U.S. FOOD & DRUG ADMINISTRATION

Meeting #2 in a Series of Public Meetings on Patient Focused Drug Development

Using Methods from PFDD Guidance 1 and Guidance 2 as Tools for Including Patient Experience Data in Clinical Trials: *Lessons Learned about Data Collection and Analysis*

July 25, 2022

#PFDD

Disclaimer

The views expressed in the following presentations are those of the individual speakers and do not necessarily represent an official FDA position.

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Welcome

Shannon Cole, MS
Office of the Center Director
Center for Drug Evaluation and Research

Agenda

11:00 a.m.	Welcome
11:05 a.m.	Opening Remarks
11:10 a.m.	Session I: Data Collection
11:50 a.m.	Session II: Ideas in Practice
12:35 p.m.	Session III: Question and Answer
1:00 p.m.	End

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Opening Remarks

Theresa Mullin, PhD
Associate Director for Strategic Initiatives
Center for Drug Evaluation and Research

Session 1: Data Collection

Objective

Provide a focused overview of data collection and analysis with an emphasis on practical implementation

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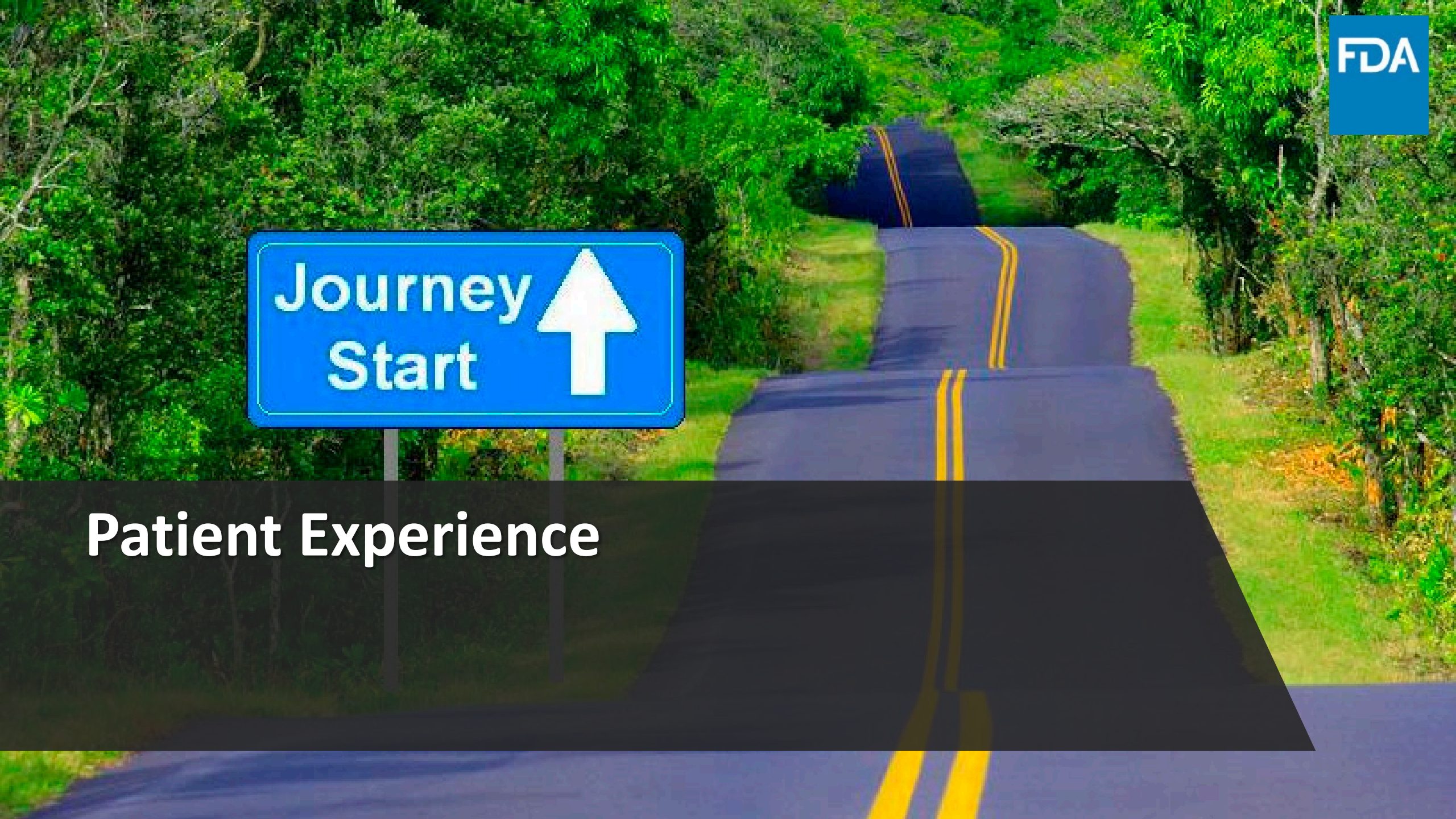
Leveraging Social Media to Capture the Patient Experience

Selena R. Daniels, PharmD, PhD
Team Leader, Division of Clinical Outcome Assessment
Office of Drug Evaluation Science
Center for Drug Evaluation and Research



Patient Experience

Importance of Patient Experience Data

Regulatory Use of Patient Experience Data

- Clinical trial design
- Trial endpoint development and selection
- Regulatory reviews including benefit-risk assessments


Patient-Focused Drug Development: Collecting Comprehensive and Representative Input
Guidance for Industry, Food and Dr
Administration Staff, and Other
Stakeholders
June 2020
Procedural
Patient-Focused Drug Development: Methods to Identify What Is Important to Patients
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders
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)
February 2022
Procedural


FDA
GUIDANCE

Collection of Patient Experience Data

QUALITATIVE

QUANTITATIVE

MIXED METHODS

Use of Social Media for Data Collection

STILL LEARNING

- Hypothesis generation
- Signal detection
- Supplement to Traditional Research

Considerations For Use of Social Media

CHOOSE AN APPROPRIATE RESEARCH DESIGN

CAREFULLY SELECT SOCIAL MEDIA SOURCE

USE APPROPRIATE METHODS TO COLLECT AND ANALYZE DATA

ASSESS DATA QUALITY

PROTECT PRIVACY

Summary

- Limited practical experience with use of social media in regulatory decision making.
- Social media may be an approach to collect qualitative and/or quantitative data to capture the patient experience.
- Use scientifically sound methods to collect robust, meaningful, sufficiently representative patient input to inform medical product development and regulatory decision making.
- Considerations for using social media data include but are not limited to the research design, social media source, data collection and analysis, data quality, and privacy.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Data Collection and Analysis: A Regulatory Perspective

Michelle Campbell, PhD
Office of Neuroscience
CDER/OND

Lili Garrard, PhD
Division of Biometrics III
CDER/OTS/Office of Biostatistics

When Developing a Treatment

What we hope for

Reality

Study Design

- When important aspects of study are not fully considered, it can potentially lead to:
  - Disconnect trade-off between patient expectations of trial and what the trial can achieve
  - Potential risk of missing data for endpoints intended for labeling
  - Lack of sufficient evidence to support labeling for non-primary endpoints
  - Uncertainty in interpretation of results

Study Design to Support Labeling

- Potential risk of missing data for endpoints intended for labeling or;
- Lack of sufficient evidence to support labeling for non-primary endpoints
  - Your study design should be well thought out to include the needed data to support all labeling claim
  - A poor study design can lead to missing data and impedes the ability to use the data for regulatory decision making

  Or
  - Unable to consider other supportive endpoints for labeling
- When designing your trial and considering potential labeling claims, your study design needs to reflect the rigor needed to collect the evidence to support these claims
  - Considerations should be taken on patient burden and minimizing missing data opportunities

Balancing Patient Expectations

- Your study design to collect data to support the trial's endpoints should reflect what is important to patients
  - There should be a balance between:
    - The mechanism of action of the medical product,
    - What is important to patients and,
    - What aspect of the disease will change from treatment
  - When this balance does not occur, incorrect data can be collected which could be unable to inform a regulatory decision

Interpretation of Data

- When we do not measure the right concept

  Or

- The concept is not measured well
  - Drawing reliable inference on benefit/risk
  - Not generalizable to target population
- Doing good measurement to minimize variability will help making treatment effect more clear
  - Especially in cases when a moderate effect is found

Clinical Meaningfulness

- There are multiple opportunities to assess clinical meaningfulness from patients during development of a medical product
- Multiple methods to assess meaningfulness should be considered
  - The choice of methodology can impact the ability of the data to inform regulatory decision making

Exit Interviews

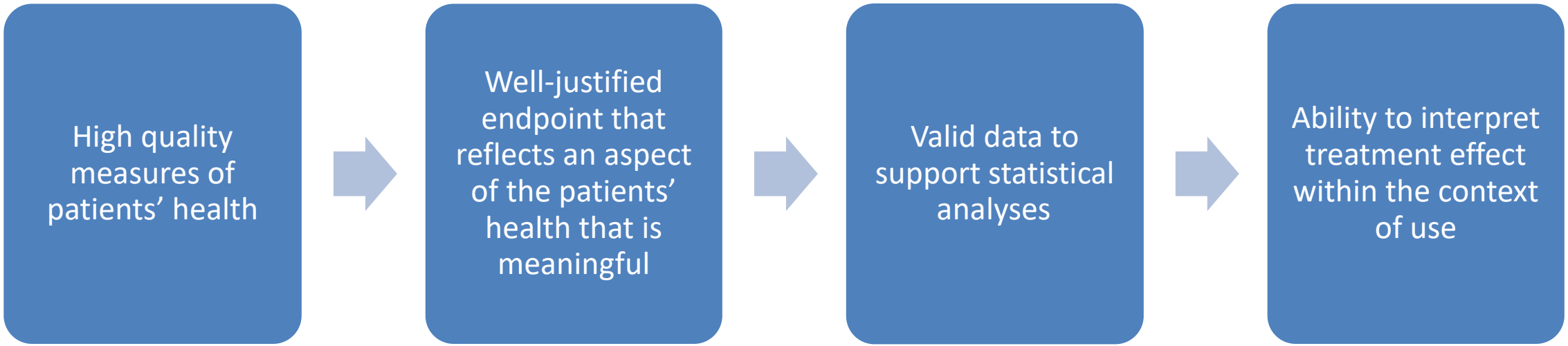
- Exit interviews can be useful if well designed to answer a specific question
- Exit interviews that are not optimally designed may not be able to inform regulatory decision making
- An exit interview may be less informative when added later during an active trial

Considerations for Future Work

- Begin discussing early and often with therapeutic review division to facilitate optimal clinical trial design and selection of endpoints (and appropriate data collection methods) that are most clinically meaningful

- Develop a scientifically sound analysis plan that addresses methodological, quality, and completeness issues

A Statistician's (Simplified) Wish



A Statistician's (Simplified) Challenge

High quality measures of patients' health

Valid data to support statistical analyses

Ability to interpret treatment effect within the context of use

Challenges with not having high quality measures make it difficult to move forward

Example Common Questions Received

- **Assuming** that content validity of COA ABC has been established for this patient population, does the Agency agree that the proposed quantitative validation plan will be sufficient to support the use of COA ABC in the pivotal trial?
- Does the Agency agree that **if** construct validity is addressed with the COA XYZ, then the instrument can support the determination of efficacy?

High Quality Measures of Patients' Health

- A **measure** is a means to capture data (e.g., a questionnaire) plus all the information and documentation that supports its use. Generally, that includes
  - Clearly defined methods and instructions for administration or responding
  - A standard format for data collection
  - Well-documented methods for scoring, analysis, and interpretation of results in the target patient population
- **High quality** = Need to do well (or to the best of our ability) on all attributes of a measure

Draft FDA guidance for industry, Food and Drug Administration staff, and other stakeholders Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (June, 2022)
https://www.fda.gov/media/159500/download

Representativeness of Patient Experience Data

- Regardless of Research methods (i.e., qualitative, quantitative, mixed methods), patients in the study sample should be representative of the target population so that study findings can be reliably extended to the target population of interest
  - Example **problem**: Initial patient experience data generated in patient sample with minimal symptom severity and pivotal study targeting more symptomatic patient population
- Important to establish representativeness before embarking on further quantitative analyses

Common Survey Response Options

- Dichotomous (yes/no, true/false)
  - E.g., have you ever been diagnosed with ABC disease?
- Numeric rating scale
  - E.g., 0-10 measuring worst pain severity
- Verbal rating scale
  - E.g., 4-point (none, mild, moderate, severe) measuring symptom severity

Example Considerations for Standardized Data Collection

- Standardized instructions and directions for data collection
- Standardized training for study personnel
- Standardized environment for participants to perform a task(s)
- Standardized devices, e.g., provide the same tablet for all participants to report responses
- Standardized case report form

Missing Data

- Missing data is inevitable; should always have a plan to handle missing data but it is important to have procedures in place to prevent missing data
- Gain understanding on reasons for missingness
  - Patients do not all experience the symptoms or functional impairment
  - Patients do not have sufficient understanding of instructions and/or tasks needed for data collection
  - Patients are not informed about the importance of data collection and how data will be used
  - Patients may experience burden due to instrument design and/or trial design
  - Programming errors
  - Informative missing vs. missing at random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Inclusive Research: Managing Barriers to Self-Report

Naomi Knoble, PhD

Division of Clinical Outcome Assessment

Patient-Focused Research

- Two broad types of barriers to self-report:
  1. Research methods are inaccessible to patients
  2. Patient is unable (e.g., related to child development, impacts of medical condition)

- Patient-focused research needs to be **inclusive** and **patient-centered** so that patients can successfully participate to their fullest ability.

Inclusive Research: Language and Culture

- Questions should be culturally sensitive, in the **patient's language or dialect**
- Seek to understand how cultural differences may impact patient responses
- For all studies, **conduct translatability assessments** early in the study development

Acquadro et al., 2018; Eremenco et al., 2018; Wild et al., 2005

Inclusive Research: Accommodating Abilities

- Ensure usability of study materials by patients, for example
  - **Low vision:** Use written materials with screen readers, large/adjustable font
  - **Fatigue:** Abbreviate study to minimize patient participation burden
- Pilot test study materials with patients for usability

Inclusive Research With Children

- Engage young children who are capable of self-report in developmentally familiar tasks
  - Drawing activities
  - Facilitate interviews with props, illustrations
  - Abbreviate activities for limited attention spans
- Plan for parent/caregiver presence and/or assistance support child participation

Matza et al., 2013

Inclusive Research: Patients with Developmental and Intellectual Differences

- **Include patients who are capable of self-report**
- Perspectives of patients with developmental and/or intellectual disabilities matter in medical product development

Inclusive Research: Caregiver perspectives

- For patients who cannot report for themselves, elicit caregiver perspectives on **observable** aspects of the patient's health
  - Signs, events, behaviors that were observed

Access and Inclusion for Representation

- Implement **inclusive strategies** for public outreach and education to foster patient engagement
  - If patients have limited internet access, meet in-person at accessible location
  - Provide access to study required technology for patients otherwise without access

FDA Guidance (2020) *Enhancing the Diversity of Clinical Trial Populations*
https://www.fda.gov/media/127712/download

Inclusive Research

- Patient-focused research needs to be **inclusive** and **patient-centered**
  - Language and culture considerations
  - Accommodating abilities with accessibility modifications
  - Inclusive research practices with children
  - Integrating caregiver perspectives

- Patient-focused research depends on accessible, inclusive practices so that all patient voices can be heard.


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Session 2: Ideas in Practice

Using Methods from PFDD Guidance 1 and Guidance 2 as Tools for Including Patient Experience Data in Clinical Trials: *Lessons Learned about Data Collection and Analysis*

Development of Research Study Materials: Lessons Learned

Robyn T. Carson, MPH
Vice President & Head, Patient Centered Outcomes Research
AbbVie

July 25, 2022

Disclaimer

The views expressed within this presentation are mine and do not represent those of AbbVie.

PFDD Guidance Series Provides Best Practices & Guiding Principles for Development of Patient Experience Data

GUIDANCE 1	GUIDANCE 2	GUIDANCE 3	GUIDANCE 4
Identifying research questions and developing a sampling strategy to collect representative patient input; data collection, management and analysis	Methods to elicit detailed, unbiased, and comprehensive input from patients, patient groups, and caregivers	Using patient input to develop or identify appropriate COAs for use in clinical trials	Developing COA-related clinical trial endpoints based upon patient input; interpreting those endpoints
Who is the Target Patient Population?	***What Concepts Matter Most?***	***What is the Right Assessment?***	***What is the Right Endpoint Definition?*** ***Is the Observed Treatment Effect Meaningful?***

Conducting Research with Patients to Identify Concepts that Matter: Key Considerations

Conduct Background Research to Inform Study Design

- Develop preliminary conceptual model and identify research gaps
- Understand competitive landscape & regulatory precedence

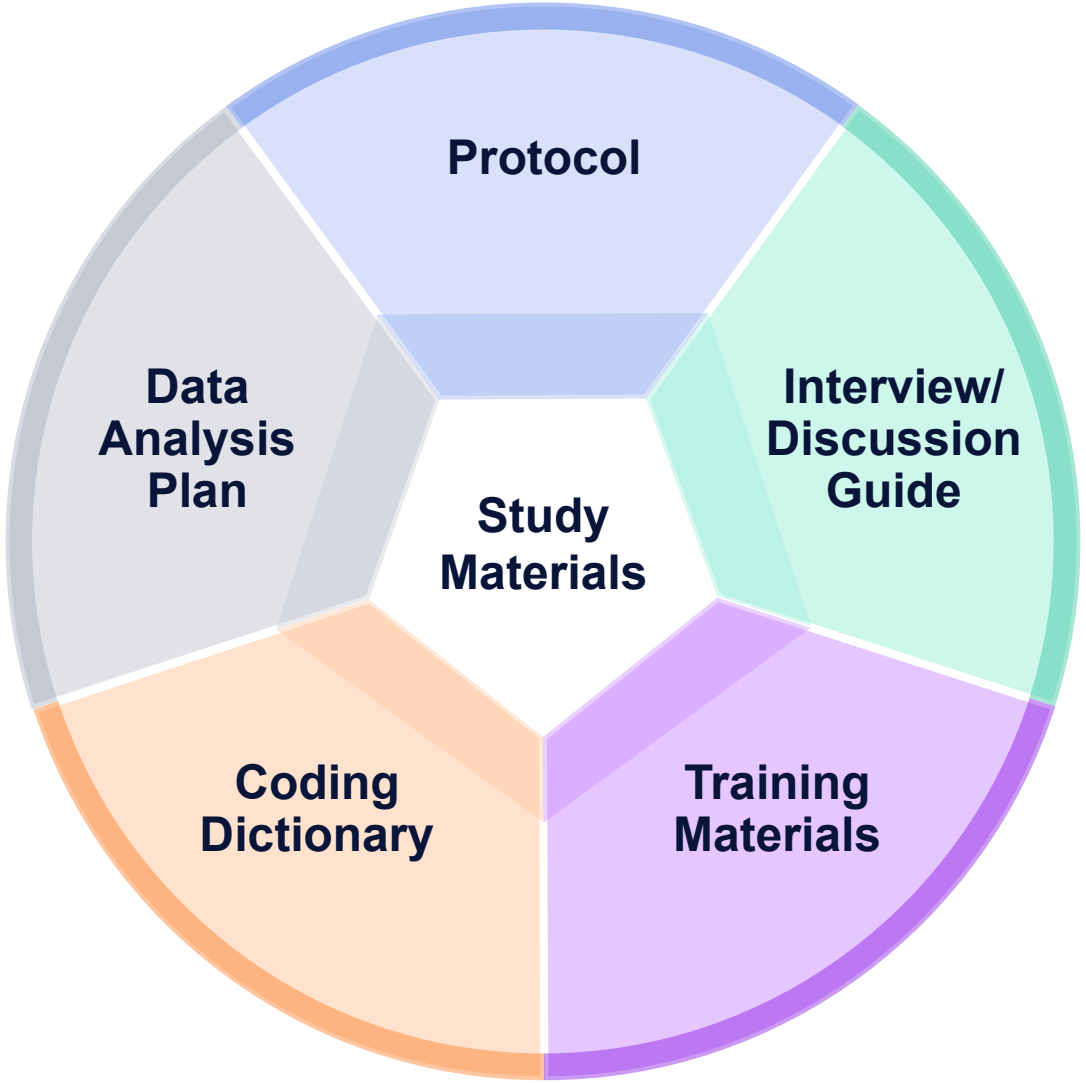
Align Research Question & Purpose to Methodology

- One size does not fit all
- Multiple methods can be utilized to inform understanding of unmet needs and patient experience with condition & treatment options

Develop Representative Sampling Strategy for Global Development Programs

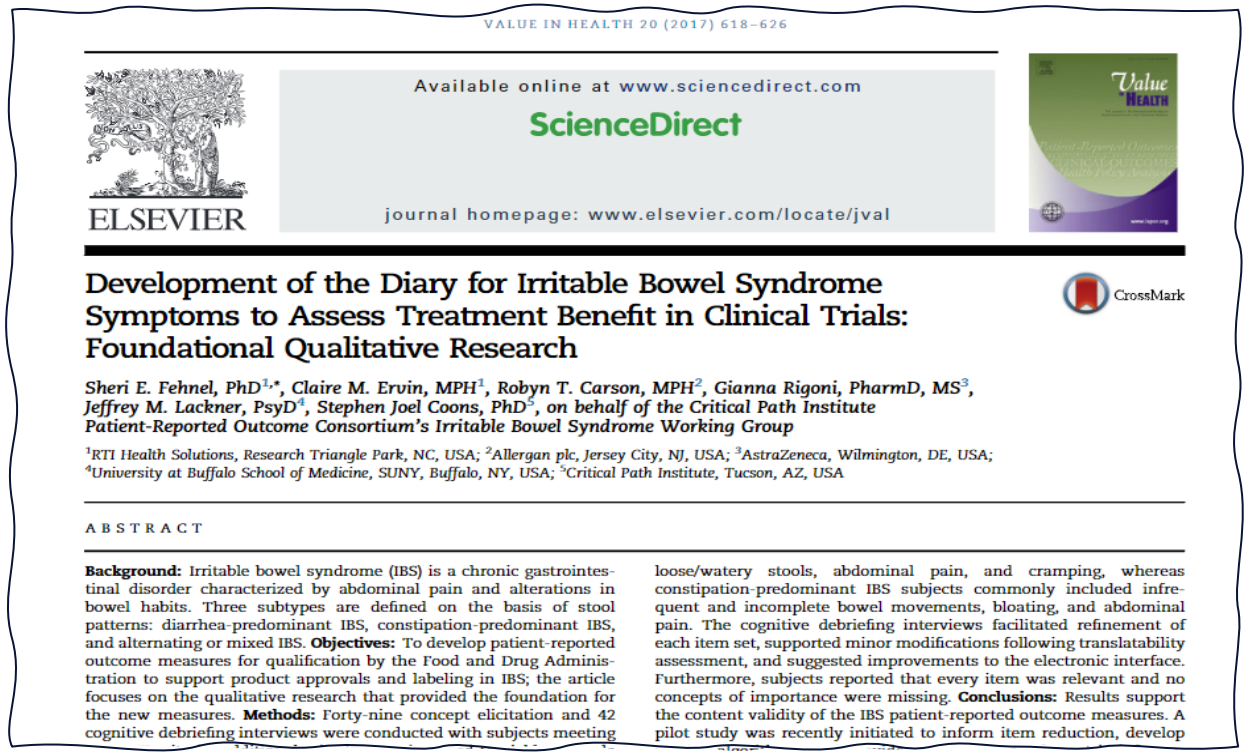
- Sample size dependent on research question, target patient population
- Align study sample with known target patient population of clinical development program
- Ensure diversity & representativeness

Developing Study Materials: Challenges & Lessons Learned



Measuring What Matters to Patients:
Case Study in Irritable Bowel Syndrome with Constipation

Elevating the Patient Voice through Identification of Concepts that Matter



VALUE IN HEALTH 20 (2017) 618–626

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

Development of the Diary for Irritable Bowel Syndrome Symptoms to Assess Treatment Benefit in Clinical Trials: Foundational Qualitative Research

Sheri E. Fehnel, PhD[1,], Claire M. Ervin, MPH[1], Robyn T. Carson, MPH[2], Gianna Rigoni, PharmD, MS[3], Jeffrey M. Lackner, PsyD[4], Stephen Joel Coons, PhD[5], on behalf of the Critical Path Institute Patient-Reported Outcome Consortium's Irritable Bowel Syndrome Working Group*

[1]RTI Health Solutions, Research Triangle Park, NC, USA; [2]Allergan plc, Jersey City, NJ, USA; [3]AstraZeneca, Wilmington, DE, USA; [4]University at Buffalo School of Medicine, SUNY, Buffalo, NY, USA; [5]Critical Path Institute, Tucson, AZ, USA

ABSTRACT

Background: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain and alterations in bowel habits. Three subtypes are defined on the basis of stool patterns: diarrhea-predominant IBS, constipation-predominant IBS, and alternating or mixed IBS. **Objectives:** To develop patient-reported outcome measures for qualification by the Food and Drug Administration to support product approvals and labeling in IBS; the article focuses on the qualitative research that provided the foundation for the new measures. **Methods:** Forty-nine concept elicitation and 42 cognitive debriefing interviews were conducted with subjects meeting loose/watery stools, abdominal pain, and cramping, whereas constipation-predominant IBS subjects commonly included infrequent and incomplete bowel movements, bloating, and abdominal pain. The cognitive debriefing interviews facilitated refinement of each item set, supported minor modifications following translatability assessment, and suggested improvements to the electronic interface. Furthermore, subjects reported that every item was relevant and no concepts of importance were missing. **Conclusions:** Results support the content validity of the IBS patient-reported outcome measures. A pilot study was recently initiated to inform item reduction, develop

Lessons Learned

1. **Patient Input & Saturation**
2. **Multi-stakeholder Effort**
3. **Engagement & Alignment with FDA**

*Granted qualification by the FDA for measurement of IBS-C symptom severity in December 2020 (https://www.fda.gov/drugs/clinical-outcome-assessment-coa-qualification-program/ddt-coa-000005-diary-irritable-bowel-syndrome-symptoms-constipation-dibss-c)

DIBSS-C, Diary for Irritable Bowel Syndrome Symptoms – Constipation; IBS-C, irritable bowel syndrome with constipation

Key Takeaways

Plan early and allow sufficient time for development of study materials

Leverage the FDA PFDD Guidance series for best practices & guiding principles

Collaborate with key internal and external stakeholders to optimize value of evidence

Reflections on the utilization of social media data: an industry perspective

Using Methods from PFDD Guidance 1 and Guidance 2 as Tools for Including Patient Experience Data in Clinical Trials: Lessons Learned about Data Collection and Analysis

Tom Willgoss, Roche

Conflicts of interest

Any opinions or information given by me are based on general industry standards and not the opinions of Roche. Any information given at the presentation should be used and disseminated by attendees at their discretion and Roche shall not be liable for any information relied upon by you or the attendees as a result of the presentation.

Agenda

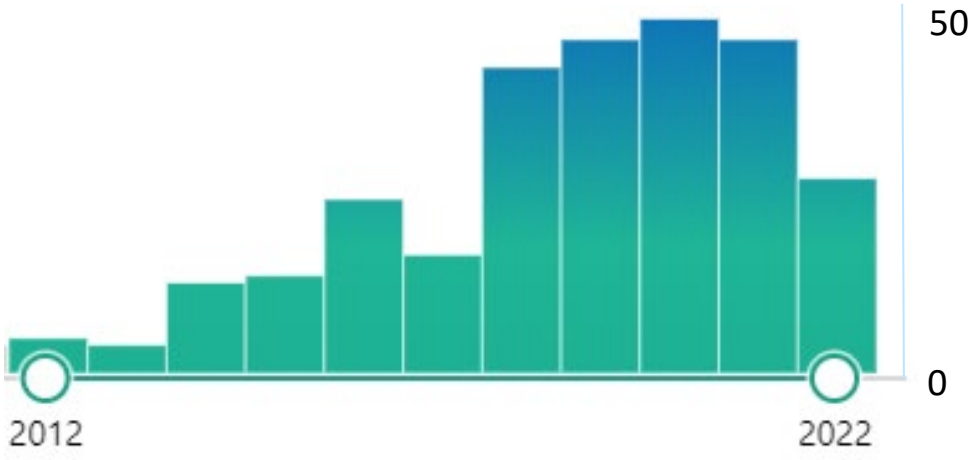
- A recent history of social media data
- Brief recap on social media data as described in PFDD 1 & 2
- How are we using social media data in our work?
- Reflections & remaining questions

A recent history of social media data utilization in our field

A lot has changed in a few decades

"There remain some important barriers to widespread use, including regulatory acceptance"

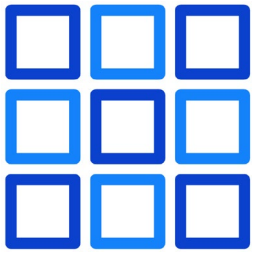
PubMed.gov "Social Media Data" AND "Patient-reported Outcomes"



Social media data remains a largely untapped insights resource for patient-centered drug development

Eliciting additional (embarrassing) concepts

Speed



Automation

Scalability & reach

Inclusion of hard to reach populations

Diversity of sample

PFDD Guidance 1 & 2 are a major step forward

Collecting Comprehensive and Representative Input

First description of social media and verified patient communities under ‘Data collection methods’.

Recognition that social media data may be valuable in early research or as a supplement for traditional methods.

Discusses strengths and limitations of generating patient input using various online methods, including social media.

Methods to Identify What is Important to Patients

Further acknowledgement of social media as an approach to collect qualitative and/or quantitative data.

Focus on practical considerations when using social media data e.g.

- Research design
- Source
- Analytical methods
- Data quality
- Privacy

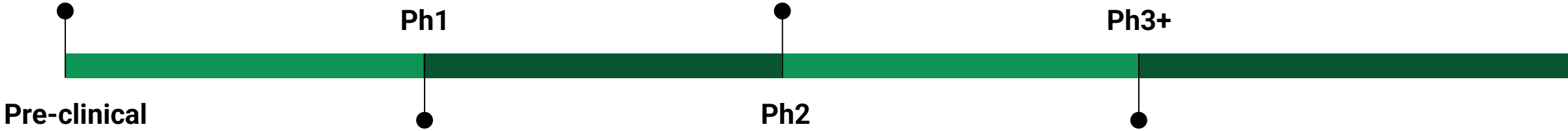
Social media data are supporting patient-centered drug development across the product life cycle at Roche

Early understanding of unmet needs & patient journey

Identify areas of high unmet need to support selection and targeting of new therapeutics, incl. Identification of sub-populations (COPD) [1]

Supporting selection/development of COAs and endpoints

Relevance of COA items, gathering insights on language use (Ophthalmology, Pan-Therapeutic)



Developing conceptual models

Complementary source of data to identify what outcomes matter most to patients. (Parkinson's disease, Angelman syndrome) [2]

Benefit-risk assessments

Safety insights to enable robust risk characterization (Breast cancer, RA) [3]

[1] Freeman TCB, et al. (2021). A Neural Network Approach for Understanding Patient Experiences of Chronic Obstructive Pulmonary Disease (COPD): Retrospective, Cross-sectional Study of Social Media Content. JMIR Med Inform, 11;9(11):e26272.

[2] Staunton, H., et al. (2022). A Patient-Centered Conceptual Model of Symptoms and Their Impact in Early Parkinson's Disease: A Qualitative Study. Journal of Parkinson's disease, 12(1), 137.

[3] Quartey, G, et al. (2022) Using Social Media To Determine Outcomes That Matter Most To Patients. Zenodo. 10.5281/zenodo.5904128. https://zenodo.org/record/5904129#.YtGBZS-B39C

Where are we today and what questions remain?

PFDD Guidance 1 and 2 supports the (pragmatic) use of social media data:

- Provides clear acknowledgement that these (robust) data are acceptable as a complimentary source of patient experience data
- Inclusion of quantitative social media data provides opportunities to generate further insights
- Strengths and limitations of various methods, as well as guidance on how to acknowledge and overcome these is particularly welcome
  - Verifying diagnosis
  - Data quality (e.g. bots)
  - Data privacy

Open questions include:

- Are there situations where social media data alone is enough? Is this likely to evolve?
- How are FDA using the data and what are the expectations of methodology, data quality, analysis plans etc.?
- Data privacy remains a complex and evolving challenge

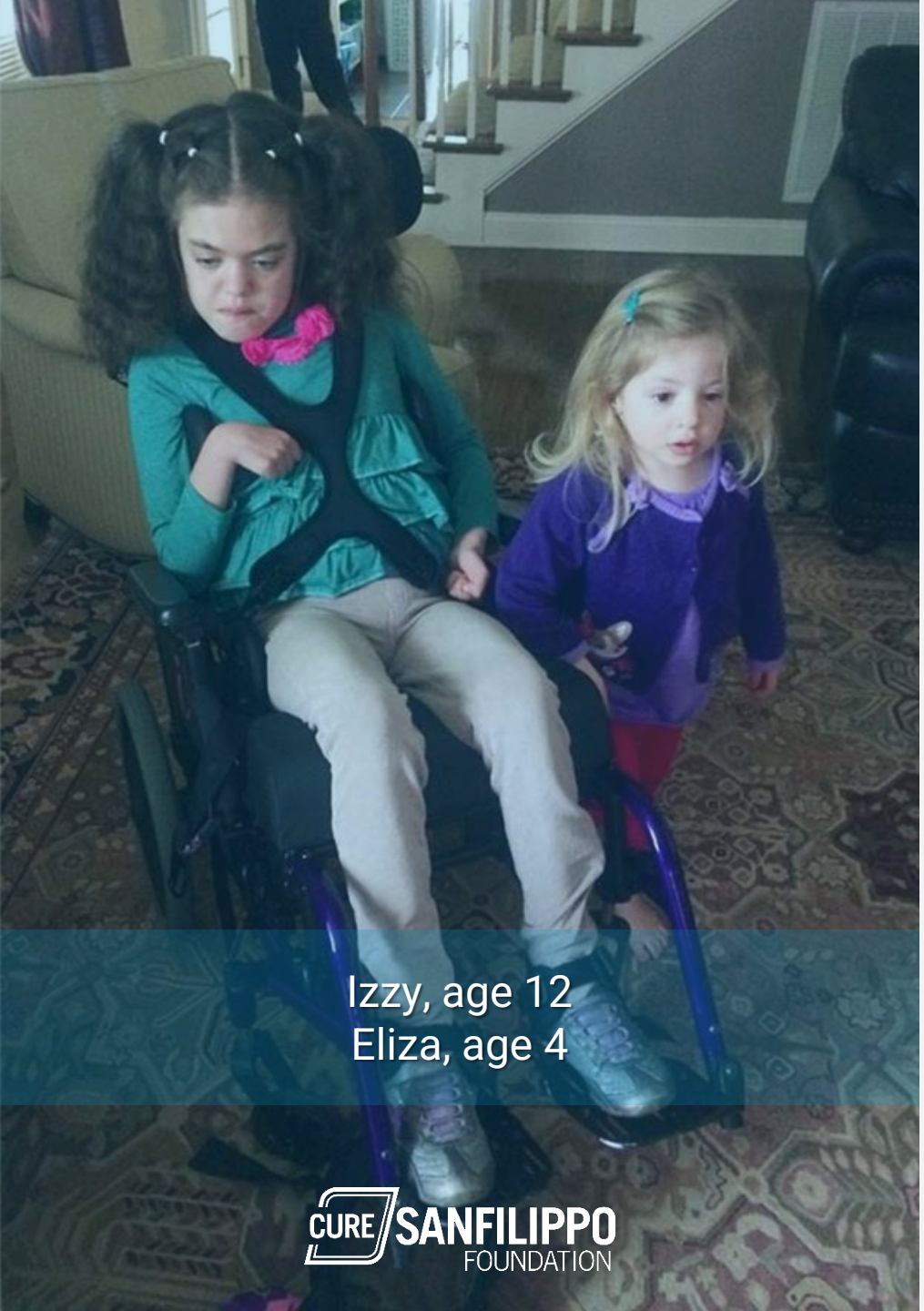
CURE SANFILIPPO FOUNDATION

Sanfilippo Syndrome (MPS III)

Study of Caregiver Treatment Priorities and Unmet Need

July 25, 2022

Cara O'Neill, MD, FAAP
Chief Science Officer & Co-Founder
Cure Sanfilippo Foundation



What is Sanfilippo Syndrome?

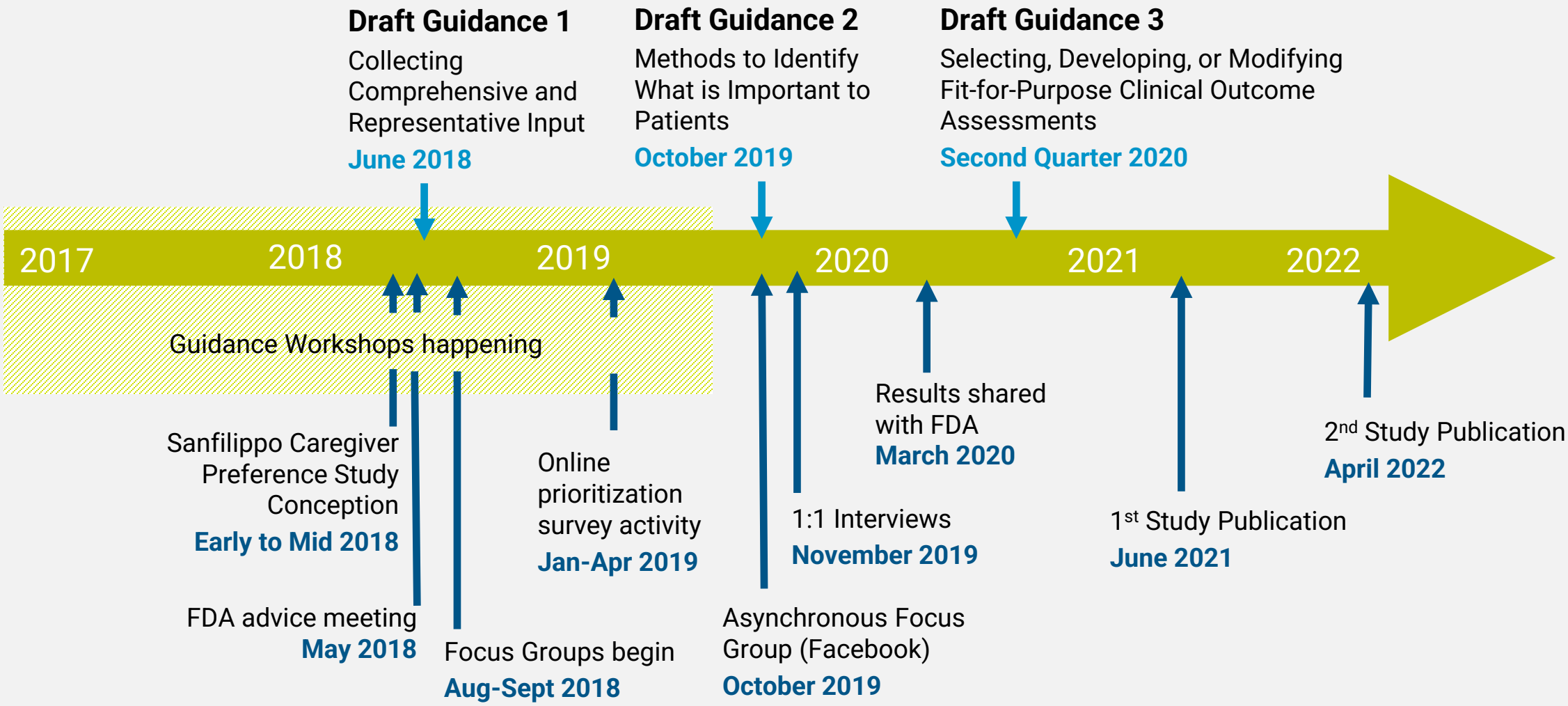
Multisystem metabolic disease with **prominent neurodegenerative and neurobehavioral** phenotype

- Autosomal recessive lysosomal disease
- Most common of the mucopolysaccharidoses (MPS)
- Enzyme deficiency leading to the **accumulation of aberrant heparan sulfate**
- 4 subtypes (prevalence A>B>C>D)
- Combined incidence is 1:70,000

Sanfilippo Caregiver Preference Study: Context

- **Clinical trial program closures** (4 plus more at risk)
  - Clinician and Caregiver-observed positive impact of treatments not measured by current tools
  - Failed drugs or Failed endpoints?
- **Increasingly restrictive inclusion age/cognitive criteria—excludes majority of living children with MPS III**
  - Sole focus on cognitive scores as primary efficacy endpoint did not appear to align with what caregivers anecdotally reported wanting in a first-generation treatment, particularly in the living population (99% symptomatic)
- **Limited publications on caregiver perspectives: focus on disease burden rather than treatment preference**

Study Timeline



Our Approach

Multidisciplinary Study Team

ADVISORY COMMITTEE:

2 social scientists: RTI International
2 industry patient advocate representatives
5 parents (1 physician/advocacy leader/parent)
1 Sanfilippo disease expert physician

EXTERNAL ADVICE: FDA

Mixed Methods

Qualitative & Quantitative
in Concurrent & Sequential manner

*Variety of research activities designed to offer opportunities for caregiver community to participate in ways that they found most accessible and comfortable

Sampling, Recruitment, Representativeness

Probability Sample Requires …

- Well-defined target population
- Sampling Frame = Listing all (or representative) individuals in target population
- Random number generator

NOT FEASIBLE

Non-Probability Sample Options …

- Convenience ★
- Purposive
- Quota
- Snowball ★

IS FEASIBLE

For advocacy groups to engage a **clinically-relevant sample**

Study Overview

Caregiver participants for all study activities | 219 in at least 1 activity

- Focus Group | 25 participants
- Survey | 164 participants
- Asynchronous Focus Group | 11 participants
- 1:1 Interviews | 19 participants

Mean age of child with Sanfilippo syndrome | 10.1 years (range 1 – 40+)

Sub-types of Sanfilippo syndrome

- A (n= 138), B (n = 43), C (n= 11), D (n = 1)

Geographic distribution | 39 U.S. states, 16 countries

Demographics, Symptoms, and Severity (n=190)

PHASE 1

PHASE 2

In-Person Focus Group (n=25)

- Disease impact
- Treatment priorities
- Inform draft survey

Online Survey (n=164)

- Symptoms frequency/ severity
- Symptoms frequency/ severity
- Best-Worst Scaling (BWS): Relative importance of treatment targets
- Caregiver worries

Advisory Committee Review

- Proposes outcome measures paired with domains of importance

Asynchronous Group (n=11)

- Validate the meaningfulness of domains identified in Phase 1 as outcome measures for clinical trials
- Reduce set of associated outcome measures for interviews
- Inform interview guide development

1:1 Interviews (n=19)

- Meaningfulness of domains and outcome measures
- Face validity of measures and items
- Attitudes related to clinical trial design
- Perceptions of benefit tradeoffs

ADVISORY COMMITTEE COLLABORATION & INPUT

Study of Caregiver Treatment Priorities and Unmet Need

Phase 1

Phase 1

In-Person Focus Groups

(n=25)

Context and Meaningfulness:

- High value on treatment outcomes targeted to **narrower aspects and subsets of developmental skills,** as well as a variety of **non-cognitive disease** manifestations

Table 3 Domains and themes: unmet treatment needs

Domain	Symptoms	Most significant impact on…
Cognitive/behavioral/psychological impact		
	Communication	Child and family
	Relationship and social deficits	Family
	Frustration	Child
	Impulse control/aggressive behaviors	Family
	Hyperactivity	Child and family
	Unsafe behaviors	Family
	Anxiety/unhappiness in child	Child
	Sleep disturbance/nighttime waking[a]	Family
Physical health impact		
	Pain/headaches (experienced and anticipated)	Child and family
	Mobility	Child and family
	Sleep problems[a]	Child
	Illness/vulnerability to illness	Child and family
	Seizures	Child
	Feeding and maintaining nutrition	Child
	Digestive issues and toileting	Family

[a] Sleep challenges were reported to have a physical impact on the child and psychological impact on the family

Porter KA, et al. Parent Experiences of Sanfilippo Syndrome Impact and Unmet Treatment Needs: A Qualitative Assessment. Neurol Ther. 2021 Jun;10(1):197-212.

Focus Group Illustrative Quotes

"Our expectations in what we would like to get from treatments for Sanfilippo are relatively small… 'cause some of those **small things have a big impact on us**."

"You know, I'll take that [my child] can **sit and enjoy doing something for three more minutes** than before. I'll even take an intensive **invasive medical procedure** to get me six more months. I'll take any of it, and I think any of it would be good for [my child]."

Prioritization Survey (Online)

Survey components:

- Demographic information
- Symptom severity
- Treatment priorities (Best-Worst Scaling (BWS) & Top 5 activities)
- Caregiver and family priorities (BWS activity)
- Disease impact on caregiver

Prioritization Survey: Sample BWS Item

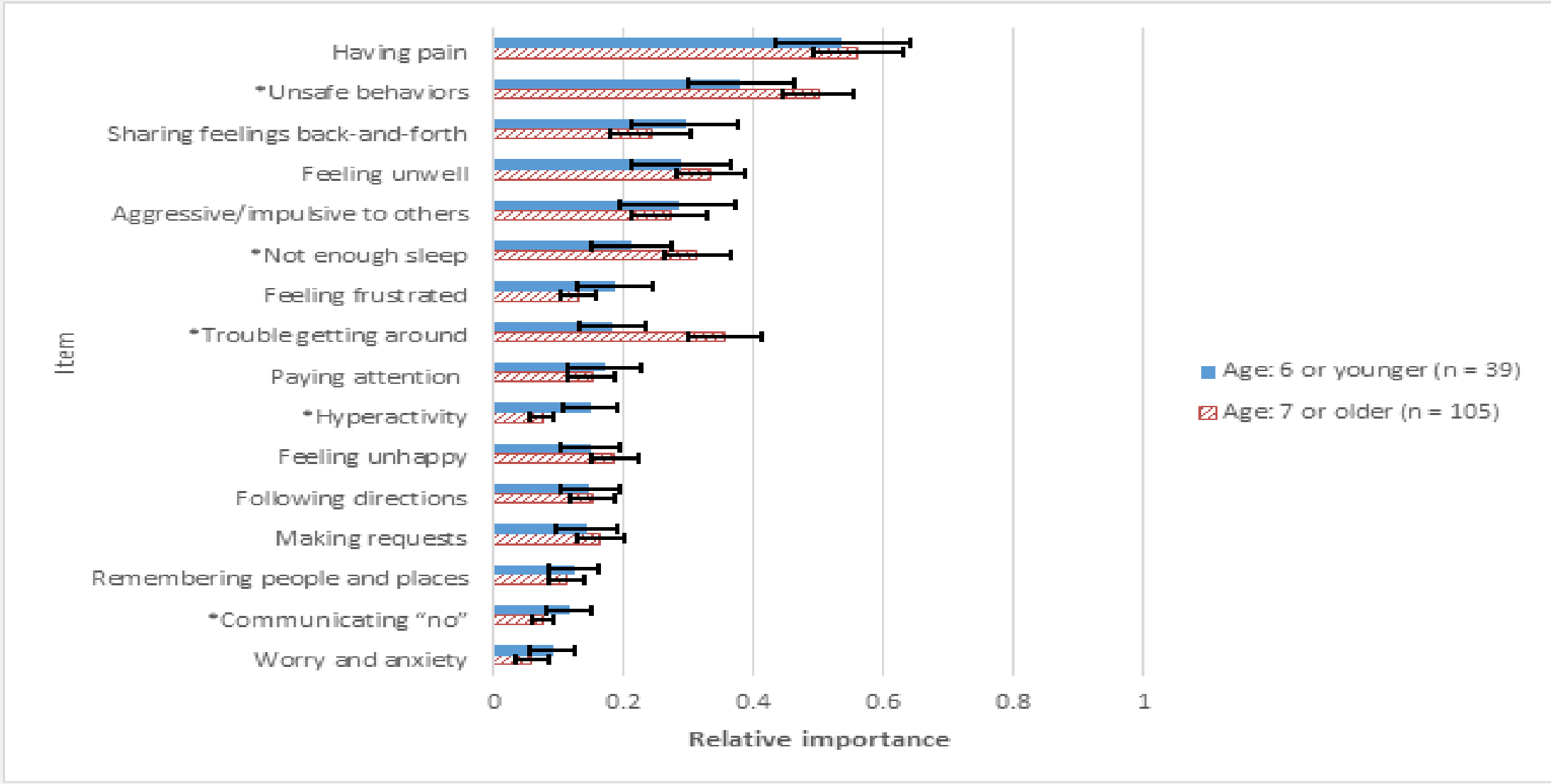
If a new treatment could improve one of these symptoms, which would be the most important to improve **for your child**? Which would be the least important to improve?

Click here for a reminder about what the items mean

Most Important		Least Important
○	Sharing feelings back and forth	○
○	Unsafe behaviors	○
●	Feeling unwell	○
○	Hyperactivity	○
○	Aggressive/impulsive to others	●

*Unpublished data–manuscript in preparation. Sanfilippo Caregiver Preference Study. Cure Sanfilippo Foundation © 2018

Prioritization Survey: Relative importance of symptoms to treat



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Neurol Ther (2021) 10:197–212
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ORIGINAL RESEARCH

Parent Experiences of Sanfilippo Syndrome Impact and Unmet Treatment Needs: A Qualitative Assessment

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ABSTRACT

Introduction: Sanfilippo syndrome (MPS III) is a rare, degenerative condition characterized by symptoms impacting cognitive ability, mobility, behavior, and quality of life. Currently there are no approved therapies for this severe life-limiting disease. Integrating patient and caregiver experience data into drug development and regulatory decision-making has become a priority of the Food and Drug Administration and rare disease patient communities.

Methods: This study assesses parents' perceptions of their child's Sanfilippo syndrome disease-related symptoms using a research approach that is consistent with the Center for Drug Evaluation and Research (CDER) guidance. This study was initiated by the Cure Sanfilippo Foundation, and all steps in the research process were informed by a multidisciplinary advisory committee, with an objective of informing biopharmaceutical companies and regulatory agencies. We explored caregiver burden, symptoms with greatest impact, and meaningful but unmet treatment needs. Data were collected from 25 parents through three focus groups and a questionnaire. Transcripts were coded and analyzed using inductive thematic analysis, and descriptive analysis of quantitative data was conducted.

Results: Participating parents' children ranged in age from 4 to 36 years. Participants endorsed high caregiving burden across all stages of the disease. Analysis revealed multiple domains of unmet need that impact child and family quality of life, including cognitive-behavioral challenges in communication, relationships, behavior, anxiety, and child safety; and physical health symptoms including sleep, pain, and mobility. Participants reported placing high value on incremental benefits targeting those

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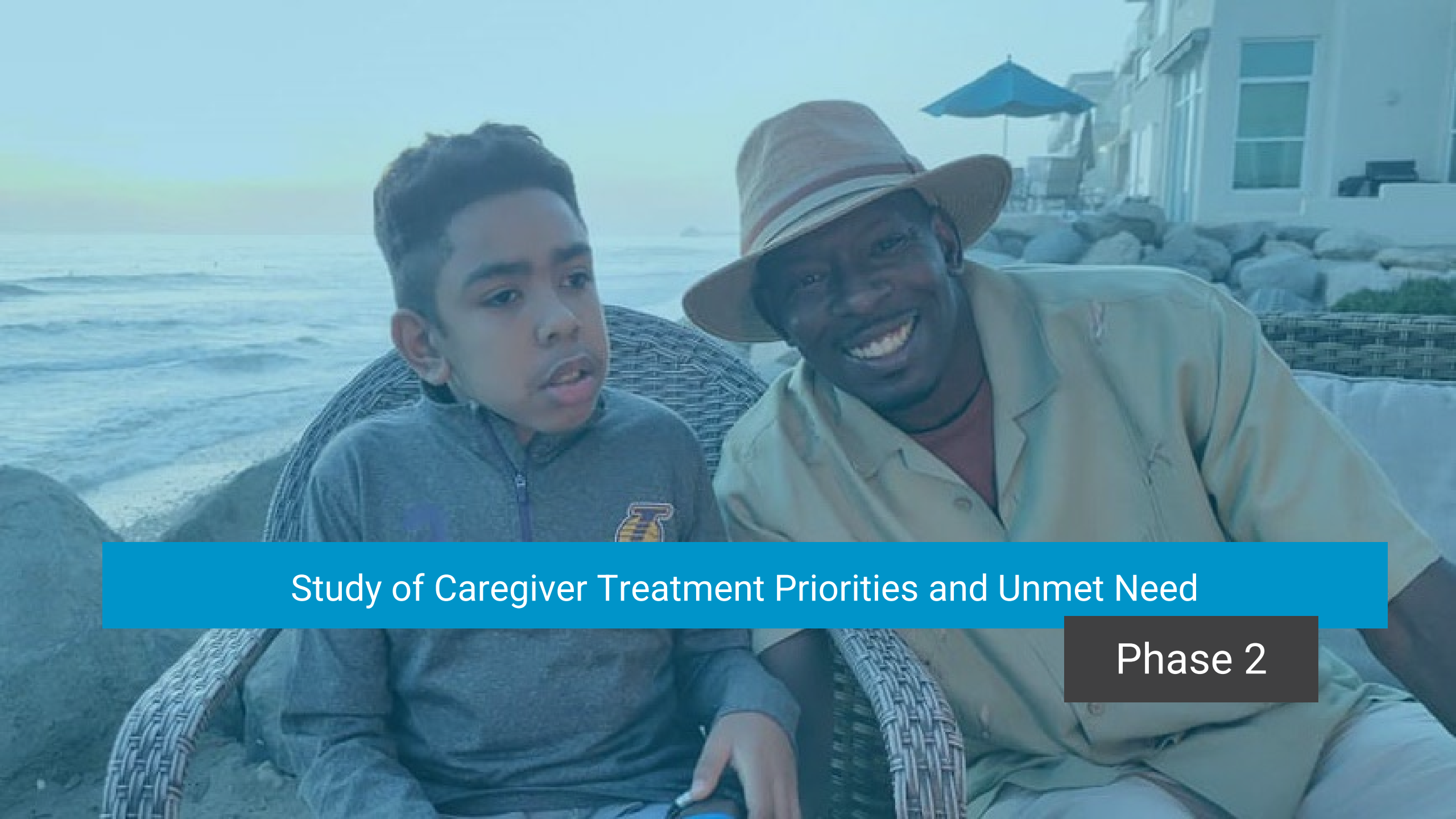
Phase 1: Methodological takeaways

In-Person Focus Groups

- It can be emotionally difficult for participants
- Use an experienced and trained facilitator
- Consider beginning and ending with positively framed discussion prompts
- Focus group participants instrumental in to informing refinement of subsequent online survey activity

Online Survey Activity

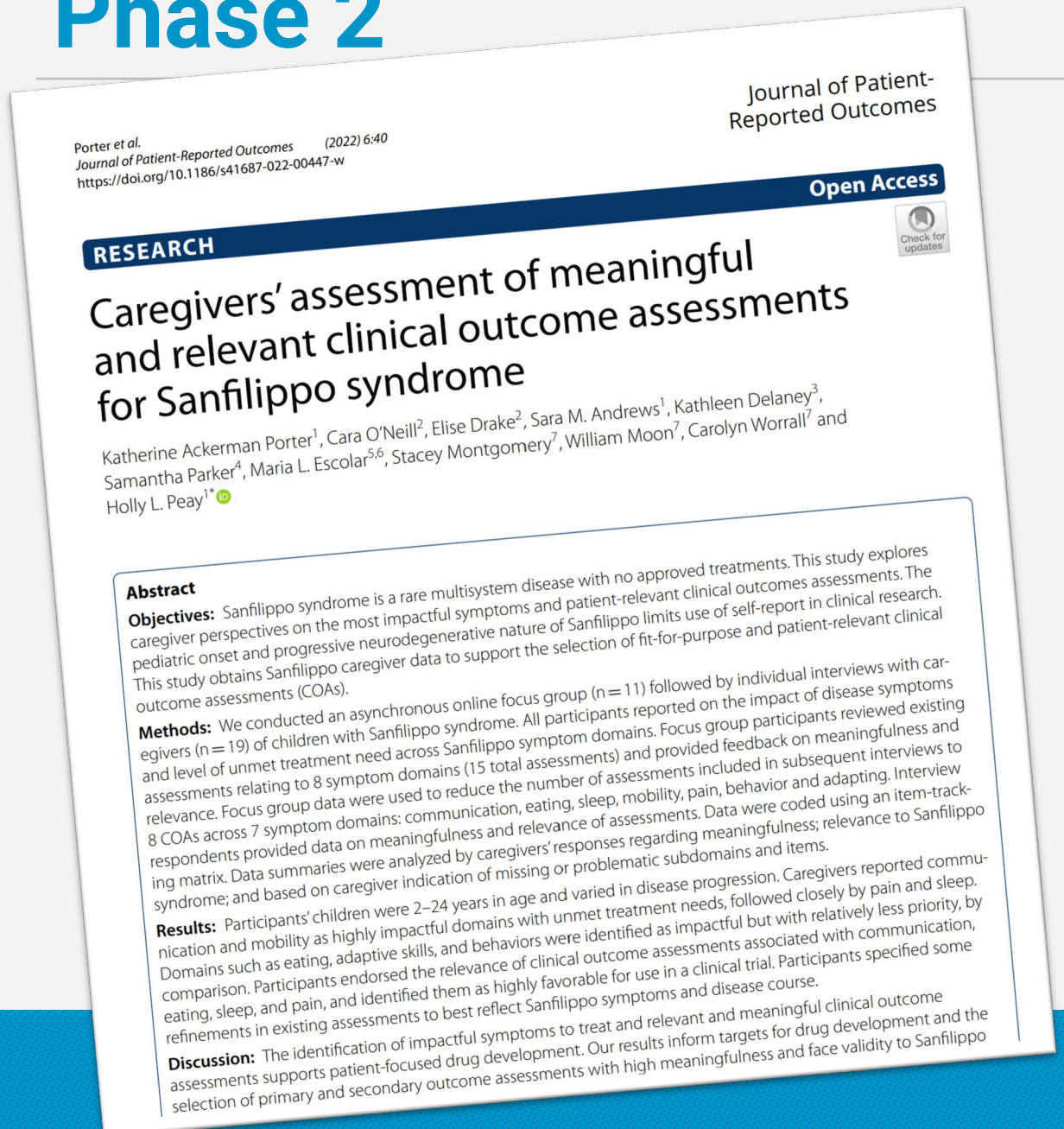
- Survey length and caregiver time constraints- still had good completion
- BWS construct was well understood and avoids problem of within set missing data
- End with positively framed reflection



Study of Caregiver Treatment Priorities and Unmet Need

Phase 2

Phase 2



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Journal of Patient-Reported Outcomes

RESEARCH

Open Access

Caregivers' assessment of meaningful and relevant clinical outcome assessments for Sanfilippo syndrome

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Abstract

Objectives: Sanfilippo syndrome is a rare multisystem disease with no approved treatments. This study explores caregiver perspectives on the most impactful symptoms and patient-relevant clinical outcomes assessments. The pediatric onset and progressive neurodegenerative nature of Sanfilippo limits use of self-report in clinical research. This study obtains Sanfilippo caregiver data to support the selection of fit-for-purpose and patient-relevant clinical outcome assessments (COAs).

Methods: We conducted an asynchronous online focus group (n = 11) followed by individual interviews with caregivers (n = 19) of children with Sanfilippo syndrome. All participants reported on the impact of disease symptoms and level of unmet treatment need across Sanfilippo symptom domains. Focus group participants reviewed existing assessments relating to 8 symptom domains (15 total assessments) and provided feedback on meaningfulness and relevance. Focus group data were used to reduce the number of assessments included in subsequent interviews to 8 COAs across 7 symptom domains: communication, eating, sleep, mobility, pain, behavior and adapting. Interview respondents provided data on meaningfulness and relevance of assessments. Data were coded using an item-tracking matrix. Data summaries were analyzed by caregivers' responses regarding meaningfulness; relevance to Sanfilippo syndrome; and based on caregiver indication of missing or problematic subdomains and items.

Results: Participants' children were 2–24 years in age and varied in disease progression. Caregivers reported communication and mobility as highly impactful domains with unmet treatment needs, followed closely by pain and sleep. Domains such as eating, adaptive skills, and behaviors were identified as impactful but with relatively less priority, by comparison. Participants endorsed the relevance of clinical outcome assessments associated with communication, eating, sleep, and pain, and identified them as highly favorable for use in a clinical trial. Participants specified some refinements in existing assessments to best reflect Sanfilippo symptoms and disease course.

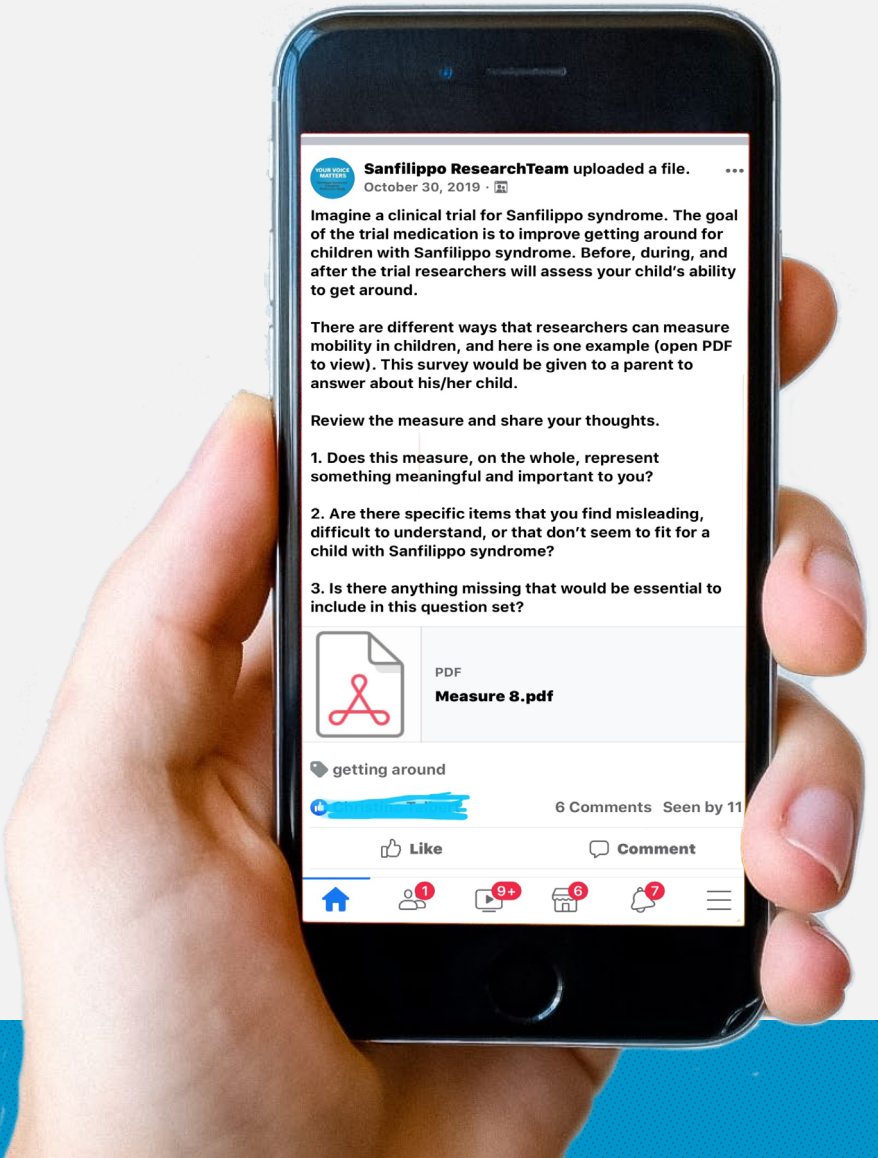
Discussion: The identification of impactful symptoms to treat and relevant and meaningful clinical outcome assessments supports patient-focused drug development. Our results inform targets for drug development and the selection of primary and secondary outcome assessments with high meaningfulness and face validity to Sanfilippo

Asynchronous Focus Group (n=11)

1:1 Interviews (n=19)

CURE SANFILIPPO FOUNDATION

Asynchronous Focus Group



Social Media Focus Group can be done with rigor, but there are limitations

Opportunities

- Inexpensive
- Avoid many geographic barriers
- Ease of use (for many)

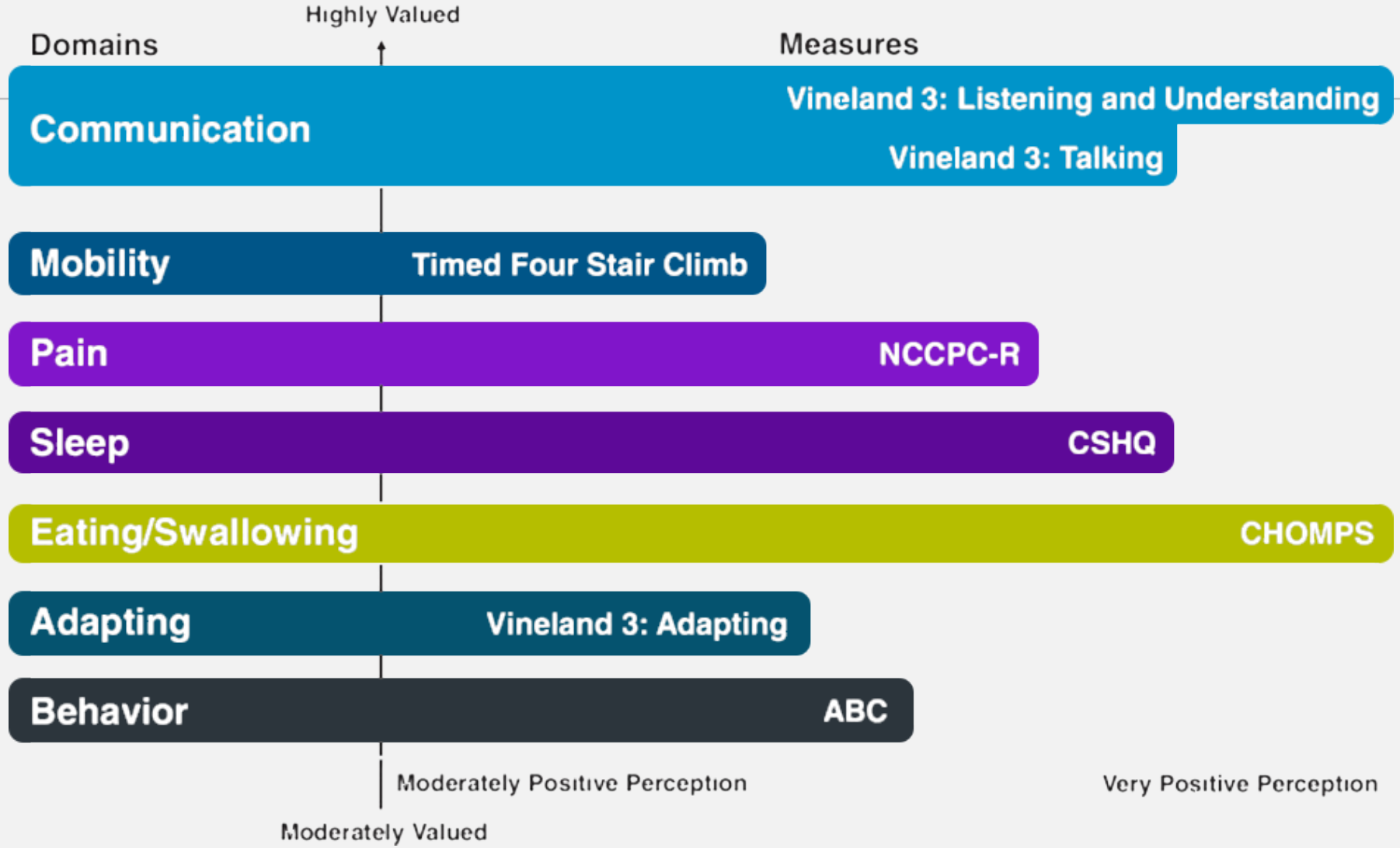
Potential Challenges

- Anonymity/Privacy - limitations despite precautions
- Can be more difficult to probe effectively in a non-person facing environment
- Internet access

Takeaway

- Good tool to use for pilot data and feedback

Comparison of caregiver valuing of outcome measure symptom domain and associated outcome measure



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Child Oral and Motor Proficiency Scale (CHOMPS)

- Domain is meaningful and relevant
- Positive perceptions as trial target and outcome measure
  - Key item suggested: **Overfilling of Mouth**
  - Other suggested items: **“finger foods” and pace of child’s eating**
- Instruction clarification: uncertainty about how to answer if the child’s ability vs. unwillingness, or if parents have instituted a workaround for ease or safety
- Response options to capture regression in Sanfilippo syndrome (i.e., **“used to”**) would be preferred
  - Current CHOMPS response options: “yes” “sometimes” “not yet”

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Study conclusions

- **Data demonstrate multisystem disease impact** and the relative prioritization of treatment targets.
- **Quality of life improving treatments valued** irrespective of impact on global cognitive ability.
- Very **high risk tolerance** for **modest benefit** is acceptable.
- **Most existing outcome measures do not account for regression**.
- Relatively **minor modifications to some existing measures would increase face validity**.

Broad Challenges for Rare Disease Preference Work

Resource challenges in rare disease small non-profit

Improving reach to increase diversity of sample

Granularity of incremental benefit in terminal diseases with no treatments

High disease burden and caregiver impact

Continued study over time as treatments emerge, medical care and diagnostics advance

Thank You

Session 3: Question and Answer

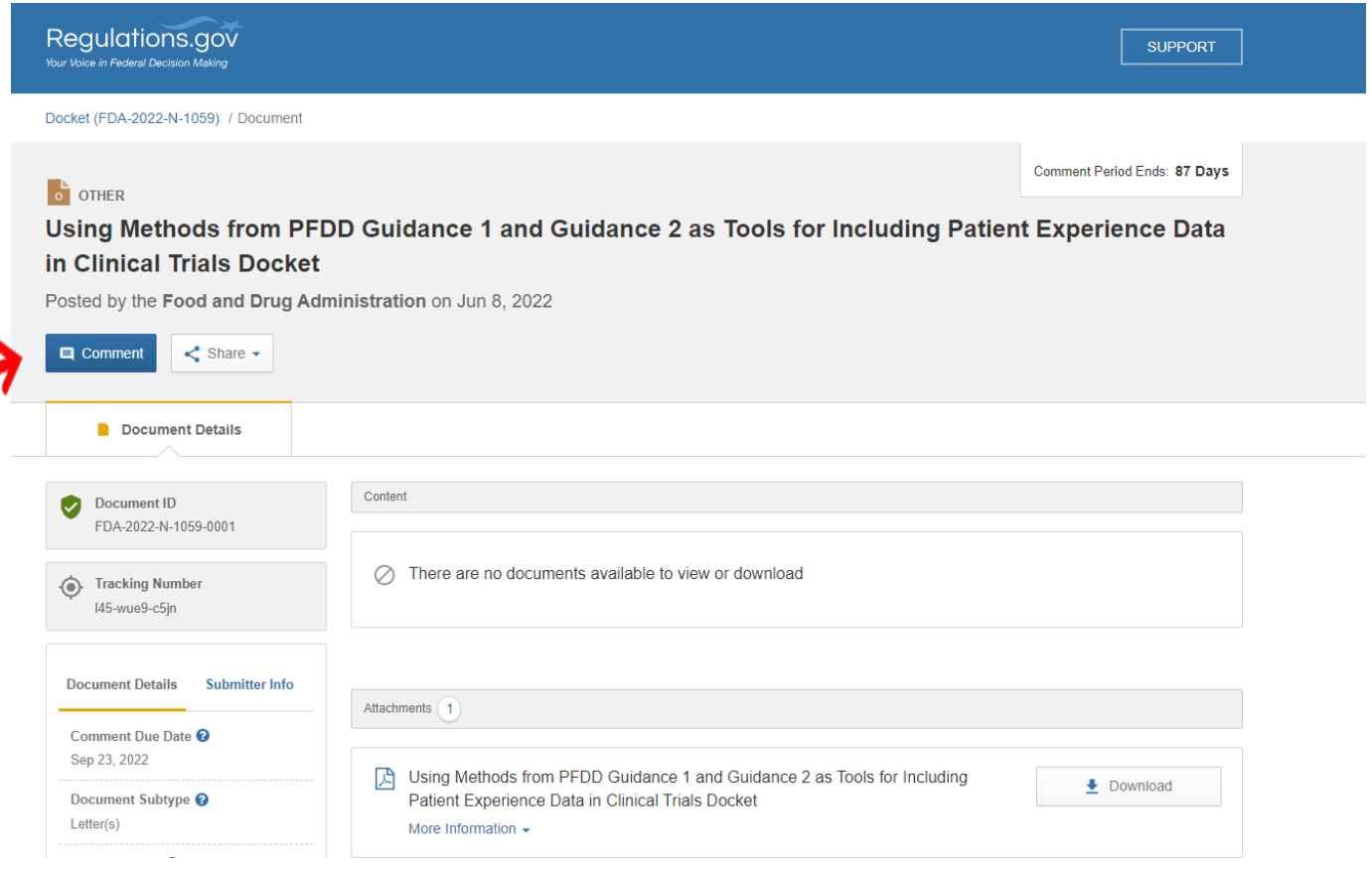
Send us your comments!

If you have examples of how you have used the PFDD Methodologic Guidance Series to advance the inclusion of the patient voice in the drug development process, please submit to the public docket for this series of meetings.

The docket will close on September 23, 2022.

How do you submit a comment?

- Please visit: https://www.regulations.gov/document/FDA-2022-N-1059-0001
- And **Click Comment**



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Thank you!