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FORWARD

FRAGILE X ONLINE REGISTRY WITH ACCESSIBLE RESEARCH DATABASE

Family Newsletter

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NEW JOURNAL PUBLICATIONS

We are excited to inform you of four new publications resulting from FORWARD, the largest resource of clinical and demographic data for the fragile X syndrome (FXS) population in the United States. FORWARD data is collected on individuals with FXS seen at specialty clinics across the country. The data were collected by clinicians at the patient visit and by parent reports for non-clinical and behavioral outcomes. **Thank you** to all the families and specialty clinics who continue to support the data collection efforts of this important longitudinal study.

Your contributions continue to make a difference.

Visit <http://forwardfx.org/journal-publications/> for a full listing of FORWARD publication.



FORWARD is supported by cooperative agreements #U01DD000231, #U19DD000753 and # U01DD001189, funded by the Centers for Disease Control and Prevention. The newsletter contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

Toilet Training in Fragile X Syndrome

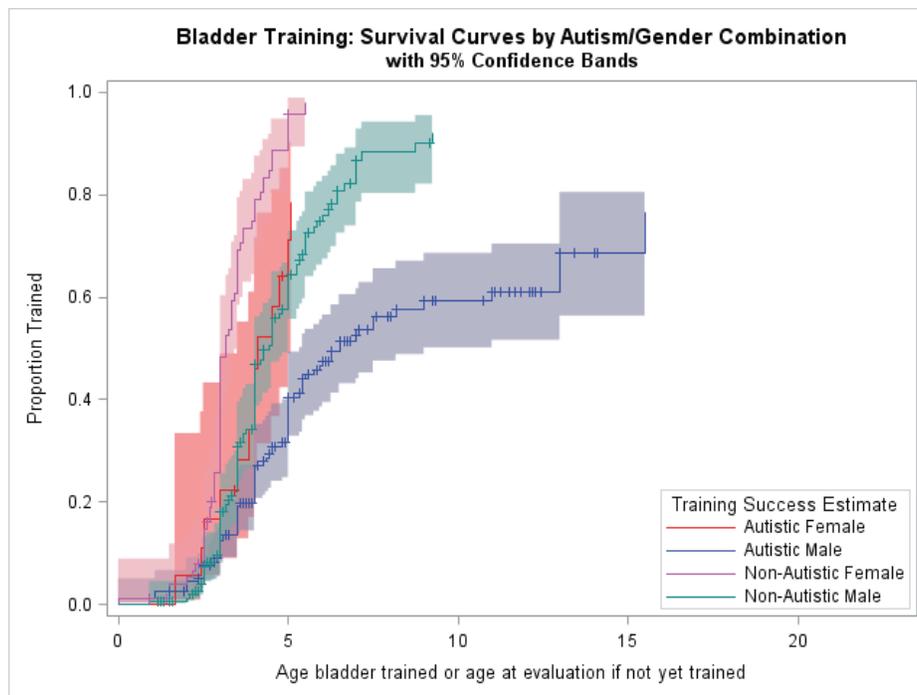
Journal of Developmental & Behavioral Pediatrics

Authors: Elizabeth Berry-Kravis, MD, PhD, Sharon Kidd, PhD, Ave M. Lachiewicz, MD, Tse Hwei Choo, MPH, Nicole Tartaglia, MD, Devadrita Talapatra, PhD, Christina Aguirre-Kolb, PhD, Howard Andrews, PhD, Karen Riley, PhD

Toilet training issues can be burdensome and a significant problem for families with children affected by Fragile X Syndrome (FXS). This groundbreaking study utilized FORWARD data on 633 individuals with FXS to fill the gap for much needed information on when children with FXS learn bladder and bowel toileting skills. By characterizing toileting milestones in children with FXS, this study helps to shed light on the factors causing delays in toilet training.

Language, behavioral irritability and autism spectrum diagnoses (ASD) presented as the main factors in predicting bowel and bladder training delays. ASD diagnosis and gender had a strong impact on age of toilet training. Males and individuals with a co-diagnosis of ASD showed a significant delay in learning toilet training skills. By 5 years of age, almost **100% of females** achieve bladder toilet training versus **70% of females** with a co-diagnosis of ASD. In comparison, about **50% of males** with FXS alone achieved bladder training by age 5 and **35% of males** with a co-diagnosis of ASD achieved bowel toilet training at the same age.

This important study will allow practitioners to help inform families about the typical toilet training process and what to expect with toilet training efforts, including how and when to implement toilet training for children with FXS.



Age is shown on the horizontal line at the bottom of the graph. This is plotted against the proportion of individuals toilet trained at a given age (eg. 0.6 would mean 6 of 10 or 60% of individuals are trained).

Berry-Kravis, E. (2019). Toilet Training in Fragile X Syndrome. *Journal of Developmental & Behavioral Pediatrics*. 40(9), 751-761.

Please visit the National Fragile X Foundation site for a more detailed summary of this publication:
<https://fragilex.org/our-research/nxf/treatment-guidelines/toileting-issues-in-fragile-x-syndrome/>

Pharmacologic interventions for irritability, aggression, agitation and self-injurious behavior in fragile X syndrome: an initial cross-sectional analysis

Authors: Eleanor Eckert, Kelli Dominick, Ernest Pedapati, Logan Wink, Rebecca Shaffer, Howard Andrews, TseHwei Choo, Chen Chen, Walter E. Kaufmann, Nicole Tartaglia, Elizabeth Berry-Kravis, Craig Erickson

Behavioral dysregulation, or the impairment of behavioral processes, is common in FXS. A regularly cited group of behaviors in individuals with FXS, particularly males, is irritability, agitation, aggression and self-injurious (IAAS) behaviors. These behaviors can put a strain on both the individual and their caregiver's quality of life and there is little information about how to manage these behaviors with medication. This publication in the Journal of Autism and Developmental Disorders presented information from a FORWARD dataset involving 415 individuals with IAAS behaviors. The study describes the psychopharmacologic management of IAAS and examines the characteristics of individuals that are treated with drug therapy for IAAS.

Findings showed that among the individuals with FXS that were exhibiting IAAS, those receiving drug treatment were more likely to be older males with significant intellectual disability. The individuals receiving drug treatment were also more likely to have comorbid autism, anxiety, hyperarousal and social impairment. The medications most used in this population are antipsychotic medications, particularly Aripiprazole and Risperidone. Both Aripiprazole and Risperidone are FDA-approved for treating irritability associated with ASD. Individuals were also prescribed drugs outside of antipsychotic medications, including Selective serotonin reuptake inhibitors (SSRIs), stimulants, non-SSRI antidepressants, alpha-agonists, mood-stabilizers, and anxiolytics. Most individuals (63%) did not experience side effects from their drug treatment.

Reported Adverse effects experienced by those on medications for IAAS	
Adverse effects	% of participants
No side effect	62.8%
Weight gain	14.4%
Sedation	8.3%
Activation/impulsivity/disinhibition	1.1%
Agitation/irritability/anxiety	5.0%
Weight loss/appetite suppression	5.0%
GI (nausea/constipation/diarrhea)	2.8%
Sleep issues/insomnia	2.2%
Tremor	2.2%
Headache	1.1%
Dizziness	1.1%
Other *	6.1%

**Other included responses like very thirsty, drooling, increased non compliance and mild activation*

Eckert EM, et al. (2019). Pharmacologic interventions for irritability, aggression, agitation and self-injurious behavior in fragile X syndrome: an initial cross-sectional analysis. *J Autism Dev Disord.* 49, 4595-4602.

Please visit <https://www.ncbi.nlm.nih.gov/pubmed/31468273> for the full publication.

Improving the diagnosis of ASD in FXS

Authors: Walter E. Kaufmann, MD, Sharon A. Kidd, PhD, MPH, Howard F. Andrews, PhD, Dejan B. Budimirovic, MD, Amy Esler, PhD, LP, Barbara Haas-Givler, MEd, BCBA, Tracy Stackhouse, MA, OTR, Catharine Riley, PhD, MPH, Georgina Peacock, MD, MPH, Stephanie L. Sherman, PhD, W. Ted Brown, MD, PhD, Elizabeth Berry-Kravis, MD, PhD

This paper published in the *Journal of Autism and Developmental Disorders* addresses the difficulty of diagnosing ASD in FXS. Although individuals with FXS are commonly diagnosed with ASD, it is a challenging diagnosis because intellectual disability and co-occurring mental health conditions can be interpreted as autistic features. Two commonly used standard measures, the Social Communication Questionnaire (SCQ) and the Social Responsiveness Scale (SRS) were examined as potential tools for improving ASD diagnosis and characterization in FXS. Researchers scientifically analyzed the SCQ and SRS and compared it to the standard DSM5 method used across clinicians to diagnose ASD in FXS. To improve diagnostic accuracy of ASD, various methodological revisions were applied to the SCQ and SRS in order to improve sensitivity and specificity of the measures.

Although the revised SCQ and SRS have an improved sensitivity/specificity balance and may be better suited for identifying ASD in males with lower cognitive function and irritability/aggression, the diagnostic accuracy of these measures is still below optimal levels, reflecting to some extent the inherent difficulty of diagnosing ASD in intellectual disability. This research suggests there are differences between the diagnosis of FXS and FXS+ASD. More work needs to be done to examine additional modifications, beyond deletion of non-informative items, that can further improve the diagnostic potential of the SCQ and SRS in FXS.

Kidd SA, et al. (2019). Improving the Diagnosis of Autism Spectrum Disorder in Fragile X Syndrome by Adapting the Social Communication Questionnaire and the Social Responsiveness Scale-2. *J Autism Dev Disord.* 2019, 1-20. doi: 10.1007/s10803-019-04148-0

Please visit <https://link.springer.com/article/10.1007%2Fs10803-019-04148-0> for the full publication.



Preventive Care Services and Health Behaviors in Children with Fragile X Syndrome

Authors: Kendra E. Gilbertson, Hannah L. Jackson, Eric J. Dziuban, Stephanie L. Sherman, Elizabeth M. Berry-Kravis, Craig A. Erickson, Rodolfo Valdez

Published in *Disability and Health Journal*, researchers from the Centers for Disease Control and Prevention and other organizations presented FORWARD data on preventive services received by children and young adults with FXS. This research can help clinicians identify preventive care services that patients with FXS may need.

Key findings:



Only one in four children and young adults with FXS met the physical activity guidance from the United States Department of Health and Human Service (DHHS). DHHS recommends children 6–17 years of age get one hour of physical activity every day, while adults need about 2.5 hours per week.



Slightly more than half of the children and young adults with FXS met the recommendation for an annual influenza vaccination.



Almost three out of four children and young adults with FXS met dental care guidance from the American Academy of Pediatric Dentistry (AAPD). The AAPD recommends children have their first dental exam at the time of their first tooth eruption, or by one year of age, followed by regular exams every 6 months for children and adults.



About nine out of ten children and young adults with FXS received the recommended immunizations between birth and 18 years of age.

Gilbertson K, et al. (2019). Preventive care services and health behaviors in children with fragile X syndrome. *Disabil Health J.* 12, 564-573

Please visit <https://www.ncbi.nlm.nih.gov/pubmed/31118158> for the full publication.