

# Measuring Pain and Symptoms in Children with Chronic Conditions

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# Outline

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- Pain and symptom experience of children with chronic conditions
- Available core outcome sets in pediatric pain (PedIMMPACT, OMERACT JIA)
  - Relevant outcome domains and measures across conditions
- Challenges in interpretation of outcomes/endpoints
- Innovations in symptom assessment (e.g., sensors, electronic diaries/ecological momentary assessment)

# Pain and Symptom Experience

- Children with chronic conditions often experience numerous symptoms
  - **Pain\*\*\*\***
  - Fatigue
  - Emotional distress
  - Sleep problems
- Health-related quality of life (HRQOL) is an important indicator of the burden of illness
- Important to study pattern of symptoms and the impact of symptoms on children's daily life

# Bothersome Pain is Very Common in Children with Chronic Conditions

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- Juvenile idiopathic arthritis
  - 76% report pain, 31% severe pain
- Sickle cell disease
  - 40-50% report monthly episodes with severe pain
- Cancer pain
  - 84% inpatients and 35% of outpatients report pain
- Inflammatory bowel disease
  - 88% of children report pain, 48% persistent



## Epidemiology and management of painful procedures in children in Canadian hospitals

Bonnie J. Stevens RN PhD, Laura K. Abbott MSc, Janet Yamada RN MSc, Denise Harrison RN PhD, Jennifer Stinson RN PhD, Anna Taddio PhD, Melanie Barwick PhD, Margot Latimer RN PhD, Shannon D. Scott RN PhD, Judith Rashotte RN PhD, Fiona Campbell MD, G. Allen Finley MD, for the CIHR Team in Children's Pain

- Multi-center study in Canada across 8 children's hospitals
- Examined management of painful procedures in inpatient units in 3822 children
- Painful procedures were common
  - 78% had one or more painful procedures in prior 24 hours; mean = 6.3 procedures per child
  - 70% of painful procedures had no pain management
- Risk for later chronic pain?

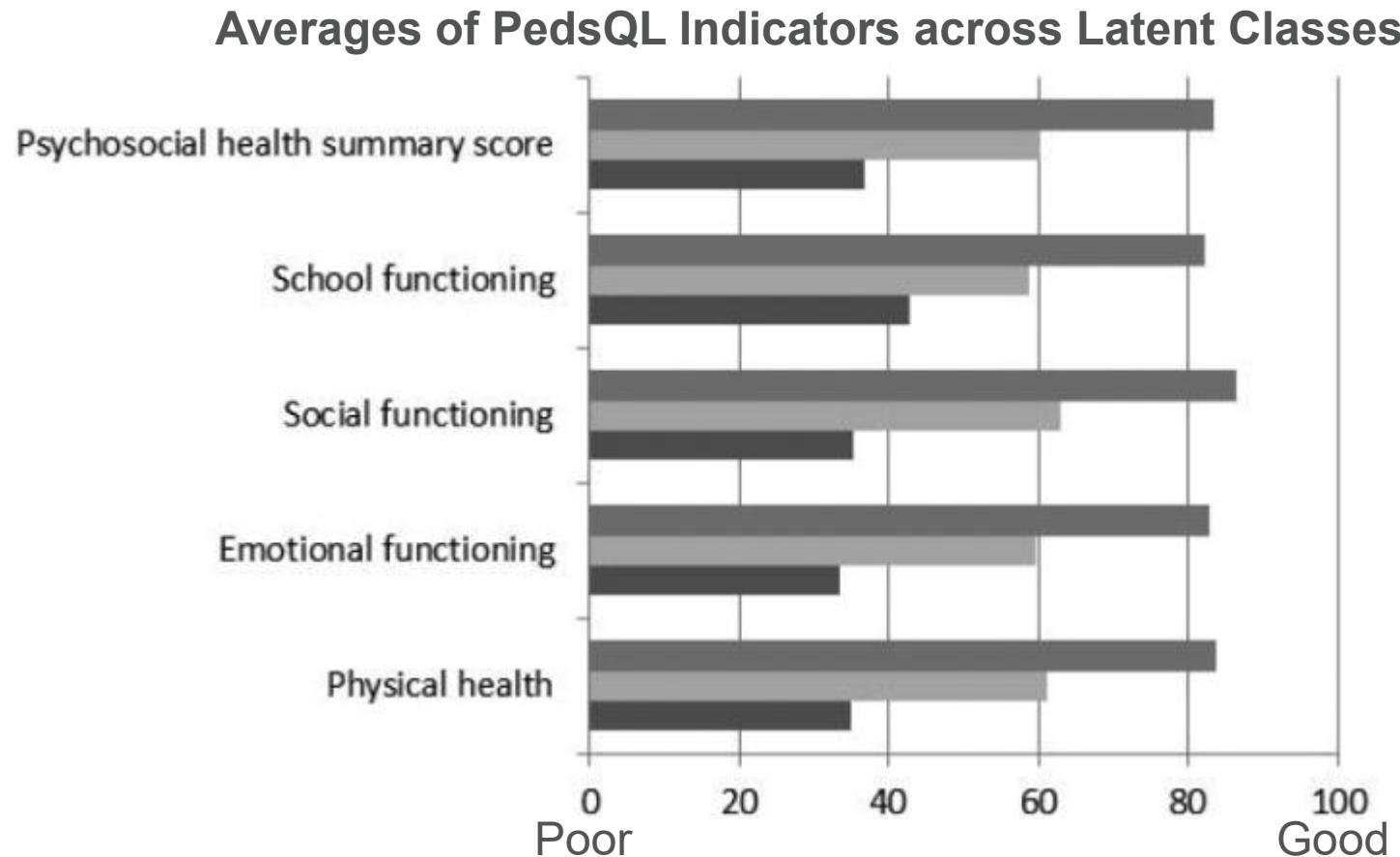
# Functional Consequences of Pain

- Broad potential impact of persistent pain on children and families
  - Can affect virtually every aspect of life
- Children: impact on school, mood, sleep, peer contact, physical activity
- Parent and family: burden (costs, time), emotional worry, family function

# What Functional Consequences do Children Report?

- Epidemiological studies (e.g., Roth-Isigkeit, et al., 2005)
  - sleep problems (53.6%)
  - inability to pursue hobbies (53.3%)
  - eating problems (51.1%)
  - school absence (48.8%)
  - inability to meet friends (46.7%)
- Increasing age more impairment

# Impact of Symptoms on Health-Related Quality of Life



# Core Outcome Sets

- A Core Outcome Set (COS) is an agreed minimum set of constructs or domains (i.e., outcomes) that should be measured and reported in all clinical trials of a specific disease or trial population
- Include stakeholders: health professionals, methodologists, patients, parents

Prinsen, et al. (2016) How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. *Trials* .



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# PedIMMPACT

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- Pediatric working group of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (PedIMMPACT)
- Met in 2006 - 26 professionals from academia, governmental agencies, and the pharmaceutical industry
- 2-stage Delphi poll and a subsequent consensus meeting to identify core outcome domains and measures that may be considered in clinical trials of treatments for acute and chronic pain in children and adolescents

# Domains Recommended for Chronic Pain Trials

Pain  
Intensity

Physical  
Functioning

Sleep

Global Tx  
Satisfaction

Emotional  
Functioning

Economic  
Factors

Adverse Events

Role Functioning

McGrath et al., J Pain, 2008



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# Available Measures for Pediatric Pain

- Recommendations include multiple validated patient-reported outcome measures to assess: (across conditions)
  - Pain intensity
  - Physical functioning and activity limitations
  - Anxiety and depression
  - Sleep
  - HRQOL



# Uptake of PedIMMPACT Recommendations

- Connelly et al. (2019): 107 randomized controlled trials of pediatric chronic pain interventions
  - **Nearly all trials included pain intensity as an outcome domain but fewer than 35% of trials included outcomes in the other PedIMMPACT recommended domains**
  - Pain impact outcomes not being included



# Measurement Challenges and Gaps

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- Lack of specificity – e.g., recommending multiple instruments within domains
- Relevance - did not incorporate perspectives of child patients and parents
- Recommendations do not address special populations: infants and pre-verbal children, children with intellectual disability and severe motor impairments
- Few measures have defined clinical cutpoints for interpreting clinically meaningful change

# Methods for Evaluating Clinical Significance

- Anchor-based methods
  - cut-points of pain intensity (>30% moderate change and > 50% substantial change)
- Distribution methods, e.g., Reliable Change Index
- Responder analysis, e.g., composite across several outcomes
- Combined or integrated methods, e.g., combining change in clinical severity category with a distribution based measure of improvement

# Disease specific COS - OMERACT Juvenile Idiopathic Arthritis



Research agenda		<ul style="list-style-type: none"><li>• Coping with illness</li><li>• Healthcare utilization</li><li>• Sleep</li><li>• Impact on social relationships</li><li>• Personal Factors</li></ul>	
Important but optional domains		<ul style="list-style-type: none"><li>• Joint Damage</li><li>• Lab signs of inflammation</li><li>• Physician perception of disease activity</li><li>• Stiffness</li><li>• Growth and Maturation</li><li>• Participation restriction</li><li>• Imaging Signs of Inflammation</li><li>• Physical activity (exercise)</li><li>• Fatigue</li><li>• Impact on emotional function, mood, cognition</li></ul>	
Mandatory domains	Mandatory in specific circumstances	<ul style="list-style-type: none"><li>• Inflammation (e.g., extra-articular) or features relevant to specific JIA category*</li></ul>	
	Mandatory in all trials	<ul style="list-style-type: none"><li>• Pain</li><li>• Joint inflammatory signs</li><li>• Activity limitation/physical function</li><li>• Patient perception of disease (overall well-being)</li><li>• Adverse Events, incl. death</li></ul>	

A Delphi process with parents, patients, healthcare providers, researchers, and regulators served to edit the domain list and prioritize candidate domains

# Developing New Core Outcome Set – Pediatric Chronic Pain Trials

- 2-stage Delphi poll with providers, children, and parents
- Consensus meeting to select domains
- Systematic reviews to identify and select one measure for each outcome

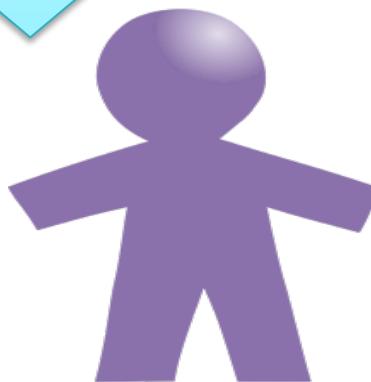
An Update and Revision of the PedIMMPACT Statement on Chronic Pain Outcome Measures for Pediatric Trials, Funded by Mayday Foundation, Palermo/Walco (PIs)

# Gathering Child and Parent Perspectives

- **We would like to know your thoughts about your treatments for chronic pain. Treatments may include physical therapy, medications, psychological or behavioral interventions, acupuncture, or other treatments.**
- Over the last few months, have you generally felt that your treatment(s) for chronic pain have been working well?
- Please tell us what aspects of your pain problem, or your daily life, have made you feel like your pain treatments are working.
- Over the last few months, have there been times when you felt that your pain treatment should be changed because you weren't improving? Please tell us the reasons why you were not satisfied with your treatment.

# Child Perspective

**“That it will **get worse as I grow older**, and for it to get to the point where I am constantly not able to **enjoy life** due to it.”**



**“I always try to play outside and stuff even when it hurts. I **never want to tell my mom** because she gets so depressed about it. I just want to stay outside, be with my friends. I want to **be like everybody else.**”**



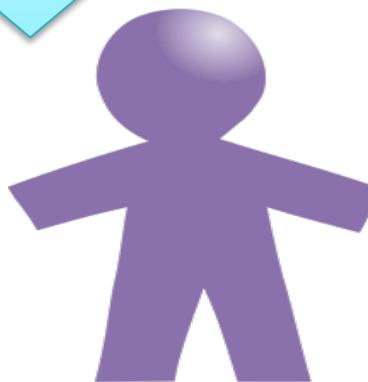
**“I think the longer, like, I’ve had the pain it’s gradually just gotten worse and worse so it was really **frustrating**. I would **stay home from school or go home early a lot.**”**



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# Parent Perspective

“This has affected us as a family entirely, in multiple ways. Either my wife or I has been with him, either both of us or one of us, to various hospitals throughout the United States trying to find a diagnosis and treatment for his pain.”



“That she will never be able to successfully fight depression in adulthood and will depend on others to care for her.”



“My main concern as always that it doesn't interrupt her school life especially as she is about to enter her senior year. Or that I won't be there for her when she goes away to college the following year or two.”



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# Innovations in Measurement

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- Objective measures/sensors
  - Actigraphy
  - Biomechanical assessments
- Electronic diaries and ecological momentary assessment

# Objective Assessment Tools

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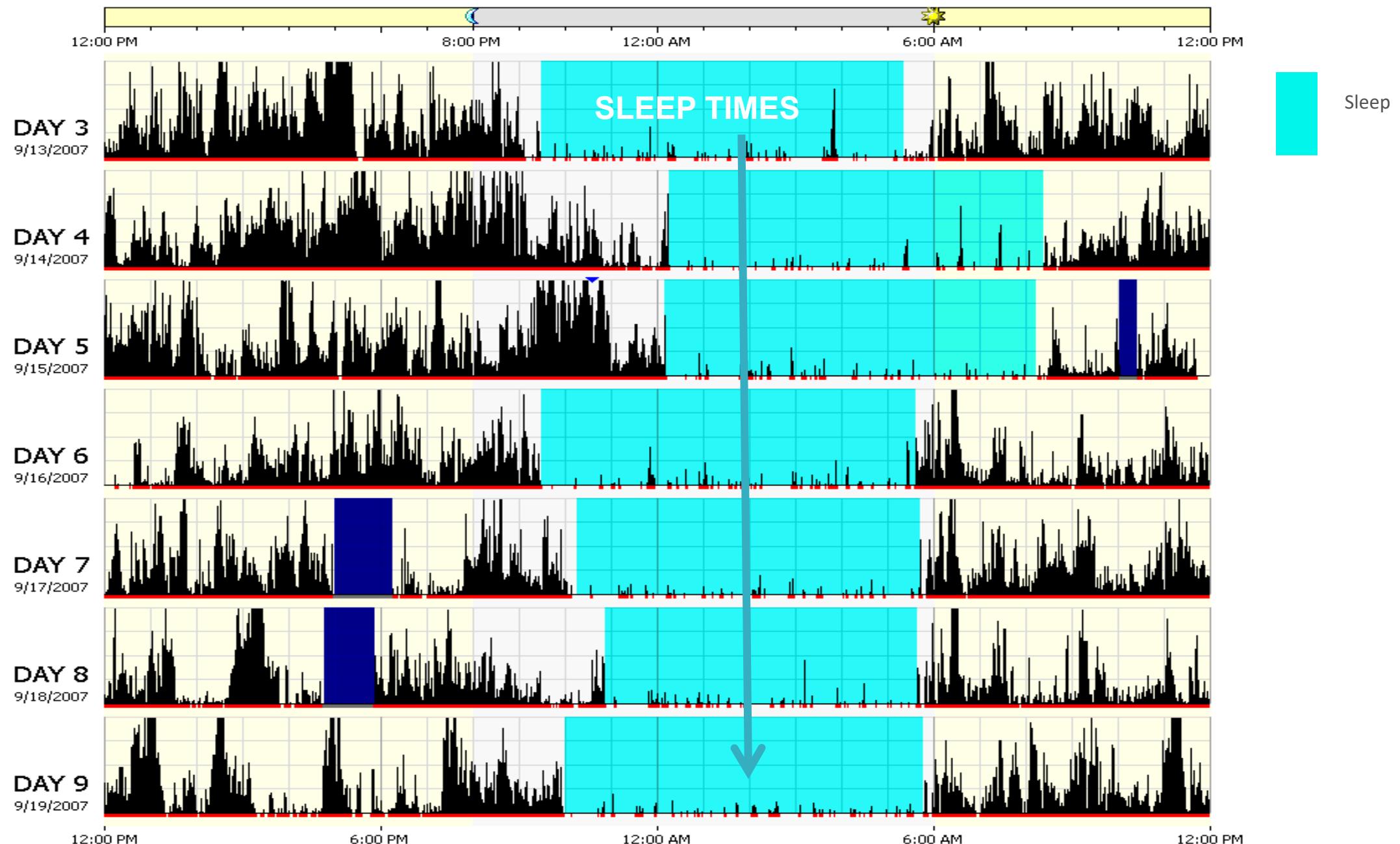
- Actigraphy- assess sleep and activity patterns
- Research vs commercial grade (Fitbit, etc)?

# Advantages of Using Actigraphy in Children and Adolescents

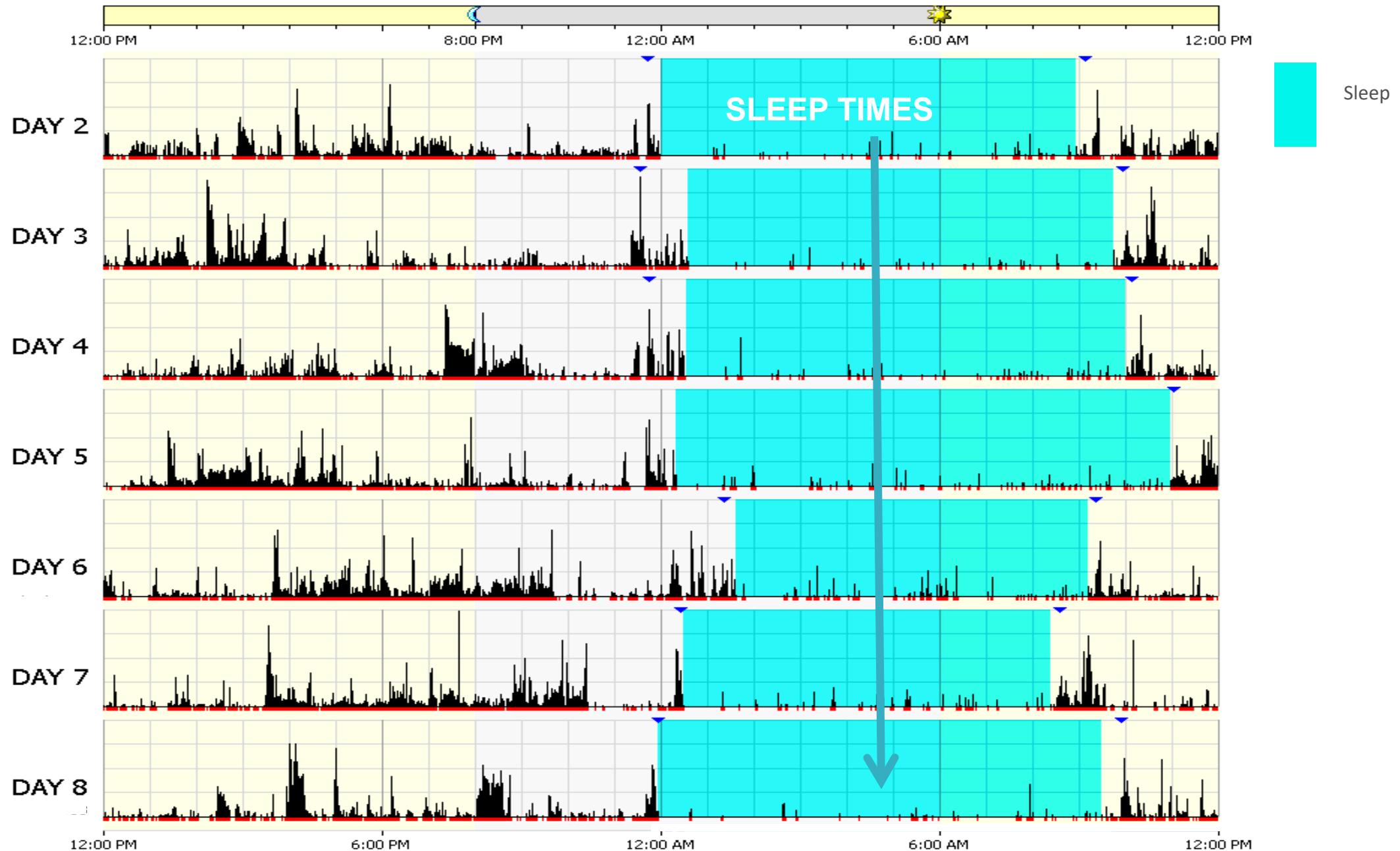
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- Relatively unobtrusive, embedded in day-to-day life
- Objective assessment tool that can complement range of information on sleep or physical activity obtained from multiple reporters
- Minute by minute (or more frequent) time stamped data

# High physical activity



# Low physical activity



# Limitations of Objective Measurement Tools

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- Normative data for pediatric pain populations is available for only some measurements
- Limited ability to understand relative levels of impairment or to determine clinically meaningful improvement in response to treatment
- Need to expand research using objective assessments in pediatric pain clinical trials to determine their appropriateness for specific outcome domains

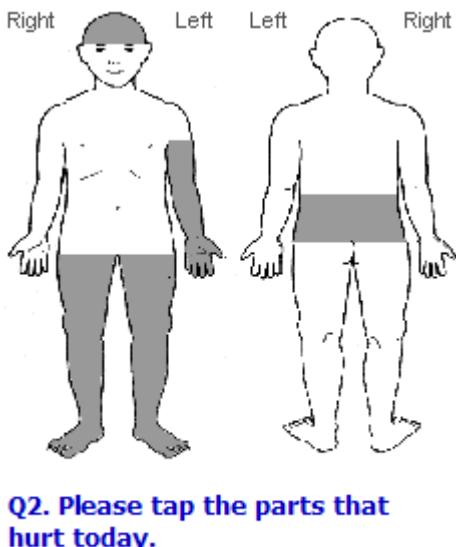
# Electronic Patient-Reported Outcomes Diaries

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- Prospective daily diary can provide information on patterns over time
  - Real time assessment; reduces recall bias, ability to determine dynamic changes in domains of interest, increased compliance
  - Well-validated for prospective pain and symptom assessment in children as young as 8 years and above

# E-diaries in Clinical Trials

- Used in multicenter clinical trials for pain and impact assessment (Heath, et al., 2017; Palermo, et al., 2016)



WebMAP

Check-in

What was your level of pain today?  
0 (no pain) to 10 (worst pain)

How difficult was schoolwork?  
0 (Not very) to 10 (Extremely)

How difficult was it to fall or stay asleep last night?  
0 (Not very) to 10 (Extremely)

Did you feel down, depressed, or hopeless today?  
0 (Not very) to 10 (Extremely)

Home Checkins Progress



# Summary and Conclusions

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- Pain and other symptoms are common and impact children's lives
- Outcome assessment is a critically important component of developing effective treatments for childhood pain
- Core Outcome Sets provide guidance on relevant outcome domains and available validated measures
- Gaps in measurement need to be addressed to encourage greater uptake of recommendations, particularly in measurement of pain impact
- Innovations in use of sensors/devices and electronic methods of outcome reporting may enhance clinical trials in pain



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