

***Resources for the Williams  
syndrome medical home  
and  
Indications for CMA following FISH  
diagnosis of WS***

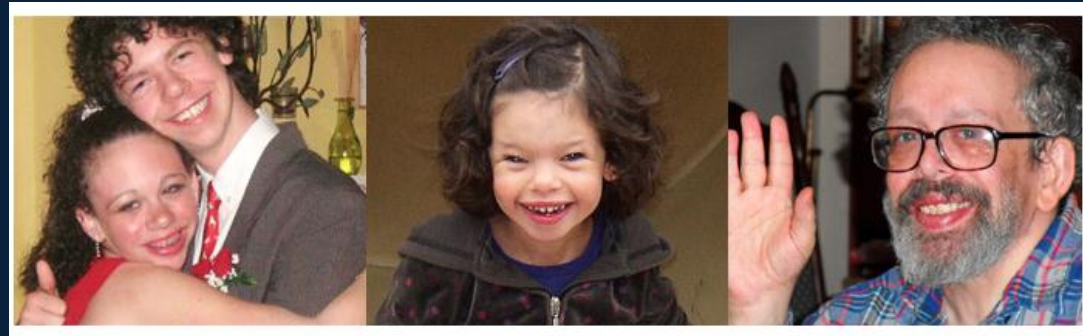
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Starting August 2015: Investigator, NIH Intramural Program NHLBI

No Financial Conflicts to Declare

# Williams Syndrome: Presenting Signs and Symptoms

- Facial Features Not Typical for Family
- Heart Murmur (abnormal echo showing narrowing)
- Failure to gain anticipated weight with irritability in infancy
- Developmental Delay
- Hypercalcaemia



Pictures from WSA website



# Clinical considerations once a diagnosis is made

- Genetics—genetic counseling and Williams specific evaluation
- Neurology—hypotonia, headaches, stroke risk
- Ophthalmology--strabismus
- Dentistry- small teeth, malalignment
- ENT/Audiology—hyperacusis, decreased hearing, increased otitis
- Endocrine—hypothyroidism, hypercalcemia, young adult onset of obesity and diabetes
- Cardiology—stenosis and/or narrowing of conducting vessels, sudden death
- GI—failure to gain weight, colic, constipation
- Orthopedics—scoliosis, flat feet
- Psychiatry—anxiety, depression, ADHD, autistic features
- Renal—calcification, hypertension, renal structural abnormalities
- OB-Gyn—GI/GU pain
- Urology—increased UTI with frequent urination symptoms (wetting, pain, etc)
- Development/Therapy
- Anesthesia risks

## WILLIAMS SYNDROME CENTER



Children's  
HOSPITAL • ST. LOUIS  
BJC HealthCare

Washington  
University in St. Louis  
Physicians

- At referral, patients can choose the number and type of services they need (or we will recommend)
- Continuous care or second opinion
- Goal of limiting the number of physicians needed to optimally care for the child/adult with WS.
- All screening goes through genetics and the child is referred if screen positive
- Follow up depending on acuity and services needed.

WILLIAMS SYNDROME  
CENTER



Children's  
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BJC HealthCare

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Physicians

Patients Seen

Infants to Adult with WS or atypical WS  
6 patients/ clinic once per month

Physicians

Genetics  
Cardiology  
Nephrology  
ENT  
Ophthalmology  
Endocrinology  
Orthopedics  
Urology  
Dentistry

Additional Services

Psychology  
Genetic Counseling  
Dieticians  
Therapy support

# Clinic Growth and New Needs

- Opened in April 2013
- 50 visits in year 1 and 74 visits year 2
- First “no-show” appointment April 2015 (show rate of 99%).

## Spring 2014 SLCH Survey Results:

- How to navigate school services
- Adult transitions (placement, guardianship)
- Feeding and nutrition
- Psychological services

# How you give the diagnosis matters to families

- Families will remember “forever” what you said at the time their child was diagnosed.
- Don’t give families outdated information or show pictures from textbooks.
- Parents want a balanced presentation that contains elements of hope.
- Parents want more than a potential problem list; they want a plan.

Parent response in a survey conducted through the Williams Syndrome Association registry, J. Waxler et al.

# Needs for the medical home

## Set of 7 brochures

- Based on needs identified through our surveys
- Identify experts in each of the fields
  - Physicians
  - Genetic counselor
  - Social worker
  - Dietician
  - Therapists
- Include the voice of the family

## Improve Screening for Neuropsychological symptoms

- Screening to identify needs prior to clinic
- More in depth testing to help with appropriate referrals



http://www.stlouischildrens.org/our-services/williams-syndrome-center/resources

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## Williams Syndrome Center

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### Resources

- Learning About Williams Syndrome
- Williams Syndrome A Parent Perspective
- Hypercalcemia/Hypercalciuria in Williams Syndrome
- Feeding Your Child With Williams Syndrome
- Guardianship, Conservatorship and Alternatives
- School and Developmental Services for Your Child
- Transition for Young Adults with Intellectual Disability

#### Williams Syndrome Center

- Conditions We Treat
- Meet the Team
- Meet Our Patients
- Diagnosing Williams Syndrome
- Treatment
- Research
- ▶ Resources

#### Patient Story



A Family Faces Williams Syndrome

#### Related Content

- ▶ Williams Syndrome: Getting to the Heart of a Rare Genetic Disorder

## LEARNING ABOUT WILLIAMS SYNDROME



### Common features

- Facial characteristics
- Heart and Blood vessels
- Hormones
- Kidneys
- Eyes
- Ears
- Connective Tissue
- Learning
- Personality

### Genetic cause

- FISH
- CMA

### Recurrence

Age specific typical features

After the diagnosis: what should we do

# WS: Parent Perspective

## YOU ARE THEIR TEACHER

- Your child is full of potential. Learning will take longer, but many of their goals will be reached, one benchmark at a time. There will be times in their journey where learning will be difficult, transitions stressful and frustration will mount, but with support from educators, medical professionals and therapists, you will learn ways to help your child achieve a level of independence that will make their lives meaningful and well adjusted.
- Don't give up on your hopes and dreams for your child. Victories are greater and the milestones sweeter. As their first teacher, you have a large hand in their success.
- As soon as possible, seek out programs that will help your child. I started with Parents as Teachers and then moved to the Early Childhood Intervention program in my county. Since then, we have participated in music therapy through her school, horse therapy and recreational programs for children with special needs.
- These programs are not only for your child, but you, too. Professionals can help you become a better teacher.
- Find the value of music. Children with WS may be highly receptive to music. Music may help your child absorb more information, reduce anxiety and increase on-task behaviors.

## YOU ARE THEIR ADVOCATE

- Along your journey, you will encounter people who do not understand. Whether it's a lack of education about WS or fear of the unknown, some people will not recognize the potential in your child.
- Ask those people, whether they are friends, family or health-care providers, to learn about WS. Share resources with them such as the Williams Syndrome Association website ([williams-syndrome.org](http://williams-syndrome.org)). If they won't learn, find others who will. It is important that you surround yourself with people who help you meet your family's needs. The result is that your child will be surrounded by caring, encouraging people.
- Find people who focus on what your child can do instead of what they cannot. Look for practitioners who are mindful of research and open to learning new things.



- Don't be afraid to ask for what you feel your child needs: ask for more time, more therapists, more support. You will find that the more educated you become about WS and what works for your child, the better advocate you can be. You never know what opportunities will arise unless you ask for them.

## YOU ARE THEIR ROCK AND CHEERLEADER

- Individuals with WS are very emotional and empathetic. This characteristic can be very endearing and at times challenging.
- Embrace the emotions of your child and learn ways to soothe them. Celebrate with them and use their desire to please as rewards for their achievements.
- In your child's times of fear and anxiety, you can use emotion to help them find comfort.
- There are many strategies that educators and doctors can share with you about helping your child overcome their fears.

## YOU ARE AN HONORARY MEMBER OF AN AMAZING COMMUNITY

- The world of WS can be lonely at times, but it doesn't have to be. Although the syndrome is relatively rare, there are amazing support groups to help you. Seek them out.

- Start with the Williams Syndrome Association. They offer support groups on social media, local events and national opportunities to meet others.
- Go to conventions and area events. By getting involved, you will find the journey more manageable and you will meet amazing people who will understand you every step of the way.

## YOU ARE HUMAN

- Accept that you'll go through stages of grief. Let yourself be mad, sad and in denial. It all leads to acceptance and eventually advocacy.
- Learn to be understanding of others in your family, as each person copes with the diagnosis differently.
- You'll find some family members and friends lose tact and don't know what to say. Forgive them. You'll find that over time, many of those same people will fall in love with your child and become important parts of their life.
- Care for yourself. Your life will change and you may feel at times like you are immersed in the world of WS, but you, your marriage, and your other relationships still matter.
- Seek out family and friends to watch your child so you can go on a date, see your friends or spend time alone. If you don't have support within your family and friends, ask your doctors and therapists about respite support. There are programs designed to give families who have children with special needs time to recharge. It's important for your mental health.

## YOU ARE ABOUT TO CHANGE FOR THE BETTER

Finally and most importantly, approach this journey with humor and a positive outlook. You will sleep again, you will feel at peace, you will find normalcy. It takes time and those first years are the hardest, but it will come. Live your life in the moment and don't focus on the fear of the future. You will come to discover the blessing you have been given. You will find that along this journey you will grow great friendships and learn amazing things. You will come to know love, pride and laughter like you have never experienced before. As a parent who has walked in your shoes, I welcome you to the amazing world of Williams syndrome.

DEVELOPMENT/SKILL	FOOD TYPES	EXAMPLES
Gaining head/neck control	Breast/Bottle	Breast milk, standard infant formulas
Can sit in a supported recline	Breast/Bottle	
*Sitting unsupported in a high chair	Purees	Stage 1 baby foods, infant cereals
Munching with front teeth	Thicker puree/soft mashed Consider introducing some sort of cup; sippy, straw, open (free flow/no spill proof valve)	Stage 2 baby foods; mashed potatoes, sweet potatoes
Lateralizing food to molars (Moving food to the sides)	Meltable hard solid	Strips of toast, Veggie Stix™/Veggie Straws™
	Soft cubes	Canned or ripe, raw diced peaches/pears/mandarin oranges
	Single texture soft food	Cubed deli meats, pancakes, soft cooked pastas
	Mixed texture soft food	Baked beans, soft chicken nuggets, noodles and sauce, chunky applesauce
	Soft table foods to appropriate size	Avocados, bananas, black beans
	Rotary Chew Jaw moves in a circular motion to grind food. <sup>1</sup>	Hard foods (dry crunchies)

## FEEDING YOUR CHILD WITH WILLIAMS SYNDROME

Society, the media, and even well-intentioned friends and family send messages to new parents about how to feed their children. Parents can usually take this information and figure out what to do to ensure their kids are getting good nutrition. But what if, as can be in the case of children with Williams syndrome (WS), your child requires a different approach to feeding and nutrition? Generally the message given is that you change or adapt foods according to a child's age. A better way to think of it may be progressing with the child's development and skill.

On the next page is a general guide to food types you may feed your child and the developmental skills your child should have when they may be introduced. For example, spoon-feeding should begin when your baby is strong enough to sit up in a high chair (supports may be used to keep them from leaning to one side). You will start with pureed foods and gradually add texture and complexity over time. As you start to notice your baby using chewing motions, chunkier and crunchier foods may be added. The time to get from one stage to the next is different for each child. It is common for a child to stay with one food type for a while before moving on to the next one, but by watching your baby during feeding time, you will know when he or she is ready to move on.



## HYPERCALCEMIA/HYPERCALCIURIA IN WILLIAMS SYNDROME



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Physicians

## RECOMMENDATIONS FOR ADEQUATE DIETARY CALCIUM INTAKE IN THE U. S.

AGE	CALCIUM INTAKE, mg/day
0 - 6 months	210
7 - 12 months	270
1 - 3 years	500
4 - 8 years	800
9 - 18 years	1300
19 - 50 years	1000
50+ years	1200

Source: US NAL

## HIGH AND LOW CALCIUM FOODS

HIGH CALCIUM FOODS	LOWER CALCIUM ALTERNATIVES
Milk, yogurt, ice cream, cheese	<b>For infants:</b> Calcilo XD specialty infant formula <b>For children and adults:</b> Rice Dream Classic Original or Rice Dream Classic Carob
Canned salmon (with bones), sardines, anchovies	Fresh (cooked) fish without bones, canned tuna fish
Tofu, white beans, chick peas, soy beans	Lima beans, black beans, green peas
Collard Greens, dandelion greens	Iceberg and romaine lettuces
Molasses	Maple syrup, dark corn syrup or honey (honey should not be given to children <1 yr old)
Calcium fortified foods such as orange juice, instant oatmeal, breakfast cereals, english muffins and other bread products with a longer shelf life	Unfortified juices and packaged goods, Examples: Tropicana Pure Premium Original orange juice, Mom's Best Cereals (Oats and Honey Blend), Bob's Red Mill Oats, fresh bread products baked from scratch

## SCHOOL AND DEVELOPMENTAL SERVICES FOR YOUR CHILD



### SPECIAL NEEDS IN THE SCHOOL SYSTEM: THE IEP

Children with developmental disabilities 3 years of age and older are generally treated within the school system. Services offered vary from school district to school district, but each school should strive to support the child to maximize their development. Most schools evaluate and set goals for a student through the development of an Individualized Education Program (IEP). The IEP is the legal document



that defines a child's special education program. It is created following a formal evaluation of the child by therapists specializing in the treatment of children with special needs. An IEP includes the disability under which the child qualifies for Special Education Services (also known as a child's classification), the services the team has determined the school will provide, the child's yearly goals and objectives, and any accommodations that must be made to assist the child's learning. A school professional may ask that a child be evaluated to see if he or she has a disability requiring intervention. Parents may also contact the child's teacher or other school professional to ask that their child be evaluated.

This request may be verbal or in writing. Parental consent is needed before the child may be evaluated. Evaluation needs to be completed within a reasonable time after the parent gives consent. Once in place, the IEP should be revisited regularly (at least yearly) to determine if goals have been met and to set new goals for the next evaluation period. Parents should play an active role in this process by discussing their wishes and concerns for their child with the evaluation and treatment teams.

### A PARENT'S PERSPECTIVE ON IEP'S

Individualized education plans can be a stressful experience for many parents, but it doesn't have to be if you approach it with proper planning, communication and a positive outlook. Here is a glimpse of the prep work and resources I've used to make the meetings run smoothly and effectively:

## TRANSITION FOR YOUNG ADULTS WITH INTELLECTUAL DISABILITY



### TRANSITION FOR YOUNG ADULTS WITH INTELLECTUAL DISABILITY

Transition is a process where young adults with challenges prepare for the future beyond the K-12 school system. Choices on the road to increased independence may include further education, specialized training or employment.

Basic transition concepts:

- Think about goals for your child's life after high school and develop a plan to get there. Consider their talents, interests and abilities and set goals to obtain the greatest degree of independence possible.
- Work with your child's high school to ensure that they gain the skills and competencies needed to achieve their desired post-school goals.
- Begin to identify and link to any needed post-school services, supports or programs before they exit the school system.
- Remember: Successful transition is complex. It takes the cooperation and involvement of parents, students, teaching professionals and community organizations to smoothly shift from school to adult life.

## GUARDIANSHIP, CONSERVATORSHIP AND ALTERNATIVES

### GUARDIANSHIP, CONSERVATORSHIP AND ALTERNATIVE PROTECTIVE ASSIGNMENTS: WHAT ARE THE OPTIONS?

Parents should try to identify the least restrictive option that is appropriate for their child. Options include (from most restrictive to least restrictive):


- **Guardianship:** the legal process of determining a person's capacity to make their own decisions regarding personal affairs (such as where he or she lives or the care he or she requires.) Guardianship is the most restrictive and limiting choice and should only be used as a last resort. "Limited" and "Total" guardianship options are available. Court orders for limited guardianship should restrict only those liberties necessary to protect the well-being of the individual while encouraging the development of maximum self-reliance and independence.
- **Conservatorship:** similar to guardianship, but differs in that it deals only with the financial affairs of an individual. A conservator has no authority to make decisions regarding the individual's personal affairs. Only a guardian has such power. "Limited" and "Total" conservatorship options are also available.
- **Advance Directives:** Legal statements that address specific areas where a child needs support. Some advance directives include: durable power of attorney for health care, durable power of attorney for property and power of attorney for case/care management. Advance directives can also be used to assist the individual in decision-making in education, health care surrogacy, representative or substitute payee, trusts, or joint checking accounts.





# Use of brochures

- In clinic
- Online—viewed nearly an average of 197x/month
- Linked to other WS websites
- Use by other non-WS clinics serving children and adults with IDD



**williamssyndrome**  
ASSOCIATION

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## WSA BLOG: HEALTH AND WELLNESS

*Posted by NanciRogers, Feb 26, 2015*

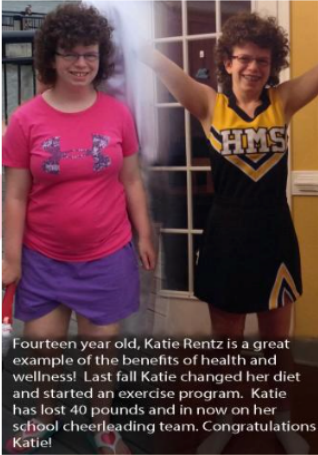
Nanci Rogers, MSN, CRNA

The WSA has always strived to provide current, relative, and quality information for individuals with Williams syndrome and their families. Medical research, education, technologies, housing, and social issues continue to be at the forefront of our concerns.

The time has come to add Health and Wellness (excellent nutrition!) to our list. Several of you may recall our initial "small" steps along this path with my "Nuts about Nutrition" column in the newsletter. Beginning this year we will be expanding the concept substantially with information on:

- the relationship between nutrition and disease;
- empowering individuals of all ages to implement "one simple change" in eating habits and lifestyle on the way to great health habits;
- linking WSA members to nutritional and fitness videos and webinars in a library on the WSA's website;
- providing a health and wellness component (recipes, fitness, research, group events, etc.) to the WSA Website and Facebook page, as well as conferences and the convention. Social media enables us to communicate a wealth of information however, it can be overwhelming. A panel that includes a dietician, medical, fitness, and holistic health representatives will help screen and review all educational material.

I am excited to be involved with the WSA and share my passion for inspiring Healthy Living. The information in this first blog is aimed at children (age 4+) and adults. An excellent general resource for feeding infants and toddlers with WS is available from the [Williams Syndrome Center at St. Louis Children's Hospital](#) (PDF).



Fourteen year old, Katie Rentz is a great example of the benefits of health and wellness! Last fall Katie changed her diet and started an exercise program. Katie has lost 40 pounds and is now on her school cheerleading team. Congratulations Katie!

# Feedback

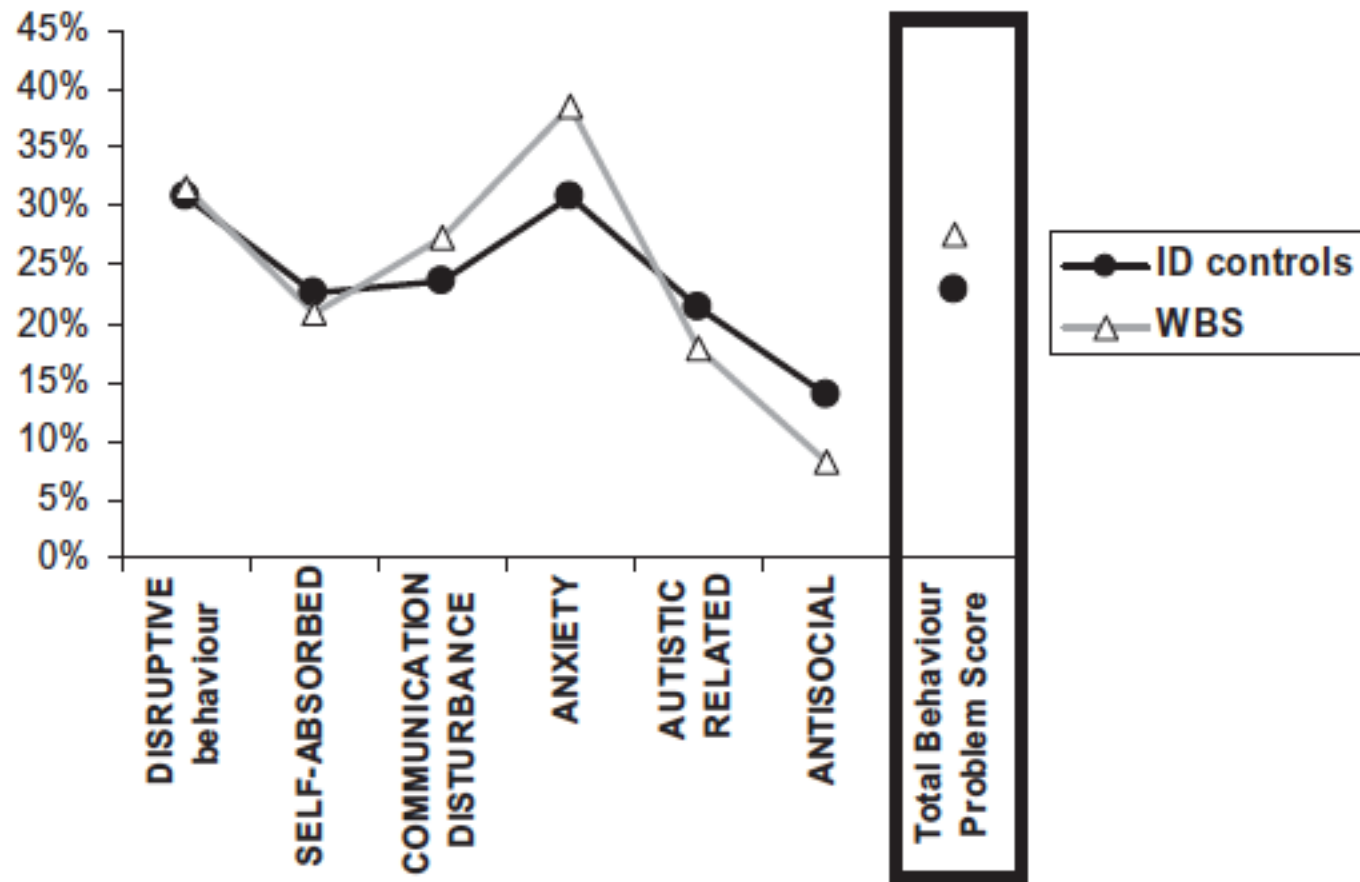
- This is a great brochure—can I link to it on my blog?
- I love Love "A Parent's Perspective" Wonderful info...very honest and exactly what we are all feeling.
- I was expecting pretty basic generalized info and instead saw how extensive the info was! I feel these will be wonderful resources for any newly diagnosed parents as well as valuable to parents who are experiencing new stages in their child's life.
- The flyers will be wonderful for awareness events and also might be good for families to share with their child's therapists/teachers/caregivers so that everyone involved in the child's care is truly educated on Williams Syndrome.
- page 5 there is a sp error "hopping" instead of happening.
- I wanted to follow up on the brochures that you had given me on "Learning About WS" and "A Parent Guide". I can't remember the exact names of the brochures, but these are close :- ) I thought both brochures were very good.
- This brochure comes out of a "wellness model" and not a "disease model." It focuses on on the strength and beauty of the WS individual and on the therapy that will help the WS children to develop to their fullest capacity.
- I had my meeting with SSD. Her OT has been removed and a new OT is being assigned this month to begin in January. You were *totally* right to encourage me to bring an advocate to that meeting.

# Gifts and Challenges

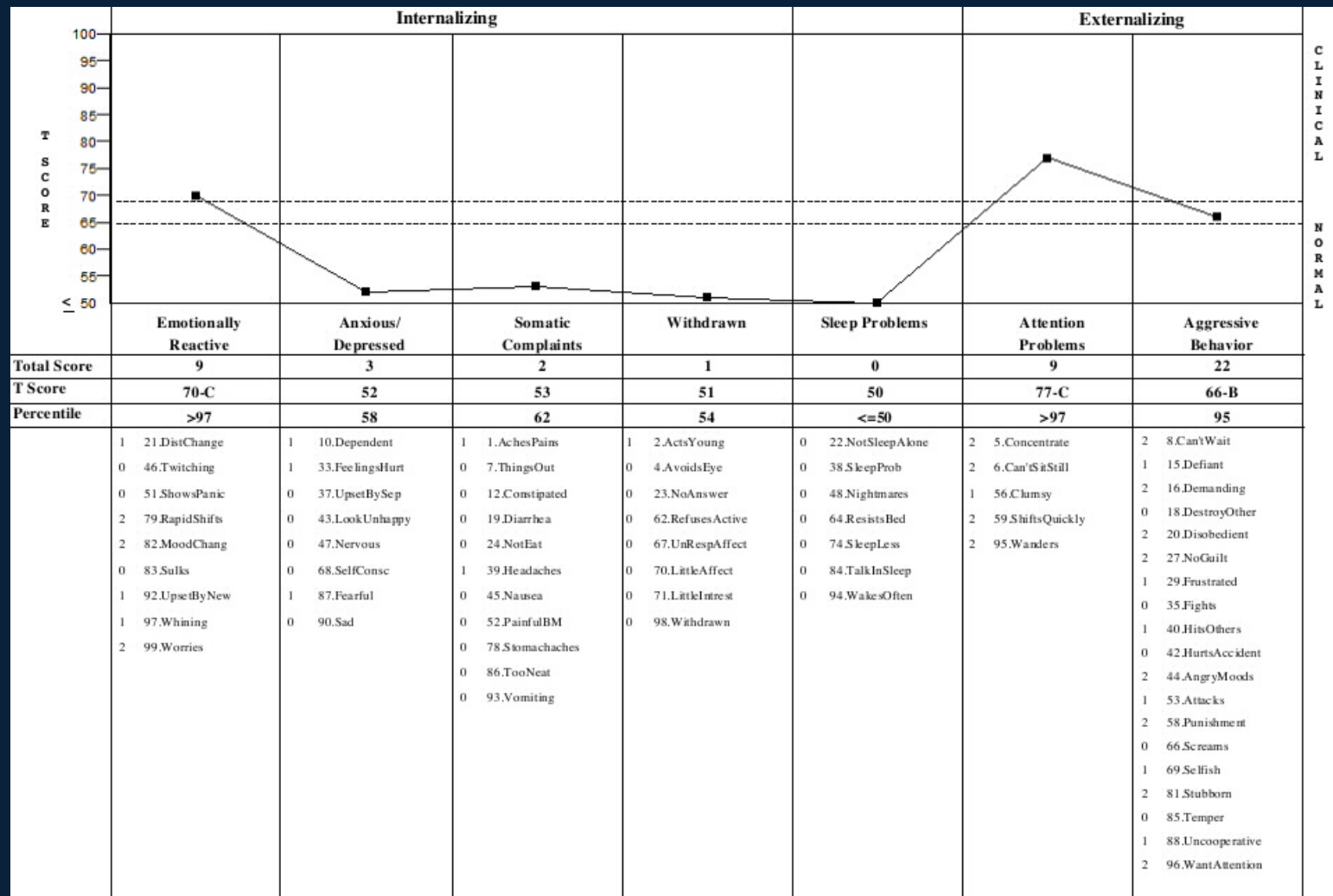
- Average IQ 55-65 (range 40s to 100s)
- Relative weakness in tasks relying on visuo-spatial skills
- Relative strengths in verbal domains
- Increased rate of ADHD (20-65%)
- Maladaptive behaviors including poor social peer interactions, owing partially to a lack of contextual social savvy.
- Hypersociability.
- High empathy.
- Lack of social fear.



# Other Behavioral Concerns

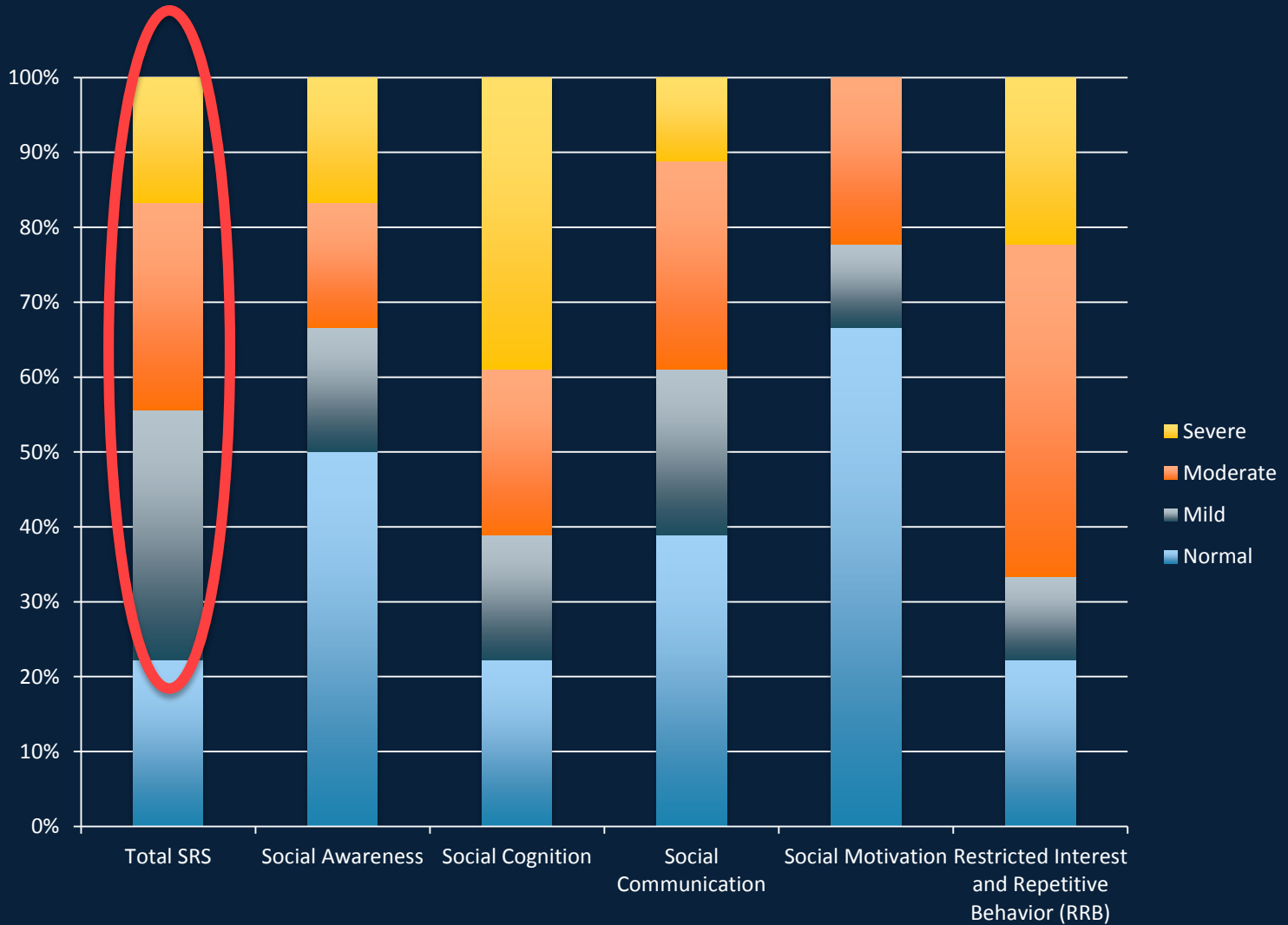


# Our data from screeners



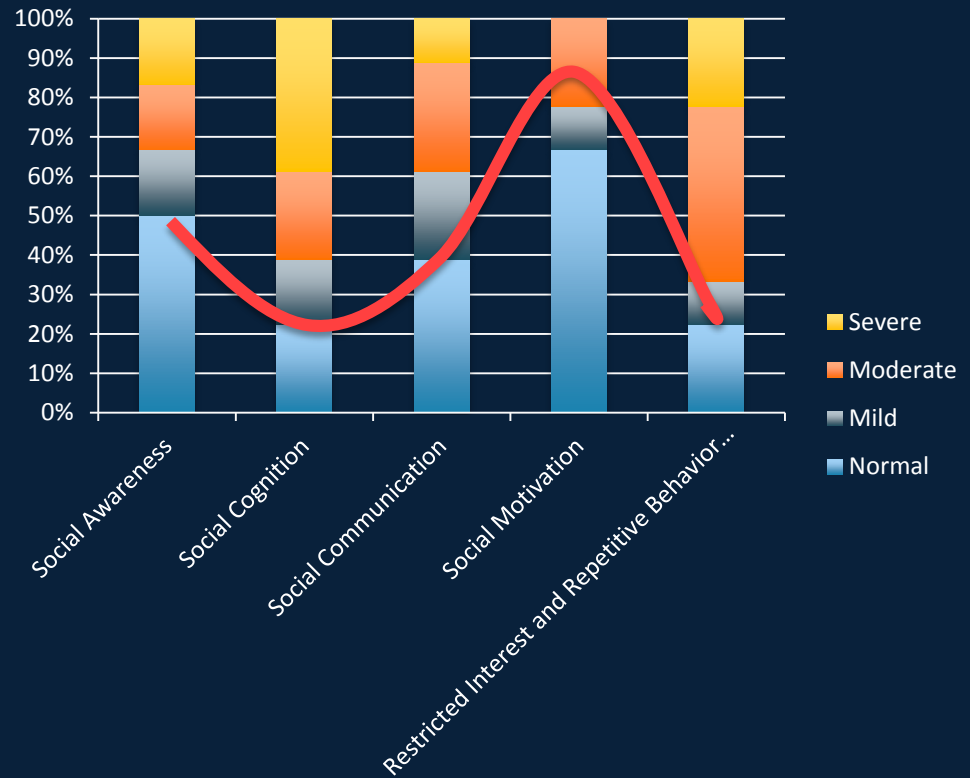
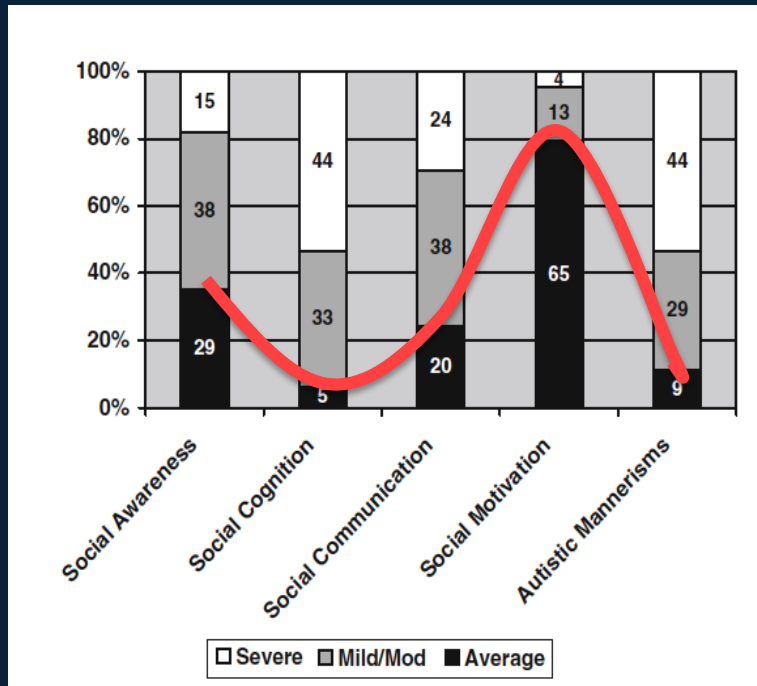
# SLCH WS Experience:

Majority of patients with autistic features

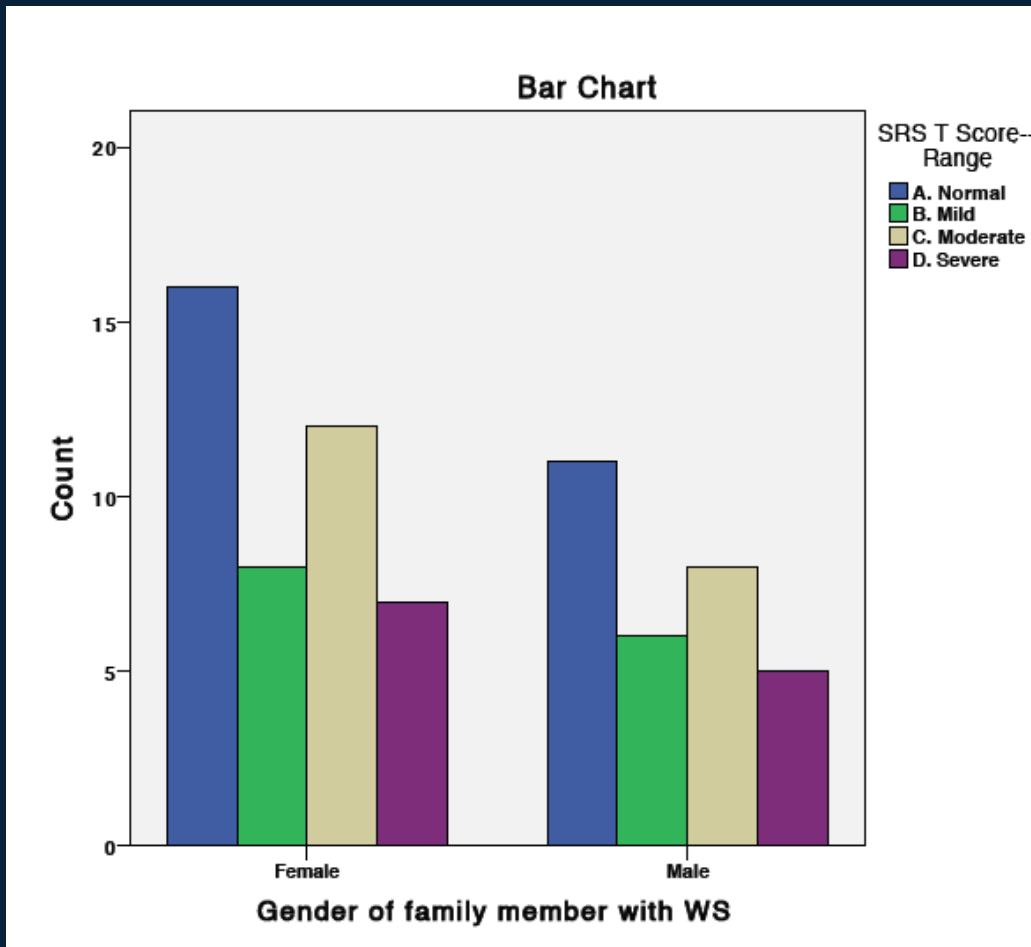


# SLCH WS Experience:

## Similar symptom spectrum but autistic features somewhat less prevalent



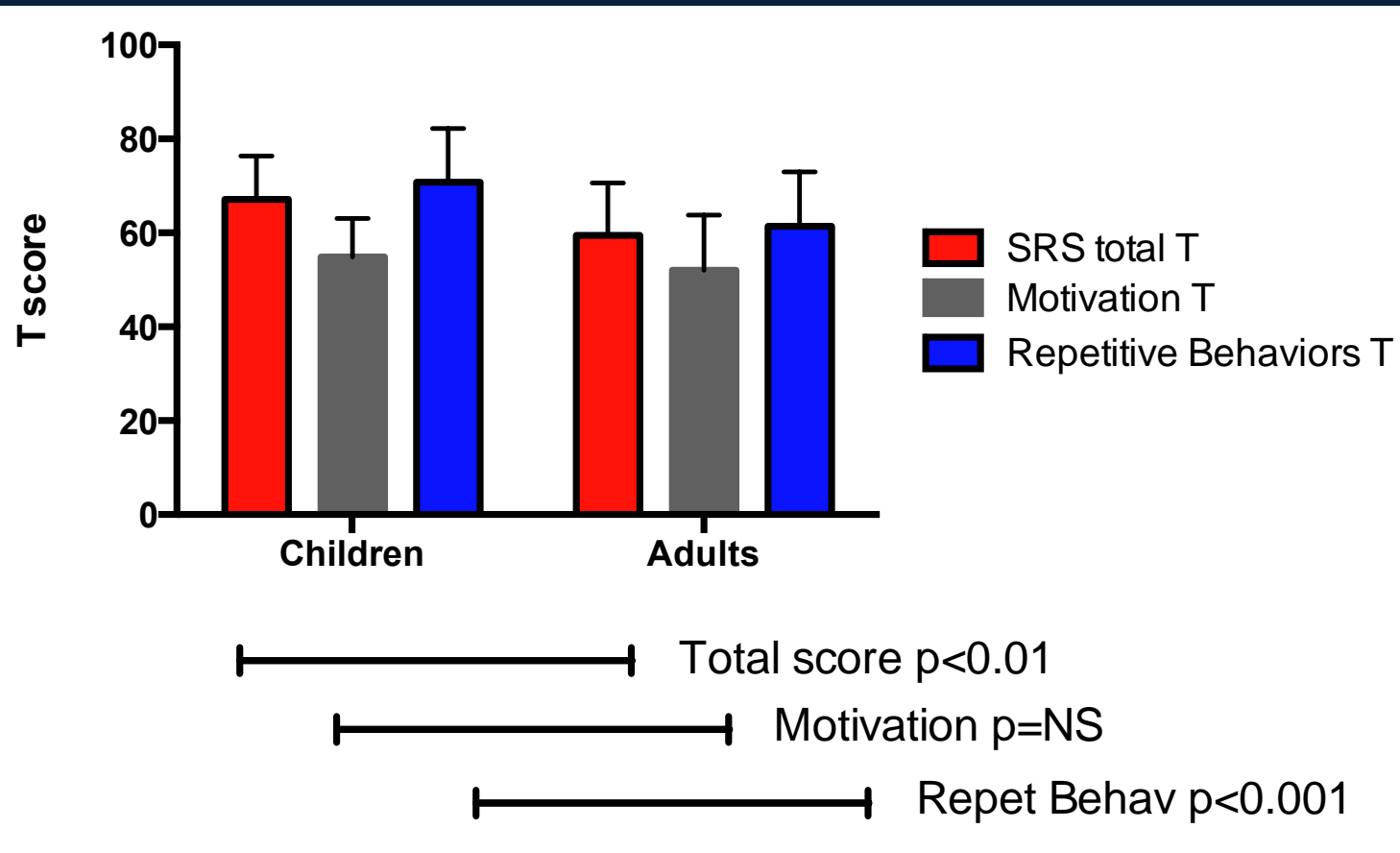
# No SRS subscore differences by gender



		Sig. (2-tailed)
<b>SRS T score</b>	Equal variances assumed	.908
	Equal variances not assumed	.909
<b>AWR T score</b>	Equal variances assumed	.964
	Equal variances not assumed	.965
<b>COG T score</b>	Equal variances assumed	.531
	Equal variances not assumed	.531
<b>COM T score</b>	Equal variances assumed	.597
	Equal variances not assumed	.601
<b>MOT T score</b>	Equal variances assumed	.865
	Equal variances not assumed	.866
<b>RRB T score</b>	Equal variances assumed	.955
	Equal variances not assumed	.955



# All ASD subscales other than Social motivation improve with age



# Impact and Areas of Potential Growth

Increased diagnosis of autism spectrum/educational autism

Increased referral for ABA

More focused discussions for behavioral concerns with time spent on options for intervention/behavioral modification at the time of the clinic visit

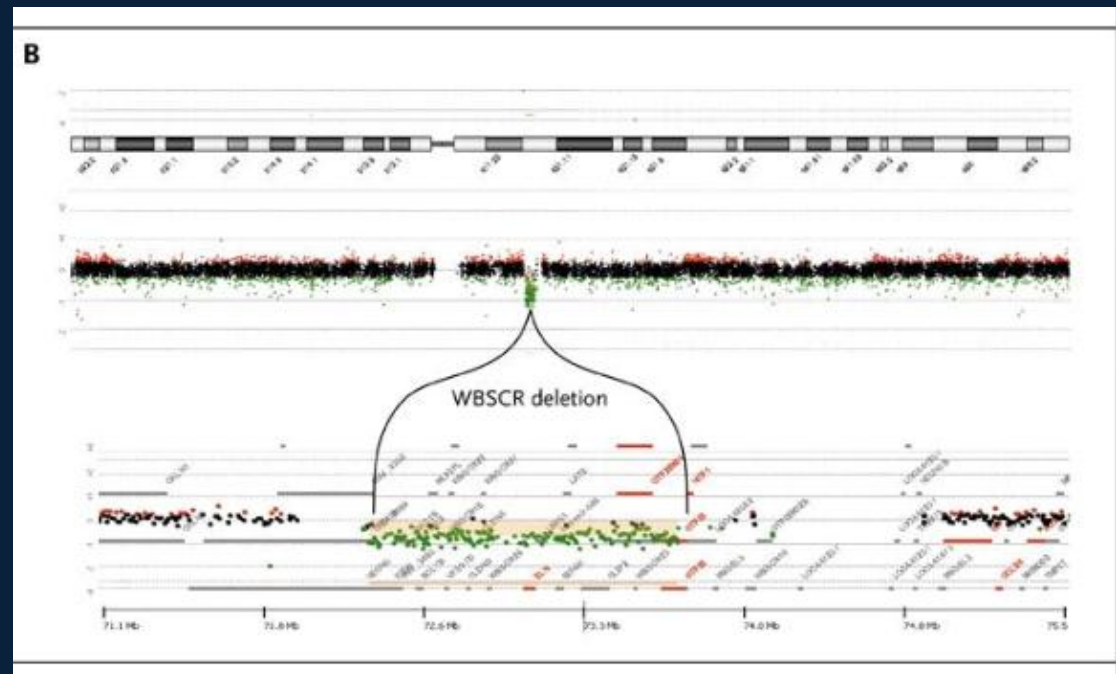
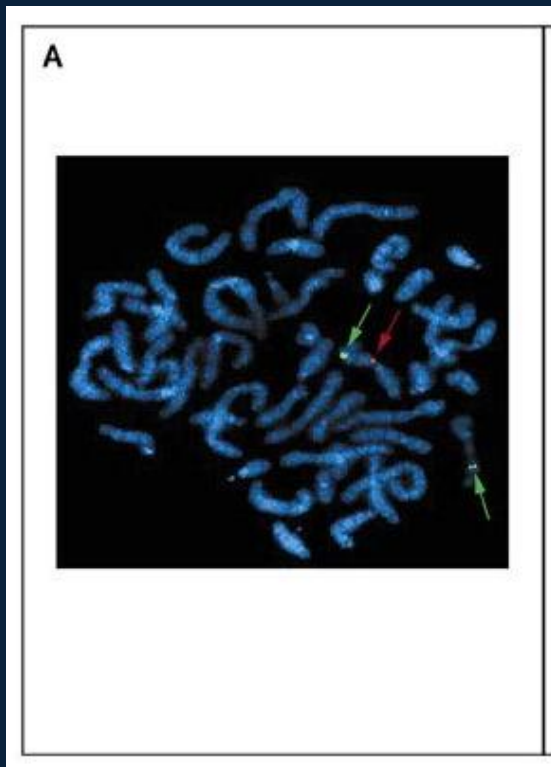
More recommendations for continued psychological services

No real increase so far in use of psychological services

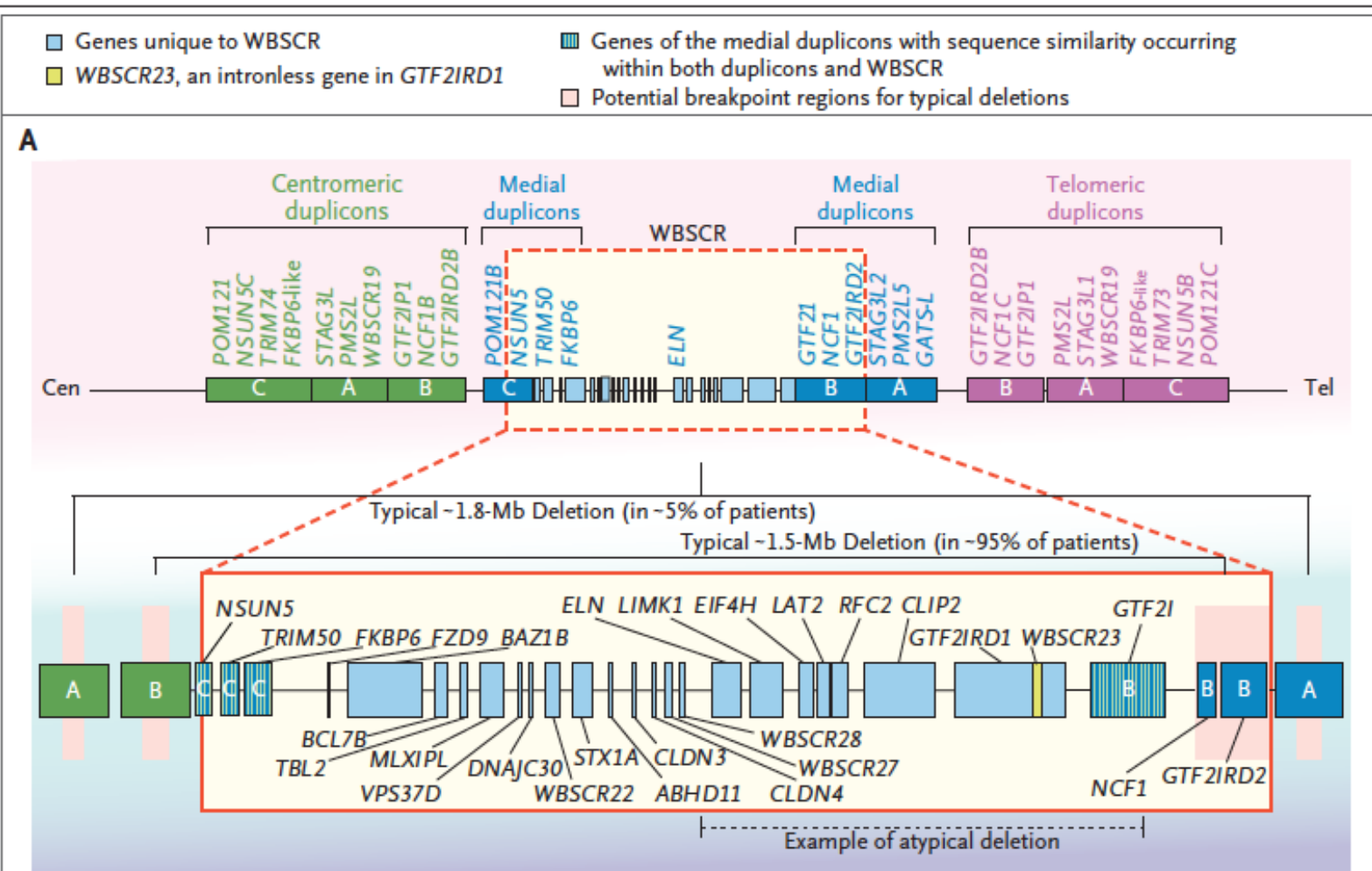
- poor insurance coverage,
- poor availability in rural and urban areas,
- poor knowledge by some providers on how to care for patients with genetic psychological problems (overmedication)

# Diagnostic testing for Williams syndrome

FISH (Fluorescent In Situ Hybridization) vs Chromosomal Microarray



# Copy number changes are mediated by flanking areas of low copy number repeat



# Deleted genes in WS critical region

Hypercalcemia  
and intracardiac  
malformations

Cardiovascular and  
connective tissue  
disease

Modifier of  
cardiovascular  
phenotypes

Osteopenia

Impaired glucose  
tolerance

??Visuo-spatial  
skills

Cognitive impairment

FKBP6

FZD9

BAZ1B

BCL7B

TBL2

WBSCR14

STX1A

CLDN4

CLDN3

ELN

LIMK1

WBSCR1

WBSCR5

RFC2

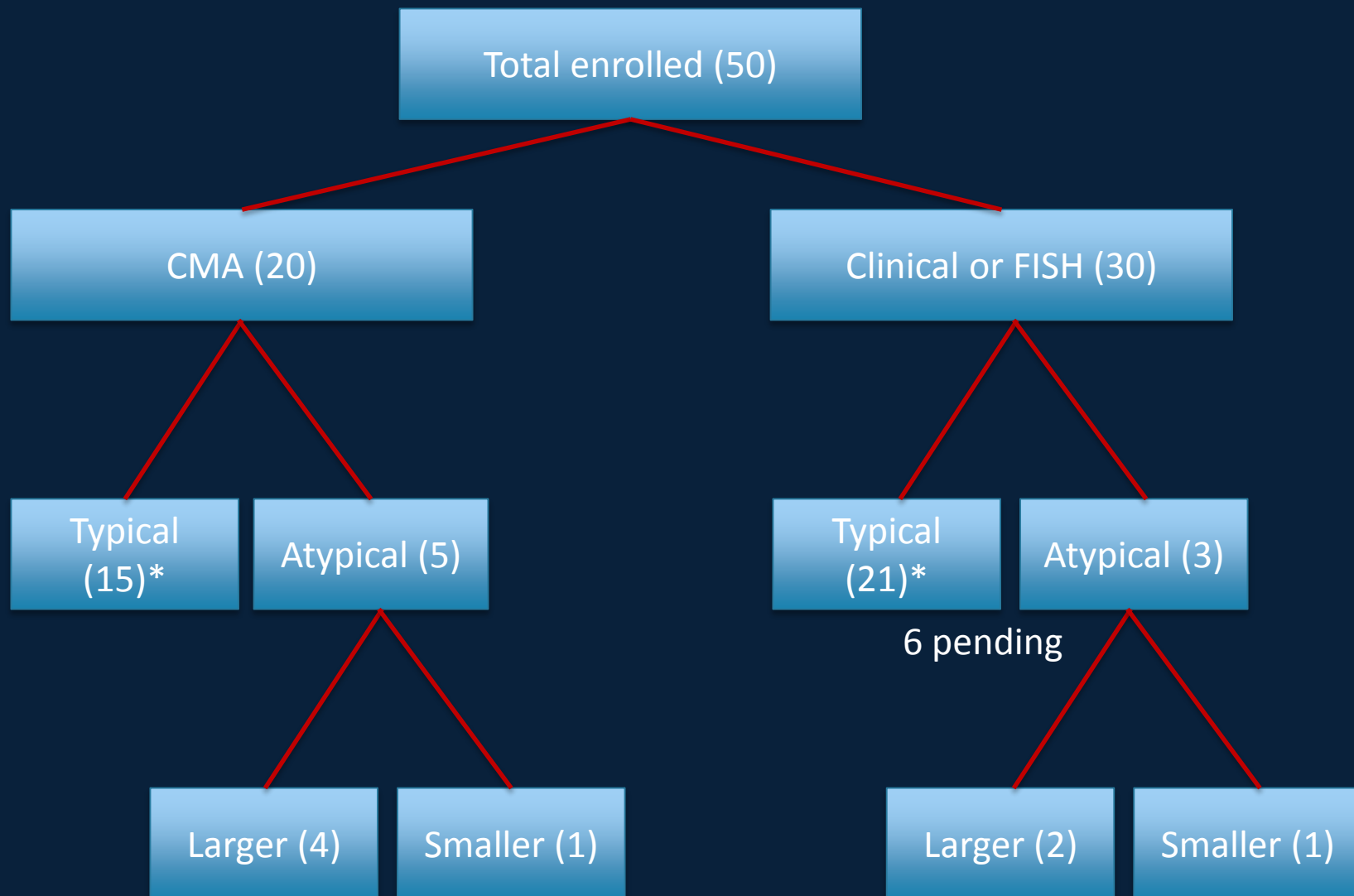
CLIP2

GTF2IRD1

GTF2I

NCF1





Del/dup/htz present but all VOUS

# Williams Critical region flanking genes



WS deletion size varied from 1.2 MB to 17 MB

Atypical deletion size present in 17% (may reflect referral bias)

Second deletions/duplications or areas of homozygosity present in significant minority (20%), most are VOUS

Experienced clinical suspicion gives high sensitivity for larger deletions, less for smaller deletions.

But outliers remain. 2<sup>nd</sup> disease? WS and MFS, WS and CDL

Research repeat of a clinical lab on one occasion led to a markedly different del size

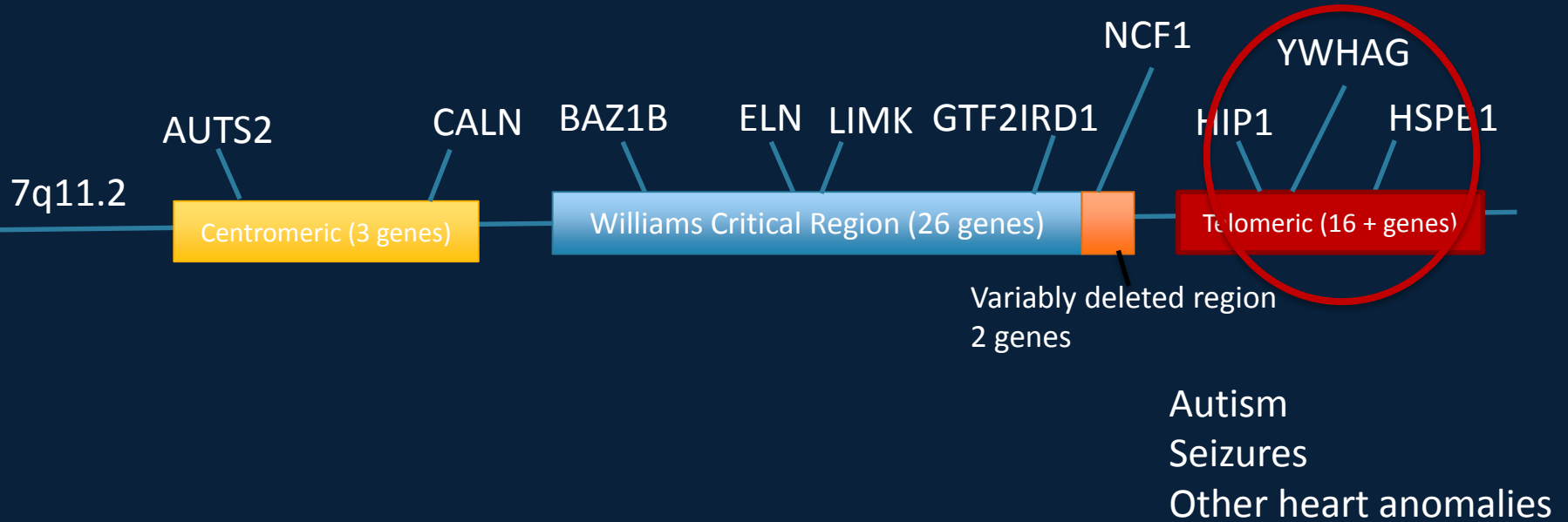
# Williams Critical region flanking genes



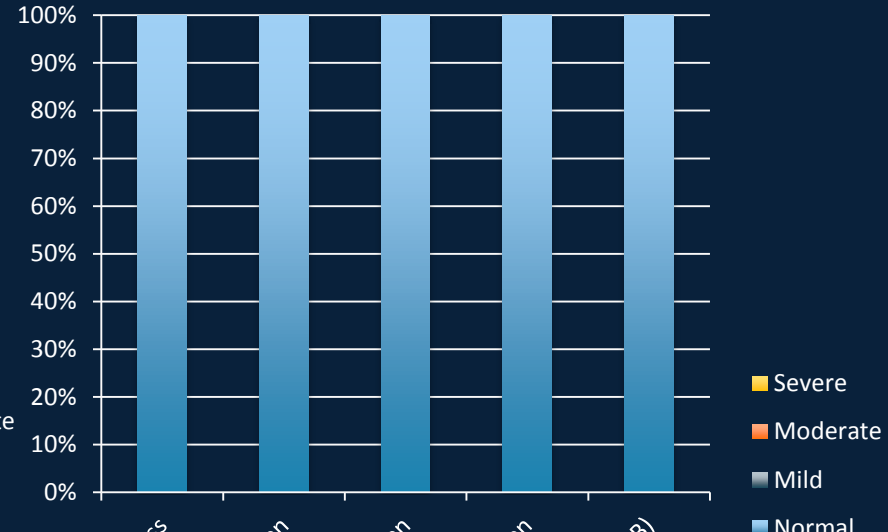
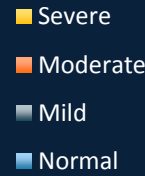
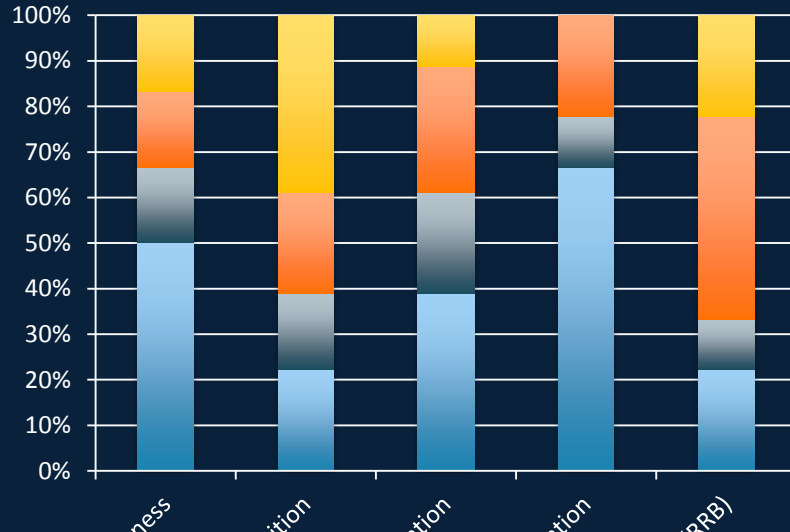
Smaller than typical head size  
Decreased speech, autism  
Spasticity



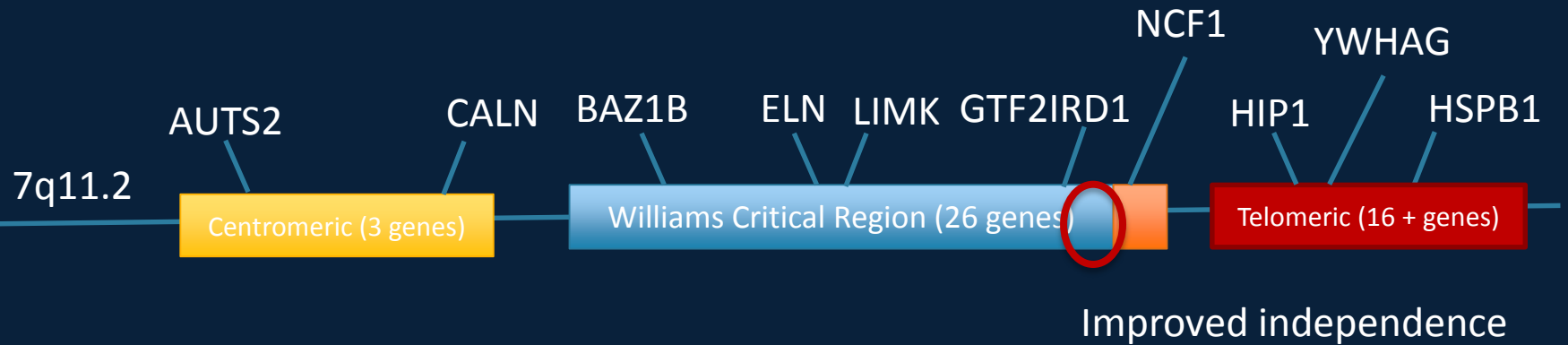
# Williams Critical region flanking genes



# Patients without GTF2i deletion report no autistic symptoms



# Williams Critical region flanking genes



# Considerations for repeat testing by CMA in those with FISH diagnosis: replicate cohort

- OFC off the WS growth chart (small)
- Frank autism (especially social motivation)
- No or very limited speech by age 3-4
- Seizures
- Higher IQ
- Normal SRS
- Facial features not typical for WS



# Thanks to:



- Kozel Lab
  - Joshua Danback
  - Li Ye
  - Michael Lugo
  - Mike Ricafort, MD
  - Destinee Shipley
- Neuropsych Evaluation
  - John Constantino, MD
  - Natasha Marrus, MD, PhD
- WS Center, Clinic brochures
  - Shabana Shahanavaz, MD
  - Anne Beck, MD
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  - Cathy Hutter, PhD
  - Karla Jacquin, MSW
  - Mary Warburton, MA CCC-SLP
  - Liz Toolin, MS, RD
  - Sarah Moonier, parent advocate



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