**Title**: **“The hardest part is allowing her to fall”: Mothers with the FMR1 Premutation and Their Experiences Raising Daughters with Fragile X Syndrome**

**Authors:** Lauren Jenner1, Thomas Christensen1, Emma Neuhauser1, Abigail Hogan1, Jane Roberts2, & Jessica Klusek1

**Introduction**: Fragile X syndrome (FXS) affects approximately 1 in 3,600 males and 1 in 4,000–6,000 females [1]. Many individuals with FXS, both male and female, live with their parents into adulthood [2]. However, there remains limited understanding of the support needs specific to females with FXS. Females with FXS present with a more variable phenotype than males, ranging from moderate intellectual disability to average or above-average cognitive functioning [3]. This has contributed to limited representation in FXS research and misconceptions about the extent of their support needs [4]. To address this gap, it is crucial to consider the family context, particularly the mother-daughter relationship. This focus is especially pertinent given that many mothers of individuals with FXS carry the *FMR1* premutation, which is associated with an increased likelihood of neuropsychiatric [5] and adult-onset health conditions [6,7], challenges that may be exacerbated by the demands of caregiving. Therefore, the central research question for this qualitative study was: What are the lived experiences of mothers with the *FMR1* premutation in raising a daughter with FXS? This question aims to explore three key aspects of the mother’s experience: 1) the dynamics of support within their relationship with their daughter, 2) how these dynamics may have evolved as they have grown older, and 3) whether these experiences have shaped the mothers’ plans for the future.

**Method**: Semi-structured interviews were completed and analyzed for ten mothers with the *FMR1* premutation (N = 10; aged 49.67-75.05 years [M = 58.32 years]) who had daughters with FXS (N = 13; aged 10.99-47.08 years [M = 25.91 years]). Among these mothers, six had daughters living at home, and half also had a son with FXS living in the household. The ethnicity of both mothers and daughters was predominantly White or Caucasian (90% and 92.31%, respectively), with two mothers (20%) and two daughters (15.38%) identifying as Hispanic or Latino. The interviews with the mothers focused on the support they provide for their daughters, the barriers they may have faced, their own *FMR1* premutation status, and their plans for the future. Interpretative phenomenological analysis (IPA) was used to identify personal and group experiential themes within their narratives. Data collection is ongoing, with a final sample of N = 15 anticipated.

**Results**: While each participant had unique experiences, five group experiential themes emerged from the analysis: 1) *balancing immediate needs with future planning*, 2) *striving for independence while managing dependence*, 3) *mutual yet distinct experiences of anxiety*, 4) *advocacy and resilience amid isolation*, and 5) *the critical challenge of building support networks*. Mothers recognized their daughters' need for support but aimed to avoid constant involvement, often choosing to "step back" and “let the situation get hard for her” until their daughters directly asked for help. They noted that this approach differed from the more hands-on care typically provided to males with FXS and was also distinct from a "typical mother-daughter relationship”. They expressed there was “nothing for that in between” in terms of available services, emphasizing that sometimes simply “having a live body at my house for her” was what their daughter needed. Many mothers were involved in their daughter’s household responsibilities, medical care, finances, and relationships — even for those living outside the household. They saw anxiety as a significant barrier to their daughters’ independence, which heightened their own worries about the future, particularly regarding the potential health implications of their *FMR1* premutation status. Mothers expressed a desire to "build a village" of support, seeking greater involvement from others in their daughters' lives while recognizing their own caregiving limitations and wanting to avoid placing additional burdens on family members. However, their unique family circumstances often complicated efforts to establish a support network outside the home.

**Discussion:** The findings emphasize the distinct challenges that females with FXS face, especially in areas of social-emotional development and independent living skills—issues that are underrepresented in FXS research, which largely focuses on males. When considered alongside emerging evidence that social challenges and anxiety become more pronounced as females with FXS approach puberty [8], and that these challenges can hinder independence in adulthood [2], this study highlights the crucial role mothers play in supporting their daughters’ journey toward independence. The results suggest that addressing the dynamics of support within the mother-daughter relationship could be a valuable focus for future research and interventions, focusing on both the daughters' needs and the pressures experienced by mothers, particularly concerning their own *FMR1* premutation status.

**References:**

1. Hunter, J., Rivero‐Arias, O., Angelov, A., Kim, E., Fotheringham, I., & Leal, J. (2014). Epidemiology of fragile X syndrome: A systematic review and meta‐analysis. *American Journal of Medical Genetics Part A*, 164(7), 1648-1658. <https://doi.org/10.1002/ajmg.a.36511>
2. Hartley, S. L., Seltzer, M. M., Raspa, M., Olmstead, M., Bishop, E., & Bailey, D. B. (2011). Exploring the adult life of men and women with fragile X syndrome: Results from a national survey. *American Journal on Intellectual and Developmental Disabilities*, 116(1), 16–35. <https://doi.org/10.1352/1944-7558-116.1.16>
3. Hagerman, R. J., Berry-Kravis, E., Hazlett, H. C., Bailey, D. B., Moine, H., Kooy, R. F., ... & Hagerman, P. J. (2017). Fragile X syndrome. *Nature reviews Disease primers*, *3*(1), 1-19. <https://doi.org/10.1038/nrdp.2017.65>
4. Bartholomay, K. L., Lee, C. H., Bruno, J. L., Lightbody, A. A., & Reiss, A. L. (2019). Closing the gender gap in fragile X syndrome: Review of females with fragile X syndrome and preliminary research findings. *Brain Sciences*, 9(1), 11. <https://doi.org/10.3390/brainsci9010011>
5. Hagerman, R. J., Protic, D., Rajaratnam, A., Salcedo-Arellano, M. J., Aydin, E. Y., & Schneider, A. (2018). Fragile X-associated neuropsychiatric disorders (FXAND). *Frontiers in Psychiatry*, *9*, 564. <https://doi.org/10.3389/fpsyt.2018.00564>
6. Sullivan, S. D., Welt, C., & Sherman, S. (2011). FMR1 and the continuum of primary ovarian insufficiency. *Seminars in Reproductive Medicine*, 29, 299-307. <https://doi.org/10.1055/s-0031-1280915>
7. Hagerman, R. J., Leavitt, B. R., Farzin, F., Jacquemont, S., Greco, C. M., Brunberg, J. A., ... & Hagerman, P. J. (2004). Fragile-X–associated tremor/ataxia syndrome (FXTAS) in females with the FMR1 premutation. *The American Journal of Human Genetics*, 74(5), 1051-1056. <https://doi.org/10.1086/420700>
8. Bartholomay, K. L., Lightbody, A. A., Ma, Q., Jo, B., Jordan, T. L., & Reiss, A. L. (2024). Cognitive and Social–Emotional Development in Girls With Fragile X Syndrome. Pediatrics, 154(4), e2023065145. <https://doi.org/10.1111/dmcn.16081>

**Affiliations:** 1 Department of Communication Sciences and Disorders, Arnold School of Public Health, University of South Carolina, 1705 College Street, Columbia, SC 29208, USA. 2 Department of Psychology, University of South Carolina, 1512 Pendleton Street, Columbia, SC 29208, USA