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# Research priorities for children with neurological impairment and medical complexity in high-income countries

CATHERINE DISKIN<sup>1</sup> | KRISTINA MALIK<sup>2,3</sup> | PETER J GILL<sup>1,4,5,6</sup> | NADA RASHID<sup>7</sup> | CAROL Y CHAN<sup>4</sup> |  
 KATHERINE E NELSON<sup>1,4,5</sup> | JOANNA THOMSON<sup>8,9</sup> | JAY BERRY<sup>10,11</sup>  | RISHI AGRAWAL<sup>11,12,13</sup> |  
 JULIA ORKIN<sup>1,4</sup> | EYAL COHEN<sup>1,4,5,14,15</sup> 

**1** Division of Paediatric Medicine, Department of Paediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada. **2** Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO; **3** Special Care Clinic, Children's Hospital Colorado, Aurora, CO, USA. **4** Child Health Evaluative Sciences, SickKids Research Institute, Toronto, Ontario; **5** Institute for Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada. **6** Centre for Evidence-Based Medicine, University of Oxford, Oxford, UK. **7** The Hospital for Sick Children, Toronto, Ontario, Canada. **8** Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH; **9** Division of Hospital Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; **10** Division of General Pediatrics, Children's Hospital Boston, Boston, MA; **11** Department of Pediatrics, Harvard Medical School, Boston, MA; **12** Division of Hospital-Based Medicine, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL; **13** Section of Chronic Disease, La Rabida Children's Hospital, Chicago, IL, USA. **14** Edwin S.H. Leong Centre for Healthy Children, University of Toronto, Toronto, Ontario; **15** CanChild Centre for Childhood Disability Research, McMaster University, Hamilton, Ontario, Canada.

Correspondence to Catherine Diskin at Black Wing 8227, Division of Paediatric Medicine, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada. E-mail: catherine.diskin@sickkids.ca

## PUBLICATION DATA

Accepted for publication 3rd August 2021.  
 Published online

## ABBREVIATION

CMC Children with medical complexity

**AIM** To identify the highest-priority clinical research areas related to children with neurological impairment and medical complexity among clinicians and caregivers.

**METHOD** A modified, three-stage Delphi study using online surveys and guided by a steering committee was completed. In round 1, clinicians and family caregivers suggested clinical topics and related questions that require research to support this subgroup of children. After refinement of the suggestions by the steering committee, participants contributed to 1 (family caregivers) or 2 (clinicians) subsequent rounds to develop a prioritized list.

**RESULTS** A diverse international expert panel consisting of 49 clinicians and 12 family caregivers provided 601 responses. Responses were distilled into 26 clinical topics comprising 126 related questions. The top clinical topics prioritized for research were irritability and pain, child mental health, disorders of tone, polypharmacy, sleep, aspiration, behavior, dysautonomia, and feeding intolerance. The clinician expert panel also prioritized 10 specific research questions.

**INTERPRETATION** Study findings support a research agenda for children with neurological impairment and medical complexity focused on addressing clinical questions, prioritized by an international group of clinicians and caregivers.

Children with neurological impairment, defined by functional and/or intellectual impairment that results from neurological disease,<sup>1,2</sup> are an important subgroup of children with medical complexity (CMC). CMC have substantial family-identified service needs, chronic conditions, functional limitations, and high healthcare use.<sup>3</sup> Children with neurological impairment account for about 28% of all CMC.<sup>4</sup> The clinical care required by children with neurological impairment and medical complexity is intensive,<sup>5</sup> requiring multiple providers in numerous locations over time and frequently relying on technological assistance for activities of daily living.<sup>6</sup> Multisystem involvement and multiple comorbidities from a characteristic pattern of co-occurring conditions are common, requiring an increased complexity of care.<sup>7–11</sup>

As high users of healthcare resources, CMC, including those with neurological impairments, have garnered

growing interest from child health researchers, healthcare providers, and policymakers.<sup>5,12</sup> Although their absolute numbers are small (<1% of all children), the impact of CMC is substantial, accounting for a quarter of inpatient bed-days<sup>13</sup> and a third of overall pediatric healthcare spending.<sup>4</sup> Much of the focus to date has been on care coordination and service delivery.<sup>14</sup> Some CMC have well-defined evidence influencing care paths, including those with advanced cystic fibrosis lung disease<sup>15</sup> and congenital heart disease, for example, children with single-ventricle physiology.<sup>16</sup>

Unfortunately, less attention has been given to establishing the evidence base to guide clinical care practice for children with neurological impairment and medical complexity.<sup>14,17</sup> Evidence for diagnosing or treating common clinical scenarios for children with neurological

impairment and medical complexity often relies on extrapolation from studies conducted on otherwise typically developing children. For example, while pneumonia is a frequent indication for hospitalization for children with neurological impairment and medical complexity,<sup>17</sup> clinical guidelines frequently exclude children with an underlying pathology<sup>18</sup> due to a lack of research in this area. Exclusion of children with neurological impairment and medical complexity from guidelines and clinical pathways creates knowledge gaps that limit evidence-based clinical practice. Furthering clinical research focused on children with neurological impairment and medical complexity supports improvements in their care and outcomes.

The consensus of clinicians and patients/caregivers is an increasingly important element of the research agenda setting<sup>19</sup> and can produce more relevant agendas while simultaneously reducing research waste.<sup>20,21</sup> We aimed to develop a list of the top priorities for clinical research, clinical topics, and specific research questions in the care of children with neurological impairment and medical complexity, reflecting the prioritization of an international expert panel consisting of both clinicians and family caregivers.

## METHOD

We conducted a modified prioritization study, which included three Internet-based surveys, conducted between 18th November 2019 and 28th June 2020. Previous literature supports the notion that three survey rounds are sufficient to achieve consensus<sup>22</sup> and these have been used in previous research priority studies.<sup>23,24</sup> Institutional review board approval was obtained from the Hospital for Sick Children, Toronto, Canada (research ethics board no. 1000063902).

### Establishment of the steering committee

A steering committee consisting of the study authors was created, reflecting clinician-researchers actively providing care to children with neurological impairment and medical complexity; the steering committee included clinician-researchers from Ireland ( $n=1$ ), Canada ( $n=4$ ), and the USA ( $n=4$ ), with a median of 10 years in practice (range 5–19y). A parent of a child with neurological impairment and medical complexity who received dedicated training to support their participation was also a steering committee member. Training focused on the basics of the research process, the role of patient advisors, and the support available to facilitate meaningful engagement. Ongoing support to the family representative was provided through the Centre for Innovation & Excellence in Child and Family-Centered Care. Further family caregiver input was obtained from the Research Family Advisory and Complex Care Family Advisory committees at the primary academic center ( $n=14$  members). These advisors provided feedback relating to family caregiver involvement, which was incorporated into the study design.

## What this paper adds

- Prioritized research areas highlighted neuropsychiatric and feeding topics in children with neurological impairment and medical complexity.
- The clinician expert panel prioritized 10 specific research questions.

### Recruitment of the clinician expert panel

The steering committee nominated a range of international clinical experts who provide clinical care to children with neurological impairment and medical complexity. A broad range of specialists (country, setting of practice [e.g. community- and hospital-based], and subspecialty) were nominated to ensure diversity and international representation and are described in the 'Results'. Recruitment was limited to physicians and nurse practitioners since the study's focus was to prioritize clinical research questions encountered in their clinical practice. To build on previous work, an invitation was extended to the principal investigator of a research prioritization study from the UK focused on the care of a broader group of children and young people with neurodisability.<sup>25</sup>

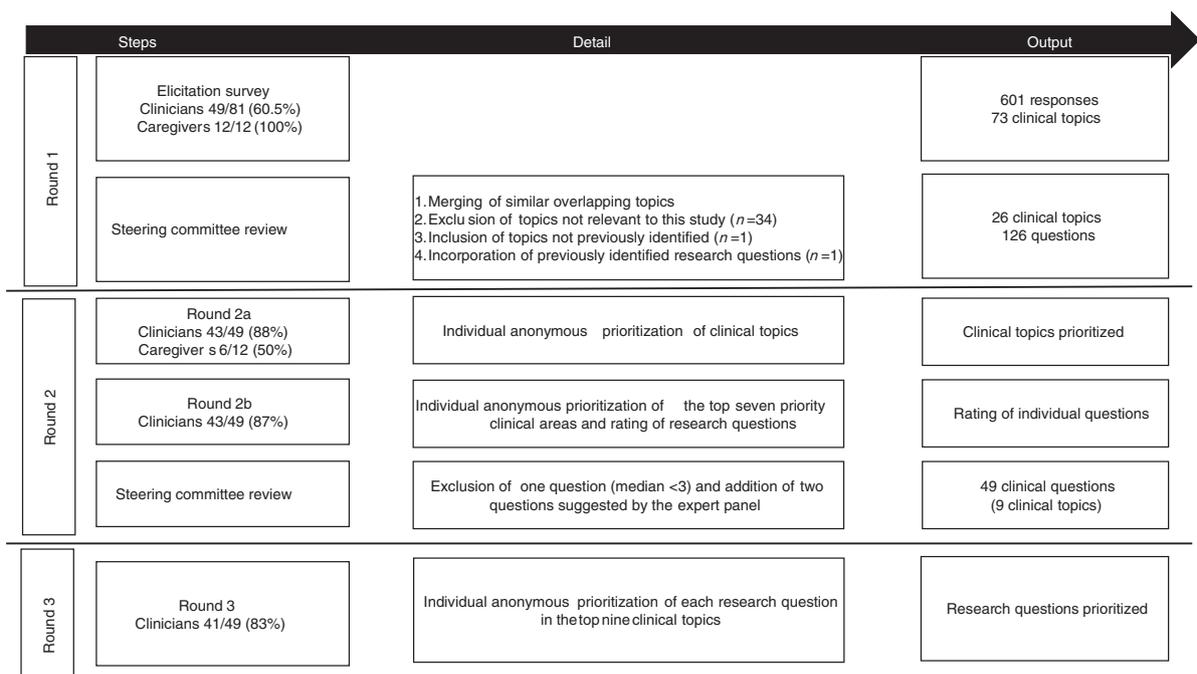
The study team invited nominated experts to participate in the study via e-mail, agreeing to a commitment including three rounds of surveys, each taking approximately 30 minutes to complete. Individuals consenting to participate were subsequently considered members of the clinician expert panel.

### Recruitment of the family caregiver expert panel

Family caregivers of children with neurological impairment and medical complexity were recruited using social media feeds. The primary institution's official Twitter account highlighted the study and the personal Twitter accounts of the study investigators (CD, JO, and EC). A Facebook page organized by family caregivers located in Ontario, Canada, also shared information about the study. Caregivers who contacted the study team by e-mail received details about the study outlining a commitment to two rounds of surveys, each taking approximately 20 minutes to complete. After completion of written informed consent, their eligibility for participation as family caregivers of children with neurological impairment and medical complexity was confirmed with details about their child's diagnosis and technology use. Eligible caregivers were subsequently considered members of the family caregiver expert panel.

### Prioritization methodology

Figure 1 outlines the three-stage prioritization methodology using online surveys.<sup>26,27</sup> Before round 1, the steering committee defined the scope of the study. We excluded topics relating to health service design or delivery, health policy, and those limited to a specific underlying disease that can cause neurological impairment (e.g. trisomy 21). Topics generated by free response in round 1 that could not be developed into specific research questions by the steering committee were excluded from further rounds. On



**Figure 1:** Study rounds and results of the data collection and surveys. The steps required for the modified, three-stage Delphi methodology using online surveys are shown. These led to the prioritization of clinical topics and research questions.

each survey round before distribution, all surveys were piloted with family caregivers ( $n=2$ ) and clinicians ( $n=2$ ) and refined based on feedback.<sup>28</sup>

The elicitation round (first survey) included open-ended elicitation questions asking for suggested priority research areas, clinical topics, and specific questions relating to the clinical care of children with neurological impairment and medical complexity. A similar survey with modified language was distributed to family caregivers. Both surveys are included as Appendices S1 and S2 (online supporting information).

The steering committee reviewed all suggestions and refined the list of clinical topics and research questions. Research questions were reframed in survey rounds 2 and 3 in the population, intervention, control, and outcome format whenever possible to ensure clarity and consistency in prioritization rounds. We also reviewed the UK prioritization results to ensure our clinical topic and research questions were complete.<sup>25</sup>

The second round included a two-part survey. Both family caregivers and clinical experts participated in round 2a, the prioritization of clinical topic areas from the perspective of future research using a 7-point Likert scale (1=not important to 7=very important). Specific research questions falling within each content area were listed to provide context and trigger additional suggestions from participants, who could provide feedback and identify missing clinical topics. The survey questions and instructions are summarized in Appendices S3 and S4 (online supporting information).

Round 2b asked clinical experts to select up to seven ‘most important’ clinical topics. Experts were then asked to rank all specific research questions falling within their top seven content areas using a 7-point Likert scale (Appendix S5, online supporting information). The third survey round asked clinical experts to rate the importance of research questions relating to the top clinical topics identified in round 2. Rounds 2b and 3 asked respondents to rank research questions based on their importance to clinical care and the current state of available evidence. This step was considered outside the scope of family caregiver expertise, so rounds 2b and 3 included only the clinician expert panel.

All study data were collected and managed using Research Electronic Data Capture (REDCap).<sup>29,30</sup>

### Data analysis

In rounds 2 and 3, analysis of the responses involved (1) calculating a frequency score (frequency of inclusion in the top seven clinical topics) and (2) calculating the median and interquartile range (IQR) of the Likert scale for each clinical topic and research question to create a rank order.<sup>28</sup> For clinical topics, the steering committee reviewed the data from round 2 graphically to determine a natural cutoff of ranked clinical topics to develop a feasible list of questions for inclusion in round 3 prioritization. Any specific research question with a median of less than 3 was removed. Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) was used throughout. In round 3, the total score was calculated based on the sum of Likert

ratings provided by clinical experts for each clinical topic. Analysis also included calculation of the median and IQR for each clinical topic.

## RESULTS

### Participants

#### Clinicians

Of the 81 clinicians invited to participate in the study, 49 (60.5%) consented to participate. Figure S1 (online supporting information) shows a flow chart of the clinician expert panel participants. Clinicians were recruited from nine different countries: USA ( $n=28$ ); Canada ( $n=9$ ); Ireland ( $n=3$ ); UK ( $n=3$ ); Australia ( $n=2$ ); Chile ( $n=1$ ); the Netherlands ( $n=1$ ); Hong Kong ( $n=1$ ); and Spain ( $n=1$ ). The most common clinical disciplinary background was medicine (86% of respondents), comprising 13 different specialties (adolescent medicine [ $n=1$ ], developmental pediatrics [ $n=12$ ], emergency medicine [ $n=2$ ], gastroenterology [ $n=2$ ], general pediatrics [ $n=16$ ], neurology [ $n=1$ ], neurodisability [ $n=8$ ], neurosurgery [ $n=1$ ], orthopedics [ $n=2$ ], palliative care [ $n=7$ ], primary care [ $n=1$ ], rehabilitation [ $n=1$ ], and respirology [ $n=1$ ]). Thirty clinicians (61%) were female and the rest were male.

Thirty-one clinicians worked in dedicated children's hospitals, seven in community hospitals (not academic centers), three in non-children's hospitals (e.g. general academic centers), two in specialty hospitals (e.g. rehabilitation and long-term acute care centers), one in a consultancy practice, and one in a respite facility. In these centers, clinicians provided a variety of services: a combination of inpatient (acute) and outpatient services ( $n=24$ ); primary care outpatient ( $n=8$ ); specialty outpatient ( $n=8$ ); and inpatient (acute) only ( $n=3$ ). One clinician worked in each of the following settings: inpatient (non-acute); emergency department; consultancy practice; and home care. Most (76%) spent more than 25% of their working week caring for children with neurological impairments and medical complexity.

#### Family caregivers

Twelve interested family caregivers met the eligibility criteria and participated (all mothers), nine from Canada (seven from Ontario, two from Alberta) and three from Ireland. The children's underlying diagnoses varied with six reporting primary neurological disorders (cerebral palsy [ $n=3$ ], brain injury [ $n=1$ ], brain tumor [ $n=1$ ], Moebius syndrome [ $n=1$ ]) and four reporting genetic disorders with neurological manifestations (trisomy 21 [ $n=2$ ], Prader-Willi syndrome [ $n=1$ ], non-specified [ $n=1$ ]). An additional respondent reported a primary mental health diagnosis ( $n=1$ ). Technology requirements described included enteral feeding tubes ( $n=4$ ) and respiratory technology ( $n=5$ ).

### Study rounds

#### Round 1

The flow chart in Figure 1 outlines the three study rounds and their output. In survey round 1, the elicitation survey

led to 601 individual comments or questions. The raw suggestions spanned 73 clinical topic areas. The supplementary material contains the full list of clinical topics suggested by clinicians (Table S1, online supporting information) and caregivers (Table S2, online supporting information) and the frequency with which they were mentioned.

After round 1, the steering committee refined the research topics and questions and merged those that overlapped highly. For example, spasticity and dystonia were combined into one clinical topic (disorders of tone including contractures). The steering committee excluded 34 topics, including those related to a specific underlying disease, for example, hypoxic-ischemic encephalopathy ( $n=12$ ), health service delivery ( $n=6$ ), no specific research question ( $n=6$ ), and research design ( $n=1$ ). Nine were acknowledged to be relevant to clinical practice but were excluded as being beyond the study scope (e.g. decision-making capacity). A single clinical topic (behavior and emotional regulation) was recommended solely by the family caregiver expert panel. The steering committee added infection control as a topic. A review of the UK prioritization study identified one additional unique question related to the use of Lycra, Kinesio Taping, or plastic among children with neurological impairment at risk for deformity secondary to spasticity.<sup>25</sup> Round 1 ended with 26 clinical topic areas and 126 related questions (Appendix S7, online supporting information).

#### Round 2

Forty-three clinicians (88% retention from round 1) and six family caregivers (50% retention from round 1) participated in round 2. To amplify caregiver input, separate rank lists were created because of the difference in panel size. We ranked topics by median Likert scores with IQRs used to differentiate between ties. Since family caregivers were separately asked to identify their 'top seven' topic areas, we created a third rank list based on the percentage of individuals choosing a given topic as in their top seven.

In the family caregiver expert panel, there were some differences when compared with the clinician expert panel. Six clinical topics were common to both panels (behavior, sleep, aspiration, irritability and pain, feeding tolerance, and child mental health); family caregivers also prioritized acute respiratory infections, enteral feeding tubes, infection control, and nutrition and growth. Clinicians' prioritization included tone, polypharmacy, dysautonomia, and chronic lung disease in their top 10 clinical topics.

Given the steering committee's concern for respondent burden in ranking the full 126 research questions proposed, the members of the steering committee considered the agreement across analyses (Table 1) and incorporated the sharp inflection point in priority scoring between the top nine clinical topics and the rest (Fig. 2) to arrive at a list for consideration for round 3. The clinician expert panel suggested an additional two questions (Appendix S8, online supporting information). A question exploring the

**Table 1:** Round 2 prioritization of clinical topics (clinical experts [*n*=49] and family caregivers [*n*=12])

| Clinician prioritization |                             |                        |              | Caregiver prioritization |                             |                 |                 |
|--------------------------|-----------------------------|------------------------|--------------|--------------------------|-----------------------------|-----------------|-----------------|
| Rank                     | Clinical topic              | Frequency <sup>a</sup> | Median (IQR) | Rank                     | Clinical topic              | Frequency score | Median (IQR)    |
| 1                        | Irritability and pain       | 28                     | 6 (6–6.5)    | 1                        | Behavior                    | 40              | 7 (7–7)         |
| 2                        | Child mental health         | 20                     | 6 (4–6)      | 2                        | Acute LRTI                  | 37              | 6.5 (6–7)       |
| 2                        | Disorders of tone           | 20                     | 6 (5–7)      | 3                        | Enteral feeding tubes       | 36              | 6 (5.25–6.75)   |
| 2                        | Polypharmacy                | 20                     | 5 (5–6)      | 4                        | Sleep                       | 35              | 5.5 (5–6.75)    |
| 2                        | Sleep                       | 20                     | 5 (5–6)      | 5                        | Aspiration                  | 34              | 6 (6–6)         |
| 3                        | Aspiration                  | 19                     | 6 (5–6.5)    | 5                        | Infection control           | 34              | 6.5 (5.25–7)    |
| 4                        | Behavior                    | 18                     | 5 (4–6.5)    | 5                        | Irritability and pain       | 34              | 6.5 (5.25–7)    |
| 4                        | Dysautonomia                | 18                     | 5 (4–6)      | 6                        | Nutrition and growth        | 33              | 5 (5–6.5)       |
| 4                        | Feeding tolerance           | 18                     | 5 (4–6.5)    | 6                        | Feeding tolerance           | 33              | 6 (5.35–6)      |
| 5                        | Chronic lung disease        | 13                     | 5 (4–6)      | 6                        | Child mental health         | 33              | 5.5 (5–6.75)    |
| 6                        | Nutrition and growth        | 12                     | 5 (3–6)      | 7                        | Chronic lung disease        | 32              | 5.5 (4.25–6.75) |
| 7                        | Acute LRTI                  | 11                     | 5 (3–6)      | 8                        | Dysautonomia                | 31              | 5.5 (4.25–6.75) |
| 8                        | Enteral feeding tubes       | 10                     | 4 (3–5)      | 9                        | Constipation                | 29              | 4 (3.5–6)       |
| 8                        | Sialorrhea                  | 10                     | 5 (3.5–6)    | 9                        | GERD                        | 29              | 5 (3.25–6.75)   |
| 8                        | Scoliosis                   | 10                     | 4 (3–5.5)    | 9                        | Polypharmacy                | 29              | 5 (3.25–6)      |
| 9                        | Osteoporosis and osteopenia | 9                      | 4 (4–6)      | 10                       | Sialorrhea                  | 28              | 5.5 (5.25–6)    |
| 10                       | Constipation                | 8                      | 4 (3–5)      | 10                       | Venous access               | 28              | 4.5 (4–5)       |
| 10                       | Neurogenic bladder          | 8                      | 4 (3–5)      | 11                       | Disorders of tone           | 27              | 4.5 (2.5–6.5)   |
| 11                       | GERD                        | 7                      | 4 (4–6)      | 11                       | Postoperative complications | 27              | 4 (3.25–6.25)   |
| 12                       | Postoperative complications | 5                      | 4 (3–5)      | 11                       | Peripubertal issues         | 27              | 4.5 (2.5–6.5)   |
| 12                       | Infection control           | 5                      | 4 (3–5)      | 12                       | Neurogenic bladder          | 26              | 4.5 (3.25–5)    |
| 13                       | Venous access               | 4                      | 3 (2–4)      | 12                       | Scoliosis                   | 26              | 4.5 (2.5–5.75)  |
| 13                       | Hip displacement            | 4                      | 4 (3–5)      | 13                       | Dental caries               | 25              | 5.5 (2.25–5.75) |
| 14                       | Hydrocephalus               | 3                      | 4 (2–5)      | 14                       | Hip displacement            | 24              | 3.5 (2.25–3.25) |
| 14                       | Peripubertal issues         | 3                      | 4 (2.5–5)    | 14                       | Hydrocephalus               | 24              | 3.5 (2–5.75)    |
| 15                       | Dental caries               | 2                      | 4 (2.5–4.5)  | 15                       | Osteoporosis and osteopenia | 23              | 3.5 (2.25–4.75) |

The top clinical topics are shaded. <sup>a</sup>The frequency score reflects the number of clinical experts who provided the top ranking for each clinical topic. IQR, interquartile range; LRTI, lower respiratory tract infection; GERD, gastroesophageal reflux disease.

role of turmeric in abdominal distension was excluded (median <3).

### Round 3

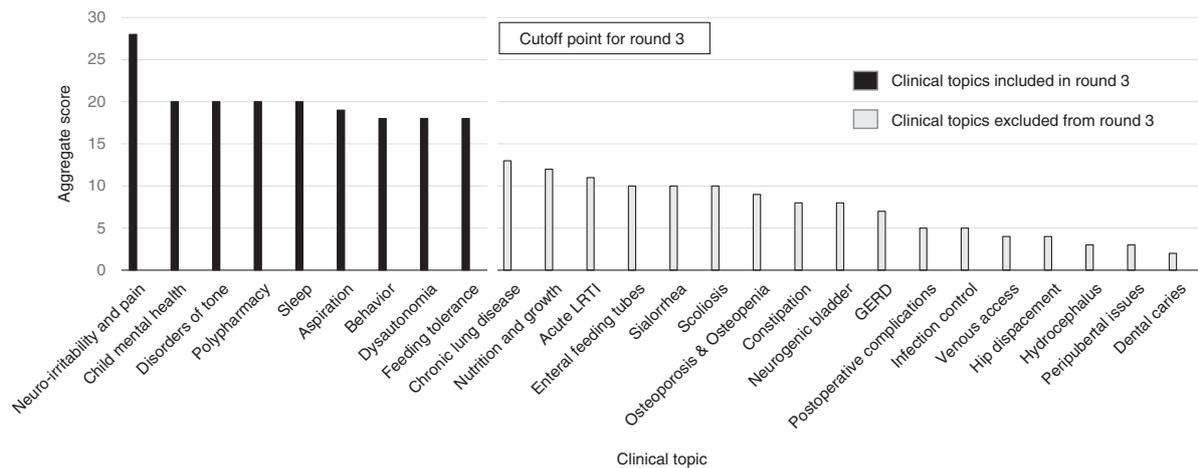
Forty-one clinicians responded to round 3 (84% retention from round 1) and prioritized the research questions related to the clinical topics in round 2. Table 2 contains the prioritized top 10 research questions. The top 10 research questions involved seven of the nine clinical topic areas, except for behavior and polypharmacy.

## DISCUSSION

This study encompassed clinicians' and family caregivers' priorities to develop a prioritization-based research agenda focused on children with neurological impairment and medical complexity. Participants were engaged throughout the prioritization process, proposing 26 clinical topics and 126 research questions that were distilled down to a prioritized list where neuropsychiatric topics (e.g. irritability and pain, sleep, child mental health) dominated, comprising 6 of 10 clinical topics. The generation of clinical topics and research questions benefited from family caregiver input. While there was relatively good concordance in clinical topics between family caregivers and clinicians, only family caregivers suggested behavior in round 1, which was subsequently prioritized by both clinicians and family caregivers. Although the study's

main aim was to develop a prioritized list of topics and questions to create a research agenda, the long list of potential research questions suggests substantial equipoise in many aspects of care of children with neurological impairment and medical complexity.

Some prioritized areas overlapped due to definitional vagaries, such as irritability and pain and dysautonomia. Other overlapping areas reflect the challenge of differentiation in clinical practice, for example, aspiration and acute lower respiratory tract infections. Some topic areas were prioritized but were challenging to frame as research questions. For instance, while in round 1, 17 clinicians highlighted irritability and pain as a clinical topic, which they frequently encounter in their practice and cannot access adequate evidence to guide management, only three questions with vaguely specified interventions and outcome metrics were developed for ratings in subsequent rounds. This observation likely reflects that irritability and pain, although undefined, has high prevalence<sup>31</sup> and highlights the challenges and complexity in diagnosing and treating pain in this population. The lack of understanding of the pathophysiology,<sup>32,33</sup> including the contribution of multiple organ systems, for example, the gut,<sup>34</sup> and limited treatment options,<sup>31</sup> translated into a lack of specific population, intervention, control, and outcome research questions. The vagueness of suggested research questions suggests that an impactful research agenda for children



**Figure 2:** Frequency score of clinical topics by clinical experts. The frequency score calculated by the frequency of inclusion among the top seven of 26 clinical topics developed after round 1 is shown. LRTI, lower respiratory tract infection; GERD, gastroesophageal reflux disease.

**Table 2:** Top 10 ranked research questions with related clinical topics

| Overall rank | Clinical topic        | Research question  | Total score | Median (IQR) |
|--------------|-----------------------|--|-------------|--------------|
| 1            | Feeding tolerance     | In children with neurological impairment and medical complexity with feeding intolerance, do blenderized formulas (e.g. home or commercially) versus other formula (polymeric or hydrolyzed) improve outcomes (e.g. nutritional health, feeding tolerance, quality of life)? | 229         | 6 (5–7)      |
| 2            | Disorders of tone     | In children with neurological impairment and medical complexity with dystonia, does baclofen versus baclofen plus gabapentin improve outcomes (e.g. pain, function)?   | 228         | 6 (5–6)      |
| 3            | Dysautonomia          | In children with neurological impairment and medical complexity with autonomic dysfunction, does propranolol versus gabapentin versus clonidine decrease symptoms of autonomic dysfunction (e.g. sweating, temperature dysregulation, blood pressure lability)?              | 228         | 5 (5–7)      |
| 4            | Irritability and pain | In children with neurological impairment and medical complexity with irritability, does gabapentin versus clonidine improve outcomes (e.g. duration of crying, discomfort)?  | 227         | 6 (5–7)      |
| 5            | Irritability and pain | In children with neurological impairment and medical complexity with irritability, does cannabidiol and/or tetrahydrocannabinol versus standard therapy (e.g. gabapentin) improve outcomes, for example, duration of crying, discomfort?                                     | 226         | 6 (5–7)      |
| 6            | Sleep                 | In children with neurological impairment and medical complexity with disrupted sleep, does melatonin versus hydroxyzine versus trazodone versus clonidine improve outcomes (e.g. sleep quality, sleep duration, daytime function)?   | 225         | 6 (5–6)      |
| 7            | Aspiration            | In children with neurological impairment and medical complexity, does exclusive enteral (tube) feeding (without oral intake) versus a feeding plan, which includes oral intake, reduce aspiration risk?  | 218         | 6 (4–7)      |
| 8            | Feeding tolerance     | In children with neurological impairment and medical complexity with feeding intolerance, does polymeric formula versus hydrolyzed formula improve outcomes (e.g. nutritional health, feeding tolerance, quality of life)?   | 218         | 5 (4–7)      |
| 9            | Child mental health   | In children with neurological impairment and medical complexity, does screening for mental health issues versus standard (no screening) improve outcomes (e.g. child mental health)?   | 217         | 5 (4–6)      |
| 10           | Disorders of tone     | In children with neurological impairment and medical complexity with dystonia not responsive to medication, does deep brain stimulation versus intrathecal baclofen improve outcomes (e.g. function)?  | 216         | 5 (4–6)      |

Two prioritized clinical topics did not have a research question ranked in the top 10 (polypharmacy and behavior). The top ranked question for the clinical topic of polypharmacy was ‘In CMC and neurological impairment, what are the demographics and clinical predictors of a medication error?’ (total score=185; median [IQR]=4 [3–6]). The top ranked question in the clinical topic of behavior was ‘In CMC and neurological impairment, what are the demographic and clinical predictors of challenging behavior (e.g. aggression) and emotional dysregulation?’ (total score=174; median [IQR]=4 [3–5]). IQR, interquartile range; CMC, children with medical complexity.

with neurological impairment and medical complexity requires greater clarity and uniformity of definitions.

The development of meaningful research, including outcome measures, will involve understanding and including those relevant and meaningful to the child and family experience. Caregiver involvement in research, including in this study, supports a more inclusive, improved research agenda.<sup>35</sup> In this study, the inclusion of behavior and emotional regulation is a result of family caregiver inclusion. Similar studies, including those that adhere to the James Lind Alliance framework,<sup>25</sup> highlight a known phenomenon: families prioritize psychosocial needs more than medical clinicians.<sup>36</sup> Professionals often prioritize basic science while caregivers will emphasize aspects of psychosocial health.<sup>21,37</sup> Despite an increased prevalence of psychiatric diagnoses among children with intellectual disabilities,<sup>38</sup> the clinician expert panel infrequently proposed related clinical topics in the elicitation phase with few research questions suggested. However, both clinicians and family caregivers subsequently prioritized both topics as research areas. This observation suggests that clinicians and researchers initially overlooked these clinical topics and yet recognize their inherent importance, presumably because of the impact on the family and child.

Clinicians and caregivers were asked to focus on clinical questions and not the entire healthcare experience of children with neurological impairment and medical complexity and their families. Despite this instruction, both groups frequently enumerated such topics (e.g. transition to adult care), reflecting the substantial impact that caring for CMC can have on families and the healthcare system.<sup>39,40</sup>

This international prioritization study incorporated the UK-based James Lind Alliance study including (1) inviting a lead researcher to participate in the expert panel and (2) incorporating some of the suggested research topics identified in that study as research questions in this study. The scope of this study differs from previously conducted studies by focusing on a subgroup of children with neurological impairment, those with medical complexity. Previous studies included all children with neurodisability or neurodevelopmental disorders or individuals of all ages with cerebral palsy.

Refinement of the various clinical topics could be the next step for clinical research in this population of children. For example, irritability is an undefined neologism. A better understanding of this clinical phenotype, including its impact on children and their families would be a foundational step for future research. We are partnering with Family Voices, a family-led organization focused on the experience of children and young people with special healthcare needs and the Lucile Packard Foundation for Children's Health to deliver a seminar series focusing on the clinical topics prioritized in this study starting in September 2021. This seminar series will bring clinicians, researchers, and families together to facilitate partnerships to design research studies related to the clinical topics addressed in this prioritization study.

## Limitations

This study has several limitations. First, family caregiver involvement was valuable but limited in the number of participants with a high dropout rate between the first and second round (50%), and their relative homogenous demographic characteristics (all were mothers from Canada or Ireland), reflecting the investigators' social media following. Second, the depth of family caregiver involvement was limited. There was only one family caregiver on the steering committee, caregivers were excluded from rounds 2b and 3, incomplete caregiver responses were recorded in round 2, and there was no youth voice in the process. Recruitment of a more diverse and larger group of caregivers and young people with neurological impairment and medical complexity may have led to a more representative group of clinical topics for prioritization.

Third, some clinical topics may not be indistinguishable (e.g. lower respiratory tract infection and aspiration) and some clinical questions overlapped. There was agreement within the steering committee that distinct clinical topics and related questions may not be mutually exclusive. For example, in clinical practice, a child with neurological impairment and medical complexity can present with respiratory illness and clinically differentiating aspiration from infection can be difficult. Fourth, non-medical health professionals who provide care for children with neurological impairment and medical complexity were excluded, for example, therapists, social workers, and nurses who are not nurse practitioners. The involvement of these professionals would likely have led to an even larger group of potential questions and may have made arriving at a prioritized list more difficult. Fifth, all family caregivers and all but one of the clinical experts were from high-income countries; therefore, they may not reflect the experience of families and clinicians in low- and middle-income countries. Sixth, the members of the steering committee were at different career stages and the decision-making process may have introduced known and unknown power differentials and biases. Lastly, while a broad group of clinicians from diverse geography, practice settings, and specialties were recruited, a different sampling of clinicians may have arrived at a slightly different prioritized list.

## CONCLUSION

This study represents a prioritization process to develop a research agenda about children with neurological impairment and medical complexity focused on addressing everyday clinical questions, reflecting clinicians' and caregivers' international prioritization. This research agenda may be informative for funders, clinicians, and others to develop and conduct research projects to improve outcomes in children with neurological impairment and medical complexity.

## ACKNOWLEDGEMENTS

The study team acknowledges the time and contribution of the expert clinicians and family caregivers who participated in the study. Ms Francine Buchanan, Research Patient & Family

Engagement Coordinator at the Hospital for Sick Children, supported the study team's effort with the family caregiver involvement. This project was supported by the Canadian Institutes of Health Research (no. FDN-143315). Dr Thomson was supported by the Agency for Healthcare Research and Quality under award no. K08HS025138.

## CONFLICTS OF INTERESTS

The authors have no conflicts of interests to declare.

## DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

## SUPPORTING INFORMATION

The following additional material may be found online:

**Figure S1:** Flow chart of the study participants (clinician expert panel).

**Table S1:** Clinical topics as suggested by the clinician expert panel

**Table S2:** Clinical topics as suggested by the family caregiver expert panel

**Appendix S1:** Round 1 survey (clinician expert panel).

**Appendix S2:** Round 1 survey (family caregiver panel).

**Appendix S3:** Round 2a survey (clinician expert panel).

**Appendix S4:** Round 2a survey (family caregiver panel).

**Appendix S5:** Round 2b survey (clinician expert panel).

**Appendix S6:** Round 3 survey (clinician expert panel).

**Appendix S7:** Clinical topics and related research questions included in round 2.

**Appendix S8:** Additional questions included in round 3.

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