CORE DIGITAL MEASURES FOR PEDIATRIC RARE DISEASES: A DISEASE-AGNOSTIC & PATIENT-CENTERED APPROACH

Identifying shared meaningful aspects of health to enable selection of digital outcomes for pediatric rare diseases

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Introduction

Pediatric rare diseases (RDs) are individually uncommon but collectively affect millions of children worldwide (1). Research in this space is hampered by small populations, phenotypic heterogeneity, and traditional endpoints that prioritize biomarkers or clinician-reported impairment over functional outcomes meaningful to families. As a result, subtle but important changes are often under-captured (2). Although digital health technologies can measure how children feel and function in real-world settings, a harmonized, patient-centered approach for selecting digital outcomes across pediatric RDs is still lacking.

To address this gap, the Digital Medicine Society (DiMe) convened a global multi-stakeholder team including patient leaders, industry and clinical experts, and government partners to define a core set of digital clinical measures for pediatric RDs. These measures provide a foundation for developing both life-changing therapies and high-quality measurement tools.

Objective

To identify shared meaningful aspects of health (MAH) across pediatric rare diseases and translate them into a modular, disease-agnostic core set of digitally enabled outcome measures.

Methods & results

Systematic literature review

- 123 sources included (66 peer-reviewed + 57 patient-experience reports)
- 73 rare diseases represented
- 1,335 extracted patient/caregiver quotations

Thematic synthesis

- Informed by methodology of Thomas and Harden (3)
- Descriptive themes organized by the International Classification of Functioning, Disability and Health (ICF) framework (4)
- Descriptive themes synthesized into analytical themes representing shared, clinically meaningful aspects of health across pediatric RDs

Modified Delphi process

- 29 multidisciplinary experts
- Weighted consensus approach
- Expert workshop for refinement of recommendations
- Selected final outcome measures + associated endpoints

Figure 1: Conceptual model of core digital measures for pediatric rare diseases

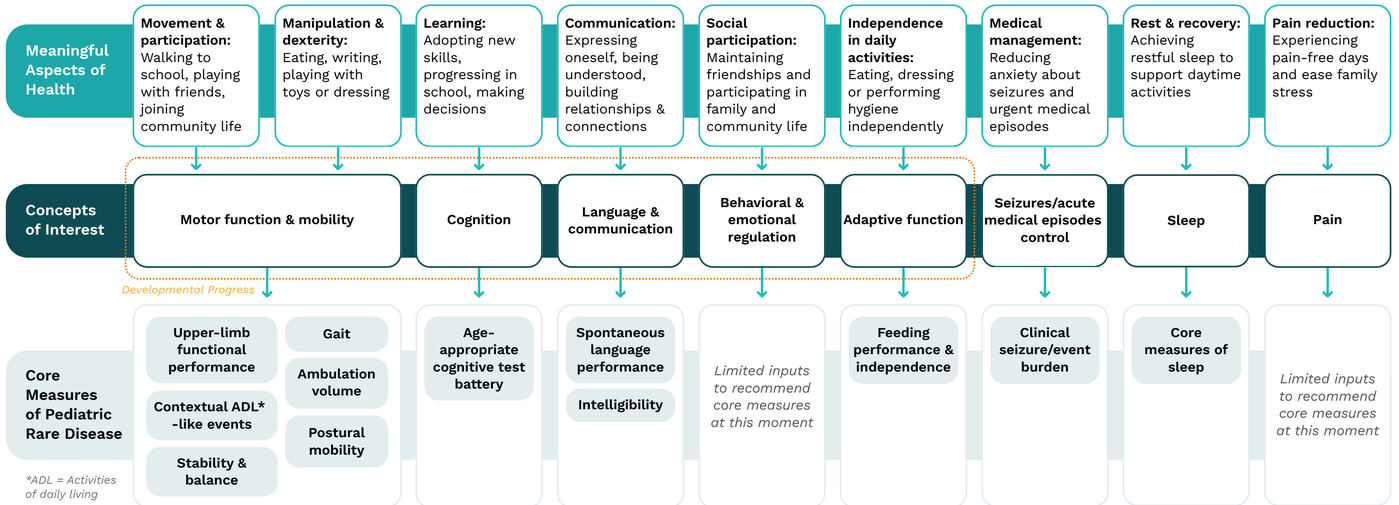
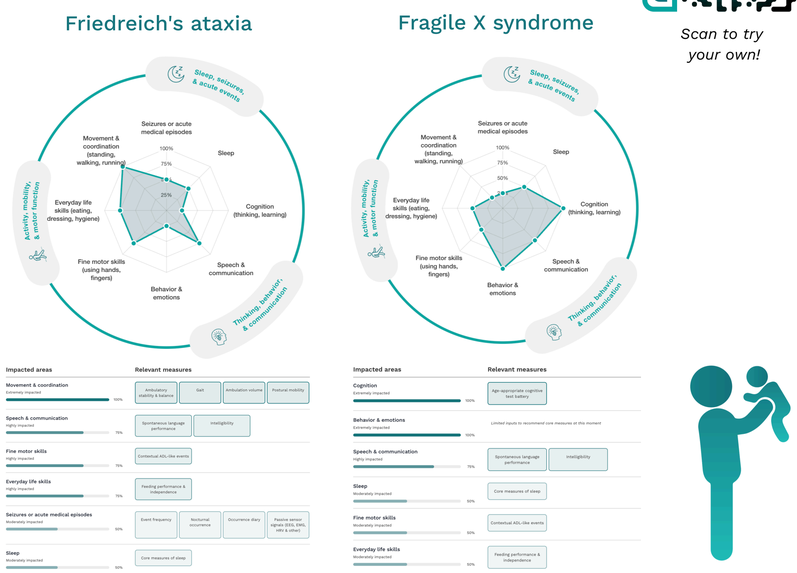


Figure 2: Phenotype-driven customization of core digital measures. This hypothetical example uses the clinical profiles of Friedreich's ataxia and Fragile X syndrome to demonstrate how the core measure set can be tailored to specific disease impacts.



Scan to try your own!

Patient & caregiver quotes

"My two biggest frustrations are losing the ability to reach for heavier things with my arms and not being able to climb the couple of stairs, which frequently prevent me from entering someone's home or getting on a bus. If I had to choose one activity that I wish I could do it is to stand up by myself."
– a patient living with Limb-girdle muscular dystrophy type 2C (LGMD2C)

"I think the biggest thing is that he can't tell us what's going on, and sometimes not being able to know makes it very hard."
– a parent of a child with GM1-gangliosidosis

"It's hard to communicate with her and it's hard for her to communicate [with us], so it effects all aspects of her life."
– a parent of a child with Galactosemia

"Seizures for Lily act like 'cleaning the chalk board' of the brain. and skills such as eating, talking or even walking need to start all over."
– a parent of a child with Phelan-McDermid Syndrome

"My daughter is four years old. I worry about the non-verbal capability, toileting issues and lack of comprehension affecting her future. I fear what the next 10, 15, and 20 years will be like."
– a parent of a child with SYNGAP1

Cross-cutting findings

Autonomy and functional independence: Across diseases and ages, families emphasized that even small gains in independence, such as feeding oneself or communicating basic needs, meaningfully improve dignity and quality of life. Improvement was defined by agency rather than clinical normalization.

Participation and social inclusion: Success was framed as the ability to participate in daily life: attending school, engaging with peers, and avoiding isolation, rather than solely reducing symptoms.

Prevention of decline: Maintaining current function was often as meaningful as gaining new skills, particularly in progressive conditions.

"Invisible" symptom burden: Pain, fatigue, and sleep disruption were common, impactful, and often under-recognized in traditional clinical assessments.

Caregiver and family impact: Child function and family well-being were closely linked; improvements in sleep, mobility, or seizure control benefited the entire household.

Key innovations

A disease-agnostic, function-first approach: Rather than developing disease-specific endpoint sets, this work identifies shared meaningful aspects of health across pediatric rare diseases and translates them into an actionable core set of digital measures.

Bridging concept to measurement: The core set explicitly links meaningful aspects of health (MAH) to concepts of interest (COI) and digitally enabled outcome measures and endpoints, creating a translational pathway from lived experience to implementable data.

Modular, phenotype-informed customization: The core set is not a fixed battery of tests but a flexible foundation that can be adapted based on population or individual needs, functional phenotypes or developmental stages.

Operationalized through a digital tool: An interactive phenotype-based tool enables tailored selection of outcome subsets while preserving alignment within the overarching core set.

Conclusion

Despite heterogeneity across pediatric rare diseases, patient-defined priorities consistently center on autonomy, participation, and quality of life. This work translates these shared requirements into a disease-agnostic, function-first set of core digital measures. By providing a modular, scalable architecture for outcome selection, we reduce endpoint fragmentation, improve cross-study comparability, and establish shared language. The core measures set accelerates more efficient, patient-centered innovation across research and care in pediatric rare disease.

SOURCES | **(1)** Nguengang Wakap, S., Lambert, D.M., Olry, A. et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. Eur J Hum Genet 28, 165–173 (2020). https://doi.org/10.1038/s41431-019-0508-0; **(2)** Dumbuya JS, Ahmad B, Zeng C, Chen X, Lu J. Assessing the effectiveness of measurement scales in evaluating the health-related quality of life in rare disease patients after treatment: a systematic review. Health Qual Life Outcomes. 2024 Dec 19;22(1):108. doi: 10.1186/s12955-024-02324-0; **(3)** Thomas, J., Harden, A. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Med Res Methodol 8, 45 (2008). https://doi.org/10.1186/1471-2288-8-45; **(4)** World Health Organization (2001). The International Classification of Functioning, Disability and Health (ICF). Geneva: World Health Organization

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