Advancing the Science of Patient Input in the Regulatory Settings

Science of Patient Input (SPI) Team
Office of Biostatistics and Epidemiology
FDA CBER

CERSI Presentation
December 2, 2020

Science of Patient Input @ CBER FDA

When patient inputs meet RWE & digital health technologies

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Patient preference studies for regulatory considerations

Sarah Stothers, RN, MSN, MPH, ORISE Fellow

Pilot study: Natural history study and rare disease RCTs

Ting-Hsuan "Joyce" Lee, MHS, ORISE Fellow

SHAPE: A reconfigurable patient friendly app for site-less study

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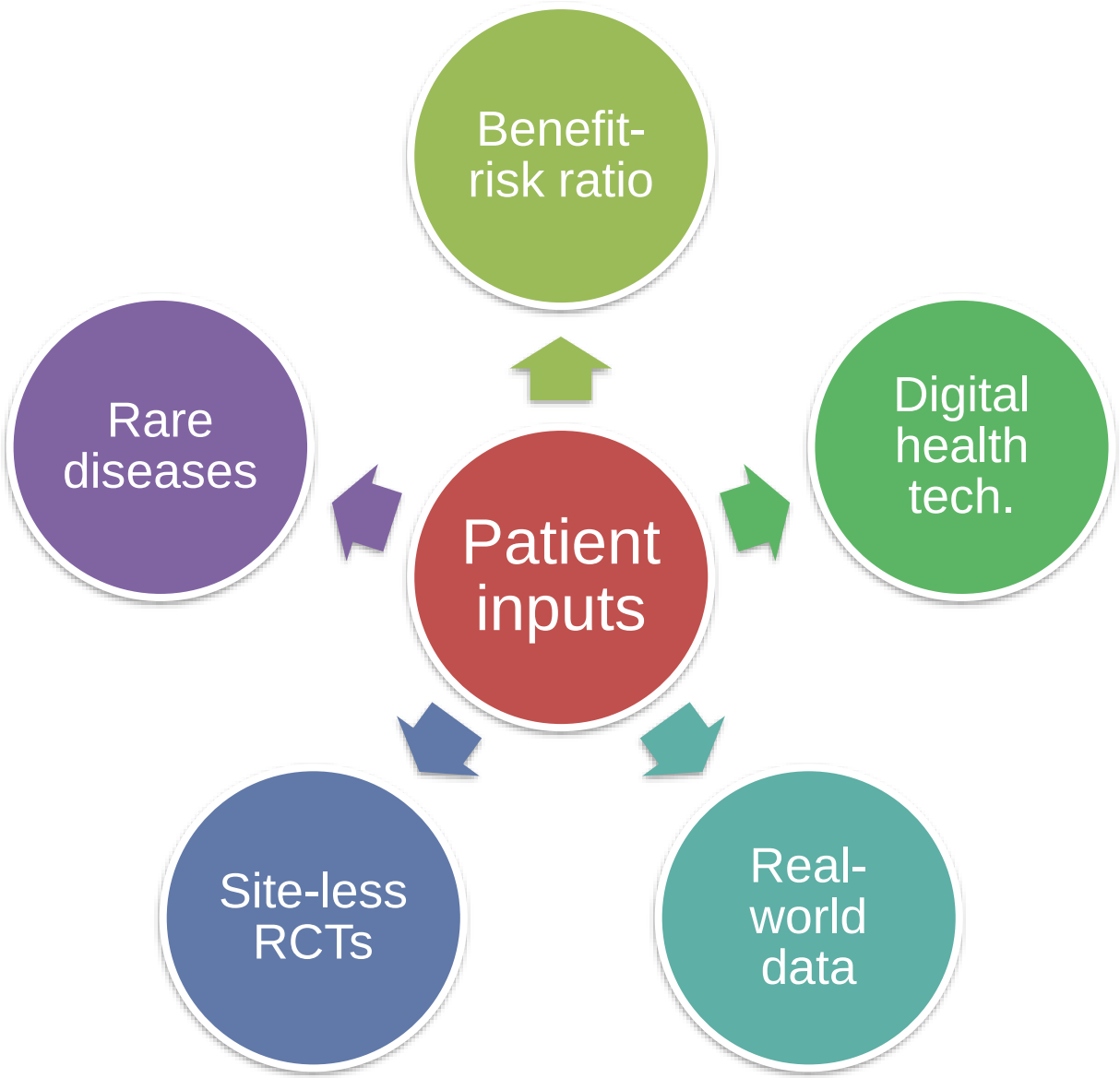
Patients Driven Regulatory Science



Why Collect Patient Input?

***Promote* Public Health**

- Increase therapy access to:
  - Vulnerable populations (e.g., elderly and children)
  - Patients with rare diseases (for advanced therapies)
  - Pregnant women
  - Immunocompromised persons
  - Identify appropriate cohorts by confirming clinical diagnosis

Opportunities

- Novel treatments may come with:
  - High rewards (e.g., potential cure)
  - New risks (e.g., cytokine release syndrome)
  - Uncertainty & unknown unknown's
- Unmet medical needs and dire conditions
- Quantitative patient preferences can inform *preference-sensitive decision-making*

1. Role of Patient Input in the Regulatory Setting

2010 The Affordable Care Act & PCORI[1]

2012 FDASIA[2] Section 1137 & PDUFA[3] V

2016 PDUFA VI

MDUFA[4] IV

Precision Medicine Initiative

21st Century Cures Act

> " …the ideal treatment is personalized to both our cells and our selves"[5]

1 PCORI = Patient-Centered Outcomes Research Institute
2 FDASIA = Food and Drug Administration Safety and Innovation Act
3 PDUFA = Prescription Drug User Fee Act
4 MDUFA = Medical Device User Fee Amendments
5 BMJ Opinion: Berger Z and deBronkart D, "Precision medicine" needs patient partnership

21st Century Cures Act

Title III, Subtitle A: Patient-Focused Drug Development

Section 3001. Patient Experience Data
Requires FDA to make public following approval of an NDA or BLA a brief statement regarding patient experience data submitted and reviewed as part of application

and submitting patient experience data
  - How to submit proposed draft guidances for consideration by FDA
  - How FDA anticipates using patient experience data, including with respect to structured benefit-risk assessment framework

Tracks PDUFA VI commitments

- **Section 3003. Streamlining Patient Input**
  Exempts FDA from Paperwork Reduction Act for collections of information under Section 569C of FD&C Act (Patient Engagement), as amended by Section 3001

- **Section 3004. Report on Patient Experience Drug Development**
  Requires FDA to publish report on website about its use of patient experience data in regulatory decisionmaking

CBER's Science of Patient Input Program

Mission: Advance the science of patient input (SPI) to help inform regulatory decision-making and policy development:

1. Clinical trial design
   - Endpoint development and selection
   - Define clinically meaningful difference
   - Relative importance of Type 1 vs. 2 error
2. Benefit-risk assessments
   - Pre-market licensing
   - Post-market surveillance

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2. Real World Data versus Real World Evidence

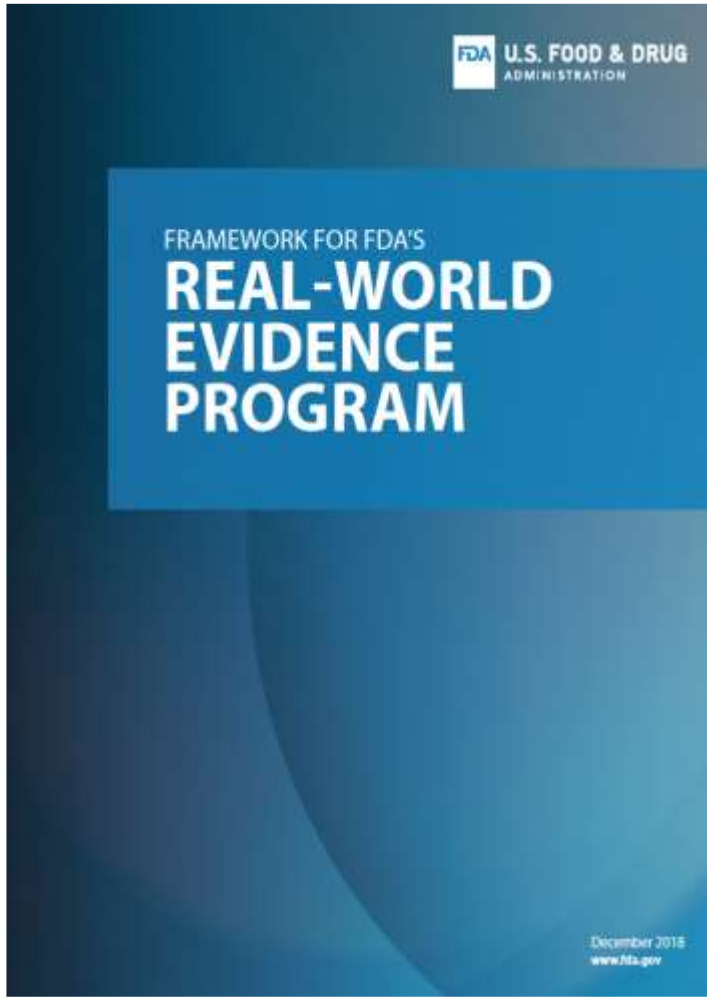
Real World Data (RWD): Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

- electronic health records (EHRs)
- claims & billing data
- data from product & disease registries
- patient-generated data including in home-use settings
- data gathered from other sources that can inform on health status e.g. mobile devices

Real World Evidence (RWE): Clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.

- Generated using many different study designs, including but not limited to, randomized trials (e.g., large simple trials, pragmatic clinical trials) and observational studies.

FDA RWE Program Framework



Framework considerations:

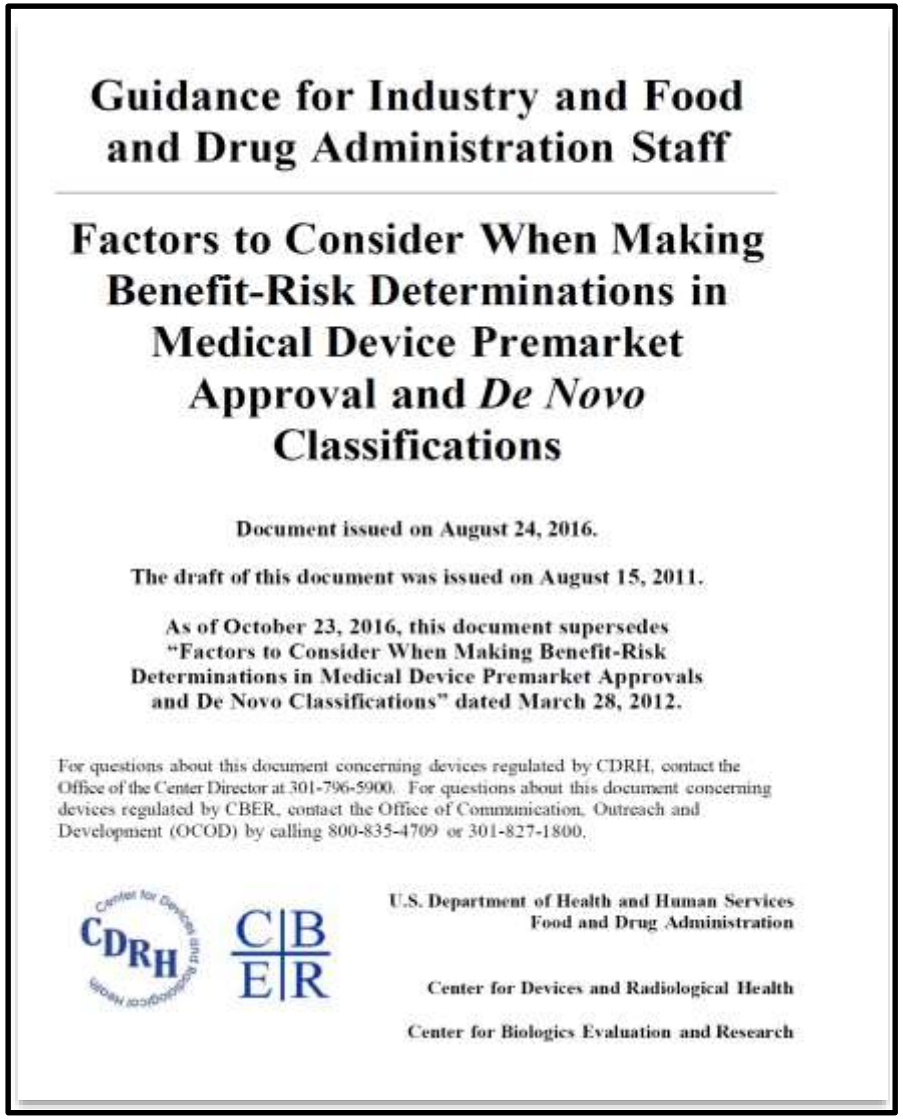
I. Are RWD fit for use in regulatory decisions?

II. Can the study design generate *adequate scientific evidence* to address the regulatory question?

III. Does the study conduct meet FDA regulatory requirements?

FDA RWE Program Framework: https://go.usa.gov/xmQnf

3. Benefit-Risk Guidance Document CDRH and CBER



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

Document issued on August 24, 2016.

The draft of this document was issued on August 15, 2011.

As of October 23, 2016, this document supersedes "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and De Novo Classifications" dated March 28, 2012.

For questions about this document concerning devices regulated by CDRH, contact the Office of the Center Director at 301-796-5900. For questions about this document concerning devices regulated by CBER, contact the Office of Communication, Outreach and Development (OCOD) by calling 800-835-4709 or 301-827-1800.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

Medical Devices (CDRH and CBER)

Factors

Benefits: Type, magnitude, probability, duration

Risks: Severities, types, probabilities, duration, false +ve & -ve

Additional Factors: Context

1. Uncertainty
2. Patient tolerance for risk and perspective on benefit
3. Severity and chronicity of the disease
4. Availability of alternative treatments
5. Risk mitigation
6. Post-market information
7. Novel technology for unmet medical need

4. Patient Tolerance for Risk & Perspective on Benefit

"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 would consider evidence relating to patients' perspective of what constitutes a meaningful benefit."

However, the guidance did not say how to submit Patient Preference Information to the Agency

CBER Patient Preference Studies

- **Preference Sensitive Decision:** Patients may be willing to tolerate higher risks in exchange for better efficacy
- **Unmet medical needs:** 1 Dire condition 2 No effective treatment on market

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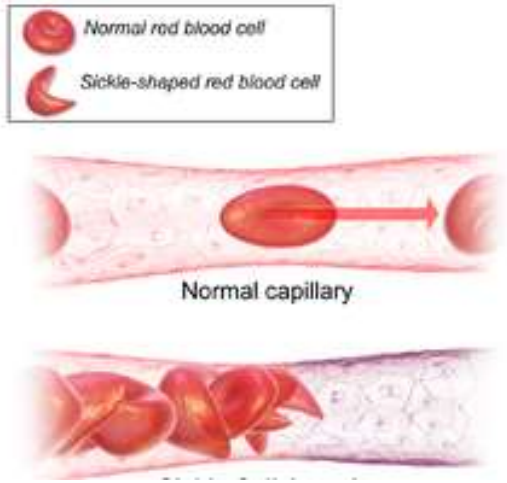
Hard-to-control Type 1 Diabetes Mellitus (T1DM)

UCSF

1 2

Sickle-Cell Disease (SCD)



DUKE

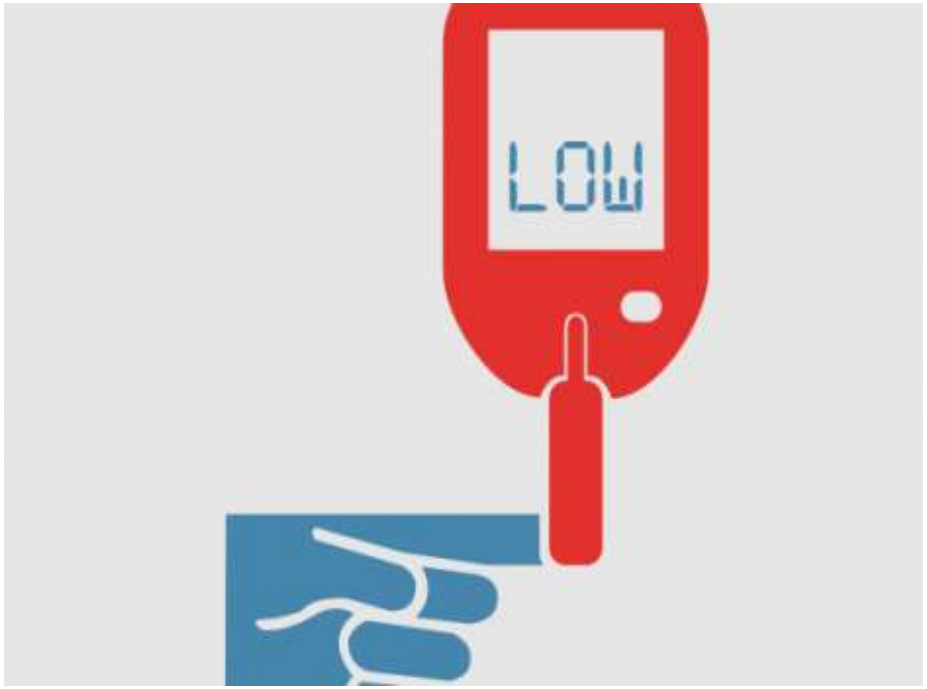
2

Osteoarthritis of the knee (KOA)

RTI

1st PPI Study: Hard-to-Control Type 1 Diabetes Mellitus

- **Patients with Type 1 Diabetes Mellitus (T1DM)** experience difficulty managing their blood glucose despite optimal insulin therapy and can experience ***hypoglycemic unawareness***
- **Islet Cell Transplantation** is a treatment strategy for patients with hard-to-control ("brittle") T1DM

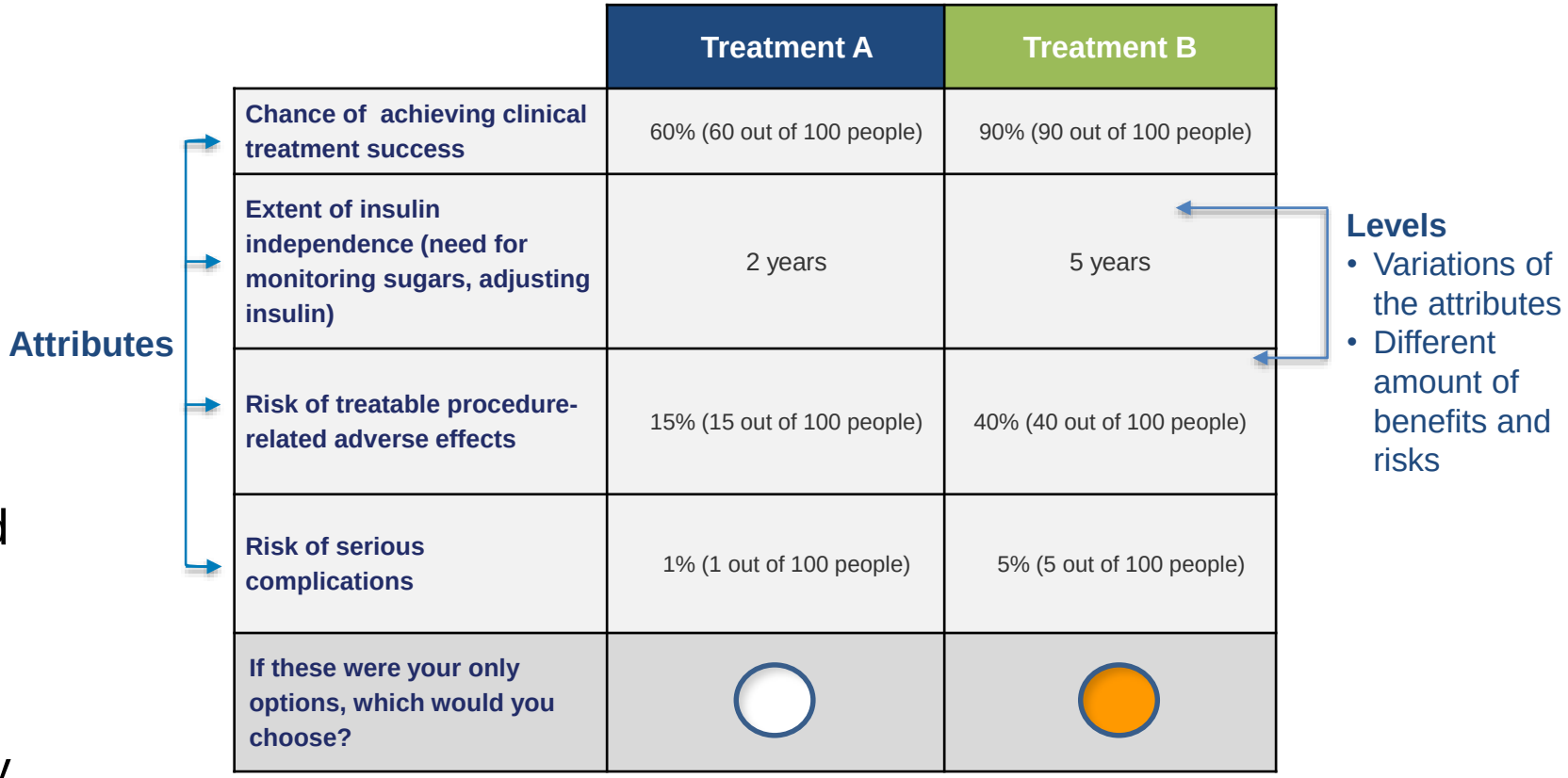


Questions for islet cell therapy PPI study

- How do patients' weigh the benefit-risk tradeoff for islet cell therapy?
- What attributes have the greatest relative importance on influencing patients' treatment preferences?
- How do these findings inform regulatory decision-making?

Preference Elicitation: Discrete Choice Experiments (DCEs)

- A well-established methodology to elicit and quantify preferences on health-care products and interventions
- Respondents choose between hypothetical treatment profiles
  - Each profile is described in terms of a number of characteristics, or 'attributes' that can be related to efficacy, safety, route of administration etc.



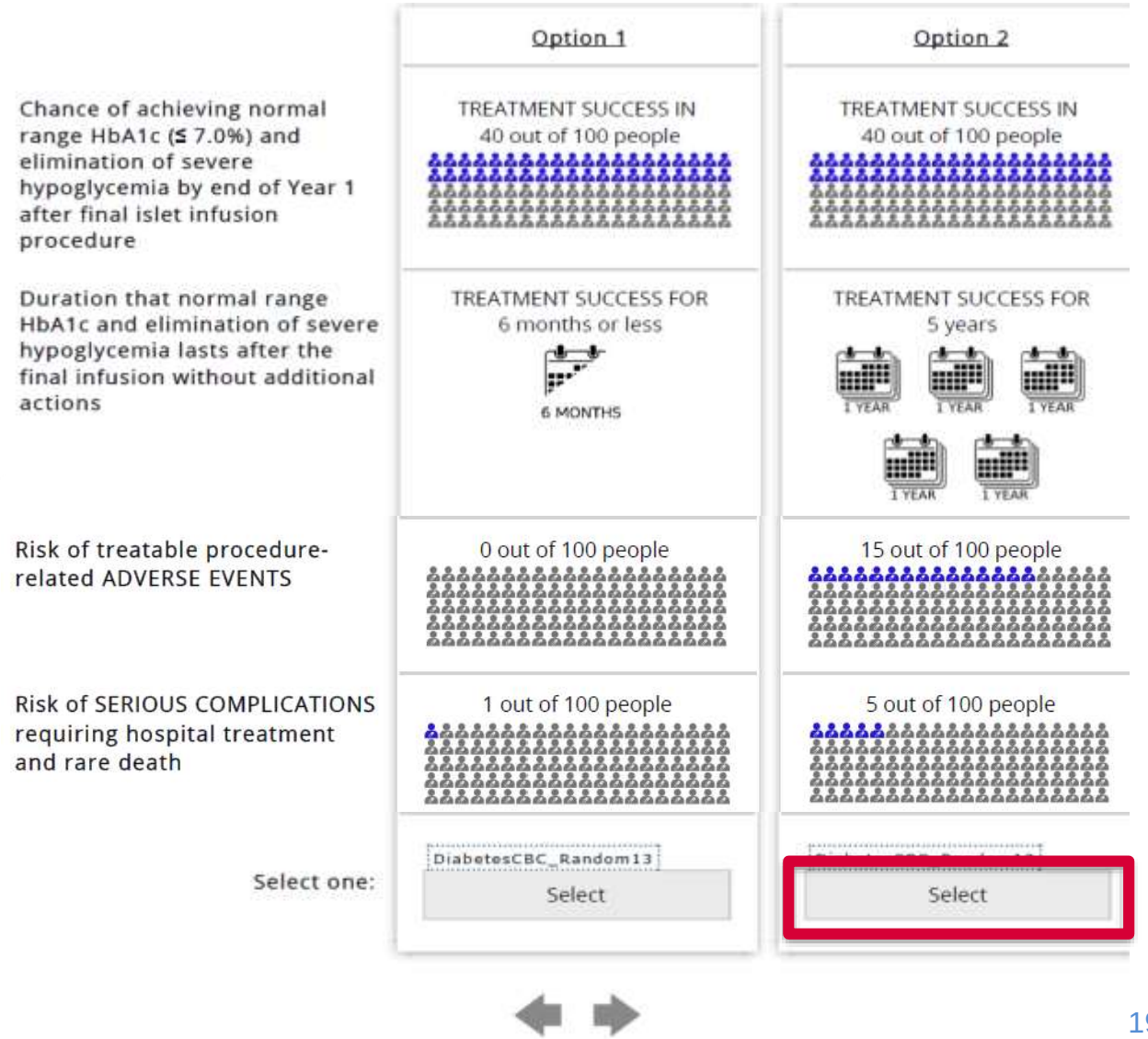
Typically, 12 – 18 questions (i.e., pairs of profiles) are shown.

T1DM Islet Cell Therapy Study Attributes

Attribute	Definition
Chance of achieving clinical treatment success	normal range HbA1c (≤ 7.0%) and elimination of severe hypoglycemia by end of year 1 after final islet cell infusion period
Success duration	normal range HbA1c and elimination of severe hypoglycemia lasts after the final infusion without additional actions
Extent of Insulin independence	not needing any insulin doses or to monitor sugars or adjust insulin to maintain your blood glucose within the first 5 years after your transplantation procedure
Expected reduction in the risk of long-term complications	high risk of developing vision loss, or moderate risk of developing kidney damage, or low risk of developing nerve damage
Risk of Treatable procedure-related adverse effects	nausea, vomiting, diarrhea, moderate bleeding, anemia, pain treated with medications, headache, tremors, confusion, high blood pressure or cholesterol
Risk of Serious complications	requiring hospital treatment and rare death (serious infections, liver bleeds, kidney damage, development of antibodies making additional transplant more difficult or cytomegalovirus infections or viral heart inflammation.
Restrictions due to life time immunosuppression	Immunosuppression (anti-rejection) medications required as long as your islet cells are working (up to 5 years or longer)
Time and support needed	if 1-3 islet cell procedures are required each requiring 3 months of extra time and support to manage your diabetes including 3-5 days hospital stay, 2 weeks intensive monitoring of diabetes, and monthly physician visits each time

T1DM Islet Cell Therapy Choice-task Example

Attribute	Levels
Chance of Achieving clinical treatment success	40 out of 100 people (40 %)
	60 out of 100 people (60 %)
	90 out of 100 people (90 %)
Success duration	0.5 years or less
	1 year
	2 years
	5 years
Risk of Treatable procedure-related adverse effects	0 out of 100 people (0 %)
	5 out of 100 people (5 %)
	15 out of 100 people 15 %)
	4 out of 100 people (4 %)
Risk of Serious complications	0 out of 100 people (0 %)
	1 out of 100 people (1 %)
	5 out of 100 people (5 %)
	15 out of 100 people (15 %)



Recruitment and Patient Characteristics

Recruitment:

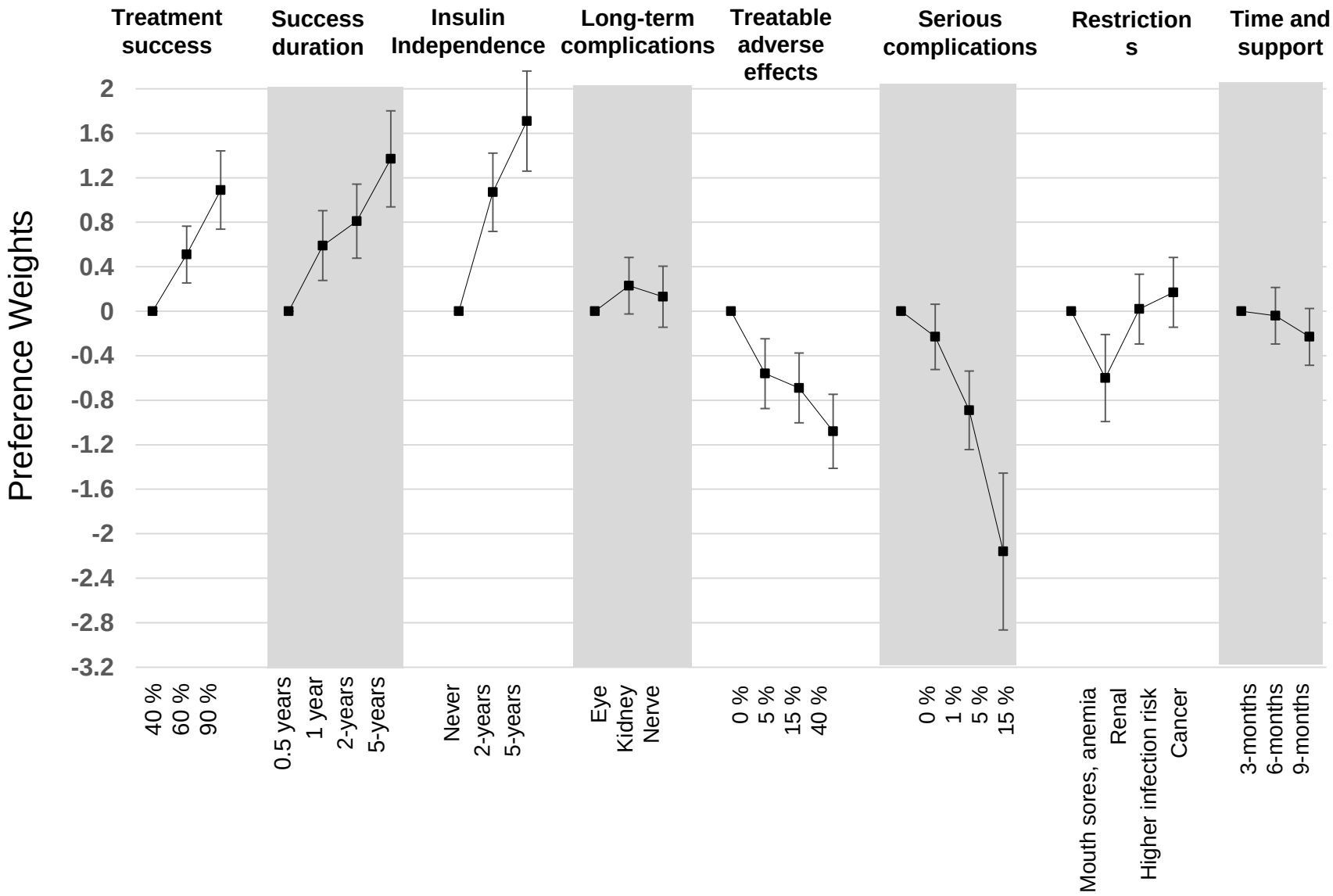
- Convenience sampling
- UCSF Diabetes Clinics
- National Diabetes Research Centers
- N = 92

Inclusion Criteria:

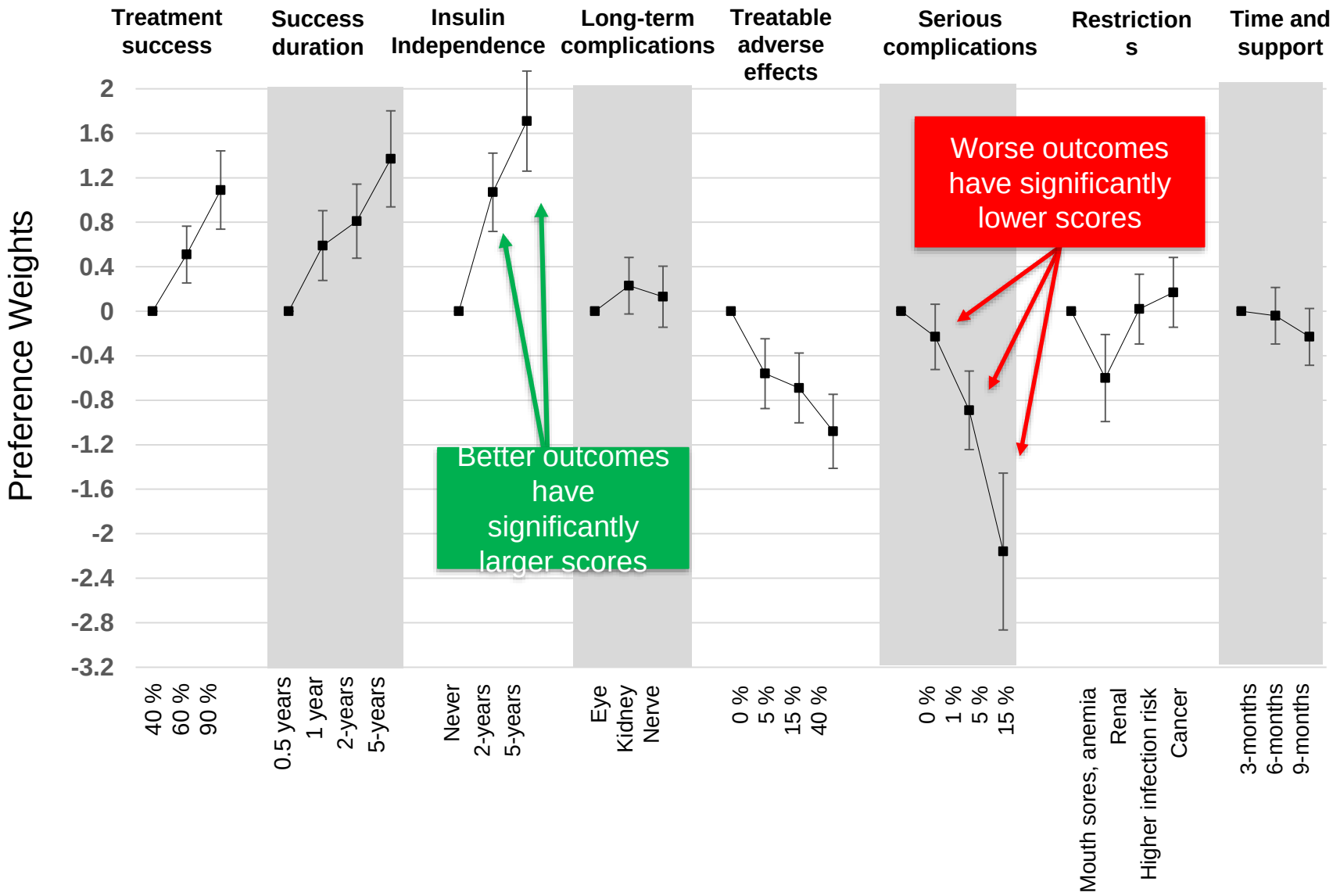
- Adults (≥ 18 years)
- English-speaking
- Physician referred Type 1 Diabetics
- Previously experienced a hypoglycemic episode

	Full Sample (N = 92) Mean (Range) / n (%)
Age	42 (20-89)
Female	46 (50%)
Race	
White	71 (77%)
Black	6 (6%)
Asian or Pacific Islander	11 (12%)
Native American	2 (2%)
Other	3 (3%)
Ethnicity	
Latino (any race)	5 (5%)
Education Level	
High School Diploma or GED	6 (6.5%)
Some College	17 (18%)
Bachelor's Degree	38 (41%)
Graduate Degree	31 (34%)
Employment Status	
Employed Full-Time	53 (57%)
Employed Part-Time	5 (5%)
Retired	10 (11%)
Homemaker or student	8 (9%)
Disabled	11 (12%)
Unemployed	5(5 %)
Income Level	
Less than $50,000	20 (22%)
$50,000 to $74,999	11 (12%)
$75,000 to $99,999	9 (10%)
$100,000 to $199,999	18 (19%)
$200,000 or more	22 (24%)
Prefer not to answer	12 (13%)
Health Insurance Type	
Medicare	20 (22%)
Medicaid	10 (11%)
Private plan through work	63 (68%)
VA or other military	2 (2%)
Disability insurance	0 (0%)
Not insured	2 (2%)

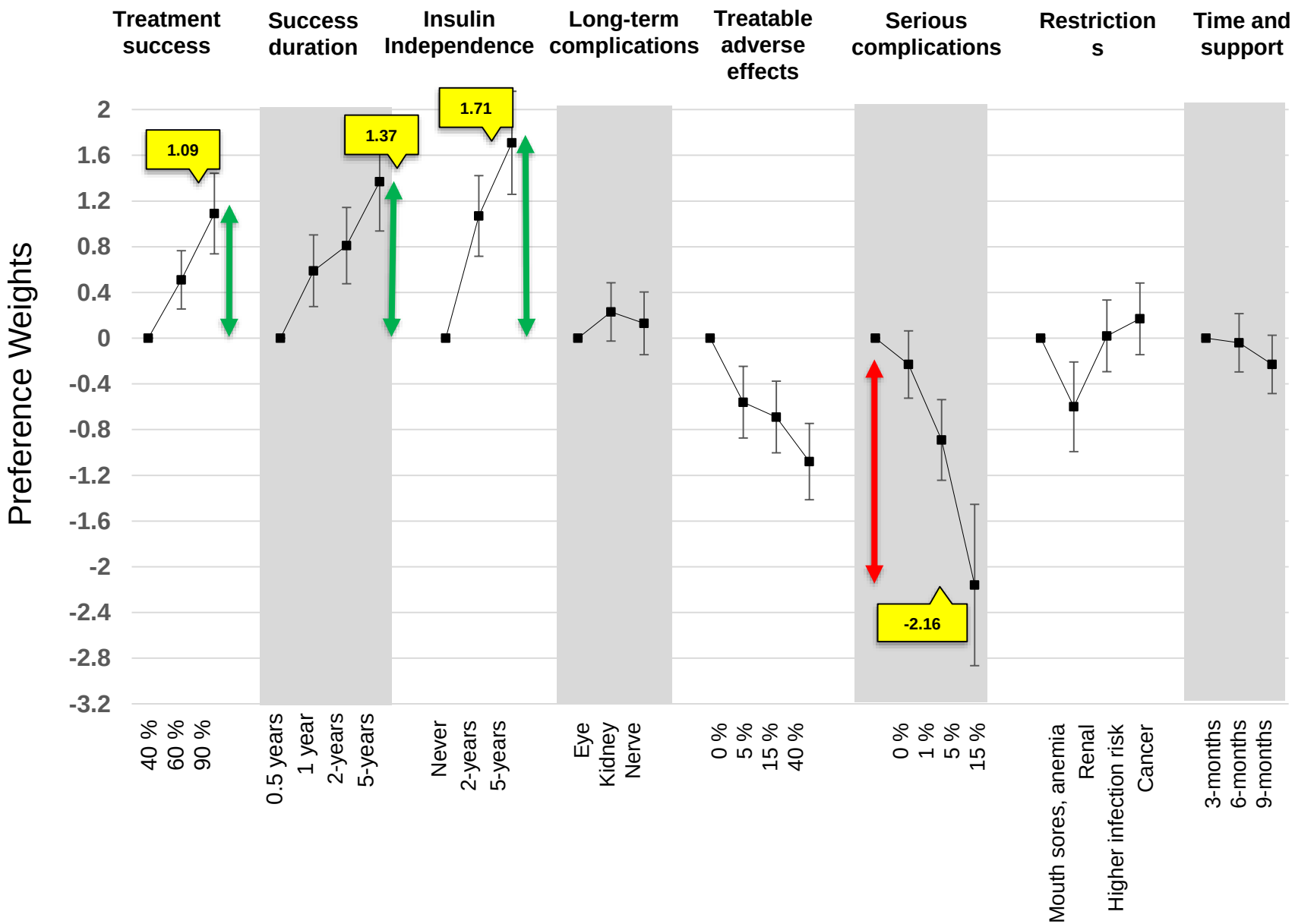
Results: preference weights



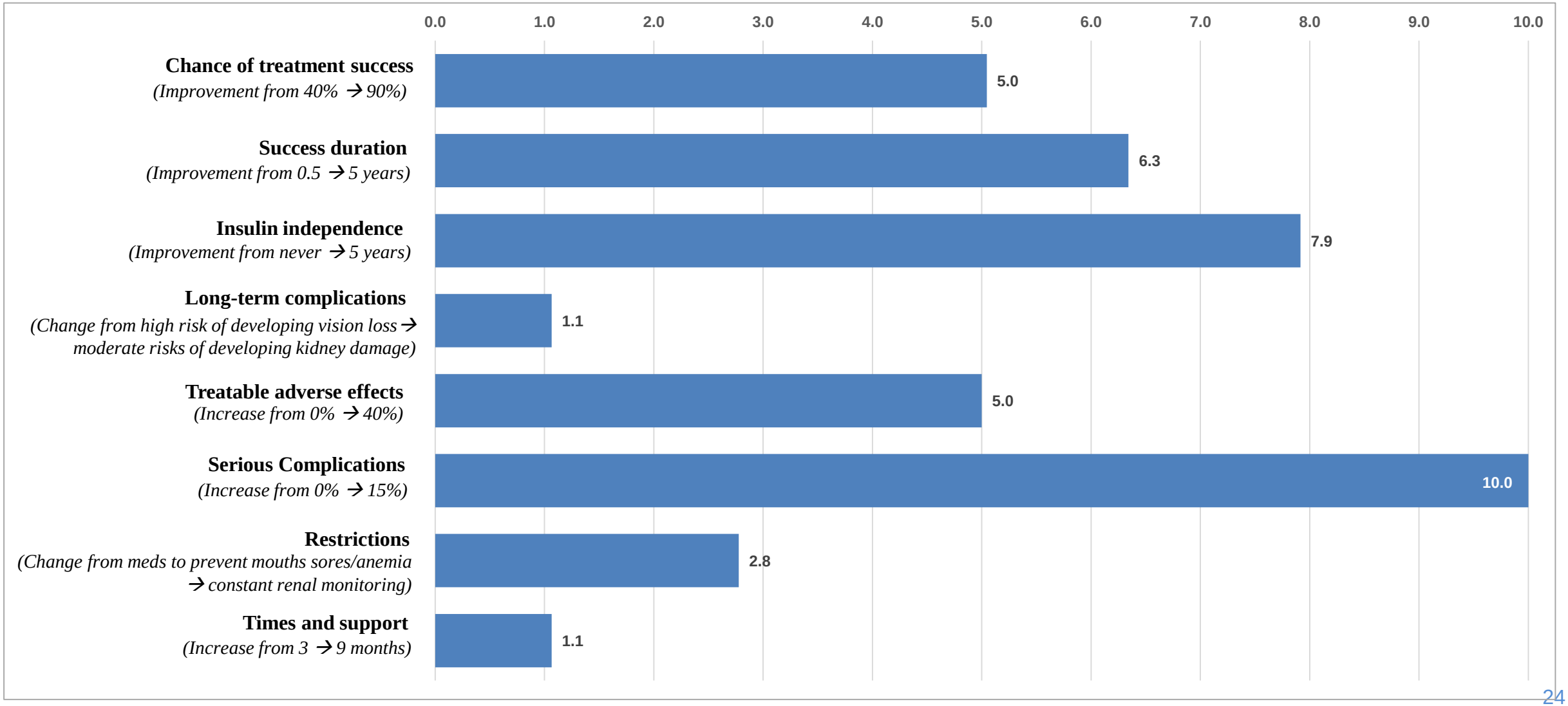
Results: preference weights



Most important attributes



Relative importance of attributes



Key Findings

- Three most influential attributes to patients' choices for islet cell treatments are:
    1. How risky of experiencing serious complications (from 0 to 15%)
    2. How independent from insulin (improvement from never to 5-years)
    3. How long treatment success lasts (improvement from 0.5 to 5-years)

- This study has demonstrated that patients are willing to make benefit-risk tradeoff when choosing islet cell treatments

- PPI data can inform regulatory considerations of islet cell treatments by attaching patients' preference weights to the outcomes observed in the clinical studies

2nd PPI Study: Osteoarthritis of the Knee (KOA)

Osteoarthritis

- Characterized by degradation of knee cartilage & bone
- Patients experience increasing pain & functional impairment

Treatment options

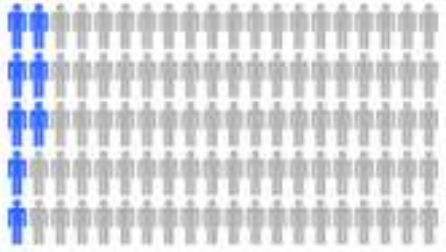
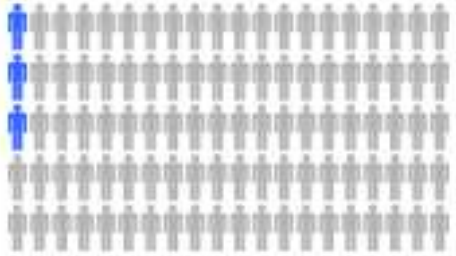
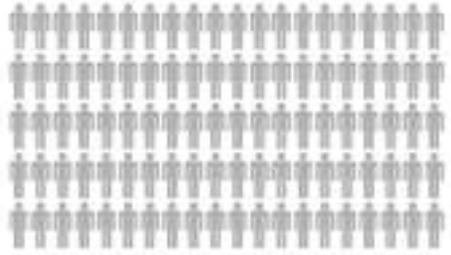
- Avail. treatments. offer symptomatic relief; *not* slow OA progression
- New therapies (cell therapies, cell or tissue-engineered products, & gene therapies) may slow OA progression

Question: Relative value of improvements in pain vs. function to patients?

KOA Study Attributes

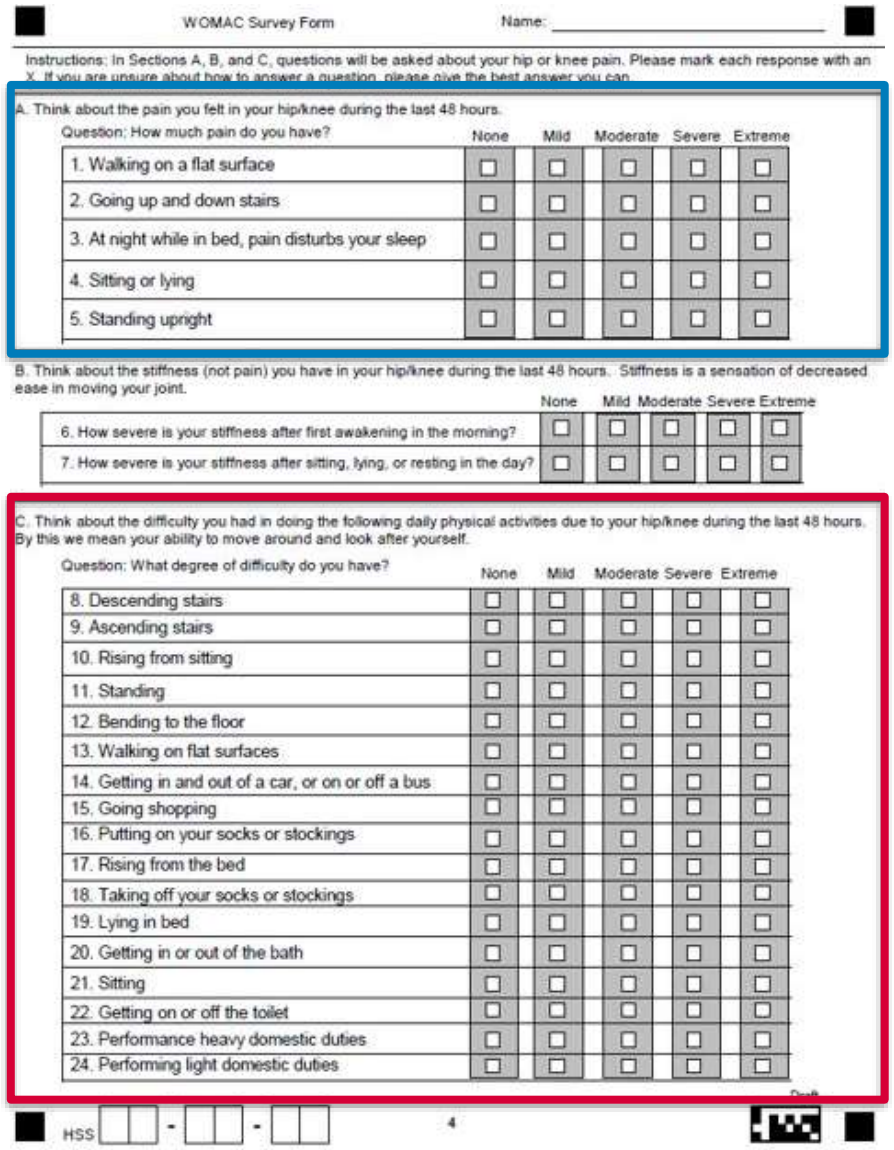
Attribute	Attribute Levels
Improvement in pain	No improvement 30% improvement in pain score 50% improvement in pain score 100% improvement (no pain)
Improvement in function	No improvement 30% improvement in activity score 50% improvement in activity score 100% improvement (no difficulty)
How long improvements last	6 months 1 year (12-months) 2 years (24-months) 5 years (60-months)
Risk of developing too much tissue inside the knee	3 out of 100 people (3%) 5 out of 100 people (5%) 8 out of 100 people (8%) 10 out of 100 people (10%)

KOA Choice Task (Question) Example

Treatment Feature	Treatment A	Treatment B	No new treatment, continue with current treatment
Improvement in pain	Improve pain from 88 to 62	Improve pain from 88 to 44	No additional improvement in pain
Improvement in ability to do day-to-day activities	Improve from 79 to 0 (no difficulty)	Improve from 79 to 39	No additional improvement in ability to do day-to-day activities
How long improvements last	5 years	2 years	No additional time
Risk of developing too much tissue inside the knee	 **8 out of 100 people (8%)**	 **3 out of 100 people (3%)**	 **No risk**
Which treatment would you choose?	☐	☐	☐

PROM to PPI

- Select a Patient-reported outcome measure (PROM) for adaptation to PPI attributes
- Translate pain and function domains from *Western Ontario and McMaster Universities Osteoarthritis Index* (WOMAC) into pre-defined attributes
  - 5-item Pain
  - 17 item Function
- Two Discrete Choice Experiments (DCEs) were developed to facilitate comparison between domain score version and single-item score version of DCE
  - Selection for single-item: “walking on a flat surface”



WOMAC Survey Form Name: _____

Instructions: In Sections A, B, and C, questions will be asked about your hip or knee pain. Please mark each response with an X. If you are unsure about how to answer a question, please give the best answer you can.

A. Think about the pain you felt in your hip/knee during the last 48 hours.

Question: How much pain do you have?	None	Mild	Moderate	Severe	Extreme
1. Walking on a flat surface	☐	☐	☐	☐	☐
2. Going up and down stairs	☐	☐	☐	☐	☐
3. At night while in bed, pain disturbs your sleep	☐	☐	☐	☐	☐
4. Sitting or lying	☐	☐	☐	☐	☐
5. Standing upright	☐	☐	☐	☐	☐

B. Think about the stiffness (not pain) you have in your hip/knee during the last 48 hours. Stiffness is a sensation of decreased ease in moving your joint.

	None	Mild	Moderate	Severe	Extreme
6. How severe is your stiffness after first awakening in the morning?	☐	☐	☐	☐	☐
7. How severe is your stiffness after sitting, lying, or resting in the day?	☐	☐	☐	☐	☐

C. Think about the difficulty you had in doing the following daily physical activities due to your hip/knee during the last 48 hours. By this we mean your ability to move around and look after yourself.

Question: What degree of difficulty do you have?	None	Mild	Moderate	Severe	Extreme
8. Descending stairs	☐	☐	☐	☐	☐
9. Ascending stairs	☐	☐	☐	☐	☐
10. Rising from sitting	☐	☐	☐	☐	☐
11. Standing	☐	☐	☐	☐	☐
12. Bending to the floor	☐	☐	☐	☐	☐
13. Walking on flat surfaces	☐	☐	☐	☐	☐
14. Getting in and out of a car, or on or off a bus	☐	☐	☐	☐	☐
15. Going shopping	☐	☐	☐	☐	☐
16. Putting on your socks or stockings	☐	☐	☐	☐	☐
17. Rising from the bed	☐	☐	☐	☐	☐
18. Taking off your socks or stockings	☐	☐	☐	☐	☐
19. Lying in bed	☐	☐	☐	☐	☐
20. Getting in or out of the bath	☐	☐	☐	☐	☐
21. Sitting	☐	☐	☐	☐	☐
22. Getting on or off the toilet	☐	☐	☐	☐	☐
23. Performance heavy domestic duties	☐	☐	☐	☐	☐
24. Performing light domestic duties	☐	☐	☐	☐	☐

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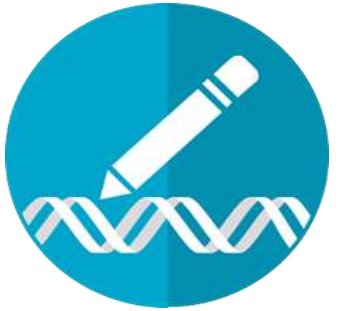
3rd PPI Study: Sickle-cell Disease

Research Questions

- Gene therapy offers a potential cure for sickle cell disease but poses high risks for patients.

  - How would patients make tradeoffs?



  - Do patients with more severe symptoms view the benefit-risk tradeoffs differently?

Sickle Cell Disease Study Attributes

Attributes	Attribute Levels
Chance of no symptoms of SCD	• 90% (9 out of 10) • 80% (8 out of 10) • 40% (4 out of 10)
Increase in life years	• None • 4 years • 8 Years
Chance of dying within first year after treatment	• No chance • 10% (1 out of 10) • 30% (3 out of 10)
Increase in lifetime risk of cancer	• No increase • Not expected • Not known

SCD Study Question Example

	Gene Therapy A	Gene Therapy B	No Gene Therapy
Chance of no symptoms of SCD after treatment (for some patients this takes up to 2 years)	8 out of 10 (80%)	6 out of 10 (60%)	No chance
Expected increase in life years after treatment	No increase	1 2 3 4 5 6 7 8 8 more years	No increase
Chance of death within 1 year after treatment	No chance	3 out of 10 (10%)	No chance
Increase in lifetime cancer risk after treatment	No Increase	Not known	No increase
	Select	Select	Select

PPI Contributions

- Patient preference information is an important complement to clinical and statistical evidence to make benefit-risk assessments
- Evidence on patient preference can be scientifically obtained
- Patient preference information can provide insights to reviewers who may have limited experience with patients of some rare diseases
- The Science of Patient Input is evolving

CBER Pilot Natural History Study

What is a Natural History Study (NHS)?

- Follows a group of people over time who have, or are at risk of developing, a specific medical condition or disease.
- Collects health information to provide understanding on how the medical condition or disease develops and how to treat it.

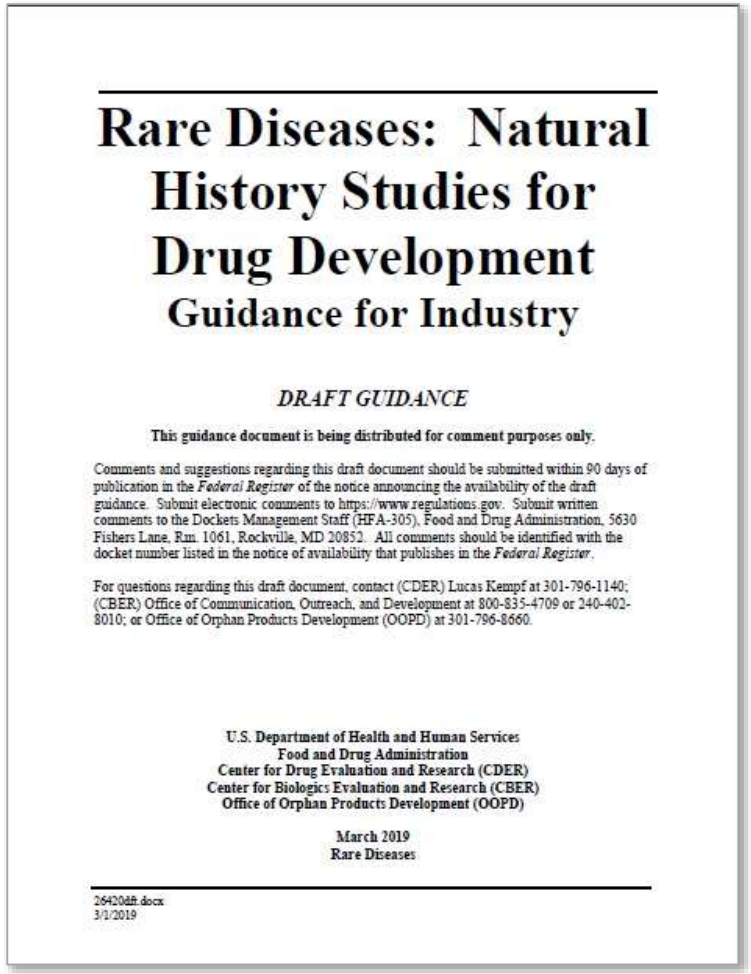
Source: The National Cancer Institute Dictionary of Cancer Terms (go.usa.gov/xvvXb)

CBER Pilot Natural History Study

Purpose of the study

Develop a pilot of a natural history study, which is designed to serve as a potential source of external controls to augment the concurrent controls of future RCTs

Draft Guidance- 2019



Rare Diseases: Natural History Studies for Drug Development

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Lucas Kempf at 301-796-1140; (CBER) Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010; or Office of Orphan Products Development (OOPD) at 301-796-8660.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Office of Orphan Products Development (OOPD)

March 2019
Rare Diseases

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Why Augment Concurrent Controls for

?

1. Patients are reluctant to enroll in clinical trials when their chance of being randomized to the treatment is 50%
2. Patients in dire conditions face an opportunity cost from being randomized to a control arm; they may become ineligible for other studies
3. Ethical considerations
4. Small population size means limited sample pool; [Tradeoff] A smaller control arm allows for a larger treatment arm

Collaborators and Selected Disease for Pilot NHS

Collaborators: National Organization for Rare Disorders (NORD) *and* IBM

Disease Area: Metachromatic leukodystrophy (MLD)

a. It is a rare disease that needs an external control for single-arm trials.

b. A product is already in the pipeline, anticipating a marketing application submission in about 2-3 years.

What is Metachromatic Leukodystrophy (MLD)?

Background

- Rare hereditary ***progressive*** disease
- Prevalence rate is estimated to be between 1 in 40,000 and 1 in 160,000

Symptoms

- Difficulty talking
- Difficulty walking
- Seizures
- Personality & behavior changes

Cause

Accumulation of sulfatides (fats) causes destruction of the myelin sheath of nerves in the CNS and PNS

Types (age of symptom onset)

- Late-infantile MLD (≤ 3 yrs.)
- Juvenile MLD (4–12 & 14 yrs.)
- Adult MLD (>14 yrs.)

Key Significances of the project

1. Use multi-stakeholder approach (including patients and caregivers, clinicians and FDA) to design and conduct study
2. Learn good research practices for designing and conducting natural history studies to augment concurrent controls
3. Explore innovative data collection methods to mitigate drawbacks of traditional natural history studies

Key Significance 1: Collaboration

1. CBER actively collaborates with multi-stakeholders (e.g., product review office, NORD, patient groups) to design study and to strive for study results that can inform regulatory decision making.

2. Listen to the patient's voice: Promote patient-focused research and product development

Key Significance 2: Report on Good Research Practices for a Natural History Study (NHS)

a. Good practices in:

I. Designing and conducting a NHS to serve as external control

II. Combining and analyzing data from:

- NHS external control, and
- Future concurrent data from the prospective RCT

III. Mimicking an RCT using analytical methods in the study design phase to control for confounding and biases

b. Pilot of a longitudinal registry that incorporates CBER's clinical data requirements

Conducting the NHS

- Study Coordinator to conduct video assessments with patients and caregivers

1. Coordinator can answer any questions the families may have
2. Less patient burden and more accuracy in data collection
3. Scheduled data entry which may reduce missing data
4. The primary endpoint (GMFC-MLD) designed to be collected by clinicians. This enables comparison with a patient reported endpoint

NORD Pilot NHS Homepage

https://rarediseases.org/mld-home-study/

Key Significance 3: Innovative Data Collection

- This study will use innovative patient-centered methods (e.g., **mobile & web-based app**) to collect **longitudinal data** and **patient perspectives** on their disease status and potential treatments

Introducing… Biologics Effectiveness and Safety Initiative (BEST)'s SHAPE

Survey of Clinical Health and Patient Experience App

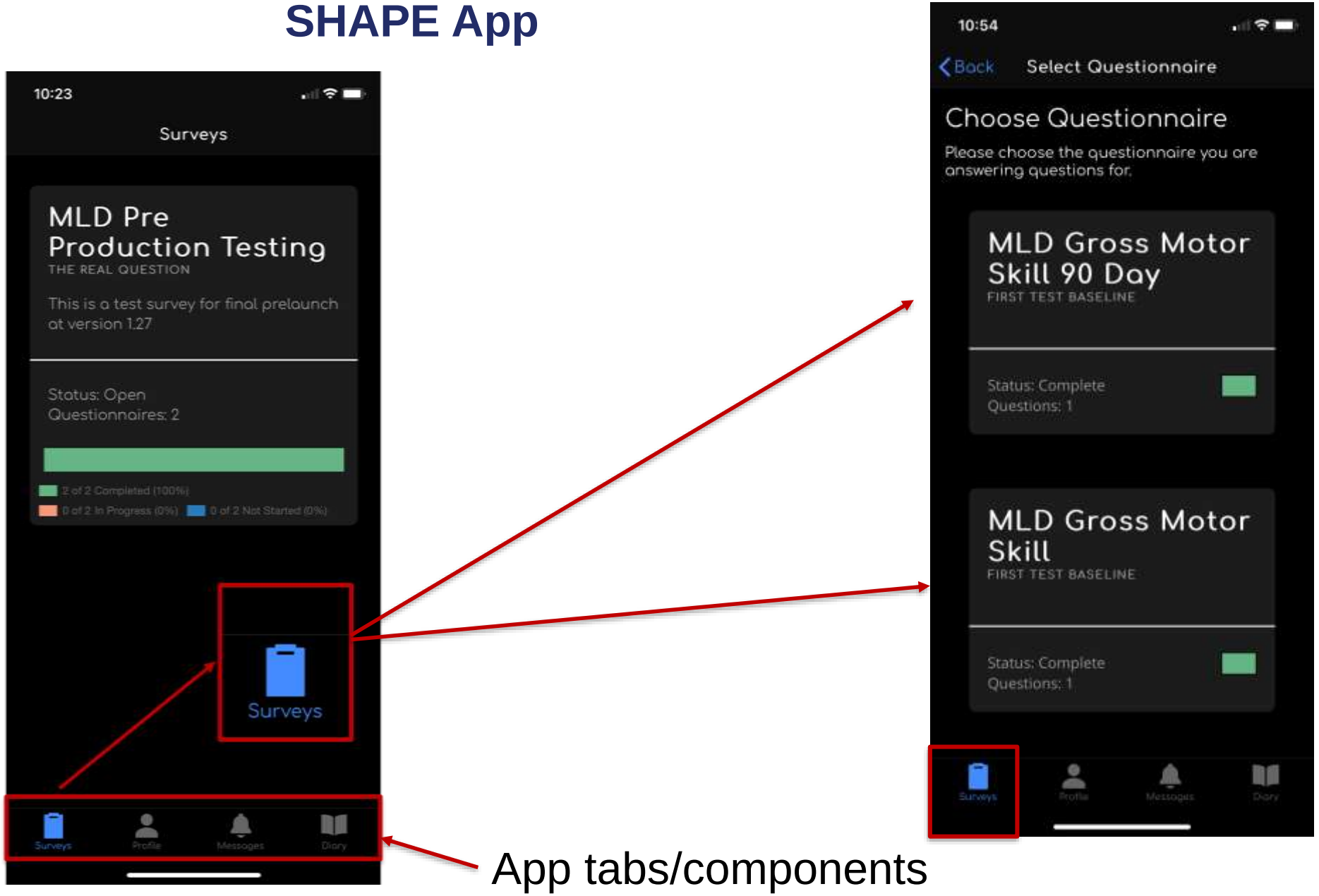
Integrate FDA/IBM Patient Experience App

Survey of Health & Patient Experience (SHAPE) App

1. Collect various endpoints:
   - Scheduled: Gross Motor Function Classification (primary endpoint)
   - Unscheduled: Relevant health events
2. Increase compliance; reduce missing data
3. Compare clinician- & caregiver-reported outcome measures (via video assessment study visits)
4. Explore linking EHR data

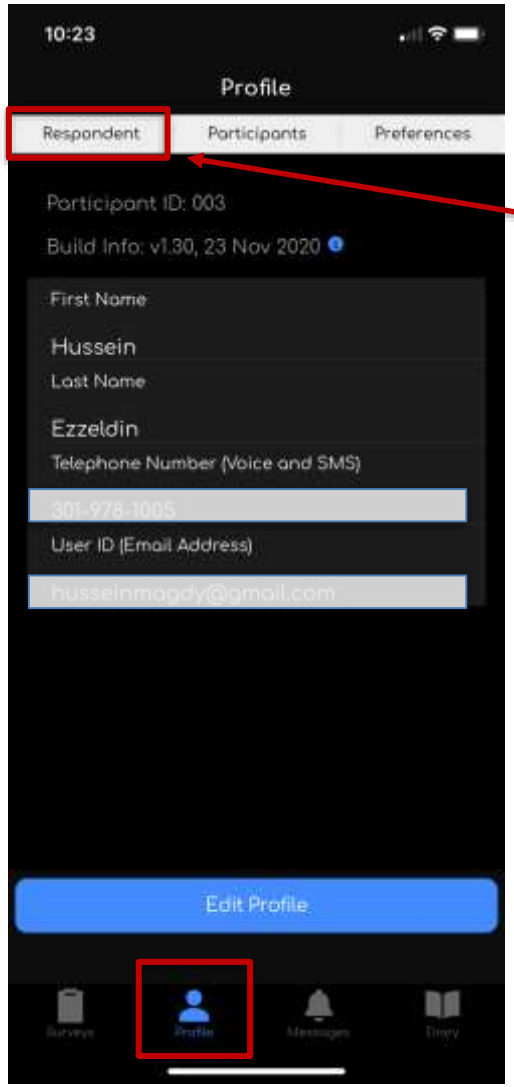
Integrate FDA/IBM Patient Experience App

SHAPE App

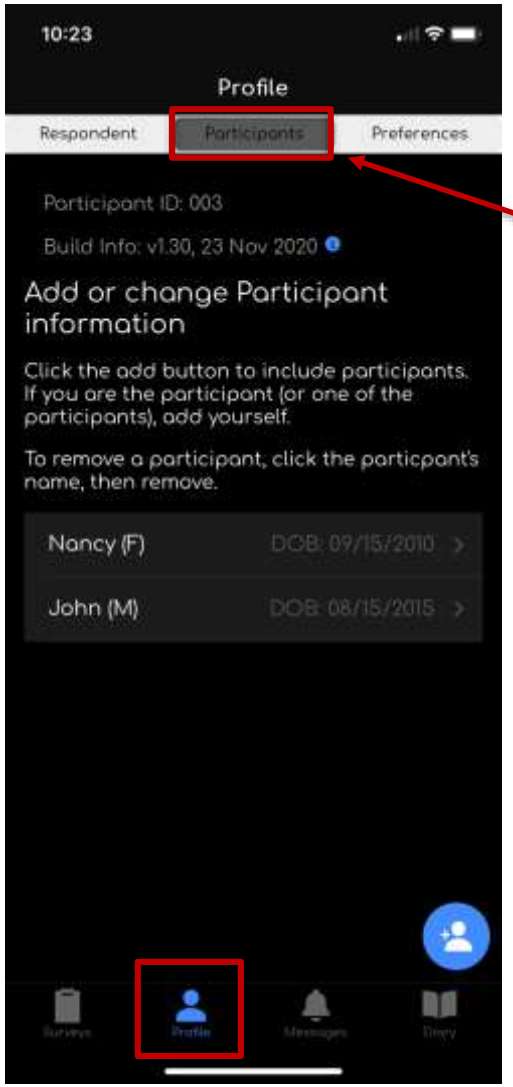


Integrate FDA/IBM Patient Experience App

SHAPE App



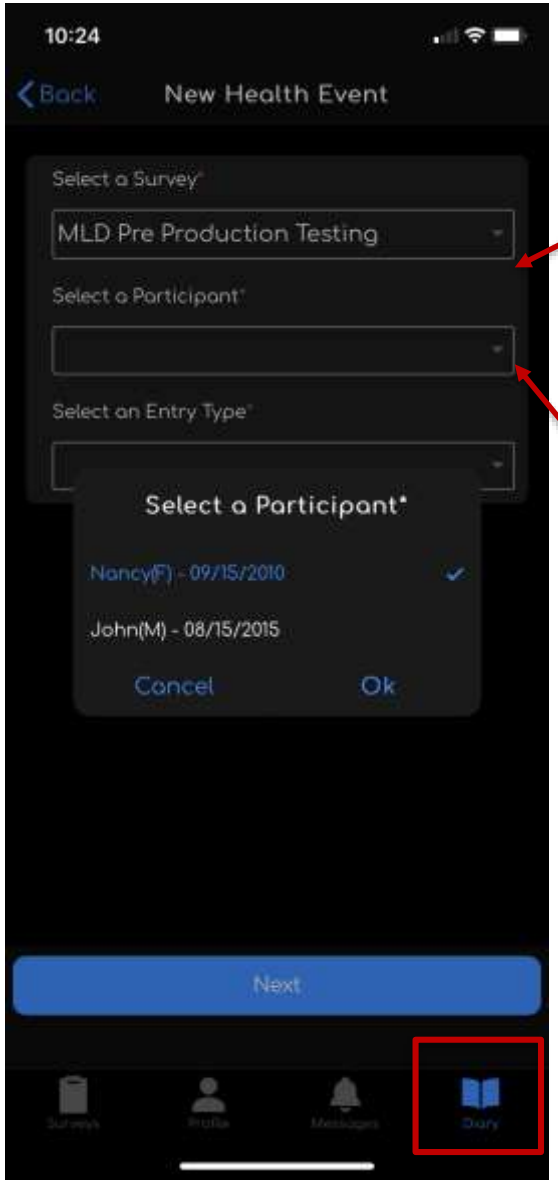
Respondent



Participant

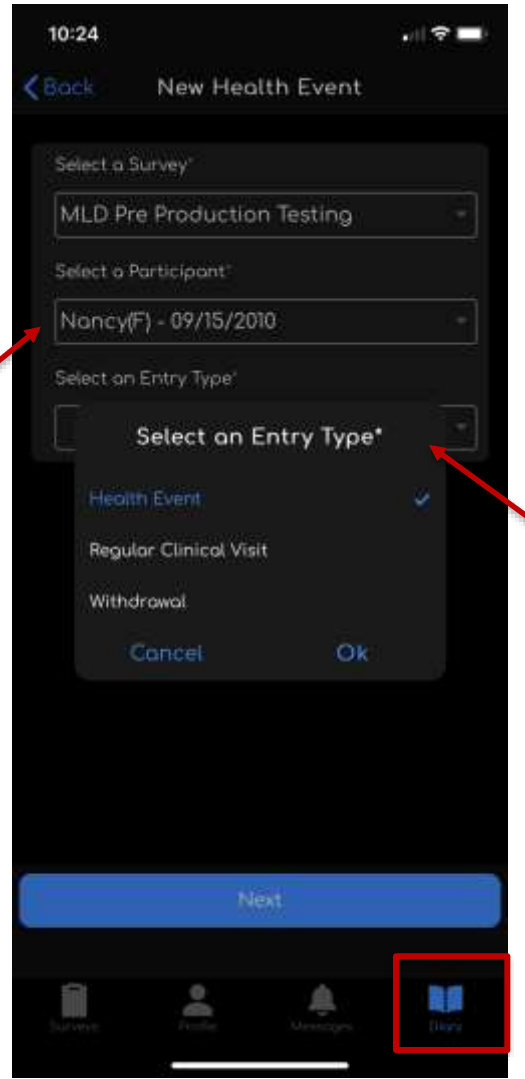
Integrate FDA/IBM Patient Experience App

SHAPE App



Survey/Study

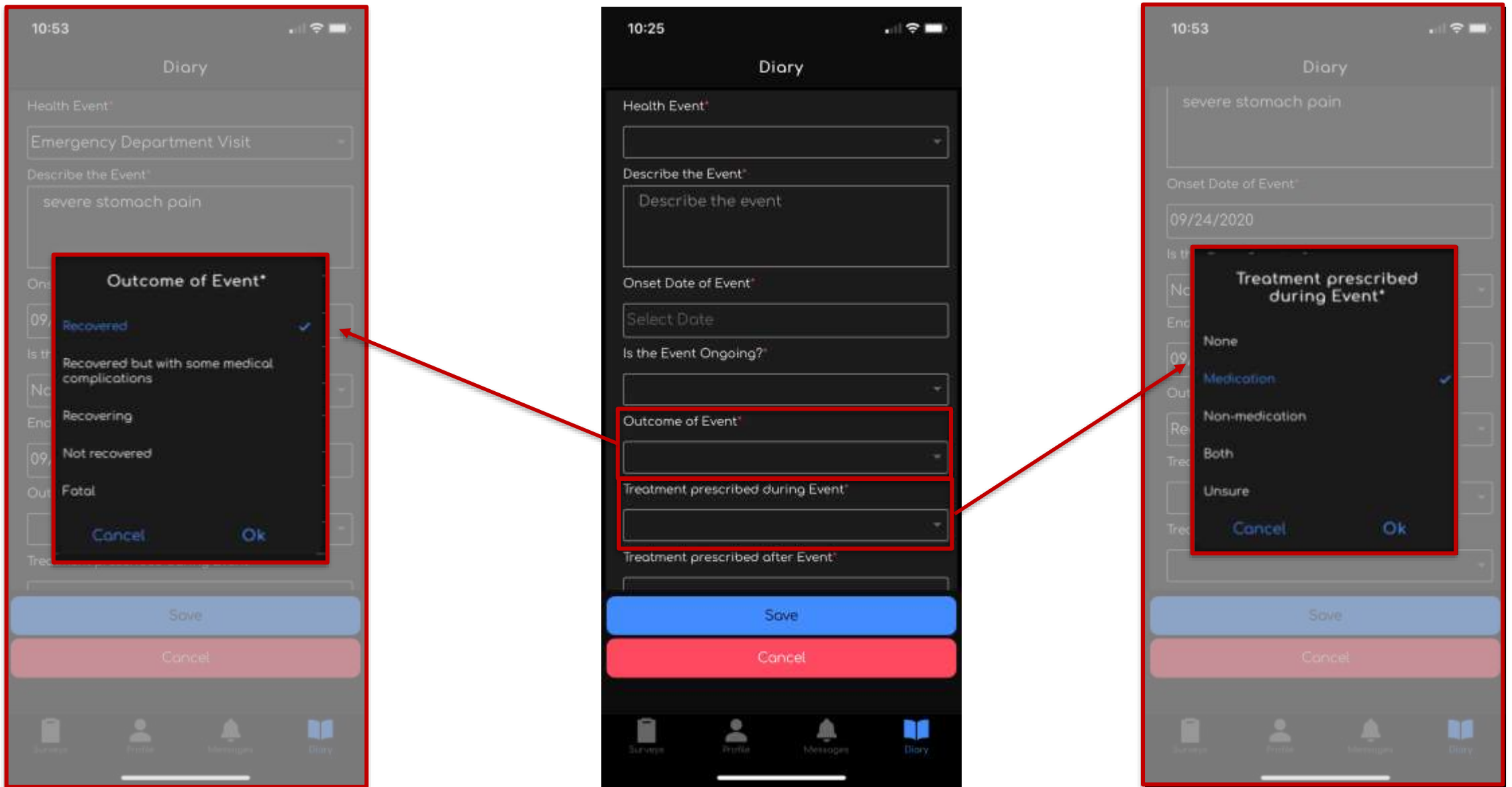
Participant



Event Type

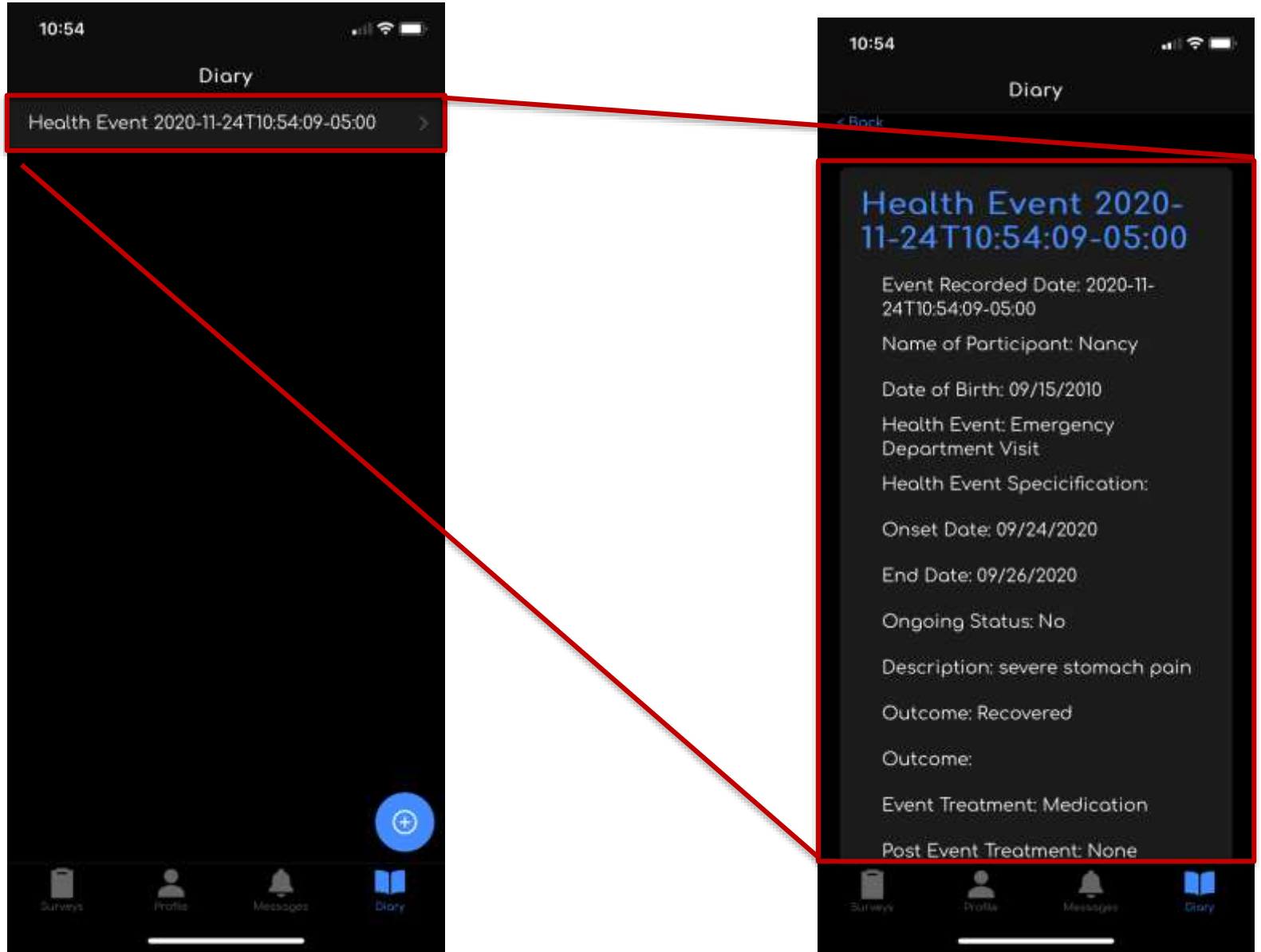
Integrate FDA/IBM Patient Experience App

SHAPE App

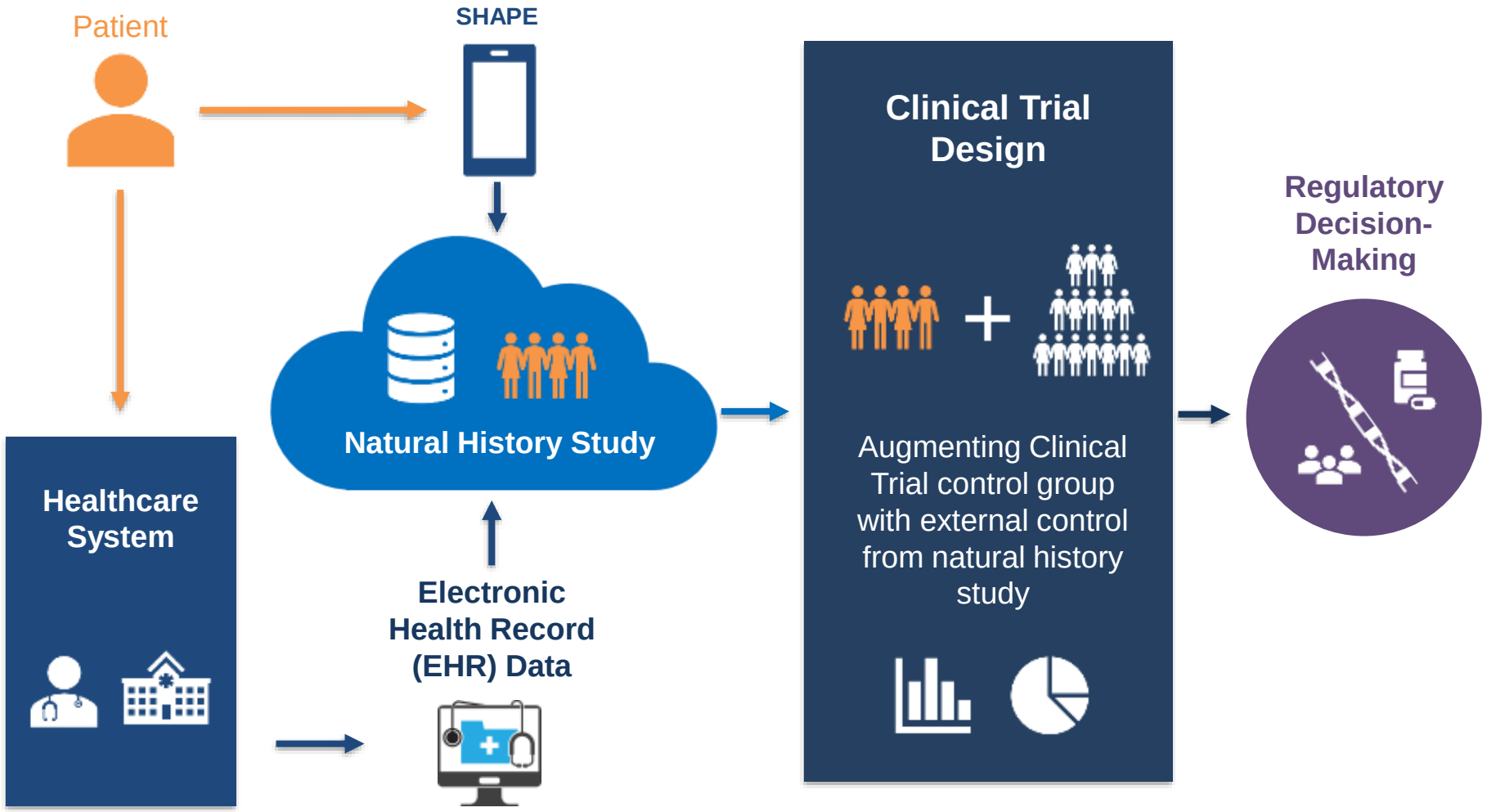


Integrate FDA/IBM Patient Experience App

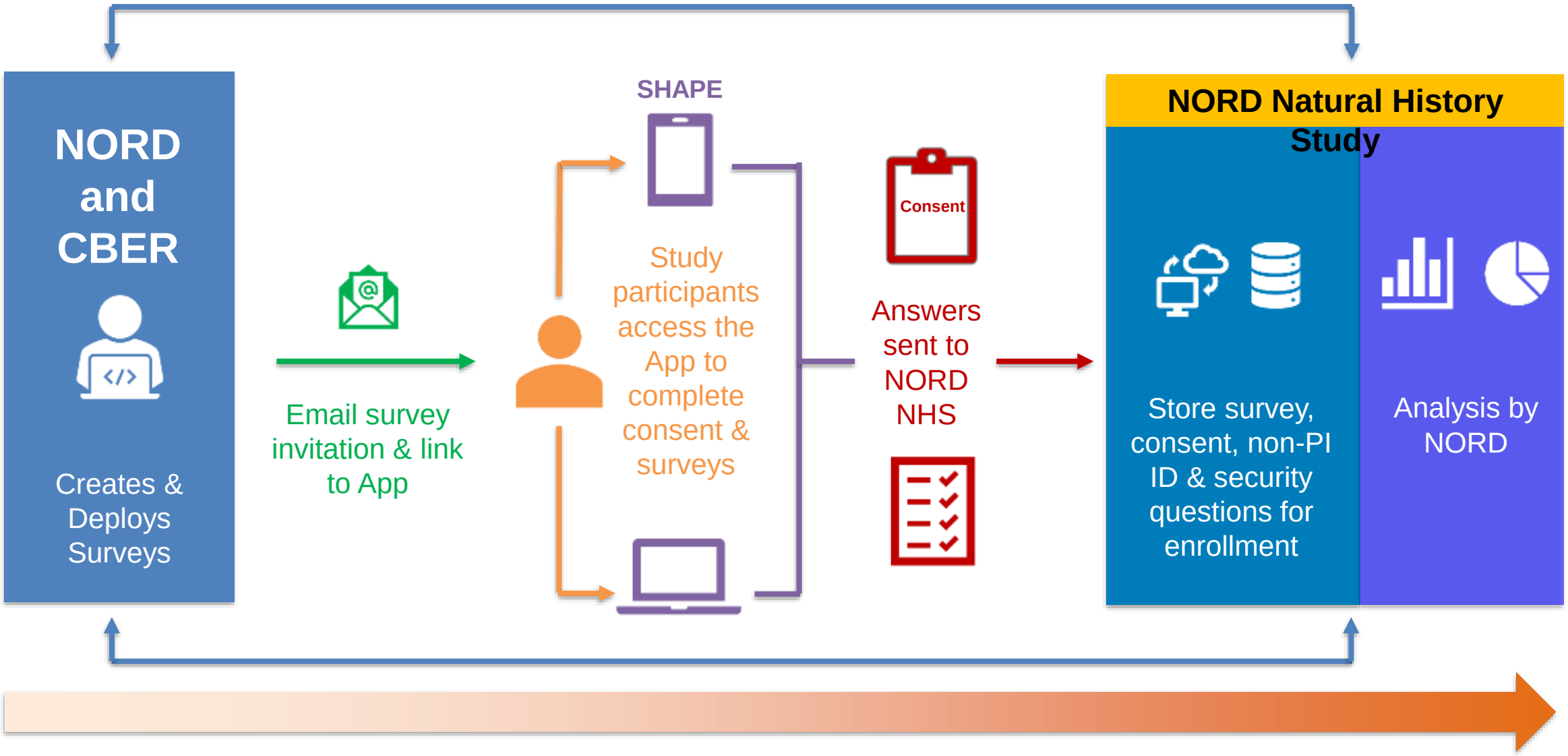
SHAPE App



Innovative Data Collection enhancing Clinical Trial Design



SHAPE Application



Take Away Messages

Patient preference information plays an increasingly important role to benefit patients and other stakeholders in the clinical trial enterprise.

Emerging breakthroughs of biologic products bring hope to address unmet medical needs; they also introduce new challenges for benefit-risk assessments.

Patient preference studies can be the key to address new challenges and make biologic innovations accessible to patients safely and efficiently.

Successfully harnessing advances in novel types of patient input requires close collaborations between patients, investigators, sponsors, and FDA.

Discussion and Questions?

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FDA U.S. FOOD & DRUG ADMINISTRATION

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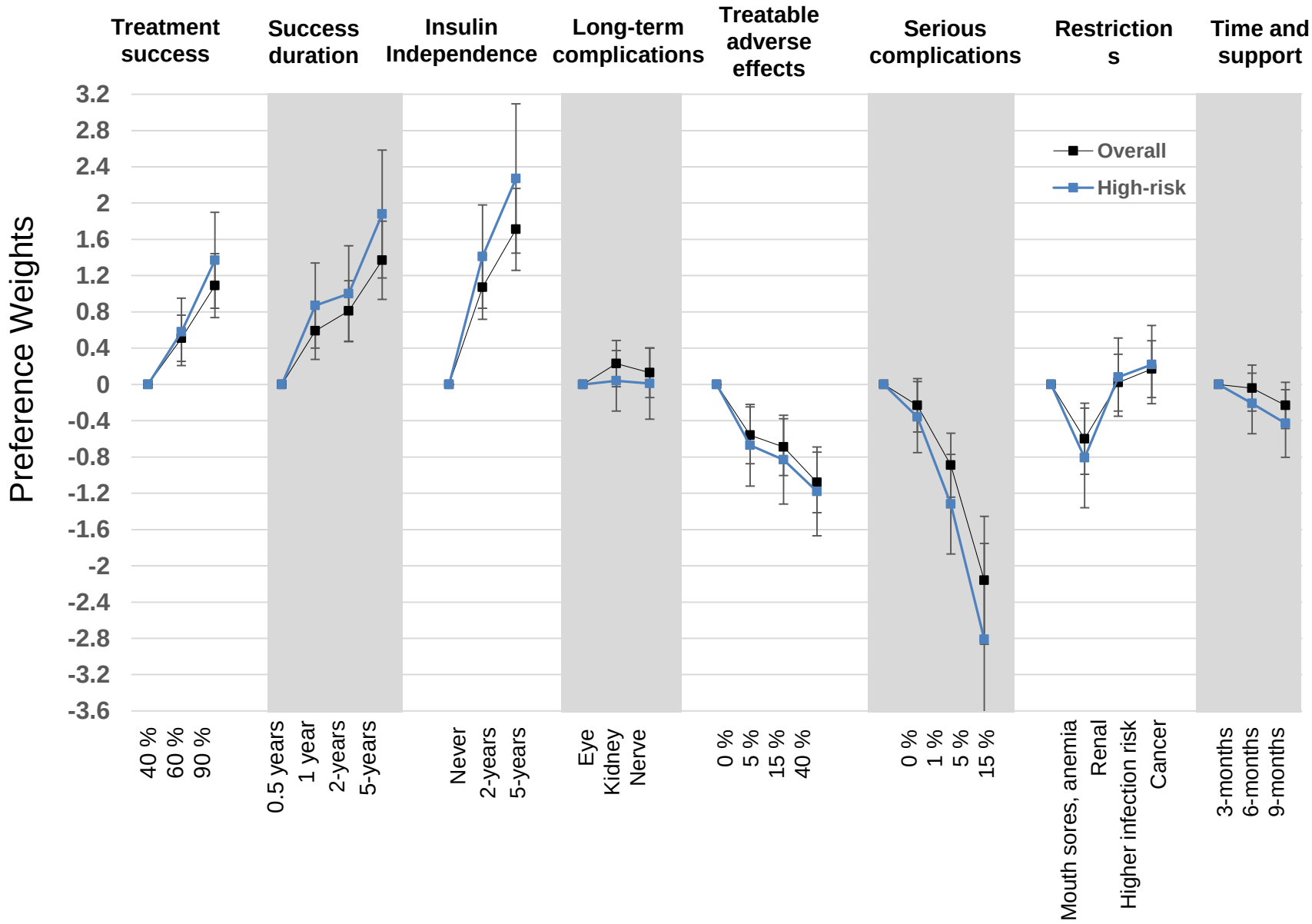
APPENDICES

Patient Clinical Characteristics

	Full Sample (N = 92) Mean (Range) / n (%)	High Hypoglycemic Risk Sample (N=78) Mean (Range) / n (%)
Diabetes Status		
Years with diabetes	22 (1-61)	23 (1-61)
Latest HbA1c		
Less than 6.5%	18 (19%)	15 (19%)
6.5% to 8%	58 (63%)	48 (62%)
Greater than 8%	14 (15%)	14 (18%)
Don't know	2 (2%)	1 (1%)
Severe Hypoglycemia Episodes (SHE)		
In the past 6 months	0.79 (0-20)	1 (0-20)
In the past 12 months	1.6 (0-40)	1.9 (0-40)
Diabetes Management		
Insulin	92 (100%)	78(100%)
Oral medications	4 (4%)	3 (4%)
Diet	37 (40%)	28 (36%)
Physical activity	32 (35%)	26 (33%)
Pancreas transplant	1 (1%)	0 (0%)
Islet cell transplant	0 (0%)	0 (0%)
Other	3 (3%)	2 (2%)
Ever Considered Islet Cell Transplant	25 (27%)	22 (28%)
Device Used for Insulin Injection		
Vial & Syringe	10 (11%)	8 (10%)
Pen (Self-Injecting)	39 (42%)	26 (33%)
Insulin Pump Single Loop	22 (24%)	22 (28%)
Insulin Pump Closed Loop	21 (23%)	21 (27%)
Self-Programmed Insulin Pump	8 (9%)	8 (10%)
Other	3 (3%)	3 (4%)
Frequency of Blood Glucose Check		
Rarely or never	7 (8%)	6 (8%)
Several times a week	18 (20%)	14 (18%)
1-3 times a day	20 (22%)	15 (19%)
4-6 times a day	18 (19%)	14 (18%)
More than 6 times a day	29 (31%)	29 (37%)

Results: preference weights – overall sample versus high-risk hypoglycemic group



Relative importance of attributes – overall sample versus high-risk hypoglycemic group