**Symposium Title**: Social determinants of health as key contributors to clinical outcomes in neurodevelopmental disabilities and associated conditions

**Co-Chairs**: Walker S. McKinney[[1]](#footnote-1), Lauren M. Schmitt1,2,9

**Discussant**: Leonard Abbeduto3,4

**Overview**: Social determinants of health (SDOH) capture “the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks” (US Department of Health and Human Services). Mounting evidence suggests that SDOH significantly influence cognitive and mental health outcomes in the general population, including IQ and internalizing symptoms. Less is known about the impact of SDOH on these clinical outcomes in individuals with neurodevelopmental disabilities and associated conditions (e.g., *FMR1* premutation). This symposium will review new findings from three studies that provide evidence of the impact that neighborhood and housing characteristics have on clinical outcomes in individuals with Fragile X Syndrome, *FMR1* premutation carriers, and intellectual and developmental disabilities. Implications for targeted intervention development and public policy solutions will be discussed.

**Paper 1 of 3**

**Paper Title**: Beyond the Protein: How Neighborhoods Shape IQ and Adaptive Behavior in Fragile X Syndrome

**Authors**: Walker S. McKinney1, Austin Corsmeier5,6, Ashley Dapore6, Christina Gross2,7, Kelli C. Dominick6,8, Craig Erickson6,8, Lauren M. Schmitt1,2,9

**Introduction**: Approximately 30% of the variance in IQ among individuals with fragile X syndrome (FXS) is accounted for by familial genetic and molecular factors, including absence or reduction in fragile X messenger ribonucleoprotein (FMRP) expression. The remaining 70% of this variance is partially accounted for by social-environmental factors (e.g., education, access to therapies, home environment, nutrition) that have not yet been comprehensively or systematically examined in FXS.

**Method**: 150 full mutation individuals with FXS (68% male) aged 4-61 years completed the Stanford-Binet, Fifth Edition (SB-5) to estimate IQ. Participants’ caregivers completed the Vineland-3 Comprehensive Interview to measure their children's adaptive skills. FMRP was quantified using our previously described (Boggs et al., 2022) Luminex-based technique. Standardized rankings of “neighborhood opportunity” were extracted based on participant home addresses at the time of testing using the Child Opportunity Index (COI), which ranks the economic, educational, and health/environmental resources of individual neighborhoods relative to national averages. To assess the impact of social-environmental factors on clinical outcomes, we used linear mixed effects models to quantify the variance in IQ and adaptive behaviors accounted for by FMRP expression and then used similar models to quantify the *additional* variance in these clinical outcomes significantly accounted for by neighborhood characteristics.

**Results**: Broadly, social-environmental factors were more strongly associated with clinical outcomes in males than in females, and these factors more strongly related to individual differences in adaptive behaviors than IQ. *IQ:* FMRP expression accounted for 3.5% and 4.9% of the variance in full-scale IQ (FSIQ) in males and females, respectively. In males, greater healthcare resources (e.g., insurance availability; nearby healthcare nonprofit organizations) significantly accounted for an additional 4.6% of the variance in FSIQ. In females, greater healthcare resources accounted for an additional 6.1% of the variance in FSIQ although this was only marginally significant (*p* = .07). *Adaptive behaviors*: FMRP expression accounted for 9.2% and 3.3% of the variance in adaptive behaviors in males and females, respectively. In males, multiple neighborhood socioeconomic and educational neighborhood characteristics significantly accounted for additional variance in adaptive behaviors, including greater economic equity (6.5%), employment opportunities (7.5%), social-economic resources (e.g., multi-caregiver households; cross-income friendships; nearby nonprofit organizations; 10%), and educational resources (e.g., teacher experience; nearby educational nonprofit organizations; 6.1%). Neighborhood characteristics were not significantly associated with adaptive outcomes in females.

**Discussion**: Our findings of stronger associations between social-environmental factors and clinical outcomes in males are consistent with historical studies of FXS (Dyer-Friedman et al., 2002; Glaser et al., 2003); this pattern may be due to the distinct service needs of males and females with FXS driven by differences in the severity of cognitive and adaptive behavioral deficits. Specifically, males with FXS may rely more on social-environmental supports to accommodate more limited cognitive and adaptive skills, whereas adaptive behavioral development in females does not require the same degree of environmental supports (e.g., specialized healthcare or educational services). Our finding that healthcare resources are related to higher IQ in males and, to a lesser extent, in females underscores the importance of policy solutions and innovative strategies (e.g., scalable telehealth services covered by insurance) that maximize healthcare access in this population. Our finding that adaptive behaviors are most strongly related to social-economic supports warrants further investigation using narrowband measures or qualitative interviews with families to identify pathways through which social supports may foster adaptive behaviors. Long-term, we hope these findings and follow-up studies will enable the development of targeted community and public health interventions that advance clinical equity for patients with FXS.

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**Paper 2 of 3**

**Paper Title**: Social Determinants of Health and Risk for Anxiety and Depression in the *FMR1* Premutation: Neighborhood Deprivation and the Mediating Role of Loneliness

**Authors**: Thomas R. Christensen[[2]](#footnote-2), Jessica Klusek1

**Introduction**: The neighborhood in which someone lives has the potential to influence social relationships, social support, and feelings of loneliness, which in turn can lead to increased feelings of anxiety and depression, particularly for aging individuals (Kearns et al., 2015). Women with the *FMR1* premutation have an expansion of 55-200 CGG repeats on the *FMR1* gene, and are at an increased risk for anxiety and depression, with lifetime prevalence at 35% and 54%, respectively (Roberts et al., 2016). Additionally, women with the *FMR1* premutation are at risk of passing the full fragile X mutation to their children. Much of the research on risk for anxiety and depression in women with the *FMR1* premutation has focused on child fragile X status and genetic factors (Loesch et al., 2015; Roberts et al., 2016), with little research focusing on the role that social determinant of health play in the *FMR1* phenotype. Understanding the role that neighborhood deprivation has on loneliness in aging women with the *FMR1* premutation and potential gene/environment interactions can illuminate risk and potential targets to reduce the anxiety and depression phenotype associated with the *FMR1* premutation. Therefore, this study seeks to inform the impact of neighborhood deprivation on loneliness in aging women with the *FMR1* premutation and the mediating role of loneliness on anxiety and depression.

**Method**: Participants included 116 women with an average age of 62 years (range = 44-81; SD = 10), 72 of whom were women with the *FMR1* premutation and 44 of whom were controls. The groups were matched on income (*p* = .931), age (*p* = .338), race (*p* = .338), and education (*p* = .946). Sixty-one of the women with the *FMR1* premutation had a child with fragile X syndrome. The Area Deprivation Index measures the socioeconomic conditions of a neighborhood by ranking census blocks based on income, education, and employment (Kind & Buckingham, 2018). The sample represents a wide range of neighborhood deprivation scores (M = 43; SD = 24). The Beck Anxiety Inventory (Beck & Steer, 1993) measured anxiety symptoms, and the Beck Depression Inventory–II (Beck et al., 1996) was used to measure depression symptoms. To measure loneliness, the UCLA Loneliness Scale (Russell, 1996) was used.

**Results**: In a general multiple linear regression model that included area deprivation, *FMR1* premutation group status, and their interaction as predictors for loneliness scores, higher levels of area deprivation predicted higher levels of loneliness (*p* = .002), and a significant interaction between group and area deprivation (*p* = .043) suggested that area deprivation was more strongly associated with loneliness in women with the *FMR1* premutation than in controls. The products of coefficient approach with bias-corrected, bootstrapped confidence intervals were used in two mediation models testing if loneliness mediated the effect of area deprivation on anxiety and depression in women with the *FMR1* premutation. The anxiety model showed full mediation (indirect effect ab = .04, 95% CI [ 0.01,0.09]) with a non-significant direct effect (*p* = .167). The depression model also showed full mediation (indirect effect ab = .07, 95% CI [0.03,0.15]) with a non-significant direct effect (*p* = .411). These results suggest that area deprivation is associated with anxiety and depression symptoms via loneliness, but not directly.

**Discussion**: To date, few studies have explored the associations between social determinants of health and anxiety and depression in the *FMR1* premutation. In the general population, area-level social determinants of health have an impact on loneliness, which have downstream effects on anxiety and depression, especially as people age. This study demonstrates that aging women with the *FMR1* premutation who live in high deprivation neighborhoods are at an increased risk for loneliness compared to women who do not carry this genetic mutation, and that the loneliness from area deprivation has downstream effects on anxiety and depression symptoms in the women with the *FMR1* premutation. Policies and interventions addressing loneliness and targeting areas with relatively higher deprivation could have a positive effect on anxiety and depression and help to address health disparities in the *FMR1* premutation population. Further research should explore the relationships between other social factors such as social relationships and social support and neighborhood deprivation and the possible downstream effects of those factors on health outcomes.

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**Paper 3 of 3**

**Paper Title**: Child Opportunity Index and Mental Health in Youth with Intellectual and Developmental Disabilities

**Authors**: Iulia Mihaila[[3]](#footnote-3), Cheng-Shi Shiu2, Katherine Buchholz3, Tracy Gladstone4, Jocelyn Kuhn5, Kristin Berg1

**Introduction**: Existing literature suggests that neighborhood environments are associated with youth physical and mental health (Christian et al., 2015). The child opportunity index is a population-level tool that provides an indicator of neighborhood resources and conditions available to youth by considering a variety of factors, including access to education, parks, food, healthcare, and safe housing (Noelke et al., 2020). It covers three domains: education, health and environment, and social and economic. The relation between neighborhood and environmental conditions and mental health among youth with intellectual and developmental disabilities remains relatively unexplored. This study aims to examine neighborhood and environmental predictors of depression and anxiety severity in youth with IDD.

**Method**: We examined baseline data from an ongoing randomized control trial investigating the efficacy of a stratified behavioral health treatment program in promoting positive mental health outcomes in a sample of 780 youth with IDD receiving care coordination services. Caregivers reported on environmental factors, including zip code (used to calculate the child opportunity index), the number of times the youth moved or changed houses in their life, how long the youth had lived in their current household, and caregiver sociodemographics. The Patient Health Questionnaire – Adolescent (PHQA) was interviewer-administered to youth with IDD to measure their depressive symptomatology and the Generalized Anxiety Disorder 7-item Scale (GAD7) was interviewer-administered to measure their anxiety symptomatology. Regression analyses were used to examine associations between neighborhood and environmental factors and depression and anxiety severity in youth with IDD.

**Results**: To date, baseline data has been collected from 276 youth with IDD, aged 13-20 years (M = 16.6, SD = 2.5). Approximately 56% identified as male, 41% as female, and 3% as another gender identity (e.g., transgender male or non-binary). Roughly 65% identified as white, non-Hispanic. Nineteen percent of youth lived in very low opportunity neighborhoods. Across youth with IDD, average PHQA and GAD7 scores were 5.4 and 4.5, respectively indicating mild depression and anxiety symptoms. Controlling for age, gender, and intellectual disability (yes vs. no), the number of times the youth moved or changed houses in their life (ß = .20, p=.002) was significantly associated with greater depression severity F(5,229)=5.10, p<.001). Similarly, the number of times the youth moved or changed houses in their life (ß = .16, p=.01) was significantly associated with greater anxiety severity F(5,226)=6.0, p<.001). The child opportunity index was not associated with depression or anxiety severity in our sample.

**Discussion**: Neighborhood conditions as described by the childhood opportunity index were not associated with mental health outcomes among youth with IDD. However, findings indicate that greater housing instability (i.e., the number of times youth move throughout their lives) may contribute to greater depression and anxiety severity among youth with IDD. This is consistent with existing literature, which suggests that a greater number of moves in childhood is associated with poorer well-being in adulthood (Oishi & Shimmack, 2010). Resources and mental health promotion services specifically targeted at youth experiencing housing instability may be beneficial.

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