



# Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

- If sharing any data or information from these slides generated by the REINS International Collaboration, please acknowledge the authors, group chairs, and specific working group.
- If using any information presented with a citation, please reference the primary source.



Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

## Endpoints for Study of Scoliosis

A. Noelle Larson, MD  
Professor, Mayo Dept. of Orthopedics  
Director, Mayo Pediatric Orthopedic Research  
Pediatric Orthopedics and Scoliosis Surgery  
[Larson.noelle@mayo.edu](mailto:Larson.noelle@mayo.edu)

# Disclosures

- Research funding
  - Orthopedic
  - Industry: funding to peds ortho research at Mayo, Globus, Depuy, Medtronic, Orthopediatrics
- Committees
  - Research Committee Chair, Pediatric Orthopedic Society of N. America



## Scoliosis - Background:

- Lateral curvature of the spine
- Occurs in up to 1/3 of NF1 patients



# How to Evaluate Scoliosis

X-rays

Physical Exam

Patient Reported Outcomes  
(Survey/Questionnaire)

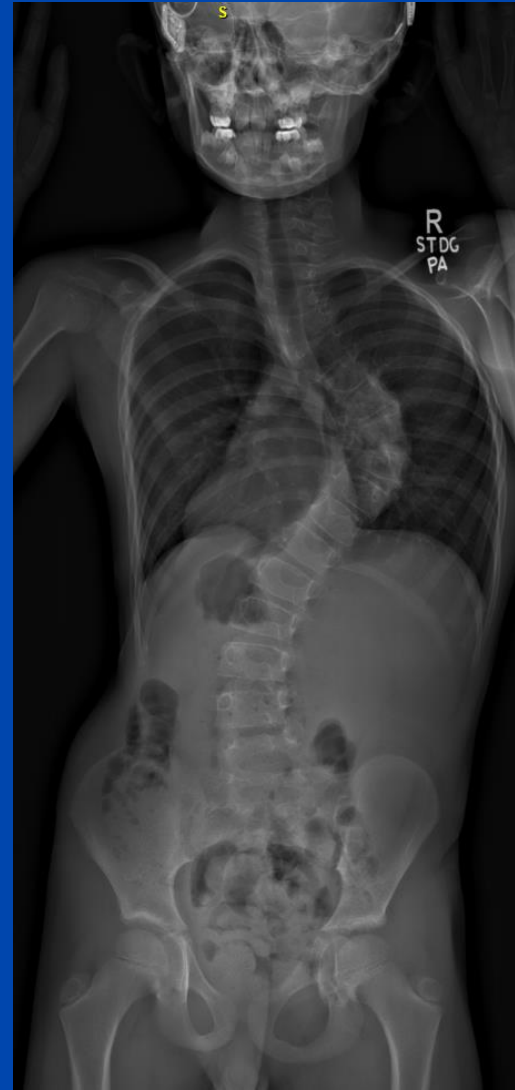


# How to Evaluate Scoliosis

X-rays

Physical Exam

Patient Reported Outcomes  
(Survey/Questionnaire)



# Severe Scoliosis Evaluations

Pulmonary Function Tests

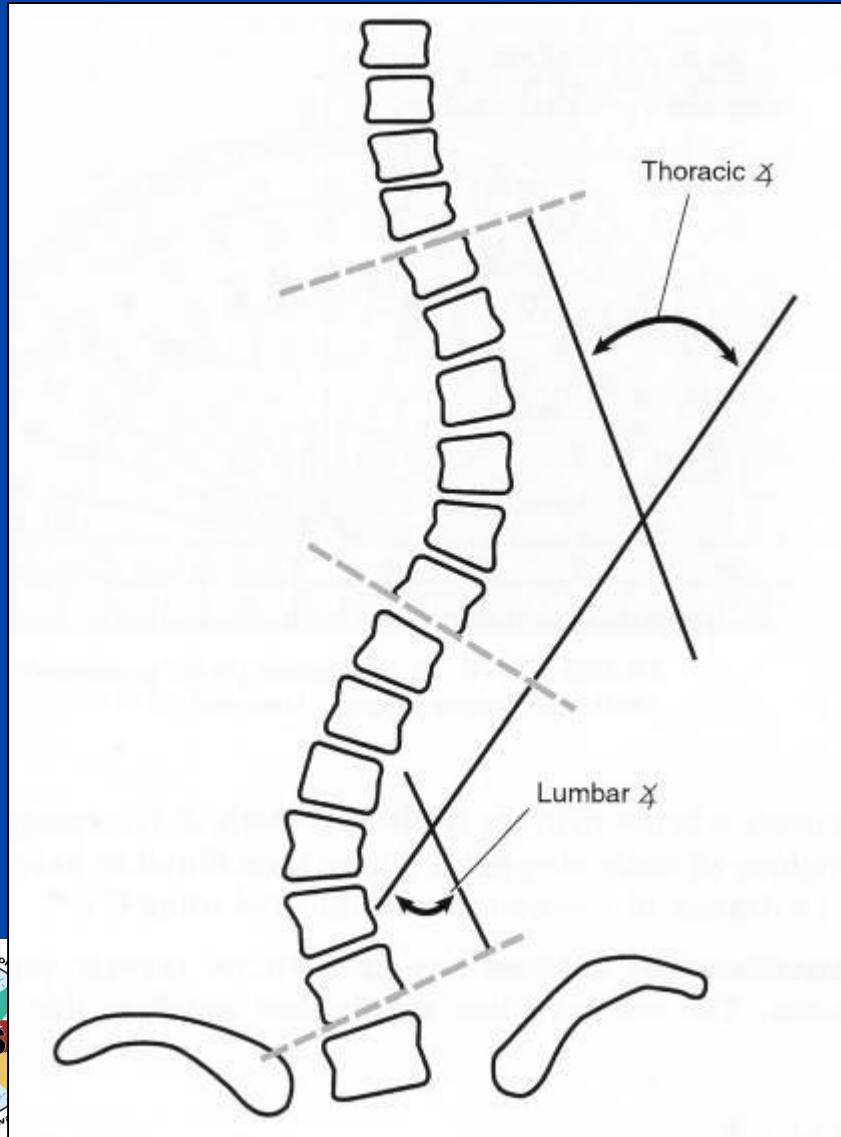
MRI (\$\$, younger child need sedation)

CT Scan

(50 x more radiation than a chest x-ray, or 500x more than a modern scoliosis x-ray)



# Scoliosis: Cobb Angle ( $\pm 5^\circ$ ) Measurement on X-ray





Spinal  
Asymmetry  
< 10°  
(no treatment)

Mild  
Scoliosis  
10° - 20°

Moderate  
Scoliosis  
20° - 45°  
(bracing in growing child)

Severe  
Scoliosis  
> 45-50°  
Surgery

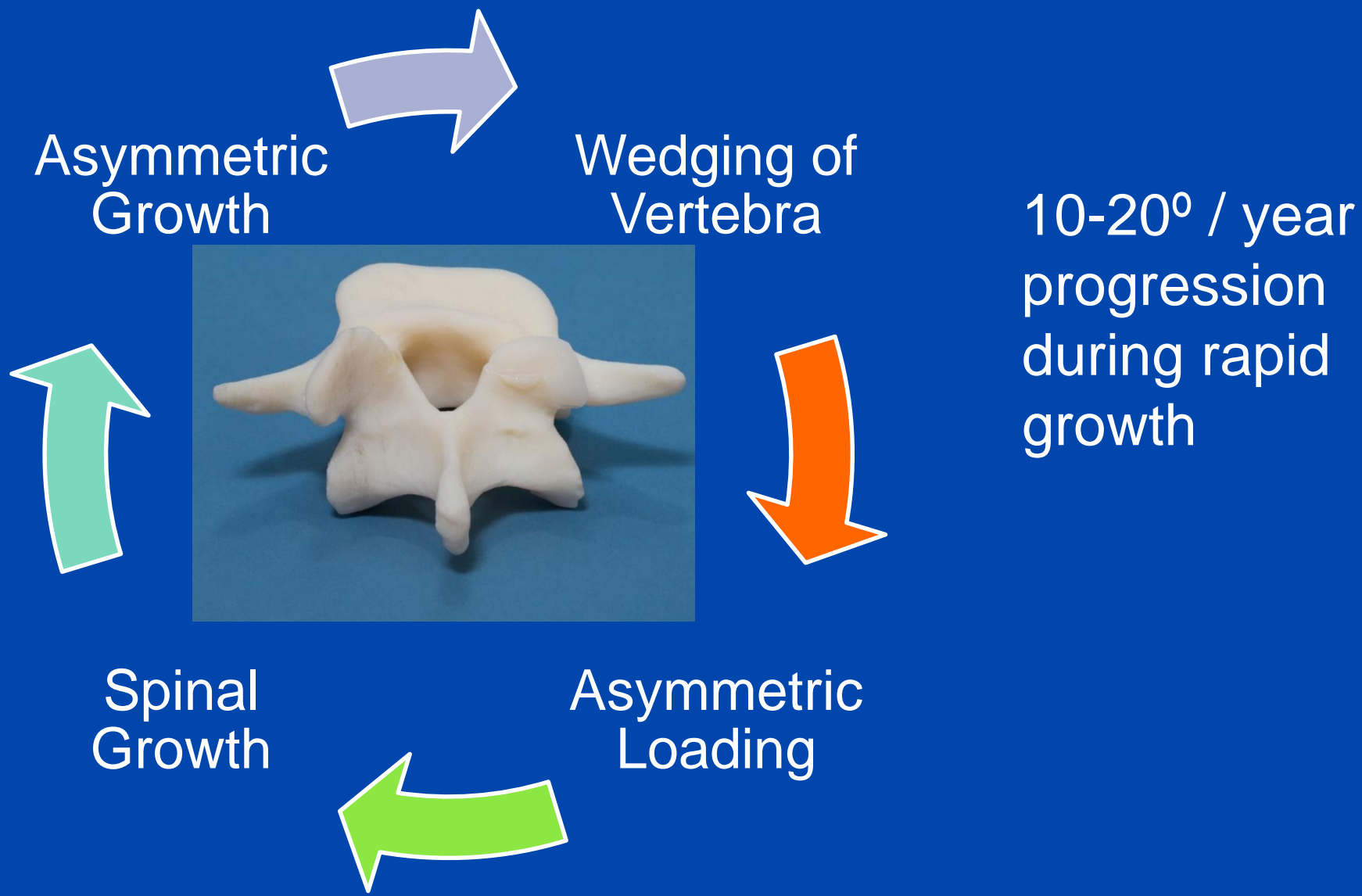


# On Exam:

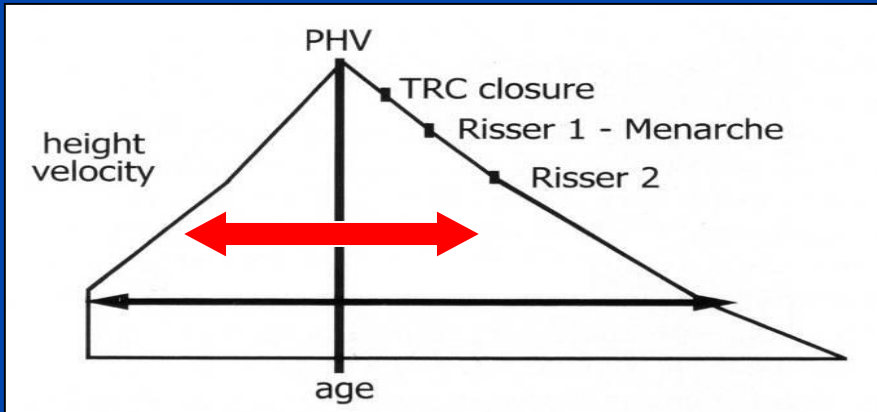
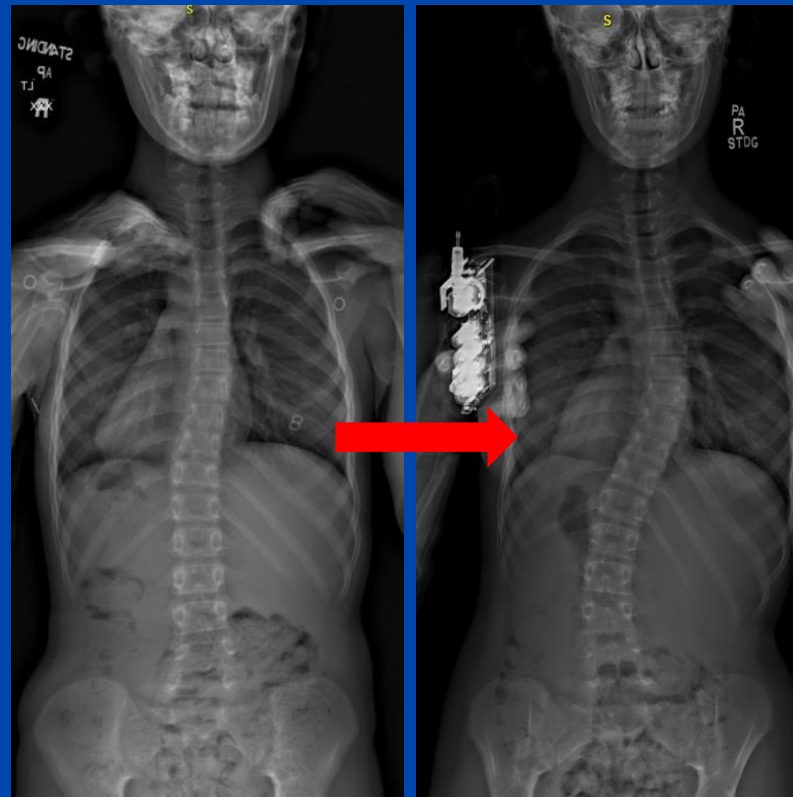
- Shoulder asymmetry
- Scapular asymmetry
- Waist asymmetry
- Right thoracic and left lumbar prominence



# Curve Gets Worse as the Child Grows

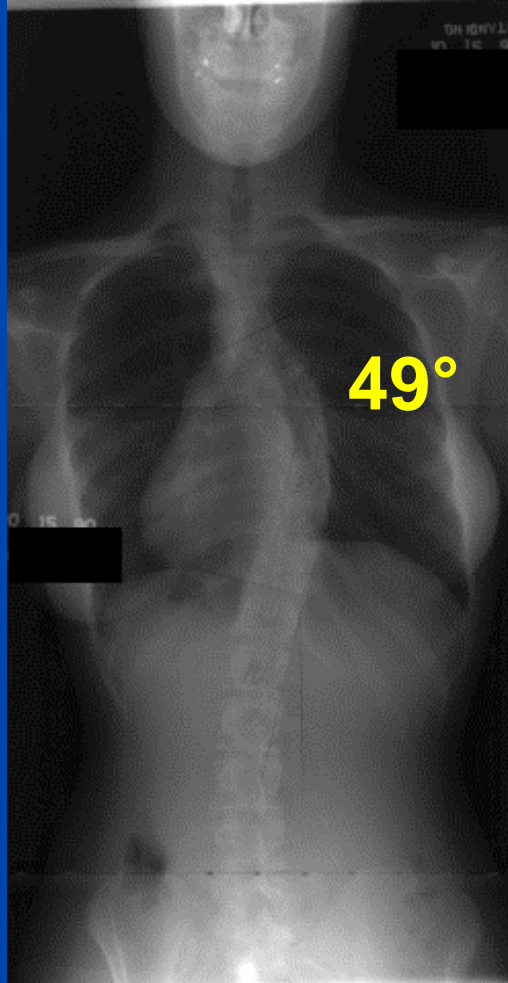


# Scoliosis Progression During Growth



# Large Curves Can Progress in Adulthood

- Curve  $> 50^\circ$ , likely to progress throughout life



22 Year Follow-Up  
1.3° per Year



# Consequence of Scoliosis

## In General Population:

- Cobb angle  $> 70^\circ$ 
  - Worse pulmonary function tests results
- Cobb angle  $> 50^\circ$ 
  - Curves progress in adulthood, surgery more difficult, more complications in adults
- Scoliosis in adulthood
  - More back pain than average adult population



# Issues for Scoliosis Specific to NF

- *In NF:*
  - *Osteopenia/osteoporosis, poor bone healing*
  - *Pain from plexiform neurofibromas*
  - *Dural ectasia (less bone to work with for surgery), can be painful*
  - *Rapid curve progression possible in children and adults*
  - *Paralysis/weakness due to spinal cord compression (severe cases)*

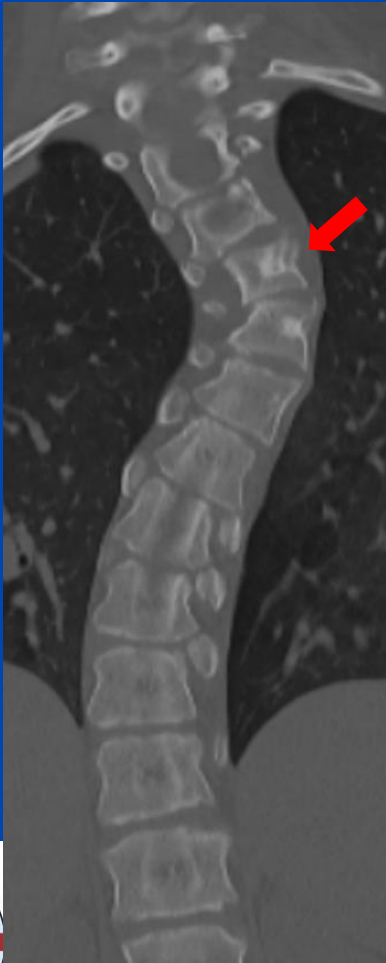




# Fusion Surgery in NF

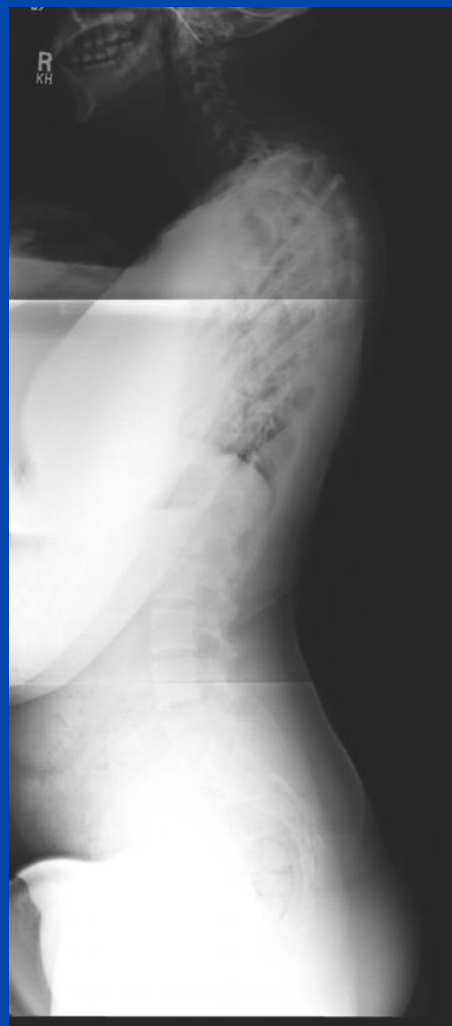
14 yo F, back pain and NF

- Erosion of vertebral bodies due to neurofibromas or dural ectasia
- Increased difficulty of placing screws in spine and achieving fusion





Now 5 years after surgery, pain has been better



# Considerations for Patient Reported Outcome Measures

- Validated
- Intuitive
- Not overly burdensome
- Clinically useful
- Can you complete form electronically on ipad/smart phone, etc.?
- Cost/ availability (some outcomes measures have associated fees to use them)
- Global relevance (translated into multiple languages, relevant to different cultures)

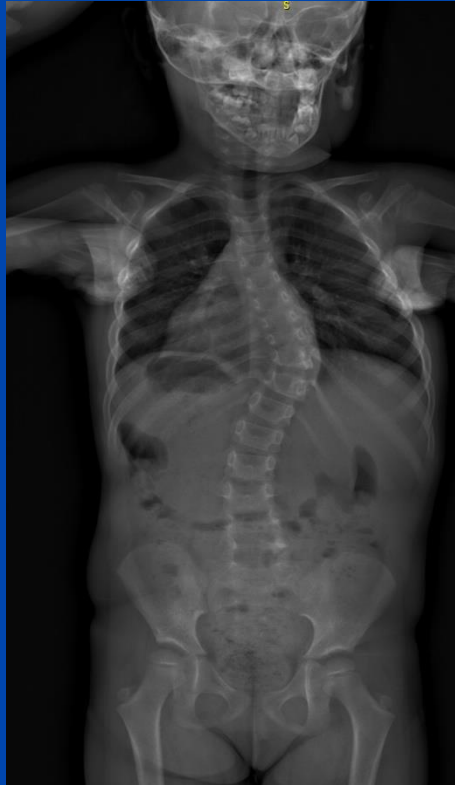


# Early Onset Scoliosis

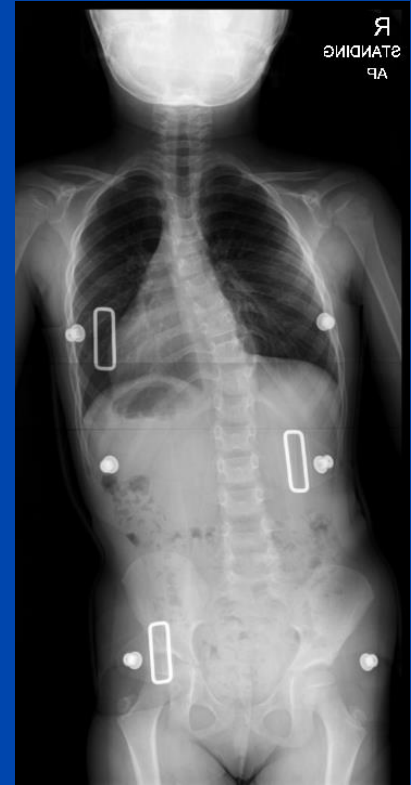
9 yo F with progressive scoliosis and NF, too young for fusion



Age 5



Age 6



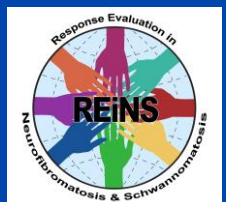
Age 7,  
in Brace



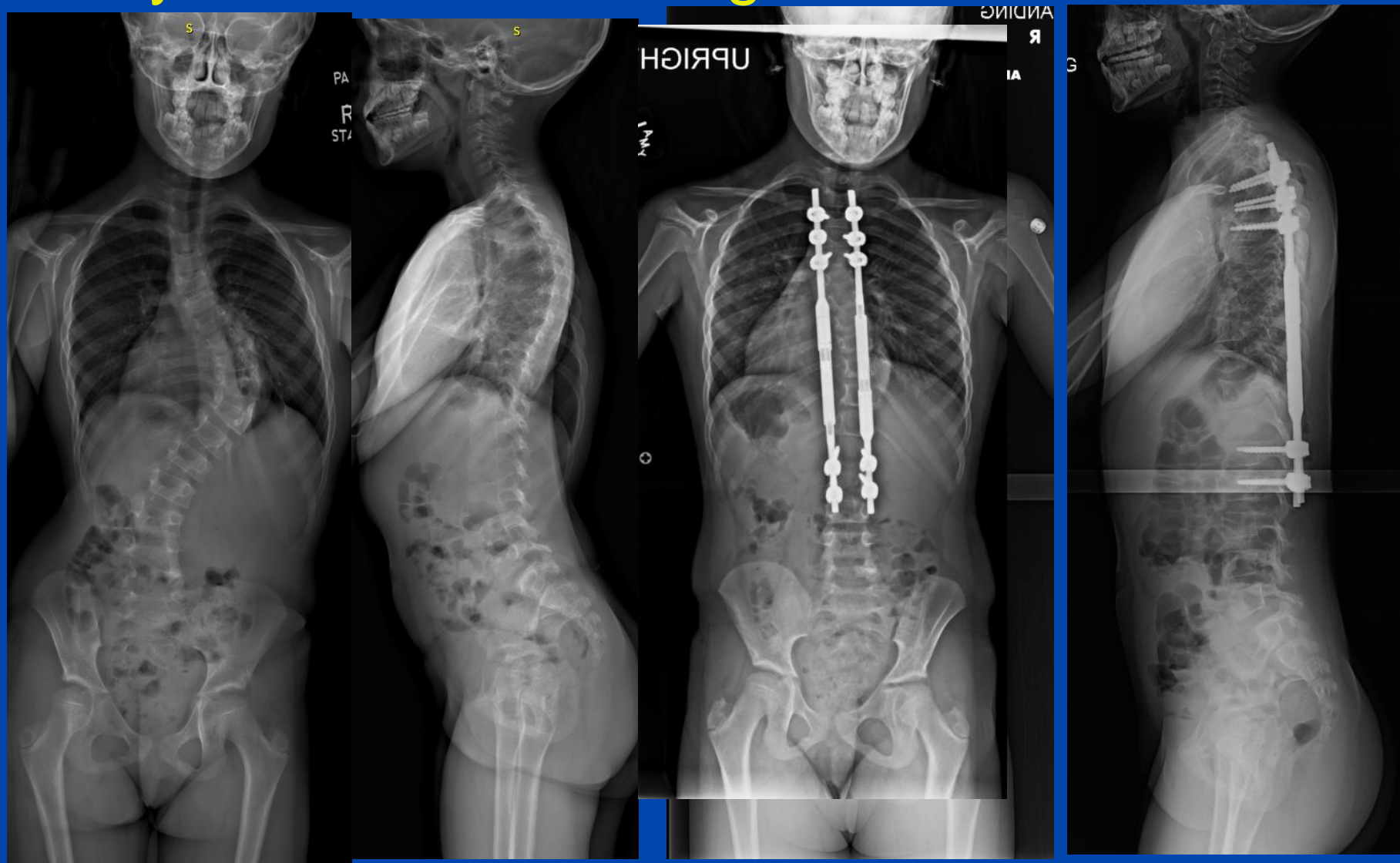
Age 8



Age 9,  
Progression  
despite bracing



# Magnetically Controlled Growing Rods



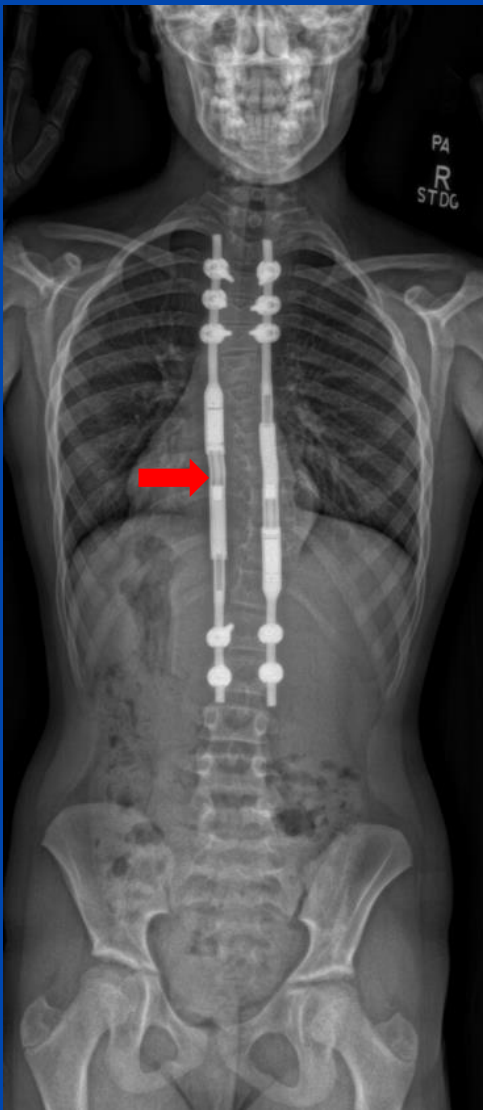




- Span dystrophic defect
- Preserve growth and allow fusion at skeletal maturity
- Lengthening in clinic 3 mm at a time, 3-4 x per year

# Magnetically Controlled Growing Rods

3 years after surgery,  
2 cm (1 in) spinal growth

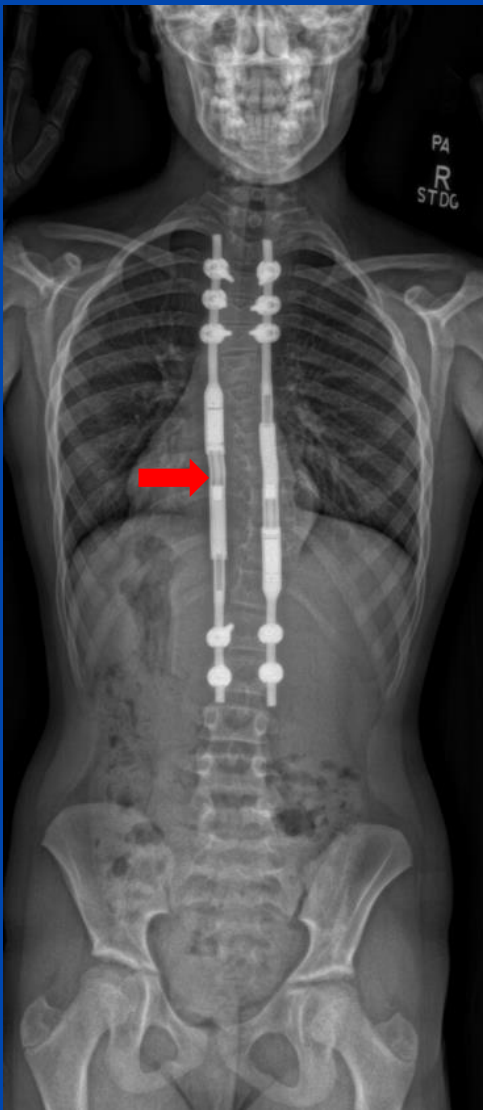


# Surgeon Outcomes

- How did surgery go?
- Did the child need a 2<sup>nd</sup> surgery?
- Was there an infection?
- How do the x-rays look?



# Did the Child's Spine Get Longer Over Time?



3 years after surgery,  
2 cm (1 in) spinal growth

Goal is 20-25 cm thoracic  
Spine height for 'normal'  
breathing, function





# Early Onset Scoliosis Questionnaire (EOSQ-24, free, validated)

- Adapted for patients with special needs (ventilator, wheelchair, nonverbal)
- Asks caregivers about breathing, finances, quality of life
- Validated, children under 10

## The Final 24-Item Early Onset Scoliosis Questionnaires (EOSQ-24): Validity, Reliability and Responsiveness

Hiroko Matsumoto, MA<sup>††</sup>, Brendan Williams, MD<sup>‡</sup>, Howard Y. Park, MD<sup>§</sup>, Julie Y. Yoshimachi, BA<sup>\*</sup>, Benjamin D. Roye, MD, MPH<sup>\*</sup>, David P. Roye Jr, MD<sup>\*</sup>, Behrooz A. Akbarnia, MD<sup>||</sup>, John Emans, MD<sup>¶</sup>, David Skaggs, MD<sup>§#</sup>, John T. Smith, MD<sup>\*\*</sup>, and Michael G. Vitale, MD, MPH<sup>\*</sup>

<sup>†</sup>Department of Orthopaedic Surgery, Columbia University Medical Center, New York, NY

<sup>‡</sup>Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY

<sup>§</sup>Department of Orthopaedics and Rehabilitation, University of Florida, Gainesville, FL

<sup>||</sup>Department of Orthopaedic Surgery, David Geffen School of Medicine at University of California at Los Angeles

<sup>#</sup>Children's Orthopaedic Center, Children's Hospital Los Angeles, Los Angeles

<sup>¶</sup>Department of Orthopaedics, University of California, San Diego, La Jolla, CA

<sup>\*\*</sup>Department of Orthopaedic Surgery, Children's Hospital, Harvard Medical School, Boston, MA

<sup>\*\*</sup>Department of Orthopaedics and Pediatrics, Primary Children's Medical Center, The University of Utah School of Medicine, Salt Lake City, UT

OFFICE USE ONLY Study ID: / / Date: / /

**General Health: During the past 4 weeks**

1. In general, you would say your child's health has been:

Poor	Fair	Good	Very good	Excellent
------	------	------	-----------	-----------

2. How often has your child been sick?

All of the time	Most of the time	Some of the time	A small amount of the time	None of the time
-----------------	------------------	------------------	----------------------------	------------------

**Pain/Discomfort : During the past 4 weeks**

3. How often has your child had pain/discomfort?

All of the time	Most of the time	Some of the time	A small amount of the time	None of the time
-----------------	------------------	------------------	----------------------------	------------------

4. How severe has your child's pain/discomfort been?

Very Severe	Severe	Moderate	Mild	No Pain
-------------	--------	----------	------	---------

**Pulmonary Function: During the past 4 weeks**

5. How difficult has it been for your child to cry/babble/speak (appropriate for age) without experiencing shortness of breath?

Difficult	Somewhat Difficult	Neutral	Somewhat easy	Easy
-----------	--------------------	---------	---------------	------

6. How often has your child experienced shortness of breath during activities?

All of the time	Most of the time	Some of the time	A small amount of the time	None of the time
-----------------	------------------	------------------	----------------------------	------------------

20. How often have you missed or have you been late for work or social events due to your child's health condition?

All of the time	Most of the time	Some of the time	A small amount of the time	None of the time
-----------------	------------------	------------------	----------------------------	------------------

21. Have you been able to spend enough time with your family/partner/spouse despite your child's health condition?

None of the time	A little of the time	Some of the time	Most of the time	All of the time
------------------	----------------------	------------------	------------------	-----------------

**Financial Impact: During the past 4 weeks**

22. How much of a financial burden has your child's diagnosis of Early Onset Scoliosis been?

Extreme burden	Quite a burden	Moderate burden	A little bit of a burden	No burden
----------------	----------------	-----------------	--------------------------	-----------

access to places?

A small amount of the time	None of the time
----------------------------	------------------



# Scoliosis Research Society Score, free, validated

- Gold standard for treatment of idiopathic scoliosis
- Extensively collected and studied for adults and children over age 10 years
- Can be converted into general scores, such as EQ-5D
- Widely translated and used globally



12. Does your back limit your ability to do things around the house?
- Never  Often  
 Rarely  Very often  
 Sometimes
13. Have you felt calm and peaceful during the past 6 months?
- All of the time  A little of the time  
 Most of the time  None of the time  
 Some of the time
14. Do you feel that your back condition affects your personal relationships?
- None  Moderately  
 Slightly  Severely  
 Mildly
15. Are you and/or your family experiencing financial difficulties because of your back?
- Severely  Slightly  
 Moderately  None  
 Mildly
16. In the past 6 months have you felt downhearted and blue?
- Never  Often  
 Rarely  Very often  
 Sometimes
17. In the last 3 months have you taken any sick days from work/school due to back pain and, if so, how many?
- 0  1  2  3  4 or more
18. Do you go out more or less than your friends?
- Much more  Less  
 More  Much less  
 Same
19. Do you feel attractive with your current back condition?
- Yes, very  No, not very much  
 Yes, somewhat  No, not at all  
 Neither attractive nor unattractive

# Oswestry Disability Index Adult, Back Pain Questionnaire

## Oswestry Low Back Pain Disability Questionnaire

Sources: Fairbank JCT & Pynsent, PB (2000) The Oswestry Disability Index. *Spine*, 25(22):2940-2953.

Davidson M & Keating J (2001) A comparison of five low back disability questionnaires: reliability and responsiveness. *Physical Therapy* 2002;82:8-24.

### Section 1 – Pain intensity

- I have no pain at the moment
- The pain is very mild at the moment
- The pain is moderate at the moment
- The pain is fairly severe at the moment
- The pain is very severe at the moment
- The pain is the worst imaginable at the moment

### Section 2 – Personal care (washing, dressing etc)

- I can look after myself normally without causing extra pain
- I can look after myself normally but it causes extra pain
- It is painful to look after myself and I am slow and careful
- I need some help but manage most of my personal care
- I need help every day in most aspects of self-care
- I do not get dressed, I wash with difficulty and stay in bed

### Section 3 – Lifting

- I can lift heavy weights without extra pain
- I can lift heavy weights but it gives extra pain
- Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently placed eg. on a table
- Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned
- I can lift very light weights
- I cannot lift or carry anything at all

### Section 4 – Walking\*

- Pain does not prevent me walking any distance
- Pain prevents me from walking more than 1 mile
- Pain prevents me from walking more than 1/2 mile
- Pain prevents me from walking more than 100 yards
- I can only walk using a stick or crutches
- I am in bed most of the time



# General Health Related Quality of Life – can be applied to all disease conditions

- SF-36 (Short-form)
- EQ5D (Euro-Qual 5D)

## SF36 Health Survey

**INSTRUCTIONS:** This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer as indicated. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is: (Please tick **one** box.)

Excellent

Very Good

Good

Fair

Poor

2. Compared to one year ago, how would you rate your health in general now? (Please tick **one** box.)

Much better than one year ago

Somewhat better now than one year ago

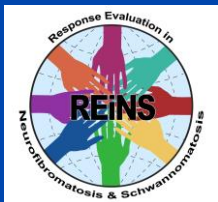
About the same as one year ago

Somewhat worse now than one year ago

Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? **(Please circle one number on each line.)**

Activities	Yes, Limited A Lot	Yes, Limited A Little	Not Limited At All
3(a) <b>Vigorous activities</b> , such as running, lifting heavy objects, participating in strenuous sports	1	2	3
3(b) <b>Moderate activities</b> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
3(c) Lifting or carrying groceries	1	2	3
3(d) Climbing <b>several</b> flights of stairs	1	2	3
3(e) Climbing <b>one</b> flight of stairs	1	2	3
3(f) Bending, kneeling, or stooping	1	2	3
3(g) Walking <b>more than a mile</b>	1	2	3
3(h) Walking <b>several blocks</b>	1	2	3
3(i) Walking <b>one block</b>	1	2	3
3(j) Bathing or dressing yourself	1	2	3



# What is PROMIS-CAT?

PROMIS<sup>®</sup> = Patient-Reported  
Outcomes Measurement Information  
System

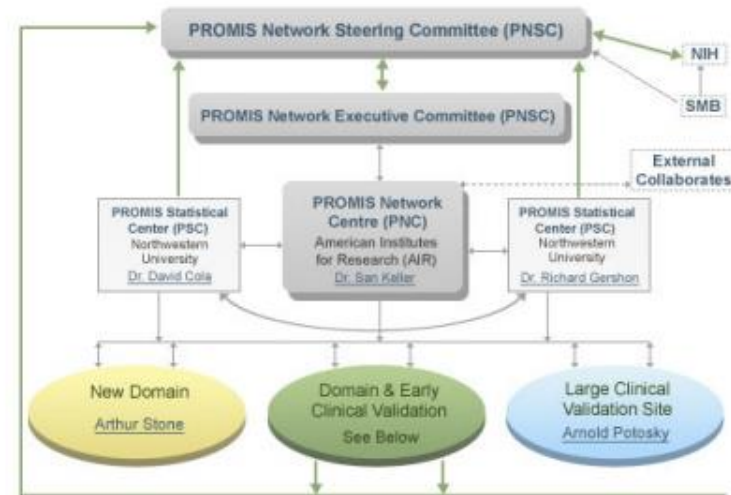
CAT=Computer Adaptive Testing



# Promis Scores – Computer Adaptive Testing (CAT)

## PROMIS®

- NIH-developed
- Validated way to measure PROs to support NIH-funded research
- Rigorously developed with IT, psychometrics, cognitive, and health survey research
- Item response theory



### Domain Development / Early Validation

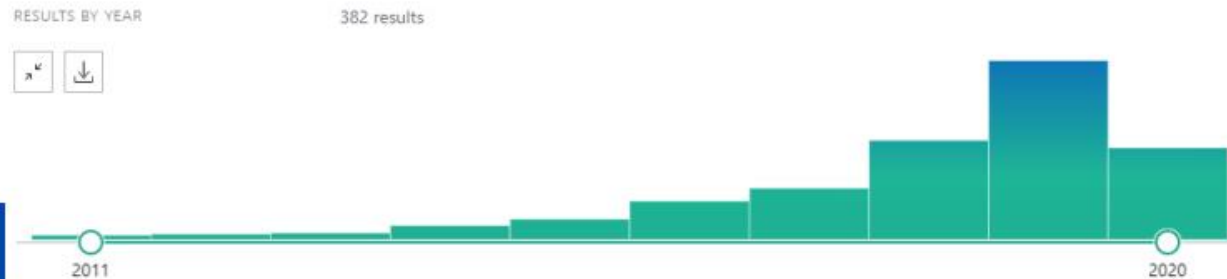
<u>Stephen Haley</u> PRO's in children and young adults w/ disabilities	<u>Darren DeWalt</u> Pediatrics: Longitudinal study linking pediatric and adult item banks	<u>Christopher Forrest</u> Pediatric PROMIS: advancing the measurement & conceptualization of child health	<u>Lisa Shulman</u> Development / validation of self-efficacy item bank	<u>Donald Patrick</u> Patient reported outcomes in routine clinical care of patients infected with HIV
<u>Kevin Weinfurt</u> Sexual functioning	<u>Dinesh Khanna</u> Development / validation of PROGIS GI distress	<u>Esi Morgan</u> Enhancing PROMIS in pediatric pain	<u>Paul Pitkonis</u> Development / validation of mental health / sleep wake function	<u>James Fries</u> Improving assessment of PF / drug safety in health and disease



# Recommended by American Academy of Orthopedic Surgeons

## PROMIS

- **AAOS** recommends PROMIS among its Instruments for Collection of Orthopaedic Quality Data
- Broad Mayo Clinic institutional support: Neurosurgery 85% compliance, Rheumatology (in progress), Oncology
- 191 articles published about PROMIS measures in Orthopedics in 2019





## Downsides of Promis

- Many different 'modules' not all the same
- Need a computer for computer-adaptive testing
- May have a ceiling effect for orthopedics (everyone scores very high, even though disability exists)
- Not disease-specific

## Advantages of Promis

- Validated
- Respected
- Can compare one disease condition to another
- Preferred by NIH



# Summary of Scoliosis Assessments

- Clinician outcomes

- Curve correction on x-ray
- Neurologic status
- Blood loss, operative time, complications

- Patient outcomes

- Disease Specific
  - SRS22
  - EOSQ-24
  - Oswestry Disability Index
- Pain scores
- General
  - Promis CAT
  - SF-36
  - SF-12
  - EQ5D



# Recommended Scoliosis Assessments

- Clinician outcomes
  - Curve correction on x-ray
- Patient outcomes
  - Disease Specific
    - SRS22
    - EOSQ-24



Thank you!

A. Noelle Larson, MD  
larson.noelle@mayo.edu