

ACTION-APS
Pain Taxonomy Meeting

July 18, 2014

A Matter of Record
(301) 890-4188

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6 **ACTTION-APS PAIN TAXONOMY MEETING**
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10 Friday, July 18, 2014
11 8:01 a.m. to 12:43 p.m.
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14 Westin Annapolis
15 Annapolis, Maryland
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1 **P R O C E E D I N G S**
2 (8:01 a.m.)
3 ACTTION Welcome and Introductions
4 DR. TURK: Welcome. Thank you all for being
5 here. My name is Dennis Turk, for those that don't
6 know me. This is going to be an exciting,
7 interesting, challenging project that we are
8 undertaking, and we are greatly appreciative. And
9 I'm speaking for the organizing committee, which is
10 Bob Dworkin, who's sitting here in the front; Roger
11 Fillingim, who's somewhere -- there he is, where I
12 can't see him -- Steve Bruehl -- Steve, where are
13 you? There's Steve Bruehl. Eva Widerstrom-Noga,
14 there she is hiding in the back.
15 We were the organizers -- perpetrators if
16 you will -- trying to put this together. I want to
17 thank APS as well as ACTTION for supporting this.
18 The intent early on was to try to get as many
19 people involved with expertise and to get support
20 from appropriate organizations to partner with
21 ACTTION, and I'll tell you a little bit about
22 ACTTION in a moment.

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1 Before I start formally doing things, some
2 housekeeping details for you to pay attention to so
3 that you're aware. By the way, so you know you are
4 in the right place, this is the ACTTION-APS
5 taxonomy meeting. If you're not here for that
6 reason, good time to leave. And let me tell you, I
7 have been to meetings where people got up and left.
8 (Laughter.)
9 DR. TURK: And the worse one was when people
10 said, "I hear they have better food next-door. I'm
11 going there." So we don't want that.
12 Housekeeping details. There is internet
13 access in the room. You may access the internet by
14 selecting "Western Conference" and using the
15 password "Western7" for those of you who have
16 computers and want to do that. Please silence your
17 cell phones or put them on vibrate or something.
18 Microphones. This is important for you to
19 know. This is going to be transcribed, and the
20 transcription of these proceedings is going to be
21 on the ACTTION website. The microphones in front
22 of you are voice activated. You don't have to push

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1 any buttons.
2 Is that correct? Yes, voice activated. Are
3 these the type that when you have a certain number
4 of people, it will block people out?
5 (Inaudible response.)
6 DR. TURK: Okay. Because we don't want to
7 pick up too much ambient noise, they are fairly
8 low. Since we're transcribing, please speak into
9 the microphone when you want to say something. And
10 please say your name because, again, this is going
11 to be transcribed. And if you've ever tried to
12 transcribe, you know what it's like to try to have
13 multiple people not saying things or not talking in
14 the microphone. So please do that. We will remind
15 you of this again because this is something that we
16 all tend to forget.
17 The meeting is being recorded and
18 transcribed. Lunch is going to be in the Capital
19 B/C Room, which is in the lobby. Check-out time is
20 12:00 tomorrow. You may check your luggage at the
21 bell stands, the usual kinds of things there.
22 Taxis may be ordered to return to the

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

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

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

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1 Networks. And if you know anything at all, you
2 need to know about ACTTION. Bob Dworkin is the
3 star of coming up with acronyms. So if in fact you
4 need an acronym for any grant you're submitting or
5 any project you're doing, Bob's company is called
6 Acronyms Are Us --
7 (Laughter.)
8 DR. TURK: -- and he's quite willing to take
9 your requests.
10 What's the mission of ACTTION? It's a
11 public/private partnership with the United States
12 Food and Drug Administration to identify,
13 prioritize, sponsor, coordinate, promote innovative
14 activities -- which is why you're here -- with a
15 special interest in optimizing clinical trials that
16 will expedite discovery/development of improved
17 analgesic, anesthetic, and addiction treatments for
18 the benefit of the public health.
19 That's what we're all about, a lot of words.
20 But the bottom line of the idea is trying to come
21 up with better methodologies, better strategies,
22 and better ways to accomplish the types of clinical

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1 trials in these different areas. And anything that
2 we can do -- one of the things -- the reason for
3 this particular working group, or group, is that
4 when you read your literatures in all your
5 different areas, I'm sure each of you have read
6 numerable articles that complain about the fact
7 that it's hard to do meta-analysis.
8 People don't agree on what the diagnostic
9 classifications are, the terminology, the
10 assessment methods, and we really need to set
11 something common. We agree, and we think that's
12 why this is one of the most important things that
13 ACTTION has undertaken, is to move this along.
14 If you want to know more about ACTTION,
15 don't try and read this, but ACTTION.org is the
16 website. You can go see. This is where the
17 transcripts will occur of this meeting. In
18 probably 4 to 6 weeks, if not sooner, we'll try and
19 get everything on there. That's to make it
20 available to you to see what was there, as well as
21 anybody else who's interested.
22 You could argue that, gee, we should have

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1 10,000 people in the room because there are people
2 in so many different areas who are interested.
3 It's just not feasible to do that. So what we
4 tried to do is identify chairs or co-chairs of the
5 working groups who are knowledgeable people, ask
6 them to populate their working groups with a set of
7 people.
8 Acknowledging that you can't possibly have
9 everybody there, we hope that we will try to enlist
10 through peer review and other methods and that
11 other groups/individuals will look at the fruits of
12 your labor, if you will, to give us feedback/input
13 on those as they go on. And they'll be mounted on
14 this particular site.
15 Now, the tattooist will be coming in this
16 afternoon because this is going to be tattooed on
17 your arm, so you can't possibly forget this.
18 What are the dimensions? We have a
19 framework for all of the classifications. You're
20 going to be hearing more about that from Roger.
21 You should have read the article. I hope you'll be
22 hearing more about it from Steve Bruehl, from Eva,

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1 from Sam Dworkin. But this is what you need to
2 keep in mind because this is the organization of
3 everything you're going to do. There are different
4 dimensions that should be considered and put into
5 every one of the conditions that you're going to be
6 examining while you're here and that we eventually
7 move forward.
8 First is what are the core diagnostic
9 criteria? Second is what are the common features?
10 These two are the ones that you're probably going
11 to spend the greatest amount of time at this
12 particular meeting. But in addition to that, we
13 also have common medical comorbidities,
14 neurobiological, psychosocial, and functional
15 consequences. And notice where putative are
16 neurobiological, psychosocial mechanisms, risk
17 factors, and protective factors.
18 The order with which these are is not to
19 emphasize priority because if you read the
20 manuscript, as you should have, there was a lot of
21 discussion in the original group that many of you
22 participated in, about the importance of looking at

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

9 UNIDENTIFIED SPEAKER: (Inaudible - off
10 mike.)

11 DR. TURK: Now today, this is July
12 2014 -- no. We are not going to do that. We're
13 going to start, and we're going to go to 2015, and
14 then we'll have mission accomplished. So you are
15 going to do this by -- now, I did exercise a
16 picture of our former president that came with
17 this. I think we want to be politically correct.
18 But this is what we're going to try and do.

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

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

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

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

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

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

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

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

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1 make sure that that information is in there because
2 it is going to be transcribed, and our
3 transcription people very much would appreciate you
4 doing that.
5 So thank you very much for being here. It's
6 a delight to have this many people. For those that
7 I don't know, I look forward to meeting you over
8 the time that we're here.
9 Roger, do you want to take over?
10 Presentation - Roger Fillingim
11 DR. FILLINGIM: Good morning, everyone. I
12 want to talk a little bit about the frameworks
13 since this is what you're going to be applying your
14 diagnostic criteria to. So first I'll give you a
15 brief history of this initiative, talk about some
16 of the issues that we discuss at the previous
17 meetings since many of you were not here. Then
18 we'll talk about the current framework and future
19 activities.
20 I'm not sure if you can read that in the
21 back, but this is sort of a timeline of this
22 initiative. Some things probably happened before

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1 September 2012; that is, Bob and Dennis and John
2 Loeser were talking about this. But September of
3 2012 is when the American Pain Society came into
4 the picture, and this became an ACTTION-APS
5 partnership.
6 Bob sent me an email in October 2012. The
7 APS board provided its initial approval. Formal
8 approval was in January of '13, and then there was
9 an announcement in the ACTTION newsletter of the
10 partnership. That was October 2012. For the next
11 six-plus months, there was a lot of planning in the
12 background. Many of you were being contacted to
13 get involved.
14 Then the Pain Research Forum, which some of
15 you may be familiar with, did an article on this
16 initiative, and that was posted in April of last
17 year. We had our launch meeting May of last year.
18 And since then, working group chairs have been
19 identified, and they've invited working group
20 members to get involved.
21 We submitted the initial article in
22 November. It was accepted in January and

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1 fast-tracked for publication. And the working
2 groups, many have been meeting via conference call,
3 and they've started their work. Of course, we're
4 here now at the second AAPT meeting. And of
5 course, in September, everyone will publish
6 their --
7 (Laughter.)
8 DR. FILLINGIM: -- oh, I'm sorry. Okay.
9 So I just thought to give you a little
10 context, I'd give you some excerpts from what's
11 going on. This is from the initial email that Bob
12 sent me, which was helpful for me to go back and
13 read to remember why we're doing what we're doing.
14 And I think it's interesting.
15 Of course, we're developing a comprehensive
16 pain taxonomy. And Bob says it's essential so that
17 consistent and accurate diagnoses are used for
18 clinical research, clinical trials, and to
19 facilitate comparisons across studies for
20 systematic reviews and meta-analyses. It's also
21 critical for regulatory reviews of new drug
22 applications. So this provides some rationale for

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1 what we're doing.
2 Then from the article published in the
3 newsletter just announcing the initiative, the aims
4 are to establish a coordinated framework for pain
5 diagnosis and classification to provide
6 evidence-based diagnostic criteria for the major
7 acute -- although we're not doing that yet -- and
8 chronic pain conditions, and to broadly disseminate
9 the pain classification and taxonomy so that it
10 will have the greatest impact.
11 So that's sort of where we came from and
12 what got this ball rolling. There were a lot of
13 discussions before the launch meeting last year
14 among those of us who were on the organizing
15 committee. I would necessarily say that we've
16 answered all of these questions, but these have
17 been questions that we've considered. And one of
18 the ones that came up as we were doing the Pain
19 Research Forum article and have talked to other
20 people is how does AAPT relate to the ongoing IASP
21 pain taxonomy efforts?
22 I suspect the most honest answer is we don't

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1 know because we don't know exactly what IASP is
2 doing, although it has to do with World Health
3 Organization and ICD-11. So it appears that
4 there's relatively little overlap.
5 We did have discussions with IASP in getting
6 this started with some back and forth. But
7 Fernando Cervero, who at that time was the
8 president, really had no problems with the American
9 Pain Society, which is a chapter of IASP, getting
10 involved in this initiative because our aims from
11 our view and his view did not overlap greatly with
12 what they were doing with taxonomy.
13 Another question that has come up is, is
14 what we're doing going to be used for research
15 only? Do we want to see it used in the clinic?
16 I think we accept that its initial
17 application is almost certainly going to be heavily
18 research focused, whether that's basic human
19 research or whether those are clinical trials. But
20 the hope is that over time, with increased
21 research, it will get disseminated into clinical
22 use as well, because it would be unfortunate to

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1 have one set of diagnostic criteria that we use in
2 research and completely different sets of
3 diagnostic criteria that are used in the clinical
4 setting.
5 The other question, initially we thought,
6 well, we'll make a book. We'll get a bunch of
7 chapters, which those of you in the working groups
8 are going to author, and we'll make a book out of
9 it.
10 As we discussed this, the plan to publish,
11 when ready, in the Journal of Pain first to make
12 these publicly available became the most obvious
13 choice. But in the end, we would like some kind of
14 a volume. Whether that's a paper book, an
15 electronic book, some other electronic medium, I
16 think is yet to be determined, but those are some
17 of the things that were talked about early on.
18 I mentioned the IASP classification. In
19 case you haven't looked at it in a while, these are
20 their axes. So they have five like we do, but
21 theirs are different than ours. And then if you
22 look at the classification system itself, you can

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1 go to many of the conditions in IASP and not know
2 exactly how to determine whether a person has that
3 condition. Right? So for many of the conditions,
4 there aren't actually diagnostic criteria proposed;
5 for some there are.
6 So we've come up with, while it does have
7 five dimensions, it is different from this. And
8 then the etiology I'll just make comment on because
9 etiology is different than mechanisms. So our
10 fifth dimension, as Dennis pointed out, is on
11 putative mechanisms. Right? And that's not the
12 same thing as etiology.
13 As you can see in some examples here,
14 diabetic peripheral neuropathy, the etiology
15 typically would be thought of as diabetes induced
16 nerve damage. There might be some general
17 mechanisms contributing, and then there are almost
18 certainly some specific mechanisms, whether we know
19 them or not. And so it's these mechanisms that
20 that fifth dimension relates to in our taxonomy.
21 So we had the launch meeting in May of last
22 year, and not all of you were here. Many of you

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1 were here. The goal of that meeting was to develop
2 a framework that all working groups could apply in
3 developing diagnostic criteria for chronic pain
4 conditions.
5 For those of you who weren't here, the
6 agenda looked something like this. We had a
7 presentation on the evolution of the Diagnostic and
8 Statistical Manual of the American Psychiatric
9 Association because that was thought of as one of
10 the models that was out there that had impacted the
11 field in terms of taxonomy.
12 Pat Mantyh and Frank Porreca gave us a nice
13 presentation on mechanisms and how they can inform
14 classification. Sam, Eva, and Steve presented
15 their experiences developing and validating
16 diagnostic criteria for different pain conditions.
17 We then talked about how we're going to develop
18 this multi-axial framework and different
19 possibilities. And then after a little blood on
20 the walls, we figured out what we were going to do.
21 Right?
22 This was a consensus meeting; not a

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

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

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

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

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

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

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

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1 illness."
2 So they go on to say, "Notwithstanding these
3 difficulties, there's consensus at this time that
4 the biology of mental illness and chronic pain is
5 insufficiently developed to support a
6 classification scheme based on integration of
7 genetics, neuroscience, and psychopathology."
8 So they've got this initiative out, this RFA
9 out, to make this happen. So despite all the money
10 they've spent on this and all the time and effort,
11 they recognize we need to spend more because we're
12 not there yet. So if they're not there yet, I'm
13 pretty confident we're not there yet for becoming
14 completely mechanism-based. And that's one of the
15 reasons this is Version 1.0. Right? We're going
16 to discover more mechanisms. Some conditions are
17 further along in that regard than others, but as
18 the evidence base develops, we're going to update
19 our classifications, especially where mechanisms
20 are concerned.

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

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

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

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

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

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1 but because I said yes instead of no I think. So
2 it's really completely arbitrary. A couple of the
3 things that we point out in the article, one is
4 characteristics of an ideal diagnostic system.
5 Apparently, it's published in a really large book,
6 which is read by a person in a white coat.
7 In addition to that, there's biological
8 plausibility. It should be exhaustive -- we're not
9 going to be exhaustive yet, but we'll
10 see -- mutually exclusive; that is if you have on
11 diagnosis, that means those same symptoms don't
12 qualify you for another diagnosis. That doesn't
13 mean you can't have two diagnoses at the same time.
14 It should be reliable, clinically useful, and
15 simple.
16 Some of the important characteristics of our
17 initiative, which we point out in the article,
18 number one, it should be evidence based. There are
19 a lot of smart people in this room, and maybe off
20 the top of your head you could tell me what you
21 think the diagnostic criteria for irritable bowel
22 syndrome are, or fibromyalgia are, and what you

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1 think is best, but we're interested in what the
2 evidence says about this. This is one of the
3 unique features of our initiative.
4 The other really unique feature is that this
5 framework is going to be applied systematically
6 across pain conditions. That's not true of other
7 taxonomy efforts that have been carried out in the
8 pain field. They tend to be isolated, and they may
9 not overlap at all in the framework that's applied
10 for TMD versus chronic widespread pain or something
11 like that.
12 So we're trying to add some cohesion to this
13 project. It will be multidimensional and
14 biopsychosocial. It will be applicable for both
15 research and clinical use. And as we've mentioned,
16 it should evolve as new evidence emerges.
17 Here's the organization as we published it
18 in the manuscript: peripheral and central nervous
19 systems; musculoskeletal pain system; orofacial and
20 head pain system; visceral, pelvic, and urogenital
21 pain; and disease-associated pains not classified
22 elsewhere. And then you see the individual working

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1 groups that emerge from those superordinate
2 categories.
3 As Dennis already put up here, here are our
4 five dimensions with the explanation that you may
5 or may not be able to read. This is taken verbatim
6 from the manuscript, so you have that already. And
7 as Dennis mentioned, this is where the majority of
8 your time is going to be focused for the next day
9 and a half to two days.
10 For the future, what you're doing today and
11 tomorrow is developing potential diagnostic
12 criteria, nominating symptoms of conditions that
13 you think and that the evidence says should be part
14 of that diagnosis.
15 Then Steve will talk about some of the
16 research activities, but it will be important to
17 evaluate the liability and validity of those
18 criteria. Ultimately, the working group will
19 finalize diagnostic criteria for each of the pain
20 conditions, and then you will disseminate that by
21 initially publishing it in the Journal of Pain, we
22 hope. And then we hope to have a broader

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1 dissemination of the combined chapters, ultimately.
2 So that's all I have to say. Are there any
3 specific questions about the framework? Does
4 anybody who was at one of these meetings want to
5 talk about everything important that I left out?
6 Yes, Lesley?
7 DR. ARNOLD: This is Lesley Arnold. I had
8 just a question for the future perhaps in terms of
9 applying these to children, adolescents, because
10 many of the conditions do occur in young people, so
11 we have to keep that in mind I think for the
12 future.
13 DR. FILLINGIM: Yes. And we do have
14 expertise in pediatric pain. I know Tonya's here,
15 apparently not for that purpose, but you're still
16 allowed to lend your expertise to the initiative.
17 Elliot Krane is here. I think we initially thought
18 about do we need specific categories for
19 pediatrics. And if memory serves, the conclusion
20 was, no, not specific categories, but each working
21 group may need input from pediatric experts. And
22 that's why we have them involved in this

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

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

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

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

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1 hear about the research activities in a little bit.
2 Presentation - Stephen Bruehl
3 DR. BRUEHL: So I'm going to answer some of
4 those questions and really raise some issues
5 related to the questions that were just brought up.
6 For those of you that weren't at the talks that we
7 gave a year ago, this will be all new. For those
8 of you that were at that talk, I added and changed
9 things around a little bit to make it fit a little
10 better with what we're doing here today.
11 So what I'm hoping, though, is that I can
12 give you a real-world example of how almost the
13 same kind of situation we're faced with here was
14 handled for a particular pain condition previously,
15 which is complex regional pain syndrome.
16 In the course of talking about this, I'll
17 talk about the kind of research we were able to do
18 that get at the issues of validity. I will also
19 try to remember -- and please remind me if I
20 don't -- to talk about the difference between
21 clinical purposes versus research purposes and what
22 impact that has because that is an important issue.

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1 For those of you who may not be familiar
2 with it, CRPS, complex regional pain syndrome, most
3 people in the U.S. think it's neuropathic. There
4 are people who disagree. But it's some kind of
5 pain syndrome. It's usually occurring in the
6 extremities. What makes it unique is that it's
7 associated with significant involvement, signs that
8 seem to suggest the autonomic nervous system is
9 involved. It used to be known as several different
10 conditions, which I'll give some names here in a
11 second.
12 I wanted to mention here, though -- keep
13 this in mind as I'm talking about the CRPS
14 examples. So what we're doing in this process is a
15 couple of key things. And we'll hand this out
16 later, the working group guidelines. Those of you
17 who haven't seen this, it's a document saying
18 here's what each working group is supposed to do.
19 One of the things you're supposed to do as a
20 working group is to do some type of systematic
21 review, and it doesn't have to be written up as a
22 review, but you want to at least look at the

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1 literature. You want to identify what the accepted
2 diagnostic criteria are in that area if there are
3 indeed any. I'm sure for many areas, there may not
4 really be anything that's accepted as the standard.
5 If there isn't a standard, or even if there
6 is a standard, what other options are out there?
7 For most areas, there are going to be competing
8 groups that may have different ways of handling
9 diagnosis of particular pain conditions, and you
10 just want to get the lay of the land, what all is
11 out there.
12 As a very specific thing you need to get as
13 a working group -- and this is very important from
14 the research perspective -- in the process of doing
15 this review, you need to identify what I've been
16 called the universe of signs and symptoms that
17 might characterize this disorder. This could be
18 test results. It might be clinical things you'd
19 see on the exam. It might be other tests you can
20 do. It might be what the patient says about their
21 syndrome.
22 Any of these things, though, that, based on

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1 the literature and your experience, you feel might
2 be kind of defining features of that pain
3 condition, you want to write those down because,
4 ultimately, that is what is going to create the
5 paperwork we need to be able to do the diagnostic
6 research on down the road.
7 So for CRPS, known prior to 1994, is reflex
8 sympathetic dystrophy, causalgia, and a variety of
9 other things. No one was ever really sure if we
10 were talking about the same condition, different
11 conditions. There seemed to be a lot of overlap.
12 It depended on whether you were in Europe or the
13 U.S. as to what terminology was used.
14 So it was a real mess because nobody -- this
15 is a really good example of how you could have a
16 bunch of treatment studies done that basically
17 leads you nowhere because every study was done on a
18 different group of patients that was defined in a
19 different way. And nobody knew what worked and
20 what didn't. I can't say that has changed a lot
21 yet, but at least we have diagnostic criteria.
22 I'm going to give you some examples. So

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1 when we went and looked at the literature on what
2 was preexisting, what we found were several things
3 that were used in a number of studies. One was
4 called Kozin's criteria. And they said you have
5 definite RSD if you've got pain and tenderness in a
6 distal extremity; signs and/or symptoms of
7 vasomotor instability undefined; swelling in the
8 extremity. And they don't even require this for
9 diagnosis but just mentioned you might have
10 dystrophic changes, so skin, hair, nail kind of
11 changes, that kind of thing.
12 So really you've got three criteria, and
13 that was it. Now, you'll notice -- this is the
14 European criteria set that was fairly dominant for
15 a number of years, called Veldman's criteria. Now,
16 they're having what's call a decision rule here.
17 You have to have at least X number out of this list
18 of signs and symptoms, which is a nice way to do
19 something because then you can alter that number
20 and change the sensitivity and specificity for
21 research purposes versus clinical purposes.
22 For example, at least for the following,

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1 unexplained diffuse pain, that's kind of similar to
2 what was mentioned in the last set. Skin color
3 asymmetry, okay, that's a vasomotor sign. That's
4 kind of similar to what was listed before.
5 Temperature, getting at vasomotor, but it's
6 a different actual objective sign. So now they've
7 split it out into two separate signs you might look
8 at.
9 Diffuse edema, limited active range of
10 motion. Range of motion wasn't even in the other
11 criteria. Signs and symptoms increase with
12 exercise. That wasn't in the previous criteria.
13 And also, they're present in an area larger than
14 the original injury, including distally.
15 So we got a little more specific about what
16 was required in this one and have an actual
17 decision rule. Gibbons & Wilson, they proposed
18 this in the Clinical Journal of Pain. They had a
19 list of various signs and symptoms, very specific,
20 and said you have to have five of these to be
21 considered having definite RSD. But you'll notice
22 some of the same things.

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1 Now, they've gotten a little more specific
2 in how they've described the pain. They're saying
3 allodynia or hyperalgesia, certain pain
4 characteristic. They've got the edema but not
5 necessarily diffuse. They have skin color or hair
6 growth lumped together. Hair growth wasn't really
7 mentioned specifically in that last set.
8 So as you can see, there is some overlap
9 between these different criteria, but each of them
10 is kind of unique. What we want to talk about here
11 is what the impact of these various things in the
12 literature is. And the basic issue is different
13 criteria mean that it is a different disease, in
14 some sense. Since we don't know the mechanisms, if
15 you have a syndrome that has a different set of
16 signs and symptoms in the syndrome, you're talking
17 about different diseases.
18 We've just presented three different sets of
19 criteria. It really is talking about three
20 different diseases potentially; we don't really
21 know. And what it means is if you've got these
22 multiple criteria floating out there, then no one

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1 knows what to use. There's nothing that's
2 considered really the gold standard. So the
3 inclination in many clinicians is to just start
4 making up your own diagnostic criteria, some
5 combination of these, or based on something you
6 heard in training.
7 It's really not the best way to do diagnosis
8 if we're trying to be able to generalize across
9 studies, especially for looking at interventions
10 and efficacy of interventions. And even just
11 clinical communication, you make a referral of a
12 patient and you want to say this patient has CRPS,
13 you want that other professional to understand what
14 you mean when you say that, that that's an agreed
15 upon language.
16 In 1994, in Orlando, they held a meeting
17 similar to this is my understanding. I wasn't
18 actually there, but they invited a group of people
19 with interest and expertise in the area and forced
20 them to sit there for two days, in Orlando, until
21 they came up with some diagnostic criteria for this
22 disorder that had previously been known by all

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

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

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

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

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

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

17 I mentioned earlier this universe of signs
18 and symptoms idea, so if you look at the
19 literature -- and this was actually a literature
20 going back a hundred years -- what you saw is the
21 1994 IASP criteria do include allodynia,
22 hyperalgesia, skin temperature and color changes,

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1 have any money.

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

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

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

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

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

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

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1 those were. Motor abnormalities can describe what
2 they were.

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

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

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

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1 and then come back later and answer certain
2 questions in terms of validating the diagnostic
3 criteria we were going to come up with.
4 What can we do to validate diagnostic
5 criteria on the cheap in a situation like this,
6 where this is basically all the data that we've
7 got? And this will be exactly what we get for AAPT
8 diagnoses. One, is the structure of the internal
9 relationships between CRPS signs and symptoms that
10 were in those 1994 diagnostic criteria valid? Does
11 it make sense to lump together vasomotor,
12 sudomotor, and edema all in one criterion? And if
13 you have any of those you get the diagnosis. That
14 was a key question.
15 Also, a key question I thought was does it
16 make sense to be able to get the diagnosis based
17 only on symptoms or should we require some
18 objective signs present when you do the exam?
19 External validity issues, do the criteria
20 and the decision rules we're using adequately
21 discriminate between CRPS patients who have known
22 other types of conditions such as diabetic

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1 neuropathy, such as various kinds of peripheral
2 neuropathy that are discrete other conditions?
3 So what we did for internal validation,
4 multi-site, we got this database form and ended up
5 with 123 patients who met the 1994 criteria. And
6 if you know how rare CRPS is, having 123 patients
7 is actually a pretty big deal because that's a very
8 large data set for that condition. We all got the
9 same information on all these people. One question
10 was, does it make sense to include objective signs
11 and subjective symptoms?
12 I'll just point out one thing here. This is
13 something we could do with the data we collect.
14 It's very simple, but it's useful. Check this out.
15 So we've got these things that the historical
16 literature said were common in CRPS, and what we
17 discover is some are more common than others. The
18 nail and skin changes, those dystrophic changes are
19 present, but they're really not very common,
20 certainly not universal. But they're common
21 enough, they might be useful in diagnosis.
22 You'll also notice that if we look at the

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1 self-reported symptoms, like the red are the most
2 common ones, so color changes, range of motion.
3 And you'll notice that if you look at the frequency
4 of signs, those same two are also the most common
5 signs. What that told us was that when patients
6 say I have this symptom, they actually are
7 reporting on a real phenomenon that may just not be
8 present that day.
9 Based on that, it was probably a good idea
10 for us to include signs and symptoms in the
11 diagnostic criteria separately because they are
12 tapping into the same things, but we might miss
13 one, miss the signs, if we don't also ask for
14 symptoms because of that lability of the symptoms.
15 So that was really the key issue that we
16 were able to come up with based on looking at just
17 simple frequencies of signs and symptoms. There
18 was nothing that every single person had, so
19 clearly we needed to have a variety of signs and
20 symptoms to look at to get the diagnosis.
21 Now, is the grouping of signs and symptoms
22 in those 1994 criteria something that holds up when

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1 you look at it based on the actual data? And
2 again, it's the one in red. And is this too low a
3 threshold if you only have to have one of these
4 based on self-report?
5 Now, we used factor analysis on that data
6 from that data sheet, and we ended up identifying
7 groups of signs and symptoms that seemed to hang
8 together. And what we found was that of that list
9 of things on that database form, what you ended up
10 coming up with, essentially, was a sensory cluster,
11 which were things like allodynia and hyperalgesia.
12 That paralleled the criterion 2 in those 1994
13 criteria.
14 You got a separate grouping of vasomotor
15 symptoms. This was the temperature and color
16 changes. That's in criterion 3, but you'll notice
17 it was a separate cluster from the sudomotor and
18 edema. So the sweating changes in the edema, for
19 whatever reason, lumped together, and they were
20 separate from the vasomotor.
21 Now, in IASP criteria, those were part of
22 the same criterion. The research was saying that

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1 it's actually two separate things. There's a
2 mechanistic reason that might be able to explain
3 why the sudomotor and edema lumped together.
4 Now, you'll notice motor and trophic
5 changes, which have been reported in the literature
6 for years as going along with this condition, were
7 not included in the IASP criteria at all, and they
8 form a separate cluster.
9 So basically, the way the current criteria
10 were written in those 1994 criteria, you didn't tap
11 at all into this feature that was acknowledged to
12 be key, and it doesn't overlap with any of the
13 other clusters. So we were actually able to get
14 some good information by doing this background
15 analysis on that very simple data sheet.
16 So we can conclude that those 1994 criteria
17 are not internally valid. And in all likelihood,
18 the way they are written, the way they are
19 structured in the decision rules involved, will
20 lead to over-diagnosis and poor specificity. This
21 says we probably need to revise the criteria. Now,
22 external validation -- so we're going to try to

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1 develop new criteria. Now we've got to be able to
2 do the external validity to demonstrate that what
3 we come up with is better than what was there in
4 the 1994 criteria.
5 So what we want to do, for external
6 validation, our big issue is can you distinguish
7 CRPS from non-CRPS pain. And if you start to think
8 about what I've already said, there's an obvious
9 problem with doing this. There's no gold standard.
10 We don't know the pathophysiology of this
11 condition, so how are you going to tell whether one
12 diagnosis is better than the other? It's not an
13 easy question to answer, and I'm the first to admit
14 that while you can address this, it has
15 limitations. It's not perfect, but it's better
16 than nothing at all.
17 The way we did this -- and it's a little
18 hard to explain this, but we've essentially -- we
19 set it up so that we've stacked the deck in favor
20 of proving that the existing criteria are the best.
21 And what we did is we said, okay, let's take those
22 1994 criteria. We're going to diagnose these

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1 patients according to those criteria. And now,
2 based on other means of diagnosis, we know that
3 this other group of patients that we've collected
4 the same data on, we know that they have painful
5 diabetic neuropathy, painful postherpetic
6 neuralgia, and discrete other conditions that we
7 know are not CRPS.
8 So we've got signs and symptoms in both of
9 these groups. And now what we're going to do is
10 say let's use those 1994 diagnostic criteria that
11 we just used to define this group to distinguish
12 between those two different groups. Now that has
13 stacked the deck. And if those are good criteria,
14 we should have 100 percent sensitivity and close to
15 100 percent specificity distinguishing those two
16 groups.
17 Now, what's nice is using that same
18 methodology, we can propose an alternative set of
19 criteria and try to do the same thing, does this
20 distinguish better than those 1994 criteria. The
21 results surprised us a little bit. So we've got
22 117 CRPS patients, and we ended up with 43 patients

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1 that had other types of neuropathic pain as a
2 comparison group.
3 We got this database form on everybody. And
4 what we found using the original IASP criteria,
5 under stacking the deck conditions, we got very
6 high sensitivity, which is what we would expect,
7 but our specificity was only .36, which is
8 horrible. It means we were way over diagnosing
9 CRPS using the existing diagnostic criteria, and we
10 thought we could improve upon that.
11 Now, I'm going to point out we want to use
12 this same type of process in doing the research for
13 any one of the conditions that we might be
14 including in our diagnostic criteria. So we might
15 be looking -- and I'm not going to give specific
16 examples, but just say within the neuropathic pain
17 working group, we might have five diagnostic
18 categories we're concerned with.
19 We might come up -- focus on one of those
20 and say I want to discriminate between people that
21 have this one and this one, these two discrete
22 diagnostic categories. Now, it may make just as

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1 much sense to pick diagnostic categories as
2 comparisons from other working groups. There's no
3 restriction on that. But we want to get a couple
4 of other comparison conditions to look at. But
5 we'll talk a little more about that later.
6 So we thought, what can we do to make the
7 diagnosis better? One might be to require the
8 presence of objective signs so you can't get the
9 diagnosis based only on self-reported symptoms.
10 That was an obvious one. We might include motor
11 and trophic changes in the diagnosis since they're
12 not in there at all now. And then we might also
13 split out those vasomotor signs and the edema and
14 sudomotor signs into two separate diagnostic
15 criteria. Those were some of the things we figured
16 we could do.
17 We actually did some research on this. We
18 had a meeting kind of like this. Again, experts
19 reviewed the research literature, existing problems
20 with CRPS diagnosis, and made recommendations for a
21 formal revision based on some research we had done.
22 The research that we did -- and I'll show you the

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1 actual criteria in a second -- allowed us to come
2 up with an improved set of diagnostic criteria that
3 addressed those issues that we thought we can
4 improve upon.
5 One thing that was key -- and this gets at
6 the question that was mentioned earlier -- is the
7 decision rules. So do you need two of these or do
8 you need three of these? We elected to actually
9 propose two separate decision rules, depending on
10 whether the purpose was clinical diagnosis where
11 you want to maximize sensitivity or whether it was
12 for research purposes, where you want to have more
13 of an emphasis on specificity.
14 Now, the clinical criteria we came up with
15 was continuing pain that was disproportionate to
16 any inciting event; at least one symptom reported
17 in three or more of the following categories. Now,
18 those four categories were taken directly from the
19 results of the factor analysis.
20 So we have symptoms. This is the
21 self-reported symptoms in three of these areas.
22 And you can see it's got temperature and skin color

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1 changes, edema, sweating changes. You've got the
2 weakness, range of motion, the dystrophic
3 changes -- tremor, dystonia -- a variety of things
4 that might meet that criterion.
5 Three was not arbitrary. Three is what we
6 ended up coming up with, but we basically tested
7 all possibilities, 1 through 4. And then you'll
8 see here -- I'll show this. You have objective
9 signs, same four categories. What we ended up
10 saying was you need two of these, but we tested 1
11 through 4 and basically looked at the ROC curves.
12 It's like how do you balance sensitivity and
13 specificity with these? What maximizes it? And it
14 turned out that the three symptoms and the two
15 signs seemed to be a nice balance of sensitivity
16 and specificity for clinical purposes.
17 You'll notice in this case our signs pretty
18 much parallel exactly what's in the symptoms, but
19 do you see it that day when they're there for the
20 exam? Research criteria, all we did is we bumped
21 up the number of signs required to 3 instead of 2.
22 And this actually did seem to increase specificity

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1 pretty -- I think it ended up being about
2 15 points.
3 You can see here -- this was actually a
4 re-validation study. This was a second go-round of
5 this with a totally new sample after we'd come up
6 with these criteria. And it turned out 1994
7 criteria, very sensitive as they should be. The
8 specificity was poor again, so we replicated that
9 finding.
10 The Budapest clinical criteria that we
11 developed, sensitivity was still very high.
12 Specificity, while not perfect, was a lot better
13 than it was with the old 1994 criteria, so we're
14 reducing over-diagnosis. If we go to the research
15 criteria, sensitivity drops, as you'd expect, but
16 specificity increases further. So we're getting
17 fewer and fewer people in our research samples that
18 don't really have CRPS.
19 That's what we came up with, the procedure,
20 since this was something we were trying to get out
21 there and use and accepted as consensus criteria as
22 we went to the IASP taxonomy subgroup and the board

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1 and said, "We've done all this. Will you make this
2 the official criteria?" And we'd actually been in
3 communication with them all along. At the
4 beginning of 2012, they finally adopted it
5 formally. So it's now official.
6 Now, it does -- I'll point this out because
7 this is something that is going to occur to you at
8 some point, and there's no good answer to it. When
9 we came up with these new criteria, the question
10 that started coming up clinically was what about
11 these people that met the old diagnosis and now
12 don't meet this? What do they have? Gee, I don't
13 know. They don't have CRPS because we've just
14 defined it.
15 We ended up with a category, which I don't
16 like. It's garbage basket. It's the same approach
17 DSM used. That's where we got the idea, was NOS,
18 CRPS NOS; looks like it, smells like it, doesn't
19 meet criteria. You don't know what else it is.
20 You can use this label.
21 Now, I don't like that approach, but this is
22 going to be something you'll probably think about

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1 as you're trying to decide how strictly to define
2 the disorders. I would say to go based on -- we
3 don't know this now, but I'd say you come up with
4 your draft criteria. We'll try to do what research
5 we can to demonstrate sensitivity and specificity.
6 And we'll use the numbers to define the criteria
7 and worry about some of these other issues later.
8 I mean, that's the whole point of AAPT, is we're
9 trying to base this on data rather than just an
10 opinion. So that's my best response to that.
11 Elliot?
12 DR. CRANE: This is Elliot Crane. Did you
13 misspeak? You said "the patients who no longer
14 meet criteria have pain syndrome NOS." They don't
15 have CRPS NOS.
16 DR. BRUEHL: No. I'm sorry. It was called
17 CRPS NOS. It was actually listed in the diagnostic
18 criteria as not really criteria, but here's what to
19 do with those people, is you can label them CRPS
20 NOS.
21 DR. SMITH: This is Wally Smith. Once
22 again, would you tell us about how you got the gold

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1 standard? It sounded like it was artificial based
2 on clinical intuition; or is it something else?
3 DR. BRUEHL: I'm sorry. The gold standard?
4 DR. SMITH: The gold standard, yes.
5 DR. BRUEHL: Yes. There is no gold
6 standard, so what we used as our gold standard was
7 the accepted criteria at the time. So that was our
8 reference point --
9 DR. SMITH: The '93?
10 DR. BRUEHL: The 1994 criteria.
11 DR. SMITH: '94?
12 DR. BRUEHL: And what the research allowed
13 us to do was to test for relative improvements over
14 those diagnostic criteria. That doesn't say that
15 we're getting at the underlying pathophysiology any
16 better because we don't know that, but we could at
17 least, using the kind of procedures I described
18 here, find out whether any criteria we came up with
19 that were a modification were better than those
20 1994 criteria.
21 DR. SMITH: How do you advise groups, like
22 the sickle cell group, that are starting with no

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1 already accepted diagnostic criteria for some
2 syndrome?
3 DR. BRUEHL: I was afraid you were going to
4 ask that. Yes. That is a tough one. And I think
5 what we're going to have to do is see what the data
6 tell us to some extent. I think there are things
7 we could do -- for example, like the factor
8 analysis -- to look at --
9 DR. SMITH: Okay.
10 DR. BRUEHL: -- some of those issues that
11 would at least give us something empirical to go by
12 when we're trying to structure the diagnostic
13 criteria. It honestly may at this point be
14 difficult, for that particular instance, to be able
15 to demonstrate that those criteria are able to
16 distinguish between sickle cell and some other
17 condition against any meaningful reference point.
18 I mean, I'm not sure what we'd use as a reference
19 point in that situation.
20 DR. R. DWORKIN: Bob Dworkin. Stephen, in
21 those situations, couldn't the criterion be an
22 expert clinical diagnosis, like one by Dr. Smith?

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

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

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

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

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1 when it comes time to pick a comparator, we can at
2 least say here's the dominant diagnostic criteria
3 that's out there for that disorder. Let's define
4 that group this way, and we'll define our other
5 group this way and see -- ability to distinguish
6 between groups by using our new criteria and then
7 modifying decision rules, things like that.
8 This is an incredibly unsatisfying way to do
9 research for me because it's really you're having
10 to kind of do things that there's a lot of smoke
11 and mirrors involved. But it really is the only
12 kind of research you can do when you don't have an
13 outside criterion to use as a reference point.
14 DR. FREEMAN: I could elaborate maybe just
15 very briefly. The challenge is, for example, with
16 diabetic peripheral neuropathy, you will have many
17 subjects. You will have them as vasomotor changes,
18 sweats, abnormalities, trophic changes, nail
19 changes, skin changes, hair changes, all of your
20 core diagnostic criteria. And so the challenge in
21 determining sensitivity and specificity is really
22 picking not [inaudible – intermittent

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1 we were going to make the assumption, going into
2 this, that if these are real disorders that have
3 some underlying mechanism, that there should be a
4 lot of overlap in the signs and symptoms that might
5 diagnose adult and pediatric patients with the same
6 condition.
7 But I think that one thing we had talked
8 about was doing kind of like in the DSM -- like the
9 DSM-IV, in depression it would say you have these
10 criteria, but then it would say, but for children
11 may come out as this symptom instead. So you'd
12 have like an option like that, where it kind of
13 modifies the criteria so you can include something
14 a little bit different if it's an adolescent or a
15 child. That is what I recollect, and that is
16 something that certainly can be discussed as we're
17 going through this process.
18 DR. R. DWORKIN: Bob Dworkin. I think this
19 is really a working group decision. So in some
20 cases, including the children, there might be, as
21 Steve is saying, a kind of qualification to the
22 criteria. In other cases, it might be an entirely

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1 audio] -- suffice it to say it is a challenge.
2 DR. BRUEHL: I think all we can do
3 reasonably is use what's out there as diagnostic
4 criteria as our reference point to start with for
5 defining the groups. And then we go look at
6 relative improvements, like when we change how we
7 diagnose it, can we improve over that.
8 DR. ZEMPSKY: Bill Zempsky. I'm going to
9 beat the pediatric horse again. I assume this was
10 all validated in an adult sample. Clearly,
11 regardless of the group we're in -- and I don't
12 even know if pediatric CRPS and adult CRPS are the
13 same disorder anyway. We're going to be challenged
14 in a lot of these groups with looking at pediatrics
15 as maybe a whole different disorder. And I wonder
16 if down the road we need to have a pediatric
17 subgroup, that after these groups have gone
18 through, look at each group's outcome and say what
19 do we need to do specifically for pediatrics.
20 DR. BRUEHL: Correct me. You guys that were
21 at that first meeting, now my recollection is the
22 way we elected to handle that was that, in general,

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1 separate diagnosis. So the osteoarthritis group
2 isn't here this week, and they're having their own
3 meeting. But I could imagine, exactly as you
4 suggest, they decide to have a sub-working group on
5 JIA because they see JIA as different enough that
6 it isn't the qualification of another adult
7 diagnosis.
8 So these decisions about how to include
9 pediatric conditions within the purview of the
10 working group really have to be made at the working
11 group level. And all of those different approaches
12 would be fine with us.
13 DR. S. DWORKIN: This is like a deja vu.
14 Sam Dworkin. This is deja vu all over again. And
15 I would really strongly just encourage the approach
16 that you outlined, beginning with experts at least
17 clumping together people who look alike and maybe
18 act alike and have common clinical characteristics.
19 And if they're well defined, then the research will
20 either validate or not the utility of using that
21 approach. And the data will begin to distinguish
22 subgroups within the groups or the errors in the

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1 diagnosis.

2 So along those lines, we call a system a

3 diagnostic and classification system. And the

4 reason for that is that diagnosis is a technical

5 term that has clear implications for treatment, and

6 classification is a bunch of researchers are going

7 to classify people by some way or another.

8 So we took a different -- the fact that we

9 took was to emphasize to be much more concerned

10 with specificity for diagnostic criteria because if

11 you had to do something to somebody that didn't

12 have the thing that you were doing to them, the

13 reason you were doing it, it was better to do

14 research on people who didn't have the condition

15 than to do treatment on people who didn't have the

16 condition.

17 So we leaned heavily towards saying before

18 we're going to call it diagnostic criteria, we have

19 to have very high specificity so there are no false

20 positives if they're going to be in treatment. We

21 could be a little bit more, or a lot more, or let

22 the data determine how much more relaxed we had to

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1 be when it came to research.

2 So the question of whether this group is now

3 a group formulating research propositions or

4 diagnostic propositions is going to depend on the

5 clinical condition. And they're going to differ in

6 their stages of development as approximating

7 diagnostic criteria.

8 But I would encourage people to begin, for

9 openers, whereas there is emphasis on research

10 criteria. It is safer. It's both politically

11 safer and scientifically safer to do. Even though

12 it takes away some of the excitement and the

13 usefulness for people right away of not focusing on

14 diagnostic criteria, it would be premature -- it

15 would be undesirably premature to come up with

16 diagnostic criteria which were not well validated,

17 and that has to take some time.

18 DR. BRUEHL: Yes, I agree with that. John?

19 DR. FARRAR: John Farrar. Sam, what you

20 were just saying I think makes good sense. We need

21 to keep in mind the reason why we need these

22 categories in the first place, and there are

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1 multiple reasons. One of them, and the primary

2 one, is ultimately treatment, how are we going to

3 treat our patients? But we also want to understand

4 and be able to explain to them why they're in the

5 condition they are. We also want to hopefully be

6 able to prevent some of this perhaps from

7 happening, give a prognosis as to what's likely to

8 happen to them, and in the real world come up with

9 some level of disability that they're entitled to.

10 Each of those are going to be distinctly

11 different. And the model that I like here is

12 postherpetic neuralgia. The definition of

13 postherpetic neuralgia is you mostly have to at

14 least had the rash.

15 Now, we occasionally say people didn't have

16 the rash and have it. But the point is that they

17 had an infection with a particular agent. However,

18 if you think about the pain that they have, it

19 depends on which neurons in their spinal cord were

20 damaged and which system was more damaged than

21 others. Mike Rowbotham's done some interesting

22 work in terms of looking at trying to differentiate

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1 those two.

2 I think the process that we're going to go

3 through here is going to run into that issue, the

4 idea of what it is that caused it and what the

5 result is, multiple times. And we need to be

6 careful not to get too caught up in trying to

7 dissect that into small pieces.

8 I just would make the point that we need to

9 keep focus, I think, on what it is that we're

10 trying to do. And it seems to me that the primary

11 goal here is to ultimately be able to make a

12 diagnosis and then ultimately treat those folks and

13 not to get too caught up into micro-dissecting

14 those particular issues, at least at the first

15 go-round.

16 Clearly, the treatment aspect of things, one

17 could argue that the best way to predicting whether

18 people are going to respond to treatment is to give

19 them the drug and see what happens, and then back

20 out of that and say, "Well --" and we all do this,

21 right? -- "must have been."

22 I think the CRPS issue comes up in what Roy

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

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

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

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

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

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

11 (Audio gap.)

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

20 Sam?

21 Presentation - Sam Dworkin

22 DR. S. DWORKIN: Thank you, Dennis.

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

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

14 (Laughter.)

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

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

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

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

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1 This is as good a summary -- it was the
2 American Dental Association definition in '83 and
3 is as good a working definition. So we're talking
4 about a persistent pain that resides in the face
5 with these opening characteristics.
6 We developed a set -- and you'll see why
7 it's deja vu all over again. We developed a set of
8 guiding principles. We didn't give such a fancy
9 title. It was a bunch of people, a smaller group
10 than this, gathered by me and a few others, that
11 had the characteristic of we knew all these people
12 to be like-minded, reasonable, non-extremists.
13 This actually turns about to be very
14 important because the people have to be willing and
15 able to work together. And we developed -- and we
16 wanted to bring some order, reduce the entropy in
17 the field. It was in a terrible state for all the
18 reasons that all of you are here. No consistency
19 in terminology, no consistency in diagnostic
20 approaches; people doing idiosyncratic things and
21 treatments all over the place totally unfounded.
22 There was very little science. So we evolved these

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1 principles.
2 The taxonomy has to include all of the
3 aspects of the patient presentation, not only those
4 that fit your particular clinical bias. The
5 classification criteria are defined by
6 evidence-based criteria. And regarding the
7 research clinical issue, if the diagnostic criteria
8 are evidence based, it's the same as saying
9 criteria based. How you get the evidence base is
10 not by asking the man on the street what do you
11 think. It's by doing rigorous scientific studies.
12 So if you're having evidence-based criteria, you
13 are having research criteria.
14 To the largest extent possible, the
15 categories are based on a single organizing
16 principle, etiology, mechanisms. You've heard
17 that. Where were we? We don't have a clue really
18 as to what causes TMD, and we don't have a clue as
19 to what sustains it. And I'll say something more
20 about the implications of maintaining the pain
21 condition. We are dealing with chronic pain.
22 Chronic means temporal factors are involved, and

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1 the dimension of chronicity is almost totally
2 ignored in the research.
3 The taxonomy had to reveal factors that
4 contribute both to initiating and prolonging the
5 disease and the illness, and we know very little
6 about that and prolonging. It's a particular now
7 pet issue of mine. It includes as a minimum both a
8 disease axis and an illness axis.
9 Very briefly, diseases are in organs, organ
10 systems and the physical structures of the body,
11 and the illness is in the person. An organ has a
12 disease. A person has an illness. They identify
13 mutually exclusive disease and illness categories
14 and subcategories, and the mechanisms accounting
15 for chronic orofacial pain must be mapped against
16 both disease and illness sustained over time.
17 You've heard these words one way or another
18 in the AAPT guidelines and the structure. That's
19 put into the group's excellent article, first
20 authored by Roger. So this is old chron now. It
21 was radical in our field and in the literature. I
22 was called because I emphasized the need to reflect

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1 an illness axis, the person in a psychosocial
2 setting, the psychological status of the person,
3 the behavior, the emotion, cognitive functioning.
4 I was called by the other side a psychosocialist.
5 (Laughter.)
6 DR. S. DWORKIN: Now, they may have been
7 correct, but for the wrong reasons.
8 (Laughter.)
9 DR. S. DWORKIN: And it anticipates an
10 evolving taxonomy to include -- this is relatively
11 new. All of this is the research diagnostic phase,
12 which took about 15 years. And then the last
13 couple of years devoting research validating those
14 early efforts and allowing them to become
15 diagnostic criteria. And then this bursting on the
16 scene of new approaches to genetics, especially
17 epigenetics, have overturned the field of genetics.
18 I'm old enough so that I thought a gene was
19 a fixed characteristic of the organism that led to,
20 without variability, that genes are invariant in
21 their function -- that's an old-fashioned
22 idea -- and brain behavior biomarkers, the

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1 explosion of the brain neuroscience, which if I was
2 younger is how I would be spending my time.
3 The taxonomy disease axes are
4 pathobiologically based and measured objectively.
5 We're saying, yes, this is probably pathobiology or
6 at least is maladaptive physiologic functioning.
7 It may be self-limiting and now pathologic in the
8 conventional sense, but there's something going on
9 because, after all, there's only one thing going
10 on. And it's the workings of the body, and we know
11 it in various ways, whether we ask questions of
12 X-rays or ask questions of people.
13 So reveal pathobiologic mechanisms that
14 differentiate disease categories, and they will
15 nowadays increasingly include brain functionings
16 that subserve maladaptive responses to the pain or
17 the physiology that's giving rise to the pain. And
18 they are specific to objectively define disease
19 entities that continue over time.
20 Continuing over time is a challenge to the
21 pathophysiologists, to the docs, because why is it
22 sustained, and what is it about chronic pain that

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1 is sustained? And what is it about chronic pain
2 that progresses? And yet, the overwhelming burden
3 of evidence is that in the most important chronic
4 pain conditions, there is no disease progression.
5 In temporomandibular disorder pain, which
6 people can have for decades, there is no rusting
7 out of the jaw joint. It does not fall off. The
8 muscles don't atrophy. In the back, similarly, a
9 chronic back patient on day 5 -- post five years
10 after their initial presentation does not look
11 different to any significant extent based on their
12 anatomic structural or physiologic findings. And
13 that's the case of TMD, and common headache,
14 irritable bowel. Irritable bowel is not a risk
15 factor for Crohn's disease, et cetera.
16 So what we are concerned with is why is the
17 pain maintained. And equally enigmatic, for many
18 of the chronic pain conditions and many of the
19 classic garden variety mental disorders like
20 depression and anxiety, they diminish with age.
21 Now, that's a challenge to both the behavioral
22 psychologists and the Axis II people. I'll talk

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1 about that more in a minute.
2 But also, if you're going to come up with a
3 mechanism, your mechanism has to account for it
4 going away. It's not so much evidence that it goes
5 away because of treatment in the highly prevalent
6 common chronic pain conditions.
7 The taxonomy's illness axes are
8 psychosocially based. And I use the term
9 "psychosocially" to include the psychological
10 status of the person, the behavior, their emotions,
11 their levels of cognitive functioning embedded in
12 the social setting or the societal setting in which
13 they exist. And it's largely measured subjectively
14 and by self-report, whereas the disease components
15 are largely measured objectively by diagnostic
16 tests that don't rely on verbal report for a sign.
17 The taxonomy illness axes also reveal
18 biobehavioral brain function based mechanisms that
19 underlie and distinguish the psychological and
20 emotional levels of function that are operational
21 over time. There is a mirror image of the behavior
22 in the neurology. We don't know how to recognize

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1 it. I like to think of it as music.
2 I even have a slide, which I may get to, of
3 Beethoven's, the score for the chorale for
4 Beethoven's 9th symphony. And it looks
5 incomprehensible to somebody who does not know how
6 to read music. And you would look at that and say,
7 "That's beautiful?" Would I pay any attention to
8 that?
9 Well, that's the music in one language, the
10 music of the score. You listen to it. It's the
11 same thing. One did not cause the other. It is
12 the same thing described in a different language.
13 And so there's going to be a biology -- not going
14 to be. There has always been a biology of the
15 psychology, and we're beginning to uncover it in
16 the most fascinating ways. And what you will
17 encounter is that this illness aspect, the impact
18 of the pain, what the person does, is going to
19 include dimensions and variables that are common
20 across almost all the pain conditions.
21 This is the commonality. The specificity is
22 in the organ system involved in the different kinds

<p style="text-align: right;">Page 97</p> <p>1 of pain. So chronic back pain takes place in a 2 different part of the body than headache or TMD. 3 And those patients are different in that way, but 4 they are common in the lives -- they have many 5 commonalities in the lives that they lead when it's 6 chronic pain.</p> <p>7 So for TMD, we begin with a stated effort to 8 develop research diagnostic criteria. We don't 9 want to overly -- it was not so much that we didn't 10 want to threaten the clinicians. We did not want 11 to arouse the large forces of the people who would 12 then be arguing against us. So we said the recent 13 diagnostic criteria and those kind of clinicians 14 that are not evidence based, they're not interested 15 in science, they don't care what you do. Go and 16 research. I don't care.</p> <p>17 So we use the biopsychosocial model implied 18 in everything that's been seen so far, 19 epidemiologic data. We created a dual axis system. 20 Axis I is the physical diagnosis, the traditional 21 approach to diagnosis that you know, and the 22 Axis II was a psychosocial profile.</p>	<p style="text-align: right;">Page 99</p> <p>1 eventually a clinician, confronting a potential TMD 2 patient, does an examination in exactly the same 3 way. And we specified the protocols for conducting 4 reliability and validity studies, first of the 5 examination, then of the criteria, and then of the 6 whole set of Axis I and II put together.</p> <p>7 If the examination is -- if your particular 8 pain condition requires a clinical examination, and 9 the clinical examination is unreliable, nothing you 10 can do will be valid. Validity has as its limiting 11 factor reliability. The validity is the square of 12 reliability. If the reliability is .9, the 13 validity is .81. That's the maximum that it can 14 attain.</p> <p>15 Working with unreliable measures of any kind 16 is like generating random numbers. Random numbers 17 are not going to be valid. And we built in the 18 requirement for periodic evidence-based revisions. 19 We would have successive iterations using the DSM 20 model.</p> <p>21 So this is the flowchart of what began 22 before 1992 because that's when we began the formal</p>
<p style="text-align: right;">Page 98</p> <p>1 A term that hasn't been mentioned so far is 2 that we required operational definitions of terms. 3 Operational means you have to state how you would 4 measure it, and you have to state your criteria in 5 measurable terms. Science requires quantities. 6 Most science, the kind of science we do 7 requires -- most of us do -- quantifying. And 8 operational definitions say things like if you 9 score -- if you got 120 on an intelligence test, 10 that's how intelligent you are.</p> <p>11 That's the danger of operational terms, that 12 what you're measuring may not be all of the 13 underlying phenomenon. So you will have to come up 14 with saying, well, what do you mean by a lot of or 15 many? You have to, as Steve has said, obsess over 16 it. Is it two? Is it three? Is it from two to 17 four? Those nitty-gritty decisions will have to be 18 done.</p> <p>19 Then we specified -- since it's a physical 20 examination in the diagnostic process for recording 21 and scoring, we've developed an examination 22 procedure. Everybody -- every researcher, and</p>	<p style="text-align: right;">Page 100</p> <p>1 activity. We were able to get a contract for small 2 amounts, something like \$80,000, from NIH to begin, 3 a bunch of people meeting, mostly meeting at 4 scientific meetings because in 1992, there weren't 5 many computers. I don't think e-mail was -- maybe 6 e-mail was in, but teleconferencing and stuff like 7 that was like Buck Rogers science fiction kind of 8 stuff.</p> <p>9 So we would meet at our annual scientific 10 meetings, IASP, ASP, dental research meetings, et 11 cetera. And so we got along with very little 12 money, just as Steve did, and we developed a set of 13 research diagnostic criteria for temporomandibular 14 disorders, which use a dual axis system as I 15 described, published in 1992. And then we began a 16 bunch of studies of the people within our group.</p> <p>17 The people within our group -- and I 18 apologize. I don't know all of you. But the 19 people within our group -- and the people in the 20 group I'll talk about later with regard to a back 21 pain effort -- had the characteristic of being 22 known to be good scientists -- and many of them,</p>

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1 but not all, clinicians; by far, not all
2 clinicians -- and respected clinicians.
3 So you had to have evidence of being
4 scientifically competent as a scientist, or if you
5 were a clinician, you had to have some weight in
6 the field. And you had to be a nice guy or nice
7 gal so that we would not have fights.
8 (Laughter.)
9 DR. S. DWORKIN: So we only had a hundred or
10 so fights, and some of them were very interesting.
11 (Laughter.)
12 DR. S. DWORKIN: And this went on for a
13 number of years. We would say, "No, it's not the
14 myalgia. It's myositis." What is myositis?
15 There's contracture. It's spasm. Can you define
16 it? If you can't operationally define it -- we
17 agree, if you cannot operationally define it, it's
18 going to fall by the wayside. And then it came
19 home to roost because they said to me -- you'll see
20 later on the implication of somatization, which is
21 now widespread pain. And they said, "What about
22 somatization?"

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1 Somatization is this flaky concept from
2 DSM-II or III about repressed sexual things giving
3 you all kinds of crazy symptoms. "You can't define
4 that and can't do research on it. So why should
5 you be allowed to have somatization on Axis II and
6 we can't have contracture on Axis I or even trigger
7 points on Axis I?" And I said, "Okay, you're
8 right. We will call it non-specific physical
9 symptoms instead of somatization."
10 That turned out to be almost like a godsend
11 because it actually describes what it is and
12 removes the whole cloud of suspicion that we are
13 secretly interpreting the symptoms to mean
14 something else that we don't know anything about.
15 We then got a large-scale grant, but this is
16 in 2001 -- that's nine years later,
17 multi-institutional, three universities, Minnesota,
18 Washington, and Buffalo -- to establish the
19 validity. Implicit in here is the reliability
20 first. And the validity, we had done data so that
21 we could show the reliability of various aspects.
22 And this was a broad sweeping approach to

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1 validating, and it was successful.
2 I want to say -- I think it's useful to say
3 that when you do a -- the purpose of doing a
4 reliability study is to be able to state what the
5 reliability is even if it's not good. But it's the
6 first approximation to what you can do. At least
7 under these standardized, this thing is repeatable
8 to a certain extent. And the same thing with
9 validity.
10 The first emphasis is that you've got to be
11 consistent, and that's reliability, and then go on
12 to the next higher, much more complex things to
13 analyze about validity, external criteria.
14 Reliability is -- inside itself, how consistent is
15 the measure?
16 If you gave it over again to the same
17 person, would they answer it the same way? If you
18 pitted one examiner against another, would each
19 examiner come up with the same physical finding?
20 And validations are much more difficult in a field
21 where there are no gold standards, are much more
22 difficult problems to attack.

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1 This study went on for five years,
2 radiologic examinations, different kinds of
3 clinical examinations. Embedded in here is
4 thorough reviews of the literature. Embedded in
5 here is thorough reviews of the literature, of the
6 criteria, the diagnostic methods, the symptoms,
7 et cetera. And we formed an international
8 consortium. I called it international consortium
9 for RDC-TMD research. I'm going to find people
10 around the world who's going to join a group for
11 RDC-TMD research? Well, about 140 people around the
12 world joined.
13 We produced 22 translations using rigorous
14 methods, state-of-the-art methods, for producing
15 translations of the RDC into 22 languages, which
16 allowed a lot of research to go on. And then the
17 consortium meetings and IASP, an orofacial pain
18 special interest group, had consensus workshops in
19 these years. We did international field trials.
20 And the objective of this was to take the RDC,
21 research diagnostic criteria, and validate that
22 they could be diagnostic criteria for use in

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1 clinical practice, and they would be evidence-based
2 diagnostic criteria for TMD.
3 Then some of the workers in this consortium,
4 the die-hards I would say, wanted to go on to
5 expand to include more than the small number of
6 common conditions, the most common conditions that
7 we could agree on, which were in the RDC. And they
8 account for 90 to 95 percent of cases.
9 We were helped because three other studies
10 came along to lend lots of supporting data that
11 were independent of the consortium. The other was
12 an IMPACT study funded by NIH, which was the
13 follow-up to this study, and then the OPPERA
14 studies. And OPPERA, I'm embarrassed to say that I
15 have been asked to be the guest editor for two
16 publications of the Journal of Pain, devoted -- for
17 one or two. And I keep tripping up over what does
18 OPPERA stand for. So OPPERA stands for
19 orofacial --
20 DR. FILLINGIM: Orofacial Pain Prospective
21 Evaluation and Risk Assessment.
22 DR. S. DWORKIN: Right.

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1 DR. FILLINGIM: It's Roger Fillingim.
2 Orofacial Pain Prospective Evaluation and Risk
3 Assessment.
4 DR. S. DWORKIN: So you've got to be careful
5 about the people who are heading this activity
6 because they come up with these acronyms that are
7 like a page long. That's not simple, and they're
8 only working on the title of what they're doing.
9 But this study was the largest single grant
10 for extramural research by the National Institute
11 of Dental Research ever awarded and
12 multi-institutional and then being followed up now,
13 and contributed just a wealth of data to allow this
14 transition, supportive validating data,
15 reliability, expanding the concepts. It allowed
16 the transition from the RDC, down through here,
17 with input from this, to the diagnostic criteria.
18 And there are now 27 translations of this in
19 process. It's not so hard because they have this
20 as a point.
21 Now we come to where we are now. This is,
22 for TMD, not so much an evolutionary stage as a

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1 translational one. What we want to do -- because
2 the taxonomy is a very invaluable thing to have in
3 existence, and TMD and every other pain condition
4 that can should be in it -- is we want to
5 translate, convert the way we put the RDC, the
6 structure of the RDC and the TMD, and the DC of the
7 TMD -- we want to convert that structure into the
8 APT structure, and I'll show you how we did it.
9 First, I'm going from the RDC to TMD, and
10 these are just examples of the differences that
11 were found in the subsequent research from these
12 very early bootstrap efforts of a bunch of
13 theoretically smart people trying to define things
14 from clinical experience, from extensive reviews of
15 the literature, and then saying, okay, the whole
16 purpose of creating the RDC is to do research.
17 The first object of research is the
18 instrument itself. And I think that that should
19 also be reassuring to some of you. Consider what
20 you are saying is not the truth. You're not really
21 inventing something. You are discovering
22 something, and you're willing -- you have the

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1 courage -- to test out what it is that you're going
2 to say. So the first test of your deliberations is
3 the test of the criteria that you are specifying.
4 And it allowed us to feel good about proceeding.
5 So the examples, the content of it, are not
6 so important other than to say that differences
7 occurred, and the data did not support, for
8 example, muscles in this region, which are the
9 elevators of the jaw. It takes very little to open
10 your jaw. But clinically, at the time that we did
11 the RDC, all the muscles of mastication were
12 considered equipotent.
13 It seemed to me, what kind of condition is
14 it? Does it matter whether you're opening your
15 mouth or closing your mouth, whether you're biting
16 down with tons of force that these large muscles
17 can produce with food or you're just opening your
18 mouth, like letting gravity do most of the work?
19 So it was kind of gratifying. These were kind of
20 like dropped. And there were a number of other
21 important changes that the data -- changes that
22 were warranted by data.

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1 This is the expanded diagnostic criteria.
2 It's offered. All the ones in yellow have no
3 evidence behind them. They are the clinical
4 impressions. The clinical guesses. The hunches.
5 These are all well-intended, smart people, too, but
6 they say -- their objective is to do for these
7 conditions in yellow.
8 You don't need them. If you want to know:
9 condylosis; idiopathic condylar resorption;
10 myofascial pain with referral; subluxation, when
11 the joint slips out and locks open or close;
12 orofacial dyskinesia. They right now defy adequate
13 description.
14 If you brought the people who put this
15 together in a room, they would not agree with each
16 other on how to define these conditions at the
17 present time. You may be somewhat in the same
18 boat. So the further back you are, the more risky
19 the stab that you take, or you should be willing to
20 take a stab because you will, if you take a stab,
21 put something out there to be systematically
22 investigated, and the advances follow from that.

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1 So this is the DC going to the APT. The
2 first thing was, well, what should we do? Which
3 portions of the TMD should we move over into the
4 AAPT, into the structure of the taxonomy that we're
5 all about here today? And it seems like a
6 self-evident -- no pun intended -- decision. But
7 should we do evidence-based disorders only or
8 should we do that whole other list? So we of
9 course have said evidence-based disorders only.
10 So this is a bunch of conditions under the
11 RDC, and these are the ones that would be in the
12 AAPT, and they have the advantage of both
13 accounting for more than 90 percent of all the
14 cases and having the evidence behind them. And
15 again, the specifics of what they are I have at
16 least on a thumb drive. I have the DC-TMD -- if
17 anybody wanted it, it would be easy to print
18 out -- copy of it. And it's available at the
19 website or the International Consortium. I'd be
20 happy to make it available.
21 So this is the DC-TMD in its current format,
22 how it looks in the publication announcing it. It

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1 has a description, a history, an exam, validity,
2 and comments for each of the conditions, which you
3 saw in the other chart for each of these
4 conditions.
5 So this is the structure of the DC-TMD in
6 its current format, and this is the structure for
7 the Axis II part, all the psychological,
8 psychosocial impact kind of measures. And they're
9 probably not surprising to any of you in the
10 chronic pain field.
11 Let me just go back. Here's the DC-TMD in
12 its current format, the way we did it. And here is
13 our first stab at trying to put that into the AAPT
14 architecture. So here's the core diagnostic
15 criteria, the common features, the common medical
16 comorbidities, the neurobiological, psychosocial,
17 and functional consequences.
18 Again, the purpose here, this will be
19 debated or worked out or ironed out perhaps better
20 in the work groups, of the TMD work group, and
21 you're certainly free to ask questions about it.
22 But my purpose here is not to present it now

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1 as the truth. This is how it really is going to be
2 in its final form. It will probably be very close
3 to this.
4 There's one more dimension, the putative
5 neurobiologic and psychosocial mechanisms, and risk
6 factors, and protective factors. We know a lot
7 about this condition without knowing hardly
8 anything about how it gets caused, let alone how to
9 prevent it.
10 So this is the AAPT chapter, article, that's
11 in preparation, almost ready to be submitted to the
12 Journal of Pain, with regard to TMD. And I
13 certainly would invite the questions and even
14 controversy over anything you see here on this
15 screen.
16 I want to just call attention to a
17 prospective for this condition. The epidemiology
18 is it ranges from 5 to 15 percent with a greater
19 prevalence among chronic cases. While the number
20 that comes up is around 12 percent averaged across
21 both genders and averaged across all ages, it's
22 important to know that the prevalence reaches -- in

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1 the population, in a population-based study -- 30
2 to 35 percent in women in their reproductive years.
3 So it is common in the literature to find
4 that the only risk factor for TMD is being a woman
5 in their reproductive years. TMD falls off
6 markedly for men. It's rare to find a man over 60
7 with TMD, and it falls markedly, but not as
8 markedly for women.
9 So it is about third in its prevalence in
10 the chronic pain conditions behind headache and
11 back pain, or back pain and headache, as the most
12 prevalent. But the prevalence issue for back pain
13 is much more -- it dwindles in significance in
14 comparison to its cost.
15 Low back pain cost more than any other
16 medical condition that afflicts people in America
17 and around the world than, for example, heart
18 disease or cancer. And by some reports, it's more
19 costly to the American public than heart disease
20 and cancer, and that's largely due to the excess
21 loss in productivity.
22 So my summary --

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1 DR. TURK: Summary.
2 DR. S. DWORKIN: I'm sorry?
3 DR. TURK: Summary
4 DR. S. DWORKIN: Yes. But my summary is
5 tricky.
6 (Laughter.)
7 DR. S. DWORKIN: Here's a short summary.
8 You can read faster than even I can talk, and it
9 only says what I've already said. I wanted to
10 take -- remember that I began about 20 minutes
11 late, right? Good. You've all read that.
12 It's really important to point out that it's
13 an iterative process that you want to establish,
14 requiring multidisciplinary effort over time.
15 Significant. We all smiled or laughed when
16 2015 -- there's no reason not to aim for 2015, but
17 it will take work. But you have the benefit of the
18 new communication technology and the
19 telecommunication, et cetera, that will make it
20 easier. We are gratified that this process that
21 has gone on for 12 or 15 years -- 20 or 22
22 years -- actually is able to fit into the AAPT

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1 structure. So that's kind of validating.
2 I wanted to take a minute, a few minutes, to
3 talk about the NIH Task Force on Research Standards
4 for Chronic Low Back Pain. A large group of
5 people, larger than these two, were -- oh, here
6 they all are -- met at the NIH Pain Consortium,
7 asked for a research task force to be created to
8 develop research standards for chronic low back
9 pain. I had the privilege and the honor of being
10 asked to co-chair it, although I am not a back pain
11 specialist at all, in any way. But we were saved
12 by having Rick Deyo. Rick Deyo is a leading back
13 pain epidemiologist, and he is a clinician as well,
14 very important work in the field.
15 I think we made a -- a couple of people.
16 Dennis Turk was in that group and was very
17 instrumental, very, very helpful to me especially
18 in an area of my responsibility, which had to do
19 with all the psychological and psychosocial
20 measures. Our top consult from NCAM is here and
21 was the NIH -- sort of like a point person for the
22 task force.

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1 The report of the NIH Task Force, the full
2 report, is on the NIH website, the Pain Consortium,
3 which is here, and I'll make it available to you
4 later. An article describing the report, briefer
5 and without so many of the details, has appeared in
6 four journals and is destined to appear in two more
7 journals. And it did three things.
8 It has identified with three products of
9 which I feel very good about. It provided a
10 definition. I was blown away by back pain had the
11 same problems that TMD did, the same problems that
12 all of you did. They could not develop an Axis I,
13 a physical dimension. There's no evidence that we
14 can -- there's hardly any evidence for anything
15 physical that's reliable and valid. I said, "Oh,
16 boy. I've been there."
17 So this is the definition of back pain, a
18 temporal aspect, and then a location -- it's
19 accompanied by a location with a drawing. The
20 person locates where the pain is in the back, and
21 then how long. But the definition is enlarged by
22 including a stratification by the impact of chronic

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

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

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

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

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1 What you could do -- and I'm just thinking
2 of options here. One option is, if you're trying
3 to come up with your draft criteria, you may end up
4 including, just as an example, five different signs
5 and three symptoms, or something like that. We
6 would be collecting data on those as well as other
7 things, other signs and symptoms and could after
8 the fact see whether it makes any difference to how
9 good those draft criteria are if we add this
10 symptom or that symptom. And you can change things
11 around after the fact as long as you collect the
12 data.
13 So the important thing is you've got to
14 include on that data collection sheet anything you
15 want to be able to answer later on in terms of the
16 research.
17 For formatting for research -- I just want
18 to present this again -- every working group for
19 every different disorder is going to need to have
20 something that is similar to this; maybe not
21 identical but similar to this.
22 Depending on the conditions, I can foresee

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1 possible situations where you might have -- like
2 with the back pain group, for example, you may have
3 enough commonalities that you can cover several
4 different proposed diagnostic categories on one
5 sheet like this because you may have -- for a
6 certain diagnoses, you may have a positive MRI
7 finding of a certain type, and another kind of
8 diagnoses, it's negative. But you can assess that
9 just with one question on this questionnaire.
10 So all of your working groups can use your
11 judgment as to how to break this out. They don't
12 all have to be separate for each different
13 condition, but they certainly can be if you want
14 to.
15 The breaking out of signs and symptoms I've
16 done on this because in CRPS, that was a very
17 important issue because of the lability of things.
18 There may be some conditions where you might not
19 have any objective signs. I'm not sure if there
20 are any like that, but it might be primarily
21 patient complaints about certain symptoms. And
22 that would be okay to do it based on symptoms only

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1 if that's all you've got and adjust the sheet
2 accordingly, or maybe others where there are many
3 objective signs, and the symptoms are relatively
4 unimportant.
5 In the end, you might elect to not even
6 include patient reports in the diagnosis, and it
7 could all be based on objective signs you see.
8 That's up to you in the individual working groups.
9 And we could actually look at the numbers for signs
10 and symptoms and determine whether that is a good
11 idea or not, or provide some empirical support for
12 the decision you make. I would tend to collect
13 signs and symptoms even if you don't plan on using
14 them just to make sure we've got that to go back to
15 and look at it later if we can make that -- if it's
16 feasible to do that.
17 The reliability issue, Sam mentioned, and
18 this is important. Reliability sets the upper
19 limit on validity. It is not feasible with no
20 money to do extensive reliability testing, although
21 I'll talk in a second a little bit about some of
22 Eva's work that relates to this. So using the

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1 dichotomous way of indicating whether a sign or
2 symptom is present is one way of reducing the
3 likelihood of unreliability somewhat, although it
4 doesn't really guarantee anything.
5 If you have measures that have known
6 reliability because they've been published before
7 and you can incorporate that as part of your
8 criteria, that's great. I do think the
9 importance -- what was not clear from the way I
10 presented this before was that there are
11 operational definitions of all these. So when it
12 says allodynia here, there's an instruction sheet
13 that says this should be tested by taking the
14 finger and -- or taking a piece of cloth and
15 stroking lightly on the upper surface of the hand,
16 and allodynia is indicated by response saying
17 that's painful.
18 There's something very specific here. Some
19 things such as the edema, we're interested in yes
20 or no, but it would be great if we could actually
21 quantify it in terms of volume or a measurement of
22 circumference based on some landmark

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22 The more we can help with that kind of

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1 thing, we realize that will help speed up the whole
2 process of getting the research done because the
3 people you're asking to help with us are busy and
4 probably don't really want to take the time to fill
5 out IRBs. And the more we can do to help with
6 that, the faster we'll get actual data.
7 Data warehousing, we're not sure yet exactly
8 how we do it. I think there is already something
9 set up that Bob has. We've got a red cap, which is
10 an online data entry procedure we could use. I
11 could program for each different working group a
12 place to enter your data just from using the
13 internet that would be fairly easy. We'll talk
14 about the specifics of that at some point in the
15 future.
16 Now, what kind of studies can we do? Eva at
17 the meeting a year ago actually presented on this.
18 But there was the option of addressing reliability
19 in a way that it doesn't require having a whole
20 bunch of patience with examiners physically
21 examining and then having to do your kappas based
22 on that. And the idea was to use vignettes. You

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1 have a very detailed case description, and then you
2 can have different clinicians try to apply criteria
3 to that vignette, and you look at the reliability
4 of that.
5 Correct me if I'm saying that wrong.
6 DR. WIDERSTROM-NOGA: Yes. I just want to
7 mention here that it was also -- Eva
8 Widerstrom-Noga. And it was not just physicians
9 that were part of the validation. It was also
10 people who were researchers. So we wanted to have
11 a rather broad representation, not just people who
12 are experts in the field with respect to clinic,
13 but also researchers. And of course, those of us
14 who are not clinically active maybe didn't do as
15 well as the clinicians. I don't really think it
16 was that big of a difference, but I think that was
17 the point I wanted to make.
18 DR. BRUEHL: Okay. So use your discretion.
19 Certainly, we want to make sure that clinicians can
20 reliably apply the criteria, that you can broaden
21 that to researchers, too, because researchers will
22 in fact be using these diagnostic criteria at some

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1 point.
2 Internal validity, that's referring to the
3 frequencies of signs and symptoms, the factor
4 analysis, the layout, how the criteria are
5 structured. Does it make sense? Does it fit with
6 reality? And we presumably would do something
7 similar to what we did with the CRPS study using
8 the data you collect on the database forms. I
9 can't tell you what we would find. I have no idea
10 what to expect with this, honestly, so we'll go by
11 what the data show and do what we can with it.
12 The external facility gold standard. I was
13 talking with Rob Edwards a minute ago. Maybe we
14 should call this bronze standard or lead
15 standard --
16 (Laughter.)
17 DR. BRUEHL: -- because we've really got a
18 not very good standard, which may in fact, in most
19 cases, end up being the current best diagnostic
20 criteria as your reference group or it may be a
21 situation like with the sickle cell, where there's
22 nothing to go by to start with, and we have to get

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1 some clinician generated, this person has it just
2 because I know what it looks like, and you get
3 agreement on that. And then that's your starting
4 point for saying whether the diagnostic criteria
5 work.
6 The point is -- and this was mentioned
7 earlier -- you've got to have a starting point
8 somewhere. Once we get that starting point, then
9 we can use that as the way to start improving,
10 incrementally improving the diagnostic criteria
11 over time.
12 Yes, Eva?
13 DR. WIDERSTROM-NOGA: This is Eva
14 Widerstrom-Noga again. I'm very interested in this
15 internal validity because factor analysis is a very
16 interesting method to use. I'm just thinking that
17 in order to do that in the best way, it's really
18 nice to have some kind of scale so you don't have a
19 dichotomous variable because then you have to
20 transform the data in a way that's kind of
21 complicated, polychoric correlation matrix.
22 DR. BRUEHL: There's actually a procedure

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

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

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

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

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1 should be aware, and you should have, if you read
2 the materials we sent you, that there is a research
3 committee. So even if we don't answer all your
4 questions or things come up about research, Steve
5 Bruehl, who will be the chair of that committee,
6 will be available to assist you along the way or to
7 address questions, or if he can't answer them,
8 bring them back to the research group.
9 So we understand that there are going to be
10 lots of questions -- I understand; I shouldn't
11 speak for everybody else -- that there may be lots
12 of questions about how to do some of the things
13 that we've talked about. But there will be
14 opportunities for you to ask us more in this panel.
15 But also as you start trying some things out or as
16 your working groups come up, that you can come.
17 And Steve will be the point person to send those
18 questions to.
19 DR. R. DWORKIN: Hi. I'm Bob Dworkin. Just
20 a couple of housekeeping things before we start.
21 If you need taxis to the airport tomorrow, arrange
22 it today around the lunch break with Valorie and

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1 Andrea outside. So that would be much better if
2 you tried to do that today rather than wait until
3 tomorrow.
4 The second housekeeping item is we'd like to
5 meet with all the facilitators -- those of you who
6 are facilitators -- and the working group
7 co-chairs -- we'll push it ahead a little
8 bit -- 5:00 this afternoon.
9 Valorie, will this room be okay for a kind
10 of 15-minute meeting at 5:00 today?
11 MS. THOMPSON: Absolutely.
12 DR. R. DWORKIN: Okay. So working group
13 co-chairs and facilitators here at 5:00, just for a
14 kind of update, make sure we're all on the same
15 page and kind of thinking about where we're going
16 tomorrow.
17 Finally, we left at everybody's place the
18 guidelines. This guidelines document for working
19 group activities had been distributed several
20 months ago to the working group chairs, but we
21 thought you should all have it. So that's what's
22 in front of you that appeared over the coffee

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1 break.
2 This morning, I think we had a bunch of
3 great talks. And of course what Steve and Sam both
4 did is present their experiences developing
5 diagnostic criteria for CRPS and TMD related
6 disorders. A third person who's done that is Eva,
7 and she was part of a group that developed
8 diagnostic criteria for spinal cord injury.
9 So I just wanted to start this Q&A
10 session -- and we have ample time for questions,
11 discussion. But I want to start by asking Eva if,
12 from her perspective, developing diagnostic
13 criteria for spinal cord injury, were there any
14 significant learnings, take-home messages, in the
15 spinal cord injury effort that you could add to
16 what Sam and Steve shared with us.
17 DR. WIDERSTROM-NOGA: Well, it took time.
18 It took time to do it. It was really important.
19 What we wanted to do was to get buy-in from the
20 things we were dealing with, with spinal cord
21 injury. We wanted to make sure that people who
22 were spinal cord injury physicians, and not

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1 necessarily other healthcare professionals, had a
2 way to review what we came up with. And also, of
3 course the pain organizations, including the -- I
4 was going to say NPSI -- NeuPSIG, which I think
5 that's when we dealt with you. So that was a
6 really important part.
7 Then of course, the taxonomy, it was
8 developed based on several previous taxonomies. It
9 was really an effort to bring together something
10 that had been very diverse in different parts of
11 the world and sometimes in the same part of the
12 world. I think we had three or four different
13 taxonomies, that we included everybody in a
14 consensus meeting, including some basic researchers
15 to get the mechanistic anchors, whatever was
16 available, into the taxonomy.
17 Then of course, we did the validation, so we
18 had like a gold standard, which was then a couple
19 of physicians' consensus, so the diagnosis that
20 people had, the pain diagnosis. And then, like we
21 mentioned before, there were a number of people
22 involved in the validation process. So there were

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1 at least two people on each diagnosis, and it was
2 tested how the consistency was between our replies
3 or our classifications.
4 Q&A and Discussion
5 DR. R. DWORKIN: Thank you. So we now have
6 a bunch of time for discussion. I think there are
7 at least two objectives for this discussion period.
8 One is to give you all the opportunity to ask Eva
9 and Steve and Sam any questions, based on their
10 experience, having done something similar over the
11 last 10 to 20 years for these other conditions. So
12 this is a Q&A part of the morning.
13 But maybe even more importantly, as
14 indicated on the agenda, this discussion period is
15 really the time to make sure we're all on the same
16 page before we break into half a dozen or so
17 working groups.
18 So we aren't going to allow you to have
19 lunch until we all consense in this room that we're
20 pretty much on the same page about what we're going
21 to be doing for the next day and a half, because
22 obviously it would be a little bit chaotic if we

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1 all go off into different directions this
2 afternoon, having different ideas of what we're
3 supposed to accomplish.
4 So let's start with are there any questions
5 for Roger, Sam, Steve and Eva about this morning's
6 presentations and about their experiences? Yes?
7 Back there?
8 DR. MACFARLANE: Thanks very much. Gary
9 Macfarlane, Aberdeen, in the United Kingdom. One
10 of the things I just wanted to ask, perhaps to
11 Dennis, is to what extent you see this as a United
12 States activity or an international activity. I
13 know that ACTTION does have an international focus.
14 I think it's really great that you've invited some
15 people from outside the United States, so just a
16 small number. And it looks as though most people
17 from outside the United States are within a single
18 working group.
19 I wonder whether you thought that had any
20 implications in terms of dissemination, the
21 ultimate take up of any criteria we come up with.
22 DR. R. DWORKIN: So Dennis answers the hard

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1 questions. I take the easy questions. That's an
2 easy question. I think our intent from the
3 beginning is that this is international. And we
4 entirely left it up to the working group co-chairs
5 to decide what the distribution of North America
6 versus outside North American working group
7 participants would be.
8 I think even though this effort is being
9 jointly sponsored with American Pain Society, we
10 think these criteria should be internationally
11 applicable. The diagnosis of chronic pain
12 conditions is not limited to one region or one
13 nation.
14 Does anyone disagree with that?
15 DR. TURK: I'd amplify it.
16 DR. R. DWORKIN: You want to amplify it?
17 DR. TURK: Yes.
18 DR. R. DWORKIN: Okay.
19 DR. TURK: Thank you for the question. Bob
20 is exactly correct. We have also invited some
21 other international people who couldn't make it for
22 different reasons, so there potentially would have

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1 been some more here.
2 The other thing that I think -- at least I'm
3 thinking, I don't want to speak for the group -- is
4 that when we start developing drafts of things
5 before they actually end up getting published, we
6 will distribute those to appropriate people from
7 different organizations, from different areas, from
8 different countries, so they can give us comments
9 on those.
10 There was no way we could have everybody
11 here we would like to have here. And even some of
12 the people that were invited here couldn't be here,
13 and several of those were from Europe.
14 DR. SARZI-PUTTINI: Sarzi-Puttini from
15 Milan, Italy. I was wondering if -- because we are
16 talking about chronicity and pain as a main
17 symptom. But what's the deal on everyday life with
18 all different types of symptoms that we call
19 centralized or dysfunctional syndrome, like chronic
20 fatigue or multichemical sensitivity? Are we
21 taking any position in doing the diagnostic
22 criteria according to these specific comorbidities

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

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

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

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

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

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

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

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

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

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

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

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

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

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

20 DR. R. DWORKIN: Can I --

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

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

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

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

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

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

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

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

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

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

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

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1 that we would then study in the research phase.

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

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

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

19 DR. FILLINGIM: Yes.

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

22 DR. STAUD: Roland Staud. I have a

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

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

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

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1 these criteria. Maybe X needs to be changed."

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

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

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

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1 approved. So they took that one and looked at
2 others.
3 In the survey that I saw that Rob Bennett,
4 who couldn't be here, did of the fibromyalgia folk,
5 at least my looking at that survey of nine people,
6 I think it was, there seemed to be fairly high
7 agreement that the existing 2010-2011 fibromyalgia
8 criteria were not necessarily -- they've missed
9 something or it's not as good as it could be, and
10 they would like to potentially modify that.
11 So you might start with that criteria as
12 your "that's the existing one right now" and see
13 how does this get improved in any way you think you
14 can in the same way you did with the CRPS.
15 DR. R. DWORKIN: The one case we're not
16 doing that is headache. As you see from the
17 materials we've distributed, we think the
18 International Headache Society has really done a
19 fine job, so that's the one example, really, where
20 we're not kind of revisiting.
21 DR. PAIVA: Eduardo Paiva from Brazil. I'm
22 just concerned about the dimensions. For example,

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1 in fibromyalgia, the more recent criteria included
2 things like the patient's perceptions of new
3 refreshing sleep, fatigue, and cognitive symptoms,
4 and probably we're going to include this in the
5 core criteria, for example, no refreshing sleep.
6 And this also can be included in comorbidities, and
7 also can be included in consequences of
8 fibromyalgia.
9 So I was just wondering if it's okay to
10 include no painful definitions in the core
11 criteria. And finally, can we repeat those
12 criteria or perceptions in the dimensions, like
13 repeating them in Dimension 2 and Dimension 3?
14 DR. BRUEHL: One thing I would point out is
15 edema's not painful, but it's a diagnostic sign for
16 CRPS and I'm sure a lot of other conditions. So
17 the individual components of the diagnostic
18 criteria, the signs and symptoms in and of
19 themselves all have to be painful. What is
20 important, though, is that they are all part of
21 defining a painful syndrome. And hopefully the
22 research would be able to help us figure out

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1 whether the fatigue adds anything to the diagnosis,
2 if it's actually crucial to it or not.
3 Yes, just because it in and of itself isn't
4 painful doesn't mean it shouldn't be included.
5 DR. PAIVA: What about repeating the symptom
6 in several dimensions?
7 DR. FILLINGIM: This is Roger Fillingim
8 again. Let's say non-restorative sleep, your
9 working group decides that's actually a specific
10 diagnostic criterion for fibromyalgia. It's one of
11 the things you can have. Let's say you've got five
12 things, and it's one of three of those five that
13 you have to have to meet criteria. I would say
14 that becomes a core criterion. And it probably
15 doesn't become something on Axis IV or Axis V
16 necessarily.
17 It's a little dicey because if it's not
18 required for the diagnosis of whatever you're
19 doing -- that is it may not be the feature against
20 which they're diagnosed, but it may be one of the
21 other features. It gets a little complex. So
22 that's going to be an individual work group

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1 decision. But I would say, let's, as much as we
2 can, avoid overlap between the criteria for
3 diagnosing the condition and then the associated
4 either consequences or risk factors.
5 But you bring up another point about which
6 there was a lot of discussion both at the launch
7 meeting and then in developing the manuscript. How
8 do you tell whether depression was a risk factor or
9 a consequence since we didn't know the person
10 before they got chronic pain ostensibly? How do
11 you tell whether obesity or non-restorative sleep
12 or whatever -- we recognize.
13 We acknowledge this in the manuscript that
14 this is a potential issue. I think it's much more
15 important for us to send the message that there are
16 psychological risk factors, premorbid psychological
17 features of an individual that put them at risk for
18 disorders, and that's clearly the case. We may not
19 always be able to tell what came first.
20 So I think we take the history as best we
21 can and make the best decision we can when we're
22 working with an individual patient and trying to

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

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

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

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

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1 this room is typical of the general population,
2 80 percent of us have some sort of pain disorder
3 for which we seek treatment. So it's not like
4 we're unfamiliar with the patients, but we are a
5 group of experts.
6 One of the key things that has really
7 developed, and obviously PCORI here in the U.S. is
8 probably the chief advocate for, is the vital
9 nature of getting patient input in helping to
10 decide what is important.
11 So in this taxonomy that's being developed,
12 and particularly the idea of developing core
13 diagnostic criteria, many of which are -- again,
14 these are the symptoms that the patients are
15 reporting. I think this will come back, if not at
16 the input of developing these, but certainly in the
17 testing of their validity, whether internally
18 and/or external validity.
19 It will be important to really assess how
20 the patients actually think these criteria are
21 because I think we've all learned over a number of
22 decades now that things that sometimes as

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1 clinicians and scientists we develop are not
2 necessarily what are the most important things to
3 the patients for whom we are trying to treat. It's
4 not clear to me yet from reading all this document
5 how that aspect is going to be incorporated in this
6 process, but I wanted to raise it because I think
7 it's something we really -- getting a greater
8 understanding of how important it is overall.
9 DR. R. DWORKIN: So just to say, we shared
10 that concern completely, and so we invited three
11 representatives of patient advocacy organizations
12 to this meeting. Two were unable to come. One was
13 here last night, but I don't see Tina this morning.
14 Oh, Tina's here. And Tina represents the
15 Neuropathy Association. So we've started in that
16 direction, Partap, and we realize there's a lot
17 more that needs to be done, and we have every
18 intention of pursuing it.
19 Chris?
20 DR. MIASKOWSKI: Chris Miaskowski. In
21 follow-up to that, I was going to ask Steve and the
22 others as well, trying to link the signs and

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1 symptoms criteria that we're going to develop to
2 the methodology for doing the research and thinking
3 about the symptoms part of that equation, vis a vis
4 the methodology with which the data is being
5 collected.
6 So I was wondering, when you did your data
7 collection, did the patient self-report or did the
8 clinician interview them and then report what they
9 thought the patient said? So I have a question
10 about that.
11 Then the second one is, related to the signs
12 and trying to come up with a specific list, was
13 consideration given to the idea that this is a
14 clinically pragmatic sign that's easily obtainable?
15 And I'm thinking about chemo neuropathy or perhaps
16 diabetic neuropathy, where the research tool is
17 often quantitative sensory testing, which doesn't
18 hang out in an oncologist or primary care
19 physician's office.
20 So can you give us some guidance about
21 thinking through that? And vis a vis what you said
22 in terms of the NIH's move with the PROMIS

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1 measures, which are online, validated, self-report,
2 how should we be thinking about this as we're
3 designing our instruments for data collection?
4 DR. BRUEHL: I can tell you what happened
5 with the CRPS. Starting with the second part of
6 your question first, the objective signs were
7 intended to be something that could be done at the
8 bedside, that you wouldn't need any fancy testing
9 to do that. That was for pragmatic reasons because
10 the reality is most people are not going to have
11 access to that kind of specialized equipment like
12 QST equipment, so didn't even want to make that
13 part of it.
14 I will say that in some of the research work
15 we did, we did collect data. Certain sites had
16 access to QST equipment and did the testing on some
17 of their patients. So we ended up having some data
18 that allowed us to look at how different diagnostic
19 criteria related to QST, but it wasn't formally
20 part of the actual criteria.
21 The subjective symptom reporting, when we
22 originally did it, was done just like a standard

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

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

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

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

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

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

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

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

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

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

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

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

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

11 DR. R. DWORKIN: Dennis?

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

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

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1 definition, a symptom is a subjected, self-report
2 of an experience that the individual is having.
3 Now, we have to ask the question correctly I think
4 to get the right information.
5 DR. R. DWORKIN: So the clinician can say to
6 the patient, do you have pain in your feet?
7 DR. MIASKOWSKI: Right.
8 DR. R. DWORKIN: And you're okay with that?
9 DR. MIASKOWSKI: Yes, I am.
10 DR. SMITH: And you're okay with that being
11 standardized as opposed to --
12 DR. MIASKOWSKI: As long as the question is
13 asked the same way.
14 DR. SMITH: -- being something -- every time
15 asked and asked the same way every time.
16 DR. MIASKOWSKI: Do you have pain in your
17 feet?
18 DR. R. DWORKIN: How about Roy, and then
19 Dennis. This is a critically important issue.
20 Thank you. Roy, and then Dennis, and then Tina.
21 DR. FREEMAN: Quite simply, the problem is
22 that there are a gazillion causes of foot pain:

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1 metatarsalgia, calcaneal spurs, plantar fasciitis.
2 I could go on, and on, and on. And it's really
3 difficult, first of all, for patients to act
4 accurately to lineate their pattern of symptoms in
5 order to differentiate those. It's pretty hard for
6 the average clinician to differentiate those.
7 I think in order to take the step perhaps
8 from the possible to the probable to the definite,
9 you may not need to bring in the German Pain
10 Consortium, but you probably need some special,
11 more objective investigations.
12 DR. R. DWORKIN: Dennis?
13 DR. TURK: Thanks, Roy. That's along the
14 lines of what I was thinking. First of all,
15 remember when Sam talked about the need to
16 potentially do more expensive types of testing, and
17 then find out that they don't matter? They're not
18 useful.
19 So for the research purposes, it may be the
20 case that you do want to consider not the full hour
21 and a half of the German network but some variation
22 of that. But if the purpose is that originally

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1 these are going to be classification with the
2 purpose of research, then you may want to gather
3 more information -- and a little bit -- it may not
4 be what the average clinician has, first of all,
5 when they find out it doesn't matter, or we might
6 find out that it really is essential, and that the
7 clinicians need to know how to do these kinds of
8 exams.
9 The second point, Chris, you raised about
10 the PROMIS measures, Sam started to show the back
11 pain task force. And they actually came up with
12 recommendations for what those measures could be.
13 As Partap's comment about the common data
14 elements, it would seem to me, to the extent that
15 you working groups decide that certain
16 psychological factors are relevant or important to
17 be assessed or considered to make use of the
18 existing either PROMIS measures or whatever the
19 common data elements -- I haven't seen all of those
20 to see what they are, but that would seem to be a
21 reasonable way -- and not that every working group
22 for every condition is going to want to say they

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1 want to have these. But if in fact you think
2 assessing this is important, then here are
3 reasonable measures or procedures that could be
4 used to enable you to address that, and it would
5 then be speaking to some common metrics.
6 DR. R. DWORKIN: Tina and then Mark.
7 MS. TOCKARSHEWSKY: Tina TockarsheWSky, The
8 Neuropathy Association. I guess the practical,
9 cautionary thought that runs through my mind and
10 listening to all this conversation is again coming
11 back to cases like diabetic neuropathy or a
12 diabetic patient, especially with the growing
13 prevalence of diabetes in this country and others,
14 being able to come away from this process with an
15 exact enough diagnostic taxonomy so that you're not
16 running into situations, which we hear on a daily
17 basis of somebody comes into a clinician, and they
18 have diabetes, and they're expressing neuropathic
19 pain, it's almost an ergo, foregone conclusion that
20 it's diabetic neuropathy. Even if the person has
21 chemotherapy induced peripheral neuropathy, we've
22 even heard situations like that.

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1 So being able to give crisp enough guidance
2 so that somebody is coming in and not falling into
3 that trap when they may have something else, and
4 they're not getting to a point of being accurately
5 diagnosed.
6 DR. R. DWORKIN: Mark?
7 DR. SULLIVAN: But on a different topic.
8 DR. R. DWORKIN: Okay. Let's hold that and
9 try and beat this topic to death. Because Steve
10 just came and whispered in my ear that this is
11 really a critical issue. And if Chris is right,
12 for all of the working groups, are we developing
13 research diagnostic criteria? Which actually in
14 psychiatry occurred before DSM-III. In the middle
15 1970s, psychiatrists developed RDC, research
16 diagnostic criteria, as did Sam for TMD.
17 DR. S. DWORKIN: Before DSM.
18 DR. R. DWORKIN: So are we, all of our
19 working groups, developing research diagnostic
20 criteria for each of these conditions or to some
21 extent and to what extent do we want these
22 diagnostic criteria to be clinically applicable?

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1 So before we get to Mark's question, which is
2 different, since that was written my Steve, I want
3 to call on Steve to say more about what I just
4 said.
5 DR. BRUEHL: I guess what struck me is that
6 I think we -- I'm including myself in the audience
7 here. We've heard mixed messages. I've kind of
8 gotten the impression that part of this is for
9 clinical diagnosis, but clearly there's the
10 importance of doing research and how do we improve
11 clinical trials. I know that in the written
12 definition, there was specifically talking about
13 getting good samples for improving clinical trials.
14 That's kind of why IMPACT was involved in this, I
15 think. Right?
16 I guess I'm just -- I'm not clear myself,
17 honestly, on what the point of this is. I keep
18 thinking towards the end result eventually being
19 something comparable to a DSM that would be out in
20 the community where it can be used to actually
21 improve communication between physicians and
22 improve eventually, hopefully, the way treatment's

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1 done.
2 I do think it makes a difference if the main
3 point is research. One, we might emphasize certain
4 aspects of the diagnosis more. We might make
5 diagnosis more complicated. We might allow use of
6 a lot more expensive than available equipment is
7 part of the diagnosis because it's just for
8 research purposes. Personally, my sense is that we
9 need to be thinking on down the road towards that
10 time when it's not going to be feasible to have a
11 lot of diagnostic equipment necessarily.
12 DR. R. DWORKIN: Roger, then Eva.
13 DR. MIASKOWSKI: Can I respond to that?
14 DR. R. DWORKIN: Chris? Sure.
15 DR. MIASKOWSKI: Chris Miaskowski. I
16 totally agree with you, Steve. And I think another
17 consideration is, for me, as I think about these
18 pain syndromes, there's an urgency now. Patients
19 need, as best -- as sensitive a set of diagnostic
20 criteria as we can come up with to begin to treat
21 them. And if this is going to be a 10-year
22 research agenda, trying to figure out the

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1 diagnostic criteria for any one of the syndromes we
2 talk about, it's not useful.
3 I mean, I really liked your presentations,
4 Steve, because as I heard your talk, it was really
5 about balancing sensitivity to specificity. And
6 maybe that's what we need to think about here
7 because to me, that is a good goal, that we will
8 get some benefit for the patient in the clinic.
9 We'll be able to do some reasonable research in the
10 clinic.
11 Your tool as you presented it looked really
12 reasonable to do. You could give that to a busy
13 clinician. They could fill it out. Yet, we could
14 include some things that would allow us to refine
15 the mechanisms perhaps or understand subgroups with
16 a particular pain diagnosis. I think there's an
17 urgency to this. I see people suffering, not being
18 diagnosed correctly. We need to think carefully
19 about this decision.
20 DR. R. DWORKIN: Roger, and then Eva.
21 DR. FILLINGIM: This is Roger. Frankly, I
22 think this is really easy.

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

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

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1 it was incorporated into the basic SCI pain data
2 set, it had to be -- the goal was to make it
3 clinically useful so that it would be implemented
4 in the clinic for treatments eventually. So that's
5 why we got so much feedback from clinicians, which
6 was very, very useful, actually.
7 Of course as a scientist, you think that
8 this is nothing. But when you incorporate it into
9 a basic clinician's clinic, it's a lot of
10 information. So I think, like Roger said, within
11 each group, one can determine how clinically useful
12 it will be.
13 DR. R. DWORKIN: Sam, in a minute. What I'm
14 hearing -- I don't know if everyone agrees. What I
15 think Roger and Eva said, I think I agree with,
16 which is these criteria, we think of them primarily
17 to start as research criteria, but they're
18 feasible -- the way it happens is feasible in the
19 clinic and feasible for a large, 600-patient, phase
20 3 trial; that there are research criteria out the
21 starting gate but have a kind of clinical
22 feasibility potential clinical utility.

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

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

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

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

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

8 UNIDENTIFIED SPEAKER: Well said. Well
9 said.

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

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

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

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1 criteria and research criteria.

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

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

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

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

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

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

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

22 DR. R. DWORKIN: Lonnie?

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1 DR. ZELTZER: I guess the question about
2 rolling this out once we put in the blue sky, as
3 Sam said -- this is Lonnie Zeltzer. We put in
4 everything we could think about, but then it's
5 going to get rolled out for sensitivity and
6 specificity in populations.
7 The question I have is a sampling technique,
8 a sampling question because if we're saying
9 functionality or pain-related functional
10 disability, bothersness or bothersome stress over
11 symptoms, is a separate access than the signs and
12 symptoms themselves without looking at a non-
13 clinical population, you're not going to get at the
14 full spectrum.
15 Also, there may be problems -- and I'll use
16 dysmenorrhea as an example. I end up seeing many
17 adolescent, postmenarchal females who are referred
18 to me by gastroenterology and have severe
19 dysmenorrhea, but that's never even asked of or
20 included as a pain problem because it's not thought
21 about. So there may be populations of pain
22 sufferers that we're missing by our sampling

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1 methodology.
2 DR. R. DWORKIN: Part of what you just said
3 relates back to Roy's question about what is the
4 comparison group. If we're trying to come up with
5 criteria for one condition against what are we
6 evaluating sensitivity and specificity.
7 Before calling on the other people with
8 hands up, I think I want to disagree with John and
9 Sam because I have to say, we do not have the
10 resources. If Roy's neuropathic pain working group
11 says we want to do punch skin biopsy on everybody
12 for these analyses, we just can't do that. If
13 another working group wants to get an hour and a
14 half QST profile from the German Research Network,
15 that ain't gonna happen.
16 So I kind of agree that we should cast a
17 wide net in terms of signs and symptoms and other
18 features of these conditions, but that net just
19 can't be so wide that it's going to be everybody's
20 kind of Christmas list of what they would like to
21 see on these patients because we just don't have
22 \$40 million to do studies like that.

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1 DR. FARRAR: But you decide that, and then
2 you back off from it.
3 DR. S. DWORKIN: Right. The final list is
4 not that.
5 DR. R. DWORKIN: That's right. We can list
6 it, but it's not going to happen in terms of the
7 actual research studies.
8 DR. FARRAR: Understood.
9 DR. HAROUTOUNIAN: Simon Haroutounian,
10 Washington University. Just to continue what Roy
11 mentioned briefly, and it has been attempted in
12 central postural pain, maybe we could come up with
13 a set of core criteria for diagnosis and then
14 specific criteria for defining how probable or
15 possible or definite the condition is.
16 So for postural pain, for example, there are
17 five criterion, then another set of supporting
18 criteria. By using this, we can decide which kind
19 of probability of condition we would like to deal
20 with within the specific study, for example, as
21 opposed to just clinical setting.
22 DR. R. DWORKIN: Steve?

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1 DR. BRUEHL: It's possible to use the
2 criteria that way. That's kind of getting at the
3 research versus clinical criteria. My take on that
4 is that you might be more interested in making sure
5 somebody's at least probable maybe for clinical
6 purposes, but a research study, you'd want to make
7 sure they're definite. Sam might say the opposite.
8 But anyway, there would be different situations
9 where your goal would be different, and you might
10 choose things in a different way.
11 I think one thing that we -- just kind of
12 implicit in all the discussion we've had is kind of
13 paralleling this with the DSM diagnostic criteria,
14 where it's a categorical diagnosis. And I think
15 there's a little bit of worry in my mind that if we
16 talk, even introduce the topic, of probable
17 diagnosis and that kind of thing, it kind of
18 weakens the whole system because then people start
19 talking about these categories that aren't really
20 the full diagnosis, and then what does that mean?
21 So I think what you're talking about can be
22 done in the research setting. Let's say we come up

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

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

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

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

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

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

14 DR. FITZGERALD: No other condition in all
15 of medicine or that these top 10 --
16 (Laughter.)

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

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

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1 balance between research criteria versus clinical
2 criteria, or are we all more or less -- if we're
3 not on the same page and the same chapter?
4 (No response.)
5 DR. R. DWORKIN: Mark?
6 DR. S. DWORKIN: I'd like to ask if Mark's
7 got a headache waiting.
8 DR. SULLIVAN: Yes. Mark Sullivan. One
9 issue raised in my mind by the mention of chronic
10 fatigue versus fibromyalgia is actually the role of
11 pain in Dimension 1. I'm assuming that we're
12 classifying pain syndromes. Are we classifying
13 chronic pain syndromes? What pain criteria are
14 universal across all categories? Pain alone I
15 doubt is enough. Is it pain of a certain severity?
16 Is it pain of a certain chronicity? Is it pain
17 with functional impact?

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

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

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

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

22 We don't have to go to lunch until about

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

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

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

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

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

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

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1 100 percent of 80-year-olds meet those criteria, so
2 be it.
3 DR. S. DWORKIN: I have to say that the
4 impact measure integrates pain intensity and the
5 psychosocial impact. So you cannot get a pain of 6
6 and no impact.
7 DR. TURK: Yes? Do you have a question?
8 UNIDENTIFIED SPEAKER: I was going to say
9 the same thing, that the impact by itself is not
10 the right thing because it's how you deal with the
11 impact. So we're not going to have 100 percent of
12 people age 80 qualifying just on impact. We
13 dropped that out because they may have an objective
14 finding, but they have no pain, or they have pain
15 and deal with it. So we have to look at all those
16 things separately.
17 DR. R. DWORKIN: So we have 5, 10, even
18 15 minutes to make sure we're all on absolutely the
19 same page before we break for lunch. And then of
20 course, after the lunch break, about 1:30, you're
21 all going to go out into the breakout sessions for
22 working groups. So raise your hand if you have

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

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1 DR. R. DWORKIN: Well, how about the
2 following? The working group should do everything
3 possible to avoid having an NOS, not otherwise
4 specified, category. But if in certain
5 circumstances they feel it's really necessary, that
6 is an option. But we would all seek to avoid
7 having what Steve described as a garbage can. Does
8 that seem reasonable?
9 UNIDENTIFIED SPEAKER: The NOS group really
10 is the high specificity group. Isn't that correct?
11 DR. BRUEHL: It's the group that's weeded
12 out by the high specificity.
13 UNIDENTIFIED SPEAKER: The high sensitivity
14 group. Excuse me, the high sensitivity group. So
15 I'm just wondering if it pays at least to have a
16 discussion within the working groups about which
17 are the -- who would be classified as high
18 sensitivity, who is being classified as high
19 sensitivity, and work it out in between, or else
20 create two different groups because, again, one is
21 going to, by definition, be the NOS group, which
22 you don't want to call NOS.

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1 DR. WASAN: Right. So you could call it,
2 for instance, indeterminate, so that the NOS
3 specification actually suggests that, yes, they
4 have a disorder, but we don't quite know what to
5 call it. So for instance, use another word such as
6 "indeterminate" or something that doesn't label
7 that as having the condition of interest. And it
8 still allows you to do all the research stuff you
9 want to do but avoid I think some of the downside.
10 DR. BRUEHL: The problem with the NOS is
11 there are no diagnostic criteria for it because the
12 condition is defined by these diagnostic criteria.
13 They don't meet it. You can call them NOS. That
14 is not a set of diagnostic criteria, so it is
15 simply a label for somebody that you have a hunch
16 might have it, but doesn't meet the criteria.
17 That's why I call it a garbage basket.
18 You don't -- I would agree with what Bob
19 said. Do everything you can not to have a category
20 that makes it sound like that's a separate
21 diagnosis because it really isn't. It's just
22 somebody -- it's the people who are weeded out by

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1 the decision rules in the diagnostic criteria. And
2 some may be close enough to meeting them that you
3 still want to label them with that label, but they
4 really don't meet it. They don't meet the
5 diagnostic criteria.
6 Now, if it turns out you've got diagnostic
7 criteria that you end up with a huge number of
8 people that would be labeled NOS, then maybe the
9 problem is the diagnostic criteria are too
10 specific, and that could be revisited based on the
11 research, potentially.
12 DR. WASAN: Just one other word that's used
13 for that is also "subthreshold." That's another
14 word to use to get around this issue.
15 DR. BRUEHL: And that might be a good one,
16 too.
17 DR. R. DWORKIN: Or how about symptom
18 deficit disorder?
19 (Laughter.)
20 DR. HASSELL: Kathy Hassell. So maybe I
21 missed it in my pre-lunch stupor, but did we decide
22 that we have a universal definition for chronic

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1 pain, and what is it?
2 DR. R. DWORKIN: No one seemed to object
3 strenuously when I said that in most circumstances,
4 it's pain that's lasted -- for most circumstances,
5 for most purposes, we consider pain that's lasted
6 at least three months, allowing the working groups
7 to have exceptions that are either pain conditions
8 that are shorter in duration or longer in duration.
9 But three months will be our benchmark.
10 DR. HASSELL: Two questions. Daily?
11 DR. R. DWORKIN: No. I think that depends
12 on the condition.
13 DR. HASSELL: Fair enough.
14 DR. R. DWORKIN: So I think we have to turf
15 this to the working groups.
16 DR. HASSELL: And severity was not included.
17 DR. R. DWORKIN: I think we said that it can
18 be any severity.
19 DR. HASSELL: Okay. Thank you.
20 DR. R. DWORKIN: We didn't really discuss
21 that. I wouldn't want to wake up -- my personal
22 feeling is I wouldn't want to wake up every morning

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1 with pain to even 1 out of 10. I might not get
2 that treated. It might not have any effect on my
3 life. But I think I've got a pain condition if I
4 wake up every morning in pain, even if it's mild
5 pain.
6 DR. PAYNE: Chris Payne. I wonder if we can
7 take a minute and just talk about lumping versus
8 splitting because in the visceral pain arena, if we
9 have a man that has ejaculatory pain versus a woman
10 who has vulvodynia, we call these different things.
11 And then if we add bladder symptoms, we call it
12 interstitial cystitis. And yet, none of these have
13 any objective findings most of the time, and we're
14 all going by symptoms.
15 So how much lumping, how much splitting, do
16 you envision going on here?
17 DR. R. DWORKIN: Maybe I want to get to
18 lunch, but I think this is up to the working
19 groups. Does anyone on the panel have anything to
20 say?
21 DR. BRUEHL: Yes. I don't have a definitive
22 response to that, but just keep in mind this is, as

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1 much as possible, suppose to be empirically driven.
2 So if the research out there that has been done on
3 those three -- just using your example, using those
4 three conditions -- indicates that there's no
5 difference in mechanisms that can be discerned, and
6 we tried to detect them, and that the symptoms are
7 similar, and the difference is only in location
8 depending on gender, use your judgment.
9 But I think you should feel free to kind of
10 think out of the box if you want to and create some
11 new diagnostic category that lumps them together,
12 if that is justified by the data. Time will tell,
13 as we investigate things further, whether that's
14 justified or not.
15 DR. R. DWORKIN: So before we break for
16 lunch, any other profound concerns that we're not
17 all on the same page?
18 DR. S. DWORKIN: I have a profound
19 suggestion that should not be at all controversial.
20 In addition to the temporal parameter, add
21 something about the location so that all the groups
22 are not just working on chronic pain of three

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1 months. You're not. You're working on chronic
2 pain of three months here, there, and say something
3 about the anatomic location in which the pain is
4 reported.
5 DR. R. DWORKIN: I think that's in Roger's
6 article. We talk about the temporal aspects of the
7 pain, the location of the pain, the intensity of
8 the pain. There certainly needs to be a discussion
9 of intensity, even if that's not a criterion
10 itself. Absolutely. And that was --
11 DR. BRUEHL: I think it was Axis II, though,
12 that we had -- it's not key to diagnosis, but it's
13 descriptive.
14 DR. R. DWORKIN: I think one last comment
15 all the way back. I can't see you because you're
16 in front of the window.
17 DR. CEUSTERS: I'm not sure whether we are
18 on this same page, but it might be that I'm the
19 only one. I'm not sure whether we understand all
20 in the same way about the syndromes and the
21 conditions and the disorders and the diagnoses and
22 so on. So I found it very useful when some said,

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1 okay, the disorder is in the body part and the
2 disease is in the person. I always tend to think
3 that the diagnosis is in the head of the physician
4 and not in the patient. And if you do that, you
5 see discordances between the two.
6 Now, given the example of the chronic pain,
7 when you are defining chronic pain, are you
8 defining something which is inside the patient or
9 is it like a diagnosis? Which is inside of the
10 head of the physician.
11 The distinction is this. When it is on the
12 side of the patient, then a patient does have
13 chronic pain or doesn't have it. There is no other
14 possibility. If it is a diagnosis, now there might
15 be a term, which is we don't know yet. If my pain
16 started a month ago, I still have it now. Then
17 according to you, what you propose as a diagnosis,
18 you would say I don't have any chronic pain. But
19 it might be that you don't know yet. If we wait
20 two months, then it became clear that already now
21 it was chronic pain.
22 So that's a clear-cut example, but reading

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

7 DR. BRUEHL: Please identify yourself.

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

10 Adjournment

11 DR. R. DWORKIN: We have to break for lunch.

12 But what I hear and what you're saying to me makes
13 perfect sense, at least in terms of that kind of
14 evolution. I wouldn't consider a patient having
15 postherpetic neuralgia unless they've had pain for
16 three or four months since their shingles.

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

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

4 Okay. I think we need to get you all to
5 lunch. The lunch break is from now until 1:30.
6 And then at 1:30, you all have working group
7 assignments. Remember the taxis, to arrange those.

8 Also, if you're a chair, co-chair, or facilitator,
9 we're meeting back here at 5. Thank you all very
10 much.

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

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