

Systematic Review of Patient Focused Drug Development Meeting Reports for Conditions Affecting Neurodevelopment

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Methodological Issue

The degree of overlap in endpoint concepts of interest across rare diseases affecting neurodevelopment is not well understood. Commonalities may be a leverage point for addressing several clinical trial methodological limitations across conditions.

Introduction

- Endpoint measurement is a significant hurdle to clinical trials in rare diseases affecting neurodevelopment, but the potential to capitalize on the collective commonness of rare disease is insufficiently tapped.
 - Psychometric efforts to improve endpoint measurement are often focused on individual conditions, so they cannot achieve the large samples required for these types of analysis.
 - To the extent that various diseases share similar endpoint concepts of interest (and by extension, similar clinical outcome assessments), these efforts may be combined.
- To support effective and systematic gathering of patient perspectives, the FDA indicated Patient-Focused Drug Development (PFDD) meetings in 2012.
 - PFDD meetings are focused on chronic conditions with few or no current therapies that have severe impact on a subpopulation.
 - The FDA initially hosted these meetings but soon expanded to supporting externally-led meetings. These are “town hall” style meetings with broad audiences including patients and other stakeholders, like industry, regulators, and clinicians.
 - An expected deliverable is a report that summarizes the results of a standardized set of survey questions. These reports are hosted by the FDA website (1).

Current Study

- We conducted the first systematic review of PFDD meeting reports, to identify commonalities across rare diseases affecting neurodevelopment in patient- and caregiver-identified concepts of interest.
- We focused on meetings that concerned a medical condition affecting neurodevelopment (per Human Phenotype Ontology Database).

Methods

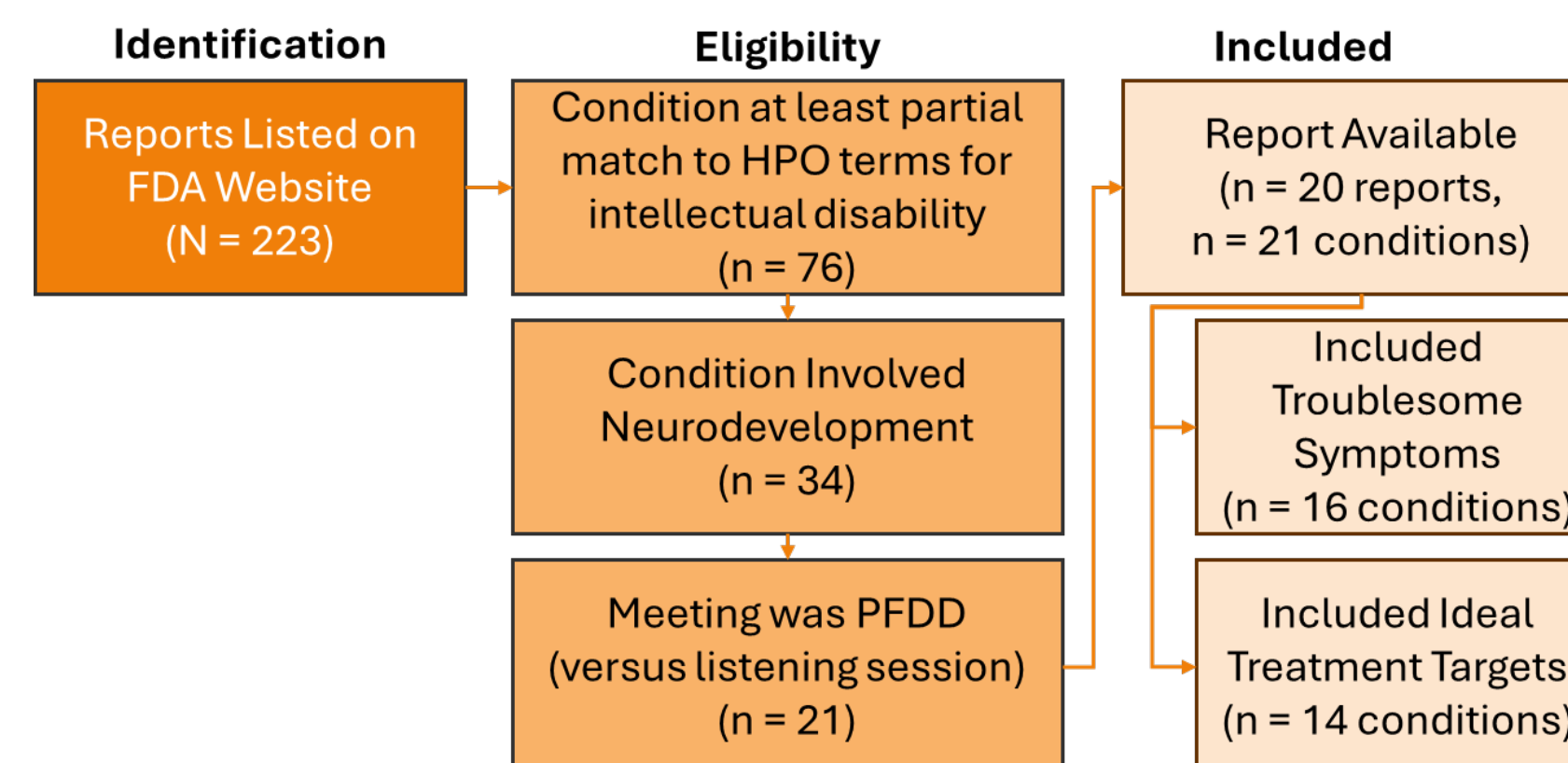
- Extracted two questions: “What are the top 3 most troublesome symptoms?” and “What are the top 3 ideal treatment targets?”
- Normalized across conditions by coding verbatim responses into concept categories. The midpoint estimate of concept endorsement for each meeting was subjected to descriptive analysis.

Conclusions

- The PFDD meeting program is essential to clinical trial development in rare genetic conditions affecting neurodevelopment.
- The results of this systematic review of PFDD meetings indicate that conditions with broad etiological heterogeneity converge upon common concepts of interest, namely cognition and communication.

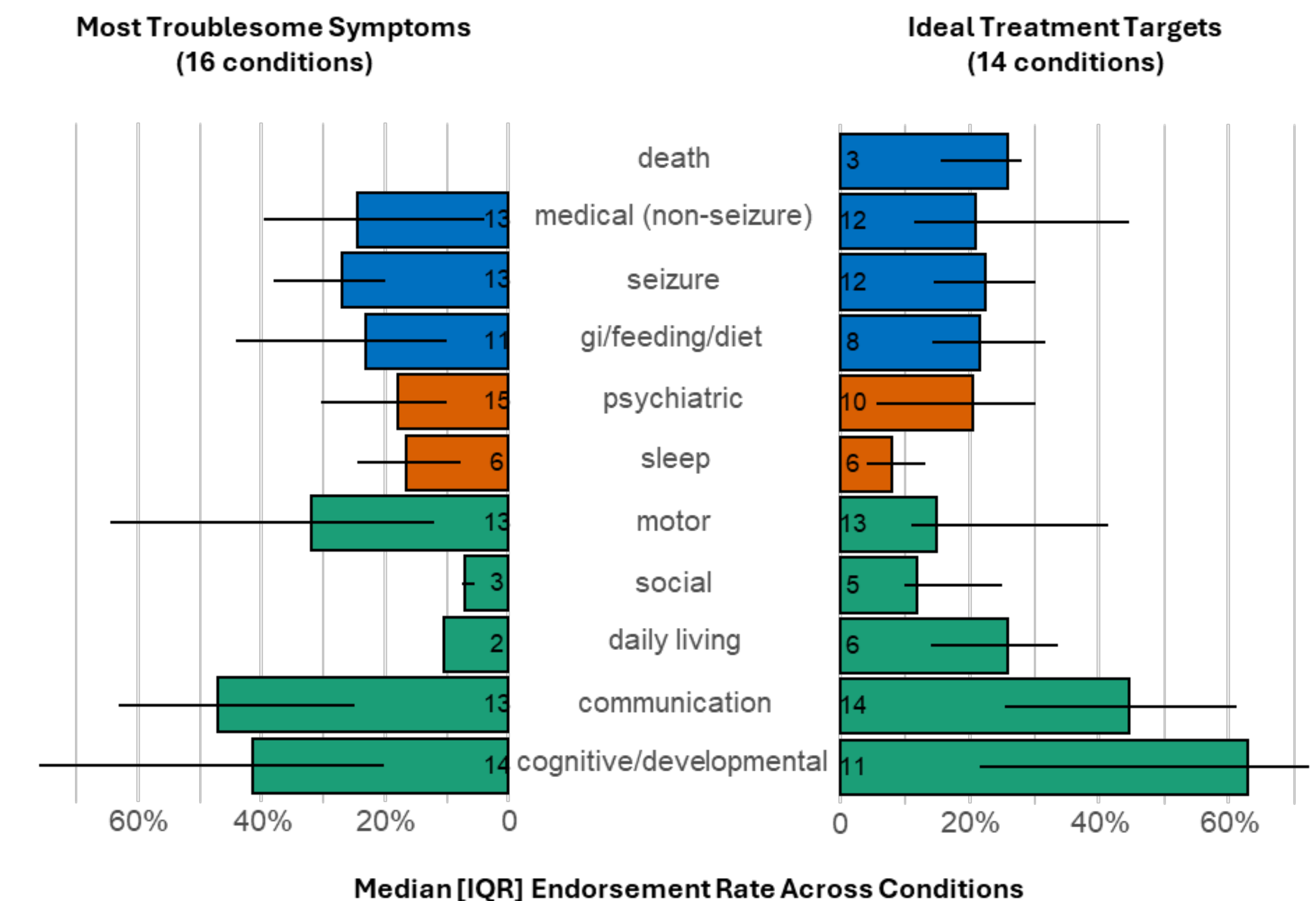
Results

Figure 1. PRISMA Diagram. Sixteen conditions from 15 meetings were eligible for inclusion. The median [IQR] sample size for each condition was 94 [54, 162] for “troublesome symptoms” and 70 [49, 108] for “ideal target.”



- Three conditions had no concept that exceeded 30% endorsement, indicating disagreement within the condition.
- In some conditions, concepts were endorsed by a majority as both most troublesome and ideal target, e.g., psychiatric symptoms in FXS (88%; 83%), communication in STXPB1 (82%; 78%), and cognitive/developmental in PMS (73%; 75%).
- Less commonly, concepts with nearly universal endorsement as troublesome were not identified as an ideal treatment target (e.g., for GM1 motor endorsed by 88% and 11%, respectively).

Figure 2. Midpoint estimates of endorsement rates by concept across all conditions. The bar indicates the median [IQR] endorsement rate for meetings which used the concept. The inset number indicates the number of meetings that used the concept. Medical concepts are colored blue, behavioral are colored orange, and developmental are colored green. Communication and cognitive had the highest rates of endorsement for both questions.



References

- <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/condition-specific-meeting-reports-and-other-information-related-patients-experience>

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