

Developing patient reported outcomes to assess pain in children and adults with NF1: Qualitative results from patient focus groups and interviews

Kari Struempfl, Ph.D.
National Cancer Institute



Outline

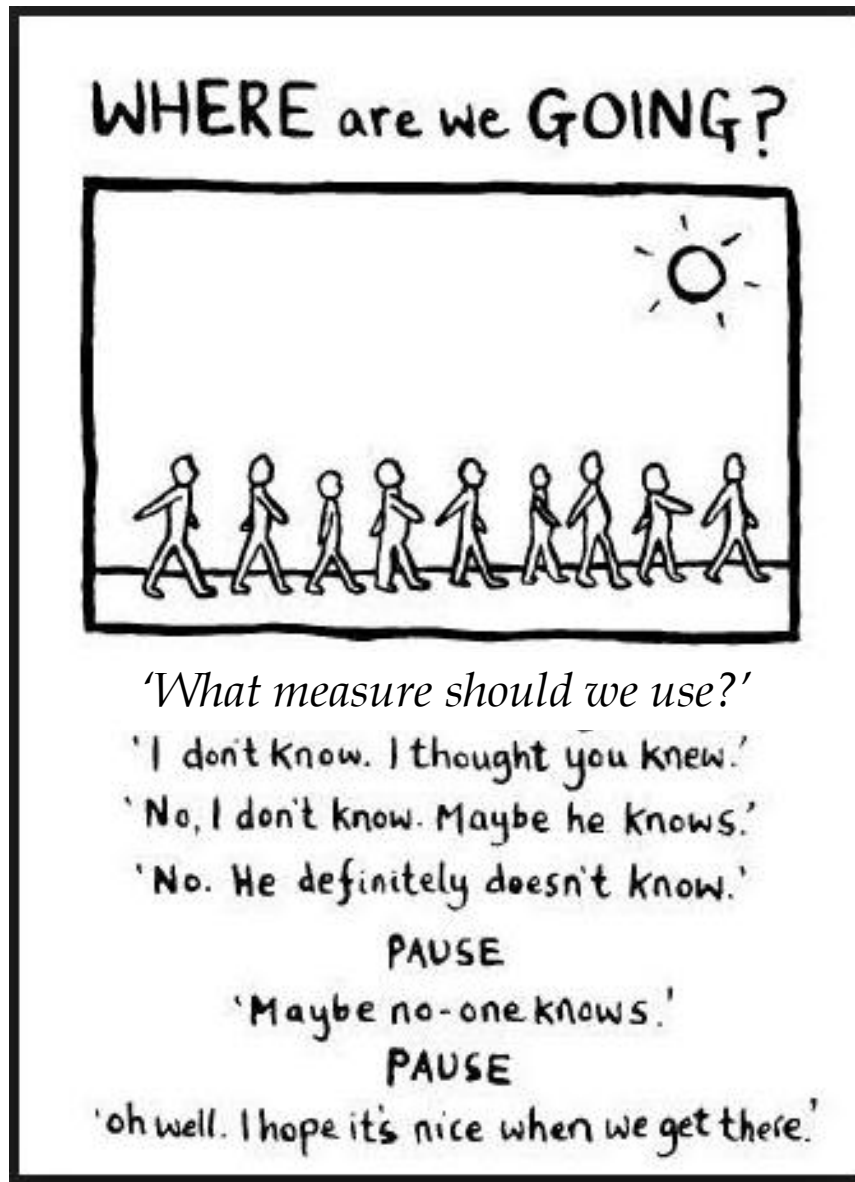
- Review the Pain Assessment In Neurofibromatosis Type 1 (PAIN) Project
- Describe patient engagement efforts
- Discuss preliminary outcomes of patient input
- Discuss barriers and benefits to patient engagement

PAIN Study

- Clinical trials are being conducted to evaluate drugs to treat plexiform neurofibromas (PNs)
- For approval of drugs to treat PNs, the FDA is requiring documented clinical benefit in addition to reduction in tumor volume
- PROs assessing changes in symptoms, such as pain, can be used to demonstrate clinical benefit
- No validated PRO measures of pain for individuals with NF1 and PNs



Difficulties with PRO selection



PAIN Study



■ Phase 1: Qualitative Research

■ Objectives

- To evaluate existing pain measures and explore potential modifications
- Make necessary modifications so measures are NF specific
- Convert the modified measures into an electronic format
- Review these changes with patients to ensure understanding and ease of use

Study Design

■ Eligibility Criteria

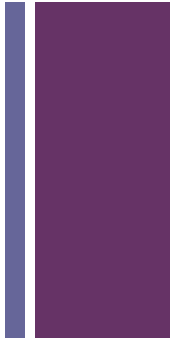
- NF1 and plexiform neurofibroma (PN)
- Age \geq 5 years old
- Report of PN-related pain (minimum of 3 on a 0-10 scale or 1 if on pain-reducing medication)

■ Lead Site (PIs)

- National Cancer Institute (Pam Wolters, PhD; Staci Martin, PhD)

■ Collaborating Sites (Site PIs)

- University of Chicago (Jim Tonsgard, MD)
- Cincinnati Children's Hospital (Betty Schorry, MD)
- Children's National Medical Center (Karin Walsh, PsyD)



Goals for Patient Engagement

- Learn from patients about their pain
 - How do they describe it?
 - How do they measure it?
 - How does it affect their life?
- Gather opinions about current pain measurement techniques
- Move away from relying only on expert opinion
 - Patients are the experts on their pain!
- Adhere to the FDA recommendations for PRO development
 - FDA Tool Development Program



Qualitative Research: Focus Groups and Individual Interviews

- Study investigators attended an intensive training on focus group development and moderation
- Scripts with open ended questions were developed to encourage free thinking and avoid leading questions
- Groups were broken into similar age groups and divided by gender to facilitate participant comfort when discussing personal topics
- We conducted a total of 15 focus groups and 39 individual interviews which resulted in a total of 79 participants

Content Analysis

- After the groups are completed, each group/interview is transcribed and content analysis is conducted to determine important topics and themes
- Initial themes developed by investigators based on existing knowledge and experiences
- New themes are created as they arise from the open ended discussions
- Each transcript is coded line by line using the identified themes



The Coding Process

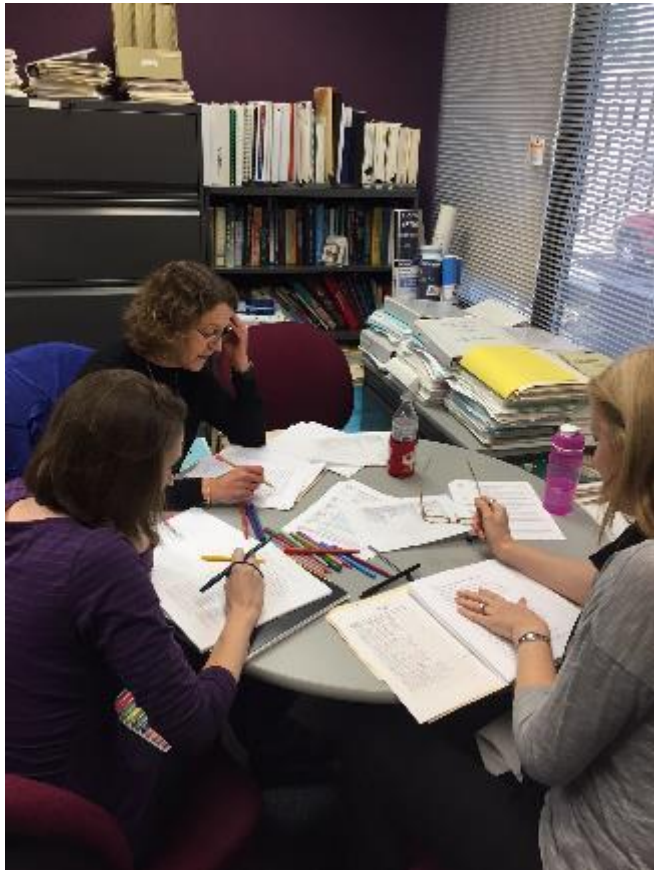
Coding Dictionary
5/26/16

Theme
<u>Recall Period</u> 110
<u>Tumor Pain</u> 102
<u>Non-tumor Pain</u> 122
<u>Unspecified Pain</u> 125
<u>Pain Variability</u> 109
<u>Pain Description</u> 103
<u>Current/Past Pain Measurement</u> 111
<u>NRS-11</u> 104
<u>PIL</u> 131
<u>PROMIS-PF</u> 128
<u>Pain Differentiation (Specific tumor pain vs others)</u> 113
<u>Recording tumor location</u> 134
<u>Overall tumor pain</u> 132
<u>Overall pain</u> 136
<u>Activity Causing Pain</u> 126
<u>Understanding of measure:</u>
<u>Did Understand</u> 123
<u>Did not understand</u> 117
<u>Changes to measure</u> 127
<u>Pain Interference</u> 120
<u>No Pain Interference</u> 106
<u>Positive</u> 108
<u>Negative</u> 121
<u>Applicability of measure to NF</u> 133
<u>Ability of measure to detect change</u> 129
<u>Physical Functioning Impact</u> 119
<u>Access to smart phone/tablet</u> 114
<u>Comfort with electronic measures</u> 107
<u>Daily Home Ratings</u> 101
<u>Ability to identify PMS</u>

2

<u>Unspecified Pain (125)</u>	Pain of unknown or unclear origin, does not clearly fit into tumor or non-tumor pain; statements where it is not clear what kind of pain the patients is talking about.
Examples	"My back hurts but they're not sure if it's from a tumor or not."
<u>Pain Variability (109)</u>	Statements about how pain changes over time. Within a day, week, over a longer period of time, like months or years. Discussions about pain "spikes" and good days versus bad days. Statements about the lack of variability, pain stability.
Examples	"One day might be a 5 and the next day might be a 9." "My pain started getting really bad when I was a teenager; before that it wasn't bad." "I feel pain in the morning, I know it's going to be bad by the end of the day." "It's unpredictable, it comes at random times." "My pain changes with the weather." "My pain is almost always at a 3."
<u>Pain Description (103)</u>	When patients describe the quality of their pain and how it feels (e.g., numb, shooting, etc). Includes recalling specific instances of painful events as long as there are descriptive words.
Examples	"Sometimes it's a stabbing pain but other times it's kind of a dull ache." "I remember when I was walking down the hall in school last year and someone ran into me and it was the worst pain ever." – (would also code as recall period)
<u>Current/Past Pain Measurement (111)</u>	How physician's measure patient's pain now or historically. Thoughts about if these measurement strategies work or do not work (also code as positive or negative). How patients have kept track of their own pain, even if not per physician.
Examples	"His doctor doesn't understand how much pain he has." "They used to ask me to do those faces." "I log my pain on an app."

The Coding Process



arm which is the most important one. Do you have another
plexiform?

INTERVIEWEE: I have a small one on my left hip but I guess like 113
for me comparing them like I kind of forget about my hip even. 109
though sometimes it hurts but like not as common and not as much
as my arm. So when I'm asked questions like this, usually like
I only answer for my arm. Because like these two questions I've
seen before together and usually they mirror each other for me,
like they are always the same number. Because like I don't 132
really add anything else to the number when I say overall.

INTERVIEWER: And that the one in your left hip and it doesn't
hurt as much as the one on your right?

INTERVIEWEE: No, not at all.

INTERVIEWER: And so if we asked you to rate them together at 113
their worst, you feel like they would be the same rating? 130

INTERVIEWEE: Yes. I mean I don't know how to like describe it
but I just kind of feel like I forget about my hip sometimes
just because like if I really had to think about it, I would say
like yes, my hip like hurts sometimes. But it wouldn't really
make like a difference in the overall pain so I kind of just
like only answer for my arm.

INTERVIEWER: Because your arm you said has this kind of base
level. It sounds like the hip one -

INTERVIEWEE: The hip one it does go down to a zero. I think my

Themes: Pain Intensity



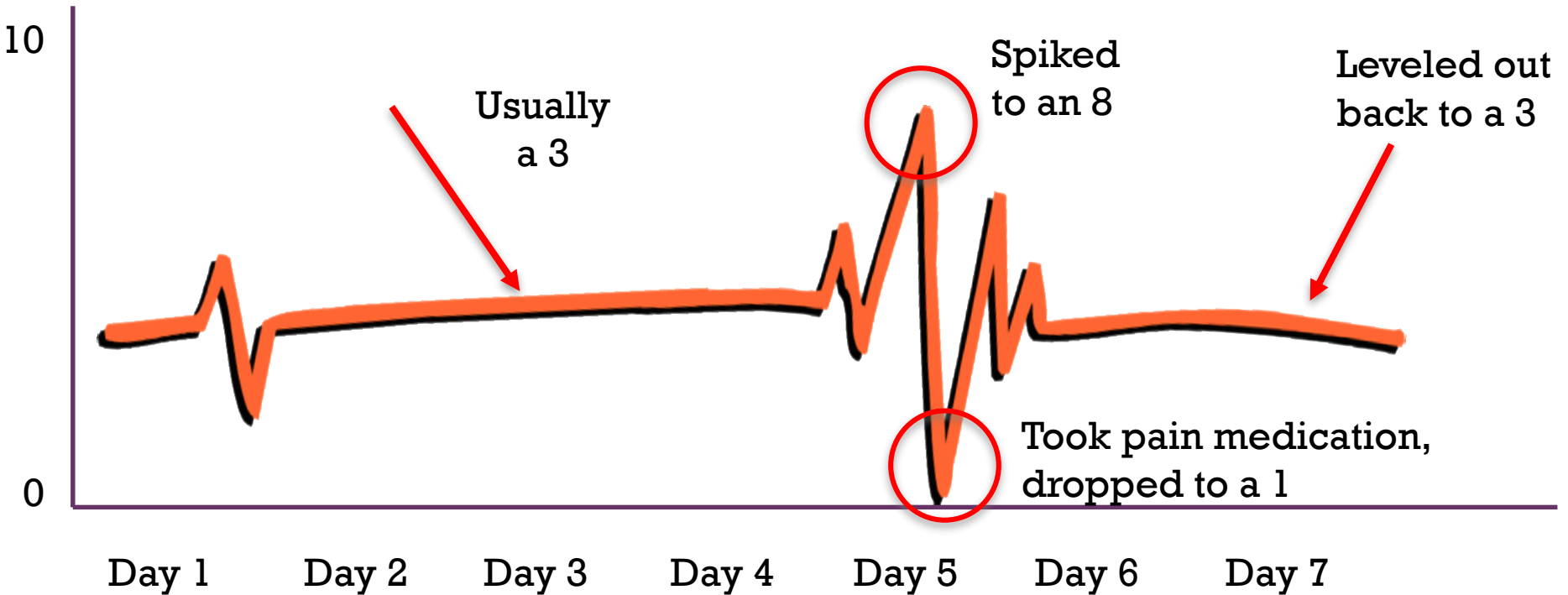
- Pain intensity is ***very difficult*** to capture for patients with NF1 and chronic pain
 - Different types of pain
 - They experience both acute pain episodes and chronic daily pain
 - Questions about “overall pain” are confusing and difficult to answer
 - Patients are answering the questions in qualitatively different ways
 - Patient’s describe pain intensity in different ways
 - The 0-10 scale
 - Descriptive Terms
 - Some measure it by the need to take pain medication

Themes: Pain Variability

- Significant amount of pain variability
 - Baseline level of pain
 - Spikes of pain
 - Good days and Bad days



Pain Variability



Just one number? Maybe if given often...

Pain Intensity and Variability

“Agony. I’ll wake up at like maybe a 5 or a 6, but by the end of the day...it goes from 5 to 6 to, I’d say even above a 10.”



“It’s like stepping on a Lego.”



“It’s always around a 3, and then just out of nowhere it will start to hurt...like an 8 and then if I hit my arm it would be a 9 or a 10.”



Pain Intensity and Variability



“Some days I might feel good, like ‘I can do this,’ then 2 to 3 days later you’re back up to a 9.”



“Some days you wake up and there’s no pain and then some days you just want to get run over by a truck.”



“Some days...it’s like a steak knife stabbing you. Sometimes it gives you that butter knife feeling, still pain, but duller.”



Themes – Recall Period

- “Past 7 days”
 - May miss “important pain events”
 - Causes patients to disregard 7 day recall period
 - ...or the 7 day period may not accurately represent the patient’s real experience of chronic pain
 - Can recall memorable pain “spikes” for longer periods of time
 - For chronic pain rely on recency (1-3 days)
 - Patients would like some way to capture pain variability



Themes – Recall Period

“This [pain] happened on Wednesday...that was 10 days ago, but nothing happened in the past 7 days.”



“I just thought of the whole week and tried to determine what was my worst day and my worst moment.”

“I can’t remember all the pain[s] that I had because I have different pains [on] different days.”



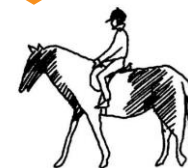
New Topics from Patients

- Daily activities lead to pain
 - Instead of pain interfering with their day-to-day life, patients reported participating in their day-to-day activities and then experiencing significant pain afterwards
 - This was not captured by our measures

“Like if you do some heavy lifting you may feel good for a minute, but later on you’re going to pay for it.”



“Because the more activity I do, the worse off I am. Like horseback riding; while I’m doing [it] I’m fine, but the day after I’m wiped and exhausted because I’m in so much pain.”



New Topics from Patients

- Difficulty with measures related to learning disabilities and other cognitive difficulties
 - Difficulty with reading – having it read either by a nurse or electronically
 - Poor handwriting/spelling – embarrassment
 - Difficulty understanding some vague/complex questions

“It’s always better if somebody asks me questions because I’m LD, so handing me a paper does nothing for me because I’m not going to understand it.”



“You want me to say ‘it hurts on the left side and it’s numbing,’ I can’t write that...for you to ask me to spell anything out, I’m not going to do it and you’re not going to know what pain I’m in because I can’t [write it.]”



New Topics from Patients



- More frequent ratings at home
 - Most participants feel that daily ratings of your pain would more accurately measure their pain
 - General willingness to complete daily home ratings if part of a clinical trial
 - Most are open to an electronic version if completed at home (i.e. an app or email)

More Frequent Home Ratings

“I would probably do it twice a day. How I feel when I wake up and...at night.”



“I would do it, but it would be hard for me because I don’t usually like doing that kind of stuff.”



“I think it [an app] would be good for me because I always have my phone with me.”



“If you’re doing a clinical trial you should do a daily diary. I could remember on a daily basis, but I’m otherwise not going to remember to tell you what I did last Wednesday unless I was in excruciating pain.”



Barriers to Patient Engagement

- **Restricted sample**
 - NF is a relatively rare disease
 - Patients must have a PN and pain
- **Logistical problems**
 - Driving
 - Time
 - Recruitment pool is often spread out over a large area
- **A small number of patients were hesitant to discuss personal information in a group**
- **Methodological restrictions**
 - Focus groups are “gold standard” in most cases, but difficult with such a restricted sample

Strategies for Managing Barriers

- Conduct research across multiple sites
 - Provides access to different populations
- Engage people the patients KNOW in recruitment
 - Doctors, clinic nurses, clinic psychologists
- Be flexible in scheduling, afternoons, evenings, weekends
- Overschedule!



Benefits to Patient Engagement in Research and PRO Development



- Patients are generally excited to participate and feel a sense of connectedness and empowerment, even patients who were initially hesitant to participate
- Adds to validity of items above and beyond expert opinion
- Follows FDA guidance for patient involvement in measure development
- Provides new and insightful information not previously considered
- Fulfilling, interesting, and fun!

Focus Group
Participant:
“I’m into it now,
let’s get it done!”



In closing...

- Engaging patients in the PRO development process is essential to create reliable and valid measures specifically designed for patients with NF1
- Acknowledgements
 - Funding: NCI Intramural Research Program and Neurofibromatosis Therapeutic Acceleration Program
 - University of Chicago (Jim Tonsguard and Cynthia Mackensie)
 - CNMC (Karin Walsh and Tess Kennedy)
 - CCHMC (Elizabeth Schorry and Sara Manning)
 - All the patients and parents who have participated in our groups and interviews

