A Scoping Review to Examine Symptoms in Children with Rare, Progressive, Life-Threatening Disorders

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Faculty/Presenter Disclosure

Presenter Name: Kimberley Widger

Relationships with commercial interests: None

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Introduction
<table>
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<tr>
<th>Quadrant 1</th>
<th>Quadrant 2</th>
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<td>Life-threatening conditions for which curative treatment may be feasible but can fail (e.g., cancer, irreversible organ failure)</td>
<td>Conditions where premature death is inevitable, but long periods of intensive treatment prolong and allow participation in normal activities (e.g., cystic fibrosis)</td>
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<th>Quadrant 3</th>
<th>Quadrant 4</th>
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<td>Progressive conditions without curative treatment options, where treatment is exclusively palliative and may extend over many years (e.g., neurodegenerative, metabolic disease)</td>
<td>Irreversible but non-progressive conditions with severe disability susceptible to health complications and premature death (e.g., anoxic brain injury, severe cerebral palsy)</td>
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Aim of the Search

• Systematically identify available literature on assessment and management of symptoms in Q3 conditions
  • Identify evidence currently available
  • Identify gaps in the literature for future research
Scope of the Search

• **180 Q3 conditions** compiled from the literature
• **10 symptoms** from the literature on these conditions
  • Behaviour problems; bowel incontinence; breathing difficulties; constipation; feeding difficulties; sleep disturbance; temperature regulation; tone and motor problems; urinary incontinence; and vomiting
  • Pain excluded as one of our team members is currently conducting a scoping review on pain in these conditions
  • Seizures excluded as good evidence already exists on the management of this symptom
Inclusion Criteria

- **A study** (E.g. not a letter to the editor)
- **Pediatric**: participants cannot be all adults
- Includes 1 of the **180 conditions** in our list
- Focus on assessing or treating one of our **10 symptoms**, or development of a symptom-focused tool or scale
- **More than one participant** (no single case reports)
- At least two participants received **same or similar treatments**
- **Not descriptive**: Study must use some way to assess symptom, even if it is of a low quality
- The **goal of a treatment must be to alleviate a symptom**, not to cure or modify the disease as a whole
Methods
PRISMA Flow Chart

Identification (n=42,153) → Duplicates excluded (n=8,679)

Initial Screening (n=33,474) → Records excluded (n=32,741)

Full Text Screening (n=708) → Full text excluded (n=477)

Included (n=82)
Identification

• Searched MEDLINE, Embase and CINAHL
  • Monthly alerts set up to keep the search current
  • No language or date limits
• Conducted a comprehensive grey literature search
• Contacted experts through listservs
• Citation chaining of cited and citing articles from included studies

Records identified through database searching (n=41,863)

Additional records identified through other sources (n=290)

Total (database + grey literature search) (n=42,153)

Duplicates removed (n=8,679)
Initial Screening

- Initial search yielded over 27,000 results once deduplicated
- Single person pre-screened results for inclusion of a condition and a symptom
- Titles and abstracts screened by two reviews
- Excluded 315 and were left with 708

Records pre-screened (n=33,474) → Records excluded (n=32,426)

Records screened (n=1,048) → Records excluded (n=315)

Full-text articles assessed for eligibility (n=708)
Full Text Screening

- Two people individually assess full-texts for eligibility
- 477 studies excluded so far, the bulk due to focus on diagnostics, cures, and lack of assessment.

Full-text articles assessed for eligibility (n=708)

Studies included in preliminary results (n=82)

Full-text articles excluded, with reasons (n=477)
- Lack of symptom focus (n=33)
- Disease modification (n=150)
- Wrong publication type (n=65)
- Wrong outcome (n=39)
- Wrong population (n=21)
- Wrong study design (n=14)
- Descriptive (n=56)
- Foreign language (n=24)
- Background article (n=17)
- Full text not available (n=1)
- Abstract only (n=44)
- Study protocol only (n=13)
Preliminary Results
• 148 of our 180 diseases are not the subject of a single study
Symptoms Covered

- Tone and Motor: 41
- Behaviour: 20
- Sleep: 17
- Feeding: 11
- Breathing: 9
- Alertness: 2
- Constipation: 2
- Bowel Incontinence: 1
- Urinary Incontinence: 1
- Temperature: 0
Rett Syndrome has a distinct clinical profile and treatments might not be relevant to other conditions.
The top 7 diseases make up the bulk of studies
For the other 173 conditions there remains very little evidence
Journals

• The 81 journal articles were found in 48 different journals
• Top 5 journals:
  • Developmental Medicine & Child Neurology (7)
  • American Journal of Medical Genetics Part A (5)
  • European Journal of Paediatric Neurology (4)
  • Movement Disorders (4)
  • Pediatric Neurology (4)
• Remaining 43 journals have 3 or less articles
  • 36 journals only have a single article
• Major general pediatric journals not represented, except for *Journal of Pediatrics*
• General pediatricians or specialists unlikely to see most of these articles
• More studies being conducted recently
• Median year is 2010
Discussion
Summary of Results

• Research focused on diagnosis, genetics, and cures
• Less focus on symptom management
• Effort concentrated on a handful of diseases that might not be generalizable to others
• Literature is dispersed and hard to access for clinicians and researchers
• More research needs to be done on these symptoms
• Research may need to combine multiple conditions with similar profiles to increase the number of participants
Next Steps

We have learned that:

• It would be difficult for clinicians to access the same evidence we found without the resources that have been available to us (for instance having a librarian on our team).

• We have to think about the gap in our knowledge about how to assess and treat symptoms in Q3 conditions as well as the difficulties in accessing the evidence we now know exists.

We will:

• Finish assessing articles for eligibility and extracting data
• Publish findings in open-access journal
Questions?