Advancing research and treatment in Fragile X Syndrome: A call for holistic, ethical, and inclusive research

Introduction:

Fragile X Syndrome (FXS) is a complex neurodevelopmental condition associated with both challenges (e.g., intellectual disabilities, cognitive and behavioural concerns) as well strengths (e.g., long-term memory, honesty, friendliness). Despite significant scientific progress over the last three decades, many people with FXS and their families continue to face fragmented care and limited evidence-based treatment options. Recent work emphasises the need for research and treatment efforts to better reflect the lived experiences, priorities, and wellbeing of those with FXS and their families (Herring et al., 2024; Johnson et al., 2024).

We call for a coordinated shift in research and clinical practice that prioritises breadth, inclusivity, and real-world impact. Future work must move beyond limited and singular approaches and instead embrace more holistic, person-centred models of care. Treatments and clinical trials must be designed and conducted with safety, ethical integrity, and meaningful impact to people with FXS at the forefront.

Key Priorities:

1. Broaden research approaches
   Research in FXS should evolve beyond narrow, deficit-focused models to reflect the full complex phenotype of FXS. This includes:
   - Integration of cognitive, behavioural, psychological, social, and physical health domains,
   - Developmental and interdisciplinary approaches,
   - Recognition of strengths, wellbeing, and adaptive functioning, alongside challenges.

2. Promote holistic and integrated treatment
   Effective care must include coordinated, person-centred care pathways that span health, education, and social systems. This includes:
   - Integrated approaches combining pharmacological, behavioural, educational, and environmental support,
   - Development and implementation of evidence-informed guidance,
   - Flexibility to tailor interventions and treatments to meet the specific needs of the person with FXS and their families,
   - A focus on functional outcomes, quality of life, and independence.

3. Ensure ethical, safe, and meaningful clinical trials
   Clinical trials must place participant wellbeing at their core. This requires:
   - Robust safeguards to ensure safety, minimise burden and maximise feasibility,
   - Understanding of the relationship of trust between the person with FXS (participant) and their family / caregiver, and how this may impact participation and results,
   - Outcome and outcome measures that are meaningful to people with FXS and their families, including both subjective (PROMs) and objective measurements (e.g. brain activity, eye tracking),
   - Greater transparency in trial design, reporting, and accessibility of findings,
   - Consideration of real-world relevance and long-term impact,
   - Attention to the dissemination and implementation of evidence in real-world settings.

4. Embed lived experience and strengths-based perspectives in research and care
   The perspectives of people with FXS and their families are essential to shaping relevant and impactful research and practice. We recommend:
   - Active involvement of people with FXS and their families in study design, outcome selection, and dissemination,
   - Attention to the reality experienced by those with FXS and allowing their expectations and desires to inform any treatment's objectives,
   - Co-production approaches that value lived experience in addition to scientific knowledge,
   - Recognition of strengths and positive aspects of FXS, alongside support needs,
   - Inclusive approaches to diagnosis and care that are supportive, respectful, and empowering,
   - The inclusion of people with FXS and/or caregivers in care guideline and care pathway development.

Guiding Principles:

All future research and clinical efforts should be:

- Person-centred, respectful, and strengths-informed,
- Holistic and lifespan-oriented,
- Ethically grounded and transparent,
- Inclusive and participatory,
- Scientifically rigorous and clinically meaningful.

Call to Action:

We urge researchers, clinicians, funders, and policymakers to work collaboratively to reshape the research and treatment landscape for FXS. By aligning with emerging integrated guidance and strengths-based perspectives, we can ensure that scientific progress translates into meaningful improvements for people with FXS and their families. A coordinated, holistic, and person-centred approach is essential to improving the lives of people with FXS.

Informing Evidence:

This position is informed by recent work calling for integrated, developmental guidance and person-centred care in FXS, which highlights the need for coordinated approaches to holistic support (Herring et al., 2024), alongside emerging perspectives emphasising strengths, neurodiversity, and supportive approaches to diagnosis and care (Johnson et al., 2024).

References:

Herring, J., Johnson, K., Scerif, G., Weight, E., Richstein, J., Crawford, H., Robinson, H., Gawarammana, R., & Ellis, K. (2024). The joys of fragile X: Understanding the strengths of fragile X and delivering a diagnosis in a helpful, holistic way. *Neurodiversity, 2.* https://doi.org/10.1177/2754633024128768

Johnson, K., Stanfield, A. C., Scerif, G., McKechanie, A., Clarke, A., Herring, J., Smith, K., & Crawford, H. (2024). A holistic approach to fragile X syndrome integrated guidance for person-centred care. *Journal of Applied Research in Intellectual Disabilities, 37*(3), e13214. https://doi.org/10.1111/jar.13214