Industry Perspective on Patient Preference Information

FDA/CERSI PPI Workshop

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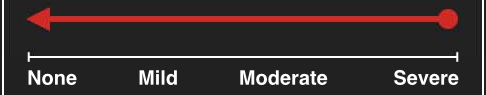
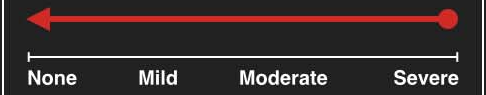
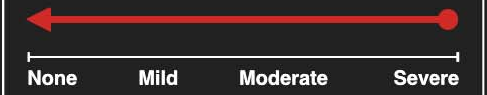
Janssen Research & Development, LLC

Outcome	Drug A	Drug B
Relief of pain		
Ability to perform work/school and social activities	No limitations	Cannot work, difficulty with chores and shopping
Annual chance of a heart attack	1 in 10,000	No chance
Which medicine would you choose if these were the only medicines available?	☐	☐

Outcome	Drug C	Drug B
Relief of pain		
Ability to perform work/school and social activities	No limitations	Cannot work, difficulty with chores and shopping
Annual chance of a heart attack	1 in 1,000	No chance
Which medicine would you choose if these were the only medicines available?	☐	☐

Outcome	Drug D	Drug B
Relief of pain		
Ability to perform work/school and social activities	No limitations	Cannot work, difficulty with chores and shopping
Annual chance of a heart attack	1 in 100	No chance
Which medicine would you choose if these were the only medicines available?	☐	☐

Endpoint	Study Drug/ 10,000 pt-yrs	Comparator Rate/ 10,000 pt-yrs	HR (95% CI)	Risk Difference / 10,000 pt-yrs
Primary efficacy (Stroke + embolism)	177	218	0.78 (0.65, 0.94)	-41 (-78, -5)
Secondary efficacy 1 (stroke, embolism + vascular death)	318	371	0.85 (0.73, 0.98)	-54 (-102, -6)
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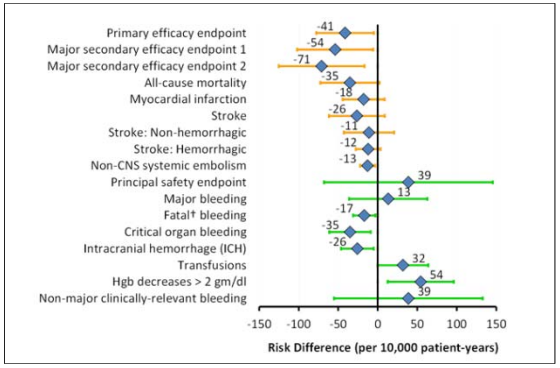
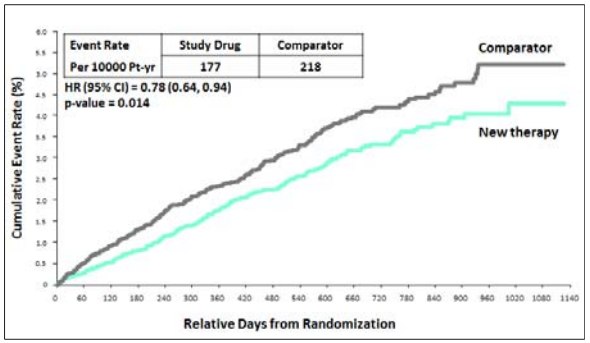
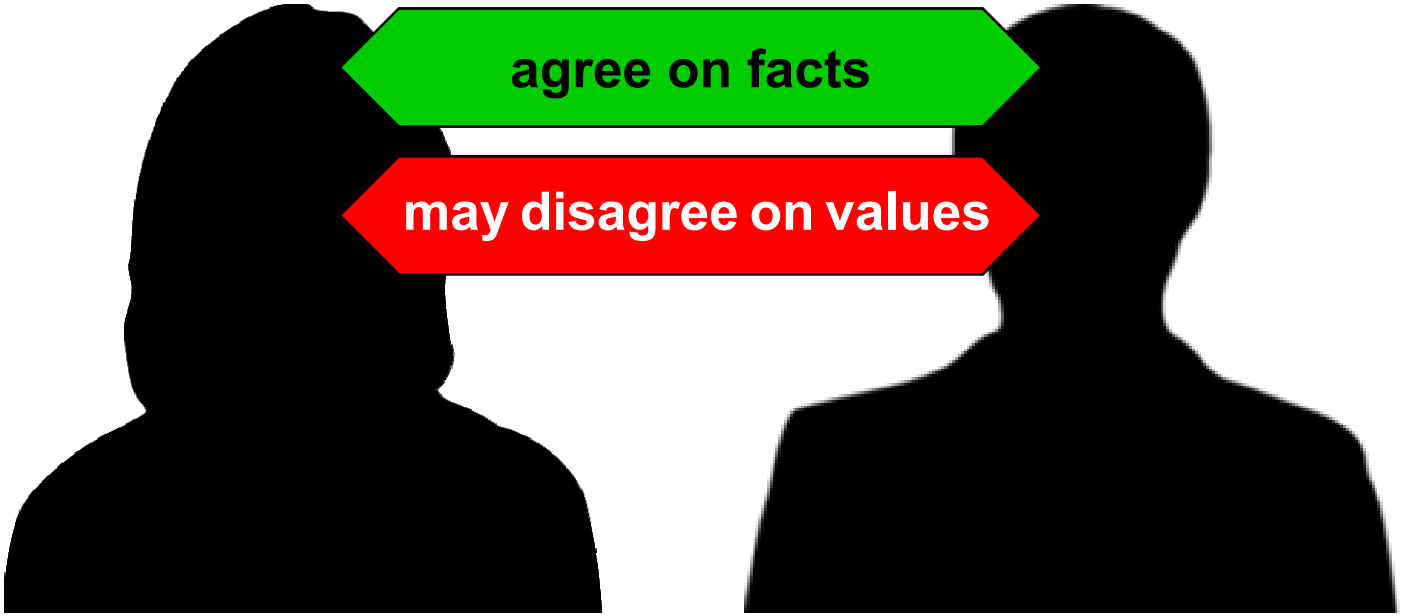




regulator **patient**



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**

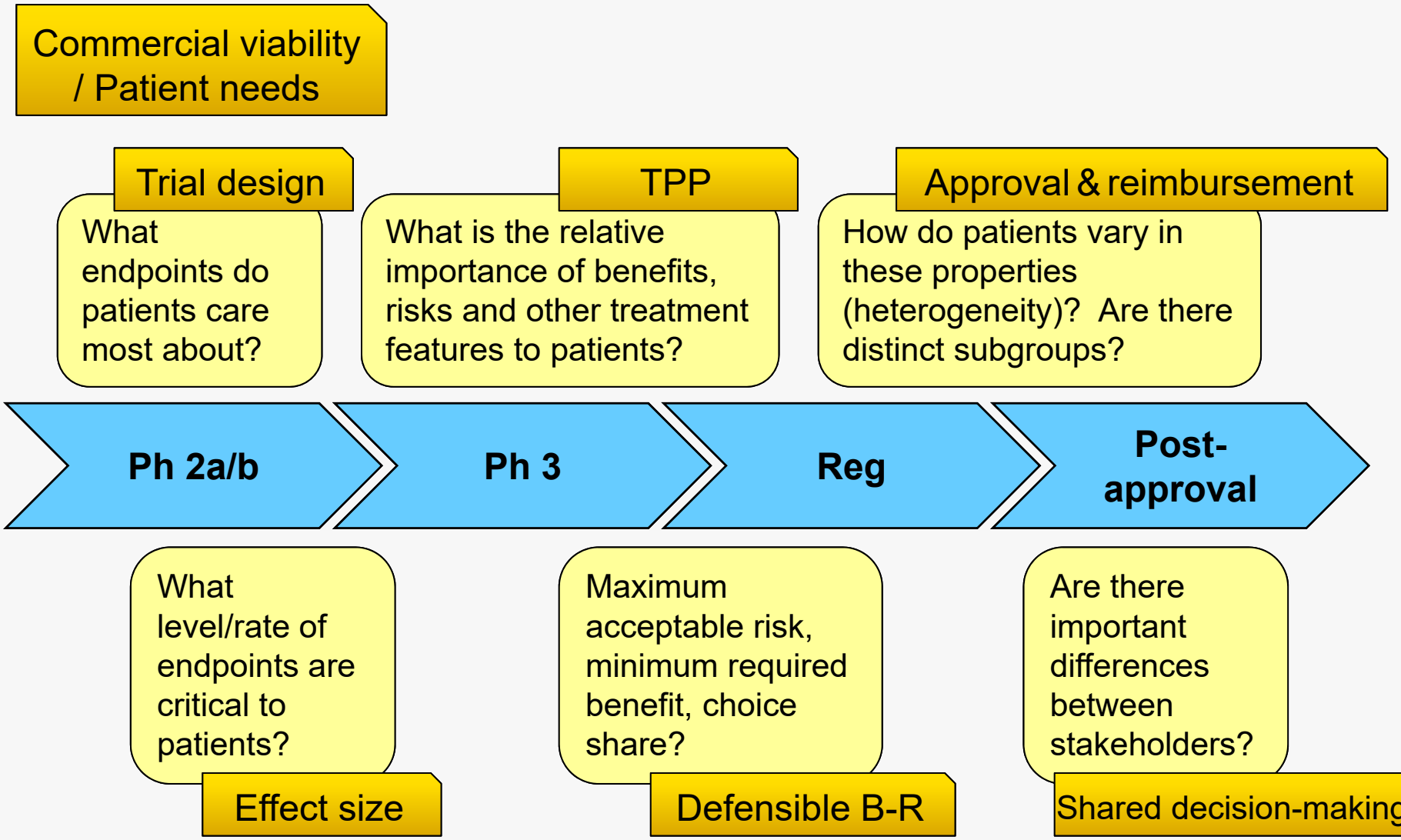
Gonzalez, Hauber, Levitan, Coplan, ISPOR 17th Annual International Meeting June, 2012.

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

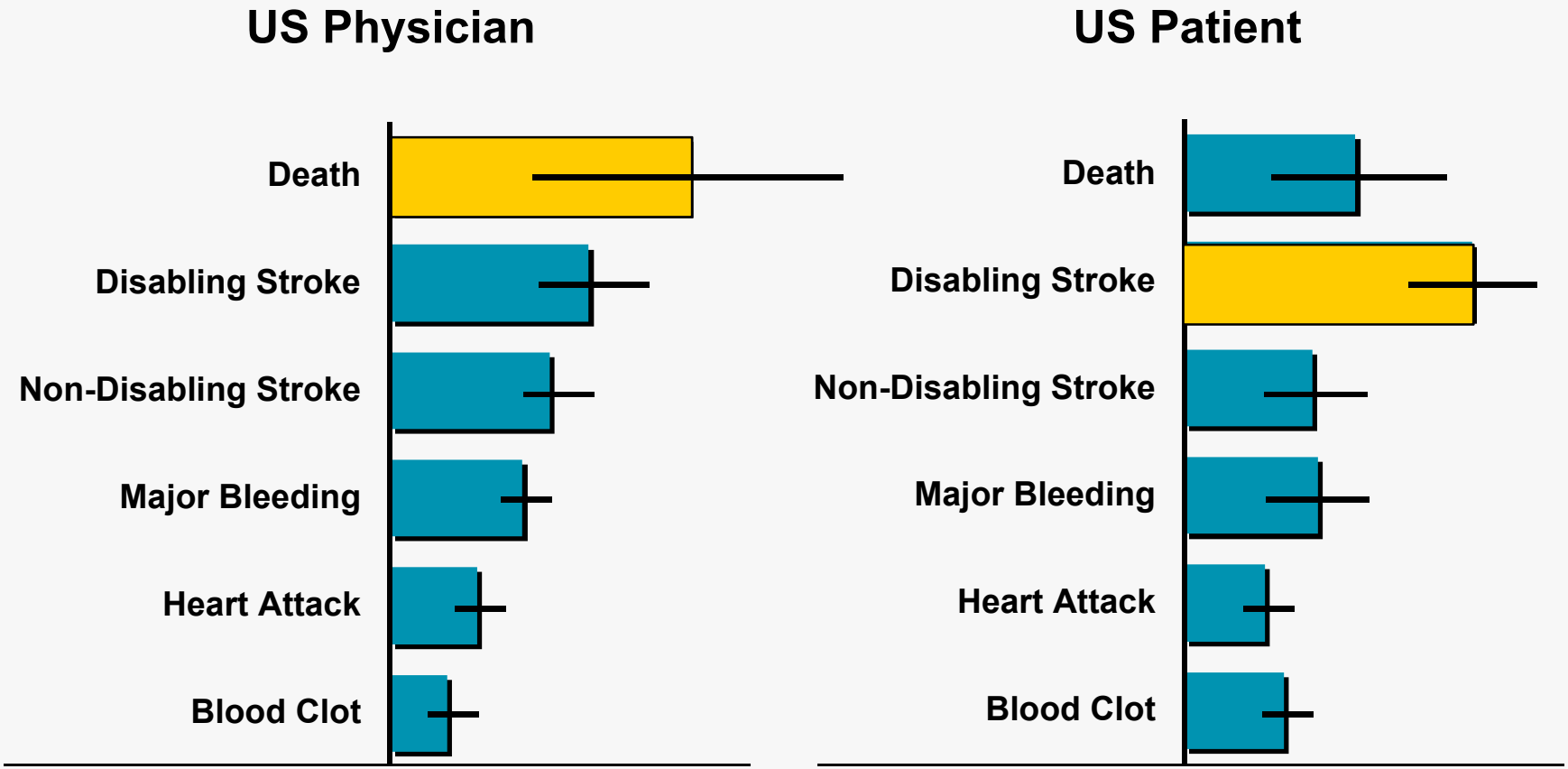
Adapted from RTI-HS and MDIC

Where Can Patient Preferences Inform the Development Lifecycle?



Identifying Differences Between Key Stakeholders

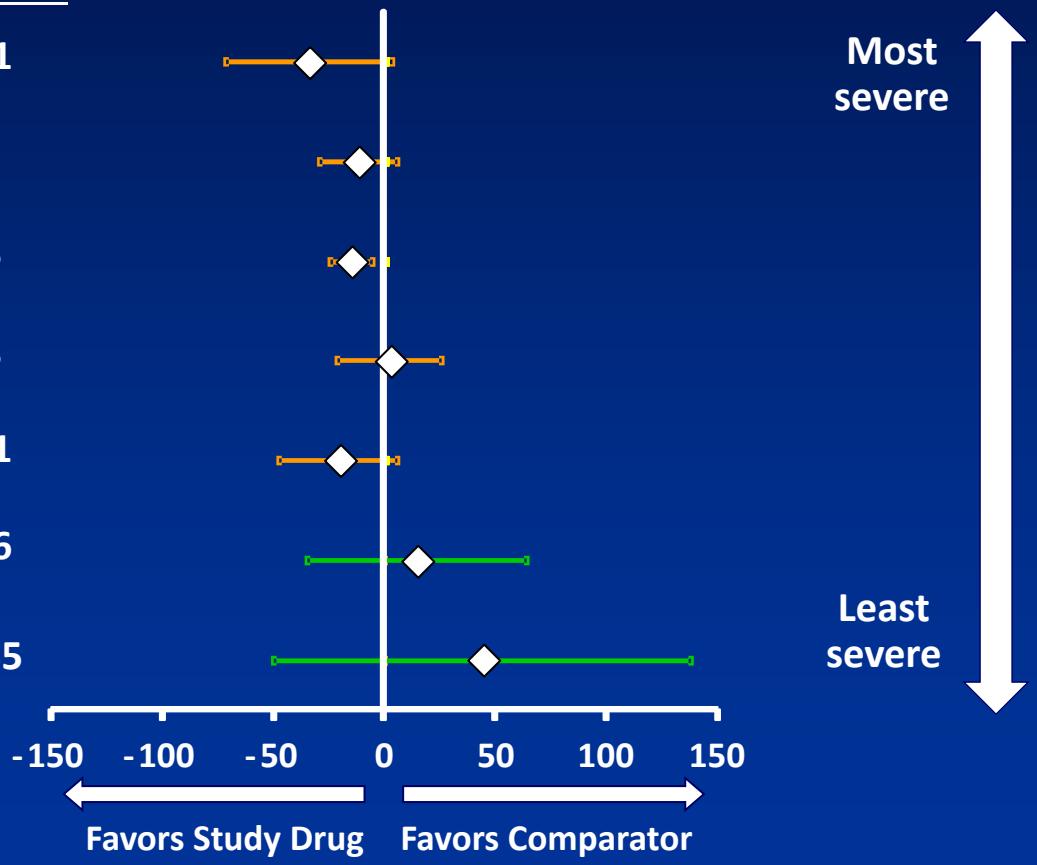
Preferences for Anticoagulants in Atrial Fibrillation



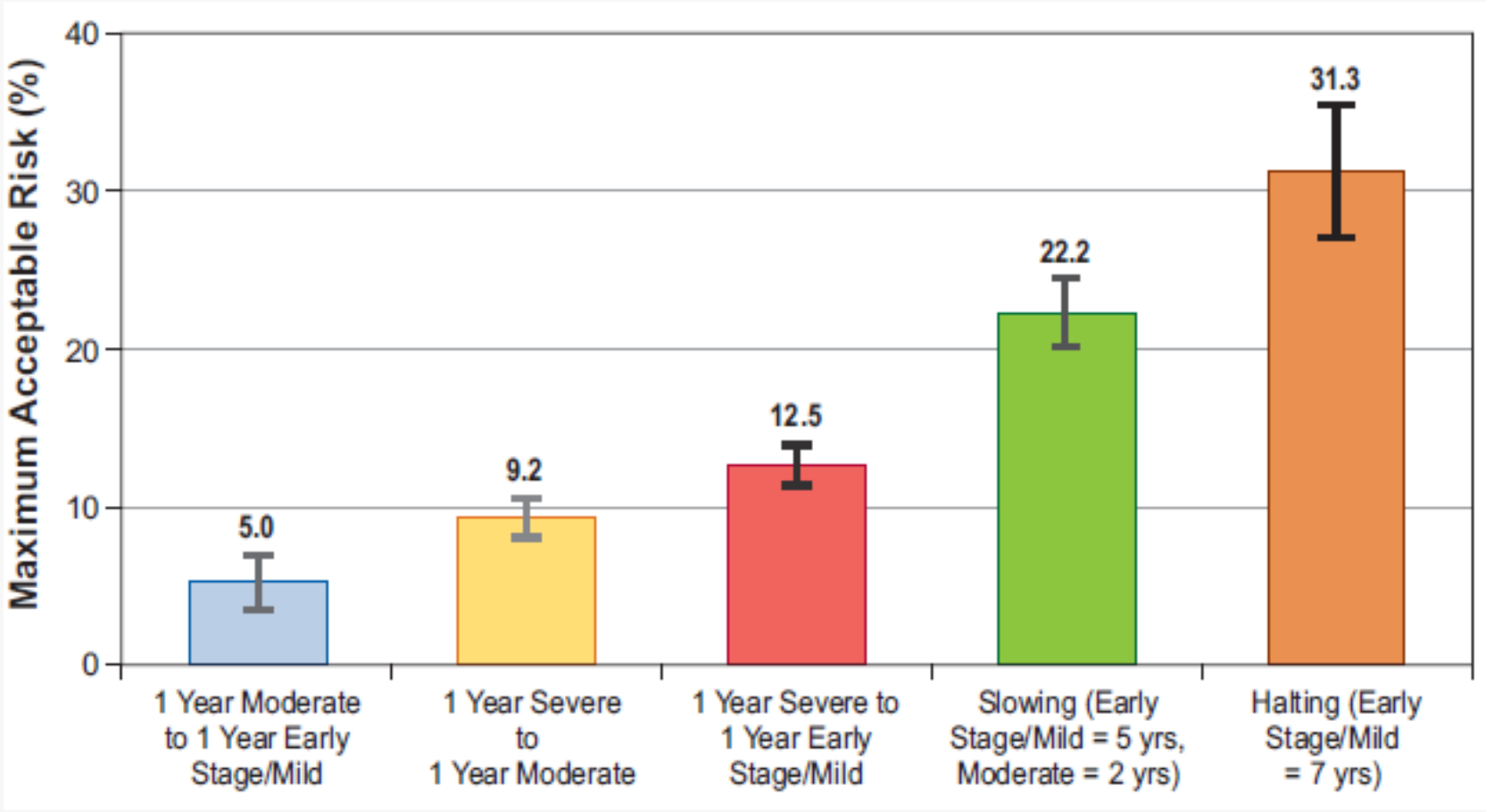
Levitan, Yuan, González, et al., ISPOR 18th Ann Int Mtg, 2013

Risk Differences by Clinical Severity/Impact
Atrial Fibrillation Example (mock data)

Endpoint	# of Events (/10,000 patient-years) Study Drug	Comparator
All-cause mortality	187	221
Disabling stroke	39	51
Non-CNS systemic embolism	3	18
Non-disabling stroke	80	78
Myocardial infarction	90	111
Major bleeding	361	346
Non-major clinically-relevant bleeding	1179	1135



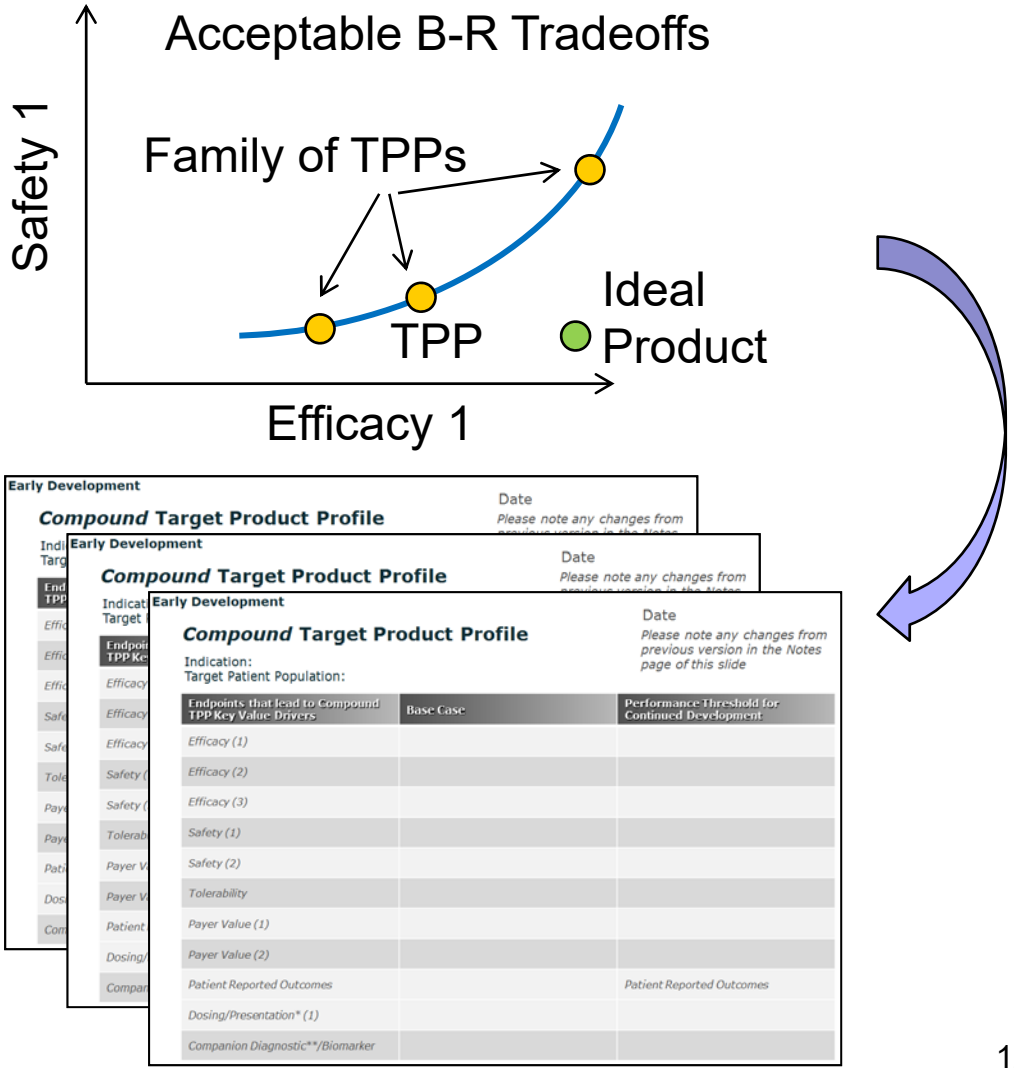
Maximum Acceptable Risk of treatment-related death or permanent severe disability due to stroke



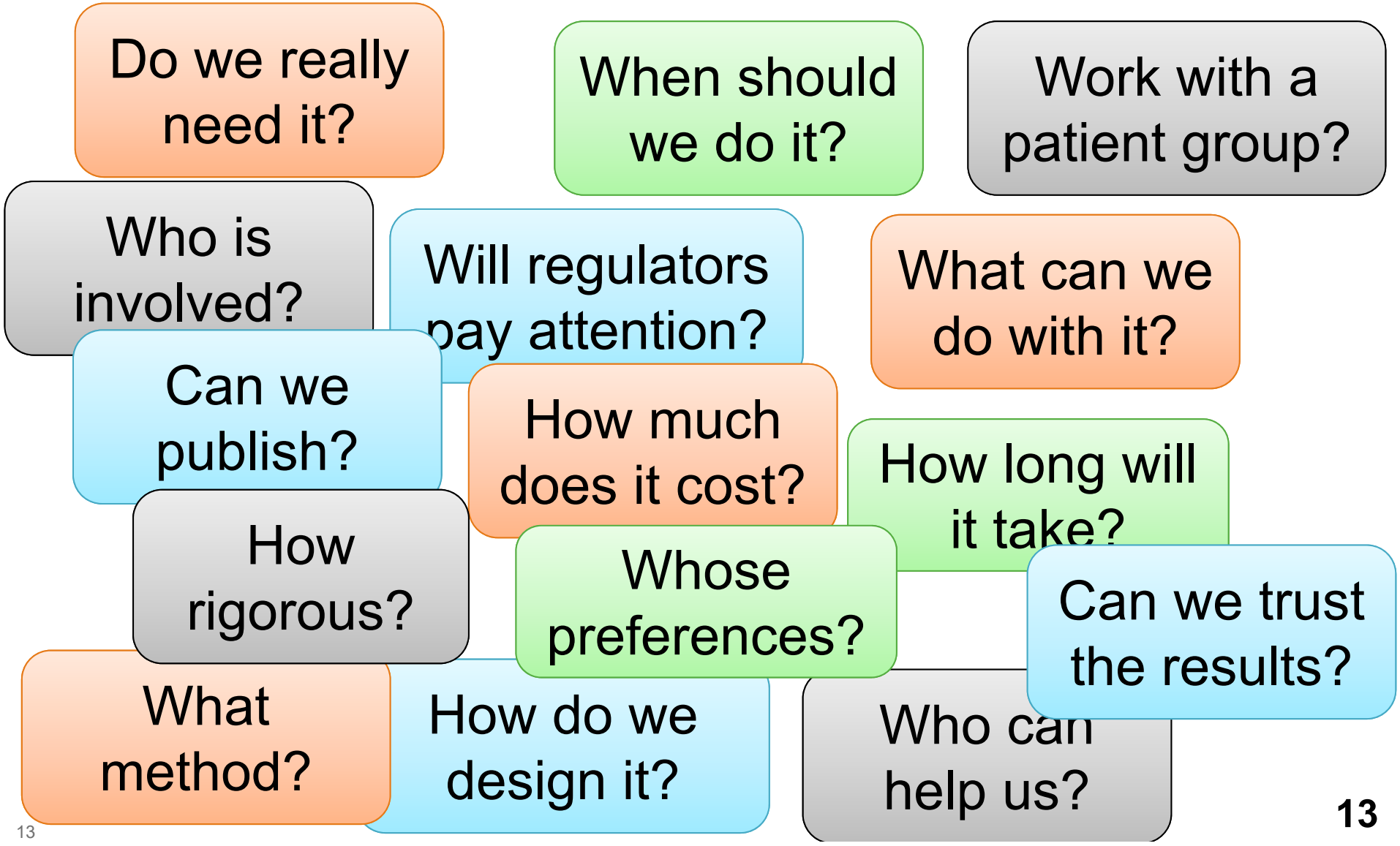
Hauber AB, Johnson FR, Fillit H, et al. Older Americans' risk-benefit preferences for modifying the course of Alzheimer disease. *Alzheimer Dis Assoc Disord.* Jan-Mar 2009;23(1):23-32

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 <u>proactive</u> flexibility for alignment between compound and TPP goals**



What Sponsors Worry About When Considering A Patient Preference Study



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Many Methods for Assessing Preferences

Group	Method
Structured-weighting	• Simple direct weighting • Ranking exercises • Swing weighting • Point allocation • Analytic hierarchy process • Outranking methods
Health-state utility	• Time tradeoff • Standard gamble
Stated-preference	• Direct-assessment questions • Threshold technique • Conjoint analysis and discrete-choice experiments • Best-worst scaling exercises
Revealed-preference	• Patient-preference trials • Direct questions in clinical trials

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

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

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

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)*

Survey pretest similar to cognitive debriefing

- 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 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

21st Century Cures

Selected sample

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

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