*ACTTION-APS*

*Pain Taxonomy Meeting*

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*July 18, 2014*

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*A Matter of Record*

*(301) 890-4188*

ACTTION-APS PAIN TAXONOMY MEETING

Friday, July 18, 2014
8:01 a.m. to 12:43 p.m.

Westin Annapolis
Annapolis, Maryland



C O N T E N T S





P R O C E E D I N G S

(8:01 a.m.)

ACTTION Welcome and Introductions

DR. TURK: Welcome. Thank you all for being here. My name is Dennis Turk, for those that don't know me. This is going to be an exciting, interesting, challenging project that we are undertaking, and we are greatly appreciative. And I'm speaking for the organizing committee, which is Bob Dworkin, who's sitting here in the front; Roger Fillingim, who's somewhere -- there he is, where I can't see him -- Steve Bruehl -- Steve, where are you? There's Steve Bruehl. Eva Widerstrom-Noga, there she is hiding in the back.

We were the organizers -- perpetrators if you will -- trying to put this together. I want to thank APS as well as ACTTION for supporting this. The intent early on was to try to get as many people involved with expertise and to get support from appropriate organizations to partner with ACTTION, and I'll tell you a little bit about ACTTION in a moment.



Before I start formally doing things, some housekeeping details for you to pay attention to so that you're aware. By the way, so you know you are in the right place, this is the ACTTION-APS taxonomy meeting. If you're not here for that reason, good time to leave. And let me tell you, I have been to meetings where people got up and left.

(Laughter.)

DR. TURK: And the worse one was when people said, "I hear they have better food next-door. I'm going there." So we don't want that.

Housekeeping details. There is internet access in the room. You may access the internet by selecting "Western Conference" and using the password "Western7" for those of you who have computers and want to do that. Please silence your cell phones or put them on vibrate or something.

Microphones. This is important for you to know. This is going to be transcribed, and the transcription of these proceedings is going to be on the ACTTION website. The microphones in front of you are voice activated. You don't have to push

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any buttons.
Is that correct? Yes, voice activated. Are these the type that when you have a certain number of people, it will block people out?
(Inaudible response.)
DR. TURK: Okay. Because we don't want to pick up too much ambient noise, they are fairly low. Since we're transcribing, please speak into the microphone when you want to say something. And please say your name because, again, this is going to be transcribed. And if you've ever tried to transcribe, you know what it's like to try to have multiple people not saying things or not talking in the microphone. So please do that. We will remind you of this again because this is something that we all tend to forget.
The meeting is being recorded and transcribed. Lunch is going to be in the Capital B/C Room, which is in the lobby. Check-out time is 12:00 tomorrow. You may check your luggage at the bell stands, the usual kinds of things there.
Taxis may be ordered to return to the

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different airports, the registration desk. And you all should have picked up your name tags. Valorie Thompson, who's sitting in the back on my right, your left, and Andrea, she's outside, they can assist you. And they have been tremendously helpful to us in organizing this meeting.
They will continue to be helpful to us in anything that comes up during the meeting or after the meeting that you need. They will help us arrange for taxis when we want to leave here, if people are going to different airports at different times. To the extent that people want to share those, that will be helpful to do. If you're in any need for any assistance, they're available to you.
So thank you, Valorie and Andrea -- please tell her that -- for all the assistance.
One of the housekeeping things that I don't see on there is where the restrooms are, which people always ask.
MS. THOMAS: (Inaudible - off microphone.)
DR. TURK: Okay. Restrooms are back toward

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the lobby, up the ramp, to the left. And I'm sure there will be signage for that.
So that's sort of the basic conference. Mute your phone. Talk into the microphone. Say your name when you're going to speak. Try not to have multiple people talking at the same time. I know that's tough because you want to jump in and get into these things.
Now, the sessions for the breakouts, those will or will not be transcribed?
MS. THOMPSON: They will not.
DR. TURK: They will not be transcribed. So therefore, this only applies when we're in this particular room. And we're not going to be taping you on the breaks.
So this is the breakout assignments, which are in your handouts for you to know. If you didn't know, these are the different working groups that are going to be here: neuropathic pain, spine pain, fibromyalgia and chronic myofascial or widespread pain, TMD and facial pain, visceral pain, cancer pain, sickle cell pain. There is one

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other working group which couldn't be here, which is on arthritides. Is that the correct work that I'm using, arthritis and other related conditions of that kind? Yes. And they will have a separate meeting to basically do what we're doing here.
We obviously didn't cover every possible area that could be covered. We couldn't do it all at one time, but these are the ones we're going to be starting with. The room assignments will appear in the meeting agenda, so you could either write them down now or see them in your agenda. We will have breakouts after lunch, and we'll remind you of these assignments at that point.
So again, this is why you're here, and this is the challenge that you all hear and you all signed on to. And I want to congratulate you for signing on. And I also want to tell you that that means you're going to have to do some work.
What is ACTTION in case you're not familiar with it? Well, this is what it stands for: Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and

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Networks. And if you know anything at all, you need to know about ACTTION. Bob Dworkin is the star of coming up with acronyms. So if in fact you need an acronym for any grant you're submitting or any project you're doing, Bob's company is called Acronyms Are Us --

(Laughter.)

DR. TURK: -- and he's quite willing to take your requests.

What's the mission of ACTTION? It's a public/private partnership with the United States Food and Drug Administration to identify, prioritize, sponsor, coordinate, promote innovative activities -- which is why you're here -- with a special interest in optimizing clinical trials that will expedite discovery/development of improved analgesic, anesthetic, and addiction treatments for the benefit of the public health.

That's what we're all about, a lot of words. But the bottom line of the idea is trying to come up with better methodologies, better strategies, and better ways to accomplish the types of clinical

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trials in these different areas. And anything that we can do -- one of the things -- the reason for this particular working group, or group, is that when you read your literatures in all your different areas, I'm sure each of you have read numerable articles that complain about the fact that it's hard to do meta-analysis.

People don't agree on what the diagnostic classifications are, the terminology, the assessment methods, and we really need to set something common. We agree, and we think that's why this is one of the most important things that ACTTION has undertaken, is to move this along.

If you want to know more about ACTTION, don't try and read this, but ACTTION.org is the website. You can go see. This is where the transcripts will occur of this meeting. In probably 4 to 6 weeks, if not sooner, we'll try and get everything on there. That's to make it available to you to see what was there, as well as anybody else who's interested.

You could argue that, gee, we should have

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10,000 people in the room because there are people in so many different areas who are interested. It's just not feasible to do that. So what we tried to do is identify chairs or co-chairs of the working groups who are knowledgeable people, ask them to populate their working groups with a set of people.

Acknowledging that you can't possibly have everybody there, we hope that we will try to enlist through peer review and other methods and that other groups/individuals will look at the fruits of your labor, if you will, to give us feedback/input on those as they go on. And they'll be mounted on this particular site.

Now, the tattooist will be coming in this afternoon because this is going to be tattooed on your arm, so you can't possibly forget this.

What are the dimensions? We have a framework for all of the classifications. You're going to be hearing more about that from Roger. You should have read the article. I hope you'll be hearing more about it from Steve Bruehl, from Eva,

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from Sam Dworkin. But this is what you need to keep in mind because this is the organization of everything you're going to do. There are different dimensions that should be considered and put into every one of the conditions that you're going to be examining while you're here and that we eventually move forward.

First is what are the core diagnostic criteria? Second is what are the common features? These two are the ones that you're probably going to spend the greatest amount of time at this particular meeting. But in addition to that, we also have common medical comorbidities, neurobiological, psychosocial, and functional consequences. And notice where putative are neurobiological, psychosocial mechanisms, risk factors, and protective factors.

The order with which these are is not to emphasize priority because if you read the manuscript, as you should have, there was a lot of discussion in the original group that many of you participated in, about the importance of looking at

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mechanisms. And the only reason that we didn't push this even harder was because we all agreed that in any many of the areas, the data just isn't there yet. It doesn't mean in the future it won't be, and we hope that this will inspire people to get into it.

So these are the AAPT dimensions. So when Roger describes for you the framework about what you're going to be doing over the days, this is what we're fitting it to. Each one of you has this on your arm because every time you're in your meetings, this is what you're trying to accomplish.

You will notice also that there are several people, or a number of people, who are not assigned to any specific working group, and they're what we're calling "facilitators." What we mean by that is that we intentionally put people, who had no particular expertise for the specific diagnostic group that they're being assigned to, to serve to help push this along.

They are not going to be the chairs of the sessions. They're not going to lead the sessions.

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But they're going to be there initially as observers. But if they see things getting into the details, or getting lost, or spending too much time, they're going to keep encouraging you and reminding you.

So you will see who those people are. They will be assigned to specific working groups intentionally. In case you're wondering, why is Dennis Turk, who has done nothing in the world of cancer pain, going to the cancer pain one, that's why I'm there; because since I don't know about cancer pain, I'm not going to get into the nuances that the experts are going to know. But I at least can try and make sure that they're moving toward this. And the same will apply for all the other working groups.

At the end of today, although it's not on the agenda, we are going to try and meet with all the facilitators and all the working group chairs probably 4:30-ish for about a half hour just to see how it went, what's happening, any difficulties that are coming up.

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So if you're a working group chair or one of the facilitators, when we break at 4:30, we'll have a little break so you can go out and use the restroom or grab some coffee or something, but then have a short meeting just to go over how things are progressing and developing and any dilemmas that you're running into.

So that's the dimensions you're going to be working on. Everything is going to be fit to that framework. The overall objective is to develop a comprehensive, evidence-based, chronic pain taxonomy that's described in the paper that is in the Journal of Pain that Roger was the first author on, eventually to do this.

Now, that does not mean tomorrow. It doesn't mean next week. It doesn't mean at the end of the two days you're here, it's all going to be accomplished. But this is what we really want to be able to do. And we realize that this is version 1.0, and as new data comes in, as new people come get involved, this will advance. But this is our first shot at this.

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For this particular meeting specifically, we want you, in your working groups as well as in the presentations this morning, to discuss important considerations and provide suggestions regarding the classifications of persons with a set of prevalent, painful conditions within each working group.

Notice that this is not intended to be exhaustive, so every working group will not cover every possible diagnosis within that classification. In some areas, there are a lot more of these; in others, there are fewer, so it's less of an issue. But the idea was we asked the working group chairs and the working groups to identify what may be the most prevalent conditions under that particular grouping. Start there, and we'll worry about some other less prevalent conditions later on.

So it's not intended to be exhaustive. So in case you're wondering how come we didn't cover disease X or condition Y, it fits under here, it's because the working group chairs decided that the

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most prevalent conditions were the ones they selected, and we may come back to those at some time in the future.

We want to propose in addition to where we are now, we want to think about a research agenda and preliminary studies necessary to validate each of the classifications. And you'll be hearing about a number of different approaches that have been used in the area of temporomandibular disorders, in the area of spinal cord injuries, in the area of old RSD -- now complex regional pain -- and how those groups have actually gone about trying to gather the kinds of information, different approaches, different models

We want you to be thinking about this because ACTTION will be able to assist, or may be able to assist, to gather some of the data to help in this validation and/or liability process. It doesn't mean that it's going to do every study that's ever needed to be done and there won't be more, but at least we can help the process. And you'll be hearing more about that as we go along.

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So in addition to working toward the classification, it's also identifying where are the weaknesses, where are holes, where is the information we need to get, what would help support what we've done, and then possibly moving forward from there.

Plan for preparation of manuscripts. We are hoping to have a manuscript as the one that Roger had put in the Journal of Pain. Because this is in combination with the American Pain Society, we're going to try to -- and we have Mark Janssen's, I believe, approval to do this, is to try publish all these articles for the specific conditions in the Journal of Pain. They won't all appear in one issue all at the same time. The idea is that as they're ready, they'll start staggering. They'll start coming out.

At the end of the process, we'll then do a compendium, which will pull all those together, plus have a set of background papers explaining the rationale and the logic, some of the information that can't go into those manuscripts. So the idea

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is that we will eventually have a compendium of all of these, but initially, it will start out with Roger's framework first. The one or two conditions that are farther along, they'll come up sooner, and those that are taking longer, later. You will see that we have some kind of time framework for this.

So this is what you're going to be doing hopefully at this meeting.

UNIDENTIFIED SPEAKER: (Inaudible - off mike.)

DR. TURK: Now today, this is July 2014 -- no. We are not going to do that. We're going to start, and we're going to go to 2015, and then we'll have mission accomplished. So you are going to do this by -- now, I did exercise a picture of our former president that came with this. I think we want to be politically correct. But this is what we're going to try and do.

So now it's going to seem, may seem -- seems to me overwhelming. We are in fact going to accomplish this plight. Working with the working groups, by working with you individually, we're

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going to push this along, which is why I said thank you for volunteering, but now you get to do the work. And of course, on your CV, you'll want to put that you were on these working groups. This is very important for your future.

So that's where we're going to go. You're going to hear less from me. This morning, you're going to hear presentations to help us get to that starting point, to get everybody on the same page, if you will, to understand where we're going, to understand about how others have done similar things in the past and how this is pulled together.

Then after, we'll have a panel to answer any questions that you may have at that point. Lunch. And then you'll go to these breakout sessions. And remember, in the breakout sessions, it does tell you where you're going to be going for the different groups. We hope you will do that. You will also have facilitators in there.

The last thing I'm going to do before I turn this over to Roger is remind you, the microphones, please speak into them. Say your name. Try to

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make sure that that information is in there because it is going to be transcribed, and our transcription people very much would appreciate you doing that.

So thank you very much for being here. It's a delight to have this many people. For those that I don't know, I look forward to meeting you over the time that we're here.

Roger, do you want to take over?

Presentation - Roger Fillingim

DR. FILLINGIM: Good morning, everyone. I want to talk a little bit about the frameworks since this is what you're going to be applying your diagnostic criteria to. So first I'll give you a brief history of this initiative, talk about some of the issues that we discuss at the previous meetings since many of you were not here. Then we'll talk about the current framework and future activities.

I'm not sure if you can read that in the back, but this is sort of a timeline of this initiative. Some things probably happened before

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September 2012; that is, Bob and Dennis and John Loeser were talking about this. But September of 2012 is when the American Pain Society came into the picture, and this became an ACTTION-APS partnership.

Bob sent me an email in October 2012. The APS board provided its initial approval. Formal approval was in January of '13, and then there was an announcement in the ACTTION newsletter of the partnership. That was October 2012. For the next six-plus months, there was a lot of planning in the background. Many of you were being contacted to get involved.

Then the Pain Research Forum, which some of you may be familiar with, did an article on this initiative, and that was posted in April of last year. We had our launch meeting May of last year. And since then, working group chairs have been identified, and they've invited working group members to get involved.

We submitted the initial article in November. It was accepted in January and

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fast-tracked for publication. And the working groups, many have been meeting via conference call, and they've started their work. Of course, we're here now at the second AAPT meeting. And of course, in September, everyone will publish their --

(Laughter.)

DR. FILLINGIM: -- oh, I'm sorry. Okay.

So I just thought to give you a little context, I'd give you some excerpts from what's going on. This is from the initial email that Bob sent me, which was helpful for me to go back and read to remember why we're doing what we're doing. And I think it's interesting.

Of course, we're developing a comprehensive pain taxonomy. And Bob says it's essential so that consistent and accurate diagnoses are used for clinical research, clinical trials, and to facilitate comparisons across studies for systematic reviews and meta-analyses. It's also critical for regulatory reviews of new drug applications. So this provides some rationale for

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what we're doing.

Then from the article published in the newsletter just announcing the initiative, the aims are to establish a coordinated framework for pain diagnosis and classification to provide evidence-based diagnostic criteria for the major acute -- although we're not doing that yet -- and chronic pain conditions, and to broadly disseminate the pain classification and taxonomy so that it will have the greatest impact.

So that's sort of where we came from and what got this ball rolling. There were a lot of discussions before the launch meeting last year among those of us who were on the organizing committee. I would necessarily say that we've answered all of these questions, but these have been questions that we've considered. And one of the ones that came up as we were doing the Pain Research Forum article and have talked to other people is how does AAPT relate to the ongoing IASP pain taxonomy efforts?

I suspect the most honest answer is we don't

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know because we don't know exactly what IASP is doing, although it has to do with World Health Organization and ICD-11. So it appears that there's relatively little overlap.

We did have discussions with IASP in getting this started with some back and forth. But Fernando Cervero, who at that time was the president, really had no problems with the American Pain Society, which is a chapter of IASP, getting involved in this initiative because our aims from our view and his view did not overlap greatly with what they were doing with taxonomy.

Another question that has come up is, is what we're doing going to be used for research only? Do we want to see it used in the clinic?

I think we accept that its initial application is almost certainly going to be heavily research focused, whether that's basic human research or whether those are clinical trials. But the hope is that over time, with increased research, it will get disseminated into clinical use as well, because it would be unfortunate to

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have one set of diagnostic criteria that we use in research and completely different sets of diagnostic criteria that are used in the clinical setting.

The other question, initially we thought, well, we'll make a book. We'll get a bunch of chapters, which those of you in the working groups are going to author, and we'll make a book out of it.

As we discussed this, the plan to publish, when ready, in the Journal of Pain first to make these publicly available became the most obvious choice. But in the end, we would like some kind of a volume. Whether that's a paper book, an electronic book, some other electronic medium, I think is yet to be determined, but those are some of the things that were talked about early on.

I mentioned the IASP classification. In case you haven't looked at it in a while, these are their axes. So they have five like we do, but theirs are different than ours. And then if you look at the classification system itself, you can

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go to many of the conditions in IASP and not know exactly how to determine whether a person has that condition. Right? So for many of the conditions, there aren't actually diagnostic criteria proposed; for some there are.

So we've come up with, while it does have five dimensions, it is different from this. And then the etiology I'll just make comment on because etiology is different than mechanisms. So our fifth dimension, as Dennis pointed out, is on putative mechanisms. Right? And that's not the same thing as etiology.

As you can see in some examples here, diabetic peripheral neuropathy, the etiology typically would be thought of as diabetes induced nerve damage. There might be some general mechanisms contributing, and then there are almost certainly some specific mechanisms, whether we know them or not. And so it's these mechanisms that that fifth dimension relates to in our taxonomy.

So we had the launch meeting in May of last year, and not all of you were here. Many of you

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were here. The goal of that meeting was to develop a framework that all working groups could apply in developing diagnostic criteria for chronic pain conditions.

For those of you who weren't here, the agenda looked something like this. We had a presentation on the evolution of the Diagnostic and Statistical Manual of the American Psychiatric Association because that was thought of as one of the models that was out there that had impacted the field in terms of taxonomy.

Pat Mantyh and Frank Porreca gave us a nice presentation on mechanisms and how they can inform classification. Sam, Eva, and Steve presented their experiences developing and validating diagnostic criteria for different pain conditions. We then talked about how we're going to develop this multiaxial framework and different possibilities. And then after a little blood on the walls, we figured out what we were going to do. Right?

This was a consensus meeting; not a

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unanimity meeting, but a consensus meeting, and we all agreed on a set of classification, dimensions, and then we discussed where we were going to go next. And here is one of the places we were going to go next.

There was a lot of discussion at that meeting and after by email. But some of the major points of discussion that we focused on at that meeting in developing this taxonomy are here. And probably the most challenging is this one: Should AAPT be evolutionary or revolutionary?

What I mean by that is, why not just throw out all the pain diagnoses we have now because most of them aren't mechanism-based. It doesn't necessarily help us with treatment to know that somebody has fibromyalgia. It doesn't tell us what mechanisms we need to target.

So why don't we throw all that out and say, okay, you have pain due to central sensitization, and ultimately due to central sensitization driven by this mechanism. And it doesn't matter to me where your pain is, why you got it, how long you've

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had it. This is your pain mechanism, and this is what we're going to treat. That's pretty radical, and it's not very practical, and we're not smart enough yet to do that even if we wanted to.

So we settled on evolutionary, and I'll try to validate our decision. There's an RFA out from the National Institute of Mental Health. Now, mental health has been doing this stuff for a long time, and they have poured a lot of money into classification. I don't know how much the American Psychiatric Association has spent, and made, on DSM, but it's a lot more than we're going to spend.

So their current RFA says, "The DSM diagnostic scheme has not assimilated recent breakthroughs in genetics and neuroscience. Most anomalies appear to link either with multiple diagnostic categories or with narrow subgroups within diagnoses." That sounds familiar. "A questionable assumption that the clusters of self-reported symptoms codified in the DSM define unique and homogenous disorders could be constraining advances in the biology of mental

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illness."

So they go on to say, "Notwithstanding these difficulties, there's consensus at this time that the biology of mental illness and chronic pain is insufficiently developed to support a classification scheme based on integration of genetics, neuroscience, and psychopathology."

So they've got this initiative out, this RFA out, to make this happen. So despite all the money they've spent on this and all the time and effort, they recognize we need to spend more because we're not there yet. So if they're not there yet, I'm pretty confident we're not there yet for becoming completely mechanism-based. And that's one of the reasons this is Version 1.0. Right? We're going to discover more mechanisms. Some conditions are further along in that regard than others, but as the evidence base develops, we're going to update our classifications, especially where mechanisms are concerned.

Then a couple of other points that are mentioned in the article, should we adopt a medical

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or a syndromal approach. You'll notice that we have a syndromal approach; that is people present with a set of symptoms that creates the condition rather than somebody presents with a specific pathophysiology and that defines the condition.

Then, how we should categorize these things? What are the groups of conditions? We could have said, okay, we're going to have an upper extremity pain disorders group, and they would cover hand OA. They would cover diabetic peripheral neuropathy of the upper extremity. And then another group who's doing lower extremities would handle knee OA and diabetic peripheral neuropathy at the lower extremities.

That didn't make a lot of sense to us, so we primarily went by organs system, if you will, nervous system, musculoskeletal system, so on and so forth, with location being another piece of the puzzle.

So we published the article back earlier this year. I'd like to note that I'm the first author not because I have any expertise whatsoever

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but because I said yes instead of no I think. So it's really completely arbitrary. A couple of the things that we point out in the article, one is characteristics of an ideal diagnostic system. Apparently, it's published in a really large book, which is read by a person in a white coat.

In addition to that, there's biological plausibility. It should be exhaustive -- we're not going to be exhaustive yet, but we'll see -- mutually exclusive; that is if you have on diagnosis, that means those same symptoms don't qualify you for another diagnosis. That doesn't mean you can't have two diagnoses at the same time. It should be reliable, clinically useful, and simple.

Some of the important characteristics of our initiative, which we point out in the article, number one, it should be evidence based. There are a lot of smart people in this room, and maybe off the top of your head you could tell me what you think the diagnostic criteria for irritable bowel syndrome are, or fibromyalgia are, and what you

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think is best, but we're interested in what the evidence says about this. This is one of the unique features of our initiative.

The other really unique feature is that this framework is going to be applied systematically across pain conditions. That's not true of other taxonomy efforts that have been carried out in the pain field. They tend to be isolated, and they may not overlap at all in the framework that's applied for TMD versus chronic widespread pain or something like that.

So we're trying to add some cohesion to this project. It will be multidimensional and biopsychosocial. It will be applicable for both research and clinical use. And as we've mentioned, it should evolve as new evidence emerges.

Here's the organization as we published it in the manuscript: peripheral and central nervous systems; musculoskeletal pain system; orofacial and head pain system; visceral, pelvic, and urogenital pain; and disease-associated pains not classified elsewhere. And then you see the individual working

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groups that emerge from those superordinate categories.

As Dennis already put up here, here are our five dimensions with the explanation that you may or may not be able to read. This is taken verbatim from the manuscript, so you have that already. And as Dennis mentioned, this is where the majority of your time is going to be focused for the next day and a half to two days.

For the future, what you're doing today and tomorrow is developing potential diagnostic criteria, nominating symptoms of conditions that you think and that the evidence says should be part of that diagnosis.

Then Steve will talk about some of the research activities, but it will be important to evaluate the liability and validity of those criteria. Ultimately, the working group will finalize diagnostic criteria for each of the pain conditions, and then you will disseminate that by initially publishing it in the Journal of Pain, we hope. And then we hope to have a broader

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dissemination of the combined chapters, ultimately.

So that's all I have to say. Are there any specific questions about the framework? Does anybody who was at one of these meetings want to talk about everything important that I left out? Yes, Lesley?

DR. ARNOLD: This is Lesley Arnold. I had just a question for the future perhaps in terms of applying these to children, adolescents, because many of the conditions do occur in young people, so we have to keep that in mind I think for the future.

DR. FILLINGIM: Yes. And we do have expertise in pediatric pain. I know Tonya's here, apparently not for that purpose, but you're still allowed to lend your expertise to the initiative. Elliot Krane is here. I think we initially thought about do we need specific categories for pediatrics. And if memory serves, the conclusion was, no, not specific categories, but each working group may need input from pediatric experts. And that's why we have them involved in this

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initiative.
Chris?
DR. MIASKOWSKI: Roger, Chris Miaskowski. I was wondering what the relationship is, if you know, between the DSM classification for psychiatric disorders and the ICD criteria, because I'm thinking about the future in terms of linking this taxonomy perhaps to reimbursement. And I think a lot of the reimbursement work happens within the context of the ICD criteria, and was that discussed at the last meeting, and are we thinking about that for the future.
DR. FILLINGIM: Yes, we did discuss that. I think we decided that we're not designing this for reimbursement purposes. We wouldn't necessarily want it to be an impediment to reimbursement purposes. And if there's ever substantial clinical uptake, which we hope there will be, it will need to be consistent with diagnoses that are used for reimbursement. So that's probably a future initiative. I don't know exactly how well DSM and ICD align, but we did talk about that. So that's

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probably a future activity.
DR. HASSELL: Kathy Hassell, hematology. In my world, I also deal with another syndrome [indiscernible] area called antiphospholipid antibody syndrome. And so for 20 years, the international community has attempted to devise classification criteria. To their dismay, it was applied clinically and found exclusion of many groups of people clinically because the classification criteria were rigorously designed for research purposes.
So I'm interested in the balance sought here. Often evidence is not present; expert opinion will be needed. But the expanse of these criteria will be different if one is seeking to include large populations of clinically affected individuals versus who you'd enroll in a research study. They can be very different. So I'd be interested in clarity about that, as best one can.
DR. FILLINGIM: You're going to talk about that, Steve?
DR. HASSELL: Okay, fair enough.

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DR. FILLINGIM: Yes. And Sam, you've been doing this with TMD with initially the research --
DR. S. DWORKIN: Sam Dworkin. I'll mention it. It was and is a real issue. In our work, we consider our system a diagnostic and classification system for the parts where we can provide operational research diagnostic criteria, and then the remaining characteristics are classification. For example, in chronic orofacial pain, we're not attempting psychiatric diagnoses of depression and anxiety, but they are certainly comorbidities that are very important.
We decided that the best tact that we could take was to be as scientific as possible, and we can't be responsible for the actions of others. So we put out the best product with the best evidence available, and hopefully let the data speak for itself. Our field has fringe elements --
(Laughter.)
DR. S. DWORKIN: -- that go their own way. And rather than being against them as a way of spending our lives, we would rather be in favor of

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advancing knowledge. So we just sloughed it.
DR. TURK: This is Dennis Turk. Sam, one of the reasons I said that to you was because I know it started out as research classification, and over time, it's evolved so that it's now become a clinical diagnosis.
DR. S. DWORKIN: Yes, but you're now giving me more speaking time, and I'm happy to -- as you know, I'll go on forever. So that's the basis of my talk.
DR. TURK: Okay.
DR. FILLINGIM: And maybe one more question, and then we'll move on.
DR. FITZGERALD: Mary FitzGerald. Will there be any attempt to validate what we come up with before publishing it? How do we know we're not the fringe elements?
(Laughter.)
DR. FILLINGIM: You've been carefully selected not to be the fringe element. And I think that's a nice segue to what Steve's going to talk about. First he'll talk about the CRPS, but we'll

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hear about the research activities in a little bit.

Presentation - Stephen Bruehl

DR. BRUEHL: So I'm going to answer some of those questions and really raise some issues related to the questions that were just brought up. For those of you that weren't at the talks that we gave a year ago, this will be all new. For those of you that were at that talk, I added and changed things around a little bit to make it fit a little better with what we're doing here today.

So what I'm hoping, though, is that I can give you a real-world example of how almost the same kind of situation we're faced with here was handled for a particular pain condition previously, which is complex regional pain syndrome.

In the course of talking about this, I'll talk about the kind of research we were able to do that get at the issues of validity. I will also try to remember -- and please remind me if I don't -- to talk about the difference between clinical purposes versus research purposes and what impact that has because that is an important issue.

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For those of you who may not be familiar with it, CRPS, complex regional pain syndrome, most people in the U.S. think it's neuropathic. There are people who disagree. But it's some kind of pain syndrome. It's usually occurring in the extremities. What makes it unique is that it's associated with significant involvement, signs that seem to suggest the autonomic nervous system is involved. It used to be known as several different conditions, which I'll give some names here in a second.

I wanted to mention here, though -- keep this in mind as I'm talking about the CRPS examples. So what we're doing in this process is a couple of key things. And we'll hand this out later, the working group guidelines. Those of you who haven't seen this, it's a document saying here's what each working group is supposed to do.

One of the things you're supposed to do as a working group is to do some type of systematic review, and it doesn't have to be written up as a review, but you want to at least look at the

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literature. You want to identify what the accepted diagnostic criteria are in that area if there are indeed any. I'm sure for many areas, there may not really be anything that's accepted as the standard.

If there isn't a standard, or even if there is a standard, what other options are out there? For most areas, there are going to be competing groups that may have different ways of handling diagnosis of particular pain conditions, and you just want to get the lay of the land, what all is out there.

As a very specific thing you need to get as a working group -- and this is very important from the research perspective -- in the process of doing this review, you need to identify what I've been called the universe of signs and symptoms that might characterize this disorder. This could be test results. It might be clinical things you'd see on the exam. It might be other tests you can do. It might be what the patient says about their syndrome.

Any of these things, though, that, based on

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the literature and your experience, you feel might be kind of defining features of that pain condition, you want to write those down because, ultimately, that is what is going to create the paperwork we need to be able to do the diagnostic research on down the road.

So for CRPS, known prior to 1994, is reflex sympathetic dystrophy, causalgia, and a variety of other things. No one was ever really sure if we were talking about the same condition, different conditions. There seemed to be a lot of overlap. It depended on whether you were in Europe or the U.S. as to what terminology was used.

So it was a real mess because nobody -- this is a really good example of how you could have a bunch of treatment studies done that basically leads you nowhere because every study was done on a different group of patients that was defined in a different way. And nobody knew what worked and what didn't. I can't say that has changed a lot yet, but at least we have diagnostic criteria.

I'm going to give you some examples. So

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when we went and looked at the literature on what was preexisting, what we found were several things that were used in a number of studies. One was called Kozin's criteria. And they said you have definite RSD if you've got pain and tenderness in a distal extremity; signs and/or symptoms of vasomotor instability undefined; swelling in the extremity. And they don't even require this for diagnosis but just mentioned you might have dystrophic changes, so skin, hair, nail kind of changes, that kind of thing.

So really you've got three criteria, and that was it. Now, you'll notice -- this is the European criteria set that was fairly dominant for a number of years, called Veldman's criteria. Now, they're having what's call a decision rule here. You have to have at least X number out of this list of signs and symptoms, which is a nice way to do something because then you can alter that number and change the sensitivity and specificity for research purposes versus clinical purposes.

For example, at least for the following,

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unexplained diffuse pain, that's kind of similar to what was mentioned in the last set. Skin color asymmetry, okay, that's a vasomotor sign. That's kind of similar to what was listed before.

Temperature, getting at vasomotor, but it's a different actual objective sign. So now they've split it out into two separate signs you might look at.

Diffuse edema, limited active range of motion. Range of motion wasn't even in the other criteria. Signs and symptoms increase with exercise. That wasn't in the previous criteria. And also, they're present in an area larger than the original injury, including distally.

So we got a little more specific about what was required in this one and have an actual decision rule. Gibbons & Wilson, they proposed this in the Clinical Journal of Pain. They had a list of various signs and symptoms, very specific, and said you have to have five of these to be considered having definite RSD. But you'll notice some of the same things.

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Now, they've gotten a little more specific in how they've described the pain. They're saying allodynia or hyperalgesia, certain pain characteristic. They've got the edema but not necessarily diffuse. They have skin color or hair growth lumped together. Hair growth wasn't really mentioned specifically in that last set.

So as you can see, there is some overlap between these different criteria, but each of them is kind of unique. What we want to talk about here is what the impact of these various things in the literature is. And the basic issue is different criteria mean that it is a different disease, in some sense. Since we don't know the mechanisms, if you have a syndrome that has a different set of signs and symptoms in the syndrome, you're talking about different diseases.

We've just presented three different sets of criteria. It really is talking about three different diseases potentially; we don't really know. And what it means is if you've got these multiple criteria floating out there, then no one

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knows what to use. There's nothing that's considered really the gold standard. So the inclination in many clinicians is to just start making up your own diagnostic criteria, some combination of these, or based on something you heard in training.

It's really not the best way to do diagnosis if we're trying to be able to generalize across studies, especially for looking at interventions and efficacy of interventions. And even just clinical communication, you make a referral of a patient and you want to say this patient has CRPS, you want that other professional to understand what you mean when you say that, that that's an agreed upon language.

In 1994, in Orlando, they held a meeting similar to this is my understanding. I wasn't actually there, but they invited a group of people with interest and expertise in the area and forced them to sit there for two days, in Orlando, until they came up with some diagnostic criteria for this disorder that had previously been known by all

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these different names.
What they came up with was complex regional pain syndrome, a new name that got rid of some of the baggage of the reflex; the sympathetic, because nobody was convinced it really was sympathetic; and the dystrophy because not everybody had dystrophy. So that was why there was a name change.
Now, they had problems like we will encounter in this room, which is different people have different opinions. People will fight for their opinions, and you may come up with something that doesn't really satisfy anybody. Hopefully, that's not going to be the end result, but there is the risk of that. So what we're trying to do here is get the highest level of agreement we can get on what the core of each of these sets of diagnostic criteria should be.
Now, they had that problem because they did not have research to base this on at that time, kind of like what we're going to have in this situation. And they had the same problem we have here, which is for CRPS, we didn't really know the

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pathophysiology. There was no gold standard to use. And really the best they could do is create a descriptive syndrome that would be used for diagnosis. So there's a lot of overlap between CRPS criterion development and what we're doing here.
Now, they were made to be -- this is what they claim after the fact. I don't know if this is actually true. They claim that they made it very broadly worded to capture all the variants that might be out there and that they were going to come back and revise them to make them better as we learn more in the process of doing research. Now, by making the criteria as broad as possible, what they actually did was made it so virtually anyone could get the diagnosis, and that's not necessarily very helpful. And that's something we have to kind of balance as we're doing this process.
So these are the criteria that were published by IASP in 1994. Again, they have one of these diagnostic criteria that's not required for diagnosis, which doesn't make a lot of sense for

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me.
So 2 and 3 are the really critical issues. This is continuing pain, allodynia, or hyperalgesia, with which the pain is disproportionate. So that was the key issue, was that it was disproportionate to what we knew had happened in terms of any injury. And then 3 is evidence at some time for edema, changes in skin blood flow, or abnormal sudomotor activity.
Now, that's basically the only signs and symptoms they're using to make the diagnosis. You'll notice "evidence at some time" means you don't have to have any objective signs on exam. It could solely be based on self-report, which to some extent for CRPS might make sense because the symptoms can be labile. You may have it one minute and not the next, one day and not the next. They do come and go.
That's well acknowledged that that happens, but this diagnosis says you can get it just based on coming in and saying I have swelling, even though you don't see it on the exam. And you're

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also lumping together a number of different things that seem very different, if that makes sense. Those are the questions we were asking when we looked at these criteria later on.
So do the criteria adequately capture the core defining signs and symptoms of CRPS? Well, I'll come back to this in a second. Is the structure of the criteria optimal? And what I'm saying with the structure, and what we're saying, is the way we've broken out the different signs and symptoms. For example, should it be a list of separate signs and symptoms or, as in these criteria, does it make sense to lump together edema, vasomotor changes, and sudomotor changes all in one diagnostic criterion?
So when I'm talking about structure, that's kind of what I'm talking about -- is that -- as well as the diagnostic decision rules. Do you have to have three of these? Do you need one of these? Does any of those qualify?
So that's another question you can ask, and both of those issues will influence the sensitivity

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and specificity when it comes down to making the diagnosis: sensitivity, essentially how well are we identifying people that actually do have CRPS; specificity, how well are we doing when we try to screen out people who don't have CRPS. And both of those are important.

For clinical purposes, you want to have very high sensitivity. For research purposes, you really want to probably emphasize specificity more because you want to make sure you don't accidentally get people into your study that don't really have it. That is where the balance comes in. As you increase sensitivity, specificity tends to go down and vice versa. You want to find some happy medium that is good enough for both, and I'll show you an example of that later.

I mentioned earlier this universe of signs and symptoms idea, so if you look at the literature -- and this was actually a literature going back a hundred years -- what you saw is the 1994 IASP criteria do include allodynia, hyperalgesia, skin temperature and color changes,

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so those vasomotor elements, sweating changes or sudomotor changes, and edema. All that was captured.

But if you look further in the literature, what you will see is a number of other characteristics widely accepted as part of the condition that weren't included in those 1994 criteria. So hair, nail, and skin changes were frequently mentioned, tremors, range of motion changes, hypoesthesia, like hemi-body hypoesthesia. Brain imaging was indicating CNS abnormalities. There was osteoporosis. So all these other things that weren't in these diagnostic criteria, is that appropriate to leave those out?

This is a really important thing. So we identified this universe of signs and symptoms, and we had to be looking ahead to improving the diagnostic criteria and doing research to be able to say that what we came up with was better than the 1994 criteria. The way we did that -- and this was done with no money at all other than our salary being paid by the institutions. But we did not

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have any money.

We got a group of researchers we identified across the country who were interested in CRPS, who were willing to make the effort to consistently collect clinical data on the patients that they saw that met those 1994 diagnostic criteria and in some patients who didn't meet those diagnostic criteria as a comparison group.

What we did in this forum is rather than try to quantify different levels of signs and symptoms, based on a 1 to 10 scale, simple dichotomous: is it present or is it absent? Let's not worry about the severity of it for now. And by doing that, it actually makes it easier to be more reliable, in some sense, because the decision is easier, is it there or not.

So what we did is we separately collected symptoms based on what was in the literature, so basically all those things that we were just talking about. They hyperesthesia is basically the allodynia, temperature, color, sweating, edema, dystrophic changes, and then you can describe what

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those were. Motor abnormalities can describe what they were.

So we just laid it out like this. We had the objective signs that you're singing on the exam that day that you see them, and it basically parallels the self-reported symptoms, gives a little more detail, for example, on color asymmetry; is it red? Is it blue pale? Is it modeled? Is there a scar present that makes it difficult to determine?

So we laid this out, and then we had some evaluation of touch, sensitivity, and also some range of motion, all of this on a single sheet, a little bit of descriptive information about where the pain was, was it bilateral, upper/lower extremity, how long had they had it, what type of injury started the condition.

By collecting this from every time a history and physical was done on a patient that we thought had CRPS or had one of these defined other conditions that were the comparison groups, we had consistent data that we could put into a database

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and then come back later and answer certain questions in terms of validating the diagnostic criteria we were going to come up with.

What can we do to validate diagnostic criteria on the cheap in a situation like this, where this is basically all the data that we've got? And this will be exactly what we get for AAPT diagnoses. One, is the structure of the internal relationships between CRPS signs and symptoms that were in those 1994 diagnostic criteria valid? Does it make sense to lump together vasomotor, sudomotor, and edema all in one criterion? And if you have any of those you get the diagnosis. That was a key question.

Also, a key question I thought was does it make sense to be able to get the diagnosis based only on symptoms or should we require some objective signs present when you do the exam?

External validity issues, do the criteria and the decision rules we're using adequately discriminate between CRPS patients who have known other types of conditions such as diabetic

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neuropathy, such as various kinds of peripheral neuropathy that are discrete other conditions?

So what we did for internal validation, multi-site, we got this database form and ended up with 123 patients who met the 1994 criteria. And if you know how rare CRPS is, having 123 patients is actually a pretty big deal because that's a very large data set for that condition. We all got the same information on all these people. One question was, does it make sense to include objective signs and subjective symptoms?

I'll just point out one thing here. This is something we could do with the data we collect. It's very simple, but it's useful. Check this out. So we've got these things that the historical literature said were common in CRPS, and what we discover is some are more common than others. The nail and skin changes, those dystrophic changes are present, but they're really not very common, certainly not universal. But they're common enough, they might be useful in diagnosis.

You'll also notice that if we look at the

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self-reported symptoms, like the red are the most common ones, so color changes, range of motion. And you'll notice that if you look at the frequency of signs, those same two are also the most common signs. What that told us was that when patients say I have this symptom, they actually are reporting on a real phenomenon that may just not be present that day.

Based on that, it was probably a good idea for us to include signs and symptoms in the diagnostic criteria separately because they are tapping into the same things, but we might miss one, miss the signs, if we don't also ask for symptoms because of that lability of the symptoms.

So that was really the key issue that we were able to come up with based on looking at just simple frequencies of signs and symptoms. There was nothing that every single person had, so clearly we needed to have a variety of signs and symptoms to look at to get the diagnosis.

Now, is the grouping of signs and symptoms in those 1994 criteria something that holds up when

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you look at it based on the actual data? And again, it's the one in red. And is this too low a threshold if you only have to have one of these based on self-report?

Now, we used factor analysis on that data from that data sheet, and we ended up identifying groups of signs and symptoms that seemed to hang together. And what we found was that of that list of things on that database form, what you ended up coming up with, essentially, was a sensory cluster, which were things like allodynia and hyperalgesia. That paralleled the criterion 2 in those 1994 criteria.

You got a separate grouping of vasomotor symptoms. This was the temperature and color changes. That's in criterion 3, but you'll notice it was a separate cluster from the sudomotor and edema. So the sweating changes in the edema, for whatever reason, lumped together, and they were separate from the vasomotor.

Now, in IASP criteria, those were part of the same criterion. The research was saying that

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it's actually two separate things. There's a mechanistic reason that might be able to explain why the sudomotor and edema lumped together.

Now, you'll notice motor and trophic changes, which have been reported in the literature for years as going along with this condition, were not included in the IASP criteria at all, and they form a separate cluster.

So basically, the way the current criteria were written in those 1994 criteria, you didn't tap at all into this feature that was acknowledged to be key, and it doesn't overlap with any of the other clusters. So we were actually able to get some good information by doing this background analysis on that very simple data sheet.

So we can conclude that those 1994 criteria are not internally valid. And in all likelihood, the way they are written, the way they are structured in the decision rules involved, will lead to over-diagnosis and poor specificity. This says we probably need to revise the criteria. Now, external validation -- so we're going to try to

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develop new criteria. Now we've got to be able to do the external validity to demonstrate that what we come up with is better than what was there in the 1994 criteria.

So what we want to do, for external validation, our big issue is can you distinguish CRPS from non-CRPS pain. And if you start to think about what I've already said, there's an obvious problem with doing this. There's no gold standard. We don't know the pathophysiology of this condition, so how are you going to tell whether one diagnosis is better than the other? It's not an easy question to answer, and I'm the first to admit that while you can address this, it has limitations. It's not perfect, but it's better than nothing at all.

The way we did this -- and it's a little hard to explain this, but we've essentially -- we set it up so that we've stacked the deck in favor of proving that the existing criteria are the best. And what we did is we said, okay, let's take those 1994 criteria. We're going to diagnose these

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patients according to those criteria. And now, based on other means of diagnosis, we know that this other group of patients that we've collected the same data on, we know that they have painful diabetic neuropathy, painful postherpetic neuralgia, and discrete other conditions that we know are not CRPS.

So we've got signs and symptoms in both of these groups. And now what we're going to do is say let's use those 1994 diagnostic criteria that we just used to define this group to distinguish between those two different groups. Now that has stacked the deck. And if those are good criteria, we should have 100 percent sensitivity and close to 100 percent specificity distinguishing those two groups.

Now, what's nice is using that same methodology, we can propose an alternative set of criteria and try to do the same thing, does this distinguish better than those 1994 criteria. The results surprised us a little bit. So we've got 117 CRPS patients, and we ended up with 43 patients

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that had other types of neuropathic pain as a comparison group.

We got this database form on everybody. And what we found using the original IASP criteria, under stacking the deck conditions, we got very high sensitivity, which is what we would expect, but our specificity was only .36, which is horrible. It means we were way over diagnosing CRPS using the existing diagnostic criteria, and we thought we could improve upon that.

Now, I'm going to point out we want to use this same type of process in doing the research for any one of the conditions that we might be including in our diagnostic criteria. So we might be looking -- and I'm not going to give specific examples, but just say within the neuropathic pain working group, we might have five diagnostic categories we're concerned with.

We might come up -- focus on one of those and say I want to discriminate between people that have this one and this one, these two discrete diagnostic categories. Now, it may make just as

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much sense to pick diagnostic categories as comparisons from other working groups. There's no restriction on that. But we want to get a couple of other comparison conditions to look at. But we'll talk a little more about that later.

So we thought, what can we do to make the diagnosis better? One might be to require the presence of objective signs so you can't get the diagnosis based only on self-reported symptoms. That was an obvious one. We might include motor and trophic changes in the diagnosis since they're not in there at all now. And then we might also split out those vasomotor signs and the edema and sudomotor signs into two separate diagnostic criteria. Those were some of the things we figured we could do.

We actually did some research on this. We had a meeting kind of like this. Again, experts reviewed the research literature, existing problems with CRPS diagnosis, and made recommendations for a formal revision based on some research we had done. The research that we did -- and I'll show you the

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actual criteria in a second -- allowed us to come up with an improved set of diagnostic criteria that addressed those issues that we thought we can improve upon.

One thing that was key -- and this gets at the question that was mentioned earlier -- is the decision rules. So do you need two of these or do you need three of these? We elected to actually propose two separate decision rules, depending on whether the purpose was clinical diagnosis where you want to maximize sensitivity or whether it was for research purposes, where you want to have more of an emphasis on specificity.

Now, the clinical criteria we came up with was continuing pain that was disproportionate to any inciting event; at least one symptom reported in three or more of the following categories. Now, those four categories were taken directly from the results of the factor analysis.

So we have symptoms. This is the self-reported symptoms in three of these areas. And you can see it's got temperature and skin color

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changes, edema, sweating changes. You've got the weakness, range of motion, the dystrophic changes -- tremor, dystonia -- a variety of things that might meet that criterion.

Three was not arbitrary. Three is what we ended up coming up with, but we basically tested all possibilities, 1 through 4. And then you'll see here -- I'll show this. You have objective signs, same four categories. What we ended up saying was you need two of these, but we tested 1 through 4 and basically looked at the ROC curves. It's like how do you balance sensitivity and specificity with these? What maximizes it? And it turned out that the three symptoms and the two signs seemed to be a nice balance of sensitivity and specificity for clinical purposes.

You'll notice in this case our signs pretty much parallel exactly what's in the symptoms, but do you see it that day when they're there for the exam? Research criteria, all we did is we bumped up the number of signs required to 3 instead of 2. And this actually did seem to increase specificity

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pretty -- I think it ended up being about 15 points.

You can see here -- this was actually a re-validation study. This was a second go-round of this with a totally new sample after we'd come up with these criteria. And it turned out 1994 criteria, very sensitive as they should be. The specificity was poor again, so we replicated that finding.

The Budapest clinical criteria that we developed, sensitivity was still very high. Specificity, while not perfect, was a lot better than it was with the old 1994 criteria, so we're reducing over-diagnosis. If we go to the research criteria, sensitivity drops, as you'd expect, but specificity increases further. So we're getting fewer and fewer people in our research samples that don't really have CRPS.

That's what we came up with, the procedure, since this was something we were trying to get out there and use and accepted as consensus criteria as we went to the IASP taxonomy subgroup and the board

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and said, "We've done all this. Will you make this the official criteria?" And we'd actually been in communication with them all along. At the beginning of 2012, they finally adopted it formally. So it's now official.

Now, it does -- I'll point this out because this is something that is going to occur to you at some point, and there's no good answer to it. When we came up with these new criteria, the question that started coming up clinically was what about these people that met the old diagnosis and now don't meet this? What do they have? Gee, I don't know. They don't have CRPS because we've just defined it.

We ended up with a category, which I don't like. It's garbage basket. It's the same approach DSM used. That's where we got the idea, was NOS, CRPS NOS; looks like it, smells like it, doesn't meet criteria. You don't know what else it is. You can use this label.

Now, I don't like that approach, but this is going to be something you'll probably think about

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as you're trying to decide how strictly to define the disorders. I would say to go based on -- we don't know this now, but I'd say you come up with your draft criteria. We'll try to do what research we can to demonstrate sensitivity and specificity. And we'll use the numbers to define the criteria and worry about some of these other issues later. I mean, that's the whole point of AAPT, is we're trying to base this on data rather than just an opinion. So that's my best response to that.

Elliot?

DR. CRANE: This is Elliot Crane. Did you misspeak? You said "the patients who no longer meet criteria have pain syndrome NOS." They don't have CRPS NOS.

DR. BRUEHL: No. I'm sorry. It was called CRPS NOS. It was actually listed in the diagnostic criteria as not really criteria, but here's what to do with those people, is you can label them CRPS NOS.

DR. SMITH: This is Wally Smith. Once again, would you tell us about how you got the gold

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standard? It sounded like it was artificial based on clinical intuition; or is it something else?

DR. BRUEHL: I'm sorry. The gold standard?

DR. SMITH: The gold standard, yes.

DR. BRUEHL: Yes. There is no gold standard, so what we used as our gold standard was the accepted criteria at the time. So that was our reference point --

DR. SMITH: The '93?

DR. BRUEHL: The 1994 criteria.

DR. SMITH: '94?

DR. BRUEHL: And what the research allowed us to do was to test for relative improvements over those diagnostic criteria. That doesn't say that we're getting at the underlying pathophysiology any better because we don't know that, but we could at least, using the kind of procedures I described here, find out whether any criteria we came up with that were a modification were better than those 1994 criteria.

DR. SMITH: How do you advise groups, like the sickle cell group, that are starting with no

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already accepted diagnostic criteria for some syndrome?

DR. BRUEHL: I was afraid you were going to ask that. Yes. That is a tough one. And I think what we're going to have to do is see what the data tell us to some extent. I think there are things we could do -- for example, like the factor analysis -- to look at --

DR. SMITH: Okay.

DR. BRUEHL: -- some of those issues that would at least give us something empirical to go by when we're trying to structure the diagnostic criteria. It honestly may at this point be difficult, for that particular instance, to be able to demonstrate that those criteria are able to distinguish between sickle cell and some other condition against any meaningful reference point. I mean, I'm not sure what we'd use as a reference point in that situation.

DR. R. DWORKIN: Bob Dworkin. Stephen, in those situations, couldn't the criterion be an expert clinical diagnosis, like one by Dr. Smith?

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So that's the best criterion we've got at present.
DR. BRUEHL: Yes.
DR. R. DWORKIN: And then you'd bootstrap your way up; you bootstrap yourself up.
DR. BRUEHL: Yes, that's a good suggestion. So, yes. I guess that would be original. But you might want to say like you have two expert clinicians and demonstrate that they have agreement that a given patient has a diagnosis, and that would be a --
DR. SMITH: Well, now you're measuring kappa scores.
DR. BRUEHL: How do you what?
DR. SMITH: Now you're measuring kappa scores in that clinical agreement.
DR. BRUEHL: Well, in that instance you are. And you're only using kappa scores to document that your expert diagnosis is reasonable. Now again, it doesn't mean that it is reasonable according to any meaningful outside standard, but it becomes something to use as a reference point.
So you might say that -- we have to think

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about this some more because I haven't really thought about this -- you've got -- your expert opinion becomes the standard. And then you say can our diagnostic criteria agree with that really well, with an expert diagnosis. And if the decision rules and layout agrees well with expert diagnosis, those criteria become a starting point for improving things in the future maybe.
Does that make sense?
DR. SMITH: Yes.
DR. BRUEHL: Okay.
DR. FREEMAN: Roy Freeman. The two challenges with this kind of research, the gold standard, which you've addressed, and the other is the comparator group when you're looking at sensitivity and specificity. And it looked like you had 40 subjects in your comparator group, PHN and DPN. And I was wondering how you chose those subjects.
To be specific, I think it would be very easy to come up with 20 patients with diabetic peripheral neuropathy who would fulfill all of

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those criteria while it would be equally easy to come up with 20 subjects with diabetic peripheral neuropathy, who would fulfill none of your criteria. So I think -- maybe to ask the question, how did you choose those 40 subjects, and what do you suggest going forward?
DR. BRUEHL: The key issue was -- like with diabetic neuropathy, you have to have the -- and this is something we talked about last night. You have to have the medical diagnosis of diabetes, and then you've got in the literature the particular patterns of pain, distal extremity pain primarily, in the context of diabetes.
I honestly can't remember exactly what it was, but the key issue was in order to get the CRPS diagnosis, that has to be no other condition that can explain it. In the case of diabetic peripheral neuropathy pain, we know that diabetes can explain it. You've got an actual disease-related neuropathy explaining the condition.
That was the key issue, was that we knew that the mechanism wasn't the same as traditional

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CRPS. And if you're going to come up with diagnostic criteria, you -- I'm trying to think of the best way to say this.
If you have two conditions that look identical, the utility of making a distinction between them is pretty low. I mean, clinically, if they look exactly the same, are they really different conditions? So part of what we were proposing was that the CRPS should look a little different based on the autonomic features that you get with diabetic peripheral neuropathy.
Now, we didn't have any great rationale for choosing DPN particularly. It was just that it was a convenient sample. It was something we could get that we knew wasn't CRPS that we could collect the same kind of data on.
For our purposes, we probably want to do a better job of defining how our comparison groups are picked. An advantage we will have in this group is that we will be doing a comprehensive literature search of diagnostic criteria for all the different conditions in each working group. So

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when it comes time to pick a comparator, we can at least say here's the dominant diagnostic criteria that's out there for that disorder. Let's define that group this way, and we'll define our other group this way and see -- ability to distinguish between groups by using our new criteria and then modifying decision rules, things like that.

This is an incredibly unsatisfying way to do research for me because it's really you're having to kind of do things that there's a lot of smoke and mirrors involved. But it really is the only kind of research you can do when you don't have an outside criterion to use as a reference point.

DR. FREEMAN: I could elaborate maybe just very briefly. The challenge is, for example, with diabetic peripheral neuropathy, you will have many subjects. You will have them as vasomotor changes, sweats, abnormalities, trophic changes, nail changes, skin changes, hair changes, all of your core diagnostic criteria. And so the challenge in determining sensitivity and specificity is really picking not [inaudible – intermittent

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audio] -- suffice it to say it is a challenge.

DR. BRUEHL: I think all we can do reasonably is use what's out there as diagnostic criteria as our reference point to start with for defining the groups. And then we go look at relative improvements, like when we change how we diagnose it, can we improve over that.

DR. ZEMPSKY: Bill Zempsky. I'm going to beat the pediatric horse again. I assume this was all validated in an adult sample. Clearly, regardless of the group we're in -- and I don't even know if pediatric CRPS and adult CRPS are the same disorder anyway. We're going to be challenged in a lot of these groups with looking at pediatrics as maybe a whole different disorder. And I wonder if down the road we need to have a pediatric subgroup, that after these groups have gone through, look at each group's outcome and say what do we need to do specifically for pediatrics.

DR. BRUEHL: Correct me. You guys that were at that first meeting, now my recollection is the way we elected to handle that was that, in general,

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we were going to make the assumption, going into this, that if these are real disorders that have some underlying mechanism, that there should be a lot of overlap in the signs and symptoms that might diagnose adult and pediatric patients with the same condition.

But I think that one thing we had talked about was doing kind of like in the DSM -- like the DSM-IV, in depression it would say you have these criteria, but then it would say, but for children may come out as this symptom instead. So you'd have like an option like that, where it kind of modifies the criteria so you can include something a little bit different if it's an adolescent or a child. That is what I recollect, and that is something that certainly can be discussed as we're going through this process.

DR. R. DWORKIN: Bob Dworkin. I think this is really a working group decision. So in some cases, including the children, there might be, as Steve is saying, a kind of qualification to the criteria. In other cases, it might be an entirely

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separate diagnosis. So the osteoarthritis group isn't here this week, and they're having their own meeting. But I could imagine, exactly as you suggest, they decide to have a sub-working group on JIA because they see JIA as different enough that it isn't the qualification of another adult diagnosis.

So these decisions about how to include pediatric conditions within the purview of the working group really have to be made at the working group level. And all of those different approaches would be fine with us.

DR. S. DWORKIN: This is like a deja vu. Sam Dworkin. This is deja vu all over again. And I would really strongly just encourage the approach that you outlined, beginning with experts at least clumping together people who look alike and maybe act alike and have common clinical characteristics. And if they're well defined, then the research will either validate or not the utility of using that approach. And the data will begin to distinguish subgroups within the groups or the errors in the

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diagnosis.
So along those lines, we call a system a diagnostic and classification system. And the reason for that is that diagnosis is a technical term that has clear implications for treatment, and classification is a bunch of researchers are going to classify people by some way or another.
So we took a different -- the tact that we took was to emphasize to be much more concerned with specificity for diagnostic criteria because if you had to do something to somebody that didn't have the thing that you were doing to them, the reason you were doing it, it was better to do research on people who didn't have the condition than to do treatment on people who didn't have the condition.
So we leaned heavily towards saying before we're going to call it diagnostic criteria, we have to have very high specificity so there are no false positives if they're going to be in treatment. We could be a little bit more, or a lot more, or let the data determine how much more relaxed we had to

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be when it came to research.
So the question of whether this group is now a group formulating research propositions or diagnostic propositions is going to depend on the clinical condition. And they're going to differ in their stages of development as approximating diagnostic criteria.
But I would encourage people to begin, for openers, whereas there is emphasis on research criteria. It is safer. It's both politically safer and scientifically safer to do. Even though it takes away some of the excitement and the usefulness for people right away of not focusing on diagnostic criteria, it would be premature -- it would be undesirably premature to come up with diagnostic criteria which were not well validated, and that has to take some time.
DR. BRUEHL: Yes, I agree with that. John?
DR. FARRAR: John Farrar. Sam, what you were just saying I think makes good sense. We need to keep in mind the reason why we need these categories in the first place, and there are

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multiple reasons. One of them, and the primary one, is ultimately treatment, how are we going to treat our patients? But we also want to understand and be able to explain to them why they're in the condition they are. We also want to hopefully be able to prevent some of this perhaps from happening, give a prognosis as to what's likely to happen to them, and in the real world come up with some level of disability that they're entitled to.
Each of those are going to be distinctly different. And the model that I like here is postherpetic neuralgia. The definition of postherpetic neuralgia is you mostly have to at least had the rash.
Now, we occasionally say people didn't have the rash and have it. But the point is that they had an infection with a particular agent. However, if you think about the pain that they have, it depends on which neurons in their spinal cord were damaged and which system was more damaged than others. Mike Rowbotham's done some interesting work in terms of looking at trying to differentiate

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those two.
I think the process that we're going to go through here is going to run into that issue, the idea of what it is that caused it and what the result is, multiple times. And we need to be careful not to get too caught up in trying to dissect that into small pieces.
I just would make the point that we need to keep focus, I think, on what it is that we're trying to do. And it seems to me that the primary goal here is to ultimately be able to make a diagnosis and then ultimately treat those folks and not to get too caught up into micro-dissecting those particular issues, at least at the first go-round.
Clearly, the treatment aspect of things, one could argue that the best way to predicting whether people are going to respond to treatment is to give them the drug and see what happens, and then back out of that and say, "Well --" and we all do this, right? -- "must have been."
I think the CRPS issue comes up in what Roy

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was saying, is that maybe the diabetic neuropathy patient actually has CRPS as a manifestation of their diabetic neuropathy, or maybe the postherpetic neuralgia has some issues related to this that are brought about in a way that makes sense. How we're going to dissect that, I'm not sure.

DR. BRUEHL: I don't think we know enough right now to be able to make sense of all that. I would agree -- and that was kind of what I was getting at earlier when I said if you have two conditions -- well, two things that currently are considered separate conditions that, when you get right down to it, look exactly the same clinically and we don't know the mechanism, what is the point of making a distinction between those two different conditions? Are they really two different conditions?

DR. R. DWORKIN: We need to come back to that question during the discussion. I've got a note to come back --

DR. BRUEHL: For anybody who didn't get a

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question answered, we do have some other time for questions. So you can bring them up. But just to keep the process going -- because some of these may get answered by some of the other presentations [inaudible - intermittent audio].

We expect there are going to be innumerable questions, which is another reason why at the end of today, we're going to be meeting with the working group chairs and the facilitators just to identify what some of those may be.

(Audio gap.)

DR. TURK: [in progress] -- initially RDC for the TMD, and over 20 years, we moved from a classification to a diagnostic system. And as he said, deja vu all over again. He's been through this over 20-plus years, so I think his perspective will be helpful to us as we think of going forward, where they've been and how they got where they're going.

Sam?

Presentation - Sam Dworkin

DR. S. DWORKIN: Thank you, Dennis.

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According to the agenda, my time is about up. But being a New Yorker, a former New Yorker, I'll talk very fast. I want to thank you for the opportunity to come back again and address these important issues. This talk was supposed to be given by Richard Ohrbach, my colleague and former student, and he's had an unresolvable conflict and could not come. So this is a joint effort by us, but in terms of first authorship, for what it's worth, this is Richard's talk.

No one has said anything about conflict of interest yet, and this is my position on conflict of interest.

(Laughter.)

DR. S. DWORKIN: I showed this before. I love this slide. It comes from a fellow named Dave Patterson, a psychologist formerly in the burn unit at Harvard Hospital in Seattle. Sometimes I wish I had a conflict of interest.

Some of the preceding talks went really great to start us off and have covered these basic mechanisms. And our task is to wind up with this.

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So my task here is to take you through the history and stuff that was encountered as temporomandibular disorder pain -- a fairly highly prevalent chronic orofacial pain developed from a set of research diagnostic criteria, which are called RDC for TMD -- into diagnostic criteria for TMD, evidence based, following the model of the earlier iterations, iterative process, that the DSM used when it went especially from II to III and III-R and IV.

This is the endpoint, and the particular condition is temporomandibular. Temporomandibular disorders are a group of related orofacial pain disorders, pain the region of the temporomandibular joint and in the musculature of the big muscles that close the jaw predominantly, the masseter and temporalis muscle, as well as the muscles that elevate the jaw to a much smaller -- the jaw kind of opens just automatically; limitations or deviations in mandibular range of motion and sounds, clicking and crepitus kinds of sounds in the joint.

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This is as good a summary -- it was the American Dental Association definition in '83 and is as good a working definition. So we're talking about a persistent pain that resides in the face with these opening characteristics.

We developed a set -- and you'll see why it's deja vu all over again. We developed a set of guiding principles. We didn't give such a fancy title. It was a bunch of people, a smaller group than this, gathered by me and a few others, that had the characteristic of we knew all these people to be like-minded, reasonable, non-extremists.

This actually turns about to be very important because the people have to be willing and able to work together. And we developed -- and we wanted to bring some order, reduce the entropy in the field. It was in a terrible state for all the reasons that all of you are here. No consistency in terminology, no consistency in diagnostic approaches; people doing idiosyncratic things and treatments all over the place totally unfounded. There was very little science. So we evolved these

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principles.

The taxonomy has to include all of the aspects of the patient presentation, not only those that fit your particular clinical bias. The classification criteria are defined by evidence-based criteria. And regarding the research clinical issue, if the diagnostic criteria are evidence based, it's the same as saying criteria based. How you get the evidence base is not by asking the man on the street what do you think. It's by doing rigorous scientific studies. So if you're having evidence-based criteria, you are having research criteria.

To the largest extent possible, the categories are based on a single organizing principle, etiology, mechanisms. You've heard that. Where were we? We don't have a clue really as to what causes TMD, and we don't have a clue as to what sustains it. And I'll say something more about the implications of maintaining the pain condition. We are dealing with chronic pain. Chronic means temporal factors are involved, and

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the dimension of chronicity is almost totally ignored in the research.

The taxonomy had to reveal factors that contribute both to initiating and prolonging the disease and the illness, and we know very little about that and prolonging. It's a particular now pet issue of mine. It includes as a minimum both a disease axis and an illness axis.

Very briefly, diseases are in organs, organ systems and the physical structures of the body, and the illness is in the person. An organ has a disease. A person has an illness. They identify mutually exclusive disease and illness categories and subcategories, and the mechanisms accounting for chronic orofacial pain must be mapped against both disease and illness sustained over time.

You've heard these words one way or another in the AAPT guidelines and the structure. That's put into the group's excellent article, first authored by Roger. So this is old chron now. It was radical in our field and in the literature. I was called because I emphasized the need to reflect

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an illness axis, the person in a psychosocial setting, the psychological status of the person, the behavior, the emotion, cognitive functioning. I was called by the other side a psychosocialist.

(Laughter.)

DR. S. DWORKIN: Now, they may have been correct, but for the wrong reasons.

(Laughter.)

DR. S. DWORKIN: And it anticipates an evolving taxonomy to include -- this is relatively new. All of this is the research diagnostic phase, which took about 15 years. And then the last couple of years devoting research validating those early efforts and allowing them to become diagnostic criteria. And then this bursting on the scene of new approaches to genetics, especially epigenetics, have overturned the field of genetics.

I'm old enough so that I thought a gene was a fixed characteristic of the organism that led to, without variability, that genes are invariant in their function -- that's an old-fashioned idea -- and brain behavior biomarkers, the

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explosion of the brain neuroscience, which if I was younger is how I would be spending my time.

The taxonomy disease axes are pathobiologically based and measured objectively. We're saying, yes, this is probably pathobiology or at least is maladaptive physiologic functioning. It may be self-limiting and now pathologic in the conventional sense, but there's something going on because, after all, there's only one thing going on. And it's the workings of the body, and we know it in various ways, whether we ask questions of X-rays or ask questions of people.

So reveal pathobiologic mechanisms that differentiate disease categories, and they will nowadays increasingly include brain functionings that subserve maladaptive responses to the pain or the physiology that's giving rise to the pain. And they are specific to objectively define disease entities that continue over time.

Continuing over time is a challenge to the pathophysiologists, to the docs, because why is it sustained, and what is it about chronic pain that

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is sustained? And what is it about chronic pain that progresses? And yet, the overwhelming burden of evidence is that in the most important chronic pain conditions, there is no disease progression.

In temporomandibular disorder pain, which people can have for decades, there is no rusting out of the jaw joint. It does not fall off. The muscles don't atrophy. In the back, similarly, a chronic back patient on day 5 -- post five years after their initial presentation does not look different to any significant extent based on their anatomic structural or physiologic findings. And that's the case of TMD, and common headache, irritable bowel. Irritable bowel is not a risk factor for Crohn's disease, et cetera.

So what we are concerned with is why is the pain maintained. And equally enigmatic, for many of the chronic pain conditions and many of the classic garden variety mental disorders like depression and anxiety, they diminish with age. Now, that's a challenge to both the behavioral psychologists and the Axis II people. I'll talk

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about that more in a minute.

But also, if you're going to come up with a mechanism, your mechanism has to account for it going away. It's not so much evidence that it goes away because of treatment in the highly prevalent common chronic pain conditions.

The taxonomy's illness axes are psychosocially based. And I use the term "psychosocially" to include the psychological status of the person, the behavior, their emotions, their levels of cognitive functioning embedded in the social setting or the societal setting in which they exist. And it's largely measured subjectively and by self-report, whereas the disease components are largely measured objectively by diagnostic tests that don't rely on verbal report for a sign.

The taxonomy illness axes also reveal biobehavioral brain function based mechanisms that underlie and distinguish the psychological and emotional levels of function that are operational over time. There is a mirror image of the behavior in the neurology. We don't know how to recognize

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it. I like to think of it as music.

I even have a slide, which I may get to, of Beethoven's, the score for the chorale for Beethoven's 9th symphony. And it looks incomprehensible to somebody who does not know how to read music. And you would look at that and say, "That's beautiful?" Would I pay any attention to that?

Well, that's the music in one language, the music of the score. You listen to it. It's the same thing. One did not cause the other. It is the same thing described in a different language. And so there's going to be a biology -- not going to be. There has always been a biology of the psychology, and we're beginning to uncover it in the most fascinating ways. And what you will encounter is that this illness aspect, the impact of the pain, what the person does, is going to include dimensions and variables that are common across almost all the pain conditions.

This is the commonality. The specificity is in the organ system involved in the different kinds

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of pain. So chronic back pain takes place in a different part of the body than headache or TMD. And those patients are different in that way, but they are common in the lives -- they have many commonalities in the lives that they lead when it's chronic pain.

So for TMD, we begin with a stated effort to develop research diagnostic criteria. We don't want to overly -- it was not so much that we didn't want to threaten the clinicians. We did not want to arouse the large forces of the people who would then be arguing against us. So we said the recent diagnostic criteria and those kind of clinicians that are not evidence based, they're not interested in science, they don't care what you do. Go and research. I don't care.

So we use the biopsychosocial model implied in everything that's been seen so far, epidemiologic data. We created a dual axis system. Axis I is the physical diagnosis, the traditional approach to diagnosis that you know, and the Axis II was a psychosocial profile.

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A term that hasn't been mentioned so far is that we required operational definitions of terms. Operational means you have to state how you would measure it, and you have to state your criteria in measurable terms. Science requires quantities. Most science, the kind of science we do requires -- most of us do -- quantifying. And operational definitions say things like if you score -- if you got 120 on an intelligence test, that's how intelligent you are.

That's the danger of operational terms, that what you're measuring may not be all of the underlying phenomenon. So you will have to come up with saying, well, what do you mean by a lot of or many? You have to, as Steve has said, obsess over it. Is it two? Is it three? Is it from two to four? Those nitty-gritty decisions will have to be done.

Then we specified -- since it's a physical examination in the diagnostic process for recording and scoring, we've developed an examination procedure. Everybody -- every researcher, and

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eventually a clinician, confronting a potential TMD patient, does an examination in exactly the same way. And we specified the protocols for conducting reliability and validity studies, first of the examination, then of the criteria, and then of the whole set of Axis I and II put together.

If the examination is -- if your particular pain condition requires a clinical examination, and the clinical examination is unreliable, nothing you can do will be valid. Validity has as its limiting factor reliability. The validity is the square of reliability. If the reliability is .9, the validity is .81. That's the maximum that it can attain.

Working with unreliable measures of any kind is like generating random numbers. Random numbers are not going to be valid. And we built in the requirement for periodic evidence-based revisions. We would have successive iterations using the DSM model.

So this is the flowchart of what began before 1992 because that's when we began the formal

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activity. We were able to get a contract for small amounts, something like $80,000, from NIH to begin, a bunch of people meeting, mostly meeting at scientific meetings because in 1992, there weren't many computers. I don't think e-mail was -- maybe e-mail was in, but teleconferencing and stuff like that was like Buck Rogers science fiction kind of stuff.

So we would meet at our annual scientific meetings, IASP, ASP, dental research meetings, et cetera. And so we got along with very little money, just as Steve did, and we developed a set of research diagnostic criteria for temporomandibular disorders, which use a dual axis system as I described, published in 1992. And then we began a bunch of studies of the people within our group.

The people within our group -- and I apologize. I don't know all of you. But the people within our group -- and the people in the group I'll talk about later with regard to a back pain effort -- had the characteristic of being known to be good scientists -- and many of them,

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but not all, clinicians; by far, not all clinicians -- and respected clinicians.

So you had to have evidence of being scientifically competent as a scientist, or if you were a clinician, you had to have some weight in the field. And you had to be a nice guy or nice gal so that we would not have fights.

(Laughter.)

DR. S. DWORKIN: So we only had a hundred or so fights, and some of them were very interesting.

(Laughter.)

DR. S. DWORKIN: And this went on for a number of years. We would say, "No, it's not the myalgia. It's myositis." What is myositis? There's contracture. It's spasm. Can you define it? If you can't operationally define it -- we agree, if you cannot operationally define it, it's going to fall by the wayside. And then it came home to roost because they said to me -- you'll see later on the implication of somatization, which is now widespread pain. And they said, "What about somatization?"

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Somatization is this flaky concept from DSM-II or III about repressed sexual things giving you all kinds of crazy symptoms. "You can't define that and can't do research on it. So why should you be allowed to have somatization on Axis II and we can't have contracture on Axis I or even trigger points on Axis I?" And I said, "Okay, you're right. We will call it non-specific physical symptoms instead of somatization."

That turned out to be almost like a godsend because it actually describes what it is and removes the whole cloud of suspicion that we are secretly interpreting the symptoms to mean something else that we don't know anything about.

We then got a large-scale grant, but this is in 2001 -- that's nine years later, multi-institutional, three universities, Minnesota, Washington, and Buffalo -- to establish the validity. Implicit in here is the reliability first. And the validity, we had done data so that we could show the reliability of various aspects. And this was a broad sweeping approach to

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validating, and it was successful.

I want to say -- I think it's useful to say that when you do a -- the purpose of doing a reliability study is to be able to state what the reliability is even if it's not good. But it's the first approximation to what you can do. At least under these standardized, this thing is repeatable to a certain extent. And the same thing with validity.

The first emphasis is that you've got to be consistent, and that's reliability, and then go on to the next higher, much more complex things to analyze about validity, external criteria. Reliability is -- inside itself, how consistent is the measure?

If you gave it over again to the same person, would they answer it the same way? If you pitted one examiner against another, would each examiner come up with the same physical finding? And validations are much more difficult in a field where there are no gold standards, are much more difficult problems to attack.

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This study went on for five years, radiologic examinations, different kinds of clinical examinations. Embedded in here is thorough reviews of the literature. Embedded in here is thorough reviews of the literature, of the criteria, the diagnostic methods, the symptoms, et cetera. And we formed an international consortium. I called it international consortium for RDC-TMD research. I'm going to find people around the world who's going to join a group for RDC-TMD research? Well, about 140 people around the world joined.

We produced 22 translations using rigorous methods, state-of-the-art methods, for producing translations of the RDC into 22 languages, which allowed a lot of research to go on. And then the consortium meetings and IASP, an orofacial pain special interest group, had consensus workshops in these years. We did international field trials. And the objective of this was to take the RDC, research diagnostic criteria, and validate that they could be diagnostic criteria for use in

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clinical practice, and they would be evidence-based diagnostic criteria for TMD.

Then some of the workers in this consortium, the die-hards I would say, wanted to go on to expand to include more than the small number of common conditions, the most common conditions that we could agree on, which were in the RDC. And they account for 90 to 95 percent of cases.

We were helped because three other studies came along to lend lots of supporting data that were independent of the consortium. The other was an IMPACT study funded by NIH, which was the follow-up to this study, and then the OPPERA studies. And OPPERA, I'm embarrassed to say that I have been asked to be the guest editor for two publications of the Journal of Pain, devoted -- for one or two. And I keep tripping up over what does OPPERA stand for. So OPPERA stands for orofacial --

DR. FILLINGIM: Orofacial Pain Prospective Evaluation and Risk Assessment.

DR. S. DWORKIN: Right.

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DR. FILLINGIM: It's Roger Fillingim. Orofacial Pain Prospective Evaluation and Risk Assessment.

DR. S. DWORKIN: So you've got to be careful about the people who are heading this activity because they come up with these acronyms that are like a page long. That's not simple, and they're only working on the title of what they're doing.

But this study was the largest single grant for extramural research by the National Institute of Dental Research ever awarded and multi-institutional and then being followed up now, and contributed just a wealth of data to allow this transition, supportive validating data, reliability, expanding the concepts. It allowed the transition from the RDC, down through here, with input from this, to the diagnostic criteria. And there are now 27 translations of this in process. It's not so hard because they have this as a point.

Now we come to where we are now. This is, for TMD, not so much an evolutionary stage as a

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translational one. What we want to do -- because the taxonomy is a very invaluable thing to have in existence, and TMD and every other pain condition that can should be in it -- is we want to translate, convert the way we put the RDC, the structure of the RDC and the TMD, and the DC of the TMD -- we want to convert that structure into the APT structure, and I'll show you how we did it.

First, I'm going from the RDC to TMD, and these are just examples of the differences that were found in the subsequent research from these very early bootstrap efforts of a bunch of theoretically smart people trying to define things from clinical experience, from extensive reviews of the literature, and then saying, okay, the whole purpose of creating the RDC is to do research.

The first object of research is the instrument itself. And I think that that should also be reassuring to some of you. Consider what you are saying is not the truth. You're not really inventing something. You are discovering something, and you're willing -- you have the

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courage -- to test out what it is that you're going to say. So the first test of your deliberations is the test of the criteria that you are specifying. And it allowed us to feel good about proceeding.

So the examples, the content of it, are not so important other than to say that differences occurred, and the data did not support, for example, muscles in this region, which are the elevators of the jaw. It takes very little to open your jaw. But clinically, at the time that we did the RDC, all the muscles of mastication were considered equipotent.

It seemed to me, what kind of condition is it? Does it matter whether you're opening your mouth or closing your mouth, whether you're biting down with tons of force that these large muscles can produce with food or you're just opening your mouth, like letting gravity do most of the work? So it was kind of gratifying. These were kind of like dropped. And there were a number of other important changes that the data -- changes that were warranted by data.

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This is the expanded diagnostic criteria. It's offered. All the ones in yellow have no evidence behind them. They are the clinical impressions. The clinical guesses. The hunches. These are all well-intended, smart people, too, but they say -- their objective is to do for these conditions in yellow.

You don't need them. If you want to know: condylosis; idiopathic condylar resorption; myofascial pain with referral; subluxation, when the joint slips out and locks open or close; orofacial dyskinesia. They right now defy adequate description.

If you brought the people who put this together in a room, they would not agree with each other on how to define these conditions at the present time. You may be somewhat in the same boat. So the further back you are, the more risky the stab that you take, or you should be willing to take a stab because you will, if you take a stab, put something out there to be systematically investigated, and the advances follow from that.

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So this is the DC going to the APT. The first thing was, well, what should we do? Which portions of the TMD should we move over into the AAPT, into the structure of the taxonomy that we're all about here today? And it seems like a self-evident -- no pun intended -- decision. But should we do evidence-based disorders only or should we do that whole other list? So we of course have said evidence-based disorders only.

So this is a bunch of conditions under the RDC, and these are the ones that would be in the AAPT, and they have the advantage of both accounting for more than 90 percent of all the cases and having the evidence behind them. And again, the specifics of what they are I have at least on a thumb drive. I have the DC-TMD -- if anybody wanted it, it would be easy to print out -- copy of it. And it's available at the website or the International Consortium. I'd be happy to make it available.

So this is the DC-TMD in its current format, how it looks in the publication announcing it. It

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has a description, a history, an exam, validity, and comments for each of the conditions, which you saw in the other chart for each of these conditions.

So this is the structure of the DC-TMD in its current format, and this is the structure for the Axis II part, all the psychological, psychosocial impact kind of measures. And they're probably not surprising to any of you in the chronic pain field.

Let me just go back. Here's the DC-TMD in its current format, the way we did it. And here is our first stab at trying to put that into the AAPT architecture. So here's the core diagnostic criteria, the common features, the common medical comorbidities, the neurobiological, psychosocial, and functional consequences.

Again, the purpose here, this will be debated or worked out or ironed out perhaps better in the work groups, of the TMD work group, and you're certainly free to ask questions about it.

But my purpose here is not to present it now

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as the truth. This is how it really is going to be in its final form. It will probably be very close to this.

There's one more dimension, the putative neurobiologic and psychosocial mechanisms, and risk factors, and protective factors. We know a lot about this condition without knowing hardly anything abut how it gets caused, let alone how to prevent it.

So this is the AAPT chapter, article, that's in preparation, almost ready to be submitted to the Journal of Pain, with regard to TMD. And I certainly would invite the questions and even controversy over anything you see here on this screen.

I want to just call attention to a prospective for this condition. The epidemiology is it ranges from 5 to 15 percent with a greater prevalence among chronic cases. While the number that comes up is around 12 percent averaged across both genders and averaged across all ages, it's important to know that the prevalence reaches -- in

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the population, in a population-based study -- 30 to 35 percent in women in their reproductive years.

So it is common in the literature to find that the only risk factor for TMD is being a woman in their reproductive years. TMD falls off markedly for men. It's rare to find a man over 60 with TMD, and it falls markedly, but not as markedly for women.

So it is about third in its prevalence in the chronic pain conditions behind headache and back pain, or back pain and headache, as the most prevalent. But the prevalence issue for back pain is much more -- it dwindles in significance in comparison to its cost.

Low back pain cost more than any other medical condition that afflicts people in America and around the world than, for example, heart disease or cancer. And by some reports, it's more costly to the American public than heart disease and cancer, and that's largely due to the excess loss in productivity.

So my summary --

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DR. TURK: Summary.

DR. S. DWORKIN: I'm sorry?

DR. TURK: Summary

DR. S. DWORKIN: Yes. But my summary is tricky.

(Laughter.)

DR. S. DWORKIN: Here's a short summary. You can read faster than even I can talk, and it only says what I've already said. I wanted to take -- remember that I began about 20 minutes late, right? Good. You've all read that.

It's really important to point out that it's an iterative process that you want to establish, requiring multidisciplinary effort over time. Significant. We all smiled or laughed when 2015 -- there's no reason not to aim for 2015, but it will take work. But you have the benefit of the new communication technology and the telecommunication, et cetera, that will make it easier. We are gratified that this process that has gone on for 12 or 15 years -- 20 or 22 years -- actually is able to fit into the AAPT

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structure. So that's kind of validating.

I wanted to take a minute, a few minutes, to talk about the NIH Task Force on Research Standards for Chronic Low Back Pain. A large group of people, larger than these two, were -- oh, here they all are -- met at the NIH Pain Consortium, asked for a research task force to be created to develop research standards for chronic low back pain. I had the privilege and the honor of being asked to co-chair it, although I am not a back pain specialist at all, in any way. But we were saved by having Rick Deyo. Rick Deyo is a leading back pain epidemiologist, and he is a clinician as well, very important work in the field.

I think we made a -- a couple of people. Dennis Turk was in that group and was very instrumental, very, very helpful to me especially in an area of my responsibility, which had to do with all the psychological and psychosocial measures. Our top consult from NCAM is here and was the NIH -- sort of like a point person for the task force.

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The report of the NIH Task Force, the full report, is on the NIH website, the Pain Consortium, which is here, and I'll make it available to you later. An article describing the report, briefer and without so many of the details, has appeared in four journals and is destined to appear in two more journals. And it did three things.

It has identified with three products of which I feel very good about. It provided a definition. I was blown away by back pain had the same problems that TMD did, the same problems that all of you did. They could not develop an Axis I, a physical dimension. There's no evidence that we can -- there's hardly any evidence for anything physical that's reliable and valid. I said, "Oh, boy. I've been there."

So this is the definition of back pain, a temporal aspect, and then a location -- it's accompanied by a location with a drawing. The person locates where the pain is in the back, and then how long. But the definition is enlarged by including a stratification by the impact of chronic

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pain and measured here operationally by these items --
DR. TURK: We have to --
DR. S. DWORKIN: Okay.
DR. TURK: We're a half hour --
DR. S. DWORKIN: Okay. I'm sorry about that. But again -- it includes a minimal data set. And those three things would be ideal things for this group someday to report in each of those things. The minimal data set is going to be something that NIH is going to require in its studies that it funds on back pain. And it's a minimal data set to bring standardization. Whatever else you want to do is okay. Include this as a minimal data set. We'll be able to compare subjects. We'll be able to compare characteristics of subjects.
I apologize for running over. I did start late, but anyway, thanks again.
DR. R. DWORKIN: Thank you. So we're a little over -- I'm Bob Dworkin. Why don't we take a 20-minute break and come back around 20 to 11:00.

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At 10:40, we'll resume. Thank you all.
(Whereupon, a recess was taken.)
DR. BRUEHL: We're about ready to get started again. If everybody can take a seat. I'm going to start zapping people with a laser in a minute to let them know they're targeted.
I did want to let you know, we're going to switch things around a little bit from what's on the agenda. Just because of all the questions that were raised about research, I thought it might be better to spend a couple of minutes talking about the research agenda first, and then we'll have the panel discussion. And that way, questions that come up that have not been answered, we can address as a group during the panel. I think that will make more sense.
So any questions that you do want to bring up, please remember to speak into your microphones and to say your names before you get started so that we can get that on the transcript.
Dennis?
DR. TURK: One more minor change. Since we

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are a little behind schedule, we're going to be moving lunch to 1:00 from 12:30.
Presentation - Stephen Bruehl
DR. BRUEHL: What I wanted to do is talk a little bit about the research agenda. And as it has already come up, I think everybody is going to have questions about how this will work in practice. And the short answer to that is I don't know because it's going to depend a lot on what we find. For example, we have the situation of some conditions where there are no current criteria to use as a reference point. There are others like TMD that basically all the work's already done, so there really may not be any significant research on those issues.
So it may differ from work group to work group. But I'm going to just talk about, in general, what our options are and how the process would work.
As I mentioned earlier, we want to identify the universe of signs and symptoms, and this means going to the literature. And this could be studies

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both that have proposed previous sets of criteria, but you can also look at any clinical studies of that condition that may have information on frequency of signs and symptoms.
So it may not explicitly have been a study that was dealing with diagnosis, but it might have information about the clinical presentation and the frequency of the different things. You can use that kind of thing to build that universe as well.
Now, keep in mind that, ultimately, this is going to have to be boiled down to a relatively short set of Chinese menu criteria, two from this and three from this. So we don't want to have 50 different symptoms on the end result criteria. Early on, you can certainly have it be over-inclusive, though, because we don't -- I mean, honestly, we don't know what's going to be important in diagnosis and what's not.
So include all the things that seem reasonable to include, but that will be winnowed down eventually by the time you get the final sets of criteria.

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What you could do -- and I'm just thinking of options here. One option is, if you're trying to come up with your draft criteria, you may end up including, just as an example, five different signs and three symptoms, or something like that. We would be collecting data on those as well as other things, other signs and symptoms and could after the fact see whether it makes any difference to how good those draft criteria are if we add this symptom or that symptom. And you can change things around after the fact as long as you collect the data.

So the important thing is you've got to include on that data collection sheet anything you want to be able to answer later on in terms of the research.

For formatting for research -- I just want to present this again -- every working group for every different disorder is going to need to have something that is similar to this; maybe not identical but similar to this.

Depending on the conditions, I can foresee

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possible situations where you might have -- like with the back pain group, for example, you may have enough commonalities that you can cover several different proposed diagnostic categories on one sheet like this because you may have -- for a certain diagnoses, you may have a positive MRI finding of a certain type, and another kind of diagnoses, it's negative. But you can assess that just with one question on this questionnaire.

So all of your working groups can use your judgment as to how to break this out. They don't all have to be separate for each different condition, but they certainly can be if you want to.

The breaking out of signs and symptoms I've done on this because in CRPS, that was a very important issue because of the lability of things. There may be some conditions where you might not have any objective signs. I'm not sure if there are any like that, but it might be primarily patient complaints about certain symptoms. And that would be okay to do it based on symptoms only

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if that's all you've got and adjust the sheet accordingly, or maybe others where there are many objective signs, and the symptoms are relatively unimportant.

In the end, you might elect to not even include patient reports in the diagnosis, and it could all be based on objective signs you see. That's up to you in the individual working groups. And we could actually look at the numbers for signs and symptoms and determine whether that is a good idea or not, or provide some empirical support for the decision you make. I would tend to collect signs and symptoms even if you don't plan on using them just to make sure we've got that to go back to and look at it later if we can make that -- if it's feasible to do that.

The reliability issue, Sam mentioned, and this is important. Reliability sets the upper limit on validity. It is not feasible with no money to do extensive reliability testing, although I'll talk in a second a little bit about some of Eva's work that relates to this. So using the

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dichotomous way of indicating whether a sign or symptom is present is one way of reducing the likelihood of unreliability somewhat, although it doesn't really guarantee anything.

If you have measures that have known reliability because they've been published before and you can incorporate that as part of your criteria, that's great. I do think the importance -- what was not clear from the way I presented this before was that there are operational definitions of all these. So when it says allodynia here, there's an instruction sheet that says this should be tested by taking the finger and -- or taking a piece of cloth and stroking lightly on the upper surface of the hand, and allodynia is indicated by response saying that's painful.

There's something very specific here. Some things such as the edema, we're interested in yes or no, but it would be great if we could actually quantify it in terms of volume or a measurement of circumference based on some landmark

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physiologically. We may not in the diagnostic criteria end up using the actual number as cutoff, but at least that gives us the option of looking at that.

So always be thinking ahead. Don't restrict yourself to only including the things you know you want to go into final criteria. Do make it a little broader. Let's get some extra information if we can, and that will give us some additional things to look at in the future potentially.

But you will need -- whatever you come up with on this sheet, anything that is physical exam based, you need to have a description -- I mean a separate page -- that says to assess this, do this, that's very explicit. And make sure it's very clear to an outsider if they were to look at this, what exactly that would -- what's required to categorize somebody as having allodynia or having whatever the measure may be.

Once you've got this universe of symptoms, you come up with a form and run the forms by me, please. I will kind of have a job to help with

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this process. So just let me know. If you get stuck on stuff, let me know, and we'll try to get that together. Once you've got the database forms that you need for clinical exams, the next step is to identify research sites.

Now, you may be a site yourself. The people involved in developing the criteria, you may see a lot of these patients that may be interested in doing that. That's an ideal situation because you're invested in this. We know you'll do a good job. If you don't, if that's not practical or you don't see enough patients, you need to get outside sites. Some options are to identify people who've done research on this previously who may have a preexisting consortium that they would be willing to incorporate this database form as part of what they do. That would be ideal if you could do that.

If it doesn't already exist, you might be able to identify a few clinics that are willing to do this, colleagues that you know and trust who'd be willing to just get the history and physical data as part of their normal exams, fill out this

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sheet. High volume is better so we can get the data faster. Specialty clinics, certain conditions may be rare enough -- like CRPS was -- where you don't see a lot in any given clinic. You have to use a bunch of sites. That's an option if you need to do it.

So use your judgment on this. We want to get data as quickly as possible, but it may take a year to get that, and that's just the way it is. But we'll see. Some of you may be really fast and in three months have all the data we need. That would be wonderful.

Money. Everybody always asks the money question. How am I supposed to do this on no money? It can be done. Not easy. It's better, though, if you have -- if you have a situation where it's going to be hard to coordinate it and you need help with that, there is the possibility of money for a research assistant and that kind of thing that might help.

Now, paying for effort for investigators is not going to happen. If you need money for

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something concrete -- like CRPS, we might want to use an infrared digital thermometer, and you need a certain one of those that's high quality, and you want it for all your sites, we can do money to do that.

That's the kind of stuff we can fund. So there's some money, not a huge amount. I'm thinking that as we're trying to organize this, we might try to have like a Skype conference or some type of video conference where I could be involved in this and kind of just make sure that from working group to working group, we're doing things relatively in a similar way.

One thing that I talked about with Bob is he had said that they might be able to provide help with preparing a standard IRB for doing this kind of research that can be modified by people at each institution to change the specifics. Obviously, the consent form format may be a little different each place but could have the basic information there to make it easier to get that completed.

The more we can help with that kind of

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thing, we realize that will help speed up the whole process of getting the research done because the people you're asking to help with us are busy and probably don't really want to take the time to fill out IRBs. And the more we can do to help with that, the faster we'll get actual data.

Data warehousing, we're not sure yet exactly how we do it. I think there is already something set up that Bob has. We've got a red cap, which is an online data entry procedure we could use. I could program for each different working group a place to enter your data just from using the internet that would be fairly easy. We'll talk about the specifics of that at some point in the future.

Now, what kind of studies can we do? Eva at the meeting a year ago actually presented on this. But there was the option of addressing reliability in a way that it doesn't require having a whole bunch of patience with examiners physically examining and then having to do your kappas based on that. And the idea was to use vignettes. You

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have a very detailed case description, and then you can have different clinicians try to apply criteria to that vignette, and you look at the reliability of that.

Correct me if I'm saying that wrong.

DR. WIDERSTROM-NOGA: Yes. I just want to mention here that it was also -- Eva Widerstrom-Noga. And it was not just physicians that were part of the validation. It was also people who were researchers. So we wanted to have a rather broad representation, not just people who are experts in the field with respect to clinic, but also researchers. And of course, those of us who are not clinically active maybe didn't do as well as the clinicians. I don't really think it was that big of a difference, but I think that was the point I wanted to make.

DR. BRUEHL: Okay. So use your discretion. Certainly, we want to make sure that clinicians can reliably apply the criteria, that you can broaden that to researchers, too, because researchers will in fact be using these diagnostic criteria at some

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point.

Internal validity, that's referring to the frequencies of signs and symptoms, the factor analysis, the layout, how the criteria are structured. Does it make sense? Does it fit with reality? And we presumably would do something similar to what we did with the CRPS study using the data you collect on the database forms. I can't tell you what we would find. I have no idea what to expect with this, honestly, so we'll go by what the data show and do what we can with it.

The external facility gold standard. I was talking with Rob Edwards a minute ago. Maybe we should call this bronze standard or lead standard --

(Laughter.)

DR. BRUEHL: -- because we've really got a not very good standard, which may in fact, in most cases, end up being the current best diagnostic criteria as your reference group or it may be a situation like with the sickle cell, where there's nothing to go by to start with, and we have to get

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some clinician generated, this person has it just because I know what it looks like, and you get agreement on that. And then that's your starting point for saying whether the diagnostic criteria work.

The point is -- and this was mentioned earlier -- you've got to have a starting point somewhere. Once we get that starting point, then we can use that as the way to start improving, incrementally improving the diagnostic criteria over time.

Yes, Eva?

DR. WIDERSTROM-NOGA: This is Eva Widerstrom-Noga again. I'm very interested in this internal validity because factor analysis is a very interesting method to use. I'm just thinking that in order to do that in the best way, it's really nice to have some kind of scale so you don't have a dichotomous variable because then you have to transform the data in a way that's kind of complicated, polychoric correlation matrix.

DR. BRUEHL: There's actually a procedure

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for doing factor analysis using dichotomous measures.
DR. WIDERSTROM-NOGA: Yes. I know because I've done it.
DR. BRUEHL: But you do lose information. The difficulty -- and it's like weighing one thing against another -- is when you've got scales that have not been previously shown to be reliable and valid, and you're trying to use that in your factor analysis, is that really an advantage over doing a dichotomous decision where you're not having to make those fine gradations, but you're losing some power with that.
I don't know the answer. I would say if you've got scales available that are known to be reliable and valid and can incorporate that in your criteria, by all means do so. And that might be possible to do something like you're saying, where you use continuous measures for everything.
Some things just by their nature may just be yes or no, and that's just the way they are. I don't know if anything more needs to be said on

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that. Ideally, it would all be based on continuous measures that have some range and variability.
DR. ZELTZER: Lonnie Zeltzer. How do you account for in this schemata where you have concomitant treatments that over time have their own morbidity, side effects -- and I'll use the example of sickle cell disease -- and you're looking over time at the development of chronic pain and characterizing that for people, kids, who are hypertransfused as part of the ongoing treatment, and they get iron overload? Then you have all the secondary effects of iron overland, using that as an example, but there may be other conditions like that.
DR. BRUEHL: I think basically that comes down to confounding of treatment with the diagnosis. You're going to change the presentation of the patient by the treatment that you're using. I don't know how to handle that, honestly. If we have a large enough sample with patients with different treatments, one could argue that those might average out. And what we see that's in

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common across all of them is the unchangeable part of things. I don't know the answer to that.
We're going to do a panel discussion with everybody -- Dennis and Bob and I think Eva -- up here in just a minute. Let's just finish talking about this if there is anything else. We'll get everybody up here, and then we can go in more detail with the questions.
I'm not sure if there are any conditions that we're dealing with where there would be what might be considered a known pathophysiology. If there is, use that as your reference point for the diagnostic criteria. That I guess would be apparent in your literature review if you're not already aware of that.
So that's basically the agenda. And then the idea would be that we collect the data. We would collate the data. And at some point say, okay, that's enough, that we can go ahead and take a look at this. And then we would do the various analyses we'll able to do and see what we can do with this.

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I think it would be nice if as we are collecting these data if each working group would continue to work on getting what their best shot at the draft criteria is because we're going to need that at some point to use in doing some of these analyses. We'll have to actually have the draft criteria.
So just give it your best shot based on what you can determine, based on what's out there already and what your consensus opinion is, and then by the time the data are collected, we'll get all that together and can work together to get the information that we can out of it. But hopefully we'll validate those draft criteria or give you ideas on what to do to improve them, ideally.
We're going to go ahead and do the panel, I think.
Q&A and Panel Discussion
DR. R. DWORKIN: Would Sam and Eva and Roger come up?
DR. TURK: While they're coming up -- this is Dennis Turk -- let me just comment that you

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should be aware, and you should have, if you read the materials we sent you, that there is a research committee. So even if we don't answer all your questions or things come up about research, Steve Bruehl, who will be the chair of that committee, will be available to assist you along the way or to address questions, or if he can't answer them, bring them back to the research group.

So we understand that there are going to be lots of questions -- I understand; I shouldn't speak for everybody else -- that there may be lots of questions about how to do some of the things that we've talked about. But there will be opportunities for you to ask us more in this panel. But also as you start trying some things out or as your working groups come up, that you can come. And Steve will be the point person to send those questions to.

DR. R. DWORKIN: Hi. I'm Bob Dworkin. Just a couple of housekeeping things before we start. If you need taxis to the airport tomorrow, arrange it today around the lunch break with Valorie and

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Andrea outside. So that would be much better if you tried to do that today rather than wait until tomorrow.

The second housekeeping item is we'd like to meet with all the facilitators -- those of you who are facilitators -- and the working group co-chairs -- we'll push it ahead a little bit -- 5:00 this afternoon.

Valorie, will this room be okay for a kind of 15-minute meeting at 5:00 today?

MS. THOMPSON: Absolutely.

DR. R. DWORKIN: Okay. So working group co-chairs and facilitators here at 5:00, just for a kind of update, make sure we're all on the same page and kind of thinking about where we're going tomorrow.

Finally, we left at everybody's place the guidelines. This guidelines document for working group activities had been distributed several months ago to the working group chairs, but we thought you should all have it. So that's what's in front of you that appeared over the coffee

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break.

This morning, I think we had a bunch of great talks. And of course what Steve and Sam both did is present their experiences developing diagnostic criteria for CRPS and TMD related disorders. A third person who's done that is Eva, and she was part of a group that developed diagnostic criteria for spinal cord injury.

So I just wanted to start this Q&A session -- and we have ample time for questions, discussion. But I want to start by asking Eva if, from her perspective, developing diagnostic criteria for spinal cord injury, were there any significant learnings, take-home messages, in the spinal cord injury effort that you could add to what Sam and Steve shared with us.

DR. WIDERSTROM-NOGA: Well, it took time. It took time to do it. It was really important. What we wanted to do was to get buy-in from the things we were dealing with, with spinal cord injury. We wanted to make sure that people who were spinal cord injury physicians, and not

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necessarily other healthcare professionals, had a way to review what we came up with. And also, of course the pain organizations, including the -- I was going to say NPSI -- NeuPSIG, which I think that's when we dealt with you. So that was a really important part.

Then of course, the taxonomy, it was developed based on several previous taxonomies. It was really an effort to bring together something that had been very diverse in different parts of the world and sometimes in the same part of the world. I think we had three or four different taxonomies, that we included everybody in a consensus meeting, including some basic researchers to get the mechanistic anchors, whatever was available, into the taxonomy.

Then of course, we did the validation, so we had like a gold standard, which was then a couple of physicians' consensus, so the diagnosis that people had, the pain diagnosis. And then, like we mentioned before, there were a number of people involved in the validation process. So there were

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at least two people on each diagnosis, and it was tested how the consistency was between our replies or our classifications.

Q&A and Discussion

DR. R. DWORKIN: Thank you. So we now have a bunch of time for discussion. I think there are at least two objectives for this discussion period. One is to give you all the opportunity to ask Eva and Steve and Sam any questions, based on their experience, having done something similar over the last 10 to 20 years for these other conditions. So this is a Q&A part of the morning.

But maybe even more importantly, as indicated on the agenda, this discussion period is really the time to make sure we're all on the same page before we break into half a dozen or so working groups.

So we aren't going to allow you to have lunch until we all consense in this room that we're pretty much on the same page about what we're going to be doing for the next day and a half, because obviously it would be a little bit chaotic if we

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all go off into different directions this afternoon, having different ideas of what we're supposed to accomplish.

So let's start with are there any questions for Roger, Sam, Steve and Eva about this morning's presentations and about their experiences? Yes? Back there?

DR. MACFARLANE: Thanks very much. Gary Macfarlane, Aberdeen, in the United Kingdom. One of the things I just wanted to ask, perhaps to Dennis, is to what extent you see this as a United States activity or an international activity. I know that ACTTION does have an international focus. I think it's really great that you've invited some people from outside the United States, so just a small number. And it looks as though most people from outside the United States are within a single working group.

I wonder whether you thought that had any implications in terms of dissemination, the ultimate take up of any criteria we come up with.

DR. R. DWORKIN: So Dennis answers the hard

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questions. I take the easy questions. That's an easy question. I think our intent from the beginning is that this is international. And we entirely left it up to the working group co-chairs to decide what the distribution of North America versus outside North American working group participants would be.

I think even though this effort is being jointly sponsored with American Pain Society, we think these criteria should be internationally applicable. The diagnosis of chronic pain conditions is not limited to one region or one nation.

Does anyone disagree with that?

DR. TURK: I'd amplify it.

DR. R. DWORKIN: You want to amplify it?

DR. TURK: Yes.

DR. R. DWORKIN: Okay.

DR. TURK: Thank you for the question. Bob is exactly correct. We have also invited some other international people who couldn't make it for different reasons, so there potentially would have

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been some more here.

The other thing that I think -- at least I'm thinking, I don't want to speak for the group -- is that when we start developing drafts of things before they actually end up getting published, we will distribute those to appropriate people from different organizations, from different areas, from different countries, so they can give us comments on those.

There was no way we could have everybody here we would like to have here. And even some of the people that were invited here couldn't be here, and several of those were from Europe.

DR. SARZI-PUTTINI: Sarzi-Puttini from Milan, Italy. I was wondering if -- because we are talking about chronicity and pain as a main symptom. But what's the deal on everyday life with all different types of symptoms that we call centralized or dysfunctional syndrome, like chronic fatigue or multichemical sensitivity? Are we taking any position in doing the diagnostic criteria according to these specific comorbidities

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or we just don't care?
DR. R. DWORKIN: Roger, do you want to talk about comorbidities? I understand that this is really a question about the comorbidity dimension.
DR. SARZI-PUTTINI: The point is, is all the pain, that chronic pain, the problem or the other symptoms, which we have comorbidity? Because to me, for example, many times it comes up in a patient with a chronic fatigue syndrome diagnosis, but for me it's fibromyalgia. So how can we stand on that? Can we put any position or we just don't take any position on that? So we don't care.
DR. FILLINGIM: This is Roger Fillingim. So I guess the way I think about that is that you're developing diagnostic criteria for chronic pain disorders and not for disorders that may be comorbid with chronic pain. So it's not the job of your work group to develop, for example, chronic fatigue syndrome criteria unless somebody convinces your work group that that's a chronic pain syndrome. Right?
But if you're developing criteria for

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fibromyalgia and symptoms that are consistent with chronic fatigue are diagnostic for fibromyalgia, according to the evidence base and then subsequently supported by research, then those diagnostic signs and/or symptoms could be part of the diagnosis of fibromyalgia.
Of course, the other issue is that other conditions are often comorbid with the primary condition that you're dealing with in your work group at the time. I think that's important to acknowledge in the write-up. It's part of the five dimensions that we identify, so it would be identified in Dimension 3.
There may be instances where there's particularly strong comorbidity, suggesting overlapping pathophysiology between a comorbid condition and the pain condition you're dealing with. And that would be dealt with in the narrative of the write-up, as far as I'm concerned.
Piercarlo, I don't know if that answers your question, but that's just some of my thoughts.
DR. BRUEHL: Can I --

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DR. R. DWORKIN: Steve, sure.
DR. BRUEHL: -- add something also? And we discussed this last night at the facilitators' meeting. So there are certain diagnoses that inherently have a comorbidity, for example, pain related to diabetic peripheral neuropathy. So diabetes is going to be automatically comorbid with that.
One thing we wanted to make sure of is that our goal is not to define diagnostic criteria for the primary disease. So in the case like a diabetes, and we've got diabetic peripheral neuropathy and pain associated with that, in the diagnostic criteria that we come up with, all we're doing is criteria for the pain component of that.
So as part of the diagnostic criteria, you might say meets the standard diagnostic criteria for diabetes as per whatever. And then you go on to list the core diagnostic criteria. So you don't need to waste your time if there are other diseases that are really inherently part of that pain condition. You don't need to come up with the

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disease diagnostic criteria, just the pain related diagnostic criteria.
I'm sorry. You were going to ask a question about that?
DR. ZELTZER: Yes. What do you do when -- and really, this is for Eva. So suppose you have two --
DR. BRUEHL: Say your name.
DR. ZELTZER: I'm sorry. Lonnie Zeltzer. I figured my hoarse voice would give me away.
What do you do when you have a lot of overlap between two different pain syndromes where -- and I'll use the example of spinal cord injury -- where maybe you don't know that the person had an injury that's likely to -- so you're just going on the symptoms. In for example, syringomyelia, where it's spinal cord related because it has to do with flow of the cerebral spinal fluid changes, without having to get -- I mean, do you get a spinal MRI and that's part of your criteria?
I'll use the example of irritable bowel

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syndrome and Crohn's disease, where obviously you could have both. But unless you have certain biomarkers and an endoscopy to really differentiate -- although you're not -- for every patient with IBS symptoms, you're not going to get an endoscopy. So how are you going to sort of tease apart those?

DR. WIDERSTROM-NOGA: Well, if we talk first about the spinal cord injury taxonomy, it's a little different approach to the AAPT taxonomy. But the taxonomy that we worked on, on spinal cord injury, we found it very important to look at all the pains that a person could have. And the reason was that when a person with spinal cord injury is treated, they're usually treated by one physician or a couple of physicians. They don't necessarily go to a pain clinic. So we wanted to incorporate all the different types of pain.

So in the diagnostic criteria, there certainly has to be some kind of -- number one is, do you have a spinal cord injury, and then what the diagnosis is of that, whether it's MRI, and also

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neurological exams are really important. So one of the things we found to be very important in -- it's kind of linked together -- our taxonomy is linked together with something that's called a basic data set, which is now adopted by NINDS as the common data element.

We found it very important to differentiate between different types of concomitant pains. And I don't know if that's what you were referring to also, that people can have, after spinal cord injury, more than one kind of pain at the same time. So we had to differentiate and evaluate all of them. So it became then tied in with the taxonomy for each pain type up to three pains.

DR. SARZI-PUTTINI: Again, Sarzi-Puttini from Milan.

DR. R. DWORKIN: Sam, and then we'll come back to you in a second.

DR. S. DWORKIN: I'd like to reinforce and extend the path that was Eva was following. If you as a clinician decide in some instances to pursue imaging to determine whether it's IBS or Crohn's

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disease, you have implicitly some set of criteria in Milan that you follow clinically. And it would be a great -- I'm looking at you, Lonnie, but not over you -- in general to write those down, to specify them because that's testable. And that's not inexpensive testing, but it is testable, and the path of the future will require that.

We needed to do that in TMD to distinguish certain conditions, whether there's really pathology in the joint, from arthritis and arthrosis kinds of complaints, to just much more -- less significant medical conditions. And we stated the criteria under which we would do the further, more elaborate testing, and then tested. And again, it was an expensive thing to test, CT scans and MRIs. Whether the testing is possible now should be separated from the idea that you want to put down everything that you think is worth testing.

DR. R. DWORKIN: Can I --

DR. BRUEHL: I'm sorry, Rob. It relates to exactly what Sam was just saying. If you have some

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kind of elaborate test that you wouldn't want to routinely subject somebody to clinically to make the diagnosis, keep in mind that future work -- once we come up with these criteria, one approach -- maybe not as a gold standard, but it certainly is an external validity issue -- is so we've got this certain MRI, something we want to see on the MRI. And we can get that in a sub-sample of patients like Sam's talking about, and then look at our diagnostic criteria for the two different disorders and see if they are distinguished. The clinical criteria distinguish patients reasonably well as they relate to the MRI findings.

That's another type of validation research to do in the future and wouldn't necessarily require including that test in the diagnostic criteria.

DR. S. DWORKIN: But you can see the potential for the taxonomy leading to research proposals, generated by this group from across disorders, working with each other to do expensive

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studies that no one of you could do by yourself.
DR. R. DWORKIN: I guess implicit in what Sam and Steve are saying is that these articles and chapters will, we expect, have a section towards the end that's research agenda; additional criteria, signs, symptoms, whatever, were considered. The research don't yet establish that they should be included in the criteria we specify, but these are obviously a focus for future studies.
DR. SARZI-PUTTINI: If we do an evaluation of Axis I and Axis II for physical or psychosocial, is the diagnosis in our diagnostic criteria mutually exclusive? So I mean, do we have to choose which one is the best? Because in the clinical practice, we know most of the time they're both present. So a pain could be nociceptive and centralized at the same time. So the only measure that you have at a certain point is when you treat the patient, then you understand what's going on.
You're not able to do the diagnosis before. I'm talking about TMD, but osteoarthritis of the knee is the same. So it could be nociceptive, but

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it could also be centralized pain. Sometimes you don't get the feeling on the diagnostic criteria, but you have the feeling after you treat the patient.
So what are we going to do with the diagnostic criteria? Do we just specify one at all, and then everything else comorbidity or we have the chance, for example, to have two types of TMD in the same patient at the same time?
DR. R. DWORKIN: I think it's a great question. Roger's going to take the first crack at it.
DR. FILLINGIM: So to me, the diagnosis is based on signs and symptoms. Now, if you have a sign that is central sensitization or generalized hyperalgesia, and your specifications detail how to operationalize that, and that's one of the criteria maybe among several that would meet the criteria for that disorder, you could specify that.
But I think what you're talking about is somebody might have TMD or fibromyalgia based on signs and symptoms, but the underlying mechanisms

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might be distinct, or they might have multiple underlying mechanisms. So that falls to Dimension 5, which is putative neurobiological mechanisms and psychosocial risk factors, and protective factors, and so on and so forth.
You can essentially code those on that dimension, and you might in your write-up indicate here are some of the potential mechanisms, risk factors, for knee osteoarthritis, central sensitization, or whatever it is, and then you specify how it is you would assess that.
So the criteria for the diagnosis would be based on signs and symptoms, and then you could separately talk about the different mechanisms that could potentially contribute to that diagnosis, if that helps.
DR. S. DWORKIN: We had tackled that head on, and we said that TMD was going to be diagnosed to the greatest extent possible, just as Roger has described, by signs and symptoms. And then we were going to further classify the patient by the psychological, psychosocial parameters and not put

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the clinician -- so that we would do measures, which would allow, in effect, elaborate screening for the possibility that the person is depressed or anxious. But we are not going to expect any non-psychiatric or non-psychologically trained behavioral therapist to diagnose depression or anxiety.
So we have a set of consequences in the AAPT format. I see that more in the -- I don't know what number it is. I think it's 3 -- 4 -- in the consequences. And the consequences are going to be uniform virtually across all the pain conditions.
So I find my patients are depressed and/or anxious, and/or seeking excessive medications, and/or abusing the healthcare system, and/or can't work, unable to function at home, in school, and that has to be recorded because that's the presentation of the patient if you examine it beyond the objective signs and symptoms. And in that arena, there are some things that you can do very different than doing the Axis I.
So we ask, and we would urge -- I would

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urge -- you to carefully specify what do you see that characterizes -- what's the phenotypical presentation of your patient? What are all the things you need to describe your patient? Whether it's TMD or the other regional syndromes that have been discussed.

DR. R. DWORKIN: Does that answer your question? I guess.

I could also imagine there would be circumstances where we'd have subtypes at the Dimension 1 and Dimension 2 level. And I don't know if this is what you were aiming at. One could imagine -- the osteoarthritis working group is not here -- that an osteoarthritis working group could say there is an inflammatory nociceptive subtype of OA joint pain and a kind of neuropathic subtype of OA joint pain. I wouldn't bet the pennies in my pocket that they're going to say that, but one could imagine they would. And I guess if the working group thought that current evidence supported those two subtypes of OA knee pain, that would be built into the list of signs and symptoms

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that we would then study in the research phase.

So I think subtypes would be possible at the Dimension 1 and 2 level, but it would depend on the working groups whether they thought the research was likely to support those subtypes. Is that consistent with what we've been thinking?

DR. FILLINGIM: Yes, I think so, although, let's take the OA example. Let's imagine that the two subtypes are identical in their presentation. It's just that the mechanisms are different. That is, the signs and symptoms are the same but with other testing, you can identify different contributing mechanisms. And I wouldn't suggest subtypes. I would suggest coding the mechanisms on Dimension 5. But this is going to be a working group issue.

DR. R. DWORKIN: There are so many different patterns of signs and symptoms.

DR. FILLINGIM: Yes.

DR. R. DWORKIN: Roland, you've been waiting for a long time.

DR. STAUD: Roland Staud. I have a

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different question. And the question is about, for conditions where already many different definitions exist, how to deal with this fact? Is the group recommending that we validate, again, all the previous conditions and compare the new definitions with the old conditions?

DR. BRUEHL: This has come up before in our discussions. The one example would be like fibromyalgia. A lot of effort has been put into developing fibromyalgia criteria and validation. Some people would say that's already been decided. There's nothing more to be done.

One thing that has to happen that's pragmatic is all of these conditions, including fibromyalgia, need to be translated to the AAPT format; so kind of just a formatting issue, you've got to get everything in the right place. Now, it may turn out that after looking at the existing literature, maybe work that's been done since those diagnostic criteria came out, that the people in your working group may go, "You know, I think they may have made a mistake in how they came up with

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these criteria. Maybe X needs to be changed."

It's okay to do that if you feel like that is justified, and we will make the effort to try to conduct whatever research we can to support that and help you decide whether that's the right thing to do or not.

So just because there are existing criteria that are pretty well accepted doesn't mean we are locked into accepting them as is exactly. If you feel there's a good reason to modify them, propose that modification, and let's test it. Hopefully that's getting at what you were asking.

DR. TURK: This is Dennis Turk. Let me just see if I can amplify that a little bit. And actually, I thought you were going to talk about the CRPS. If you remember Steve's presentation, there were several different classifications out there. Then there was the one that they actually thought was the IASP one, which was there "gold standard" if you will. That was the classification. But they felt they wanted to see if in fact there were things missing or could be

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approved. So they took that one and looked at others.

In the survey that I saw that Rob Bennett, who couldn't be here, did of the fibromyalgia folk, at least my looking at that survey of nine people, I think it was, there seemed to be fairly high agreement that the existing 2010-2011 fibromyalgia criteria were not necessarily -- they've missed something or it's not as good as it could be, and they would like to potentially modify that.

So you might start with that criteria as your "that's the existing one right now" and see how does this get improved in any way you think you can in the same way you did with the CRPS.

DR. R. DWORKIN: The one case we're not doing that is headache. As you see from the materials we've distributed, we think the International Headache Society has really done a fine job, so that's the one example, really, where we're not kind of revisiting.

DR. PAIVA: Eduardo Paiva from Brazil. I'm just concerned about the dimensions. For example,

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in fibromyalgia, the more recent criteria included things like the patient's perceptions of new refreshing sleep, fatigue, and cognitive symptoms, and probably we're going to include this in the core criteria, for example, no refreshing sleep. And this also can be included in comorbidities, and also can be included in consequences of fibromyalgia.

So I was just wondering if it's okay to include no painful definitions in the core criteria. And finally, can we repeat those criteria or perceptions in the dimensions, like repeating them in Dimension 2 and Dimension 3?

DR. BRUEHL: One thing I would point out is edema's not painful, but it's a diagnostic sign for CRPS and I'm sure a lot of other conditions. So the individual components of the diagnostic criteria, the signs and symptoms in and of themselves all have to be painful. What is important, though, is that they are all part of defining a painful syndrome. And hopefully the research would be able to help us figure out

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whether the fatigue adds anything to the diagnosis, if it's actually crucial to it or not.

Yes, just because it in and of itself isn't painful doesn't mean it shouldn't be included.

DR. PAIVA: What about repeating the symptom in several dimensions?

DR. FILLINGIM: This is Roger Fillingim again. Let's say non-restorative sleep, your working group decides that's actually a specific diagnostic criterion for fibromyalgia. It's one of the things you can have. Let's say you've got five things, and it's one of three of those five that you have to have to meet criteria. I would say that becomes a core criterion. And it probably doesn't become something on Axis IV or Axis V necessarily.

It's a little dicey because if it's not required for the diagnosis of whatever you're doing -- that is it may not be the feature against which they're diagnosed, but it may be one of the other features. It gets a little complex. So that's going to be an individual work group

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decision. But I would say, let's, as much as we can, avoid overlap between the criteria for diagnosing the condition and then the associated either consequences or risk factors.

But you bring up another point about which there was a lot of discussion both at the launch meeting and then in developing the manuscript. How do you tell whether depression was a risk factor or a consequence since we didn't know the person before they got chronic pain ostensibly? How do you tell whether obesity or non-restorative sleep or whatever -- we recognize.

We acknowledge this in the manuscript that this is a potential issue. I think it's much more important for us to send the message that there are psychological risk factors, premorbid psychological features of an individual that put them at risk for disorders, and that's clearly the case. We may not always be able to tell what came first.

So I think we take the history as best we can and make the best decision we can when we're working with an individual patient and trying to

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assign the criteria to them.
In the article you're going to write, I think it's very important to acknowledge that depression can be a consequence of this condition. Depression can be a risk factor for this condition. In that instance, it can go in both Dimension 4 and Dimension 5.
DR. R. DWORKIN: Gloria?
DR. BACHMANN: Gloria Bachmann. I'd like to suggest one other outcome to this. Robert Wood Johnson Foundation is really promoting a culture of health, which is what pain embodies because pain does affect every aspect of a person's life. And it had several panels, web-based panels, that discuss exactly what we're doing.
I would suggest that that would be another outcome, to contact the foundation and suggest that we have this type of panel discussion on a national and international basis with their support because it is so important, and we do have leaders in pain here.
I think the other two aspects that I think

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we should emphasize is the issue of gender. I know the Canadians are now looking at all research from male/female animal, and I think we should probably permeate that in our discussion. And the other is age.
It's been brought up several times, the pediatric patient versus the adult patient. But it's really where does pediatrics end? It's really a continuum of age, and I think we've brought it up several times that someone may have a pain syndrome when they're premenopausal and have adequate estrogen, and in the postmenopause, they may have other aspects of pain that the reproductive aged female may not have, but the post-reproductive aged female may.
So I think those two points of gender and age are clearly important in anything that we do publish.
DR. R. DWORKIN: One could imagine, in fact, like with DSM III, IV, V, that those would be standard sections, actually subsections, in each of our articles and chapters, age and gender. And

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with respect to the first point you made, Gloria, about Robert Wood Johnson, I promise that we will pursue that only if you promise to help us with it.
DR. BACHMANN: Yes, absolutely.
DR. R. DWORKIN: Good. Thank you.
Yes, Partap?
DR. KHALSA: Partap Khalsa. For those of you who don't know me, I'm the representative from the NIH Pain Consortium to this meeting. I had two points I wanted to make, and I mentioned this to Dennis this morning early. But in this general context, I thought it would be worthwhile bringing it up to the group as a whole because Eva mentioned it early in her talk, and that is the effort by the NINDS, National Institute of Neurological Diseases and Stroke, which is a component of NIH, to develop a common data elements framework. And they have done so already for two pain conditions, one's on stroke, which David was mentioning, and also recently -- I think the more recent one was specifically related to headache.
I guess what I'm raising here, both for the

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steering committee as well as for the individual working groups, is to consider whether there is an intersection between the efforts of this group and this common data elements framework that NIH and NINDS specifically is developing and maintaining.
In particular, since these are -- at least initially, the taxonomies that are being developed are specifically to enable -- or to facilitate anyway, if not enable -- future research, and clearly NIH is going to be a contributor to that. So having these taxonomies that intersect well with this common data elements framework I think would be a benefit in terms of getting them implemented and having something really useful. So that's one.
The second thing is I'm struck by this -- let me rephrase that. I have become really aware of -- and I think NIH at large is particularly sensitive -- of the importance of getting patient input into developing what's important. And this process we have here today, as we're all experts, I think probably it's fair to say all of us are also patients. And probably if

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this room is typical of the general population, 80 percent of us have some sort of pain disorder for which we seek treatment. So it's not like we're unfamiliar with the patients, but we are a group of experts.

One of the key things that has really developed, and obviously PCORI here in the U.S. is probably the chief advocate for, is the vital nature of getting patient input in helping to decide what is important.

So in this taxonomy that's being developed, and particularly the idea of developing core diagnostic criteria, many of which are -- again, these are the symptoms that the patients are reporting. I think this will come back, if not at the input of developing these, but certainly in the testing of their validity, whether internally and/or external validity.

It will be important to really assess how the patients actually think these criteria are because I think we've all learned over a number of decades now that things that sometimes as

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clinicians and scientists we develop are not necessarily what are the most important things to the patients for whom we are trying to treat. It's not clear to me yet from reading all this document how that aspect is going to be incorporated in this process, but I wanted to raise it because I think it's something we really -- getting a greater understanding of how important it is overall.

DR. R. DWORKIN: So just to say, we shared that concern completely, and so we invited three representatives of patient advocacy organizations to this meeting. Two were unable to come. One was here last night, but I don't see Tina this morning. Oh, Tina's here. And Tina represents the Neuropathy Association. So we've started in that direction, Partap, and we realize there's a lot more that needs to be done, and we have every intention of pursuing it.

Chris?

DR. MIASKOWSKI: Chris Miaskowski. In follow-up to that, I was going to ask Steve and the others as well, trying to link the signs and

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symptoms criteria that we're going to develop to the methodology for doing the research and thinking about the symptoms part of that equation, vis a vis the methodology with which the data is being collected.

So I was wondering, when you did your data collection, did the patient self-report or did the clinician interview them and then report what they thought the patient said? So I have a question about that.

Then the second one is, related to the signs and trying to come up with a specific list, was consideration given to the idea that this is a clinically pragmatic sign that's easily obtainable? And I'm thinking about chemo neuropathy or perhaps diabetic neuropathy, where the research tool is often quantitative sensory testing, which doesn't hang out in an oncologist or primary care physician's office.

So can you give us some guidance about thinking through that? And vis a vis what you said in terms of the NIH's move with the PROMIS

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measures, which are online, validated, self-report, how should we be thinking about this as we're designing our instruments for data collection?

DR. BRUEHL: I can tell you what happened with the CRPS. Starting with the second part of your question first, the objective signs were intended to be something that could be done at the bedside, that you wouldn't need any fancy testing to do that. That was for pragmatic reasons because the reality is most people are not going to have access to that kind of specialized equipment like QST equipment, so didn't even want to make that part of it.

I will say that in some of the research work we did, we did collect data. Certain sites had access to QST equipment and did the testing on some of their patients. So we ended up having some data that allowed us to look at how different diagnostic criteria related to QST, but it wasn't formally part of the actual criteria.

The subjective symptom reporting, when we originally did it, was done just like a standard

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clinical history. The questions were asked in a standardized way. I mean, they tried to stick to what was on the sheet. But since then, we have gone to investigating the possibility of having patients fill out a form where they report on those key symptoms because we ended up taking those diagnostic criteria and making a severity scale out of it, which is a lot more practical if you can just have the patient reporting on that and be able to use that for severity.

DR. R. DWORKIN: So Chris, one thought about your question is that even though we seem to have a consensus here, at least at first the criteria we're developing are more comfortable within a research context, and they will then evolve in terms of their clinical applicability.

I guess I agree with what Steve is saying. We don't want to go so far that what we're developing are really kind of tight research criteria that require sensory profiling by the German Neuropathic Pain Network that takes an hour and a half of QST. There's this balance between

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research criteria for chemotherapy induced peripheral neuropathy, but what you might want to do in a phase 2 trial with 30 patients. And I think that's going to be up to the working groups to find that balance between what's feasible in a clinical setting for medium- to large-scale research and what you might want to do in your own lab with 20 patients.

DR. MIASKOWSKI: This is Miaskowski again. Bob, I think we have to have some sense of which way to go. I actually believe we need to think are we designing criteria that are going to be clinically useful. And then have in almost a column, these are the add-ons for research or the other way. I think that's a crucial decision because it's going to be very -- I think it may be very different.

DR. R. DWORKIN: Could you flesh that out with respect to chemotherapy induced peripheral neuropathy, which you're intensely interested in?

DR. MIASKOWSKI: My bias would be to have the patient self-report their symptoms just because

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we've done that enough. And I can tell you, in cancer, we know when patients report their functional status and a clinician reports their functional status, they're not correlated. So I believe it's a much sounder approach to give patients a clear sense of what it is you were asking them and have them rate it.

Clinicians today have a very limited amount of time, in truth. So we have to come up with what I believe are very, very crisp signs that we can -- that the tools are available to ascertain those in the clinic, and we believe these are a finite list that -- and we have to test it, obviously. But these are the ones we believe are the most sound to lead to a diagnosis, and then which are the ones that may enhance that, or give us the subgroups or the profiles.

I think that's a critical question we need to struggle with. I'm not sure I know the answer at this point.

DR. R. DWORKIN: So you're suggesting -- this would be relevant to the

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neuropathic pain working group -- that you would be comfortable with a diagnosis of chemotherapy induced peripheral neuropathy, diagnostic criteria that were entirely based on patient-reported --

DR. MIASKOWSKI: No, I'm not saying that. But I'm saying that the sign part of it, we need to be clear that that information is able to be obtained in a relatively discrete amount of time with tools that are readily available in the clinic.

DR. R. DWORKIN: Dennis?

DR. SMITH: This is Wally Smith. Chris, can you distinguish between three things -- and I know you probably don't mean the former -- spontaneously reported symptoms, symptoms reported in response to a survey by a clinician as part of usual care, and physician-judged or clinician-judged symptoms and signs?

DR. MIASKOWSKI: I don't think a clinician can judge a symptom. A symptom is self-report. The patient has to tell you yes or no to that. The clinician judges the sign. By virtue of

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definition, a symptom is a subjected, self-report of an experience that the individual is having. Now, we have to ask the question correctly I think to get the right information.

DR. R. DWORKIN: So the clinician can say to the patient, do you have pain in your feet?

DR. MIASKOWSKI: Right.

DR. R. DWORKIN: And you're okay with that?

DR. MIASKOWSKI: Yes, I am.

DR. SMITH: And you're okay with that being standardized as opposed to --

DR. MIASKOWSKI: As long as the question is asked the same way.

DR. SMITH: -- being something -- every time asked and asked the same way every time.

DR. MIASKOWSKI: Do you have pain in your feet?

DR. R. DWORKIN: How about Roy, and then Dennis. This is a critically important issue. Thank you. Roy, and then Dennis, and then Tina.

DR. FREEMAN: Quite simply, the problem is that there are a gazillion causes of foot pain:

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metatarsalgia, calcaneal spurs, plantar fasciitis. I could go on, and on, and on. And it's really difficult, first of all, for patients to act accurately to lineate their pattern of symptoms in order to differentiate those. It's pretty hard for the average clinician to differentiate those.

I think in order to take the step perhaps from the possible to the probable to the definite, you may not need to bring in the German Pain Consortium, but you probably need some special, more objective investigations.

DR. R. DWORKIN: Dennis?

DR. TURK: Thanks, Roy. That's along the lines of what I was thinking. First of all, remember when Sam talked about the need to potentially do more expensive types of testing, and then find out that they don't matter? They're not useful.

So for the research purposes, it may be the case that you do want to consider not the full hour and a half of the German network but some variation of that. But if the purpose is that originally

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these are going to be classification with the purpose of research, then you may want to gather more information -- and a little bit -- it may not be what the average clinician has, first of all, when they find out it doesn't matter, or we might find out that it really is essential, and that the clinicians need to know how to do these kinds of exams.

The second point, Chris, you raised about the PROMIS measures, Sam started to show the back pain task force. And they actually came up with recommendations for what those measures could be.

As Partap's comment about the common data elements, it would seem to me, to the extent that you working groups decide that certain psychological factors are relevant or important to be assessed or considered to make use of the existing either PROMIS measures or whatever the common data elements -- I haven't seen all of those to see what they are, but that would seem to be a reasonable way -- and not that every working group for every condition is going to want to say they

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want to have these. But if in fact you think assessing this is important, then here are reasonable measures or procedures that could be used to enable you to address that, and it would then be speaking to some common metrics.

DR. R. DWORKIN: Tina and then Mark.

MS. TOCKARSHEWSKY: Tina Tockarshewsky, The Neuropathy Association. I guess the practical, cautionary thought that runs through my mind and listening to all this conversation is again coming back to cases like diabetic neuropathy or a diabetic patient, especially with the growing prevalence of diabetes in this country and others, being able to come away from this process with an exact enough diagnostic taxonomy so that you're not running into situations, which we hear on a daily basis of somebody comes into a clinician, and they have diabetes, and they're expressing neuropathic pain, it's almost an ergo, foregone conclusion that it's diabetic neuropathy. Even if the person has chemotherapy induced peripheral neuropathy, we've even heard situations like that.

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So being able to give crisp enough guidance so that somebody is coming in and not falling into that trap when they may have something else, and they're not getting to a point of being accurately diagnosed.

DR. R. DWORKIN: Mark?

DR. SULLIVAN: But on a different topic.

DR. R. DWORKIN: Okay. Let's hold that and try and beat this topic to death. Because Steve just came and whispered in my ear that this is really a critical issue. And if Chris is right, for all of the working groups, are we developing research diagnostic criteria? Which actually in psychiatry occurred before DSM-III. In the middle 1970s, psychiatrists developed RDC, research diagnostic criteria, as did Sam for TMD.

DR. S. DWORKIN: Before DSM.

DR. R. DWORKIN: So are we, all of our working groups, developing research diagnostic criteria for each of these conditions or to some extent and to what extent do we want these diagnostic criteria to be clinically applicable?

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So before we get to Mark's question, which is different, since that was written my Steve, I want to call on Steve to say more about what I just said.

DR. BRUEHL: I guess what struck me is that I think we -- I'm including myself in the audience here. We've heard mixed messages. I've kind of gotten the impression that part of this is for clinical diagnosis, but clearly there's the importance of doing research and how do we improve clinical trials. I know that in the written definition, there was specifically talking about getting good samples for improving clinical trials. That's kind of why IMPACT was involved in this, I think. Right?

I guess I'm just -- I'm not clear myself, honestly, on what the point of this is. I keep thinking towards the end result eventually being something comparable to a DSM that would be out in the community where it can be used to actually improve communication between physicians and improve eventually, hopefully, the way treatment's

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done.

I do think it makes a difference if the main point is research. One, we might emphasize certain aspects of the diagnosis more. We might make diagnosis more complicated. We might allow use of a lot more expensive than available equipment is part of the diagnosis because it's just for research purposes. Personally, my sense is that we need to be thinking on down the road towards that time when it's not going to be feasible to have a lot of diagnostic equipment necessarily.

DR. R. DWORKIN: Roger, then Eva.

DR. MIASKOWSKI: Can I respond to that?

DR. R. DWORKIN: Chris? Sure.

DR. MIASKOWSKI: Chris Miaskowski. I totally agree with you, Steve. And I think another consideration is, for me, as I think about these pain syndromes, there's an urgency now. Patients need, as best -- as sensitive a set of diagnostic criteria as we can come up with to begin to treat them. And if this is going to be a 10-year research agenda, trying to figure out the

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diagnostic criteria for any one of the syndromes we talk about, it's not useful.

I mean, I really liked your presentations, Steve, because as I heard your talk, it was really about balancing sensitivity to specificity. And maybe that's what we need to think about here because to me, that is a good goal, that we will get some benefit for the patient in the clinic. We'll be able to do some reasonable research in the clinic.

Your tool as you presented it looked really reasonable to do. You could give that to a busy clinician. They could fill it out. Yet, we could include some things that would allow us to refine the mechanisms perhaps or understand subgroups with a particular pain diagnosis. I think there's an urgency to this. I see people suffering, not being diagnosed correctly. We need to think carefully about this decision.

DR. R. DWORKIN: Roger, and then Eva.

DR. FILLINGIM: This is Roger. Frankly, I think this is really easy.

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(Laughter.)
DR. FILLINGIM: No, I'm being honest here. Regardless of whether we think we're developing research diagnostic criteria or clinical criteria, the truth, they're going to be used for research before they're used in the clinic because we're not tying them to billing. At least that's true in this country. And the early adopters are going to be researchers anyway. But that's sort of orthogonol to how complicated we make the criteria.
Let's say our full intent is to develop these criteria for use in clinical trials and clinical trials only. They still need to be simple, otherwise the cost of clinical trials is going to be so prohibitive such that the few pharma companies that are left are going to run away from pain.
So we need to make these -- well, first, each working group needs to look at the evidence base, the current diagnostic systems that are out there, and propose the criteria that, according to the evidence and their expert opinion, best capture

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that disorder. And then they need to decide what's the simplest way to gather the data to determine whether a patient meets these criteria. And if it's between rubbing them with a Q-tip and testing them with a $100,000 piece of equipment, the Q-tip wins.
So they still need to be practically useful. And then if the working group wants to go on and say other approaches to perhaps more definitively determine the nature of the hyperalgesia or the allodynia, or whatever might include quantitative sensory testing as done like this, but that's not required for the diagnostic criteria.
DR. R. DWORKIN: Eva, and then Sam.
DR. WIDERSTROM-NOGA: Yes. I just had a small comment. I think this is an extremely important issue, too. The clinical utility was actually something that we had in mind when we worked on the spinal cord injury pain taxonomy, not necessarily to start with.
So it's very consistent with what Roger said, that initially there was a taxonomy, but as

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it was incorporated into the basic SCI pain data set, it had to be -- the goal was to make it clinically useful so that it would be implemented in the clinic for treatments eventually. So that's why we got so much feedback from clinicians, which was very, very useful, actually.
Of course as a scientist, you think that this is nothing. But when you incorporate it into a basic clinician's clinic, it's a lot of information. So I think, like Roger said, within each group, one can determine how clinically useful it will be.
DR. R. DWORKIN: Sam, in a minute. What I'm hearing -- I don't know if everyone agrees. What I think Roger and Eva said, I think I agree with, which is these criteria, we think of them primarily to start as research criteria, but they're feasible -- the way it happens is feasible in the clinic and feasible for a large, 600-patient, phase 3 trial; that there are research criteria out the starting gate but have a kind of clinical feasibility potential clinical utility.

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Sam?
DR. S. DWORKIN: I certainly can't disagree with that. But we're here because there are no diagnostic criteria for any of the conditions that the people in this room represent. And why is that? Are we dumb? Are we inadequate? No, we're about the smartest that there are. There's something wrong or inadequate about our model system, and we need to kind of shatter it and put it together again in ways that allow us to advance.
So to say the problem is complicated now is the way a cockpit of a plane is complicated when you go and stick your head in and see this myriad of dials and switches. And you hope what? You hope somebody understand what they mean to each other, especially the pilot. So the task here is not to make the complicated simple. The task is to make the complicated complex. The difference between complexity and complication is they both have the same number of parts in them, but in a complex situation, the relationships among the parts are known.

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Chronic pain is complex, and it will not yield to simple solutions. We know that because we are smarter than simple. There has not been -- in the 50 or 75 years of intense pharmacological research, there has not been a single safe analgesic for chronic pain that is both effective and safe over time, and there have not been stupid people working on those issues.

My strong intuition and understanding of this -- and if we had had this discussion and took the tactics implied here in 1990, we would not have in 2014 a simple -- a relatively simple -- clinical set of criteria for diagnosing TMD, and we did it through research that involved them.

I just would make the case, stress yourself. Pick your own brains and the brains of everybody else. Put down everything that you think is potentially relevant, and then sort it out through your discussions into hierarchies of immediate and less relevance, and design and think about how to get the data on the things you think about because you've got some good ideas. I know that because I

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had good ideas, and everybody I worked with had good ideas. We have to get them out of ourselves in a way unfettered by the requirement for simplicity. That can be a secondary requirement, but the first one is blue sky, and then arranging them in hierarchies. And it's research that's going to provide the answer.

UNIDENTIFIED SPEAKER: Well said. Well said.

DR. S. DWORKIN: Thank you, whoever said that.

MS. FITZCHARLES: Mary-Ann Fitzcharles from Montreal. I think there's one other dimension that we have to keep in mind. We're thinking of the clinic and the research agenda, however, payers and the American legal world are going to pick up on anything that we produce.

So even if we develop criteria, and we say this is purely clinical, we have to clearly understand that it's going to be picked up very quickly by our payers, and we've got to decide is there going to be a difference between the clinical

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criteria and research criteria.

DR. R. DWORKIN: There are lots of other comments on this issue. John?

DR. FARRAR: We started off by saying that we thought that this should be evidence based. And I think if we come back to that, there may be a solution to this issue. I liked what Sam just said. I'm John Farrar if I didn't say before.

In developing a prediction rule for use in clinical work, we often will reduce it over the period of time that we're using it to try and come up with a minimal number of criteria that will best predict in our patients. But that's not where we start.

We start, as I think you were suggesting, in putting down everything that's potentially useful in those circumstances, and then doing some thinking about and some research towards understanding the relative sensitivity and specificity of those particular items; looking at and developing via well-known statistical techniques, prediction rules to try and understand

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how those various pieces work; understanding how some of the comorbidities and the other issues that we're dealing with in the beginning, that should go with this, influence those decisions. And at the end of the day, we can hopefully reduce that data set to a useable data set.

Building on what Stephen showed, the issue is -- you can say this is the model that we would use if you want high sensitivity, but low specificity -- and this is the model that you should use if you want to have a slightly lower sensitivity but really specific. So I think the answer to the question is that we start out by putting down everything possible, and then reduce that set -- start with that, and then reduce that set to a useable format depending on what the goals are of that particular use.

DR. S. DWORKIN: I would just like to add -- this is Sam again -- if this is not the kind of group that's going to do it, no one's going to do it.

DR. R. DWORKIN: Lonnie?

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DR. ZELTZER: I guess the question about rolling this out once we put in the blue sky, as Sam said -- this is Lonnie Zeltzer. We put in everything we could think about, but then it's going to get rolled out for sensitivity and specificity in populations.

The question I have is a sampling technique, a sampling question because if we're saying functionality or pain-related functional disability, botherness or bothersome stress over symptoms, is a separate access than the signs and symptoms themselves without looking at a non-clinical population, you're not going to get at the full spectrum.

Also, there may be problems -- and I'll use dysmenorrhea as an example. I end up seeing many adolescent, postmenarchal females who are referred to me by gastroenterology and have severe dysmenorrhea, but that's never even asked of or included as a pain problem because it's not thought about. So there may be populations of pain sufferers that we're missing by our sampling

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methodology.

DR. R. DWORKIN: Part of what you just said relates back to Roy's question about what is the comparison group. If we're trying to come up with criteria for one condition against what are we evaluating sensitivity and specificity.

Before calling on the other people with hands up, I think I want to disagree with John and Sam because I have to say, we do not have the resources. If Roy's neuropathic pain working group says we want to do punch skin biopsy on everybody for these analyses, we just can't do that. If another working group wants to get an hour and a half QST profile from the German Research Network, that ain't gonna happen.

So I kind of agree that we should cast a wide net in terms of signs and symptoms and other features of these conditions, but that net just can't be so wide that it's going to be everybody's kind of Christmas list of what they would like to see on these patients because we just don't have $40 million to do studies like that.

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DR. FARRAR: But you decide that, and then you back off from it.

DR. S. DWORKIN: Right. The final list is not that.

DR. R. DWORKIN: That's right. We can list it, but it's not going to happen in terms of the actual research studies.

DR. FARRAR: Understood.

DR. HAROUTOUNIAN: Simon Haroutounian, Washington University. Just to continue what Roy mentioned briefly, and it has been attempted in central postural pain, maybe we could come up with a set of core criteria for diagnosis and then specific criteria for defining how probable or possible or definite the condition is.

So for postural pain, for example, there are five criterion, then another set of supporting criteria. By using this, we can decide which kind of probability of condition we would like to deal with within the specific study, for example, as opposed to just clinical setting.

DR. R. DWORKIN: Steve?

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DR. BRUEHL: It's possible to use the criteria that way. That's kind of getting at the research versus clinical criteria. My take on that is that you might be more interested in making sure somebody's at least probable maybe for clinical purposes, but a research study, you'd want to make sure they're definite. Sam might say the opposite. But anyway, there would be different situations where your goal would be different, and you might choose things in a different way.

I think one thing that we -- just kind of implicit in all the discussion we've had is kind of paralleling this with the DSM diagnostic criteria, where it's a categorical diagnosis. And I think there's a little bit of worry in my mind that if we talk, even introduce the topic, of probable diagnosis and that kind of thing, it kind of weakens the whole system because then people start talking about these categories that aren't really the full diagnosis, and then what does that mean?

So I think what you're talking about can be done in the research setting. Let's say we come up

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with 10 diagnostic criteria that are part of diagnosis of X condition, and formally we may say that 5 of those are required for the diagnosis. You might later go back and do research and change that decision rule to 4 or 3 or 8 of those symptoms, but you're still using the same structure. I don't know that we want to include that as part of the actual diagnostic materials, though.

DR. FITZGERALD: Mary FitzGerald. Two main questions. One is about the rule of exclusionary or negative signs and symptoms. Where do you want those to come in? For example, they have pain, but it's not cancer. It's pain in a diabetic, but they haven't had chemo. Would you like those to be on the way in? So before you ever get to Axis I in this patient, you've already excluded cancer, for example.

The second thing is about active ongoing disease processes. They have pain in the limb, but all biopsies are negative. They have bowel pain, but they don't have Crohn's. Is that exclusionary

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on the way in or they can have Crohn's and bowel pain?

DR. R. DWORKIN: I think that's part of Dimension 1. Steve, Roger, Sam?

DR. BRUEHL: I would say it's part of Dimension 1. In the CRPS criteria, I didn't mention it, but that last criterion up there in the Budapest criteria is that there's no other condition that better explains the symptoms. So DSM for many conditions, it will say you don't get this diagnosis if the following conditions are present. And I think that can be all part of Axis I.

DR. FITZGERALD: No other condition in all of medicine or that these top 10 --

(Laughter.)

DR. BRUEHL: I think if you have very specific things that can easily be confused, you would want to mention the specific diagnoses.

DR. R. DWORKIN: So before we finally return to Mark, who's been incredibly patient, any other comments about this challenging issue of the

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balance between research criteria versus clinical criteria, or are we all more or less -- if we're not on the same page and the same chapter?

(No response.)

DR. R. DWORKIN: Mark?

DR. S. DWORKIN: I'd like to ask if Mark's got a headache waiting.

DR. SULLIVAN: Yes. Mark Sullivan. One issue raised in my mind by the mention of chronic fatigue versus fibromyalgia is actually the role of pain in Dimension 1. I'm assuming that we're classifying pain syndromes. Are we classifying chronic pain syndromes? What pain criteria are universal across all categories? Pain alone I doubt is enough. Is it pain of a certain severity? Is it pain of a certain chronicity? Is it pain with functional impact?

If you look at previous efforts at pain epidemiology, like the WHO survey that Mike Von Korff was involved in, they set a threshold. Pain that interferes with an important daily activity prompted at healthcare seeking. So I think we have

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a debate that cuts across all groups about what is the nature of the pain that we're classifying. I've heard it's chronic, but I don't know how severe it is, and I don't know if it's functionally impaired. But I think we need to debate that before we break up into groups.

DR. R. DWORKIN: So I hear three questions, great questions. Do we have a shared criterion of what chronic means? How are we defining chronic? Is it three months? Is it six months? Is it more days of the month than most? So what does chronic mean? Are we setting a threshold for severity if I have one out of -- on a zero to 10 scale, one out of 10 pain, but I have it everyday. Is that chronic?

Then the third thing Mark mentioned -- and this really does go to DSM-III, IV, V -- are we requiring some impact of the pain on the person's life? Or if I've got 8 out of 10 pain everyday, but I'm functioning just fine, do I not get in our book?

We don't have to go to lunch until about

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12:45. Those are three great questions. Comments?
DR. SULLIVAN: And I think they probably need to be held in common across all the groups. I would vote for something that's universal so that we're talking the same language. I think that's what's different. You guys did separate efforts -- CRPS, RSD, spinal cord injury -- independent efforts. But we have an umbrella thing that I think probably needs to define pain for Dimension 1 in the same way.
DR. R. DWORKIN: So, Mark, do you want to make a proposal for those three things?
(Laughter.)
DR. R. DWORKIN: Definition of chronic pain, do we need a threshold for severity and does there need to be functional impact?
DR. SULLIVAN: You know, I think what was used in the WHO study is as good as anything, which is I think we do need a chronicity, probably a more inclusive, like a 3-month rather than a 6-month one would make sense to me. And I also would vote that it has to have some functional impact; otherwise,

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your osteoarthritis group is everybody.
DR. R. DWORKIN: So are we comfortable to make some progress? Because we don't want to spend all day before lunch. I would propose that our definition of chronic pain is pain that's lasted at least three -- in most circumstances, we consider chronic pain, pain that's lasted at least three months. The qualifier of a no circumstance allows the working groups to have exceptions of conditions where it might be less than three months or other exceptions where they might want to make it six months because there is maybe rapid resolution in months 4 and 5.
So are we comfortable enough with a shared definition of chronic pain that in most circumstances it's pain that's lasted three months?
DR. TURK: I would like you to hear Sam's comment because this was directly one of the issues that the back pain took up. And we wrestled with all this and came up with a definition. So why don't you mention that?
DR. S. DWORKIN: Right, part of it. And

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it's entirely in line with Mark's thrust of his remarks that's consistent with -- that is, the research task force that was establishing standards for research on chronic back pain came up with a definition of chronic pain, which had this temporal aspect, and then an impact measure for which there is evidence, a lot of it reported on and generated by Michael Von Korff but other people, so that -- but to answer the question, it was a functionality, the impact.
Rather than -- although we had in that task established a criteria, at this point for this group, I would strongly urge that that kind of impact measure be incorporated in the definition and the criteria for what is high and low impact, for which there is good data on back pain, there's good data on TMD, and that's an empirical issue to be evaluated. But the principle is that chronic pain that matters -- and matters either as a public health issue, as a cost issue, lives of people -- has to include -- an impact is as good a term as any.

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DR. R. DWORKIN: This is a very important decision. So you're saying, Sam, that if I've got knee OA or postherpetic neuralgia, and my pain is 6 out of 10, I've had it for six months, but it doesn't depress me, and I'm continuing to work at full productivity, I don't have a chronic pain syndrome?
DR. S. DWORKIN: No. You have a chronic pain syndrome whose impact is 1 on a score of -- the definition does not stand alone. The definition is coupled to the stratification of impact.
DR. R. DWORKIN: But that's our fourth dimension, right, where we talk about psychosocial consequences of pain.
DR. S. DWORKIN: Yes, but this is very operational and part of it is integrated into the definition.
DR. R. DWORKIN: So I just want to know whether I'm in the book or not. So I am in the book?
DR. S. DWORKIN: Yes, if you want to include

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those menus.
DR. R. DWORKIN: Because one could have argued, using the DSM model, that if there's zero functional impact, it's not a disorder, but you're not saying that.
DR. S. DWORKIN: I can't think about it that quickly. I think if it's a zero --
DR. R. DWORKIN: Are you saying that, Mark?
DR. S. DWORKIN: It can't be --
DR. R. DWORKIN: If there's zero functional impact --
DR. S. DWORKIN: Impact --
DR. SULLIVAN: I don't think we want to say that 100 percent of 80-year-old people in this country have an osteoarthritis pain syndrome.
DR. BRUEHL: I think part of the issue, if we stop thinking about it as syndrome and replace it -- just thinking about it with disorder. You can have a syndrome that is not really a state of disorder. I think what we're concerned about in the diagnosis is a condition that is a disorder that requires intervention.

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DR. R. DWORKIN: Roger's frowning, so I'm going to call on Roger because he's frowning.
DR. FILLINGIM: Another concern about the impact is, when I went to my doctor three months ago, I had the disorder, and it was impacting my life. But with successful treatment that I need to continue, it's no longer affecting my life. If my diagnosis goes away, my insurance company no longer provides my treatment. And since I don't have that chronic pain condition anymore because its impact has been reduced by treatment, I can't get the treatment that reduces its impact.
So the chronic pain -- and by the way --
DR. SULLIVAN: That's completely [inaudible]. The diagnosis doesn't go away. The reimbursement doesn't go away.
DR. FILLINGIM: And I'll say in the article and at the launch meeting, we decided we were dealing with chronic pain conditions; not disorders, not diseases, not syndromes. Conditions. And if the OA group comes up with criteria for OA that are evidence based, and

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100 percent of 80-year-olds meet those criteria, so be it.
DR. S. DWORKIN: I have to say that the impact measure integrates pain intensity and the psychosocial impact. So you cannot get a pain of 6 and no impact.
DR. TURK: Yes? Do you have a question?
UNIDENTIFIED SPEAKER: I was going to say the same thing, that the impact by itself is not the right thing because it's how you deal with the impact. So we're not going to have 100 percent of people age 80 qualifying just on impact. We dropped that out because they may have an objective finding, but they have no pain, or they have pain and deal with it. So we have to look at all those things separately.
DR. R. DWORKIN: So we have 5, 10, even 15 minutes to make sure we're all on absolutely the same page before we break for lunch. And then of course, after the lunch break, about 1:30, you're all going to go out into the breakout sessions for working groups. So raise your hand if you have

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real profound doubts about whether we're on the same page or not. Ajay?
DR. WASAN: This is Ajay Wasan. I wanted to just have a real quick discussion about "not otherwise specified" as a category because it's easy and convenient to put that in every single diagnostic kind of category. I think it's really problematic for this group.
In DSM, NOS on the one hand actually resulted in a lot of people getting treatment that they might not have otherwise got. On the other hand, it's also resulted in a lot of people being given a psychiatric diagnosis which they may not actually have.
So if we stick to our primary focus, which I see it as what Sam has defined as coming up with criteria, primarily or at least initially, for use in clinical research studies, I think we're better off not -- as a group, hopefully we can come to some agreement, as in a consensus, that we're not going to use NOS. That would be my preference, and I'm happy to discuss it.

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DR. R. DWORKIN: Well, how about the following? The working group should do everything possible to avoid having an NOS, not otherwise specified, category. But if in certain circumstances they feel it's really necessary, that is an option. But we would all seek to avoid having what Steve described as a garbage can. Does that seem reasonable?

UNIDENTIFIED SPEAKER: The NOS group really is the high specificity group. Isn't that correct?

DR. BRUEHL: It's the group that's weeded out by the high specificity.

UNIDENTIFIED SPEAKER: The high sensitivity group. Excuse me, the high sensitivity group. So I'm just wondering if it pays at least to have a discussion within the working groups about which are the -- who would be classified as high sensitivity, who is being classified as high sensitivity, and work it out in between, or else create two different groups because, again, one is going to, by definition, be the NOS group, which you don't want to call NOS.

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DR. WASAN: Right. So you could call it, for instance, indeterminate, so that the NOS specification actually suggests that, yes, they have a disorder, but we don't quite know what to call it. So for instance, use another word such as "indeterminate" or something that doesn't label that as having the condition of interest. And it still allows you to do all the research stuff you want to do but avoid I think some of the downside.

DR. BRUEHL: The problem with the NOS is there are no diagnostic criteria for it because the condition is defined by these diagnostic criteria. They don't meet it. You can call them NOS. That is not a set of diagnostic criteria, so it is simply a label for somebody that you have a hunch might have it, but doesn't meet the criteria. That's why I call it a garbage basket.

You don't -- I would agree with what Bob said. Do everything you can not to have a category that makes it sound like that's a separate diagnosis because it really isn't. It's just somebody -- it's the people who are weeded out by

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the decision rules in the diagnostic criteria. And some may be close enough to meeting them that you still want to label them with that label, but they really don't meet it. They don't meet the diagnostic criteria.

Now, if it turns out you've got diagnostic criteria that you end up with a huge number of people that would be labeled NOS, then maybe the problem is the diagnostic criteria are too specific, and that could be revisited based on the research, potentially.

DR. WASAN: Just one other word that's used for that is also "subthreshold." That's another word to use to get around this issue.

DR. BRUEHL: And that might be a good one, too.

DR. R. DWORKIN: Or how about symptom deficit disorder?

(Laughter.)

DR. HASSELL: Kathy Hassell. So maybe I missed it in my pre-lunch stupor, but did we decide that we have a universal definition for chronic

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pain, and what is it?

DR. R. DWORKIN: No one seemed to object strenuously when I said that in most circumstances, it's pain that's lasted -- for most circumstances, for most purposes, we consider pain that's lasted at least three months, allowing the working groups to have exceptions that are either pain conditions that are shorter in duration or longer in duration. But three months will be our benchmark.

DR. HASSELL: Two questions. Daily?

DR. R. DWORKIN: No. I think that depends on the condition.

DR. HASSELL: Fair enough.

DR. R. DWORKIN: So I think we have to turf this to the working groups.

DR. HASSELL: And severity was not included.

DR. R. DWORKIN: I think we said that it can be any severity.

DR. HASSELL: Okay. Thank you.

DR. R. DWORKIN: We didn't really discuss that. I wouldn't want to wake up -- my personal feeling is I wouldn't want to wake up every morning

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with pain to even 1 out of 10. I might not get that treated. It might not have any effect on my life. But I think I've got a pain condition if I wake up every morning in pain, even if it's mild pain.

DR. PAYNE: Chris Payne. I wonder if we can take a minute and just talk about lumping versus splitting because in the visceral pain arena, if we have a man that has ejaculatory pain versus a woman who has vulvodynia, we call these different things. And then if we add bladder symptoms, we call it interstitial cystitis. And yet, none of these have any objective findings most of the time, and we're all going by symptoms.

So how much lumping, how much splitting, do you envision going on here?

DR. R. DWORKIN: Maybe I want to get to lunch, but I think this is up to the working groups. Does anyone on the panel have anything to say?

DR. BRUEHL: Yes. I don't have a definitive response to that, but just keep in mind this is, as

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much as possible, suppose to be empirically driven. So if the research out there that has been done on those three -- just using your example, using those three conditions -- indicates that there's no difference in mechanisms that can be discerned, and we tried to detect them, and that the symptoms are similar, and the difference is only in location depending on gender, use your judgment.

But I think you should feel free to kind of think out of the box if you want to and create some new diagnostic category that lumps them together, if that is justified by the data. Time will tell, as we investigate things further, whether that's justified or not.

DR. R. DWORKIN: So before we break for lunch, any other profound concerns that we're not all on the same page?

DR. S. DWORKIN: I have a profound suggestion that should not be at all controversial. In addition to the temporal parameter, add something about the location so that all the groups are not just working on chronic pain of three

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months. You're not. You're working on chronic pain of three months here, there, and say something about the anatomic location in which the pain is reported.

DR. R. DWORKIN: I think that's in Roger's article. We talk about the temporal aspects of the pain, the location of the pain, the intensity of the pain. There certainly needs to be a discussion of intensity, even if that's not a criterion itself. Absolutely. And that was --

DR. BRUEHL: I think it was Axis II, though, that we had -- it's not key to diagnosis, but it's descriptive.

DR. R. DWORKIN: I think one last comment all the way back. I can't see you because you're in front of the window.

DR. CEUSTERS: I'm not sure whether we are on this same page, but it might be that I'm the only one. I'm not sure whether we understand all in the same way about the syndromes and the conditions and the disorders and the diagnoses and so on. So I found it very useful when some said,

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okay, the disorder is in the body part and the disease is in the person. I always tend to think that the diagnosis is in the head of the physician and not in the patient. And if you do that, you see discordances between the two.

Now, given the example of the chronic pain, when you are defining chronic pain, are you defining something which is inside the patient or is it like a diagnosis? Which is inside of the head of the physician.

The distinction is this. When it is on the side of the patient, then a patient does have chronic pain or doesn't have it. There is no other possibility. If it is a diagnosis, now there might be a term, which is we don't know yet. If my pain started a month ago, I still have it now. Then according to you, what you propose as a diagnosis, you would say I don't have any chronic pain. But it might be that you don't know yet. If we wait two months, then it became clear that already now it was chronic pain.

So that's a clear-cut example, but reading

Roger's paper, I see several of those kind of confusions. And I think that they should be discussed at least. If it's not here, then at least in the different working groups, and that each working group understands clearly what all those different things are.

DR. BRUEHL: Please identify yourself.

DR. CEUSTERS: Excuse me. I'm Werner Ceusters from University of Buffalo.

Adjournment

DR. R. DWORKIN: We have to break for lunch. But what I hear and what you're saying to me makes perfect sense, at least inn terms of that kind of evolution. I wouldn't consider a patient having postherpetic neuralgia unless they've had pain for three or four months since their shingles.

But then, what about the patient who's had pain for two months? And this goes back to what Ajay was saying. That's a kind of subacute condition or a subclinical condition, and the working groups need to deal with that. There should be some text, some footnotes, some



elaboration of those kind of aspects of the conditions that don't fit into -- or fall in between the cracks, don't fit into the criteria.

Okay. I think we need to get you all to lunch. The lunch break is from now until 1:30. And then at 1:30, you all have working group assignments. Remember the taxis, to arrange those. Also, if you're a chair, co-chair, or facilitator, we're meeting back here at 5. Thank you all very much.

(Whereupon, at 12:43 p.m., the plenary session was adjourned.)

## B

## C

## E

## F

## G

## H

## J



## K



## L

## M

## N



## O

## P

## S

## T