Caregiver-defined Unmet Needs to Support Patient-Centred Trial Design and Value Considerations in Multiple Sulfatase Deficiency (MSD)

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BACKGROUND

- Multiple sulfatase deficiency (MSD) is an ultra-rare, progressive pediatric-onset neurodegenerative disorder characterized by delayed diagnosis, absence of disease-modifying therapy, and substantial unmet needs. In ultra-rare diseases, uncertainty around patient-centred outcomes particularly constrains early clinical development and value assessment and is further amplified in pediatric research where trial participation is contingent on caregivers defining acceptability and meaningful benefit.
- This REMEDi4ALL study aimed to engage caregivers early to determine key elements of unmet medical need, identify meaningful outcomes, and procedural criteria for patient-centred clinical trial design in a drug repurposing program for MSD.

METHODS

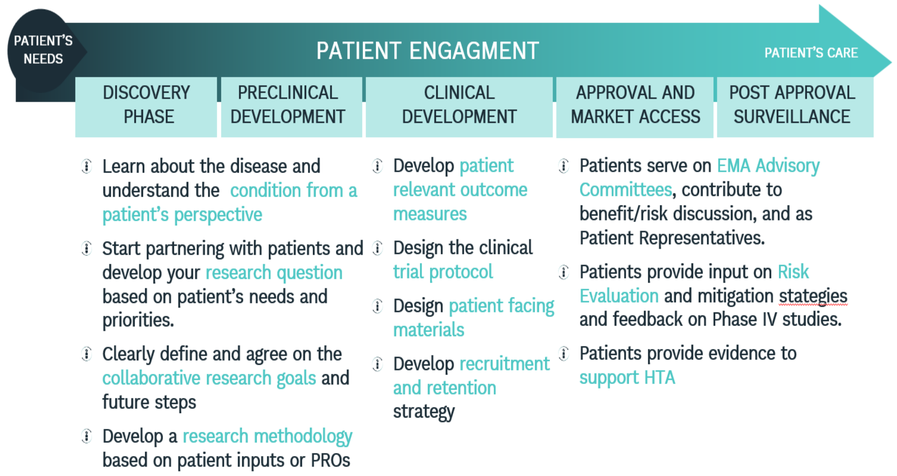

Figure: REMEDi4ALL Patient Engagement Framework

- Semi-structured individual and group interviews were conducted with caregivers affected by MSD to explore lived experience, treatment expectations, risk-benefit considerations, and clinical trial participation. Interviewees came from 3 different methods of recruitment, all of which were coordinated by the REMEDi4ALL patient engagement team
- Thematic analysis was applied to identify caregiver-defined unmet needs, meaningful benefits (to be translated into patient-centred outcomes), and trial acceptability considerations. Findings were integrated and mapped to clinical trial design considerations, supporting outcome selection and protocol refinement.

RESULTS

Therapeutic Gaps	Lack of disease-modifying treatments; need for therapies that stabilise disease progression; limited options for symptom control (pain, vomiting, sleep); uncertainty around long-term benefit
Clinical Care Gaps	Fragmented care coordination; limited clinician familiarity with MSD; challenges managing multi-system symptoms; variability in treatment decisions; difficulties in care transitions
Trial Delivery and Participation Gaps	Travel burden; disruption to daily routines; burden of invasive procedures; need for flexible trial design; importance of clear communication and consistent contact; caregiver involvement in decisions
Measurement and Evidence Gaps	Lack of patient-centred outcomes; underrepresentation of pain, vomiting, sleep, and stability; limited capture of caregiver burden; reliance on biomarkers; need for low-burden data collection (e.g. home sampling)
Supportive and Mental Health Care Gaps	Limited psychological support; emotional burden of caregiving; impact on family and siblings; need for respite care; lack of structured peer support

- Participation of families affected by MSD in clinical trials requires a personalised, patient-centred approach. Understanding the child's disease status and daily routine is key to building effective relationships with trial teams and supporting recruitment and retention.
- Caregivers expressed willingness to participate if pain is minimised, communication is transparent, and individual care needs are respected.
- Shared decision-making, with clear expectations and options, is essential, alongside a consistent point of contact for clinical and logistical support.
- Side effects of greatest concern are those requiring additional management and disrupting established routines, such as constipation causing pain and reduced nutritional intake.
- Travel burden can be mitigated by distinguishing mandatory site visits from those conducted locally and providing appropriate support during extended periods away from home.

IMPLEMENTATION

- This study demonstrates how early caregiver engagement can generate decision-relevant evidence to inform biomarker and patient-relevant endpoint selection and support scientific advice discussions.
- These findings highlight the importance of incorporating patient-centred outcomes, pragmatic endpoint strategies such as low-burden biomarker collection, and flexible trial designs that minimise disruption to family routines.
- They contribute to ongoing efforts to formalise patient-defined value in MSD and provide broader insights for patient-centred trial design in ultra-rare diseases.

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