

Title: Development of a conceptual model to inform a clinical outcome assessment strategy in adolescents and young adults with Fragile X Syndrome

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BACKGROUND: Published literature recognizes a significant heterogeneity in the extent of behavioral and cognitive deficits across individuals with Fragile X syndrome (FXS). This poses significant challenges when developing a clinical outcome assessment strategy for FXS clinical trials. The current study sought to identify the key symptoms and its associated impacts to the individual and his caregiver to support the development of a conceptual model for adolescents and young adults with FXS aged 13-30 years.

STUDY DESIGN: A strategic peer-reviewed literature search was conducted using the Medline[®], Embase[®] and PsycINFO electronic databases to identify relevant concepts in FXS. Supplementary searches were conducted in Google Scholar, conference proceedings, and the reference lists of selected articles. The abstracts identified from the search were reviewed and key relevant concepts included in the conceptual model. As a result of the limited qualitative literature pertaining to FXS, online resources such as publicly available online blogs and forums were also reviewed. Transcripts from previously conducted qualitative interviews with caregivers of individuals with FXS were also analyzed for any relevant symptom or impact concepts.

RESULTS: The literature search identified 418 articles, with five then selected for full-text review based on the inclusion of direct patient/caregiver quotes relevant to the experience of 13-30 year-olds with FXS. Additionally, two online resources and six caregiver interviews were reviewed. The symptom and impact concepts identified in this review were categorized into eight separate domains within the conceptual model: behavior, cognition, speech and communication, sensory perception, emotions, social, activities of daily living (ADL), and caregiver impacts. Key symptom concepts included developmental delays in both learning and verbal communication, hyperactivity and impulsive behavior, and issues with short-term and working memory. The impact of symptoms associated with FXS included a lack of independence when completing ADLs, social behavior and communication issues, and emotional reactions such as anxiety and frustration.

CONCLUSIONS: Findings from the literature review, online materials and caregiver interviews were largely consistent and supported the development of the FXS conceptual model, which can be used to identify key outcome measures for potential use in clinical trials. Concept elicitation interviews with caregivers of individuals with FXS and clinicians are recommended to further support the concepts identified in this review.