported preferring subcutaneous administration of RITUXAN HYCELA over intravenous rituximab and the most common reason was that administration required less time in the clinic. After Cycle 8, 66 of 620 patients (11%) preferred rituximab intravenous administration and the most common reason was that it felt more comfortable during administration. Forty eight of 620 patients (7.7%) had no preference for the route of administration. Twenty nine subjects of 620 (4.7%) received Cycle 8 but did not complete the preference questionnaire.

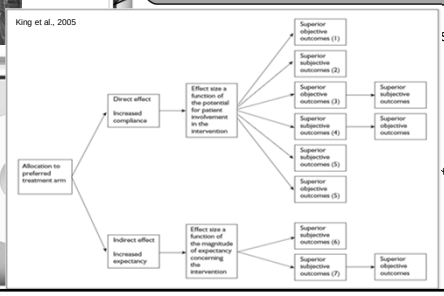

Now Playing
STAIRWAY TO HEAVEN
Led Zeppelin
IV
2:20
-1:38
MENU
"There's still time to change the road you're on"
Regulatory use of stated preference methods:
Label should include patient experience data.
Experience-based preference evaluation could be included in labelling
equal exposure to two treatments is required
or at least experience in previous lines
Proxies for preference
Satisfaction
Patient-perceived benefit-risk
Patient preference information in routine clinical practice a cornerstone of EBM


*"It keeps holding on; And it's holding strong; Even though I tried to break it; Heaven knows that I can't shake it"*

- If strong preferences are observed, this may undermine the credibility of the RCT if comparison is preference-sensitive
  - **Recruitment**
  - **Retention**
  - **Behaviour modification**
    - Trial outcomes = function of treatment +/-
      - Motivation
      - Adherence
      - Expectations


*"It keeps holding on; And it's holding strong; Even though I tried to break it; Heaven knows that I can't shake it"*

King et al., 2005




s may

+/-


*"You loosed the chains*
*….*
*But I still haven't found;*
*What I'm looking for"*

- Patient Preference Information (PPI) to be used:
  - **Sponsor:**
    - Identifying outcomes of interest
    - Determining commerciability
    - Trial design
  - **Decision-makers**
    - Regulators; to inform B-R decision-making
    - Payers; reimbursement for choice
    - Prescribers; individual-PPI
- **BUT**….. focus on:
  - **Patient experiences**
  - **Valuation of outcomes**
  - **Individualised trade-offs**

**Not stated preference methods**


*"I get by with a little help from my friends"*

Denise Bury
Stephen Joel Coons
Daniel Eek
Sonya Eremenco
Adam Gater
Heather Gelhorn
Chad Gwaltney
Lori McLeod
Charlie Nicholls
Jean Paty
Anna Ryden


*"Lean on me when you're not strong and I'll be your friend; I'll help you carry on"*

- Regulatory considerations of PROs: which would enhance stated PPI:
  - **Content validity**
  - **Context of Use**
  - **Test-retest (internal validity)**
  - **Interpretable (meaningful) responses**
  - **Interdependencies**
  - **Comprehensiveness**
  - **Cognitive reframing**
  - **Cognitive overload**
  - **Desirable responding**
  - **Subjective norm**
  - **Generalisability**
  - **Missing data**


*"Stop right now; Thank you very much"*

# Examining the Role of Patient Preferences to Inform Regulatory Decisions

## My views on stated preference methods via a tour of my music collection

Matt Reaney, Global Head of Clinical Outcomes
May 23 2018

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**THIRD PLENARY:**
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**Bennett Levitan, MD, PhD**
Janssen Research & Development
Titusville, NJ, USA

# Considerations for Patient Preference Studies to Inform Regulatory Decisions

**ISPOR 2018 Meeting**
**May 23, 2018**

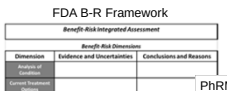
***Bennett Levitan, MD-PhD***

**Senior Director, Benefit-Risk Assessment**
**Department of Epidemiology**
**Janssen Research & Development, LLC**

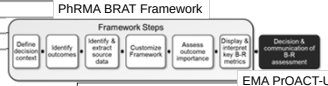
## Structured Benefit-Risk: B-R Frameworks

- **Set of principles, guidelines and tools for selecting, summarizing and communicating evidence for B-R decisions**
- **Preference can inform many elements common to all frameworks**

FDA B-R Framework




PhRMA BRAT Framework

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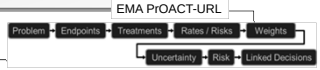
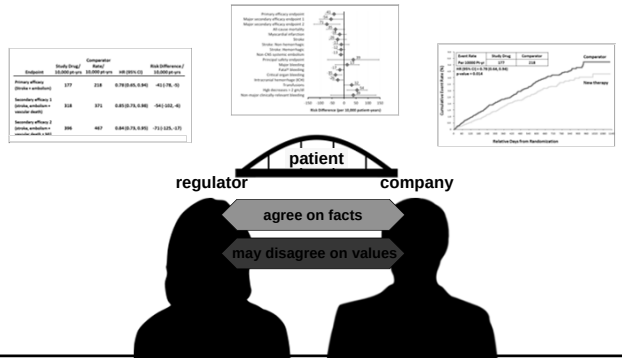


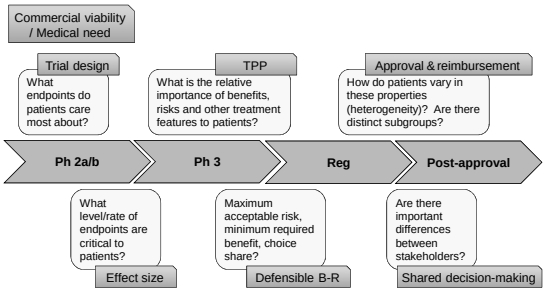



## Three Types of Patient Preference Information

| Type | What it Measures |
|---|---|
| **Attributes** | What Matters |
| **Relative Importance** | How much it matters |
| **Tradeoffs** | What tradeoffs patients are willing to make between benefits, harms, and other aspects |

Adapted from RTI-HS and MDIC

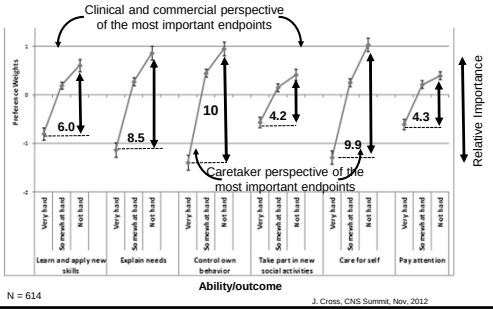
## Where Can Patient Preferences Inform the Development Lifecycle?




## Which endpoints do patients care about? Example: Fragile-X Syndrome

- **Rare genetic condition impacting development**
  - Learning and intellectual disabilities, cognitive impairment, behavioral challenges (ADHD, autism, social anxiety)
  - No cure – educational, therapeutic support
- **Preference study conducted to prepare for phase 3 study**
  - Intent was to identify which endpoints or components of existing instruments were most important to patients
  - Survey administered to family members, given patient cognitive limitations

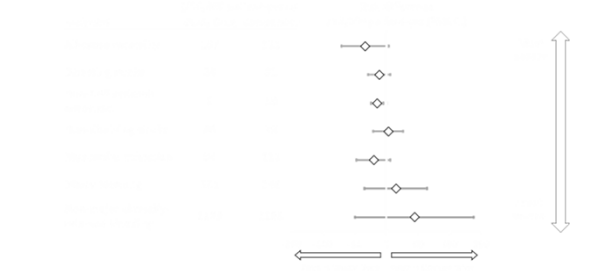
## Preference Survey Identified Large Gap Between Clinician and Patient Caretaker Beliefs on Endpoint Importance




N = 614

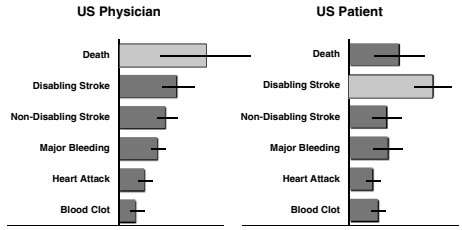
J. Cross, CNS Summit, Nov, 2012

## Preferences Supporting B-R in FDA Advisory Committee Atrial Fibrillation Example (mock data)



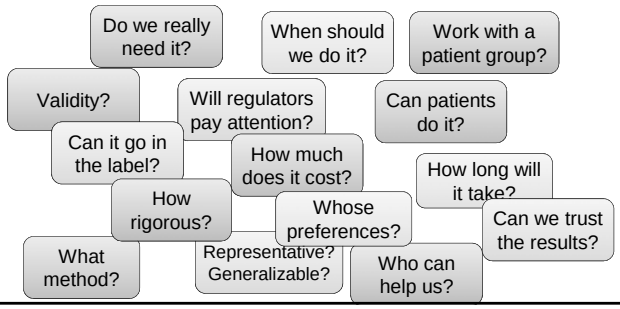
## Identifying Differences Between Key Stakeholders

Preferences for Anticoagulants in Atrial Fibrillation




Levitan, Yuan, González, et al., ISPOR 18th Ann Int Mtg, 2013

## What Sponsors Worry About When Considering A Patient Preference Study




## Patient Experience Section included in Rituxan Hycela Label (Approved 2017)

**RITUXAN HYCELA™ (rituximab and hyaluronidase human) injection, for subcutaneous use**
**Initial U.S. Approval: 2017**

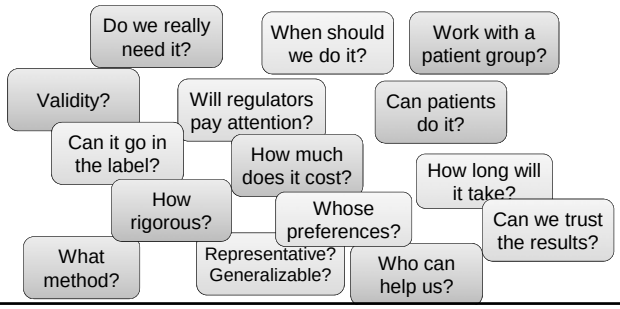
**14 CLINICAL STUDIES**
14.1 Follicular Lymphoma
14.2 Diffuse Large B-Cell Lymphoma (DLBCL)
14.3 Chronic Lymphocytic Leukemia (CLL)
14.4 Patient Experience

**14.4 Patient Experience**

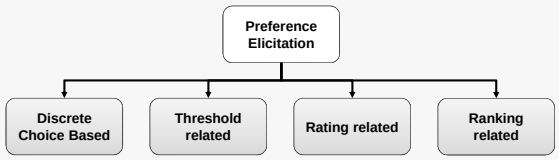
Previously untreated adult patients outside of the United States with CD20+ diffuse large B-cell lymphoma (DLBCL) or CD20+ follicular non-Hodgkin's lymphoma (FL) Grades 1, 2, or 3a were randomized to receive a standard chemotherapy regimen (CHOP, CVP, or bendamustine) and either RITUXAN HYCELA 1,400mg/23,400 Units at Cycles 2–4 (after the first cycle with intravenous rituximab) or a rituximab product by intravenous infusion at Cycles 1–4. After the fourth cycle, patients were crossed over to the alternative route of administration for the remaining 4 cycles. After Cycle 8, 477 of 620 patients (77%) reported preferring subcutaneous administration of RITUXAN HYCELA over intravenous rituximab and the most common reason was that administration required less time in the clinic. After Cycle 8, 66 of 620 patients (11%) preferred rituximab intravenous administration and the most common reason was that it felt more comfortable during administration. Forty eight of 620 patients (7.7%) had no preference for the route of administration. Twenty nine subjects of 620 (4.7%) received Cycle 8 but did not complete the preference questionnaire.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761064s000lbl.pdf

## What Sponsors Worry About When Considering A Patient Preference Study




## Several Classes of Preference Elicitation Methods




**Variety of similar techniques within each class**

Soekhai V, et. al.
ISPOR 20th Annual European Congress, Nov, 2017
IMI PREFER, WP4

## Growth of Regulatory Expectations, Guidance and Initiatives in Patient Engagement, B-R, and Patient Preferences

| Regulatory/Govt | Trade/Acad Orgs | Pub Private/Prof | Patient Groups |
|---|---|---|---|
| CDRH | PhRMA | imi | FasterCures |
| CBER | BIO Biotechnology Industry Organization | Clinical Trials Transformation Initiative | Parent Project Muscular Dystrophy |
| PDUFA VI MDUFA IV | AdvaMed | MDIC | National Health Council |
| 21st Century Cures | efpia | Patient Focused Medicines Development | JDRF |
| ICH | ISPOR | | The Michael J. Fox Foundation for Parkinson's Research |
| pcori | IAHPR International Academy of Health Preference Research | | |

Incomplete list

## Approaches to Address These Concerns – selected examples

**Survey Development**

- Use good research practices guidelines
- Focus on the research question (keep it simple)
- Qualitative interviews / studies before (bottom-up approach)
- FDA's open approach – early discussions and protocol review
- Consortia approach
- Fund larger, more representative samples

## Focus the Preference Survey on the Research Question

**Factors influencing whether patient preference information may be valuable for regulatory review**

| | |
|---|---|
| Patients as stakeholders | • Patients' benefit-risk preferences different than providers or regulators<br>• Patient subgroups with different preferences would make different decisions<br>• Importance of personal familiarity with the disease (e.g. very subjective endpoints, lifestyle indication, rare disease) |
| Benefit-risk trade-offs (preference sensitive) | • Benefit-risk balance is not obvious (e.g. clear benefit with rare serious risks)<br>• Time separation of benefits and harms<br>• Considerable uncertainty about benefits and harms |
| Regulatory novelty | • Lack of regulatory precedent for population or indication<br>• New technologies in existing area or existing technology in a new area |

Medical Device Innovation Consortium Patient-centered Benefit-risk Framework, http://mdic.org/wp-content/uploads/2015/05/MDIC_PCBR_Framework_Web.pdf

## Two approaches to developing patient preference studies

- Product-evaluation (top-down) approach
  - Disease and preference experts define features and priorities
  - Often applies to existing products / services or those in development
  - Survey pretest similar to cognitive debriefing
  - Example: CDRH weight-loss preference study *(Ho et al., 2015)*
  - Typically faster and less expensive

Can be used for well-understood disease context and endpoints

- Issues-identification (bottom-up) approach
  - Patients define relevant features, priorities and need in qualitative interviews
  - Not necessarily specific to the features of an existing product
  - Survey development similar to concept elicitation
  - Example: PPMD Duchenne Muscular Dystrophy Studies *(Hollin et al., 2015; Peay et al., 2014)*
  - Typically takes more time and funds

Needed to understand relevant attributes and meaningful changes

## Approaches to Address These Concerns – selected examples

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**Survey Testing**

- Pretesting
- Comprehension tests
- Internal validity tests
- Pilot survey

## Potential Internal Validity Tests

- Repeat questions
- Elapsed time
- Dominated pair (mostly DCE)
- Straight-lining or patterning (e.g. all column A)
- Domination (always deciding based on a single attribute)
- Monotonicity tests
- Transitivity tests
- Scope tests (check for recoding of levels)
- Face validity
- Internal consistency (variance) of a subject's utilities

- Tradeoff between sample size, cognitive burden and tests
- None are definitive, but can be very informative collectively

## Approaches to Address These Concerns – selected examples

**Survey Development**

- Use good research practices guidelines
- Focus on the research question (keep it simple)
- Qualitative interviews / studies before (bottom-up approach)
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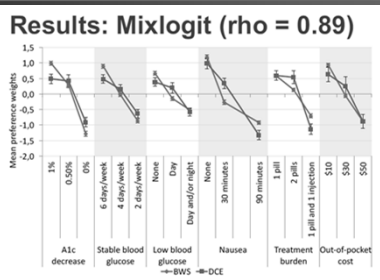
**Survey Testing**

- Pretesting
- Comprehension tests
- Internal validity tests
- Pilot survey

**Repetition**

- Repeat survey in a new sample
- Used different sample sources
- Conduct survey with more than one method

## Multiple Methods
## BWS vs. DCE, Type 2 diabetes treatments




BWS = best-worst scaling
DCE = discrete choice experiment

Janssen, Segal and Bridges. The Patient. vol 9, issue 5, 2016

## Sample Source – Can be very important to use more than one – ex: panels vs. RCTs

**On-line Panel**

**Advantages**
- **Many options readily available in many countries**
- **Generally inexpensive**
- Can perform probabilistic sampling to match basic criteria

**Concerns**
- **Self-report**
- Can be challenging to meet some inclusion/exclusion criteria
- Limited associated clinical data
- **Selection bias – those who join on-line panels**

**Randomized Clinical Trial**

**Advantages**
- **Trusted diagnoses and history**
- **Associated clinical data**
- Longitudinal sampling
- Health authority focus on work
- Revealed choice by dropouts

**Concerns**
- Many regulatory and legal requirements
- Huge management overhead
- ePRO vendor limitations
- Huge increase in cost
- **Differs from real-world patients**
- **Selection bias – those who choose to enter RCTs**

## Approaches to Address These Concerns – selected examples

**Survey Development**
- Use good research practices guidelines
- Focus on the research question (keep it simple)
- Qualitative interviews / studies before (bottom-up approach)
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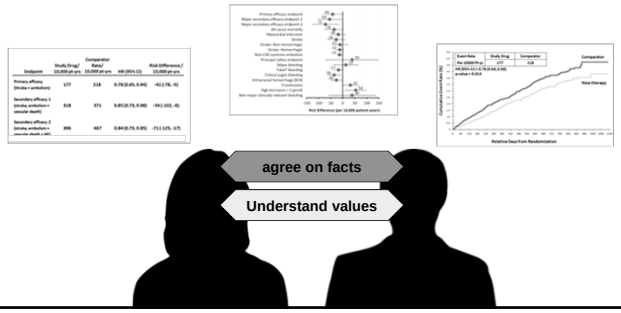
**Survey Testing**
- Pretesting
- Comprehension tests
- Internal validity tests
- Pilot survey

**Repetition**
- Repeat survey in a new sample
- Used different sample sources
- Conduct survey with more than one method

**Post-Survey**
- Terminal questions (easy to understand, answers consistent with my preferences, relevance of vignette and attributes, etc.)
- Compare to other patient experience data
- Subject interviews ("why")
- Sanity tests ("Do the results make sense")

## A Goal for Preference Studies

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## THIRD PLENARY:
## Examining the Role of Patient Preferences to Inform Regulatory Decisions

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