Welcome!

Please be seated by 8:55 AM ET

The webinar will go live at 9:00 AM ET

Advisory Panel on Rare Disease: In-Person Meeting

September 27, 2017

9:00 AM – 3:30 PM

Welcome, Introductions, and Setting the Stage

Matt Cheung

Chair, *Rare Disease Advisory Panel*

Vincent Del Gaizo

Co-Chair, *Rare Disease Advisory Panel*

Housekeeping

- Today's meeting is open to the public and is being recorded
  - Members of the public are invited to listen to the teleconference and view the webinar
  - Meeting materials can be found on the PCORI website
  - Anyone may submit a comment through the webinar chat function, although no public comment period is scheduled
- Visit www.pcori.org/events for more information

Housekeeping (cont.)

- We ask that panelists stand up their tent cards when they would like to speak and use the microphones
- Please remember to state your name when you speak

Conflicts of Interest

- Welcome to the Rare Disease Advisory Panel meeting. I want to remind everyone that disclosures of conflicts of interest of members of the Advisory Panel are publicly available on PCORI's website. Members of the Rare Disease Advisory Panel are reminded to update your conflict of interest disclosures if the information has changed, in addition to completing your annual disclosure. You can do this by contacting your staff representative.
- Finally, if the Rare Disease Advisory Panel will deliberate or take action on a matter that presents a conflict of interest for you, please inform one of the co-chairs so we can discuss how to best address the issue.

Agenda

Agenda Item	Time
Welcome and Setting the Stage	9:00 AM – 9:30 AM
International Rare Diseases Research Consortium (IRDIRC) and Patient-Centered Outcome Measures	9:30 AM – 10:00 AM
Core Outcome Set for Pediatric Rare Disease	10:00 AM – 11:30 AM
Break	11:30 AM – 11:45 AM
Developing PCORI Informational Resources to Better Serve the Rare Disease Community	11:45 AM – 12:30 PM
Lunch	12:30 PM – 1:15PM
Presentation Materials for PCORI's Rare Disease Portfolio	1:15 PM – 1:45 PM
Break	1:45 PM – 2:00 PM
Case Study: PCORI Rare Disease Funded Study in Urea Cycle Disorders	2:00 PM – 3:00 PM
Closing and Next Steps	3:00 PM – 3:30 PM

Introductions

- Please quickly state the following:
  - Name
  - Stakeholder group you represent
  - Position title and organization

Introductions: Current Panelists

Introductions (cont.)

Vincent Del Gaizo ***(Co-Chair)***

Owner, *Plaza Dry Cleaners*

Representing: Patients, Caregivers and Patient Advocates

Introductions (cont.)

Matt Cheung, PhD, RPh ***(Chair)***

Adjunct Professor, *Pharmacy Practice, University of the Pacific*

Representing: Payers

Introductions (cont.)

Julie Abramson

Project Manager and Architect, *Hennepin County*

Representing: Patients, Caregivers, and Patient Advocates

Introductions (cont.)

Kathleen Gondek, MS, PhD

Vice President, *Global Health Economics Outcomes Research and Epidemiology, Shire PLC*

Representing: Industry

Introductions (cont.)

Lisa Heral, RNBA, CCRC

Registered Nurse, *Pacific Quest and Bay Clinic - Hawaii*

Representing: Patients, Caregivers, and Patient Advocates

Introductions (cont.)

Cindy Luxhoj, MUP

Executive Director and Founder, *Alagille Syndrome Alliance*

Representing: Patients, Caregivers, and Patient Advocates

Introductions (cont.)

Stephen Mathai, MD

Associate Professor, *Johns Hopkins University School of Medicine*

Representing: Researchers

Introductions (cont.)

Yaffa R. Rubinstein, MS, PhD

Rare Disease Patient Registries and Bio-repositories Special Volunteer,
National Information Center of Health Services Research & Health Care Technology at the NLM/NIH

Representing: Researchers

Introductions (cont.)

Marcia Rupnow, MS, PhD

Vice President of Value Evidence and Outcomes, *GlaxoSmithKline*

Representing: Industry

Introductions (cont.)

Maureen Smith, MEd

Board Member, *Canadian Organization for Rare Disorders (CORD)*

Patient Member, *Ontario Ministry of Health and Long Term Care*

Representing: Patients, Caregivers, and Patient Advocates

Introductions (cont.)

James J. Wu, MSc, MPH

Senior Manager, *Global Health Economics, Amgen Inc.*

Representing: Industry

RDAP Panelists (cont.)

Patricia Furlong*

Founder, President and CEO, *Parent Project Muscular Dystrophy*

Representing: Patients, Caregivers, and Patient Advocates

Naomi Aronson, PhD*

Executive Director, *Clinical Evaluation, Innovation, and Policy, Blue Cross and Blue Shield Association (BCBSA)*

Ex-Officio Member from PCORI's Methodology Committee

**Not attending today's meeting*

RDAP Panelist Resignations

Marshall Summar, MD

Represented: Clinicians

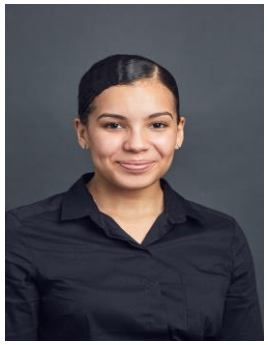
Michael Kruer, MD

Represented: Researchers

Rare Disease Advisory Panel – PCORI Staff

Yen-pin Chiang, PhD
Deputy Chief Science Officer
Office of the Chief Science Officer

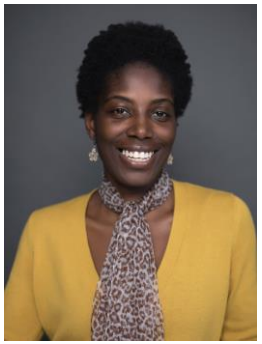
Parag Aggarwal, PhD
Senior Program Officer,
Healthcare Delivery and Disparities Research



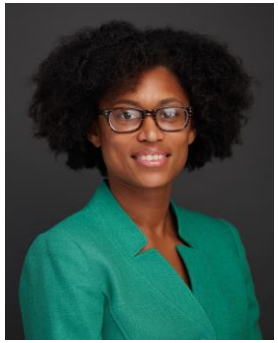
Dionna Attinson
Program Assistant,
Healthcare Delivery and Disparities Research

Sarah Philbin, MPH
Program Associate
Clinical Effectiveness and Decision Science

Allison Rabinowitz, MPH
Program Associate
Office of the Chief Science Officer



Tomica Singleton
Senior Administrative Assistant,
Healthcare Delivery and Disparities Research



Gyasi Moscou-Jackson, PhD, MHS, RN
Program Officer,
Healthcare Delivery and Disparities Research

Patient-Centered Outcome Measures in Rare Diseases

Thomas Morel

PCORI's Rare Disease Advisory Panel

September 27th, 2017

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

About IRDiRC

To deliver treatments for the 7,000 rare diseases, we need…

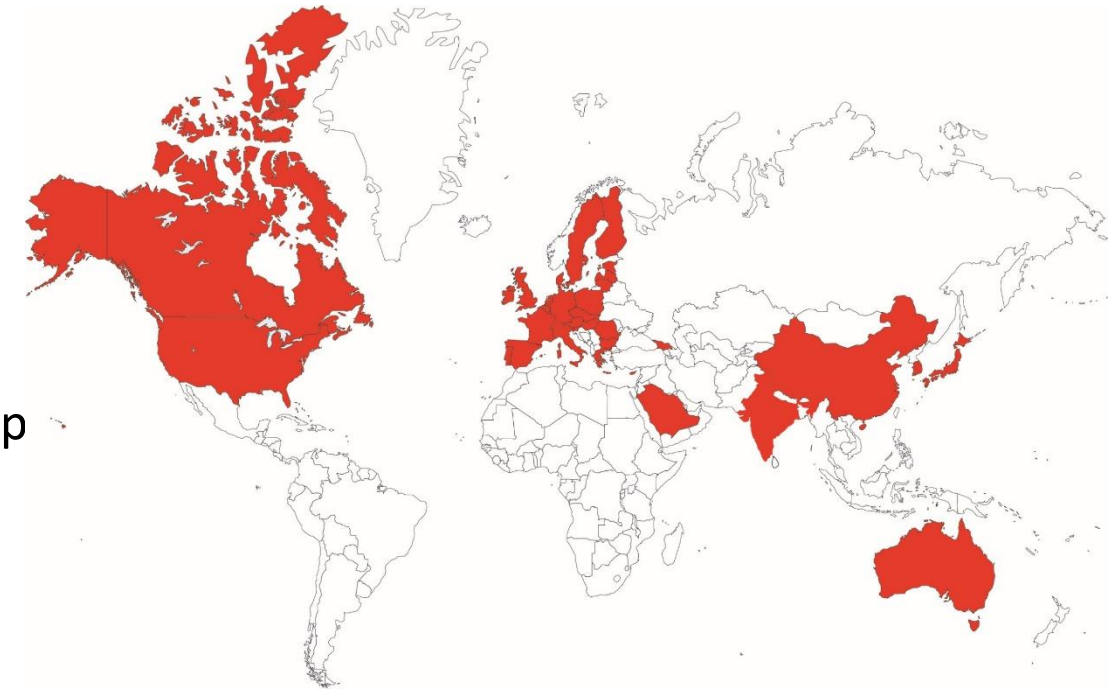
- A change in the ecosystem of research and development
- Appropriate funding
- Collaboration

IRDiRC
INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

An international co-operation to stimulate, better coordinate & maximize output of rare disease research efforts around the world

IRDiRC: Member Organizations

- 49 IRDiRC members
  - 23 funding agencies
  - 13 companies
  - 4 institutes
  - 2 ministries
  - 2 consortia
  - 6 patient advocacy group

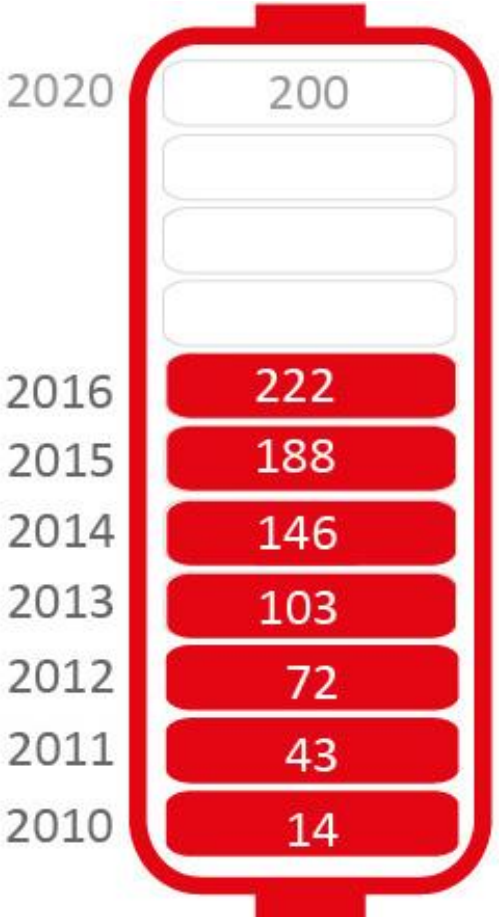


IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Number of New Orphan Drugs

- IRDiRC's goal to deliver 200 new therapies was achieved in late 2016 – **three years earlier than expected**

- Between 2010 and 2016, over 200 new drugs have reached the market, covering about 170 rare diseases.

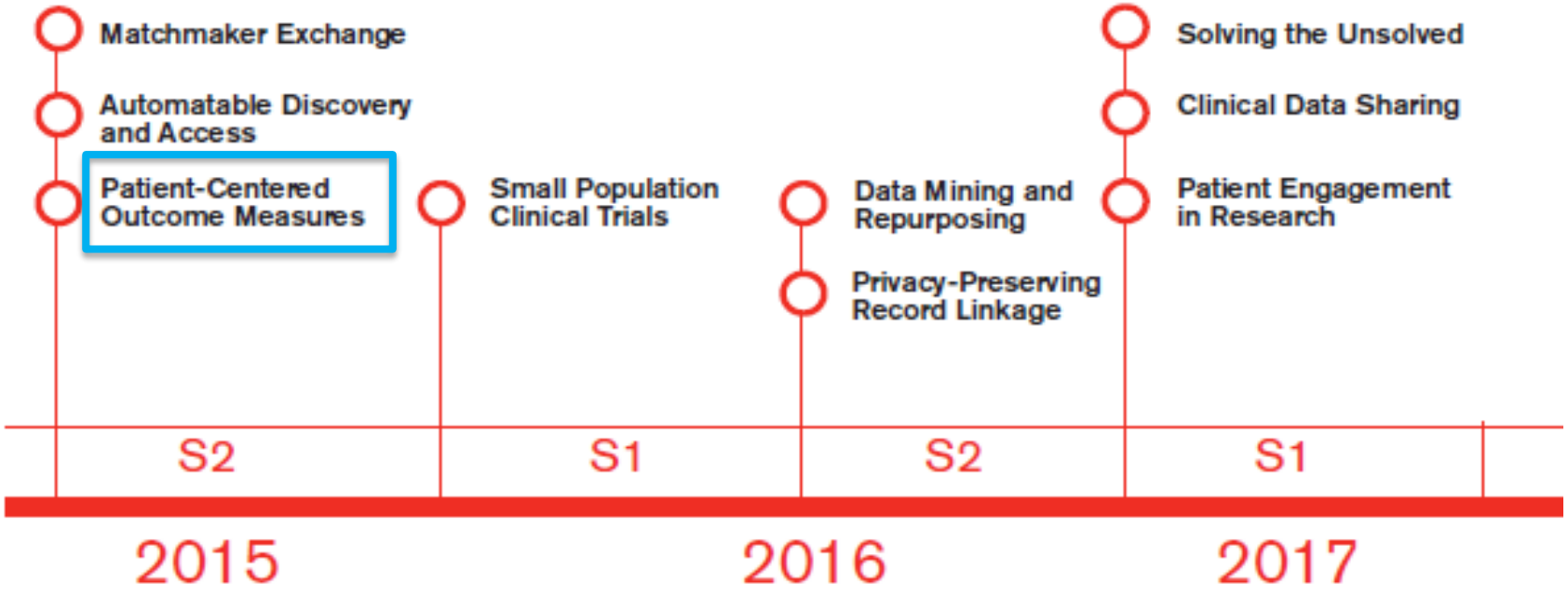


Updated on www.irdirc.org

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Task Forces in Action

- Actionable projects to ensure IRDiRC meets its objectives for the rare diseases community are carried out by Task Forces



IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

IRDiRC Goals, by 2027

- All patients coming to medical attention with a suspected rare disease will be diagnosed within one year if their disorder is known in the medical literature; all currently undiagnosable individuals will enter a globally coordinated diagnostic and research pipeline

- 1,000 new therapies for rare diseases will be approved, the majority of which will focus on diseases without approved options

- Methodologies will be developed to assess the impact of diagnoses and therapies on rare diseases patients

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Nature Commentary: http://www.nature.com/uidfinder/10.1038/548158c
CTS Past Perspective: http://onlinelibrary.wiley.com/doi/10.1111/cts.12501/full
CTS Future Perspective: http://onlinelibrary.wiley.com/doi/10.1111/cts.12500/full

IRDiRC's work on Patient-Centered Outcome Measures

Current paradoxes in rare diseases

Growing acceptance that rare disease patients have the **clearest view of the health outcomes that matter**

An **acceleration of RD research** (attested by the increase in orphan designations)

Overall clinical trial **success rates in RD are improving**

Growing reliance on **surrogate outcomes** in trials that may not reflect treatment benefits that patients value

Regulators, HTA agencies and Payers are **increasingly difficult** over the acceptance of surrogate endpoints and the question over 'patient relevant outcomes'

Recurring late-stage drug development **failures** across a few RDs

Is the lack of consensus over the most important outcomes to study contributing to delays or denials of patient access to new therapies?

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

IRDiRC's PCOM Taskforce

- Set up in 2015
- Explore how and to what extent patient-centered outcome measure initiatives can be expanded to target rare disease research and improve feasibility and quality of trials

- A multi-disciplinary team
- A report issued in 2016: http://www.irdirc.org/wp-content/uploads/2016/03/PCOM_Post-Workshop_Report_Final.pdf

- **Developing PCOMs for rare diseases is a '*necessity*'**

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

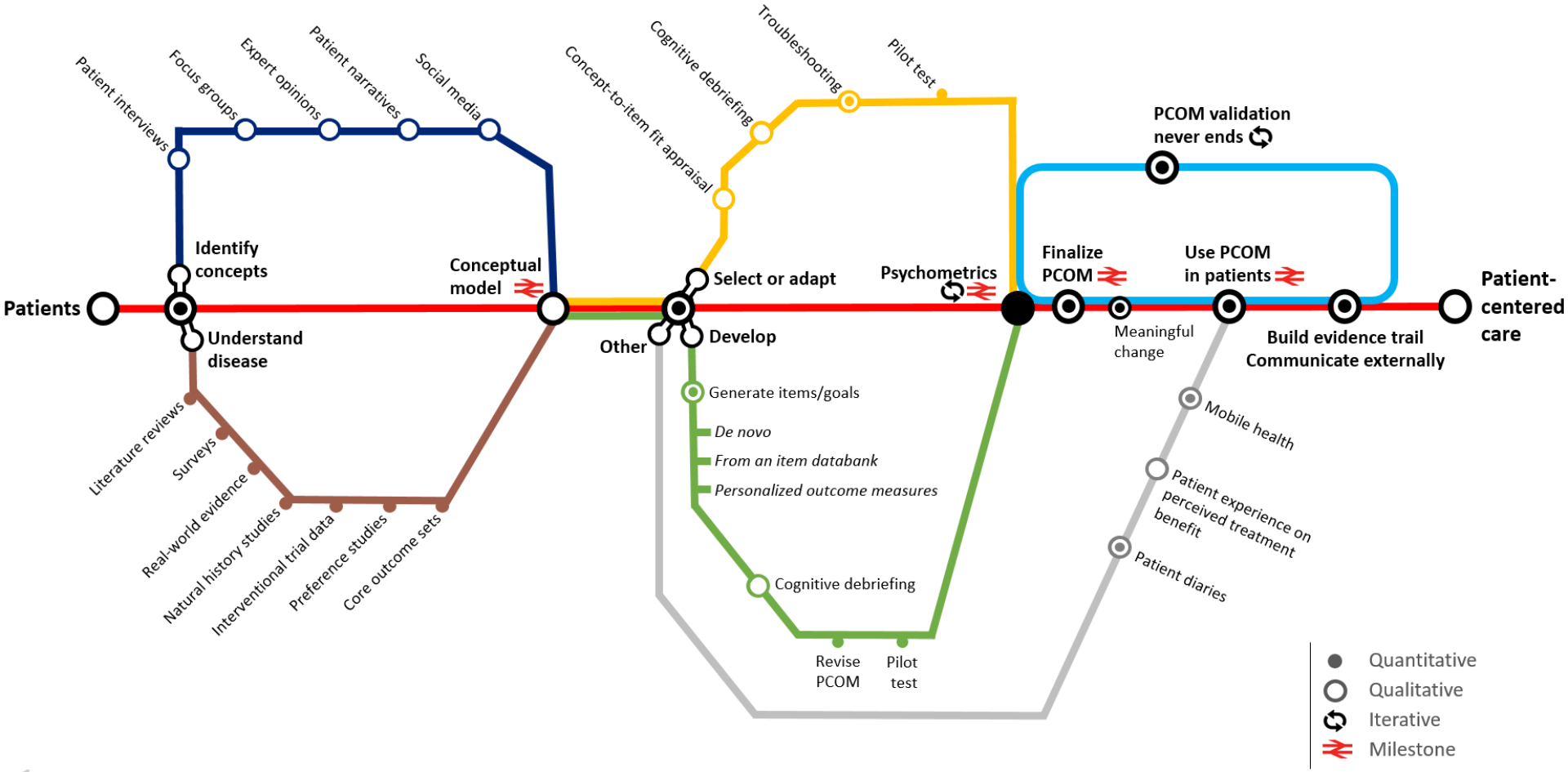
A call for action

Forthcoming Opinion by Morel et Cano (Orphanet Journal, in press)

- PCOMs bring **benefit for all healthcare stakeholders**
- **PCOMs are anchored to Patients**, their daily experience of disease, their preferences, concerns, hopes, values
- A lot of **good PCOM work is on-going** across the RD community: a need to disseminate, train, educate
  - The Opinion includes references to many PCOM projects in rare diseases, including 7 illustrative case studies
- **Two methodologies best-suited in rare diseases**:
  - Mixed Methods Psychometric Research
  - Rasch Measurement Theory (RMT)

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

The ‘rail tracks’ to PCOMs



IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Policy Recommendations

- **Collaboration** – PCOM as a pre-competitive activity (e.g. CoreHEM)
- **Alignment** – need to build agreement on evidentiary requirements
- **Integration** – use of PCOMs in value frameworks, registries, outcome-based agreements
- **Innovation** – seize the opportunity offered by new methodologies and technologies (e.g. wearables)
- **Communication** – disseminate PCOM best practices, publish, train

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Thoughts about Core Outcome Sets in rare diseases

With thanks to:
Stefan Cano
Anna Mayhew
Antoine Regnault

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

- COS should be **driven conceptually**
- Concepts should be elicited **directly from patients/caregivers**
- **Heterogeneity** across/within paediatric rare diseases will be a challenge to identify core outcomes, magnified by the geographic variability of care settings and societal values

- **Thought # 1**: Focus on Burden of Care in families (i.e. distal dimensions of disease): economic cost, emotional impact, social interactions/relationships etc.
- **Thought # 2**: Each condition will require their own special focus on concepts: key challenge! To identify what can be considered common (and what isn't) should be prospective
- **Thought #3**: Be mindful of the need for measurement continuum across ages (and care settings)

Catalyzing registry-based randomized comparative effectiveness trials for inherited metabolic diseases in children: establishing a core outcome set and data collection tools

- Strategy for Patient-Oriented Research (SPOR) catalyst grant study funded by the Canadian Institutes for Health Research (2017-2018)
- Lead investigator: Dr. Beth Potter, Associate Professor, School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa

---

Maureen Smith, MEd

Member, RDAP and PCORI Ambassador
Representing: Patients, Caregivers, and Patient Advocates

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Overview

- Inherited Metabolic Disorders (IMD): Large group of single but distinct gene defects, no standardized patient-centered measures
- Project Aim: Establish core outcome set for future comparative effectiveness trials
- 2 patient engagement experts as co-investigators included in multi-stakeholder research team
- Core outcome sets for Phenylketonuria (PKU) and Medium-chain acyl-CoA dehydrogenase (MCAD) patients, under age 12, many of which will be generalizable to other IMDs
- COMET initiative: http://comet-initiative.org/studies/details/995

uOttawa

CIMDRN RCRMMH

CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

Potential Generalizability of the Core Outcome Set

- We anticipate that we will end up with a number of common outcomes and also a number of outcomes that are disease-specific, which is why we are conducting this process separately for PKU and for MCAD deficiency but we are doing the work in parallel.
- We chose two IMDs that are about as different from one another as possible within the realm of IMDs.
- Our family advisory forum includes some members whose children have IMDs other than PKU and MCAD deficiency, and the physicians on our team also have experience with a range of IMDs.

Developing a Core Outcome Sets for Pediatric Rare Diseases

Gyasi Moscou-Jackson, PhD, MHS, RN

Program Officer, Healthcare Delivery and Disparities Research

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Overview

- Background
- Methods
- Results
- Comparison of Results with PCORI-funded Portfolio on Pediatric Rare Diseases
- Discussion and Next Steps

- *Related Materials*
  - Conceptual framework of core outcomes for prioritization

Core Outcome Sets Overview

- A “Core Outcome Set (COS)” is an agreed minimum set of outcomes or outcome measures. It is a recommendation of ‘what’ should be measured and reported in all trials in a specific area. (COMET, Core Outcome Measures in Effectiveness Trials)

- COS development is most beneficial when a variety of stakeholder perspectives (including patients) are included

- Currently no published COS for pediatric rare diseases that are cross-cutting (i.e., they may not be applicable or explicitly intending to apply to multiple specific pediatric rare diseases)

RDAP Interest in Core Outcome Sets

- During the Fall 2016 RDAP meeting, the RDAP initially expressed an interest in developing a core outcome sets for rare disease studies. During this meeting, panelists discussed:
  - Benefits and challenges to developing a COS
  - Continuing the discussion at a future RDAP meeting

- At the Spring 2017 RDAP meeting, the following key questions were discussed:
  - What is a COS for rare diseases?
  - What is the problem we are trying to solve?
  - How should we go about solving this problem?
  - What can PCORI do with a COS for rare disease?

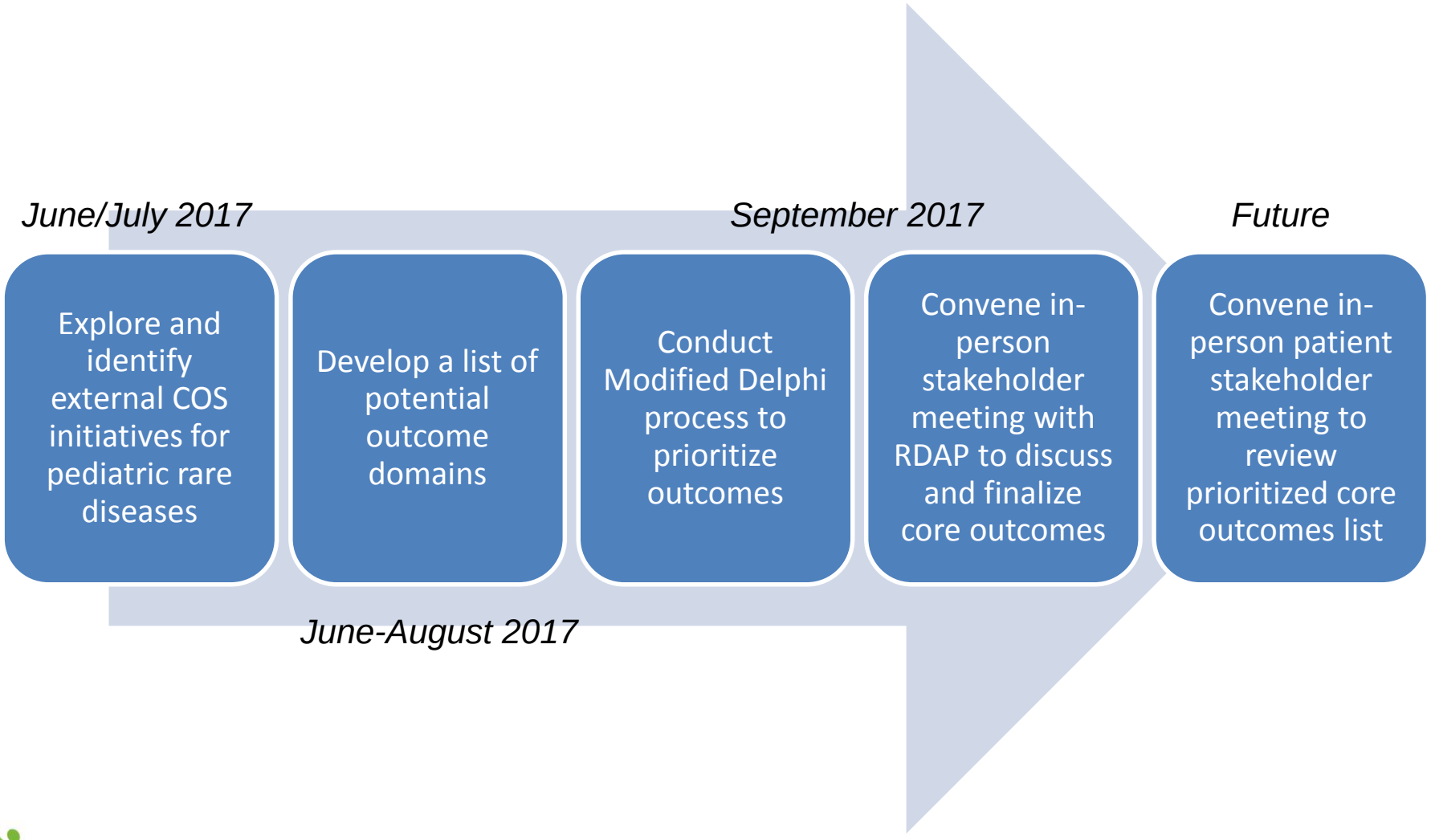
RDAP Interest in Core Outcome Sets (Cont.)

- Highlights from Spring 2017 discussion:
  - "Core" refers to outcomes common to ALL rare diseases and are important to patients
  - A COS would help:
    - Make rare disease research more patient centered
    - Aid evidence synthesis across different rare disease studies
    - Improve quality of care by measuring outcome important to patients
  - The COS would not replace or be used in-lieu of a disease-specific outcomes, but would be a starting point for outcome selection in studies
  - The RDAP agreed that it was important to focus on pediatric rare diseases because most rare diseases affect children
  - The COS should be built on NIH's PROMIS domains and will be finalized with patient input to ensure patient-centeredness

RDAP Interest in Core Outcome Sets (Cont.)

- Next steps from the Spring 2017 RDAP Meeting:
  - Explore and identify external COS initiatives for pediatric rare diseases
  - Identify existing core outcome sets for children as a starting point
  - **Identify the minimum set of PROs that should be measured in studies of children with rare diseases.**
  - Focus on:
    - **'What' should be measured NOT 'how' the outcome will be measured (i.e., operationalization of the outcome).**
    - PROs that are generally applicable to a broad set of pediatric rare diseases.
  - Incorporate NIH PROMIS measures
  - Identify common outcomes across PCORI funded studies in pediatric rare diseases

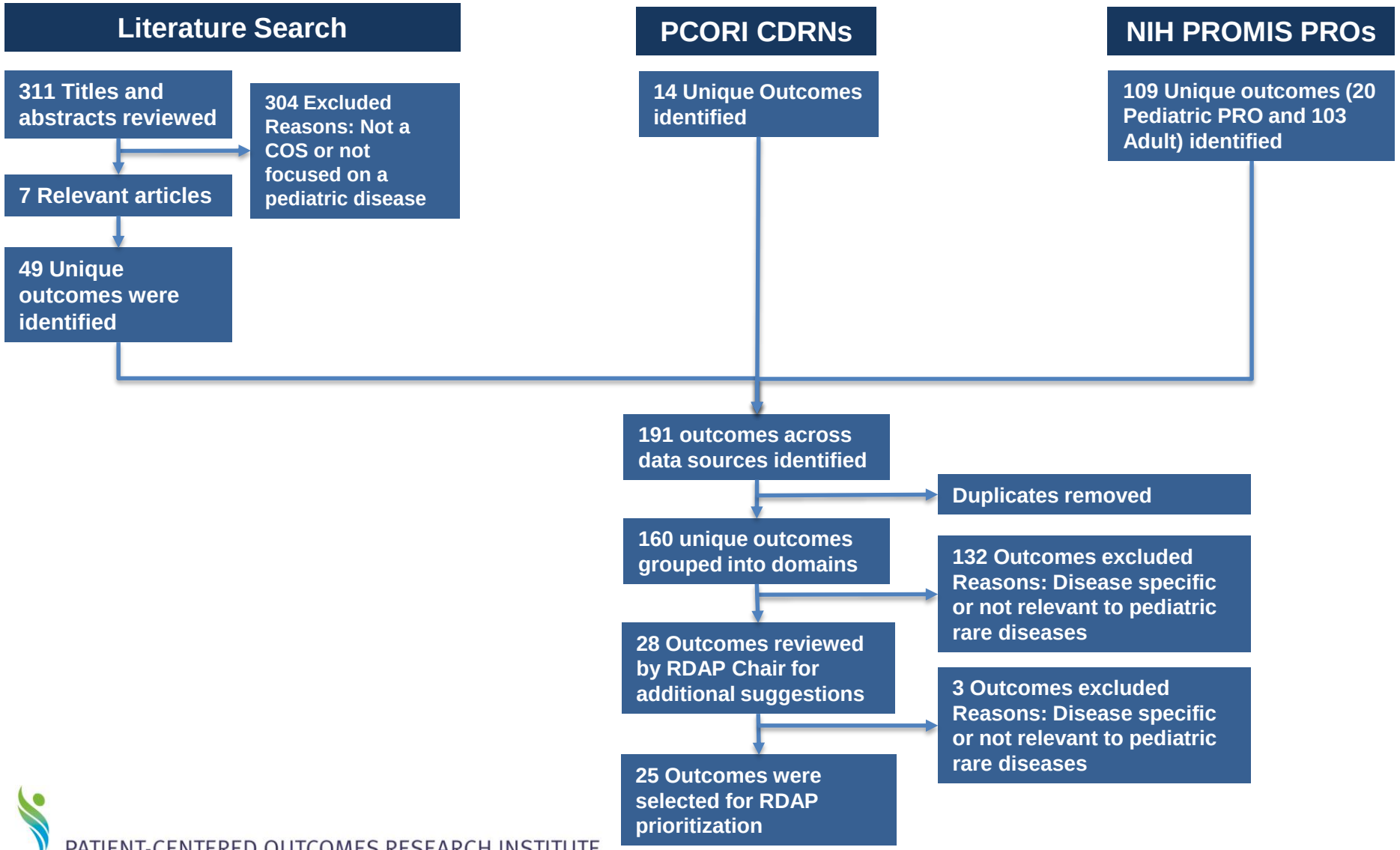
Overview of COS Development Process



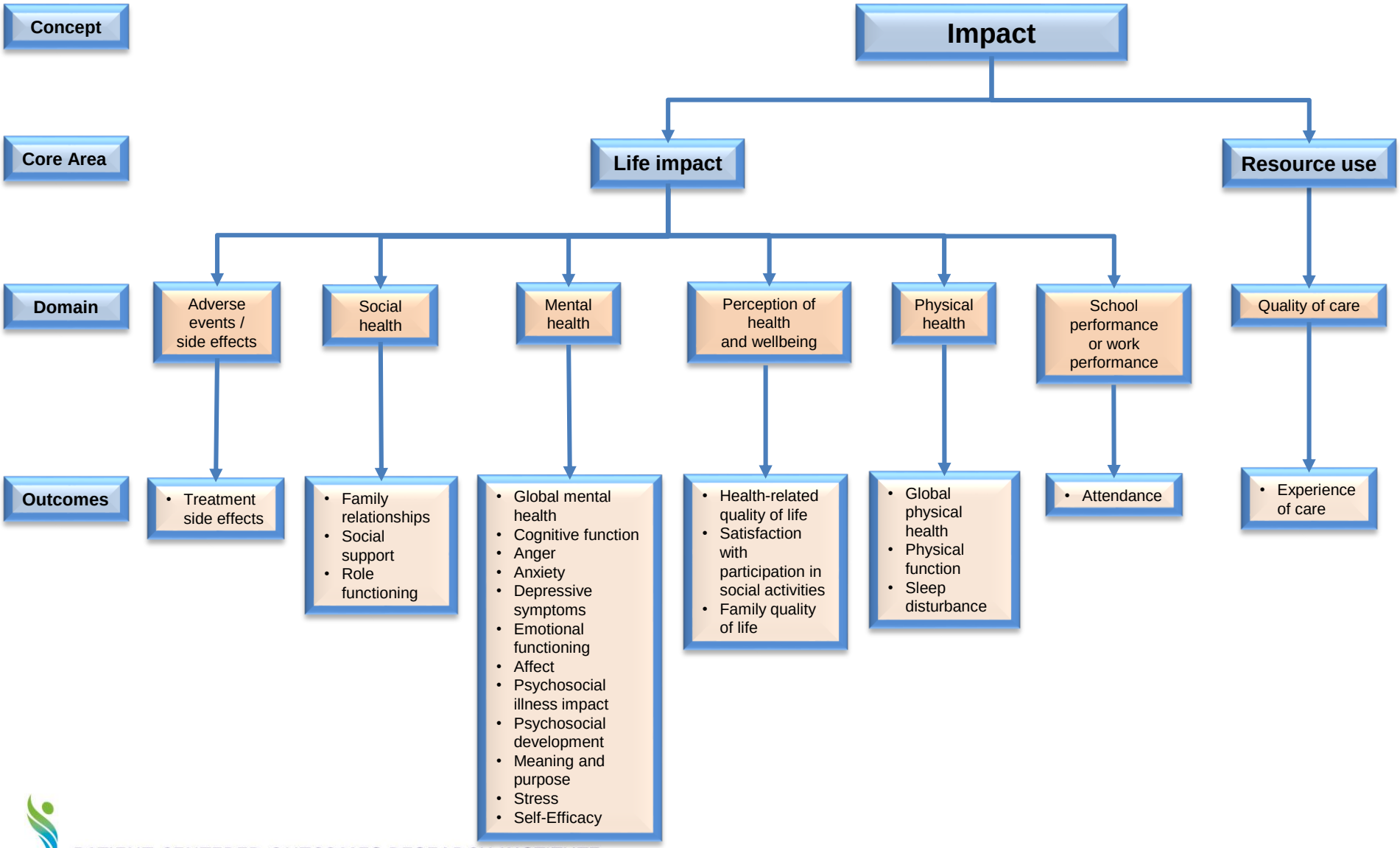
Development of Outcomes List

- PCORI staff performed a literature review for core outcome sets in pediatric common and rare diseases
  - 7 published pediatric disease-focused core outcome sets were identified (i.e., childhood asthma, JIA, childhood eczema, etc.)
  - 0 published pediatric rare disease core outcome set
- PCORI staff also reviewed:
  - NIH PROMIS pediatric and adult health measures
  - PCORI's PCORnet common data model
- In total, 191 outcomes were identified across sources
- After refinement, a final list of 25 unique outcomes was presented to the RDAP for prioritization

Development of Potential Outcomes List (Cont.)



Conceptual Framework for Outcomes Prioritized



RDAP Prioritization of Outcomes Process

- Modified Delphi was used to prioritize outcomes (one survey plus in-person meeting)
- RDAP ranked the final list of outcomes based on their importance for pediatric rare diseases.
- **The goal was to identify the minimum set of PROs that should be measured by researchers (and clinicians) in studies of children with rare diseases.**
- The focus was on:
  - 'What' should be measured NOT 'how' the outcome will be measured (i.e., operationalization of the outcome).
  - PROs that are generally applicable to a broad set of pediatric rare diseases.

Results from RDAP Prioritization

- Total number of surveys received=9

Table 1. Ranking for outcomes receiving >3 weighted average score

	Total Respondents Scoring 1-4 N	Not Important 1 N (%)	Somewhat Important 2 N (%)	Important 3 N (%)	Very Important 4 N (%)	Weighted Average
Cognitive function	8	0 (0)	0 (0)	2 (25)	6 (75)	3.75
Health-related quality of life	8	0 (0)	1 (13)	0 (0)	7 (89)	3.75
Treatment side effects	8	1 (13)	0 (0)	0 (0)	7 (89)	3.63
Global physical health	8	0 (0)	1 (13)	1 (13)	6 (75)	3.63
Physical function	8	0 (0)	1 (13)	2 (25)	5 (63)	3.5
Anxiety	8	0 (0)	0 (0)	5 (63)	3 (38)	3.38
Depressive symptoms	8	0 (0)	0 (0)	5 (63)	3 (38)	3.38
Emotional functioning	8	0 (0)	0 (0)	5 (63)	3 (38)	3.38
Sleep disturbance	8	0 (0)	1 (13)	4 (50)	3 (38)	3.25
School attendance	8	0 (0)	1 (13)	4 (50)	3 (38)	3.25
Psychosocial development	8	0 (0)	2 (25)	3 (38)	3 (38)	3.13
Family quality of life	8	0 (0)	2 (25)	3 (38)	3 (38)	3.13
Experience of care	8	0 (0)	2 (25)	3 (38)	3 (38)	3.13

Results from RDAP Prioritization

- Total number of surveys received=9

Table 2. Outcomes receiving ≤3 weighted average score

	Total Respondents Scoring 1-4 N	Not Important 1 N (%)	Somewhat Important 2 N (%)	Important 3 N (%)	Very Important 4 N (%)	Weighted Average
Psychosocial illness impact	8	0 (0)	2 (25)	4 (50)	2 (25)	3
Stress	8	0 (0)	2 (25)	4 (50)	2 (25)	3
Family relationships	8	0 (0)	2 (25)	4 (50)	2 (25)	3
Global mental health	8	0 (0)	1 (13)	7 (89)	0 (0)	2.88
Anger	8	0 (0)	4 (50)	4 (50)	0 (0)	2.5
Affect	8	1 (13)	2 (25)	5 (63)	0 (0)	2.5
Peer relationships	8	0 (0)	4 (50)	4 (50)	0 (0)	2.5
Social support	8	1 (13)	2 (25)	5 (63)	0 (0)	2.5
Self-efficacy	8	0 (0)	6 (75)	1 (13)	1 (13)	2.38
Meaning and purpose	7	1 (14)	3 (43)	3 (43)	0 (0)	2.29
Satisfaction with participation in social activities	8	1 (13)	4 (50)	3 (38)	0 (0)	2.25
Satisfaction with social roles and activities	8	1 (13)	5 (63)	2 (25)	0 (0)	2.13

What projects are in the PCORI portfolio of rare diseases involving children?

As of March 2017, PCORI has 15 active or completed patient-centered CER projects on rare diseases which involve children*, an investment of $37 million.

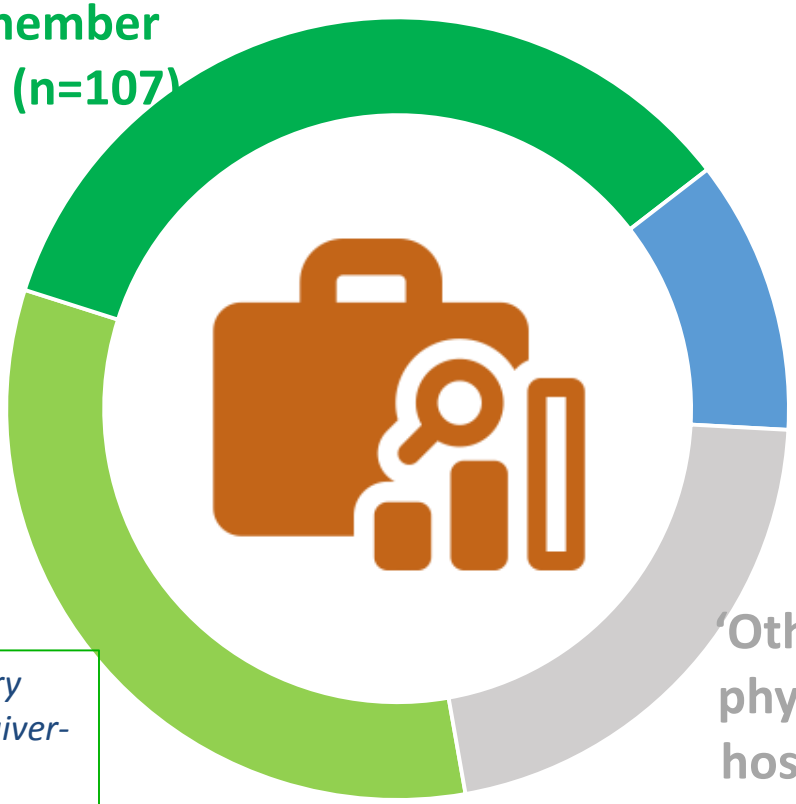
Conditions:

- Acute myeloid leukemia
- Cerebral palsy
- Chiari type I malformation (CM) and syringomyelia (SM)
- Disorders of sex development
- Duarte galactosemia
- Eosinophilic esophagitis
- Hydrocephalus
- Kawasaki Disease
- Pediatric Crohn's Disease
- Pediatric transverse myelitis
- Polyarticular juvenile idiopathic arthritis
- Spinal cord injury and spina bifida
- Urea cycle disorders
- All rare diseases (study of genomic testing reports)

* Note that 2 studies of sickle cell disease are not included in this sample.

Who is reporting the outcomes being studied in PCORI projects on rare diseases?

Two-thirds of outcomes in PCORI's CER rare disease projects are children are patient- or caregiver-reported



Five studies had at least one primary outcome that was patient- or caregiver-reported

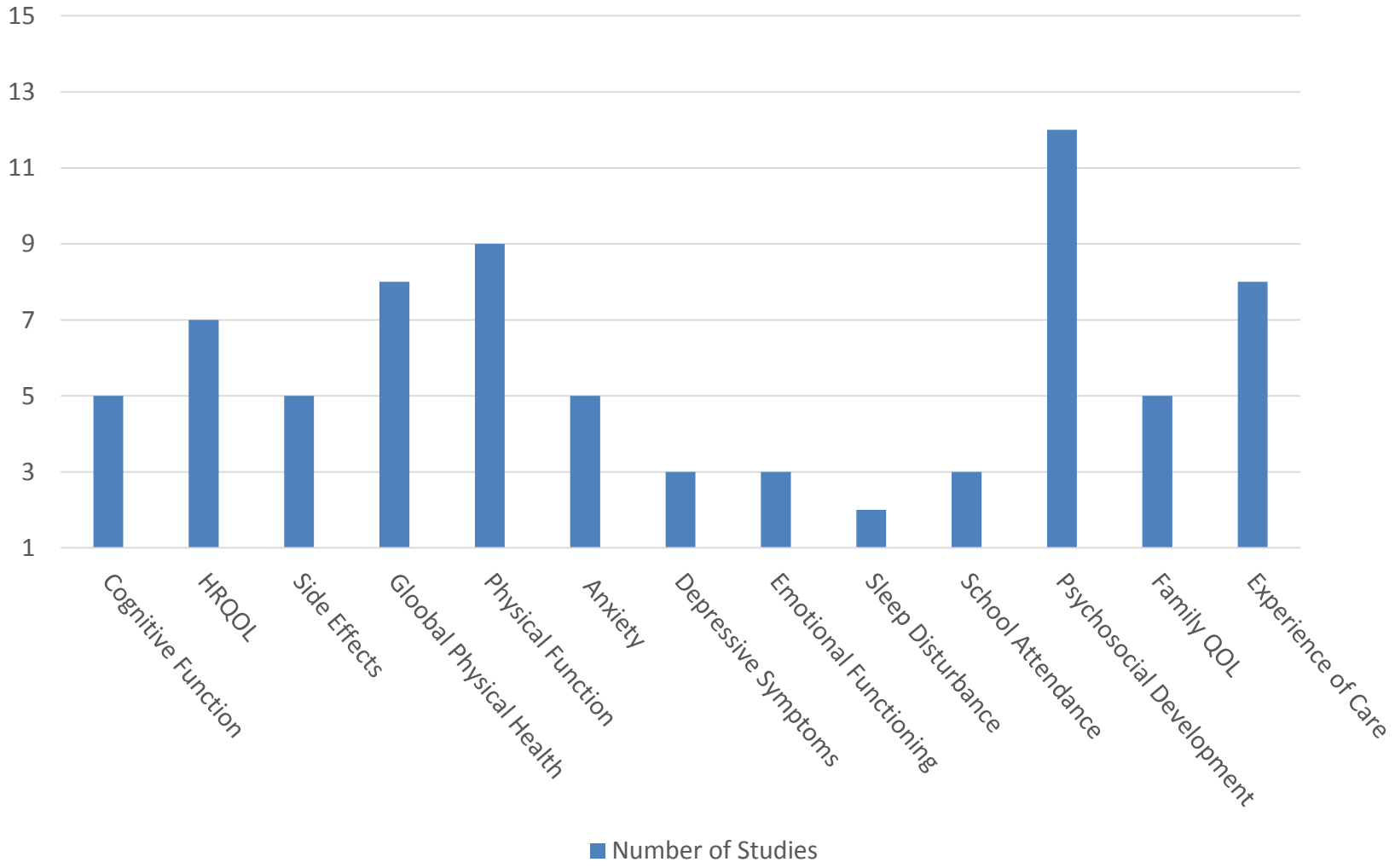
Projects often measure outcomes across more than one reporter category.
Analysis includes active/completed rare disease CER projects that involve children (n=15 as of March 2017).
Analysis excludes Methods, Pilots, PPRNs and CDRNs, MOUs and Engagement Awards

What *health status and well-being* outcomes are patients and caregivers reporting in PCORI CER projects on rare diseases that involve children?

There are 113 **health status and well-being outcomes** *reported by patients and caregivers* across 11 projects on rare diseases involving children.

- Psychological health status (n=42; 7 studies)
  - Anxiety, cognition, depression, emotional status, executive functioning, worry etc.
- Psychosocial status (n=37; 10 studies)
  - Family activities/impact, health-related quality of life, peer relations, social functioning, etc.
- Physical health status (n=32; 7 studies)
  - Mobility, physical functioning, visual motor functioning, etc.
- General health and functioning (n=2; 1 study)
  - Global health

Prioritized Outcomes among PCORI-funded Studies on Pediatric Rare Diseases



Discussion and Next Steps

- What is the overall impression of the results?
- What is the consensus for prioritization of top outcomes?
  - Which outcomes, if any, were not rated as important that should be?
  - Which outcomes, if any, were rated as important that should not be?
  - Are there outcomes that are missing, but important to include in a core outcome set for pediatric rare diseases?
- What are the next steps?

Break

11:30 – 11:45 a.m.

pcori®

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Developing PCORI Informational Resources to Better Serve the Rare Disease Community

Parag Aggarwal, PhD

Senior Program Officer, Healthcare Delivery and Disparities Research, PCORI

William Silberg

Director, Communications, PCORI

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Current Available Resources

- **PCORI-Funded Rare Disease Projects and Related Resources (Current)**
  https://www.pcori.org/get-involved/join-advisory-panel/advisory-panel-rare-disease/pcori-funded-rare-disease-projects-and
  *This page was created for the Spring meeting

- **Research Spotlight on Rare Diseases (PDF)**
  https://www.pcori.org/sites/default/files/PCORI-Research-Spotlight-Rare-Disease.pdf
  *This is one of our one-pagers that were intended to bring together key information about PCORI's high-priority research topics. These one-pagers are being expanded into one of the new Research Topics pages (below), and the plan is to have a Rare Diseases page in the very near future. The RD one-pager could then be updated to include a link to the RD topic page, where someone would get more information. Perhaps the RD topic page could be modeled similarly to the Transitional Care mini-site (below)

- **PCORI's New Research Topic Pages**
  https://www.pcori.org/research-results/research-topics
  *We currently have 7 online, with more to come in the weeks and months ahead.
    - Cardiovascular Disease
    - Cancer
    - Pain Care and Opioids
    - Kidney Disease
    - Multiple Sclerosis
    - Dementia and Cognitive Impairment
    - Transitional Care

- **PCORI's Transitional Care (TC) mini-site**
  https://www.pcori.org/research-results/topics/transitional-care
  *This is a multi-page Research Topic page, highlighting the 21 transitional care projects under PCORI's TC Evidence to Action Network, and related information.

Lunch

We will resume at 1:15 PM ET

Presentation Materials for PCORI's Rare Disease Portfolio

Parag Aggarwal, PhD

Senior Program Officer, Healthcare Delivery and Disparities Research, PCORI

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

PCORI's Focus on Rare Disease Research

Presenter Name

Presenter Title

Date

pcori®

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Presentation Overview

- PCORI: Background and Mission
- PCORI's Rare Disease Research Focus
- Award Type: Eugene Washington PCORI Engagement Awards
- Award Type: Pipeline to Proposal (P2P) Awards
- Award Type: Research Awards
- Rare Disease Specific PCORI Resources

PCORI: Background and Mission

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

About PCORI

- Authorized by Congress as an independent research institute through the Patient Protection and Affordable Care Act.
- Funds comparative clinical effectiveness research (CER) that engages patients and other stakeholders throughout the research process.
- Seeks answers to real-world questions about what works best for patients based on their circumstances and concerns.

PCORI: Mission and Strategic Goals

PCORI helps individuals make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from **research guided by patients, caregivers, and the broader healthcare community.**

Our Strategic Goals:

- Increase quantity, quality, and timeliness of useful, trustworthy research information available to support health decisions
- Speed the implementation and use of patient-centered outcomes research evidence
- Influence research funded by others to be more patient-centered

We Fund Comparative Clinical Effectiveness Research (CER)

- Compares the effectiveness of two or more interventions with proven efficacy
- Answers questions that matter to patients and other clinical decision makers
- Measures benefits in real-world populations
- Describes results in subgroups of people
- Helps consumers, clinicians, purchasers, and policy makers make informed decisions that will improve care for individuals and populations
- Patient-centered

Note: We do not fund cost-effectiveness research

We Fund Patient-Centered Outcomes Research (PCOR)

PCOR is a relatively new form of CER that….

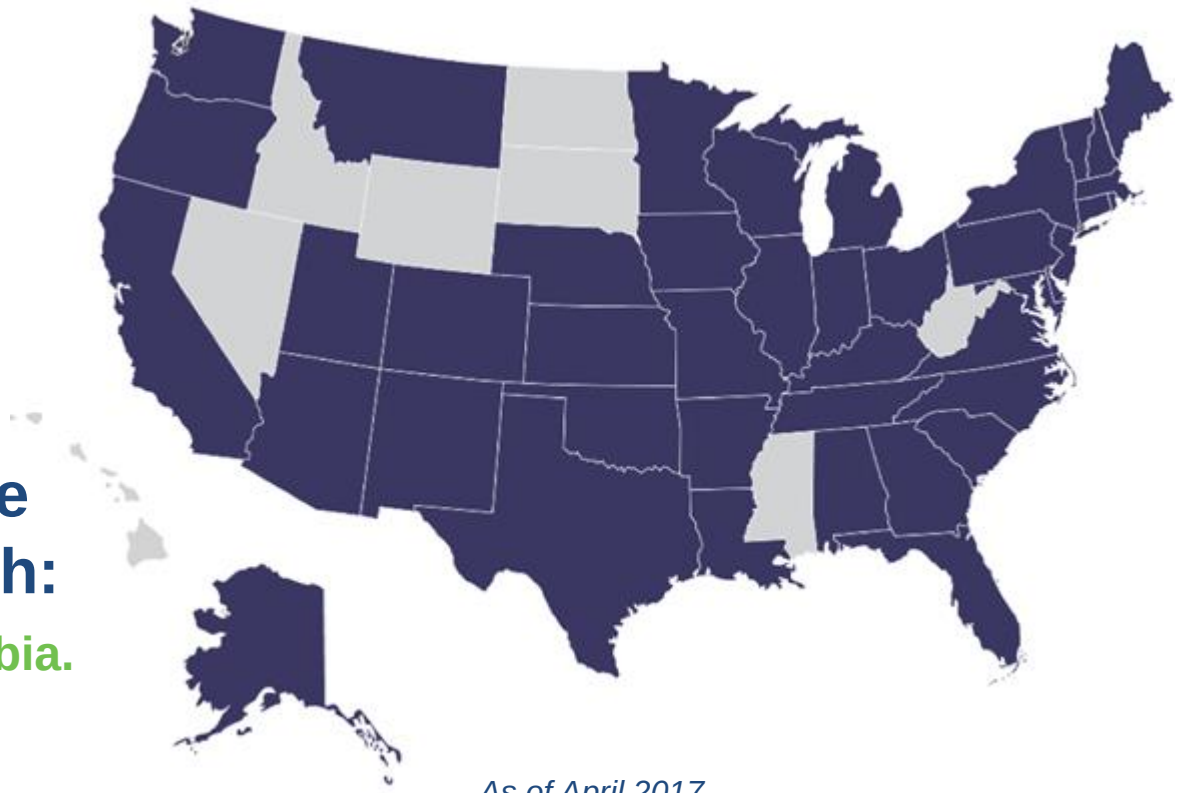
- Considers patients' needs and preferences, and the outcomes most important to them
- Investigates what works, for whom, under what circumstances
- Helps patients and other healthcare stakeholders make better-informed decisions about health and healthcare options

Snapshot of PCORI Funded Projects

Total number of research projects awarded:
440*

Total funds awarded:
$1.61 billion

Number of states where we are funding research:
42 (plus the District of Columbia. Canada. Sweden, and Italy)



As of April 2017

***784 total projects that include engagement, research infrastructure, and coordinating center awards**

Who Are Our Stakeholders?

- Payers
- Clinicians
- Caregivers/Family Members
- Purchasers
- Hospital/Health Systems
- Policy Makers
- Patients/Consumers
- Industry
- Patient/Caregiver Advocacy Organizations
- Training Institutions

Who Can Apply for PCORI Funding?

- Any private sector research organization

Non-Profit Organizations

For Profit Organizations

- Any public sector research organization

Universities/ Colleges

Hospitals or Healthcare Systems

Local, State, or Federal Government

Laboratories

- Foreign Organizations or Nondomestic Components of Organizations based in US, **if clear benefit to US healthcare system**

NOTE

PI **must** be an employee of the prime applicant institution. Individuals are not eligible to submit research applications to PCORI.

PCORI's Rare Disease Research Focus

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Snapshot of PCORI-Funded Rare Disease Projects

Number of Rare Disease projects:

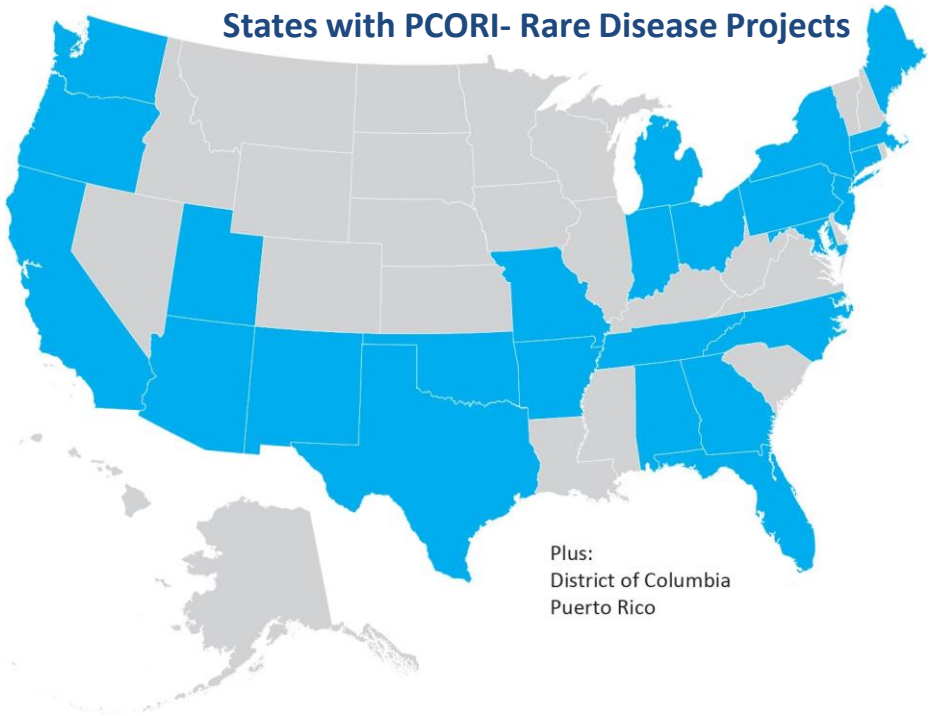
26 Engagement Awards
14 Pipeline to Proposals
27 Research Awards

Amount awarded to Rare Diseases:

$4.1 million in Engagement Awards
$575,000 in P2P Awards
$80 million in Research

Number of states where we are funding Rare Disease research:

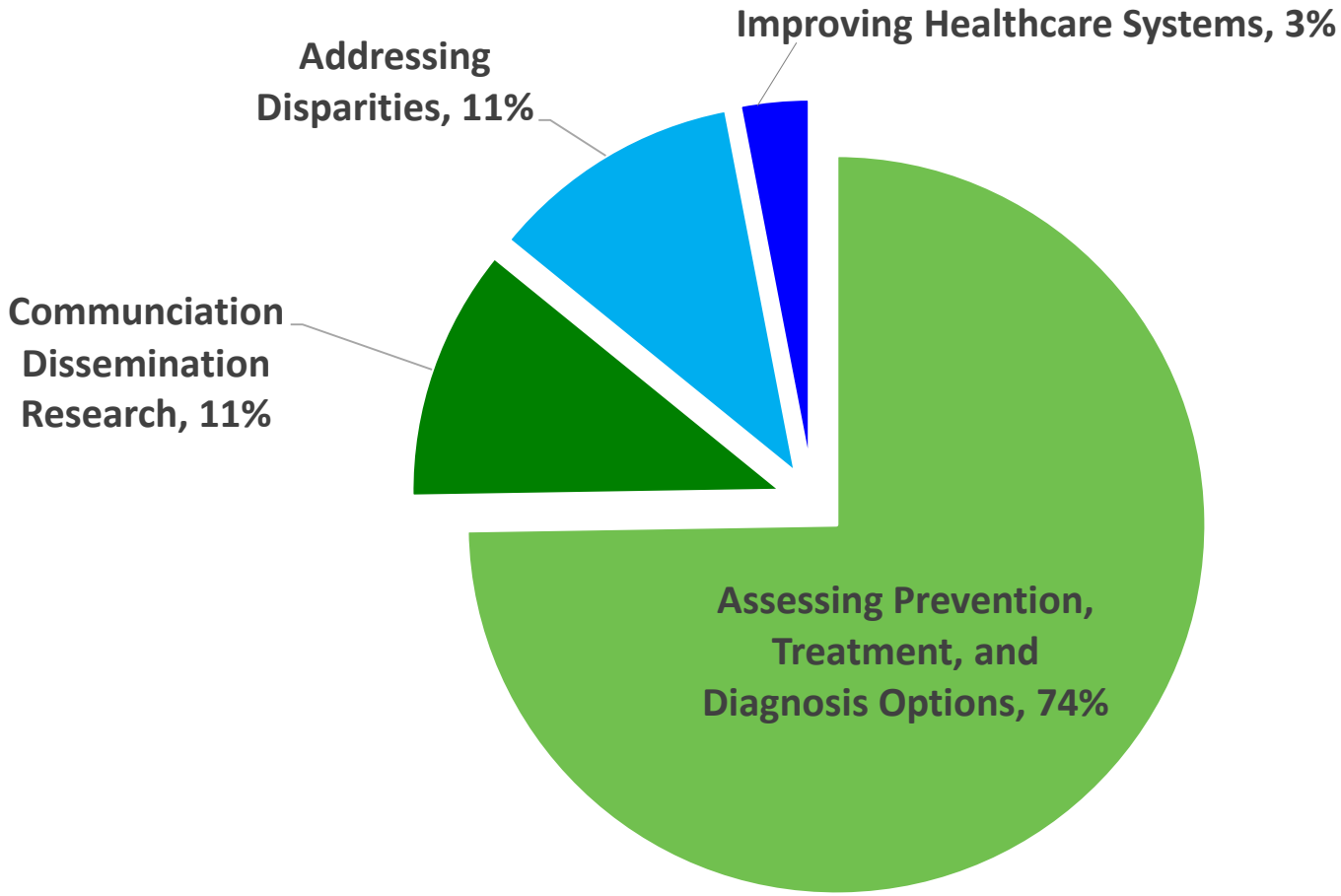
25 (plus the District of Columbia and Puerto Rico)



As of September 2017

Rare Disease Portfolio

Proportion of projects by PCORI priority area



N=27
Categories are mutually exclusive
Active and completed projects awarded through December 2016 (Cycle 1 2016)

Rare Disease Portfolio

Accelerating PCOR Methods and Infrastructure Projects

Patient Centered Adaptive Treatment Strategies (PCATS) using Bayesian Causal Inference

Bin Huang, PhD
Cincinnati Children's Hospital Medical Center
Cincinnati, OH

Engaging Patients and Caregivers Managing Rare Diseases to Improve the Methods of Clinical Guideline Development

Dmitry Khodyakov, PhD, MA
RAND Health
Santa Monica, CA

Design and Methodological Improvements for Patient-Centered Small n Sequential Multiple Assignment Randomized Trials (snSMARTs) in the Setting of Rare Diseases

Kelley Kidwell, PhD,
University of Michigan
Ann Arbor, MI

Rare Disease Portfolio

Number of projects across care continuum

N=27
Categories are mutually exclusive
Active and completed projects awarded through December 2016 (Cycle 1 2016)
Excludes Methods

Rare Disease Portfolio

Specific conditions

Acute Myeloid Leukemia
Cerebral palsy
Chiari type I malformation (CM) & syringomyelia (SM)
Disorders of Sex Development
Duarte galactosemia
Eosinophilic Esophagitis
Hydrocephalus
Idiopathic Subglottic Stenosis
Lupus nephritis
Kawasaki disease
Myasthenia Gravis
Non-CF bronchiectasis
Pediatric Crohn's Disease
Pediatric Transverse Myelitis
Polyarticular Juvenile Idiopathic Arthritis
SATB2-Associated Syndrome
Sickle Cell Disease
Spinal Cord Injury and Spina Bifida
Systemic Scleroderma
Urea cycle disorders

Projects awarded through December 2016 (Cycle 1 2016)
Excludes Methods

Award Type: Eugene Washington PCORI Engagement Awards

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Program Overview

- A programmatic funding opportunity -- not research awards
- Support projects that will build a community better able to participate in patient-centered research (PCOR) and comparative clinical effectiveness research (CER), as well as serve as channels to disseminate study results
- Projects will produce deliverables that are useful to awardees, PCORI, and the broader PCOR community for increasing patient and stakeholder engagement in PCOR and CER

*As of April, 2017

Engagement Awards Portfolio Overview

Number of awards:

256*

Amount awarded:

$51.4 million

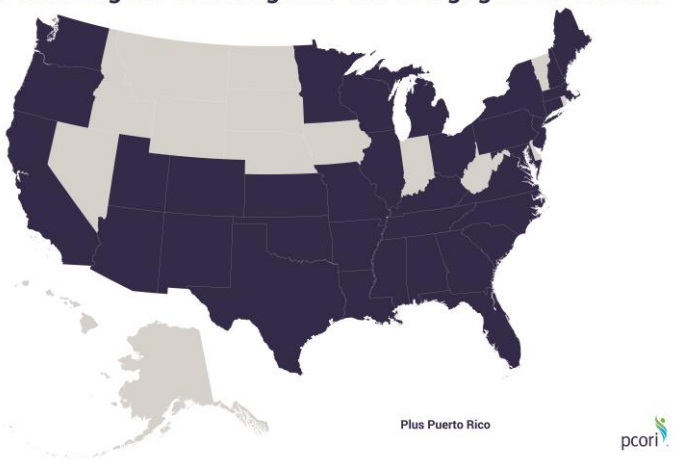
States with funded projects:

35 **(plus DC and Puerto Rico)**

26 are Rare Disease Related

$4.1 million has gone towards funding Rare Disease projects

States with Eugene Washington PCORI Engagement Awards



**As of April, 2017*

Types of Engagement Awards

- **Engagement Award (EA) projects**
  - build **knowledge** base about how patients and other stakeholders want to participate in PCOR/CER or receive research findings;
  - implement **training** or skill **development** initiatives to build capacity for engaging in PCOR; and
  - strengthen channels for **disseminating** research findings.
- **Engagement Award Initiative Notice (EAIN)** supports **meetings/conferences** that align with PCORI's mission and strategic plan, and facilitate expansion of PCOR/CER in areas such as:
  - Research design and methodology
  - Research development
  - Dissemination and implementation

Awards of **up to $250,000** per project, up to **two years** in duration

Award Type: Pipeline to Proposal (P2P) Awards

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Pipeline to Proposal Awards (P2P)

Mission

- The P2P program aims to build a national community of patient, stakeholder, and researcher partnerships that have the expertise and passion to participate in patient-centered outcomes research within their communities that leads to high-quality research.
- In addition, the P2P program is a funding mechanism to develop and strengthen the engagement in proposals submitted for funding**.**

Purpose

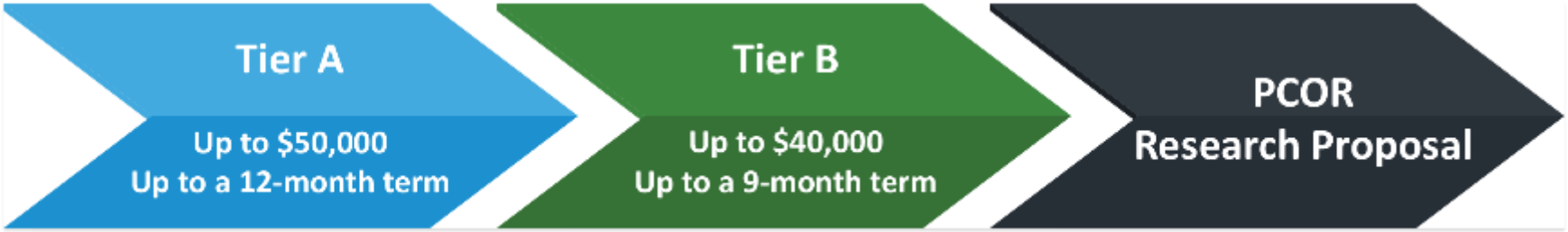
- Build capacity and cultivate the development of proposals with sound scientific rigor and **robust patient engagement**.

Overarching Goals of P2P

- Enabling the non-researcher community (including individual patients) to drive partnership development and research project (flip the funding)
- Developing research partnerships, infrastructure and a diverse, skilled PCOR community especially in underserved and underrepresented communities
- Creating a robust Dissemination and Implementation network that recognizes the PCORI brand
- Submission of high quality PCOR/CER proposals to PCORI and other funders with strong engagement plans
- Learning about promising pre-engagement practices and methods in the P2P (P2P as a learning laboratory) and share with broader research community

New Two-Tiered Program

Projects participate in a two-tiered funding mechanism, which supports concentrated partnership development in Tier A and proposal development in Tier B. Each tier is designed to help patients and communities take another step toward producing community-led PCOR proposals.



*P2P awards already in progress will continue to move through the old three-tiered program structure.

For More Information:

Engagement Awards Program

- Web Page: www.PCORI.org/eugene-washington-awards
- Email Address: ea@pcori.org
- Contact Number: 202-370-9312

Pipeline to Proposals Program

- Web Page: http://www.pcori.org/funding-opportunities/programmatic-funding/pipeline-proposal-awards
- Email Address: p2p@pcori.org

Award Type: Research Awards

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

The Research We Fund is Guided by Our National Priorities for Research

Assessment of Prevention, Diagnosis, and Treatment Options

Improving Healthcare Systems

Communication & Dissemination Research

Addressing Disparities

Accelerating PCOR and Methodological Research

Assessment of Prevention, Diagnosis, and Treatment Options

Seeks to fund investigator-initiated research that:

- Compares the effectiveness of two or more options that are known to be effective but have not been adequately compared in previous studies.
- Among compared population groups, investigates factors that account for variation in treatment outcomes that may influence those outcomes in the context of comparing at least two treatment approaches.

Assessment of Prevention, Diagnosis, and Treatment Options

Available funds: Up To $32 Million

Budget: $2 million in direct costs

Project Period: 3 years

Improving Healthcare Systems

Seeks to fund investigator-initiated research on effects of system changes on:

- Patients' access to high quality, support for self-care, and coordination across healthcare settings.
- Decision making based on patients' values.
- Experiences that are important to patients and their caregivers, such as overall health, functional ability, quality of life, stress, and survival.
- The efficiency of healthcare delivery, as measured by the amount of ineffective, duplicative, or wasteful care provided to patients.

Available funds: Up To $16 Million

Award Types

- Large Awards
  - Up to $5 million in direct costs
  - Up to 5 years
- Small Awards
  - Up to $1.5 million in direct costs
  - Up to 3 years

Communication and Dissemination Research

Seeks to fund investigator-initiated research in:

- Clinician engagement with CER.
- Translating research, decision support interventions, and risk communication. For this funding announcement, studies of decision support aids are not encouraged.
- Distribution of CER to patients, caregivers, and providers.

Communication & Dissemination Research

Available funds: Up To $8 Million

Budget: $1.5 million in direct costs

Project Period: 3 years

Addressing Disparities

Seeks to fund investigator-initiated research that:

- Compares interventions to reduce or eliminate disparities in patient-centered outcomes.
- Identifies/compares promising practices that address contextual factors and their impact on outcomes.
- Compares health care options across different patient populations.
- Compares and identifies best practices within various patient populations for information sharing about outcomes and research.

Available funds: Up To $8 Million

Budget: $1.5 Million in direct costs

Project Period: 3 years

Addressing Disparities

Improving Methods for Conducting Patient-Centered Outcomes Research

Seeks to fund investigator-initiated research that addresses gaps in methodological research relevant to conducting PCOR to benefit all healthcare stakeholders.

Focuses on:

- Methods for patient and other stakeholder engagement in research
- General analytic methods
- Design-specific analytic methods
- Analytics for data networks
- Usability, interpretability, and clinical meaningfulness of patient-reported outcomes
- Issues related to human subjects protections
- Improving methods of recruitment and retention of participants into PCOR/CER

Available funds: Up To $12 Million

Budget: $750,000 in direct costs **Project**

Period: 3 years

We are Particularly Interested in Research That…

Focuses on high-priority conditions

- Affecting large numbers of people across a range of populations
- Placing a heavy burden on individuals, families, specific populations, and society
    - This includes many rare diseases

Funding Mechanisms

- Broad Funding Announcements
- Pragmatic Clinical Studies
- Targeted Funding Announcements

PCORI's Broad Funding Announcement

- Supports research on investigator initiated research topics that address questions of importance to patients and other stakeholders.
- The announcement includes 5 different types of awards that align with PCORI's National Priorities for Research

Overview

Awards range from $750,000 – $5,000,000 in direct costs per project and are generally 3 years in duration

Pragmatic Clinical Studies

- Addresses critical evidence gaps, including topics of special interest to stakeholders, National Academy of Sciences, Agency for Healthcare Research and Quality
- Seeks to produce information that can be directly adopted by providers
- Often conducted in routine clinical settings
- Though often large, usually less complex protocols than traditional trials

Overview

Awards can be up to $10 million direct costs per project and are generally 5 years in duration

Targeted Funding Announcements

- Seek research proposals on the highest-priority questions identified through PCORI's topic generation and research prioritization process
- Examples:
  - Clinical Management of Hepatitis C Infection
  - Treatment of Multiple Sclerosis
  - Management of Care Transitions for Emerging Adults with Sickle Cell Disease

Overview

Budget and project duration vary by funding announcement

http://www.pcori.org/research-results/how-we-select-research-topics/generation-and-prioritization-topics-funding-4

Help with selecting a PCORI Funding Program

- A list of all open, closed, and upcoming funding announcements can be found here: http://www.pcori.org/funding-opportunities

- If you are not sure which is best for you, contact the PCORI Helpdesk:
  - Email: sciencequestions@pcori.org
  - Phone: (202).627.1884
  - Online: http://www.pcori.org/PFA/inquiry

- **PCORnet**: PCORI's National Infrastructure
  - Clinical Data Research Network (Rare Disease cohorts)
  - Patient-Powered Research Network (Rare Disease-specific)
  - Archived Webinar: http://www.pcori.org/events/2017/pcornet-101
  - Contact: pmo@pcornet.org

Rare Disease Specific PCORI Resources

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

New Page for Rare Disease Resources

PCORI-Funded Rare Disease Projects and Related Resources

View listings of PCORI-funded rare disease clinical effectiveness research projects, as well as projects on coordination and engagement with the rare disease research community, and related resources.

Applicant Resources

- Guidance for RD Orgs for Research Awards
- FAQs for Rare Disease Applicants

Webinars & Other Events

- Webinar: PCORI Funding for Rare Diseases (2015)
- Town Hall: Management of Care Transitions for Emerging Adults with Sickle Cell Disease
- Rare Diseases Roundtable (2013)

Blogs, Feature Stories, Videos & Other Resources

Blogs

- Big Data versus a Rare Disease

Here you can find:

- All of PCORI's funded Rare Disease projects
- Applicant resources (Rare Disease specific)
- Past webinars
- Rare Disease PCORI-produced media, videos, and blogs

http://www.pcori.org/get-involved/join-advisory-panel/advisory-panel-rare-disease/pcori-funded-rare-disease-projects-and

Learn More

www.pcori.org

info@pcori.org

twitter

YouTube

Thank You

Presenter Name

Presenter Title

Presenter's Contact Information (Optional)

pcori®

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

RDAP Discussion

- What are most beneficial parts of the presentation?
- What components do panelists recommend be added or removed from the presentation?

Break

1:45 – 2:00 p.m.

pcori®

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

CER-1502-27816

COMPARATIVE EFFECTIVENESS OF THERAPY IN RARE DISEASES: LIVER TRANSPLANTATION VS CONSERVATIVE MANAGEMENT OF UREA CYCLE DISORDERS

PCORI RDAP Meeting

September 26, 2017

Outline

- Overview of Urea Cycle Disorders and management
- Overview of PCORI-sponsored rare disease project
- Preliminary results
- Lessons Learned

Outline

- Overview of Urea Cycle Disorders and management
- Overview of PCORI-sponsored rare disease project
- Preliminary results
- Lessons Learned

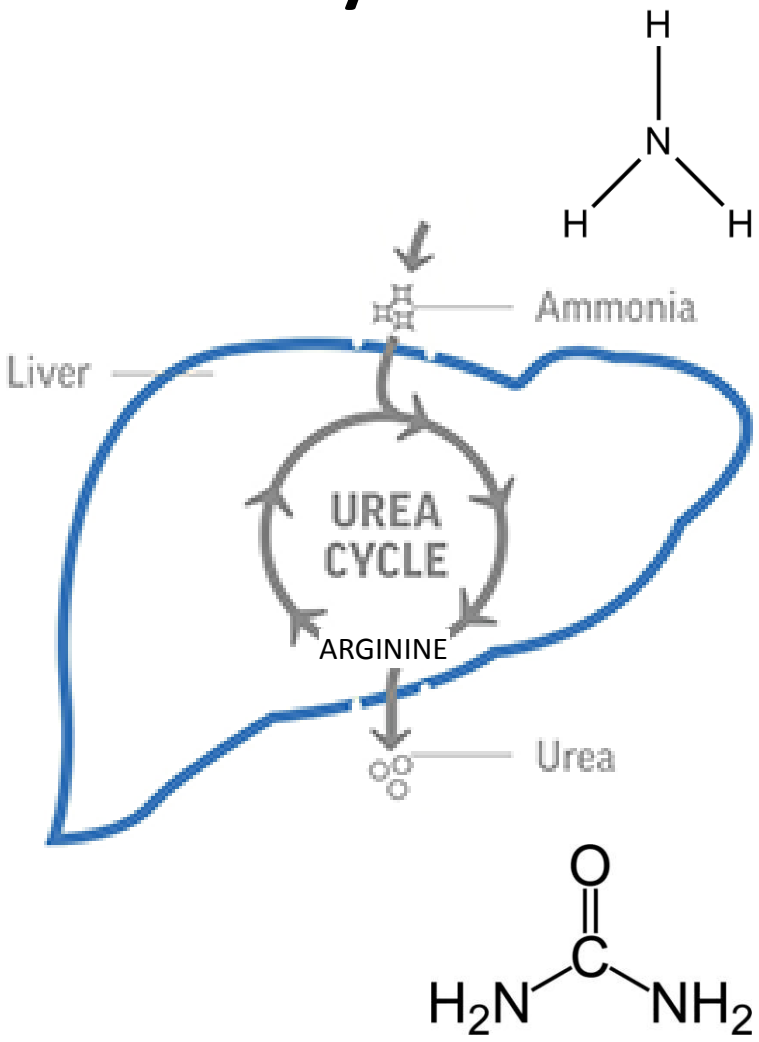
Overview of the urea cycle

- Essential mammalian biochemical pathway

- Has two roles:

  1) Convert ammonia into urea

  2) Make arginine (an amino acid)

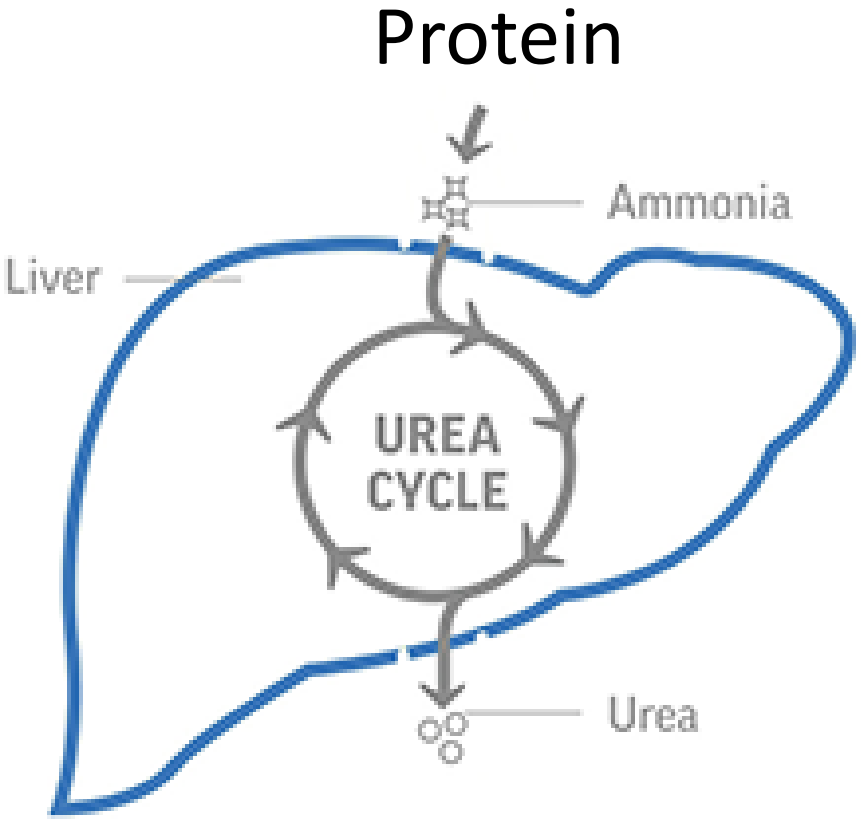


http://www.horizonpharma.com/wp-content/uploads/2015/04/UCD2.png

The urea cycle

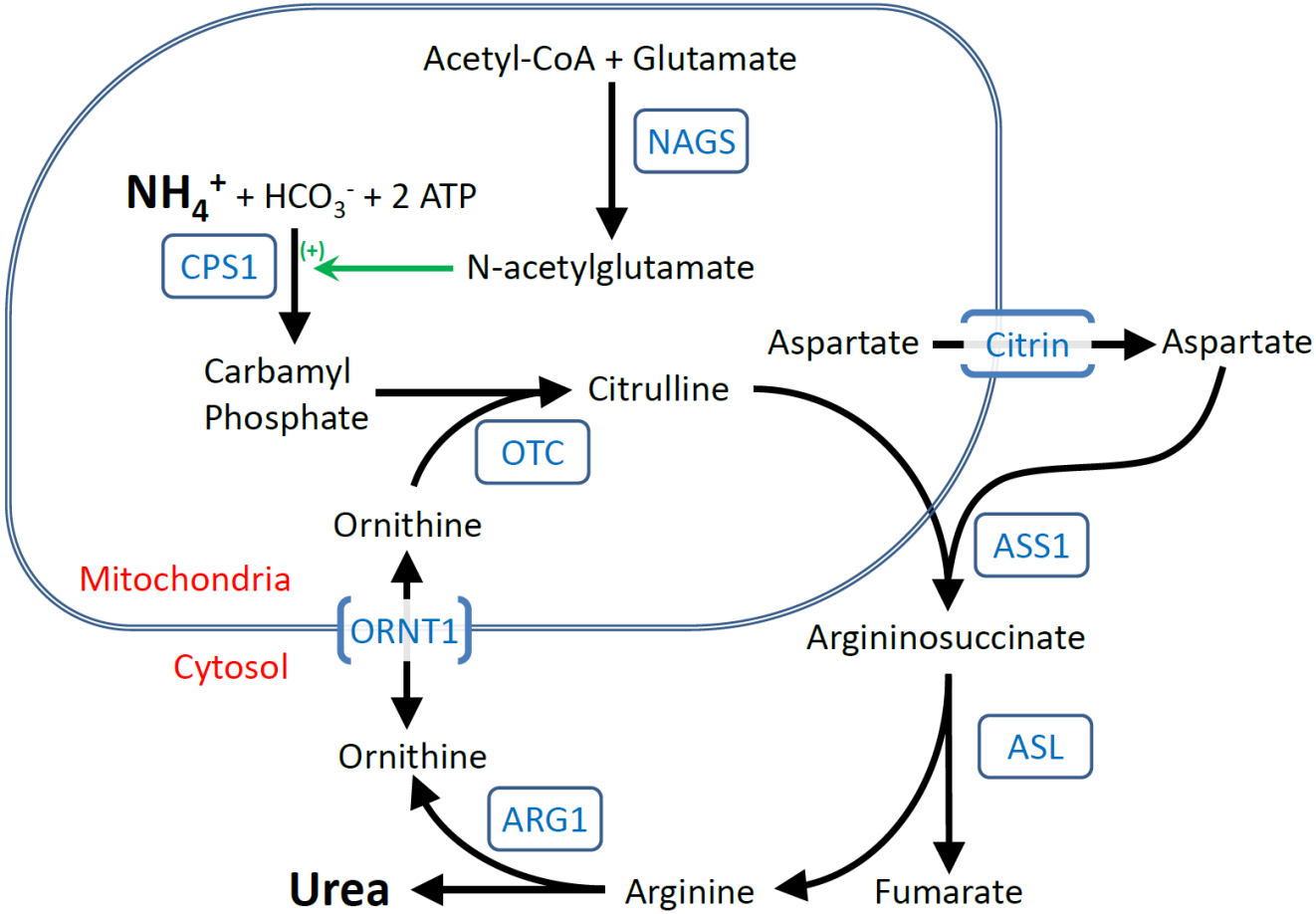
- Ammonia (NH_3) is a form of waste nitrogen which comes protein degradation

- The urea cycle requires the coordinated function of 6 ENZYMES and 2 transporters



http://www.horizonpharma.com/wp-content/uploads/2015/04/UCD2.png

The hepatic urea cycle



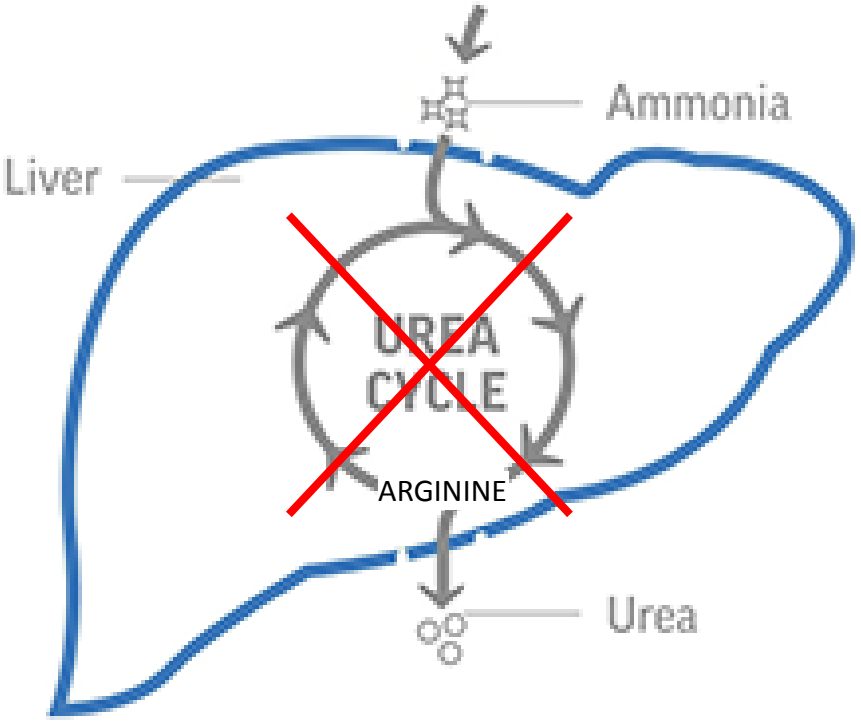
Urea cycle disorders

- A defect in one of these transporters or enzymes or may block urea cycle function

- This can result in

1) Build up of ammonia
2) Decreased arginine production

Incidence ~ 1: 35,000



Medical management of urea cycle disorders

1) Limited dietary protein intake
   - Special medical formulas
2) Alternative pathway medications
3) Arginine/Citrulline supplementation
4) Prevention and treatment of intercurrent illness

Outcomes in UCDs are still suboptimal with medical management

- Death (Batshaw et al. MGM 2014)
- Neurocognitive deficits (Waisbren et al., JIMD. 2016)
  - IQ, Working memory, Executive functioning
- Liver disease (Laemmle et al. PLoS One. 2016)

Liver transplant in UCDs

- Liver transplant eliminates hyperammonemia
  - Eliminates need for special diet or medications
- ‘Swaps’ one condition for another
- Improving morbidity/mortality associated with liver transplant
- Increase in the proportion of liver transplants due to UCD (Perito et al. Liver Transplantation 2014)

Outline

- Overview of Urea Cycle Disorders and management
- Overview of PCORI-sponsored rare disease project
- Preliminary results
- Lessons Learned

Study Aims - PCORI CER-1502-27816

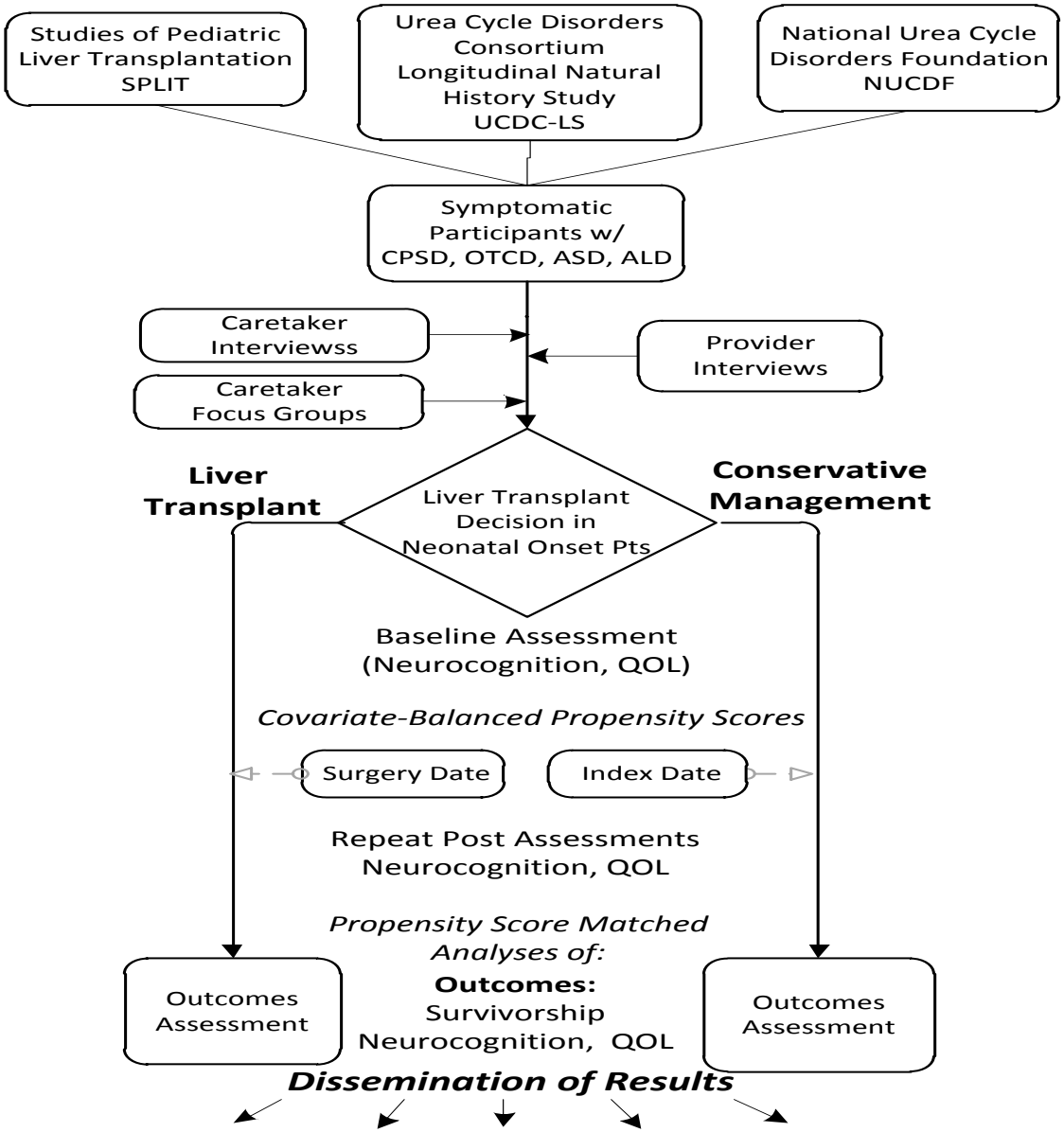
- **<u>Randomized controlled trial is not possible</u>**

- **Aim 1:** To study two urea cycle disorder (UCD) patient cohorts, one managed conservatively and the other treated by liver transplantation, comparing survival rate, neurocognitive function and patient reported quality of life.

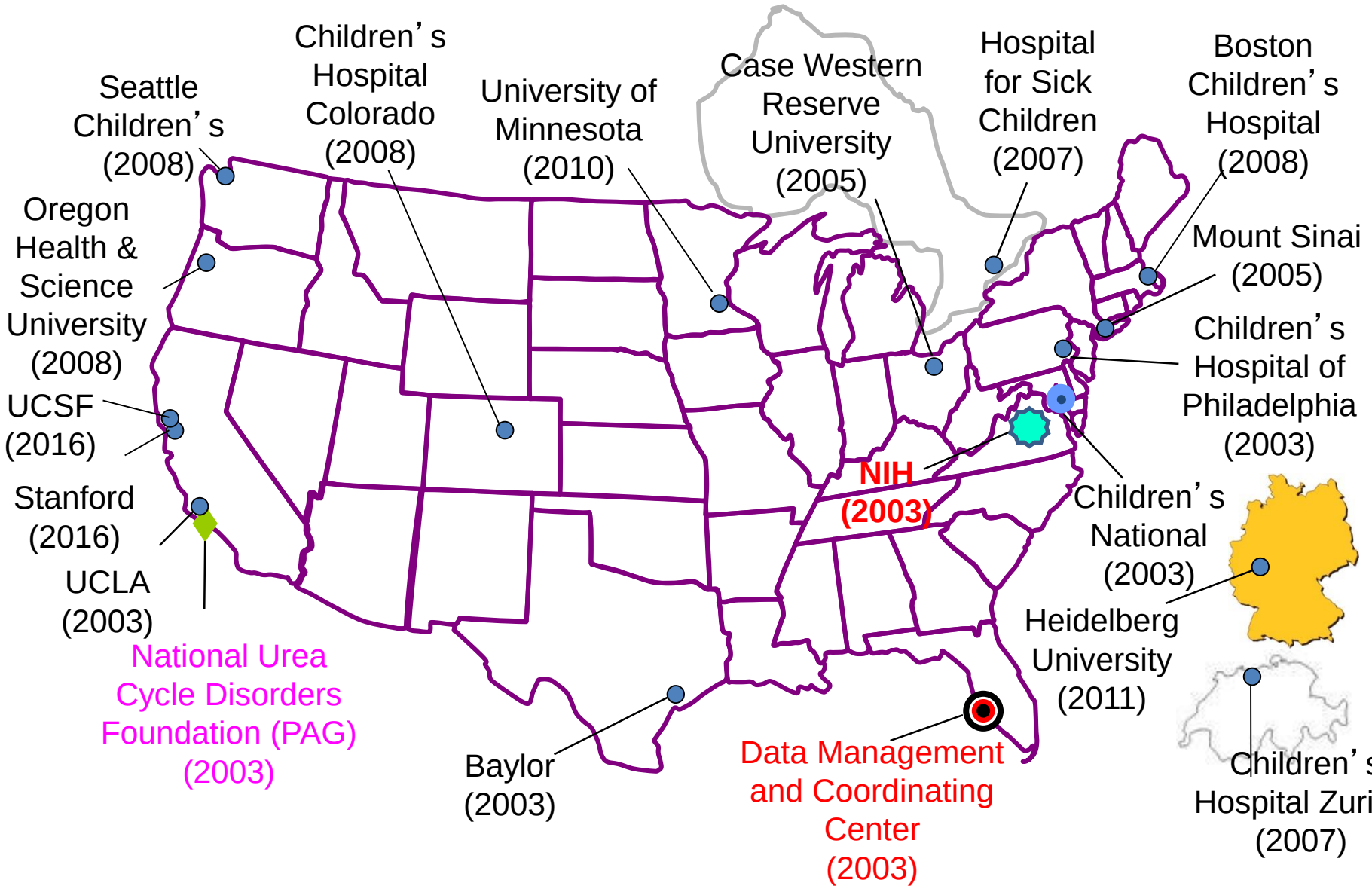
- **Aim 2:** To examine, through a representative sample of pediatric patient caretakers and medical providers, including the treating physician and other clinicians on the team, how UCD treatment decisions are made, describing the factors that influence the patient/family's decision to continue conservative management or elect liver transplantation.

- **Aim 3:** To develop a dissemination strategy for study findings of Aim 1 that aligns with the decision-making considerations and process illustrated through Aim 2 and which is responsive to the expressed needs of UCD patients and their caretakers.

STUDY DESIGN



Urea Cycle Disorders Consortium (UCDC)



Outline

- Overview of Urea Cycle Disorders and management
- Overview of PCORI-sponsored rare disease project
- Preliminary results
- Lessons Learned

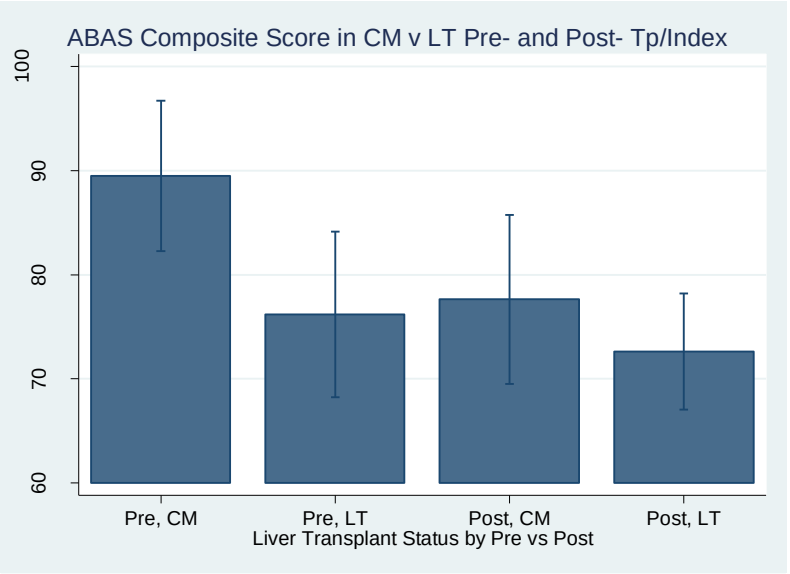
Aim 1

- Study two urea cycle disorder (UCD) patient cohorts, one managed conservatively and the other treated by liver transplantation, comparing survival, neurocognitive function and patient reported quality of life.

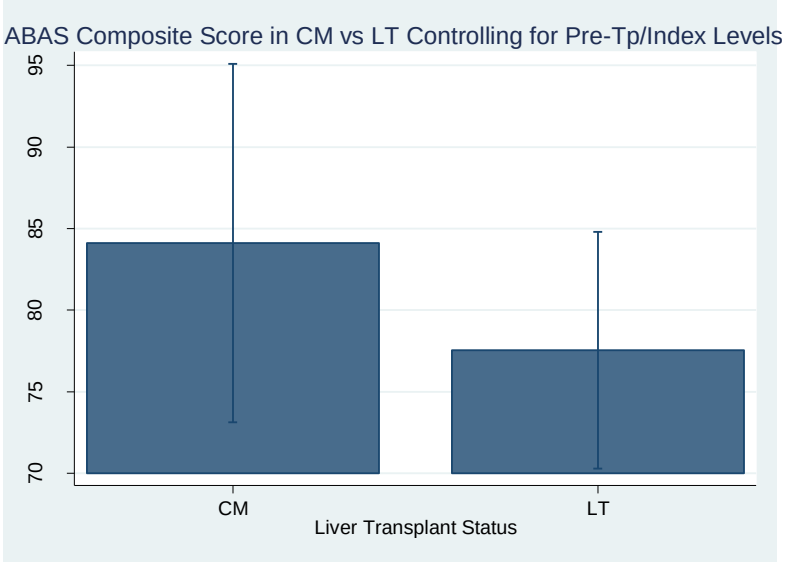
- Data accrued from 169 subjects
  - 86 conservatively managed (CM) and 83 Liver transplant (LT)

Preview: Neuropsych (NP) Comparison by Traditional Methods

- Sufficient pre/post NP data only for ABAS comparisons (Adaptive Behavior Assessment System)



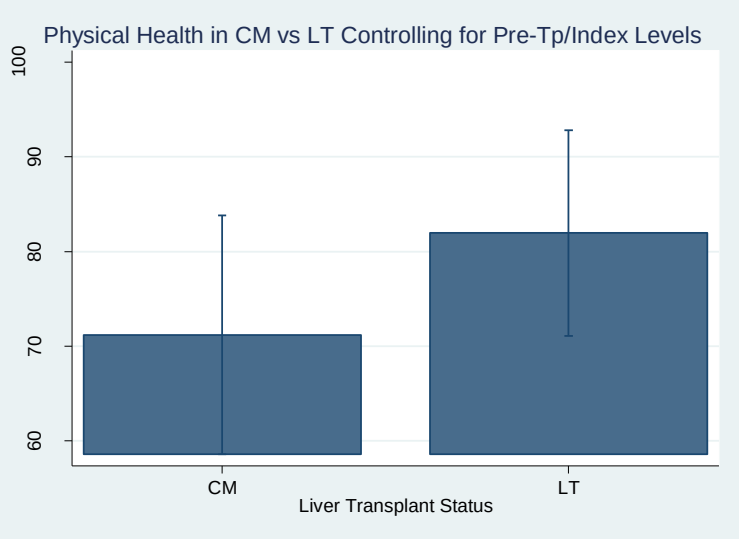
- Controlling for Pre Levels, Post ABAS Scores suggest narrowing of difference

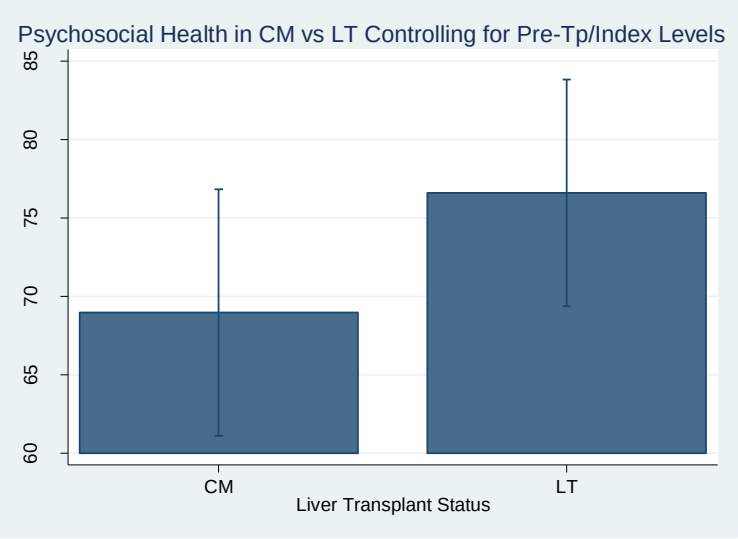


Preview: Quality of Life (QOL) Comparison by Traditional Methods

- Sufficient pre/post QOL data only for parent PEDS/QL comparisons

- Controlling for Pre Levels, Post Physical and Psychosocial QOL Scores suggest advantage for LT over CM





Comparability in Dx and Age

- Reasonable Sample Sizes
  - 86 CM and 83 LT
- Large Differences in:
  - Type and Method of Dx
  - Index vs. Transplant Age
- Not shown is greater similarity in demographic characteristics

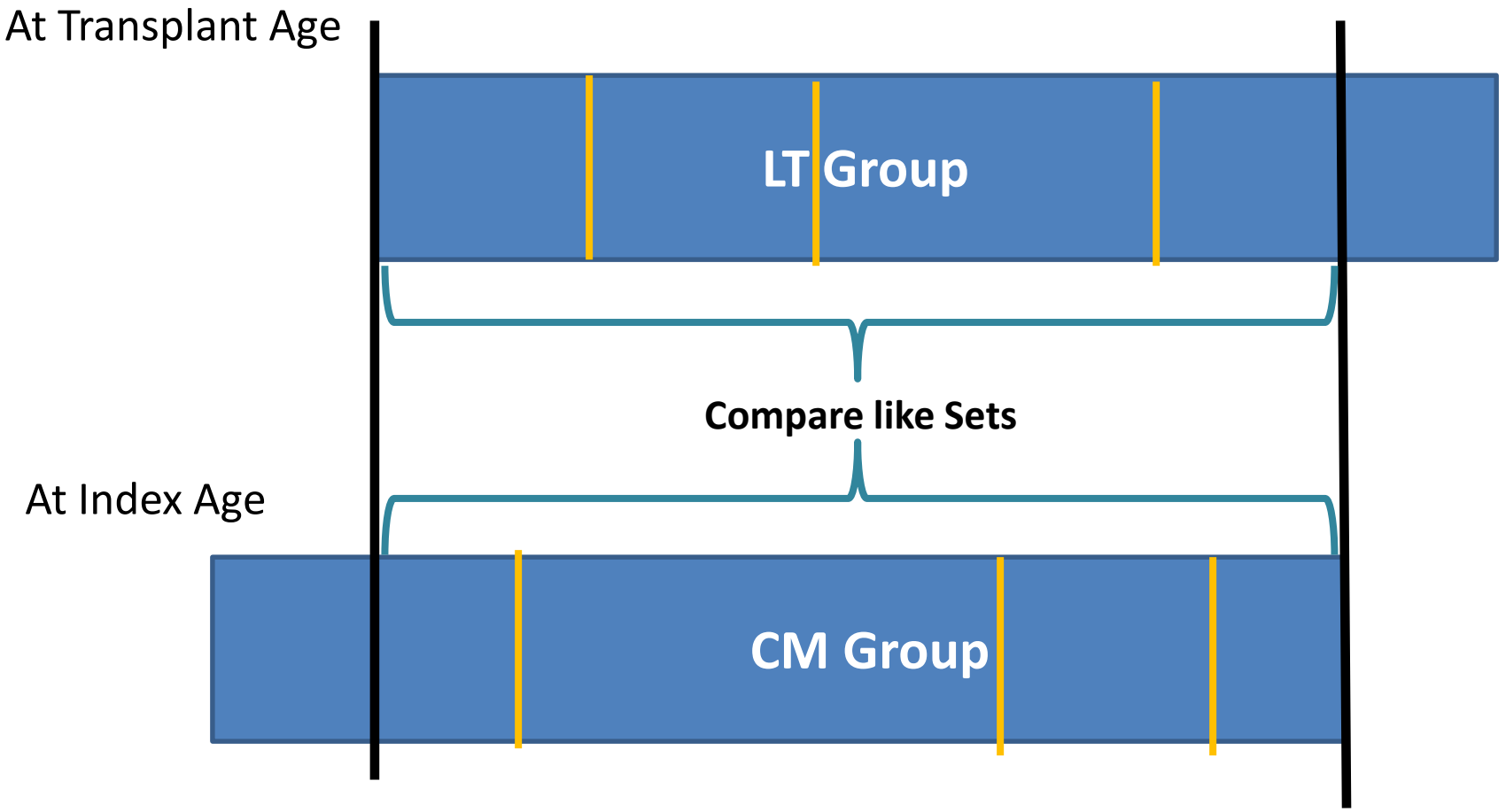
Characteristics	Consrv. Mgmt		Liver Transp		
	N	Col %	N	Col %	p-value
Total	86	100	83	100	
UCD Diagnosis					0.005
CPS1	2	2.3	10	12.0	
OTC	24	28.0	33	39.8	
ASD	25	29.1	22	26.5	
ALD	36	41.9	18	21.7	
Diagnosis Method					0.001
Clinical Presentation	42	48.8	65	78.3	
Family History	13	15.1	4	4.8	
Newborn Screening	28	32.6	14	16.9	
Unknown	3	3.5	0	0	
Transplant/Index Age (mos)					<0.001
<6 mos	7	8.2	15	18.1	
6-<12 mos	5	5.8	24	28.9	
1- <3 yrs	52	60.5	24	28.9	
3- <5 yrs	14	16.3	8	9.6	
5- <7 yrs	3	3.5	7	8.4	
7+ yrs	5	5.8	5	6	

Comparability in Severity

- Important Differences in:
  - Indicators of Severity
- Greater Severity in the Transplant Group

Severity Indicators	Consrv. Mgmt N	Consrv. Mgmt Col %	Liver Transp N	Liver Transp Col %	p-value
Total	86	100	83	100	
Pre-Transplant/Index Events					
Hyperammonemia (HA)					<0.001
None	21	24.4	0	0	
1	18	20.9	10	12	
2	9	10.5	5	6	
3-5	17	19.8	20	24.1	
6+	21	24.4	48	57.8	
HA w/ Intracranial Pressure					0.15
0	77	89.5	64	77.1	
1	8	9.3	13	15.7	
2	1	1.2	2	2.4	
3+	0	0	4	4.8	
HA with Coma					0.17
0	81	94.2	72	86.7	
1	5	5.8	5	6	
2+	0	0	4	4.8	

Covariate Balanced Propensity Scoring (CBPS) Analysis



Covariate-Balanced Propensity Scoring(CBPS) an Alternative to an RCT

RCT

- Random Tx Assignment
  - removes Tx determinant bias
  - removes other sources of bias
- Blinding
  - avoids reporting bias

CBPS

- Propensity Scoring
  - Balances key Tx predictors
- Covariate Balancing
  - Balances other characteristics
- Instrumental variable
  - Account for Transplant differences by center
- Choice of Outcomes
  - Death is free of reporting bias
  - Objective neuropsych testing
  - QOL is subjective

Future Steps

- Continued enrollment (window closes March 1, 2018)
  - Ensure complete and update assessments from UCD subjects
  - Identify potential subjects through multiple avenues
- Scoring and analysis to begin thereafter

Aim 2

- To examine, through a representative sample of pediatric patient caretakers and medical providers, including the treating physician and other clinicians on the team, how UCD treatment decisions are made, describing the factors that influence the patient/family's decision to continue conservative management or elect liver transplantation.

- Interviews of 35 caretakers and 26 providers completed

Preliminary Caretaker Data Analysis

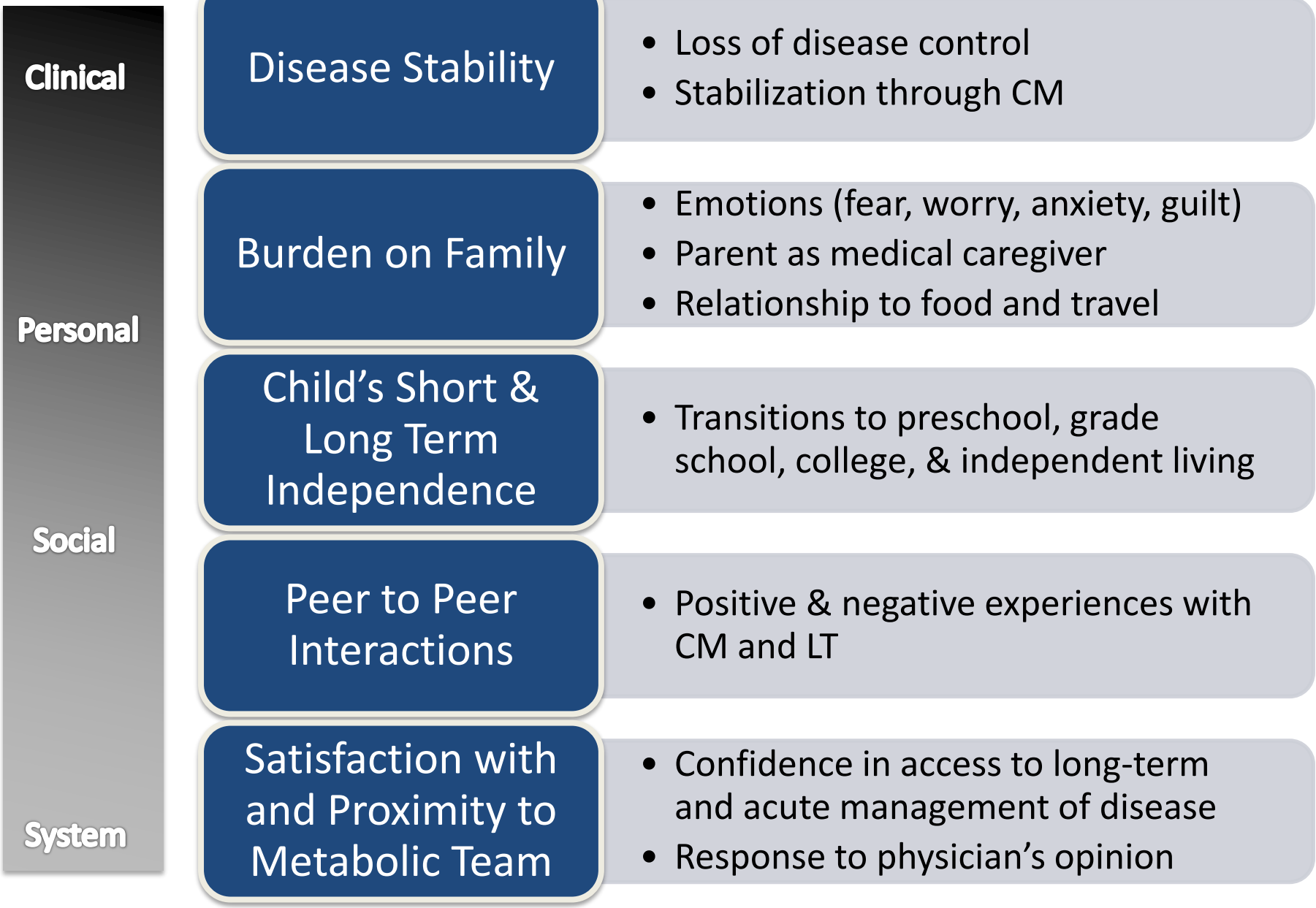
- Thematic content analysis
  - Multiple rounds of line by line open coding of interview transcripts by 3-4 researchers
  - Development of preliminary coding structure
  - Codebook revised and refined in response to additional rounds of coding and consensus building

Preliminary Findings: Phases of Childhood Development:

- Major changes during key phases of child's development appear to act as a catalyst for caretakers to consider (or reconsider) liver transplant as a viable treatment option

Preliminary Findings: The Tipping Point

- Caretakers who opt for transplant appear to have reached a **tipping point** when they feel they are no longer able to manage their child's disorder through diet and medication
  - This tipping point may come rapidly, after several years (e.g. in response to a major transition in child's life), or never
  - A variety of clinical, personal, social, and system level factors influence if, when, and how families affected by UCD reach this point


Clinical
Personal
Social
System
Disease Stability
Loss of disease control
Stabilization through CM
Burden on Family
Emotions (fear, worry, anxiety, guilt)
Parent as medical caregiver
Relationship to food and travel
Child's Short & Long Term Independence
Transitions to preschool, grade school, college, & independent living
Peer to Peer Interactions
Positive & negative experiences with CM and LT
Satisfaction with and Proximity to Metabolic Team
Confidence in access to long-term and acute management of disease
Response to physician's opinion

Future Steps for Analysis

- Continue to refine coding structure and expand on findings:
  - Code remaining caretaker interviews
  - Code provider interviews and assess for congruence/divergence of themes
  - Integrate focus group data into analysis and assess for congruence/divergence of themes
- Utilize findings to inform development of dissemination strategy (Aim 3)

Outline

- Overview of Urea Cycle Disorders and management
- Overview of PCORI-sponsored rare disease project
- Preliminary results
- Lessons Learned

Engagement with patient advocacy organization has been crucial

- Input into study design, focus groups, recruitment
- 8 of 9 new subjects in Aim 1 study enrolled to this study by National Urea Cycle Disorders Foundation
- Essential to dissemination efforts

Families with UCDs are often enthusiastic to participate in research

- Enrollment targets for Aim 2 rapidly reached
- Feedback to NUCDF about participation in research has been positive

Develop innovative solutions to barriers in subject enrollment

- Many patients with UCDs have very brittle health, so travel is difficult
  - Logistically challenging
  - Increases risk of metabolic decompensation
- If patients cannot come to us, why not go to them?
  - Home neuropsychological assessments

Minimize regulatory hurdles

- Benefit of IRB-reliance agreement or central IRB in expediting study start-up

- Due to rare nature of disease, major effort is often in the study start-up
- Are there innovative ways to improve this process?

Utilizing existing infrastructure has accelerated this study

- RDCRN – Urea Cycle Disorders Consortium
  - Access to: potential subjects, investigators, coordinators, neuropsychologists
  - Existing UCDC-NUCDF collaboration

- Can we improve clinical trial infrastructure for rare diseases?

Thank you!

- CNHS
  - Nicholas Ah Mew
  - Mendel Tuchman
  - Katie Rice
  - Robert McCarter
  - Jacqueline Sanz
- NUCDF
  - Cindy Le Mons
  - Janice Bartos
- GWU
  - Anne Rossier Markus
  - Maya Tuchman Gerstein
  - Kirk Williamson
  - Kan Z. Gianattasio
- SPLIT
  - Ravinder Anand
- Other collaborators
  - Benjamin Goodlett
  - Susan Waisbren

Closing and Next Steps

Matt Cheung

Chair, *Rare Disease Advisory Panel*

Vincent Del Gaizo

Co-Chair, *Rare Disease Advisory Panel*

Parag Aggarwal, PhD

Senior Program Officer, *Healthcare Delivery and Disparities Research, PCORI*

Gyasi Moscou-Jackson, PhD, MHS, RN

Program Officer, *Healthcare Delivery and Disparities Research*

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Closing and Next Steps – Future Discussion Topics

- **RDAP Discussion:**
  - Review results of RDAP prioritization survey.
  - Outreach for future panelists.
- **Potential Future Topics:**
  - Cross-cutting topics and development of a PCORI Funding Announcement (PFA)
  - Linking clinical outcomes to patient-reported outcomes (PROs) and utilizing PCORnet.

Thank You!

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE