Development of a Conceptual Model & COA Measurement Strategy in Propionic Acidemia / Methylmalonic Acidemia
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BACKGROUND
• Propionic acidemia (PA) and methylmalonic acidemia (MMA) are both ultra-rare, multi-systemic, and often lethal conditions, which require significant expertise and care. The diverse nature of patient manifestations and the potential overlap with other conditions can result in significant challenges in diagnosis and management (Sikirica et al, 2018; Zhou et al, 2018; Forny et al, 2021).

OBJECTIVES
• To develop a conceptual model in PA and MMA.
• To evaluate potential COA measures as fit-for-purpose (FFP) in PA/MMA clinical trials.

METHODS
• A conceptual map was developed following a structured interview-guided approach with patients with PA/MMA and their caregivers, disease experts, and patient advocates to identify and prioritize core concepts for measurement.
• Interviews were audio-recorded and transcribed for analysis. Thematic analysis identified important concept areas, including signs/symptoms and health-related quality of life (HRQoL) domains.
• Interviews were conducted in-person or via teleconference, and followed a semi-structured interview guide with a focus on capturing the true experiences and perspectives of patients and caregivers.
• Thematic areas were mapped to the conceptual model and outcomes identified for further evaluation.
• The conceptual model was developed according to the MetabolQoL 1.0 guidelines and was iteratively refined to address gaps and overlaps.

RESULTS
• A majority of caregivers interviewed were female (n=15, 71.4%), a majority were working (n=15, 71.4%), and the majority of patients had a diagnosis of PA (n=19, 90.5%).
• The most commonly reported signs/symptoms included vomiting (n=19, 95.8%), seizures (n=16, 80.0%), and respiratory issues (n=18, 90.0%). Other signs/symptoms included headaches (n=11, 55.0%), food aversion (n=13, 65.0%), and gastrointestinal issues (n=15, 75.0%).

CONCLUSIONS
• This is the first conceptual model for PA/MMA identifying core concepts of patient/caregiver importance.
• The Cogstate, NIH Toolbox Motor Battery, and Bayley™4 were determined to be FFP for measuring cognitive and/or motor function (depending on age of patient) [Zeltner NA, Baumgartner MR, Bondarenko A, Ensenauer R, Karall D, Kölker S, et al. Development and Psychometric properties, and other instrument details in the intended context-of-use, PMCID: PMC5740049.]

REFERENCES

CONTACT INFORMATION
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