Patient- & Family-Oriented Outcomes for Inborn Errors of Metabolism: A Systematic Review

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on behalf of the Canadian Inherited Metabolic Diseases Research Network (CIMDRN)

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Context & Background

The Canadian Inherited Metabolic Diseases Research Network (CIMDRN)

- Canadian Institutes of Health Research (CIHR)-funded multidisciplinary practice-based research network (core funding 2012-2017)
- Aims to develop evidence-informed approaches to health care for rare pediatric inborn errors of metabolism (IEM)
- For IEM and other rare diseases, increasing recognition of the need for evidence regarding the experiences and needs of patients and their families
  - Emphasis on patient-centred, personalized care

Patient-Oriented Outcomes Research

- Patient-oriented outcomes research has emerged as a priority more generally:
  - E.g., North American initiatives: Strategy for Patient Oriented Research (SPOR, Canada), Patient Centered Outcomes Research Institute (PCORI, US), Patient-Reported Measurement Information System (PROMIS, US)
- Increasing discussion in literature of related concepts: e.g., patient-informed care (Gardiner, 2008) personalized medicine (Hamburg, 2010)
- Work addressing patient-oriented outcomes for children and families remains preliminary (e.g., PROMIS Pediatrics) relative to that for adults
- Particular relevance to rare genetic diseases: clinical heterogeneity is typical, value of interventions is sensitive to patient preference

Patient-Centered Outcomes Research Institute www.pcori.org; Strategy for Patient-Oriented Research www.cihr-irsc.gc.ca/e/41204.html; Gardiner R. (2008) In: Bos L., et al. (eds.) Amsterdam: IOS Press; Hamburg, MA et al. (2010) *N Engl J Med;* Morris, C. et al. (2009) http://phi.uhce.ox.ac.uk/pdf/PROMs_WithChildren_Oxford_2009.pdf ; Irwin et al. (2012) *Health Qual Life Outcomes*

Objective

- To support CIMDRN's expert working group in developing self-reported measures of patient and family experiences with IEM by systematically reviewing the published literature to identify existing patient-oriented outcome measures and constructs
  - Aim to review studies of pediatric patients with complex chronic diseases where care pathways and outcomes are relevant to IEM
- Patient/family-reported data collected by CIMDRN will be linked to data collected on clinical interventions and outcomes

Methods

1. **Protocol:** structured study protocol developed by CIMDRN's expert working group using existing knowledge of the literature and an iterative consensus process to specify aims, methodological approach and delineate key concepts.

2. **Search:** comprehensive search strategy iteratively and collaboratively developed between subject matter and information science experts, emphasizing MeSH categories and keywords derived from the protocol.

3. **Study selection:** pre-specified criteria from the research question and protocol were applied to a 10% random sample of the search yield to inform iterative development of an operationalized screening tool using the PICOS typology:

Patients	Pediatric (i.e. ≤18yrs) w/specific diagnoses of chronic, complex diseases relevant to IEM
Interventions	Not applicable
Comparators	Not applicable
Outcomes	Patient-/family-oriented, self-reported, and measured by self-administered instrument(s)
Studies	Primary research (i.e., no reviews, editorials) , >5 study subjects, published between 2002-2012, any research design, peer-reviewed journal articles (i.e., no abstracts,)

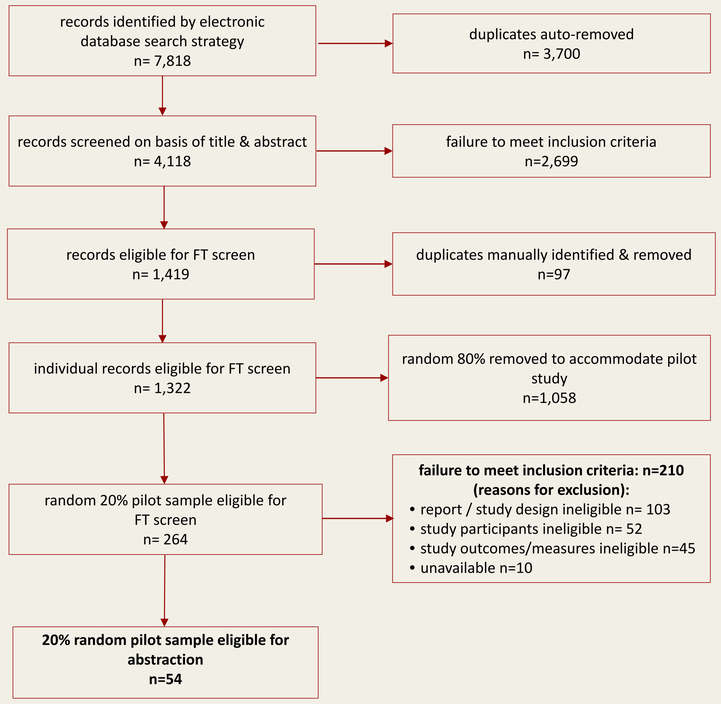
Two independent reviewers screened all records at the title/abstract and full-text level with discrepancies addressed by discussion and consensus, and guided by conceptual definitions derived from the study protocol.

4. **Data collection:** structured data abstraction form developed and piloted using a 20% random sample of articles included in the study; data were abstracted for this pilot sample by one reviewer and validated by a second researcher with discrepancies resolved by discussion and consensus.

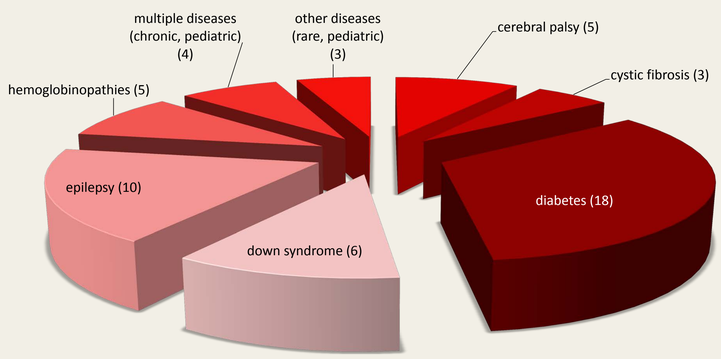
5. **Descriptive analyses:** a framework specific to the classification of constructs was not identified; several sources e.g., PROMIS Pediatric (Irwin, 2012) & McDowell (2009) informed and corroborated our otherwise qualitative approach to establishing and assigning constructs to domains.

Schardt, C. (2007) *BMC Med Inform Decis Mak;* Irwin et al. (2012) *Health Qual Life Outcomes;* McDowell (2006) *Oxford University Press;*

Results: PRISMA Study Flow Diagram



Pilot Results: Study Characteristics



Studies of patient/family oriented outcomes by disease category (N=54)

Study characteristics

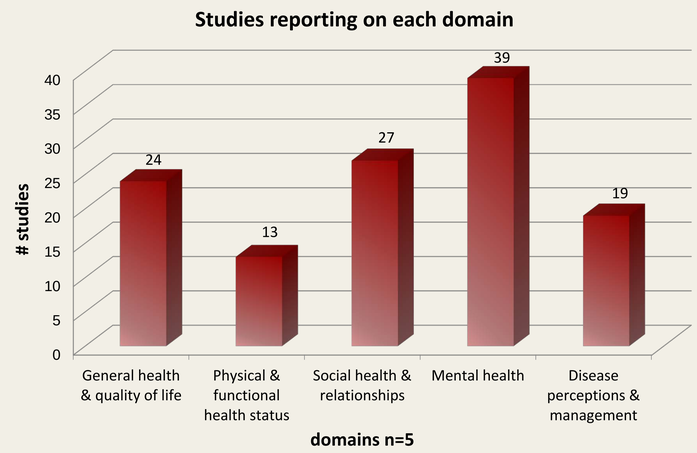
Disease category	Mean # eligible children	Range # eligible children	# Studies w/control group	Primary unit of analysis
Cerebral palsy (5 studies)	126 (4 papers; 1 NR)	95-205	0	Child – 3 studies Caregiver/Child Dyad – 1 study Family – 1 study
Cystic Fibrosis (3 studies)	48	23-76	1 (33%)	Child – 1 study Caregiver – 2 studies
Diabetes (18 studies)	82 (17 papers; 1 NR)	16-187	4 (22%)	Child – 11 Caregiver/Child Dyad – 7 studies
Down Syndrome (6 studies)	176 (4 papers; 2 NR)	33-440	3 (50%)	Caregiver – 5 studies Family – 1 study
Epilepsy (10 studies)	141 (8 papers; 2 NR)	37-375	1 (10%)	Child – 5 studies Caregiver – 1 study Child/Caregiver Dyad – 1 study Sibling – 1 study Family – 1 study
Hemoglobinopathies (5 studies)	48	38-65	1 (20%)	Child – 1 study Caregiver – 2 studies
Multiple (chronic, pediatric diseases) (4 studies)	48	29-73	2 (50%)	Child – 2 studies Caregiver – 2 studies
Other (rare, pediatric diseases) (3 studies)	36	15-67	2 (66%)	Child: 1 study Caregiver: 2 studies

Pilot Results: Outcome Measures & Constructs

- Total independent measures identified in pilot sample n= 128
- Total constructs identified n=77
- Total emergent construct domains n=5

Constructs (n=77) by domain, unit of analysis & Measures (n=128) → examples-only below

Construct domain	Constructs: unit/anal	Constructs: construct labels	Exemplar measures used within construct domains: measure name	# studies/ construct domain	respondent
General (global) health status & quality of life (6 constructs)	child	• health status • quality of life • satisfaction with daily life	Child Health Questionnaire (CHQ)	4	parent (4)
			PedsQoL	8	child (1), parent (2), child-parent dyad (4), sibling (1)
	caregiver	• health status • quality of life • satisfaction with daily life	Short-Form 36 Health Survey (SF-36)	2	parent (2)
Physical health & functional status (13 constructs)	child	• cognitive function • functional status • gross motor function • injuries • pain • physical activity • physical health • sleep problems • feeding problems	Health Utilities Index (HUI-23)	1	child-parent dyad
			Gross Motor Function Classification System (GMFCS)	1	parent
	caregiver	• fatigue • sleep problems • somatization • functional capacity	Epworth Sleepiness Scale (ESS)	1	parent
Social health & relationships (17 constructs)	child	• social competence • social interaction • social persistence • social support • loneliness • scholastic impact	Scales of Independent Behavior—Revised (SIB-R)	1	parent
			Brother-Sister Questionnaire	1	sibling
	caregiver	• marital relationship • social support	Dyadic Adjustment Scale (DAS)	2	parent (2)
	family	• resources • life-changing events • impact • quality of life • conflict • function • social support • stress • coping	Diabetes Family Conflict Scale (DFCS)	3	child-parent dyad (3)
			Family Inventory of Life Events and Changes (FILE)	2	parent (2)
Mental health (28 constructs)	child	• emotional problems • behavior problems • psychosocial disease impact • life-changing events • independence • life skills • task persistence • mental health • mood • personality traits • anxiety • depression • emotional distress • coping • self concept	Child Behavior Checklist (CBCL)	8	parent (8)
			Children's Depression Inventory (CDI)	5	child (4), sibling (1)
			Strengths and Difficulties Questionnaire (SDQ)	3	parent (2), child-parent dyad (1)
	caregiver	• psychosocial impact • diagnostic trauma • personal vulnerability • life-changing events • sense of coherence • coping • mental health • anxiety • distress • depression • hopelessness • stress • optimism	State-Trait Anxiety Inventory (STAI)	3	parent (3)
			Center for Epidemiological Studies of Depression Scale (CES-D)	4	parent (4)
			Parenting Stress Index (PSI)	4	parent (4)
Disease perceptions & management (13 constructs)	child	• perceived disease severity • disease self-management • treatment adherence	Illness Perception Questionnaire - Revised (IPQ-R)	1	child-parent dyad
	caregiver	• perceived child vulnerability • perceived disease severity • perceived intervention effect • satisfaction w/intervention • disease management • over-protectiveness	Diabetes Family Responsibility Questionnaire (DFRQ)	2	child-parent dyad (1), parent (1)
			Diabetes Responsibility and Conflict Scale	2	child-parent dyad (2)
	family	• disease management • health care utilization • satisfaction w/care • need for services	Family Needs Assessment Tool (FNAT)	1	parent



Key Messages & Next Steps

Key Messages

- Studies of complex, chronic pediatric disease: many measures of patient/family-reported outcomes representing a broad range of constructs;
- Systematic review is a challenging methodological approach to studies investigating patient-oriented outcomes and measures (e.g., large study yield, reporting details not always adequate to determine self-administration)

Next Steps – completed review will:

- Inform development of tools to collect patient-centered data for CIMDRN;
- Serve as an important resource for researchers in clinical pediatrics, for identifying patient/family-centred outcomes and measurement tools

Funded by: (TR3-119195)

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

CIMDRN RCRMMH

Administered and supported by:

uOttawa Faculté de médecine Faculty of Medicine