



# CARRIER COURIER

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INTERNATIONAL  
FRAGILE X  
PREMUTATION  
REGISTRY

## WELCOME

Dear all,

For nearly 25 years, I have spent most of my working hours focused on fragile X-associated conditions, primarily working with research participants that visit us at the MIND Institute at UC Davis, here in Sacramento, California. You might assume that I have full understanding of the lived experiences of these individuals, at least for those living in the United States. Humbly, I have come to realize that I really do not.

Several years ago, when social media became a prominent way for us to share our experiences and gain support from others, I joined Facebook groups associated with fragile X syndrome and FXTAS. I joined only to learn about the experiences, struggles and successes of individuals affected by fragile X and their families and to stay informed about concerns that I could help address in my research or clinical work. I haven't *contributed* really anything other than an occasional "thumbs up", "like", or "heart" emoji. I guess I mainly wanted to be a listener and not stick my nose where it doesn't belong. What I quickly realized is that the comments and questions shared by men and women with FXTAS and their caregivers are often heart-wrenching, and they have opened my eyes to the real life impact of this disease. The declines in self-care, changes in personality, uncontrollable tremors, falls and injuries, deteriorating memories, the many illnesses and life events that seem to accelerate the decline, as well as several memorials all remind me of the importance of finding effective treatments for FXTAS as soon as possible. This brings me to the focus of the 3rd edition of the newsletter.

While both men and women are impacted by FXTAS, it is much more prominent in men who carry the premutation. Currently, the registry is over 85% female, and male premutation carriers are very under-represented. *If we are going to find effective treatments, and even a cure for FXTAS, we need our prospective research samples to be representative.* Right now, the Registry would not produce a representative group of participants. **Help us share the Registry opportunity with men who carry the premutation!** Please reach out to your brothers, uncles, fathers, grandfathers or other men with the premutation and encourage them to join the registry. Their potential engagement in research is SO IMPORTANT.

Speaking of important research, Deborah Hall, Michelle Tosin and their colleagues at Rush University, along with several collaborators are working to finalize and validate a very important clinical assessment measure called the **FXTAS Rating Scale**. As you may know, we use clinical trials to learn whether treatments are effective and beneficial to patients. One of the most important aspects of clinical trial design and execution is the "primary outcome measure." This is the tool used to measure the most important clinical problems of a disease, and whether or not improvements occur during the treatment period. The FXTAS Rating Scale is being developed to serve this critical purpose for future trials. The work is a true partnership between the clinical researchers and people with the premutation, including FXTAS. Participation in these measure development studies is an absolutely essential step along the path towards identifying effective treatments and making them available to patients. The study led by Drs. Hall and Tosin highlighted below has been approved by the Registry governance committee, and flyers have been sent to registrants who may be eligible to participate. If you receive an email about this study, I sincerely hope you will give it consideration and reach out to the team.

Thank you for being a part of the International Fragile X Premutation Registry. By growing the Registry we are able to demonstrate the community of individuals living with the fragile X premutation are interested and ready to participate in research to better understand the condition and improve their quality of life. We believe in the power of this project and could not do it without your involvement. Thank you.

David

A handwritten signature in black ink, appearing to read "David".

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## REGISTRY UPDATE

We have over 1000 individuals registered from 49 U.S. States and 39 countries. We launched the Spanish version of the registry on December 27th, 2021 and we now have registrants from 6 Latin American countries. 81% of the registered participants are females and 19% are male. We continue to encourage all family members, individuals who carry the premutation and controls (individuals who do not carry the premutation or have Fragile X syndrome) to register.

**Thank you to those who visited our booth at the National Fragile X Foundation Conference! We had a great response with an additional 150 new registrants since then.**



Feel free to contact [HS-IFXPR@UCDavis.edu](mailto:HS-IFXPR@UCDavis.edu) if you have any questions or to check if you are already included in the Registry.

## INTERNATIONAL SPOTLIGHT

Did you know the idea for the International Fragile X Premutation Registry was first presented by Dr. David Hessel at the International Premutation Conference in Rotterdam, The Netherlands three years ago?

The next conference will take place in New Zealand in February of 2023. Many of the IFXPR Leadership team and Advisory Committee members are planning to attend and looking forward to connecting with other professionals and patient advocacy organizations interested in and dedicated to the fragile X premutation.



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## WE'RE IN A CLINIC NEAR YOU!

Have you or a loved one recently attended an in-person clinic appointment? You may have seen the IFXPR registry posters. Pretty cool, huh?

We are spreading awareness to individuals carrying the premutation and their family members by providing materials in clinic that make it easy to register. Keep your eye out for the IFXPR posters at the UC Davis MIND Institute, Rush Medical Center, University of Colorado, and University of Michigan.

## APPLICATION FOR RESEARCHERS IS OPEN!



### JOIN THE INTERNATIONAL FRAGILE X PREMUTATION REGISTRY TODAY!

Adult fragile X premutation carriers AND family members who do not have a fragile X mutation are eligible.

#### WHY REGISTER?

- Get involved and contribute to future discoveries that will help us understand how the premutation affects health.
- Let researchers know you are interested in participating in research, including future treatment studies that focus on conditions such as FXTAS and FXPOI.
- Stay connected with the worldwide premutation community as the registry expands.
- Get updates on new discoveries with our newsletter, The Carrier Courier.

Need help registering? No problem! If you have FXTAS, your loved ones can help you register.

Help us build an amazing resource by enrolling at [fragilex.org/ifxpr](http://fragilex.org/ifxpr)

It only takes 15 minutes!



Our application for research recruitment support is open to researchers all around the world!

Many researchers have reached out to learn more about the application process and we have had two research requests already!

Researchers are also actively applying for grant funding for various projects on the premutation condition. We are looking forward to supporting their future projects!

Remember, researchers will not be given any of your information, including your contact information. You will only receive information from the Registry team and it will be your choice to contact the researcher to learn more about their project.

Curious about the application process? You can take a look at the [here](#).

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## RESEARCH CORNER

### PARTICIPATE IN A GROUNDBREAKING STUDY THAT WILL VALIDATE THE FIRST RATING SCALE FOR FXTAS

More than two decades have passed since **Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS)** was first described, and despite advances in FXTAS research, treatment of this condition remains focused on addressing symptoms – not treating the core causes.

For this reason, in the last 16 years a group of scientists has been dedicated to improving **the first rating scale** created to measure **FXTAS motor symptoms**. By doing so, we will be better able to see if future treatments are making a difference.

The development of a measurement instrument (such as a rating scale) is not a straightforward process, given the complexity of methods used to study large numbers of individuals. This becomes particularly challenging when it comes to **rare diseases** such as FXTAS.

We hope that this newsletter reaches many **Premutation Carriers with and without FXTAS**, motivating them to participate in the last phase of the **FXTAS Rating Scale validation study**.

Highlighted here is the example of Ms. Sue Fishman, who volunteered to participate in the study during the recent National Fragile X Foundation International Conference, held last July in San Diego, CA. After the conference, Ms. Fishman contacted the researchers at **Rush University** and scheduled the participation of her 3 sisters.

The photos of Sue demonstrate the motor exam conducted by the neurologist Dr. Deborah Hall, PhD, using the FXTAS Rating Scale.

Take this opportunity to help improve treatment for those currently with FXTAS and for those who may develop it in the future.

#### For more information

Call: 312-563-3855

Email: [michelle\\_tosin@rush.edu](mailto:michelle_tosin@rush.edu)

Link: [https://redcap.link/fxtas\\_research\\_opportunity](https://redcap.link/fxtas_research_opportunity)



Tosin MHS, Stebbins GT, Goetz CG, Hagerman RJ, Hessler D, Zolecki MA, Todd PK, Leehey MA and Hall DA (2022) Fragile X-associated tremor ataxia syndrome rating scale: Revision and content validity using a mixed method approach. Front. Neurol. 13:977380. doi: [10.3389/fneur.2022.977380](https://doi.org/10.3389/fneur.2022.977380)

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## MY STORY by Sue Fishman

Little did we know what life had in store for us and all the kind, caring, and helpful people we would meet along the way! We were so excited when our first son David was born in 1976. He was a beautiful baby. However, early on I knew something wasn't quite right. David cried all the time, he would make a fist as he cried while his body tightened up like a tight rubber band. A mother's intuition told me that something wasn't right or normal. When I talked to the pediatrician, he thought I was a nervous mother and told me not to worry about it and that David was on the slow end of normal. Still, I continued to worry throughout his first year. When he was 18 months old there was a Child Find program for preschoolers in Boulder Colorado and they tested David. They found that he was developmentally delayed. Shortly thereafter, he began to receive early intervention services. Initially, services were provided in the home, but eventually David went to the nearby university where he was enrolled in a speech and language preschool program. It was assumed that this would fix David's developmental delays which, at the time, were attributed to fetal stress at birth.

Our second son, Jason, was born in 1979 and shortly thereafter we moved to the Hampton Roads area of Virginia. David was enrolled in the special education preschool program. When Jason turned two, he was enrolled in the same program. Both boys were now labeled as being developmentally delayed and both received speech and occupational therapy. Multiple evaluations took place over the next seven years and in 1987 the boys were finally diagnosed with fragile X syndrome after bloodwork was completed. After 11 years of searching for the reasons for David's and then Jason's developmental delays, we had our diagnosis. But we were uncertain as to what it all meant and so immediately began the search for information.

I am from a family of nine children, so I knew I needed to inform my family about what I had just learned about our genetic make-up. Although I have nineteen nieces and nephews, no one seemed to be affected with fragile X except for my two sons. We didn't know if my mother or father was the carrier, so we went to a geneticist for further testing. At the time, and as a result of the test being less sophisticated than the one currently in use, we were told that everyone's test results were negative for fragile X and that I was a spontaneous mutation!

Fast forward nine years when we decided to take David and Jason to the Denver Fragile X clinic and have a complete battery of tests done and to get help with developing an educational plan for the boys. At the time, I mentioned to Dr. Randi Hagerman that I was told I was a spontaneous mutation. She just looked at me and said, "I don't think so." She recommended that my sisters and mother all be tested. It turned out my late father was the carrier as were all my sisters. Once my sisters realized they were carriers, their children were also tested. Two females were diagnosed with the full mutation. (Both girls went through public school, college, and graduate school and are, today, married and living full lives. Later, one of my nieces did in vitro fertilization and has two beautiful neuro-typical children.)

The challenges of being a fragile X carrier started appearing in my body when I was age 35 and started having irregular menstrual cycles. My doctor at the time told me I was just stressed so I switched doctors only to find out I was in menopause. I informed them that research was showing that women who were fragile X carriers went through early menopause, (Now referred to as Fragile X-associated primary ovarian insufficiency or FXPOI), but none of my doctors were familiar with the studies. It was recommended that I start a regiment of hormone replacement therapy to help protect my heart and bones and to help prevent osteoporosis and I remained on the therapy for the next 15 years.

I lead a fairly active life. I enjoy playing tennis, volunteer work and involvement in activities of our sons and daughter. I had a full-time job as a reading specialist at the local school district. In my late 50s I started noticing my hands had developed a tremor and my writing wasn't as neat as it was before. At the 2010 NFXF International Conference in Detroit, I talked to Dr. Hagerman again and she suggested that I might have FXTAS.

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We moved to St. Louis in 2011 and I began to see Dr. Deborah Hall in Chicago. The only symptoms of FXTAS that I was exhibiting was a hand tremor and I currently have no balance issues that are common to FXTAS. Along with medication prescribed by Dr. Hall, I wear weighted wristbands (Tone-y-Bands) that seem to help with my tremors. I have participated in many research projects for FXTAS at Rush University and it is my hope that by participating in research I will be helping others.

I am not limited in what I do in life, and I try to live life to the fullest. I exercise three or four times a week at the gym, play the piano, enjoy reading, am a board member of the Fragile X Resource Center of Missouri, tutor ESL adults, and tutor children in reading. Helping others gives me a sense of purpose in life.

Recently my husband and I became empty nesters! We never thought we would get to this point but now we are here and enjoying the fruits of our labor after 46 years. Our sons have flown from the nest and are succeeding independently, are living in their own apartment and are very happy. Our journey has taken us to places we couldn't have imagined; we've been blessed with three amazing children, and we look forward to our next chapter in life.

As I look back on the road we traveled, I think of all the progress that has been made in the world of fragile X thanks to research. So much more is known today and organizations like the National Fragile X Foundation, along with the new International Premutation Registry, are important to continuing the quest for effective treatments and a cure, as well as a better quality of life for those impacted by fragile X. There is hope for the future.



Sue and her sisters to take in FXTAS research study (Diane, Ann, Nancy, Sue)



Fishman Family Portrait: Melissa, Sue, Jason, Jack and David



David and Jason in their new apartment (October 2022)





To learn more about the International Fragile X Premutation Registry, visit [www.fragilex.org/ifxpr](http://www.fragilex.org/ifxpr)

The International Fragile X Premutation Registry was created to facilitate and encourage Fragile X premutation research, including future medication and non-medication treatment and intervention studies that could positively impact you and your loved ones quality of life. Fragile X premutation-associated conditions include Fragile X-associated tremor/ataxia syndrome (FXTAS) and Fragile X-associated primary ovarian insufficiency (FXPOI).

The IFXPR has taken great care to design and implement a HIPAA- and GDPR-compliant registry to aid researchers in the Fragile X premutation field. The Registry is a tool, not a research project, and therefore all data entered into the Registry is not publicly available. Below are a few helpful reminders:

- No data is given to researchers or pharmaceutical companies. Data entered by registrants is only used to understand opportunities that are relevant to the registrant (e.g., sending FXPOI opportunities to only those females with FXPOI in the registry).
- Registrants are not directly contacted by researchers. Families are only sent IRB-approved materials after review and approval from the Governance Committee about the potential project. It is the registrant's choice whether or not to contact the researcher.
- Registrants can request their data be removed from the Registry at any time. Please contact the Registry team at [HS-IFXPR@UCDavis.edu](mailto:HS-IFXPR@UCDavis.edu) for details.
- You can find more information about the design, implementation, and safety of the Registry on the IFXPR webpage and in the consent form of the Registry





**The Registry was created in partnership with an international advisory committee of dedicated Fragile X professionals from some of the world's most respected institutions. Special thanks to our Advisory Committee members:**

David Hessel PhD, UC Davis

Sundus Alusi MD, The Walton Center, UK

Robert Miller, NFXF

Karen Lipworth, Fragile X Association of Australia

Hilary Rosselot, NFXF

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