

ACTION-APS-AAPM
Pain Taxonomy (AAAPT) for Acute Pain

April 28, 2016

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Page 4	<p>1 P R O C E E D I N G S</p> <p>2 (8:07 a.m.)</p> <p>3 Welcome and Introductions</p> <p>4 DR. TURK: Good morning. Please take your</p> <p>5 seats so we can get started. Thank you.</p> <p>6 My name is Dennis Turk, and I am happy to</p> <p>7 have all of you here at the AAAPT meeting. And I</p> <p>8 will formally introduce things in a moment, but let</p> <p>9 me just get started with a couple of housekeeping</p> <p>10 slides, make sure everybody -- there will be coffee</p> <p>11 around, so you can get up and get coffee if you</p> <p>12 want to. There will be plenty of coffee breaks for</p> <p>13 you to do that.</p> <p>14 Okay, so let's just do a little bit of</p> <p>15 housekeeping. Now, you probably don't want me</p> <p>16 reading all this to you. You can read it yourself,</p> <p>17 and you know most of these things. The only thing</p> <p>18 I'll emphasize is the restrooms, which we always</p> <p>19 get asked to, out the door to the left, next left,</p> <p>20 through double doors, and you'll find them. So</p> <p>21 those are always the important things.</p> <p>22 Standing in the back, with the blue top, is</p>	Page 4

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1 Valerie Thompson. She and Andrea Speckin are the
2 organizers of this meeting. They can help you and
3 handle all details that you bump into as far as
4 your room or your flights, or anything of that
5 kind, any questions you have. They are our saviors
6 and have been with us, Bob Dworkin and myself, for
7 a long time, so we count on them to really keep
8 things going, so any questions you have.

9 The speakers, if you have any slides, the
10 gentleman in the pink shirt, my left, will be happy
11 to help you set those up if you haven't already
12 given them to them as well.

13 So let's just make sure you've had a chance
14 to look over the housekeeping. Nothing
15 particularly unusual. We already heard that it's a
16 bit warm in here, so we're taking care of that.
17 The microphones are the types you have to push the
18 button on. They're not voice activated. And if
19 one person is speaking, obviously you won't be able
20 to get in there. It will light up red when you do
21 it, and then you turn it off or it goes off on its
22 own.

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1 Okay. So let me introduce the welcomers for
2 you. This meeting, as you may know, is a joint
3 collaboration with the ACTTION public-private
4 partnership, which I'll tell you more about during
5 my formal presentation, and the American Pain
6 Society and the American Academy of Pain Medicine.
7 And that is, we're bringing these organizations all
8 together with our real objective, which is to get
9 accomplished at this meeting, and you'll hear more
10 about that.

11 But I want to welcome our two welcomers.
12 First Dr. Dan Carr from Tufts University, the
13 president of the American Academy of Pain Medicine.

14 Are you president or president-elect?
15 DR. CARR: President.
16 DR. TURK: You're president. Okay, Dan.
17 And then when you're done, we'll introduce Greg,
18 and then back to me.

19 DR. CARR: Thank you very much, Dennis. And
20 I have to reflect personally that I had the
21 privilege to be at the first couple of IMMPACT
22 meetings that really produced very high impact

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1 papers that have been widely cited, and I feel very
2 proud to have maintained that relationship over the
3 years. And I think Bob and Dennis, we'll have a
4 spontaneous round of applause to thank the two of
5 them.

6 (Applause.)
7 DR. CARR: Sorry. That wasn't on the
8 schedule, but I just lost control of myself.

9 So I also want to thank everyone in this
10 room. It is a dream team of people who are
11 incredibly and uniquely well informed, both about
12 issues relating to taxonomy, the structure of
13 ACTTION and AAPT, and also acute pain. So this is
14 an amazing group.

15 I think I have to give a special thanks to
16 Henrik Kehlet for distance travelled, although
17 Steve Stanos, and John, and Greg and the Washington
18 contingent might equal the thousands of miles of
19 travel. But it is just a fantastic group of
20 people.

21 So could I have the first slide?
22 Hmm, is that my first slide? It looks like

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1 a harbinger of something. In any case -- oh, the
2 boxes didn't project. But this is what we're here
3 to do. We're here to develop a framework for a
4 comprehensive and evidence-based ACTTION-APS-AAPM
5 pain taxonomy for acute pain.

6 Acute pain. Now, for some of the people in
7 this room, acute pain never stopped being
8 important, and they contributed and made advances
9 in practice. But I would say that at the present
10 time, we can look back over the last 15 or 20 years
11 and look at an interval where the period of acute
12 pain didn't seem to be that interesting.

13 I'd say it might have been viewed as a
14 mechanical thing, as a quality, internal quality
15 assurance thing. But I'd say that it's been very
16 gratifying to see in the last handful of years a
17 true resurgence of interest and NIH funding for
18 acute pain.

19 I'm going to quote a position paper, a
20 survey of the state of acute pain that was first
21 authored by Patrick Tighe, who is one of people
22 here today, but also included Mike Kent and Trip

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1 Buckenmaier, and several other people from AAPM.
2 And this survey said, well it looks like there is
3 resurgent interest, and this began around the
4 2010s.
5 For one thing, the application of multimodal
6 therapies and enhanced recovery after surgery has
7 been increasingly the norm. It saves money, it
8 allows people out of the hospital more quickly.
9 And we now have effective, proven, multimodal
10 regimens to accomplish that. They're not perfect.
11 They don't work for everybody equally. But they're
12 reliable enough that the treatment of acute pain
13 has become integrated into the fabric of daily
14 care.
15 By doing so, looking back historically,
16 using multimodal regimens, assessing pain,
17 titrating pain treatments to pain scores, and so
18 on, there's been a demonstrable reduction in
19 adverse events. There is also a likely reduction
20 in the chronification of acute pain and also costs.
21 Of course, there's increased patient
22 satisfaction, and I guess personally I don't know

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1 how many of you are following what's going on in
2 the U.S., but there's controversy about even asking
3 questions about pain. Be that as it may, I think
4 just sitting here in this room, most of us would
5 agree that if patients are happier, that's a good
6 thing.
7 So here are the hypotheses that I would see
8 driving this meeting. First of all, the hypothesis
9 is there's an opportunity to advance acute pain
10 research, and I think practice, by revisiting the
11 taxonomy of acute pain from an inter and
12 multidisciplinary perspective. And we certainly
13 have assembled the right people to do that.
14 The next hypothesis is that the recent and
15 ongoing experience with the taxonomy of chronic
16 pain under the AAPT aegis can guide the process for
17 acute pain. And third, the chronic pain process,
18 the AAPT process, may not be perfectly
19 generalizable to acute pain, so we have to work out
20 a few things about that.
21 I've reviewed the slides that people
22 submitted, and thank those of you who did so, so I

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1 know that this is duplicative. But this will also
2 serve a little bit as an introduction to the first
3 speaker's talk, namely by Roger Fillingim, in that
4 earlier and ongoing process, there were five key
5 dimensions that were identified of relevance to
6 taxonomy.
7 In particular, there were core diagnostic
8 criteria that allowed one to define or decide if a
9 certain condition were present. And I'll speak to
10 this later in my longer talk, but I think there's a
11 little bit more emphasis on diagnosis in the
12 chronic pain effort than there is in the acute pain
13 effort where the cause is often very clear.
14 Also, there are common, and by common it's
15 really meant frequent features of that condition,
16 so there are additional characteristics and
17 non-pain features: common medical comorbidities
18 that co-occur with high frequency, consequences in
19 the neurological, psychobiological, and function,
20 such as sleep, and then putative neurobiological
21 and psychosocial mechanisms, risk factors, and
22 protective factors.

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1 So you'll see this way of thinking. This is
2 a way of organizing one's thought about the
3 taxonomy, and I'm sure Roger will touch upon that.
4 I'll throw out some ideas, the purpose, in
5 this few minutes of introductory remarks, not to
6 gender debate about this. But if I go back and
7 look at that Tighe, et al. acute pain medicine
8 shared interest group paper, their working
9 definition of acute pain was, " the physiologic
10 response and experience to not just stimuli that
11 can become pathologic, is normally sudden at onset,
12 time limited, and motivates behaviors to avoid
13 actual or potential tissue injuries."
14 In that same state of acute pain paper, it
15 was pointed out that the experience of acute pain,
16 as we think about it, generally has an exciting
17 event, it's of sudden onset, it's time limited, and
18 has the potential to develop into a pathologic
19 condition.
20 So I'm throwing these out not to debate them
21 per se, but to kind of begin to have us get our
22 heads around two traditionally distinct constructs,

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1 the one construct being chronic pain, it's long
2 established, you don't have the opportunity to
3 intervene at the beginning because the patient
4 comes to you long after the beginning; then you
5 have acute pain, it's a somewhat different context,
6 and I'll go into that in a longer talk.

7 I read with great interest the initial
8 publication from the AAPT effort, which was first
9 authored by Roger. And I, for the purposes of this
10 meeting, wanted to call to your attention one
11 portion of this, which said that, in considering
12 the approach to take, whether to take an
13 evolutionary approach or revolutionary approach,
14 they said, and Roger wrote, that a revolutionary
15 approach to chronic pain taxonomy might completely
16 abandon current diagnostic labels and approaches
17 based on anatomical structures and organ systems in
18 favor of an approach that prioritizes the
19 neurobiological mechanisms underlying chronic pain.

20 I think we'll hear a great talk. I've had a
21 sneak preview of Tim Brennan's slides, and I think
22 you'll be well informed by his talk.

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1 But having weighed whether to do an
2 evolutionary or revolutionary way forward, they
3 decided I think to pull back a little because there
4 was inadequate knowledge of mechanisms. The area
5 was just not there yet to support this
6 revolutionary approach.

7 Also, ultimately, these products need to
8 have some impact on the real world. And Roger
9 wrote that, "Clinicians and scientists comfort with
10 classical systems and the reluctance to change
11 tipped the balance back towards an evolutionary
12 approach."

13 Now, I am a member, or I should say
14 survivor, of the IASP task force on taxonomy. And
15 as a young faculty person, coming into the task
16 force was an experience I will never forget in my
17 lifetime because the heat and passion of battle,
18 even sustained over internet, was staggering to me,
19 that people could be so passionate.

20 I think ultimately -- I may not be doing
21 this justice, John, but I think it's not inaccurate
22 to say that ultimately the entire task force was

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1 fired because they did nothing but fight, or the
2 amount of productivity relative to the amount of
3 fighting was viewed as too low, so it was
4 reconstituted.

5 This also being the week of Passover, I
6 thought, well, we can't actually have services
7 here, but I came across this quote from the
8 wonderful scholar Maimonides, and we're looking
9 about over 800 years ago. And in one of his
10 writings on Judges, which is a tremendous thing to
11 read in terms of conflict of interest and so on,
12 very modern, he had this thought that, "Two
13 scholars who dislike each other are forbidden to
14 sit together in judgment for this might lead to the
15 rendering of a perverted judgment. Prompted by
16 hostility, each will be inclined to refute the
17 arguments of the other."

18 So who knew that he served on committees?
19 (Laughter.)

20 DR. CARR: Who knew that he was a member of
21 the task force on taxonomy? But I think we're
22 really in good shape because we have a very

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1 congenial and positive group of people here.

2 Actually, I see Rob Hurley in the back, and
3 I didn't mean to leave you out from the acute pain
4 effort.

5 But we are benefiting by a great group.
6 We're benefiting by a formula that's been worked
7 out. It's an amazing formula that Bob and Dennis
8 have worked out over the years. I guarantee this
9 will produce something, and the question is how
10 much and how extensive, and that depends upon all
11 of you.

12 So I'm going to turn the podium over to my
13 colleague, Greg Terman, and thank you for being
14 here and traveling here.

15 DR. TERMAN: Good morning. I don't have any
16 slides, but I didn't want to pass up an opportunity
17 to welcome you and thank you for being here on
18 behalf of the American Pain Society for this
19 collaborative meeting.

20 Discussing development of framework for
21 acute pain taxonomy, I think it's very timely.
22 Some of you may have read on blogs or in the papers

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1 about the recent CDC guidelines and people
2 describing, with satisfaction or with horror, the
3 acute pain part of those guidelines, and probably
4 not having read the fine print, which says it isn't
5 concerning the traumatic or perioperative acute
6 pain, which is, really, most of the patients that
7 I've taken care of over the last close to three
8 decades of being an acute pain doc.
9 So I think this is a great opportunity. I'm
10 pleased to say that the American Pain Society is
11 becoming more and more interested in acute pain,
12 certainly based on the joint APS perioperative
13 guidelines that were just published earlier this
14 year.
15 I think that's going to continue or increase
16 as those of you that have kind of looked or are
17 involved in the Federal Pain Research Strategy
18 through NIH, there's certainly a considerable
19 portion of that effort around acute pain. So I
20 think that's really outstanding, and certainly as
21 an acute pain doc I find it very good.
22 If we're going to discuss or treat or

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1 research acute pain, it might be useful if we know
2 what we're talking about. So I look forward to
3 this meeting in terms of thinking about taxonomy of
4 acute pain, and I thank you again for coming.
5 DR. TURK: Thank you, Dan and Greg.
6 Actually, when Dan was speaking about Maimonides
7 quote, I was remembered of a cartoon that I once
8 saw, which basically said that the only thing two
9 experts will agree on is that the third expert is
10 an idiot.
11 (Laughter.)
12 DR. TURK: So perhaps we'll be able to
13 figure something out for the group here.
14 Again, I'm Dennis Turk from the University
15 of Washington, and I want to welcome all of you
16 here from ACTTION, which stands for Analgesic,
17 Anesthetic, Addiction, Clinical Trials,
18 Innovations, Opportunities, and Networks. Whew! I
19 got through that whole thing.
20 One of the things you're going to learn, you
21 already heard Dan mention IMMPACT, which is another
22 acronym that some of you may be familiar with,

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1 Initiative on Methods, Measurement, and Pain
2 Assessment in Clinical Trials. Dr. Dworkin, who is
3 the perpetrator of these acronyms, is a
4 card-carrying member and fellow with the American
5 Academy of Acronymnilia [ph], so therefore we're
6 going to add yet one more acronym to the group
7 here, and that will be the AAA -- AAAPT.
8 You've also heard mention about the chronic
9 pain guideline, and you'll hear a formal
10 presentation of that from Roger Fillingim.
11 But just to understand how that began, it
12 was essentially a group like this that got together
13 trying to see could we come to some agreement about
14 the relative and appropriate dimensions that would
15 be considered in a taxonomy. And bemoaning what
16 had occurred to the original classification that
17 Harold Merskey had created for the International
18 Association for the Study of Pain, which was used
19 by almost no one, if anyone -- and to my knowledge,
20 there's only been one study that's actually tried
21 to evaluate it. I did it. We concluded that it
22 was totally unreliable, that raters could not use

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1 that system to come up with anything reliable. So
2 bemoaning that was some of the impetus.
3 We did have interesting meetings. We didn't
4 argue and scream nearly as much, I don't think, as
5 the IASP taxonomy, but we were able to hammer some
6 things out. And I think the manuscript that you
7 saw gives you a wonderful idea of what we're trying
8 to do with that.
9 It's expanding. There are working groups
10 in -- what, Bob? -- 9 areas or 8 areas, that are
11 working for specific disorders to come up with
12 classifications that will fit within that
13 classification.
14 The background papers for the AAPT taxonomy
15 will be appearing in a supplement in Journal of
16 Pain, which will be out probably September/October
17 if all goes well. It will have much more detail
18 and rationale as backup for what Roger produced in
19 that particular paper, and really articulating much
20 more clearly the dimension. So you can look
21 forward to receiving that.
22 Let me just move ahead. This is to welcome

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1 you officially. I have the logos of all the
2 relevant organizations. Consider yourself
3 welcomed. I should say, by the way, when we were
4 talking about the distance people came, we forgot
5 Knox Todd, who came I think the longest -- how many
6 miles did you come, Knox?
7 DR. TODD: Oh, so many miles.
8 DR. TURK: How many hours did it take you to
9 get --
10 DR. TODD: Eighteen.
11 DR. TURK: Yes, I think Knox with Argentina.
12 Yes, I think Argentina may be the furthest
13 distance, but it definitely took the most amount of
14 time for somebody to get here. So in addition to
15 Henrik and anybody else that we've got here from
16 Europe, also to thank Knox for making this long
17 trek here.
18 We really did try to get people who were
19 knowledgeable across the spectrum of acute pain
20 areas so that we went from post-op, to visceral, to
21 cancer, to emergency room, et cetera. And the
22 people around the room, some of you may not know

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1 each other, so what I thought I would do is very
2 quickly, and if you could do this quickly, just say
3 who you are, where you're from, what university
4 you're from. And let me tell you, there will be a
5 quiz at the end, so you must stay awake and
6 remember who you have beside you.
7 So Bob, why don't we start with you. They
8 already know who you are, but go ahead.
9 DR. DWORKIN: Bob Dworkin, University of
10 Rochester.
11 DR. TURK: Knox?
12 DR. TODD: Knox Todd. I was the founding
13 chair of the Department of Emergency Medicine at
14 the University of Texas MD Anderson Cancer Center
15 for the last five years. In December made a career
16 change and live in Mendoza, Argentina. And if
17 anyone wants to come down and sample the wine or
18 the olives, we'd be happy to have you.
19 DR. MACKEY: Sean Mackey, Stanford
20 University.
21 DR. BUVANENDRAN: Kumar Buvanendran from
22 Rush University Medical Center, Chicago.

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1 DR. KEHLET: Henrik Kehlet, Copenhagen
2 University, Denmark.
3 DR. FILLINGIM: Roger Fillingim, University
4 of Florida.
5 DR. RAJA: Srinivasa Raja, Johns Hopkins
6 University in Baltimore.
7 DR. MCLEAN: Sam McLean. I'm an emergency
8 physician from the University of North Carolina.
9 DR. SCHREIBER: Kristin Schreiber. I'm an
10 anesthesiologist and pain researcher at Brigham and
11 Women's Hospital in Boston.
12 DR. BELFER: Inna Belfer. Former University
13 of Pittsburgh, now FDA.
14 MS. GORDON: I'm Deb Gordon. I'm a nurse
15 from the University of Washington in Seattle.
16 DR. STACEY: I'm Brett Stacey, and I
17 [inaudible – off mic] if I should leave. I'm also
18 from the University of Washington and I run the
19 [inaudible – off mic].
20 DR. KENT: I'm Mike Kent from Walter Reed.
21 DR. TIGHE: Patrick Tighe, University of
22 Florida.

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1 DR. TURK: Stop for one second. Those two
2 gentlemen right there are going to be taking the
3 minutes, the notes from this particular meeting.
4 They're going to be drafting up the manuscript that
5 you're all going to be involved with. So be very
6 kind to them and make sure that you give them good
7 information.
8 I should also say, to stop right now, the
9 slide presentation that you're going to be seeing,
10 we've already had people ask about them, we
11 will -- I'm not sure how long, but in a couple of
12 weeks get these all up on the ACTTION website, so
13 that you will be able to download these for those
14 who are interested.
15 For those of you who did slides, if you have
16 any proprietary information in any of those, let us
17 know, and we'll make sure those don't get included.
18 But everything else will become available to
19 everyone, both in this room, but also anyone
20 outside who was not able or was not invited to
21 attend because of the space limitations.
22 Sorry. Okay, Trip?

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1 DR. BUCKENMAIER: Trip Buckenmaier,
2 Uniformed Services University, [inaudible – off
3 mic].
4 DR. POLOMANO: Rosemary Polomano, University
5 of Pennsylvania.
6 DR. STANOS: Steven Stanos, Swedish Health
7 Systems, Seattle, Washington.
8 DR. WEISMAN: Steve Weisman from the Medical
9 College of Wisconsin and Children's Hospital
10 Wisconsin.
11 DR. SURESH: Santhanam Suresh from Lurie
12 Children's Hospital and Northwestern University in
13 Chicago.
14 DR. WU: Chris Wu, Hopkins.
15 DR. BRUMMETT: Chad Brummett, University of
16 Michigan.
17 DR. HURLEY: Rob Hurley, Medical College of
18 Wisconsin and [inaudible – off mic].
19 DR. EDWARDS: David Edwards, Vanderbilt.
20 DR. SCHUMACHER: Mark Schumacher, UCSF.
21 DR. TURK: Jen?
22 DR. GEWANDTER: Jen Gewandter, University of

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1 Rochester.
2 DR. COHEN: I'm Robert Cohen. I've been at
3 Beth Israel Deaconess Medical Center, part of
4 Harvard Medical School, and now I'm with Analgesic
5 Solutions.
6 DR. BRENNAN: Tim Brennan, University of
7 Iowa.
8 DR. RAHMAN: Siamak Rahman, University of
9 California, Los Angeles.
10 DR. DESJARDINS: Paul Desjardins, Rutgers
11 and Tufts.
12 DR. BRUEHL: Steve Bruehl, Vanderbilt
13 University.
14 DR. LOESER: John Loeser, University of
15 Washington.
16 DR. SCHACHTEL: Bernie Schachtel, Yale
17 University.
18 DR. TURK: Terrific. As you probably picked
19 up, we've got a range of disciplines, a range of
20 different areas where people come from outside the
21 United States, within the United States. We really
22 do have, as Dan said, a dream team.

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1 So consider yourself welcomed. Make sure
2 you get a chance to interact with your colleagues.
3 There are plenty of coffee breaks, plenty of lunch
4 breaks, other opportunities for you to do that.
5 What we've learned from a number of these
6 meetings is that the conversations and discussions
7 that go over among those breaks actually are very
8 useful and informative because they often then feed
9 back to subsequent discussions. So we encourage
10 that as much as you want to do that.
11 Okay. Let's go forward. What are the
12 objectives? You heard sort of Dan do this, to
13 review the AAPT classification -- you've heard more
14 about that than you're probably going to want to
15 hear -- from chronic pain, determine its
16 appropriateness and any modifications required to
17 extend to acute pain.
18 To disseminate these considerations,
19 observations, suggestions and research agenda by
20 publishing a peer-reviewed journal. That
21 peer-reviewed journal will possibly be a combined
22 publication of the Journal of Pain and Pain

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1 Medicine for the two organizations that are here.
2 This can be done -- so don't worry about the
3 logistics, but it can come out simultaneously in
4 two journals if the editors and the publishers are
5 willing. So far, they've been very positive, so
6 that shouldn't be a problem.
7 In order to accomplish these objectives,
8 some herding of the participants is needed.
9 (Bob Dworkin nods no.)
10 Now, notes on the gentle art of herding,
11 participants don't like to be herded. In fact, you
12 can't readily -- AAPT participants, we can't get
13 them to do much of anything, but we keep trying
14 anyhow. Participants like to herd themselves, but
15 you're not very good at it, so you sometimes need a
16 little assistance.
17 Participants understand that they sometimes
18 need to be herded, however, that doesn't make them
19 any less recalcitrant or easier to herd. And harsh
20 herding usually has negative consequences.
21 So that's what we've learned, and here we
22 are, the happy team who is going to help herd you

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1 because we want to do this. Remember, the goal is
2 at the end of the two days, day and three-quarters,
3 is to have enough information available, discussing
4 the important and relevant issues, that will then
5 end up with Patrick and Michael in their hands to
6 get it pulled together.
7 They will create a draft of the manuscript.
8 It will be circulated to all of you, all of whom
9 are invited, encouraged, wish to be co-authors as
10 long as you sign off that you are willing to do
11 that. We hope you will provide comments.
12 Let me explain to you about doing
13 manuscripts with this many authors. It is
14 difficult and slow. We appreciate, greatly
15 appreciate, if in fact when you have a draft sent
16 to you or some question comes to you, you respond
17 as quickly as reasonable. Don't drag this out.
18 Comments like, great, thanks, are not real
19 helpful in the early stages of a draft, so it's
20 useful if you have comments that we can contribute
21 to this. When we then circulate subsequent drafts,
22 again, the faster we can turn this around, the

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1 better.
2 When we get the inevitable comments back
3 from the journal reviewers, we tend to make the
4 changes and address those, assuming they're
5 relatively minor, identify those changes in usually
6 red font on the next draft you'll see, and
7 encourage you to pay attention specifically to the
8 red font.
9 People sometimes say, oh, I forgot I didn't
10 read this section carefully and there's something
11 else I want to change. We prefer you not do it at
12 that point since it's been through review, so try
13 to stick to it. Paul is shaking his head because
14 he's been with us as a first author, a lead author
15 on one of these particular manuscripts. So we
16 encourage you to do that. Okay?
17 So you've heard the logistics. You know
18 what you're being asked to do. You now know all
19 your neighbors and friends. I'm not going to do
20 the quiz, but I will expect you to know each other.
21 Now we do have name tags. You can understand about
22 the housekeeping.

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1 So Bob, unless you have a question and
2 you've already -- I introduced Valerie, who you
3 saw, who we thank, and our gentleman in the back on
4 my left who is taking care of the slides and the
5 audio/visuals. Should speakers have any questions,
6 talk to them.
7 Bob, any comments you'd like to make? Okay,
8 then consider yourself welcomed. You gentlemen can
9 step down, and I'll call Roger Fillingim up, who is
10 going to be our first speaker.
11 Roger is a professor at the University of
12 Florida. He has been past president of the
13 American Pain Society, and he was most importantly
14 the lead author of the AAPT Chronic Pain guideline.
15 He herded the cats. His picture is there.
16 He was one of the key herders of the cats and was
17 able to produce that manuscript. He can tell you
18 stories offline, horror stories, if he wants to,
19 about getting the cats herded. But it's my
20 pleasure to have Roger come and sort of give you
21 the background, which you've been sensitized to.
22 The manuscript was circulated. Hopefully,

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1 you all read that. So Roger, they're all yours.
2 Presentation – Roger Fillingim
3 DR. FILLINGIM: Thanks very much, Dennis.
4 My job is to just give you some background
5 on the chronic pain taxonomy. As Dan pointed out,
6 one of the goals is to determine the extent to
7 which the chronic pain taxonomy can inform the
8 AAAPT and what modifications might be needed. So
9 I'm going to tell you about the process we went
10 through and give you a sense of how the sausage was
11 made.
12 Dennis mentioned the acronyms. If you're
13 not aware, Bob directs a clinical research acronym
14 program, also known as CRAP.
15 (Laughter.)
16 DR. FILLINGIM: If any of you are
17 interested, I think it's a great resource.
18 (Laughter.)
19 DR. FILLINGIM: So this is just an overview
20 of what I'm going to talk about today. I'll give
21 you a brief history, talk about some of our
22 conceptual considerations during the development,

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1 highlight the current framework that you've already
2 heard a little bit about, and then talk about where
3 AAPT is going in terms of future directions.
4 This is just a timeline sort of from
5 inception to slightly past today. Dennis referred
6 to the Journal of Pain supplement that's getting
7 into its final stages in terms of article
8 submissions and revisions. So we think that's
9 going to come out in about September.
10 But this all started back in September of
11 2012 when Bob emailed me -- I was then president of
12 APS -- and proposed this. I'll tell you a little
13 bit more about that. And the APS board approved
14 that shortly thereafter.
15 We then planned for the AAPT launch meeting,
16 which occurred in May of 2013, so that's about
17 three years ago, right? And then you can see the
18 other activities from about -- so we had our second
19 AAPT meeting in July of 2014, and since that time,
20 the working groups, and I'll tell you about those
21 shortly, have been developing their diagnostic
22 criteria.

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1 So this is some of the text from Bob's
2 initial email to me, and I bolded some text to give
3 you a sense of why Bob and Dennis thought this was
4 an important idea. But a comprehensive pain
5 taxonomy is essential so that consistent and
6 accurate diagnoses are used for clinical research,
7 clinical trials, and to facilitate comparisons
8 across studies for systematic reviews and
9 meta-analyses. And it's also critical for
10 regulatory reviews of new drug applications.
11 So that was a large part of the rationale
12 for getting things going in the first place. I
13 mentioned May of 2013 was our launch meeting. And
14 our goal was to develop a framework, much like our
15 goal here this week -- to develop a framework that
16 all working groups could apply in developing
17 diagnostic criteria for chronic pain conditions.
18 Here's essentially the agenda that we
19 followed at that meeting. We had Chuck O'Brien, a
20 psychiatrist who has been involved in the
21 diagnostic and statistical manual of the American
22 Psychiatric Association. And at that time,

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1 essentially, he had to leave the meeting because
2 DSM-5 was being unveiled in California or
3 something. So he told us a little bit about some
4 of the history there, because we thought that the
5 DSM process was, in some ways, a model for what we
6 might be thinking about with chronic pain.
7 Then we had some discussion of chronic pain
8 mechanisms. And then we had three presentations by
9 individuals who had been involved in developing
10 evidence-based diagnostic criteria and conducting
11 research on those criteria. So that was Sam
12 Dworkin for TMD, Eva Widestrom-Noga with spinal
13 cord injury pain, and then Steve Bruehl, who is of
14 course with us here today talking about complex
15 regional pain syndrome, just to give us some ideas
16 of the process whereby diagnostic criteria get
17 developed and then tested.
18 I then talked some about, at that point,
19 what was our thinking about how we might develop a
20 multi-axial framework, and then there was lots of
21 discussion. And ultimately, we developed work
22 groups, decided on the core diagnostic criteria

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1 that would be part of our framework, and then
2 talked about where we were going to go from there.
3 So that's sort of how the meeting unfolded in a
4 nutshell.
5 You've heard both me and Dennis mention this
6 upcoming Journal of Pain supplement. The rationale
7 for this -- and you can see a list of the articles,
8 most of which are already accepted. A couple of
9 them I think are in the revision phase right now.
10 But as we think about our working groups, who are
11 developing diagnostic criteria, we didn't want
12 every working group to have to reiterate, here's
13 how you should assess pain. Here's how you should
14 assess psychosocial mechanisms.
15 If that happened nine times, that's a huge
16 waste of journal space, so we wanted to give some
17 foundational information and references that all of
18 the working groups could refer to. And so that's
19 the rationale for this supplement, which we hope to
20 see later this year.
21 So let me dig down into the meeting a little
22 bit and some of the things we were thinking about

<p style="text-align: right;">Page 37</p> <p>1 leading up to the meeting and during the AAPT 2 meeting. Of course, we were talking about 3 diagnostic criteria, but there are sort of 4 overlapping and confusing terminologies that get 5 thrown around. And in fact, we had to decide what 6 are we calling these things. Are these chronic 7 pain diseases, disorders, conditions, syndromes? 8 This comes primarily from the psychiatric 9 literature. If you distinguish among these terms, 10 a disorder is a medical concern, an abnormality, an 11 aberration, and this is generally used when the 12 pathophysiological process is not well-known. 13 A disease refers to a known pathological 14 process that leads to one or more disorders. And a 15 diagnosis is a procedure used to decide whether or 16 not a certain disorder or disease is present in a 17 patient. And I believe we settled on chronic pain 18 conditions, if my memory serves, so we skipped all 19 of these terms. 20 If we think about diagnosis -- I think this 21 is relevant to our work here, and it certainly was 22 relevant to our work in AAPT -- the purpose of</p>	<p style="text-align: right;">Page 39</p> <p>1 chronic pain. The open question is whether 2 different diagnostic manifestations of a basic 3 pathological process have been divided into 4 multiple diagnostic silos creating artifactual 5 comorbidity in certain circumstances. 6 So are we making distinct disorders or 7 conditions out of something that's actually one 8 pathological process, and that creates many 9 comorbidities that we see? 10 As I say, this is relevant to chronic pain. 11 We know we have overlapping conditions in the 12 chronic pain space. And one of the articles coming 13 out in the JoP supplement addresses these 14 overlapping pain conditions. So to what extent are 15 these actually distinct disorders versus 16 reflections of some global underlying 17 pathophysiology? 18 Another thing we wanted to keep in mind as 19 we develop AAPT is what are the characteristics of 20 an ideal diagnostic system? And here are some of 21 those characteristics here. So there should be 22 some biological plausibility, which you might</p>
<p style="text-align: right;">Page 38</p> <p>1 diagnosis is to guide treatment and prognose. 2 There are other secondary purposes to which 3 diagnosis has been applied, but those are far less 4 important, in my view. 5 So what we should be thinking about as we 6 develop diagnostic criteria is will these criteria 7 help us decide what treatments need to be 8 perpetrated on these patients, and that's really 9 the ultimate goal. And it might help us tell 10 patients what they can expect, what the course of 11 their condition is likely to be? 12 That implies that treatment is based on 13 diagnosis. And now we know that this isn't 14 necessarily true at present, but we would like it 15 to be true in the future. This is one of my 16 favorite cartoons, "We can't find anything wrong 17 with you, so we're going to treat you for symptom 18 deficit disorder." We never treat people until 19 after we've diagnosed them. 20 So another conceptual concern is this issue 21 of lumping versus splitting, again from the 22 psychiatric literature, but certainly relevant to</p>	<p style="text-align: right;">Page 40</p> <p>1 interpret as the diagnostic system should be 2 translatable into pathophysiological mechanisms. 3 The diagnostic system ideally would be exhaustive, 4 that is it allows you to characterize all of the 5 pain conditions that might be encountered by a 6 clinician. 7 The diagnostic categories should ideally be 8 mutually exclusive so that you can tell that if a 9 person has X, that's different from a person who 10 has Y. Now, a given person could have both X and 11 Y, but those would be two separate conditions. 12 Then of course, it should be reliable, and 13 that requires some research to determine the 14 reliability of the system. 15 As Dan alluded to, we were concerned and we 16 opted for evolution rather than revolution because 17 we wanted the system to be clinically useful and 18 also useful for research. And if you take too far 19 a leap, it's difficult to encourage people to 20 continue using a system. And then ideally, the 21 diagnostic system would be simple enough for people 22 to understand and apply. So these are some of the</p>

<p style="text-align: right;">Page 41</p> <p>1 principles we were shooting for in the development 2 of AAPT. 3 At the time that we were contemplating 4 development of AAPT, this was essentially the state 5 of pain classification, and I think this is largely 6 true still today. There are multiple diagnostic 7 systems proposed by different groups with no 8 uniformity of structure or approach. 9 Even the three presentations that we had by 10 Sam and Eva and Steve at that time, those were 11 completely independent initiatives. There was no 12 guiding framework. So they did quite good work and 13 quite good research, but in completely different 14 spaces. 15 Unlike those three systems, most of the 16 diagnostic criteria out there have very little 17 evidence supporting their reliability or validity. 18 And of course, they're based primarily on signs or 19 symptoms, which, as I have mentioned, can overlap 20 considerably. The diagnostic studies that are 21 performed -- and this is certainly still 22 true -- typically emphasize tissue damage, which as</p>	<p style="text-align: right;">Page 43</p> <p>1 peripheral neuropathy, the etiology is that 2 someone's got diabetes, and that's producing nerve 3 damage, let's say. 4 Then you could think about general 5 mechanisms. Well, they've got peripheral nerve 6 damage, they may have altered central pain 7 processing. That's sort of a description, not an 8 actual mechanism. Then to get to a specific 9 mechanism, you might propose that there's some 10 dysregulation of TRP channels or something else 11 that is driving the pain. And as you can see, we 12 start struggling when we get far over to the right 13 of what the actual mechanisms are because, again, 14 we don't have the evidence yet. 15 Another point of discussion is how do we 16 categorize these conditions? Should we categorize 17 them based on location in the body so that all 18 lower extremity conditions go together? And those 19 get to be separate from upper extremity conditions. 20 And well, maybe that sounds interesting, except 21 that that would mean diabetic peripheral neuropathy 22 of the lower extremity and diabetic peripheral</p>
<p style="text-align: right;">Page 42</p> <p>1 we all know, at least in the chronic pain space, 2 has limited relationship with the actual pain that 3 people report. And then, pain diagnoses typically 4 provide limited information regarding the 5 mechanisms underlying the pain experience. 6 Ideally, we were going to try to address as 7 many of these shortcomings as we could, given the 8 evidence that's available to us at the present 9 time. And as has been mentioned, a major point of 10 discussion, and probably what we spent more time 11 and more angst over than anything, is should AAPT 12 be evolutionary or revolutionary? This boiled down 13 to can we make a completely mechanism-based 14 classification system? 15 I think even people who would have loved a 16 mechanism-based classification system recognize 17 that the answer to that question is no. We don't 18 know enough about mechanisms, yet. And if you 19 think about mechanisms, there are different kind of 20 constructs that are important here. 21 So there's etiology, right? That's not 22 mechanisms. So if you think about diabetic</p>	<p style="text-align: right;">Page 44</p> <p>1 neuropathy of the upper extremity are completely 2 different categories even though they share the 3 same process. 4 So what we decided on was sort of a hybrid 5 approach of system, essentially organ system, 6 bodily system, with some consideration of location, 7 anatomical location. So we have peripheral and 8 central neuropathic pain, which are disorders of 9 the peripheral and central nervous system. We have 10 a variety of musculoskeletal conditions here. 11 According to site, we have things that 12 happen above the neck. And you'll note that the 13 AAPT system has stayed away from developing 14 classification for headache because that's already 15 been done quite extensively by the international 16 headache group, but we are addressing TMD and other 17 orofacial pains, and we have visceral pelvic and 18 urogenital pain; and then disease associated pains 19 that don't get covered anywhere else. And our two 20 groups here are cancer pain and pain associated 21 with sickle cell disease. 22 So that's the compromise we settled on, and</p>

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1 I think it works fairly well. You might quibble
2 with it, but after a lot of discussion, this is
3 where we ended up.
4 As you know, we published a Focus article.
5 I should give you a disclaimer here. I'm not the
6 first author because I have any expertise or
7 particular knowledge here. I'm the first author
8 because Bob and Dennis cornered me, and I panicked
9 and said yes.
10 (Laughter.)
11 But it's actually a great process to go
12 through, and it was very interesting and enjoyable
13 actually to write the article.
14 Some of the important characteristics that I
15 think AAPT exhibits and strives for, number one, we
16 want the criteria that get developed -- they're not
17 out yet but working groups are working on
18 them -- we want them to be evidence-based.
19 We wanted a framework that could be
20 systematically applied across pain conditions so
21 that all chronic pain conditions classified under
22 the AAPT framework follow the same system, which is

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1 new to the pain world.
2 We wanted them to be multidimensional and
3 biopsychosocial. We want these criteria to be
4 applicable for both research and clinical use,
5 recognizing that the uptake initially may be
6 greater for research use, but we certainly want
7 them to be incorporated into clinical
8 applicability. And very importantly, we want these
9 criteria to be living. We want them to update and
10 evolve based on new evidence.
11 As you've already seen, and as is in the
12 article, these are the dimensions we developed,
13 certainly, the core diagnostic criteria, you really
14 have to specify these, then we can talk about
15 common features. These are characteristics of the
16 condition that are frequent, if not typical, but
17 aren't required to meet criteria for that
18 condition.
19 There are common medical comorbidities that
20 we thought it would be helpful to specify. And
21 then these two, I can tell you reviewer feedback
22 and a lot of discussion at the meeting focused on

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1 these two categories. With a patient sitting in
2 the office today, how do we know that the
3 neurobiological and psychosocial and functional
4 characteristics that they display today, how do we
5 know whether those are consequences or causes of
6 their pain? And the frank answer is we don't,
7 right.
8 But we thought it was important to
9 acknowledge that both occur. And there is good
10 evidence in the literature that depression, for
11 example, has been found to be both a risk factor
12 that increases likelihood of development of future
13 chronic pain, as well as a consequence of chronic
14 pain.
15 We thought it was particularly important to
16 acknowledge that there are a variety of
17 neurobiological and psychosocial mechanisms that
18 are indeed risk factors, that are causal in the
19 development of these pain conditions, and in fact
20 there are protective factors that prevent people
21 from developing these conditions.
22 We wanted this specifically to be

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1 incorporated because that's an incredibly important
2 aspect of the evolution of the system. As we learn
3 more about mechanisms driving chronic pain, this
4 gives us a place to specify those mechanisms.
5 So this is the framework that we came up
6 with from which the working groups are developing
7 their criteria.
8 Now, these are the nine working groups
9 numbered here. So we have one group working on
10 peripheral and one group working in central
11 neuropathic pain. Then we have three groups
12 working on conditions of the musculoskeletal
13 system. We have a group working on
14 temporomandibular disorders, a group working on
15 visceral pelvic and urogenital pain, and then two
16 groups working on disease associated pain.
17 So that's what's going on right now, and we
18 have seen some draft criteria come through, so the
19 working groups are indeed making progress, albeit
20 at different rates.
21 It's also important to point out that right
22 now we're in the AAPT-1 phase. So AAPT-1 is

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1 diagnostic criteria based on available evidence,
2 and that comes from literature reviews, existing
3 criteria for those conditions, secondary data
4 analyses and expert consensus. So those are the
5 first criteria that will be published.
6 Then we fully plan for there to be an
7 AAPT-2, where after these working groups publish
8 their diagnostic criteria, they do studies of the
9 reliability and validity of those criteria and
10 refine those criteria based on new research that is
11 conducted.
12 At one point in time, we had imagined this
13 would all occur before publication of any of the
14 criteria, and we realized we might all be retired
15 before that would happen. And indeed, we could
16 imagine that after the AAPT-1 criteria come out,
17 independent groups might decide to do research on
18 these criteria and help inform the evolution of the
19 system.
20 In terms of future activities, we hope that
21 in the next year the diagnostic criteria from all
22 of the working groups will be submitted and

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1 published in peer-reviewed journal articles. And
2 then we intend next year to have a launch meeting
3 to talk about the research activities that need to
4 be conducted to get to AAPT-2.
5 Then, we'd also like -- while these will be
6 published at different times in different articles,
7 we would like to bring them together into one
8 volume so that if somebody wants to have this on
9 their shelf, or on their computer if it's
10 electronic, they can have a combined volume of all
11 the criteria.
12 So I think the task today is to think about
13 what can we take from the chronic pain taxonomy and
14 apply that to an acute pain taxonomy, and I think
15 we'd do well to strive for all of these
16 characteristics. I doubt we will get much argument
17 from this group about the importance of these.
18 But I think it's a very open question how
19 these different components of the framework for
20 chronic pain translate into a framework for acute
21 pain. That's going to be the result of our
22 discussions here that will be informed by a number

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1 of excellent presentations, and I know Dan will be
2 talking about distinctions among the various stages
3 of pain. But to a large degree, this is our task
4 here. And that's all I have.
5 (Applause.)
6 Questions and Comments
7 DR. FILLINGIM: Yes, thank you.
8 DR. TURK: We have a few minutes for
9 questions and comments. And just one other thing I
10 wanted to note is, if you look at that list of the
11 nine working groups, that is not an exhaustive list
12 of every possible chronic pain diagnosis.
13 What we wanted to do was pick exemplars, and
14 hopefully that the template or the framework that
15 Roger described would be used for all kinds of
16 other conditions that other groups could look at.
17 But there was no way we assumed that we could
18 handle every one of the possible diagnoses for
19 chronic pain, but those were exemplars picked
20 because either they were highly prevalent or
21 particularly interesting cases for demonstration.
22 The last thing I'll say before the other

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1 questions is that the supplement that you've heard
2 about will be published in the Journal of Pain.
3 And it will be open access, so it will be available
4 for anyone who wants to get access to it. We're
5 also thinking about -- is this definite,
6 Bob -- mailing out copies of it to IASP and APS
7 members.
8 DR. DWORKIN: No, we've requested that the
9 publisher figure out how to send copies on a free
10 basis to all the members of IASP in addition to all
11 the members of APS, and that should happen. We
12 can't think of any reason why they can't figure out
13 how to do that.
14 DR. TURK: Questions for Roger?
15 DR. RAJA: So in the broad categories that
16 you had, for example, I can think of cancer pain
17 having some neuropathic issues, some
18 musculoskeletal. I mean, there are multiple
19 categories that may be involved in a certain
20 diagnosis. How do you resolve that issue?
21 DR. FILLINGIM: Yes, and we did have
22 considerable discussion about that, and that's why

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1 that kind of category is disease associated pains
2 not classified elsewhere. So if it's a clearly
3 neuropathic pain, we expect it very well will be
4 covered within one of the neuropathic pain working
5 groups.
6 If it's a disease associated pain that's not
7 covered anywhere else, that's where we expect those
8 disease associated pains will be classified in that
9 group. And, you know, there may be some overlap.
10 There may be the cancer pain working group
11 describes neuropathic cancer pain and refers back
12 to peripheral neuropathic pain criteria or
13 something like that.
14 Yes, Bob?
15 DR. DWORKIN: So, Raj, actually what's
16 evolved in a couple of situations for exactly the
17 reason you're intimating, is a bit of a kind of
18 negotiation between different working groups. So
19 in fact, it's ended up that chemotherapy induced
20 peripheral neuropathy, the criteria for that are
21 being included within the cancer pain working group
22 because the cancer pain specialists really wanted

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1 to do CIPN.
2 But of course, the other polyneuropathies
3 are being done by the peripheral neuropathic pain
4 working group, and so we've had to make sure that
5 there's coordination between what's being done by
6 the cancer working group for CIPN and what's being
7 done by the peripheral neuropathic pain group for
8 diabetic, HIV, idiopathic, small fiber sensory
9 neuropathy, et cetera, criteria, and I think we've
10 successfully done that.
11 The other example of this is lumbosacral and
12 in cervical radiculopathy, which could either be
13 obviously in the peripheral neuropathic pain group
14 or the spine pain group. And it's those
15 neuropathic low back pain and upper back pain
16 conditions are going to be done by spine pain, and
17 they could just have easily have been done by the
18 neuropathic pain working group.
19 So there are examples where there had to be
20 negotiation about which working group does what.
21 And we just have to make sure, as Roger said, that
22 we can cross reference that. It's kind of

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1 unavoidable in a way.
2 DR. RAJA: Yes, I'm just looking at an
3 example of a patient I saw two days ago. The
4 patient admitted with a history of sickle cell
5 disease, quote/unquote "in acute crisis with
6 basically bone pains." So do you call that patient
7 as musculoskeletal pain or do you call that as
8 other sickle cell pain?
9 MALE SPEAKER: Yes. Just in response to
10 that, just mention that what you're going to
11 discover very quickly is conditions are what they
12 say they are. So the way we end up defining sickle
13 cell pain would either include or exclude those
14 people by the way that it's been worded in there.
15 DR. FILLINGIM: Chad?
16 DR. BRUMMETT: I want to get a sense of what
17 wasn't on the page without turning it into a gossip
18 column. If you look at something like fibro being
19 categorized as musculoskeletal and you call
20 post-stroke pain central, you've got vulvodynia as
21 now genitourinary, right. So we're
22 compartmentalizing again.

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1 I know what you think. Like we've talked,
2 and you've got a nice slide showing all these
3 overlap. Is this the right direction? I mean, are
4 we servicing the pain community by continuing to
5 call FM a musculoskeletal condition given that we
6 know so much about what drives pain in
7 fibromyalgia, vulvodynia?
8 We've got a lot of data out there. It seems
9 surprising in 2016 that we're going to put
10 something out there like this that seems like a
11 step backwards. I'm curious how those
12 conversations evolve because you do describe it in
13 terms of how you made those decisions. But without
14 making this gossipy, help me understand how you get
15 to that point.
16 DR. FILLINGIM: So I guess one reality is
17 that a patient with vulvodynia has different
18 symptoms and a different presentation than a
19 patient with fibromyalgia. They can tell each
20 other apart, and we can tell them apart. So
21 they're not identical conditions. They may share
22 pathophysiological mechanisms, although I still

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1 don't think we know enough about those mechanisms.
2 We can say the central nervous system is
3 involved. Well okay, the central nervous system is
4 a big thing. How does that help me guide
5 treatment? I can't do a brain transplant. What
6 components of the central nervous system are
7 involved? And why do some people only have
8 symptoms or primarily have symptoms in their
9 bladder or genital organs, and other people seem to
10 have symptoms that they believe and that sound like
11 are musculoskeletal in nature?
12 At some point, we may figure that out. And
13 that's sort of why we sort of stuck with an
14 evolutionary rather than revolutionary approach.
15 So what you're asking about is why didn't we
16 go revolutionary. And one issue is I don't think
17 we know enough about specific mechanisms yet, and
18 another issue is that I don't think the research
19 and clinical world is ready for that yet.
20 But one thing we did talk about is, as
21 working groups specify putative neurobiological and
22 psychosocial mechanisms, it would be ideal, for

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1 example in an electronic system, if we could type
2 in, give me all the conditions that involve altered
3 central processing of pain, or disturbances of
4 noradrenergic functioning, and it might come up
5 with different ones. And it sort of starts
6 educating us and pointing us towards shared
7 mechanisms that might underlie these different
8 conditions.
9 But what you're asking is the very tension
10 that we dealt with. I think we erred on the side
11 of practicality and interpretation of the state of
12 the evidence at this point in time. And, you know,
13 I think there are still plenty of people who would
14 respectfully disagree with that decision.
15 DR. BRUMMETT: Thank you.
16 DR. FILLINGIM: Sam?
17 DR. MCLEAN: Roger, one thing that's
18 interesting to me is -- I think it's phenomenal
19 that you've done this amazing work. The dimensions
20 make sense. It all makes sense, but the dimensions
21 of core diagnostic criteria, common features,
22 comorbidities, et cetera, it's interesting

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1 that -- and I say this because it potentially has
2 relevance for acute pain, is that in terms of this
3 taxonomy of chronic pain, it seems like we need to
4 have diagnostic criteria for these pain disorders
5 using these dimensions.
6 We need to come up with something structured
7 for all the reasons that Roger so eloquently said
8 in his -- that you've said. But why do we need to
9 subdivide them as peripheral nervous system,
10 central nervous system, musculoskeletal?
11 I get Chad's concern about, oh, is this
12 going to mean that people in the peripheral camp
13 are going to see this as a vouching of fibromyalgia
14 as a peripheral disorder rather than a central
15 disorder, where it seems like it's an
16 argument -- you could argue that you don't even
17 need to make -- you don't need to -- what if you
18 just said, this is our diagnostic criteria for
19 fibromyalgia?
20 We're not categorizing it as musculoskeletal
21 versus under central. This is like we are
22 developing these categories. You seem to get all

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1 the benefits of the categorization without having
2 to worry about someone saying, well, wait a minute,
3 you put it under musculoskeletal. I see it as
4 central because, you know, it's obvious these
5 things are mixed.
6 So for the acute pain, we could think about
7 at least doing these domains and coming up with
8 criteria, but not saying, and we're going to fit
9 this acute sickle pain under musculoskeletal or
10 under -- because it's an argument that it doesn't
11 matter, it's not relevant for our purposes, and
12 it's just going to create contention or be
13 misunderstood.
14 DR. FILLINGIM: No, I think that's a fair
15 point. Again, I think part of it was practical,
16 how do we develop working groups and what are the
17 working groups going to be? Is there going to be a
18 central pain working group? Oh boy, well what
19 belongs in central pain and what doesn't? And as
20 far as I can tell, the central nervous system is
21 involved in every pain condition. So that makes it
22 difficult.

<p style="text-align: right;">Page 61</p> <p>1 So at some level, we deferred to existing 2 structures and also the putative locations of the 3 pain complaint. 4 DR. MCLEAN: I can see how that would have 5 arisen out of the functional desire to have some 6 overarching group above the individual diagnostic 7 groups, and so kind of coming out of that. And 8 again, just with that tension of there could be a 9 functionality of doing that, but maybe the ultimate 10 diagnostic criteria we don't want to put under 11 those sorts of sub-categories, again, simply for 12 the reasons that show a need to and -- 13 DR. FILLINGIM: Yes. Bob? 14 DR. DWORKIN: There's another very simple 15 minded answer to this question, and I acknowledge 16 that it's very simpleminded, which is we adhere to 17 the IASP definition of neuropathic pain, which is 18 that it's cause by, as you know, all know, lesion 19 or disease in the somatosensory nervous system. 20 And that's how we defined the conditions in the 21 peripheral neuropathic pain bucket and the central 22 neuropathic pain bucket. They're all completely</p>	<p style="text-align: right;">Page 63</p> <p>1 high risk/low risk -- it seems like maybe out of 2 your five key dimensions that 4 and 5 were meant to 3 get at that. But I wonder if we can somehow make 4 that of more prominence, be more in the -- work it 5 into the structure of actually categorizing them 6 because I think it may be really important to 7 treatment and how to practically use this. 8 DR. FILLINGIM: Yes, and that was the 9 thinking there, that a person who meets the core 10 diagnostic criteria for a given pain condition, two 11 different people, both of whom meet those criteria, 12 might have vastly different psychosocial and 13 neurobiological mechanisms driving their pain, as 14 well as consequences to their pain, which can 15 greatly impact decisions about pain treatment. 16 So I think as we move toward this acute pain 17 taxonomy, it's important to think about how best to 18 allow individualization and personalization of 19 diagnosis and description of pain conditions while 20 creating criteria that can be broadly applied. 21 That's another tension that's important to deal 22 with in this process.</p>
<p style="text-align: right;">Page 62</p> <p>1 consistent with possibly one exception, with the 2 IASP definition. 3 DR. MCLEAN: But a disease might obviously 4 involve multiple mechanisms and be much dirty, so 5 that we say, well, wait a minute -- someone says 6 that's musculoskeletal, and it's bone pain, and 7 it's tissue ischemia induced. 8 DR. DWORKIN: I think at the time our 9 feeling was that fibromyalgia was explicitly 10 excluded by the IASP definition of neuropathic pain 11 from being a neuropathic pain condition. So in a 12 very simple way, that made the decision easy for 13 us. 14 DR. FILLINGIM: Yes, Kris? 15 DR. SCHREIBER: So I also think this is a 16 great step forward, and it seems like a good 17 framework for us. I was just wondering, in terms 18 of getting towards precision medicine and taking 19 into account individual differences between 20 patients that may be really, really important in 21 how we go about treating them -- like I'm thinking 22 about someone going into surgery, like they may be</p>	<p style="text-align: right;">Page 64</p> <p>1 Yes, Brett? 2 DR. STACEY: One of the things that I am 3 always intrigued by is the focus on the underlying 4 pathophysiology, like for instance with the 5 neuropathic pain definition, because a lesion to 6 the sensory part of the nervous system is not 7 sufficient to cause pain. Most people with 8 diabetic peripheral neuropathy, the majority of 9 them don't have pain. 10 So we get very excited about the things we 11 can test with our available diagnostic criteria, 12 yet, if we're a clinician seeing someone with a 13 pain problem in front of us, the imaging, the lab 14 results, do not distinguish those with pain versus 15 those without. 16 So I'm very nervous about this 17 pathophysiology stuff thinking that that's part of 18 the diagnostic criteria because I think it's an 19 abstraction. We know a lot about people's 20 structures. You know spinal imaging doesn't really 21 help us much with telling us why this person has 22 pain and why we label this patient as having facet</p>

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1 arthropathy, or foraminal stenosis, or whatever it
2 is. But we can see things, but then we make this
3 association, and that association is a big leap of
4 faith.
5 DR. FILLINGIM: Yes, I don't disagree.
6 Yes, Steve?
7 STEVE: Aren't we potentially looking at
8 clumps of forest and trying to come up with labels
9 for the clumps of forest when, when it comes to
10 acute pain, what we really need to define are the
11 trees in that clump of forest?
12 So if you have someone who has a burn
13 injury, and that is their primary acute pain
14 diagnosis that should allow you to develop
15 treatment plans and to prognosticate, but they may
16 also have really, really significant biologically
17 based anxiety that completely messes up how they
18 personally deal with their pain, it seems to me
19 that that's a different diagnosis.
20 Our job isn't to treat and prognosticate
21 about that anxiety diagnosis. Our job in this
22 meeting is to come up with the taxonomy to actually

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1 define those other categories. And that's a
2 different way of looking at it because, I mean, we
3 all understand the comorbidities and how they
4 interact and nothing is simple, but if you really
5 are looking at defining a taxonomy, it has to be
6 simple. It can't be complex.
7 I've been struggling for months dealing with
8 the cockamamie structure you guys came up with --
9 (Laughter.)
10 STEVE: -- because it's really hard for me
11 to take that and do anything clinical with it.
12 DR. FILLINGIM: In fact, we thought about
13 calling it the cockamamie AAPT.
14 (Laughter.)
15 DR. FILLINGIM: But there was some -- no,
16 but I think this is a good point, Steve, because
17 what we're talking about is -- the core diagnostic
18 criteria for burn pain can be defined, I
19 assume -- I don't know anything about burn pain but
20 you guys do -- but then, on these other dimensions,
21 which are not required for that diagnosis, some
22 patients may have strong psychosocial drivers of

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1 their pain phenotype and other patients may not.
2 And that's why there's this sort of
3 multidimensional approach to the framework.
4 So you all can decide how this applies to
5 acute pain and which parts of a multidimensional
6 framework are important. But you're right, there
7 has to be something that's a core criteria for the
8 pain condition itself because the anxiety is not
9 the pain. It's something that accompanies the pain
10 either as a driver, or a consequence, or both in
11 some patients.
12 DR. SCHUMACHER: Mark Schumacher, UCSF. To
13 expand on the difficulty rather than clarifying,
14 what is the target audience for the products? So
15 I'm facing two issues, as many are here. One is
16 UCSF, as well as other institutions, are centers of
17 excellence in pain education, and there's a
18 national effort. So we're looking at ways to
19 simplify approaches of learning at the
20 undergraduate across all professional schools.
21 Then in addition, as you know, many of us
22 are launching efforts to develop ACGME sponsored

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1 regional and acute pain fellowships. And these are
2 the two targets that we are wrestling with, and I
3 would hope that the products that would come from
4 this -- I know I'm a newbie here -- but the product
5 would at least gesture to those audiences. I think
6 it's going to be very important in the long run.
7 Thank you.
8 DR. FILLINGIM: Patrick and then Henrik.
9 DR. TIGHE: Roger, my understanding of this
10 approach is that we have several dimensions, and
11 then there are the exemplar pain objects that are
12 described by the dimensions to create the
13 diagnostic pattern. So that ends up being, at
14 least from my understanding, a relatively flat
15 structure.
16 Is there any intention to add some vertical
17 depth of clustering this, similar to the DSM
18 structure where you have a hierarchal
19 representation of types, and subtypes, and
20 sub-subtypes organized under some type of
21 structure, or was this intended to be flat with
22 specific diagnoses running in parallel to the

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1 attributes at hand, specified by the dimensions?
2 DR. FILLINGIM: I can't answer that because
3 I'm not sure I understand the question. So what
4 would be -- give me an example of the DSM vertical
5 piece you're talking about.
6 DR. TIGHE: So we might start with mood
7 disorders, and then we'd separate under anxiety
8 versus depression, and then within depression, you
9 would have certain subtypes. Is there a plan to
10 move along something for the chronic pain, or is it
11 meant to be separate free to those nine exemplars?
12 DR. FILLINGIM: I'm not sure we talked about
13 things at that level, and maybe that's this
14 categorization that some people have already mildly
15 objected to, which is there's musculoskeletal pain,
16 and within that there's different types of
17 musculoskeletal pain or neuropathic pain or
18 whatever.
19 I don't know that that's sort of an exact
20 parallel, but that's probably the closest that we
21 come at this point. But, you know, if we get smart
22 enough, that might change, and there might be a

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1 different vertical structure. And maybe we'll
2 satisfy Chad, and there will be centralized pain or
3 something like that, and there will be different
4 conditions that come under that.
5 Bob or Dennis?
6 DR. DWORKIN: I don't know if this is what
7 you're thinking of, Patrick. We sort of have a
8 hierarchy. I don't know that we've thought about
9 it explicitly, but it's not an exciting one. It
10 would be something like neuropathic pain,
11 peripheral neuropathic pain, polyneuropathies,
12 diabetic, idiopathic, CPIN, HIV.
13 So that's a kind of hierarchy. I don't know
14 that we've emphasized it, but it exists. It
15 certainly exists in the way that we're structuring
16 it.
17 MALE SPEAKER: [Inaudible - off mic].
18 Actually, it just doesn't seem like -- it seems
19 like the fundamental goal here is that when someone
20 says low back pain, that we're using the same
21 criteria, which is such a huge thing because
22 there's nothing [inaudible - off mic]. That is a

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1 massive benefit. To try to characterize these
2 things in ways, which, really, they're very
3 dirty -- let's take PTSD under anxiety disorders.
4 PTSD has overwhelming comorbid depression
5 with it. Depressive symptoms are a huge part of
6 PTSD. We don't need to go into these vertical
7 silos that are inherently going to be wrong and
8 they're going to be -- when you talk about
9 bone -- okay let's say sickle cell, you would mark
10 that area with the peripheral nerve in it. You've
11 got a neuropathic component. Someone seeing these
12 patients.
13 What utility is there for making vertical
14 structure that's going to inherently be wrong or
15 incorrect when we're simply trying to come up with
16 diagnostic criteria that can be used uniformly
17 around the world?
18 DR. FILLINGIM: Steve, I think you had a
19 comment on this.
20 STEVE: Yes. Those are great questions. I
21 think one thing that -- and this is going to be
22 several years before we can ever do this. But I

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1 think were we to put together a AAAPT taxonomy
2 successfully, based on whatever we come up with
3 here today, keep in mind we can always go after the
4 fact, assuming we're collecting data, and answer
5 those questions about taxonomy empirically, because
6 in all likelihood, we are wrong about how we would
7 lump things together and the assumptions we would
8 make.
9 But I think one thing we've learned that is
10 really important from the initial AAPT for chronic
11 pain is that we have to start somewhere. And we
12 may come up -- well I'm not going to say may. We
13 will come up with something that is imperfect. And
14 if we have a starting point -- and you'll see in my
15 talk tomorrow why it's beneficial to have some
16 starting point. That gives us something to work
17 with to try to improve that and opens up the
18 possibility of empirically looking at other things.
19 I just wanted to make a comment that we had
20 a couple of questions about the multiple
21 dimensions. The Dimension 1 is the core diagnostic
22 criteria. It would be useful in education settings

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1 because it is really like a cookbook.
2 It's like if you want to know what this
3 condition looks like, read Dimension 1, and this
4 will tell the core features, to somebody who
5 doesn't know that condition, what it would look
6 like in clinical practice and how you would go
7 about assessing.
8 The Dimensions 2 through 5 are messier, and
9 I get the feeling that some people are a little bit
10 uncomfortable with that. In the original AAPT, it
11 was recognized that not every condition has the
12 same comorbidities, not every condition has the
13 same factors that are impacting on it or
14 consequences of it.
15 So it had to be kind of different for
16 everybody, and we didn't -- and I'm kind of
17 realizing as we're talking about this, we never
18 really got down to saying how you would
19 systematically assess all 5 dimensions for a given
20 patient. So it's kind of left up to you to decide
21 how to assess 2 through 5.
22 I don't know if it's doable to do more than

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1 that or not, but I think that's something that
2 could be discussed today, or would you want to
3 include, for example, anxiety assessment officially
4 in every disorder on a particular axis.
5 DR. FILLINGIM: Dennis?
6 DR. TURK: Although we didn't discuss the
7 assessment of those in Roger's paper, in the
8 supplement, at least the chapter that I did and the
9 one that Rob Edwards did, are focused in on how do
10 you go about assessing these things.
11 So if you believe that emotional factors are
12 relevant across conditions, what are the ways that
13 you could go about assessing that in an efficient
14 way? So we did try to go into that without
15 recommending specific measures but just giving,
16 laying out, here are the ones that have been most
17 commonly used.
18 You know, a tension that I've heard, and I
19 think Steve is picking up on this, and one that I
20 think John Loeser -- this goes way back to when we
21 first talked about this, is although those of us
22 who did that manuscript all believe that all five

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1 of those dimensions are important to consider, that
2 many people will look at 1 and stop.
3 This is what's happened in the old DSM-4 is
4 that people rarely use these subparts. It's what
5 happened in the old IASP classification, people
6 stuck with the first one. And unfortunately, if
7 you're going to put a priority, if you're going to
8 list these in any way, if you have to list the core
9 at first, everything else then becomes secondary.
10 That was a tension we had at the meeting and
11 I'm picking up from the comments here, is how do
12 you balance the fact that for every individual is
13 an individual. And regardless of what the nature
14 of the pathology may be, all of these other factors
15 have influence, and how are you going to see them.
16 So the question will there ever be
17 subgroups, empirically we may identify that within
18 one classification there are subtypes of people.
19 Not everybody with painful diabetic neuropathy also
20 has this set of other characteristics. So we may
21 get there, but we're not there by any means.
22 Roger put up AAPT-1 and AAPT-2. Well, we

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1 have 3, 4, 5. As the data comes along, what we had
2 hoped was the structure would be useful to help us
3 advance, and it will be modified as we go. But at
4 least people attend to those important dimensions
5 as they're thinking about their patients as a
6 group, and then the individual patient by patient.
7 When you get to that level, then you're
8 going to have to make some decisions as a
9 clinician, which may or may not exactly follow
10 everything that's in the classification. But at
11 least we would like you to think about more than
12 just Dimension 1.
13 DR. FILLINGIM: Steve?
14 STEVE: [Indiscernible – audio distorted].
15 MALE SPEAKER: Speak louder.
16 STEVE: Okay. My colleagues -- or if a
17 doctor's doing musculoskeletal medicine this
18 afternoon, are going to do probably seven or eight
19 ultrasounds for tendinopathy on patients, if they
20 even think about looking at catastrophizing and
21 some other things, even though these patients are
22 sent for acute pain, if the dimensions work the

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1 right way, just for them to screen for some of
2 these things is going to be a benefit.
3 So if we look at our acute pain guys or
4 sports medicine guys, they rarely look at that
5 until 3 months or 6 months, or until they refer
6 them to a pain doctor.
7 So within the dimensions -- hopefully, this
8 is actually going to be helpful. I think we're
9 maybe jumping way ahead. But some of these basic
10 ideas, even though it's very common to us to think
11 about psychosocial variables and all that on the
12 chronic pain side, the acute pain clinicians rarely
13 think about it.
14 So those dimensions could actually work even
15 if they're starting to use a screening tool. So
16 maybe that would be in the 4th and 5th dimension to
17 look at those things.
18 I'm just kind of throwing that out there. I
19 think we always think of pain clinicians versus the
20 guys doing acute pain, where it is based on
21 mechanisms. But we could give them more options to
22 kind of work in a hierarchal way. That's all.

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1 DR. FILLINGIM: And I could see that being a
2 huge benefit if this kind of invigorates acute pain
3 care and diagnosis with the biopsychosocial model
4 much more than it's invigorated now.
5 Dan?
6 DR. CARR: So I'd like to, for the sake of
7 advancing the conversation, try to make explicit
8 what I think is implicit in many of the comments,
9 mainly that while the classification is fine, it
10 comes from a tradition of looking at mechanisms in
11 a sense that are cellular, or the more micro scale
12 the more secure one feels about a mechanism or its
13 value, and progressively assigning less and less
14 value to the more macro scale things, such as these
15 social interactions or the presence of risk
16 factors, but we know that those are very, very
17 important.
18 Actually, I was delighted to see, in the
19 slides that Knox will show, a reference to Roselyne
20 Rey, who wrote on the history of pain, to say that
21 with the successes of the scientific method,
22 medicine's concept of illness shifted from

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1 something that befell an individual with that
2 individual's complex life and social interactions,
3 to something was a physiological process that was
4 just hosted by the host who happened to be the host
5 of the process.
6 So where I'm going with this is to wonder if
7 there might not be another access or another
8 dimension, certainly for chronic pain, but I think
9 also for acute pain, that captures the social
10 interactions or meaning of the pain or of the
11 illness.
12 We're often inclined to focus on these micro
13 scale mechanisms, and I'll get into that in my own
14 talk, yet we go out and practice in the real world,
15 and all these distracting irrelevant things, like
16 the meaning of the illness, the economics, the
17 patient's family, these are kind of brushed aside
18 because we think we're focusing on the real
19 mechanism.
20 Not that this classification is wrong, but
21 it's the things that we're trained to brush aside
22 which may be major determinants of outcomes in the

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1 acute pain setting as well as the chronic pain
2 setting.
3 So I guess I'm calling for another axis or
4 something to be added that renders explicit the
5 implicit feeling of clinicians that when you get
6 down to an individual level, there are a lot of
7 these factors that we're trained to brush aside
8 that actually are really, really important.
9 DR. TURK: That's in Dimension 4. We'll
10 look carefully at Dimension 4, and when you see the
11 supplement paper, many of the things you just
12 mentioned get embedded in there.
13 So it's this tension that we keep talking
14 about, which is what's priority and important makes
15 the secondary uninteresting. We were trying -- and
16 we never resolved it well, how to make sure that
17 it's not one's more important than the other, that
18 all of these should be considered as you're
19 evaluating your patient.
20 However, if you don't start with the
21 presenting symptoms and signs, you're going to not
22 be able to even start with somebody. But that

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1 doesn't mean you don't do all these other things.
2 It only means that these then are relevant.
3 I keep using the word we'd like you to
4 consider, so I don't care if you're in acute care,
5 I don't care if you're primary care, or chronic
6 care, these factors should be things in your mind
7 when you see that patient; not they're secondary,
8 they're uninteresting, they are small, once I know
9 the pathology I'm done, because every one of the
10 clinicians in here knows that knowing the
11 pathology, you're not done with that patient. You
12 can have very different responses from people.
13 Henrik has had his hand up for a while, and
14 we're going to get to him.
15 DR. KEHLET: It was the same question.
16 DR. FILLINGIM: Bernie?
17 DR. SCHACHTEL: No, I agree. I mean, we're
18 really talking about a patient-centered approach
19 towards acute diagnosis, treatment, and prognosis.
20 And I think that all this can be simplified in some
21 ways by taking the first grouping, the signs and
22 symptoms that you were just talking about, Dennis,

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1 to the question that I think Steven was asking
2 before about how do we treat the patient.
3 Well, in many cases, that patient comes to
4 you with, let's call it post-operative pain, but
5 the catastrophizing, the magnification from the
6 past, may seriously implement -- rather, affect his
7 or her perception of pain and how he or she
8 responds when you even ask for a grading of pain.
9 DR. TURK: We tried to capture that, and
10 probably it slipped by in the phrase
11 biopsychosocial, that is all of these should
12 consider all of those factors in the individual
13 patient and in the classification.
14 So that was our attempt, but I know John
15 Loeser and I, Bob, went round and round about the
16 dilemma of not letting it turn out that you only
17 pay attention to what historically has been just
18 the physical pathology.
19 But you've heard it enough times here. It's
20 still a problem by calling one core, and then these
21 other comorbidities, characteristics, potential
22 causes and consequences. It's not those are

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1 and combining it with a third axis, if I can use
2 your terminology, because what's important to the
3 patient may be really what matters.
4 I refer to the phrase, I think it was in
5 your third ranking there, third categorization for
6 chronic pain, you used the word "descriptors" of
7 pain. And often the patient will describe his or
8 her pain not in conventional, shall we say
9 evaluative terms, but more qualitative, and often
10 emotional or effective terms, where on the case of
11 acute pain, especially in sensory terms. And
12 that's what matters to the patient.
13 So I think perhaps we could consider a
14 more -- I don't know want to use, and perhaps I
15 shouldn't use the term "holistic." But originally
16 I had described this in earlier papers as patient
17 directed endpoints. And now the terminology, which
18 is more accepted, is patient centered endpoints.
19 Maybe what you're getting at, Dennis, if I
20 understand you correctly, is we really have to look
21 at all of those dimensions beyond the very first to
22 get to what really matters to the patient. It gets

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1 secondary, it's just that they need to be there.
2 But we ran into the dilemma -- Roger remembers this
3 well -- is how do you deal with what's going to be
4 where you start, and that's the dilemma we ran
5 into.
6 MALE SPEAKER: Roger, could I just respond
7 one second?
8 DR. FILLINGIM: Yes.
9 MALE SPEAKER: Perhaps it's the way we
10 present it, not as a list as opposed to a Venn
11 diagram, that there are interceptions of all of
12 these dimensions. And maybe that way, the reader,
13 the educator, the clinician will also see them as
14 interrelating as opposed to sequential or, as you
15 said, primary and secondary.
16 DR. FILLINGIM: Yes?
17 MALE SPEAKER: So I just wanted to second
18 what Mark Schumacher had said. One of the
19 important things is the ASGME's under consideration
20 for the acute pain fellowship. I think here's an
21 opportunity for this group to influence how
22 teaching is carried out across the United States.

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1 And not only that, but convert these individuals
2 from being just block jocks to actually creating an
3 acute pain paradigm that people can follow through.
4 So here's an opportunity, but just to follow
5 up, I think there is a real need to move this
6 agenda rather rapidly than to sit around because in
7 the event the ACGME does approve this, there is a
8 likelihood that this could even be up and about for
9 '17. So we have to keep that in mind.
10 DR. FILLINGIM: Okay, thanks. Yes, Paul?
11 DR. DESJARDINS: Roger and Bob, just a
12 question directed to both of you to bring in a
13 different dimension of the discussion. There are,
14 at least at last count, 200 companies developing
15 therapeutic agents, devices, techniques, who are
16 looking at various acute pain conditions.
17 They come to it with a very simplistic
18 question, where do I start? Do you have a model?
19 Can you show me one study where I could get a basis
20 for making a decision the concept works for this
21 group of categories? And this has been a
22 discussion that has gone on at least for 35 years

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1 in my discussions with FDA colleagues, and they're
2 common questions.
3 So with that as a preface to the question,
4 to what extent have the chronic pain positions,
5 this position paper on categorization, how much
6 does that influence the discussion about the
7 developing drugs or devices for chronic pain? Has
8 it crossed over to that? And does that provide a
9 model for sort of how we might have a better
10 roadmap going forward?
11 DR. CARR: So Paul, that's a great question,
12 and I have to disclose that from the outset, the
13 way I thought about the chronic pain effort is that
14 it's potentially inclusion and exclusion criteria
15 for clinical trials. And that if we succeeded at
16 our job and developed valid, reliable, clinically
17 useful criteria, that these will be what's used in
18 clinical trials.
19 It's up to this group to decide whether to
20 think about the acute pain diagnostic criteria the
21 same way, but I think most if not all of us in the
22 chronic pain effort started off thinking of these

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1 as inclusion/exclusion criteria. They would of
2 course be helpful in education, in the clinic,
3 et cetera.
4 DR. FILLINGIM: And if I could just add to
5 that. If I go back to Patrick's question about
6 sort of vertical structures, is there a group of
7 pain conditions for which compound X is helpful?
8 And what falls under that group? And what's the
9 prototypical or accessible model for that group of
10 conditions?
11 That would have been lovely to do with
12 chronic pain. I don't think we're actually there
13 yet. It might be more feasible for acute pain, but
14 that will unfold as the discussion.
15 MALE SPEAKER: I'd make a response to that
16 also. Just to add, when you brought that up, I
17 heard -- and not to put John on the spot, but you
18 said how much impact does it have. John says
19 "Absolutely none at all."
20 (Laughter.)
21 MALE SPEAKER: Now, here's the point I want
22 to make though, is that I'll talk tomorrow a little

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1 bit about our experience with complex regional pain
2 syndrome diagnostic criteria. And I can tell you
3 that once those were published, what happened was
4 about 10 years, they started being adopted
5 internationally, once they were published in Pain,
6 started being adopted internationally. And now if
7 you look on the clinical trials website, you see
8 everybody is using them, and it has become the norm
9 to use this.
10 So even though you are rightfully skeptical,
11 I think it is possible if people are dissatisfied
12 with what exists now, I think there is a very good
13 chance that these will be adopted if they're well
14 thought out.
15 DR. FILLINGIM: Sean?
16 DR. MACKEY: I want to add my compliments to
17 what you and the group did. And just thinking
18 ahead from an operational standpoint, ultimately,
19 you want to use this classification system not only
20 for pure research purposes, but ideally you'd like
21 to get it in the hands of clinicians to be able to
22 classify and characterize large numbers of

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1 patients.
2 As I'm thinking as a clinician and thinking
3 of the folks in the trenches, they're already
4 inundated with these other classification systems.
5 So the question is, was there consideration, and
6 should there be consideration here, towards tying
7 in more closely with an existing classification
8 system, like ICD-10 or SNOMED, that's been around
9 for decades; identifying the features of it that
10 are working, and then build on those features and
11 add in the things that we would want to have it
12 expressed in either chronic pain or acute pain.
13 But not ask the clinicians to learn yet another
14 classification system when they're already
15 struggling with ICD-10 as it is and there's these
16 other systems that are already in place.
17 DR. FILLINGIM: I can say by my recall, we
18 didn't really consider sort of ICD-9 or 10 and
19 trying to match with that. Whether that was an
20 error, I don't know. And maybe that's something
21 for the group to discuss here on whether that's
22 important for acute pain. But I think you hit on

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1 another tension, which is it's got to be clinically
2 useful and not such a burden over and about what
3 clinicians are already asked to do.
4 DR. MACKEY: Right now, clinicians are
5 terrible with diagnosis. We build into our EMR
6 data, and the quality of the data is just
7 absolutely terrible. We're hoping ICD-10 will
8 help, but we have to teach clinicians how to
9 diagnose and how to code it properly and integrate
10 it into their workflow, which they're not doing
11 now.
12 I love this classification system. No
13 concerns about it. Other than the operational
14 nature of it, we're trying to get this into the
15 real world to collect huge amounts of data.
16 DR. FILLINGIM: Yes, that's a good point.
17 Patrick, maybe this will be the last
18 question before the break. Are we on schedule for
19 a break now? Yes, Patrick?
20 DR. TIGHE: For the third dimension, has
21 there been discussion to create an exhaustive list
22 of terms to capture the range of possible values

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1 for that dimension? So is there a range of common
2 features that you can choose from to describe
3 something?
4 If that list were comprehensive but also
5 complete, meaning finite, you had to choose from
6 something there and you had stage upgrades, then
7 you'd have a structured way of rolling this up and
8 categorizing different types of pain. I didn't
9 know what the vision was for how you intended to
10 characterize each of those dimensions.
11 DR. FILLINGIM: Yes, I can say I don't -- at
12 least I haven't thought about a comprehensive list
13 like that. But the supplement that's coming out
14 takes a more conceptual approach and gives
15 examples, not a comprehensive list but examples of
16 ways to assess different dimensions of the
17 taxonomy, but not sort of comprehensive in the way
18 you're suggesting that might be useful in an EMR
19 type of sense and for text analytics and that kind
20 of thing.
21 Did you have a quick question, Deb?
22 MS. GORDON: Well, I'm sitting here as a new

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1 person to this, but also as a clinician thinking
2 that the diagnostic criteria for acute pain seems
3 to be less of an issue. When someone's in front of
4 you and they've had a big incision or they've had a
5 big burn -- so I'm thinking of it very differently
6 in terms of do we have to look at tissue type, the
7 visceral pain versus myofascial pain, or is
8 ischemia different from in cellulitis or infection?
9 It just seems like it's kind of a different set of
10 things we're going to be talking about.
11 DR. FILLINGIM: Yes. So what I hear you
12 saying is, you guys have it easy. We took on a
13 much more difficult task for the chronic pain
14 taxonomy, and we should all be congratulated.
15 (Laughter.)
16 (Applause.)
17 DR. FILLINGIM: So we'll take our break now
18 until what -- are we back at 10:00? Is that right?
19 10:15. Great.
20 (Whereupon, at 9:47 a.m., a recess was
21 taken.)
22 DR. TURK: Welcome back. Obviously there

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1 was lots of discussion going on, which means we're
2 succeeding. Roger did a terrific job. The
3 conversation or discussion that we were having
4 after Roger's presentation is exactly what we need
5 to get out there, realizing that Patrick and
6 Michael are going to take all this information, and
7 by the end of tomorrow we're going to have a
8 definitive draft manuscript for you to see.
9 So we're going to now have our next
10 presentation. The man who is already introduced,
11 Dan Carr, so you already know who he is. And he's
12 going to give us a little bit of a perspective on
13 acute, subacute, and some other concepts that are
14 particularly important.
15 Dan obviously is the president of the
16 American Academy of Pain Medicine, and he is from
17 Tufts University, and other places.
18 DR. CARR: And long-term member of IMMPACT.
19 DR. TURK: That, too.
20 Presentation – Dan Carr
21 DR. CARR: So once again, I thank everyone
22 here. It's a phenomenal group. And what I was

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1 going to be talking about, the title is Key
2 Distinctions Among Acute, Subacute and Chronic
3 Pain. I'll emphasize them, but I'm going to cover
4 some more ground, so I thought I'd start out with
5 this slide.
6 I heard about this quote from my friends at
7 Cochrane in Oxford, and they do this all the time.
8 If you have a systematic review or a clinical
9 trial, just because you can discern a difference,
10 is that really important?
11 I think this would be a nice thought to keep
12 in mind for the conference going forward, that if
13 we come out with some theoretical idea or
14 hypothesis that's very intellectually attractive,
15 but no one uses it, it's not helpful, it doesn't
16 add value, then we probably have failed.
17 So if we are trying to make a difference,
18 then that will determine whether this has been
19 worthwhile. It's not enough for there just to be a
20 difference, it has to make a difference.
21 So we're fortunate to have in the room
22 people, certainly I'm thinking of John, who were

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1 there at the outset of this definition of pain.
2 It's always struck me. If you look at the
3 definition, there are two things that have struck
4 me.
5 The first is how I came to realize that
6 every word was fought over. So certainly pain
7 would not be pain unless it were unpleasant, and
8 that gets to the anecdote about Howard Fields'
9 proposal for the term algosity. And we know there
10 had to be actual or at least potential damage, or
11 described in such terms.
12 In subsequent iterations, the insights were
13 added that language or verbalization were not
14 required. But I'm not 100 percent sure why this
15 particular collection of words was arrived at, but
16 one thing that's always struck me is that this
17 emphasizes the real time.
18 Now, you can argue that this is certainly
19 applicable to chronic pain or persistent pain, but
20 the wording itself I think did not initially
21 address the important role of plasticity and
22 chronification of pain. And I have some ideas

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1 about it.
2 I personally feel that it was building on
3 the wonderful successes of neurophysiologists, in
4 particular electrophysiologists, of the '30s, '40s,
5 and so on, who were able to map out pathways, study
6 properties of neurons by doing real time stimulus
7 and recording. But that's the definition.
8 So I'm going to give you what I would call
9 context or constructs to guide this notion of where
10 we need to go as differentiated from where AAPT has
11 been. I'll give you a personal take on this, but I
12 think it represents the thoughts of many people,
13 that if we're thinking about the context in which
14 we are constructing a taxonomy, and we're thinking
15 about chronic pain, issues of making the diagnosis
16 are very important. And you will hear from world
17 authorities later, Steve Bruehl is going to talk
18 about this, the criteria. It's already come up.
19 When clinicians think about chronic pain,
20 behavioral dimensions are embedded and integral to
21 this, things like suffering, trauma, anxiety. If
22 we see a patient with chronic pain, we presume that

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1 their pain is centralized, and hence, they have
2 hyperalgesia, other things. But we're also
3 frustrated because by the time, as a clinician, we
4 see a person with chronic pain, there's no
5 opportunity to prevent or even modify the inciting
6 event.
7 Also, the intensity of pain, as we all know,
8 is only one of several outcome domains that Bob and
9 Dennis have pioneered in constructing and helping
10 us think about. For the most part, I'd say the
11 patients we see with chronic pain are stable
12 medically. And as I just mentioned, I have had a
13 feeling that the chronicity is something that's
14 underweighted in what I would call a real-time
15 definition.
16 Finally, just as a practical matter, there's
17 an outpatient culture of care. So what we're
18 thinking about is in John's diagram, which is
19 nociception caused pain, which led to suffering,
20 and which frequently leads to pain behavior.
21 In contrast, and I've worked on acute pain
22 services as well, the diagnosis is usually less of

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1 intensity.
2 So for example, as we had our discussion
3 after Roger's talk this morning, as we're thinking
4 about things that may be important, this issue of
5 social, families, the connectedness, might in fact
6 turn out to be as strong a determinant of outcome
7 or long-term outcome as whether a person is a
8 placebo reactor.
9 So we've addressed placebo reaction, but
10 there are a number of other behavioral or social
11 issues connected with expectation that could work
12 in a negative way.
13 I think as Sean pointed out, we're in an era
14 where people are collecting data. We have normal
15 routine use of electronic data capture, so we have
16 objective outcomes that can be easily captured in
17 terms of big databases, like length of stay, or
18 incidence of complications.
19 On the other hand, in the acute pain
20 setting, patients are often unstable medically.
21 They may be post-op, they may have fluid shifts,
22 they may be hypotensive, they may have had trauma,

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1 an issue. Making the diagnosis is less of an
2 issue.
3 Anatomy is relevant. It may not be relevant
4 from a mechanistic point of view, but in a
5 practical sense, if someone has a lower extremity
6 procedure, it makes sense to do a block, epidural
7 spinal, whereas it may not be relevant in a head
8 and neck operation.
9 For the most part, the framing of this, and
10 you'll hear a wonderful framing and summary of this
11 from Tim Brennan later, it emphasizes I'd say the
12 periphery and cellular or micro mechanisms. And of
13 course, we have an opportunity not just to
14 intervene early, but even to prevent pain.
15 Although pain intensity has been criticized,
16 justly, as not capturing the complexity of the pain
17 experience, nonetheless, it's a really good outcome
18 measure. And thinking ahead to the points that
19 Bernie made and Paul made, in terms of getting
20 drugs approved, we have an opportunity to have
21 quite a bit of influence going forward if we can
22 add value to the traditional reliance on pain

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1 whatever, to the thoracic cavity, they may have
2 respiratory issues, organ damage, and so on. Or if
3 they're ill enough to be in the hospital, maybe
4 they have something like pancreatitis or sickle
5 disease where you really have to keep the vital
6 signs supported.
7 That gets to the last point, which is that a
8 lot of the acute pain assessment and treatment is
9 conducted in an inpatient culture of acute care.
10 And that goes for labor as well where there's a lot
11 of observation, a lot of scrutiny, interventions
12 take place quickly.
13 So maybe this is a bit of an exaggeration,
14 but to illustrate that mentality of focusing at the
15 micro level, I'm positive that this title of an
16 article, whose senior author was John Levin and it
17 appeared in a supplement after one of the IASP
18 world congresses, I'm positive this was chosen to
19 be a little provocative. But the title that he
20 gave the article was called The Fundamental Unit of
21 Pain is the Cell, so I think that embodies one
22 extreme.

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1 So what are we talking about here? I think
2 when we construct acute pain versus chronic, we
3 have something like this ball in a well. If
4 there's a little bit of disruption for a little bit
5 of time, then that ball which started at A rolls up
6 the side a little bit and then it kind of settles
7 back down. But we often think that if the
8 intensity of the pain stimulus or the intensity of
9 the trauma passes some threshold, kind of roll that
10 ball up to point B, and if it's over that
11 threshold, it gets pushed over to the right, and
12 we're in a whole different ball game.
13 But I'm going to propose to you that maybe
14 we've over simplified. And I think it's
15 fascinating to hear the conversation and discussion
16 from clinicians this morning that we feel that
17 there's more that we could capture, that there are
18 things that are not captured yet, that might be
19 very important for outcome or judging the success
20 of any therapy. These are these social things.
21 I'll get at that in a moment.
22 So we're developing analgesics, and if you

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1 were a group of students, well I often show a slide
2 like this, but before I put the slide on the screen
3 I ask them, what do you think is the everyday
4 common analgesic that has the greatest benefit to
5 risk/ratio?
6 Of course, the answers are Tylenol, aspirin
7 and so on. But in our daily life as a species, all
8 the time, children get injured, and all the time
9 their mothers, generally their mothers or care
10 providers, nurture and provide reassurance, and
11 it's a great intervention. It works 99 percent of
12 the time. There's no ill effect that I'm aware of.
13 So what's going on here? Well, this is a
14 picture taken from the stage of a marionette show
15 in Paris. And you can see these kids look to me
16 like they're 6 or 7 years old. They're completely
17 engrossed in this, but what they're watching are
18 traditional marionettes with strings. It's obvious
19 these are not -- they don't look anything like a
20 living person. They're puppets.
21 You can think about your nieces or nephews
22 or kids or grandkids watching cartoons on TV that

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1 they know are cartoons. But they get so wrapped up
2 in it that they're lost in it. And I bet if you
3 took any one of the kids and said, Pierre, you know
4 this is a marionette, right? He would probably
5 say, yes it was, but they just can't help
6 themselves, they get drawn into things.
7 So this leads to the issue of what's going
8 on. How can they get so drawn into this? And as
9 we know, we are well beyond the classic view of
10 pain where there's some passive registration of
11 nociception, and we don't much think about what's
12 going on. Our current view is that this is a
13 complicated thing. There's a network of brain
14 structures. It takes in nociception, but other
15 inputs and memories, and actively constructs an
16 internal model of reality, and we don't really know
17 how that model works. It's probably really
18 complicated. It is really complicated.
19 We know from work -- and this is from Sean's
20 lab, that -- and I'm just reminding you of this,
21 everyone in the room knows this -- that empathy for
22 another's pain is as effective in some regions of

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1 the brain in activating those regions as is pain in
2 oneself.
3 Looking at another dimension of this, this
4 classic study by Tor Wager looked at rejection
5 paradigms and found that if you looked at negative
6 affect induced by pain or rejection, that there was
7 a similar overlap in many regions that are
8 activated by both circumstances.
9 So if we wanted to look back and say, well,
10 the issues of the experiential side of pain are now
11 attracting more attention because we're in a
12 situation where we can speak with people, they can
13 report how they're feeling, and at the same time we
14 can do imaging, this has placed greater weight on
15 the experiential side of pain.
16 So it's often worthwhile to look back and
17 see, well, who has talked about this. There is an
18 immense literature, as old as all of literature,
19 that refers to pain. The actual origins of this
20 Book of Job probably took place in the 6th century
21 before the common era, even though they were later
22 incorporated into the Bible, this was an older

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1 story.

2 Job had some illness. He had some kind of a
3 rash. He felt bad. And what was the result? The
4 result was that the people around him, even the
5 children, rejected and vilified him. So this
6 language is really strong emotional language. He
7 said, "They abhor me. They flee far from me. They
8 spare not to spit in my face." So very strong
9 language.

10 There were a couple of articles, I'm happy
11 to give the references to you, written by some
12 Greek anesthesiologists. One was around 2000, one
13 was about 2010. They looked at Greek medical
14 writing in general in the first article and in
15 Hippocrates in the second article, and traced out
16 different terms of relevance to anesthesia and also
17 analgesia and pain.

18 It's very striking that the Greeks were
19 outstanding in their linguistic ability to relate
20 experiences because they didn't require any
21 technology to do this. They could just observe
22 themselves and others. Some of the writings are

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1 just remarkable.

2 But the point of showing you this is that
3 they differentiated at least three different types
4 of pain. The word "algos" is derived from a root
5 meaning to care or look after. And this tended to
6 be used in the context of somatic pain, and there
7 are many compound forms that link this to pain in a
8 certain area.

9 On the other hand, the "odyne" was the
10 psychic dimension of pain. And the literal
11 translations of the context in which it's used and
12 the compound forms are things that don't look that
13 different from the McGill Melzack scale. These
14 were just literal translations of what these
15 compound forms meant, fearful or terrible, acute or
16 hot and cold.

17 Then there was this other term called
18 "poine." Poine is the root for payback, or
19 retribution, or penalty. It is believed to come
20 from an earlier Indo-European root meaning to pay,
21 or atone, or compensate.

22 Certainly, this is the way it appeared in

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1 the Book of Job. There was the immediate
2 assumption that Job displeased God, or had done
3 something wrong. And from the outset, his illness
4 was viewed by his community as payback for
5 something, and much of the Book of Job is spent
6 trying to figure out what he did.

7 In Latin, this evolved and kept its meaning
8 to mean penalty, like penitentiary for instance.
9 And even in English, it kept the connotation of
10 punishment, and there's some legal language, like
11 something being punishable on pain of death. And
12 in that context, it doesn't mean nociception, it
13 means penalty.

14 So I would propose to you that, to me, it
15 looks like the word that we've chosen, that we've
16 settled upon, of several different dimensions, is
17 the one that has a social or transactional meaning.

18 I'm glad that Bernie is here. He'll
19 recognize this table. This is the table from the
20 famous Lou Lasagna article with Beecher on the
21 powerful placebo. And they used the term
22 "reactors" instead of responders as we would, or

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1 "non-reactors."

2 I'm not quite sure how they came up with
3 these categories, but they characterized the
4 individuals whom they observed in terms of whether
5 they had a certain attribute or did not. And it's
6 striking to me that if you look at things that
7 differentiated, the placebo reactors from the ones
8 who are not reactors, this one, you can't quite see
9 this here, but there's a statistical relationship.

10 If the patient liked everyone in the
11 hospital, or if they thought the care was
12 wonderful, and if you looked at regular
13 churchgoers -- I would come away from this saying
14 that the original construct I showed you a few
15 slides ago, where you have one kind of conceptual
16 compartment and that's acute pain, and that's
17 mechanistic, it's all about what the cell is doing
18 versus the construct we've made of chronic pain is
19 a false dichotomy.

20 I know this whole talk is in a sense
21 creating a false dichotomy, but I'm trying to
22 emphasize the fact that when you look at the

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1 literature, there are already many cues, including
2 Beecher's own observations of people who didn't
3 feel a bullet when they were wounded in battle
4 because it was a way out of battle versus those in
5 everyday life back in his Boston practice who did
6 feel the same injury much stronger.
7 If you look at this literature on acute
8 pain, there actually is a substantial framing of
9 acute pain, and that relies on memory inputs. We
10 asked our Tufts students last year, we were
11 inspired by CNN because when the Pope visited the
12 U.S., they did a quick word cloud and they said,
13 "Write three words about the Pope." One of them
14 was opposite of Trump.
15 (Laughter.)
16 DR. CARR: But others were things like
17 compassionate. It's true. So anyway, we thought,
18 you know what, it's pain month; why don't we do
19 this?
20 So the question is what three words should
21 the world know about pain? We sent it out to our
22 mass mailing list, students, friends, alumni,

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1 faculty. And this is what they came up with. And
2 we didn't cue them at all, this was it. This was
3 the whole thing.
4 So I would propose to you that to people who
5 either have pain or are close to or treating those
6 with pain, this experiential aspect of suffering
7 and shame is really very important. And
8 nociception or the magnitude of pain itself is just
9 one component of this. There's a couple of words
10 like "discomfort" that fit in. But fundamentally,
11 this was more about the experience of loneliness.
12 Now, Leo Goudas and I wrote an article some
13 time ago -- so I've been beating this drum for a
14 long time -- it stated in the Lancet article that
15 acute versus chronic is oversimplified. And if we
16 look at work, which was available even back in the
17 '90s on the expression of genes, let's say in
18 dorsal horn, you could see c-Fos expression within
19 tens of minutes of an acute injury.
20 So what I propose to you is to try to think
21 about acute pain as the initiation phase of
22 persistent pain that is mediated through a cascade,

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1 which in most circumstances in acute pain is
2 triggered by tissue injury. And as in many other
3 complex systems, like you think of the butterfly
4 effect, a small change in the initial state of the
5 host or in some aspect of the nociceptor stimulus
6 produces major differences in the detailed manner
7 in which this process unfolds.
8 So should we be thinking about acute pain as
9 the initial phase of pain the disease? We know
10 that injury triggers a cascade of responses. We
11 know the peripheral and central nervous systems
12 have evolved to promptly adapt and reorganize and
13 remember.
14 So there's an essentially programmed
15 instability. In other words, it's like a
16 mousetrap. A mousetrap is a contrivance, which
17 works because it's unstable. It's all set to get
18 triggered with a little stimulus of a mouse paw on
19 the cheese. But our nervous system has also that
20 programmed aspect, and it's programmed to achieve
21 instability.
22 So we know that there is a lot of chronic

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1 pain after surgery, and it's a really interesting
2 question, why the number needed to harm isn't one?
3 Why doesn't everybody get chronic pain after
4 everything? There's been a lot written, and I'm
5 certainly going to defer to Tim and others in this
6 room about the chronification of pain. But this is
7 a key new appreciation that's been driving this
8 whole area.
9 So acute versus chronic pain, maybe that's
10 oversimplifying. Maybe there's a disease state,
11 and you can think of this like infection, or like
12 tumors, where my understanding is that every day we
13 make a number of tumorous cells or cancer cells,
14 but our body mostly cleans them out. And when we
15 shift our ability to do that, let's say getting
16 older, immunosuppressed, that's when they continue
17 to grow. But the process is always potentially
18 going to occur at any time.
19 So maybe there's a chronic disease state
20 that may begin within hours or even tens of minutes
21 of acute injury. And I would say that the
22 techniques to effectively suppress that cascade and

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1 the following benefits have perhaps been
2 inadequately studied. The mechanisms of how the
3 pain normally resolves, through these, for one
4 example, a compound class called resolvents, are an
5 intriguing area of study.
6 So we're here at this juncture where the
7 people who study pain in the acute setting have
8 focused on the micro scale, kind of a bottoms up.
9 But we know, and it's especially intriguing to hear
10 about big data from Mike and Sean, that maybe we
11 can benefit from thinking about pain as a
12 population-based phenomenon. Maybe we can add
13 something to that.
14 So I'm proposing to you that maybe this
15 question of when does acute pain, maybe it's
16 misleading. Maybe we've been misled by framing the
17 question that way because we're equating time
18 course and mechanism. But we know that there are
19 many instances of prolonged pain or repetitive
20 nociception that can be resolved, and there's no
21 chronic pain thereafter.
22 I was intrigued and I referred to this, I

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1 was very influenced by a paper that Henrik Kehlet
2 wrote with Fred Perkins probably 15-20 years ago,
3 looking at risk factors for persistent surgical
4 pain. And they used the term "psychosocial
5 factors" as kind of a term because we knew there
6 were some patients, and we know this in the acute
7 pain clinical world, that are not going to do well.
8 We don't have a convenient way of dealing
9 with that, but I think there's a clue there that it
10 may be very valuable to transpose or take over some
11 of the dimensions that were used in AAPT that
12 traditionally we tend to reserve for chronic pain
13 into the acute pain setting and do more with them.
14 So we need to distinguish between this
15 concept, and I gave you some samples from the acute
16 pain shared interest group of AAPM, that acute pain
17 is tied up with intense nociception versus the
18 onset of this reorganization process that we call
19 chronic.
20 So if you look at the literature, and I
21 don't mean to oversimplify this, but in some crude
22 way, it looks like the chronic post-surgical pain

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1 risk is somehow proportional to the magnitude of
2 peripheral nervous system injury and the magnitude
3 of sensitization that in turn can be triggered by
4 poor pain control or high pain intensity.
5 But there's so many factors that modify
6 this: genetics, epigenetics, cognition, the
7 relative weighting, the intensity, whether
8 inhibitory processes are mobilized. These are all
9 influenced by a lot of things.
10 So in the sense of keeping on track and
11 allowing time for discussion, I was thinking, well,
12 what can I also do. I don't know if you recognize
13 this lady. She's a very important lady, and she
14 was important in our family's life. She's a living
15 author who said, "If we can have confidence in our
16 decisions and launch enthusiastically into action
17 without any doubts holding us back, we'll be able
18 to achieve much more."
19 I'm quoting from her wonderful book called
20 The Life Changing Magic of Tidying Up. It has to
21 do with cleaning your house out and how that
22 changes life.

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1 So I'm going to leave you with that note,
2 and we can either start the next one early or do
3 some questions afterwards. How would our mentors
4 want to proceed? Take questions. Okay.
5 DR. TURK: A comment before I take
6 questions. We were told by the transcriber, please
7 talk into the microphone because she can't hear.
8 So it's not just whether you can hear us, it's
9 whether she can hear us in the transcribing. So
10 even if it's awkward and you're turning around, try
11 to use your microphone.
12 DR. CARR: Should I repeat my talk?
13 (Laughter.)
14 DR. CARR: But that's okay, I've rehearsed
15 the spontaneous insights. So actually, I did have
16 a spontaneous insight. Thanks to Dennis with his
17 use of the analogy of the herd, that we are a herd,
18 of course many people observed, including
19 Aristotle, that we, man is a social animal, or
20 people are social animals.
21 So if you think about this, there are many,
22 many examples of pack animals or herds that when

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1 one of their members becomes wounded, or ill, for a
2 brief period of time, they will be supportive. You
3 know, these are like the things you see on YouTube
4 where the elephants are trying to get the other
5 elephant up and get it to walk and so on. But at a
6 certain point, if that injured elephant can't
7 continue with the migration and the herd has to get
8 going, or can't help the wolf pack feed itself, the
9 members of the herd turn on that animal and drive
10 it away or even will attack it. There's a lot of
11 examples of that.

12 So I don't know if this adds anything to the
13 debate, but I was thinking in some implicit way,
14 when we think about acute pain, we're probably
15 thinking about that first phase where the member of
16 the pack or the herd has been injured.

17 We're willing to put a lot of resources in.
18 We're going to do fancy nerve blocks. We're going
19 to use ultrasound guides. We're going to put an
20 epidural, whatever. We're going to get that person
21 through. But then I think as time persists, and
22 the person doesn't reenter their functional role,

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1 they tend to get stigmatized, and there's certainly
2 a large literature on stigma and pain. And they
3 also stigmatize themselves.

4 I was intrigued by that quote from Steve
5 Hyman that maybe this notion of depression and pain
6 can -- maybe they're actually the same thing, that
7 maybe there is a way of behaving where the person
8 figuratively will crawl back into a cave and either
9 get better and rejoin the herd or not get better
10 and at least will not be a burden for the herd if
11 they die off in some cave.

12 Maybe they're the same thing. And that's
13 that second phase that we've been seeing in animals
14 all the time, where the herd expels the animal, and
15 the animal goes along with it and just slinks away
16 quietly back into the shadows. So I think, to me,
17 this is at some level resonant with the notion of
18 acute versus chronic pain.

19 DR. TURK: Is that a cautionary note, Dan?
20 Are you saying that if people don't go along with
21 what we want, we're going to attack them?
22 (Laughter.)

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1 DR. CARR: That's a great idea. That's a
2 good suggestion. I was thinking that you were
3 going to say slink into the shadows. I don't know.

4 MALE SPEAKER: [Inaudible - off mic].
5 (Laughter.)

6 DR. CARR: Yeah. You mean lemmings? I
7 don't know.

8 Henrik, this is the person we want to hear
9 from.

10 DR. KEHLET: No, that was wonderful, Dan.
11 But I think we only have two days to discuss the
12 taxonomy of acute pain, and I simply think we
13 should decide on a time frame for that acute pain
14 and leave the question about transition to chronic
15 pain.

16 That is too complicated, and I must admit, I
17 think that your review on that was quite
18 superficial. So I will suggest that we stay on
19 acute pain and decide on a time frame and not going
20 into persistent acute pain.

21 But I want to hear what you say. We have
22 been in that area for so many years, it's so

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1 complicated.

2 DR. CARR: So when you say time frame,
3 you're saying we should say acute pain is a new
4 injury and it causes nociception for X number of
5 days or hours?

6 DR. KEHLET: Yes.

7 DR. CARR: Would you make an opening bid
8 about X?
9 (Laughter.)

10 DR. KEHLET: I would suggest something
11 around one week. Because the further you get out,
12 the more complicated it gets.

13 DR. CARR: Well, I certainly don't feel
14 motivated to argue about it. It is incredibly
15 complex, but I don't see why we couldn't try both.
16 If we don't spend all our time working out
17 complexities that are too difficult and we're never
18 going to get done, but if we acknowledge that
19 operationally we can take one week, it's not that
20 different than saying chronic pain is whatever,
21 3 months or 6 months.

22 That doesn't undermine the motivation to

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1 study mechanisms of chronic pain, but you can do
2 both. You can say in practice, we can say acute
3 pain is a week.
4 Dr. Buckenmaier?
5 DR. BUCKENMAIER: Frustratingly, that
6 approach of providing some sort of time frame that
7 we're going to work in has been a real problem,
8 particularly with the soldiers that I've been
9 dealing with on the battlefield. It is a
10 continuum. It is a process. I've recognized
11 neuropathic symptoms in a fresh amputee literally
12 hours after their injury.
13 So trying to compartmentalize and not look
14 at pain as a disease process that has an acute and
15 a chronic component, like [inaudible – mic fades]
16 processes, makes it difficult to actually build a
17 system then to manage it.
18 It's the silos that have literally been
19 killing us in the military where we do things very
20 effectively in the acute setting on the
21 battlefield, but that provider never gets to see
22 the consequences of that pain approach months or

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1 years down the road because that system wasn't
2 established.
3 So decisions we made with opioids, very
4 early on that made lots of sense in the acute
5 setting as we're dealing with the trauma, that
6 provider doesn't see the damning outcome as that
7 opioid monkey is on the back of that soldier trying
8 now to deal with his healed injuries but lifelong
9 chronic pain that still makes him an unproductive
10 citizen.
11 So I think we have to look at it as a
12 spectrum, a continuum. And trying to part an
13 artificial time frame on it only creates more
14 problems than in my opinion are actually going to
15 solve.
16 DR. CARR: Steve?
17 STEVE: Yeah. I think that's an acute
18 condition that clearly looks like it's neuropathic
19 pain. And then in our original AAPT for chronic
20 pain, we've got neuropathic conditions that look a
21 particular way. And presumably they would look
22 pretty similar if they've got comparable underlying

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1 neuropathic mechanisms.
2 Since we have, by definition, set up a
3 chronic pain and a separate acute pain taxonomy, it
4 kind of leaves us with this challenging problem of
5 having conditions that should look similar if
6 they're both neuropathic, but we've said they're
7 different, and we've arbitrarily dichotomized a
8 continuum.
9 Pragmatically, we kind of have to do that, I
10 think. And I guess the question is, just for
11 future reference as we're thinking about this, is
12 there a way to make that cutpoint, agreeing it's
13 arbitrary, but making a cutpoint between acute and
14 chronic in a way that makes sense that's flexible
15 that doesn't box you into difficult situations like
16 you're talking about.
17 So I think that is a really important issue
18 that needs to be addressed in this. I don't think
19 we're going to be able to totally avoid talking
20 about time frames because somehow we're going to
21 have to separate these from the chronic pain
22 conditions. But I think that maybe there are ways

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1 of wording it to be flexible about it.
2 DR. CARR: Bob, we have a few -- everyone
3 will be heard. Bob?
4 DR. DWORKIN: So the FDA sponsored a
5 workshop I think about 4 or 5 years ago that some
6 of us were at to address the question of
7 extrapolation of efficacy from one acute or chronic
8 pain condition to another. If a drug works in X,
9 is it likely to also work in Y?
10 The consensus of that workshop was
11 published, and in that piece on extrapolation,
12 acute pain was defined as up to 30 days, and
13 chronic pain was 90 days or longer. And that was
14 done to be consistent with IASP.
15 Of course, that leaves a middle 2 months
16 that we called subacute pain, not being very
17 creative. That would be a starting point if we
18 wanted to adhere to what is consistent with IASP,
19 what is consistent with the FDA's way of thinking
20 about these things. I'm not advocating for it, but
21 it certainly is a way to start.
22 The only other thing I'd want to say is in

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1 the discussions that led up to this meeting, an
2 additional dimension for acute pain that was
3 proposed to add to the five that Roger discussed,
4 would be a dimension that focused on the temporal
5 aspects of the particular acute pain condition. So
6 there would be a dimension that really discussed,
7 for whatever acute pain condition, what are its
8 temporal characteristics.

9 As Dennis mentioned earlier, the two of us
10 know very little about acute pain, but the way I
11 think about this is if we've got diagnostic
12 criteria for renal colic, the temporal dimension is
13 basically going to say that this is an acute
14 condition that typically resolves and doesn't lead
15 to chronic pain; whereas, for acute traumatic pain,
16 surgical pain, et cetera, the temporal dimension
17 would have a discussion of risk factors for
18 chronicity.

19 So that would be one way to address the
20 temporal aspects, which is to add a dimension that
21 specifically describes those features when
22 relevant.

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1 DR. CARR: Can I just ask you a question,
2 and back to Henrik, and everyone else will be
3 called on and have their say. But as long as the
4 idea is in here, what would you do if there were a
5 decision to make 30 days or 7 days? How would that
6 fit into the big picture? Do you just say we're
7 going to define acute pain as pain within X time?
8 What would you do with that idea?

9 DR. DWORKIN: Well, what I would do, I think
10 it depends on the condition. So the acute pain
11 condition I think I know the most about is acute
12 pain in patients with herpes zoster. So for that,
13 I would think a week is a little too short. And if
14 I was responsible for coming up with diagnostic
15 criteria for acute pain in herpes zoster, I'd be
16 thinking about pegging it either to the period
17 until the rash is completely healed and there's
18 been loss of all scabs or up to 3 to 4 weeks.

19 That would be a kind of mildly interesting
20 discussion. Do you define acute shingles pain
21 based on the rash or based on just what we know
22 about the kind of epidemiology of the acute phase?

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1 And other conditions it might be no more than a
2 week or hours, or perhaps in some conditions, it's
3 hours.

4 So I think it would be condition specific.
5 But I think once you get beyond 30 days, you're
6 really kind of transitioning to a subacute
7 chronicity kind of process.

8 DR. CARR: So let me ask Henrik, how would
9 you have put that in the final document? Because
10 if the document just said acute pain is pain
11 lasting up to X days, let's say it was 30 not
12 necessarily 7, then is that the end of it? And
13 then what value has this enterprise added?

14 DR. KEHLET: No, no. It is no way the end
15 of it, but we have to deal with the problems around
16 acute early pain, and I thought that was the
17 purpose of this meeting. Because if we go into the
18 persistent thing, we would need another at least
19 two days.

20 There are so many challenges in acute pain
21 by categorizing patients, overlapping pain
22 conditions, pre-op opioid users, all the

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1 psychological issues. And it has never been
2 addressed in all these pain trials because people
3 just say patients and pain and analgesics, and lump
4 it all together. And the future will be to divide
5 it up in different pain patients.

6 DR. CARR: Well, I see this is echoing what
7 Roger was pointing out earlier, that we could be
8 revolutionary and take a purely mechanistic state
9 of the art, or evolutionary. And I think that AAPT
10 succeeded in introducing new important valuable
11 content in an evolutionary way. Maybe we'll do the
12 same thing. I'm not sure.

13 There are a lot of people that have
14 questions. Bob, did you have one other thing to
15 add? And then we'll start getting all the hands?

16 DR. DWORKIN: I just wanted to say I
17 completely agree with Henrik. If I'm doing a
18 clinical trial to look and see whether pregablin is
19 efficacious for acute pain in patients with herpes
20 zoster, I don't need to think about PHN.

21 I could have a dimension in my diagnostic
22 criteria that some patients with shingles develop

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1 PHN, but for my inclusion and exclusion criteria
2 for a study of whatever drug for acute pain in
3 zoster, I don't need to think about PHN. So in
4 that sense I completely agree with Henrik.
5 DR. CARR: Okay. But before getting the
6 hands, I would say that what if we were having this
7 conversation about placebo? In other words, what
8 if we decided that not addressing whether a
9 proposed enrollee in a clinical trial was a placebo
10 responder or not might impair the quality of the
11 trial or our ability to detect --
12 What if these other things that we're
13 lumping as psychological factors, what if they had
14 an equally great magnitude upon ultimately the
15 effect size of the trial? Maybe it's time to dig a
16 little deeper and bring those out into the
17 sunlight.
18 DR. DWORKIN: But that's still the
19 acute -- that's a question of for my trial of
20 zoster, do I include individuals who are depressed,
21 but that still has nothing to do with the
22 chronification. That's, you know, during their

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1 shingles are they depressed, are they
2 catastrophizers, and maybe I want to exclude those
3 to improve my assay sensitivity.
4 I don't think Henrik would disagree that if
5 you're doing a trial of acute post-operative pain,
6 you want to pay a lot of attention to the patients'
7 mood and physical function, but you don't
8 necessarily need to take into account the risk of
9 the patient still having pain 6 months later.
10 DR. CARR: Okay, there were a number of
11 hands up, so now as promised we're going to go
12 around. Yes, please?
13 DR. SCHREIBER: So I was just going to say
14 from a clinical standpoint, we are still concerned
15 about chronification of pain in that we know the
16 acute pain is going to end, and obviously we want
17 to treat that, but I think there's a great amount
18 of importance about whether it becomes chronic.
19 I mean, if it's a separate discussion and a
20 separate interest group, then it is, but I think it
21 is a really important thing. And it will guide our
22 treatment of the patients, like say in the

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1 perioperative period. You know, like do I want to
2 give this person -- are they going to respond to
3 X drug in terms of preventing chronic pain? It's
4 an important question, but maybe a separate one
5 from whether it's going to impact their acute pain.
6 DR. CARR: Let's see. Srimi, then Deb,
7 Sean, Dr. Edwards, and then we'll get over to this
8 side of the room.
9 DR. RAJA: Dan, your initial title said key
10 distinctions among acute, subacute, and chronic, so
11 to respond to this duration question, in your
12 opinion, when does acute become subacute?
13 DR. CARR: You know, you saw that I avoided
14 that issue because I was propagandizing for the
15 continuum. Yes, there's some he doesn't know, I
16 don't know. I mean, when does acute become
17 subacute, I don't know. I think the word
18 "subacute" is a word that we apply to kind of patch
19 a gap without much thinking about it.
20 We could retrofit some definition around the
21 word "subacute," but it would be some derivative of
22 a derivative of a hypothesis. You know, it would

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1 be the pain between acute and chronic.
2 So I think in subacute, the concept we have
3 is that there's some organizing process, which is
4 continuing to follow that initial injury, and it's
5 either going to go back to baseline or go off in
6 its direction of chronification.
7 To Kristin's point, though, I think we often
8 are confronted with patients that are prevented
9 from being discharged because their pain intensity
10 is too high. So the pain trajectory, even acutely
11 as our friends in PAIN OUT have seen, is a pretty
12 good predictor in many instances of chronification,
13 and it's very practical. It's not like you can
14 think about it later because the problem is already
15 there right now. I don't know if you want to add
16 something, Srimi.
17 DR. RAJA: No, I think the reason I was
18 thinking of is you can define the duration of acute
19 pain as pain that either resolves or becomes
20 subacute. And the question is, what is that
21 duration.
22 DR. CARR: Okay, we'll leave the question on

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1 the floor. And we said we would have a few other
2 people, so it's Deb next, and then Sean, and then
3 Dr. Edwards.
4 MS. GORDON: Thanks, Dan, for your talk.
5 There's a lot in there. I mean, I want to agree
6 with Henrik that I think we do have to continually
7 stay within scope of what we can achieve, but I
8 don't think we can completely separate it.
9 I'm thinking of all the work we're all doing
10 right now to kind of identify complex pain patients
11 in the pre-anesthesia clinic and doing
12 catastrophizing screening, and resiliency
13 screening, and looking at prevention. I mean, you
14 mentioned prevention is so unique about acute pain,
15 but part of the goal of acute pain is preventing
16 chronic pain.
17 So that issue about expectation setting and
18 intervention on the psychosocial factors, the
19 pre-habilitation, the categorization of patients
20 before they come to a planned surgery, and then how
21 you quickly get them through that acute phase and
22 prevent subchronic persistent pain. I just think

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1 it's going to be -- it's going to stick together.
2 DR. CARR: Okay. Sean? And by the way,
3 Dennis informed me we'll maybe in the overall
4 discussion period take questions from this side
5 just to stay on track time-wise.
6 DR. MACKEY: I want to acknowledge the
7 tensions of what I'm hearing from Henrik, who I
8 agree with. We don't have it figured out. There's
9 so many questions that we have, and at the same
10 time highly support what you're saying in this
11 continuum of pain. These arbitrary distinctions
12 between acute and chronic probably just don't
13 [inaudible – mic fades] and want to advocate
14 strongly that we allow a classification system that
15 will allow us to capture that continuum, so that we
16 can better understand what Henrik has so eloquently
17 stated.
18 Much like in the pediatric pain realm, we're
19 all appreciating the developmental aspects of pain,
20 and there's great efforts now to try to understand
21 that developmental progress from when these kids
22 have chronic pain into adulthood.

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1 We want to be able to characterize when
2 people have acute pain and move into chronic pain.
3 So parallelism with this group's effort with what
4 has been done in chronic pain I think would be
5 incredibly important.
6 Secondly, it would allow us, if we did align
7 and have parallelism, to be able to better classify
8 that patient who comes into the surgical or acute
9 pain setting who has chronic pain, to classify that
10 person's chronic pain and at the same time
11 characterize the acute pain in that episode.
12 DR. CARR: Okay. Dr. Edwards, last
13 question.
14 DR. EDWARDS: Sure, Sean said it greatly. I
15 was just thinking practically when we have patients
16 present to us, they're going to present somewhere
17 along the continuum, not at the beginning in a
18 research model, but 7 days, 12 days into an acute,
19 subacute pain episode.
20 To be helpful to non-pain specialists,
21 that's always the question, they never know who to
22 consult. Do they consult a chronic pain service or

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1 an acute pain service, and what stage. And we help
2 them define what stage this patient's at. So if we
3 can't come up with some kind of plan for this at
4 the outcome of this meeting, that's going to
5 continue to plague us. Thanks.
6 DR. CARR: Thank you. I think those
7 questions are -- there will be a lot of time that's
8 built in already to discuss and handle further
9 questions. We just can't handle right now because
10 we have to move on to the next speaker.
11 DR. TURK: Thank you. It's great to have
12 the questions. And the fact that we actually have
13 more questions than time is perfect because what
14 that means is that you're engaged, and you're
15 interested, and there are a lot of things to work
16 out. The worst meeting I've ever had was we said
17 are there any questions, and we sat there for
18 45 minutes and no one said a word. So that's not
19 very helpful.
20 Now, I'm going to go to our next topic, and
21 there will be opportunities, as Dan implied, for
22 discussion. This is not over. This is just

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1 weighing out some of the issues that you're going
2 to be wrestling with over the next day and a half.
3 Going to our next speaker -- and we're a few
4 minutes behind, but don't worry about that -- Tim
5 Brennan. Most of you know Dr. Brennan, or
6 Professor Brennan I should say, from the University
7 of Iowa. He is a professor there as well as the
8 vice chair for research. And he's going to give us
9 a little bit of pathophysiology of acute pain with
10 a question mark at the end, I notice. So let's see
11 what he has to tell us.
12 Presentation – Tim Brennan
13 DR. BRENNAN: So when Dennis and Bob asked
14 me to give this talk, and they talked about our
15 meeting getting together, they talked about
16 creating a straw man, so I will throw out the first
17 bit of straw here.
18 My talk, I was given this topic. I created
19 a little bit of a template of slides and sent them
20 out. It's biased towards post-operative pain
21 because those are most of the patients I see as
22 well as post-traumatic pain. And I do basic

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1 research and am familiar with mechanisms and
2 mechanistic research.
3 Bob sent me the mechanistic preprint from
4 the chronic pain working group. No help. I could
5 have picked up a textbook, read all the mechanistic
6 work and the latest review article on mechanism,
7 and I refrained from doing that. So I put this,
8 sort of off the top of my head, but 25 years of
9 acute pain and 25 years of pain research. Here it
10 goes.
11 The conclusion, I'll begin with a conclusion
12 that not very easily can we use mechanisms to
13 classify acute pain, or let's take the other side
14 to this and say we're part way there, and we need
15 more information.
16 I think Kris included procedural, so we're
17 going to review some pain mechanisms from Brennan's
18 point of view off the top of his head. There's a
19 few references in here, but there's not many.
20 So Kris mentioned procedural pain, that may
21 help us a little bit, and I'm going to talk about
22 acute pain. What am I going to talk about? We can

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1 take nociceptive mechanisms, neuropathic,
2 inflammatory, et cetera. We can say, oh, it's
3 sensitization. That's how we're going to
4 characterize acute pain. That's how we're going to
5 categorize it.
6 No, we're going to do it by mediators. This
7 condition has factor Z, the other condition it's
8 not there. Now, let's look at treatment. We got a
9 drug; completely eliminates that acute pain
10 problem, and that drug is totally ineffective in
11 another acute pain problem, or we're going to look
12 at tissue injured.
13 So with respect to procedural pain, I called
14 it nociceptive pain. Treatment is local, and it
15 involves peripheral nociceptor activation and
16 central nervous system nociceptive pathway
17 activation. I put a time on there as minutes.
18 Let's get it on the table now. It can involve
19 freezing or a burn lesion, it can be involved in
20 injection. Those of us over 50 know distention for
21 a gastroenterologic procedure.
22 It usually involves transduction of heat;

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1 you know we can burn things. Cold. We can use
2 cold, nociceptive cold for procedures, and
3 mechanical stimuli like distention or injection.
4 And it involves transmission through both
5 peripheral and central nociceptive pathways. And
6 is not pathophysiological, but we used our Levin's
7 review article. We used our transduction
8 mechanisms in acute pain. But it's not
9 pathophysiological, so let's take some
10 pathophysiological pain mechanisms and see where this
11 going to get us.
12 Now, if we're going to be -- we've got time,
13 we thought we had time to separate acute and
14 chronic pain, but we haven't gotten there yet. And
15 when I look at these mechanisms, I'm going to refer
16 back a little bit to chronic because the time may
17 be a little bit muddled, as you've just said. But
18 if we've got these acute pain mechanisms, are they
19 really unique and different than chronic pain, and
20 how are we going to use them.
21 So here's the start. We can take our
22 nociceptive mechanisms, mechanical, heat, cold, and

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1 I added chemical, and they transduce these acute
2 stimuli, so we could say a sharp needle, something
3 burning, ice, holding ice in your hand for a long
4 time.
5 Chemical is a little bit ignored, but lemon
6 juice in your eye is acid, and it's extremely
7 painful. So we do transduce chemical stimuli as
8 well. Neuropathic, I just said that's caused by
9 nerve injury and inflammatory.
10 I put immune-mediating. Basic scientists in
11 pain have overstated and over utilized
12 inflammation, so everybody injects something that's
13 brutally inflammatory and says, well, it's present
14 in chronic pain, therefore we're studying chronic
15 pain. And this in pain mechanisms, I think the
16 pain research field has taken this broad
17 inflammatory topic and said as is good for all of
18 us, formalin causes inflammation, look at it, it's
19 bad.
20 But this is a tough one because we've got
21 immunologists who are very detail oriented and have
22 markedly affected their pain patients, but we've

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1 used it really broadly. And I left it
2 immune-mediated, and we'll move on to that.
3 I could pick an example. Swelling after a
4 sprain, maybe even throbbing, nociceptive or
5 ischemia. If you've seen my slides, I'm going to
6 throw out ischemia as a mechanism not well
7 appreciated.
8 We talked about seeing acute neuropathic
9 pain. We know we cut, stretch, and inflame nerves
10 during injury, trauma, surgery, et cetera. And we
11 can find acute inflammatory conditions, and I put
12 an easy one out there for me because I'm talking
13 off on my own here without reading any of the
14 rheumatology literature.
15 But almost all of these, as I'm going to
16 show you, are components of acute pain condition.
17 We may not recognize neuropathic pain, but nerves
18 are cut, and we're not exactly sure of the
19 consequences.
20 So let's keep going in the detail here. We
21 think that nociceptive mechanical is an important
22 part of acute pain mechanisms. I mentioned

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1 swelling. We can get release with elevation and
2 reducing swelling. It must be there. When we take
3 a deep breath after abdominal surgery, we stretch
4 the abdominal muscles. It's notable to be pain and
5 so stretch or a mechanical component is clearly
6 evident in acute pain. And if we cough, we
7 contract the middle of the muscle and stretch the
8 outer part of the muscle and also can produce pain.
9 So any evoked pain with activities has a
10 mechanical nociceptive component, and most acute
11 pain we think has evoked components, as Henrik
12 taught us in the early '80s and '90s.
13 So chemical is understated. I put ischemia
14 as an example of chemical transduction in
15 pathophysiologic mechanisms, and I put hypoxic
16 lactic acidosis in as an example of a chemical
17 transmission. Compartment syndrome after trauma.
18 That's great, so I've got an ischemic condition
19 there. We can put that into our category, but I'll
20 tell you that that mechanism looks to be operative
21 with fracture and bone remodeling.
22 I showed almost none of my own slides from

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1 my usual lectures on acute pain mechanisms, but I
2 threw a few in at the end to show you wounding,
3 loss of blood flow, and coagulation will produce
4 this ischemic mechanism, and of course, it occurs
5 during a heart attack as well.
6 But when the NGF trials came out in
7 osteoarthritis, I listened to someone lecture about
8 osteoarthritis, that mechanism is also present
9 there. If I get this wrong, please correct me, but
10 endochondral bone has no nerves or blood vessels.
11 When it becomes inflamed, there's high oxygen
12 consumption, inflammation, neovascularization, new
13 innervation, and pain from osteoarthritis.
14 So I went back to chronic pain, not my
15 intention to overlap, but we'd love to have
16 specific acute pain mechanisms. When I was working
17 on ours that I'll show you a little bit of
18 information, I was struck by the osteoarthritis
19 literature.
20 So I think Trip mentioned acute neuropathic
21 pain. Henrik told me a couple years ago, oh yes,
22 there is acute neuropathic pain in surgery,

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1 surgical and traumatic nerve injury, so there are
2 some studies on thoracotomy, acute zoster.
3 Phantom at least must be acute -- acute phantom
4 must be neuropathic. Inguinal hernia, iliac bone
5 harvest are others hypothesized to be acute
6 neuropathic pain.
7 All trauma has nerve injury to some degree.
8 Every time, usually tissue is innervated and nerves
9 are cut, and its role in acute pain I'd say is
10 noted. We think that's there and that's present.
11 I'm a little bit -- I'm going to struggle that
12 using a neuropathic pain scale in the acute
13 post-operative period is demonstrating that a
14 patient has neuropathic pain, but the literature is
15 sort of moving this direction. Certainly, the
16 acute phantom; we'd have to give them that.
17 I really struggle with the broad term of
18 inflammation, but it's generated a huge amount of
19 basic science, research on pain and pain
20 mechanisms. Almost any tissue injury or trauma is
21 associated with some form of inflammation. We
22 could talk about inflammation using markers. We

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1 can talk about it as leukocytes, and we can talk
2 about it as TNF.
3 So I actually threw out a few references
4 here to talk about a variable role of inflammation
5 in post-operative pain. I'll begin with a
6 meta-analysis on dexamethasone for Northwestern
7 that basically said it's a mixed effect, and I'll
8 come back to treatments, and I'll be redundant in
9 some of the information.
10 If you look at NSAIDs in COX-2 inhibitor
11 trials, you can look at -- here's a recent
12 intravenous ibuprofen trial that was really weak
13 for any benefit in open abdominal hysterectomy.
14 And I think Henrik's database website recommended
15 specific treatments for specific surgeries that I
16 think was in agreement with this weak effect of, in
17 this case of an NSAID.
18 If we look at parecoxib in hip replacement,
19 we'd say there's a moderate to strong effect. And
20 if we looked at the dental literature and third
21 molar extraction, I reach back to 1986 in which
22 they showed a strong effect of NSAIDs in the dental

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1 literature.
2 I'll just point out a TNF's inhibitor high
3 utility in autoimmune acute pain conditions. I
4 think maybe we'll touch on that tomorrow. And
5 certainly it has a role in acute joint infection.
6 Bob would go back -- we could go back and
7 forth on whether acute zoster is inflammatory or
8 whether it's neuropathic or certainly a
9 combination, but you can see that these injuries
10 are multifactorial and redundant and use a variety
11 of mechanisms. And who is to say a simple surgical
12 incision through the abdomen doesn't have all
13 nociceptive components, neuropathic, and
14 inflammatory components to it. Thus, the
15 categorization of pain mechanisms is all inclusive.
16 So I put mechanical and chemical, and I
17 dropped heat and cold. They are great for modeling
18 the pain system and categorizing nociceptors, but I
19 don't think -- we can argue this after
20 lunch -- that those are really stimuli we're really
21 interested in, in acute pain management.
22 Injury occurs throughout. We think acute

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1 neuropathic injury exists but is not consistently
2 diagnosed. And it's difficult to diagnose. I
3 really struggle with the neuropathic surveys as
4 their use in the acute pain period. I had a burn
5 surgeon come up to me and say, I gave the LANSS
6 scale to all my burn patients, and they've all got
7 neuropathic pain. And I winced and kept it to
8 myself.
9 Immune-mediated responses are common, and we
10 can get some separation if we pay attention to the
11 rheumatologists and their autoimmune conditions.
12 Okay. We're all excited about
13 sensitization, and I hear, not infrequently, acute
14 pain, well, that's peripheral sensitization, and
15 chronic pain, certainly that's central
16 sensitization. And going to the IASP
17 definitions -- I just put them up there as a
18 reminder of increased responsiveness of
19 nociceptors -- central sensitization was broadened
20 by ISAP. I call this recent. When you've been
21 around a long time, 2008 is recent, but it is
22 increased responsiveness of any part of the central

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1 nervous system nociceptive pathway.
2 I read the Hopkins article, Raj was included
3 in that, and they called, true central
4 sensitization, and it was inspiring to read, a
5 really rigorous characterization of central
6 sensitization.
7 So Dan, I stayed broad, but acute pain
8 minutes to weeks, we'll throw it out there. That's
9 good. And in the sensitization, I said early acute
10 pain, off the top of my head, as high local amounts
11 of pain mediators and sensitizing agents, and a
12 prominent peripheral nociceptor activation and
13 sensitization. However, with the broad definition
14 by the IASP that anything activated in the central
15 nervous system is now central sensitization, using
16 the very broad definition, this is occurring as it
17 makes its way up to the central nervous system.
18 I'm going to posit that in chronic
19 pain -- I'll put it out there. Chase me down at
20 lunch if you disagree -- there are less local
21 mediators in chronic pain conditions, but
22 nevertheless, it's still peripherally maintained.

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1 We do trigger points in myofascial pain. We get a
2 pretty good response.
3 I threw out , I think chronic pain, a lot of
4 chronic pain has structural problems rather than
5 mediator problems, neuromas. Steve mentioned
6 tendinopathy. I'm glad he did that as we're
7 onboard. But central sensitization may be more
8 prominent in chronic pain than acute pain. And I
9 think I was hurt [indiscernible] -- did nerve
10 blocks on upper extremity phantom and had a
11 50 percent response rate.
12 So we still can't get far from chronic pain
13 with this sensitization topic. There is central
14 sensitization in acute pain. The area of secondary
15 hyperalgesia is one surrogate of central
16 sensitization. It's only one, and it has a limited
17 clinical relevance. Certainly in the acute pain
18 setting, we can talk about central sensitization's
19 engagement of affect of anything supraspinal. I'll
20 leave it at that.
21 Acute phantom pain may have a strong
22 component of central sensitization. And I think I

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1 was worried about too many slides, but every time
2 somebody's getting a shoulder replacement, and they
3 get a nerve catheter, and we dose it up with local
4 anesthetic, it relieves their chronic pain almost
5 invariably. So even using peripheral versus
6 central sensitization as something to try to define
7 our acute pain doesn't separate, even difficult to
8 separate from chronic pain.
9 Most acute pain is strongly driven by
10 peripheral sensitization, certainly in days, maybe
11 up to weeks. The importance of peripheral
12 sensitization even in chronic pain patients
13 prevents using it I think or makes it very
14 difficult to categorize acute pain. And the role
15 of central sensitization, we already threw that out
16 there. I think it's central, et cetera, and
17 chronic pain is an area of active study by Roger
18 and others.
19 Okay. I didn't get too far with pain
20 mechanisms. This is up for discussion, but I don't
21 have very far to go. But certainly, if we can find
22 a mediator that's generated in one condition but

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1 not another, we can maybe classify our acute pain.
2 So I did go pick one of these articles like
3 John Levin had the lists of mediators. I don't
4 remember if this was dental or not. And these
5 are -- if we're doing basic science, if we're doing
6 that, we need to recognize our limitations. So I
7 changed theirs to hypothesized mediators, and
8 they're redundant in various acute pain states.
9 So well, prostaglandin, that's a good one,
10 and I struggle with histamine. But CGRP, NGF, all
11 these, substance P, we've thrown out these. You
12 can pick up a review article. We're still there in
13 all these mediators. But at least I tried. Come
14 back and challenge me after lunch.
15 Clinically evident mediators in human
16 studies, we could go with prostaglandins, and I
17 said acute pain states. We'll go with
18 prostaglandins. If you'll bear with me, I think
19 Pfizer did some trials in acute pain that had some
20 markers in there, a little bit of a signal there.
21 Polycytokines, I haven't seen it, maybe you
22 have. Nitric oxide, bradykinin, the darling

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1 molecule of the '80s. Platelet activating factor,
2 wonderful. TNF-alpha, not in acute pain. So
3 everybody, all the rheumatoid arthritis patients
4 who come in loaded with their TNF-alpha don't come
5 back and say, you don't even need to see me, I
6 don't have any acute pain. It must be my
7 infliximab that I'm taking. It's completely
8 eliminated my acute pain. I don't see anything
9 there; maybe you do. But TNF-alpha in acute pain
10 states, unless it's an acute rheumatologic
11 condition, is different.
12 Substance P, no, didn't make the clinical
13 trials. Give me this for migraine at least; that
14 looks positive. ATP acid and lactate, those are
15 mine I added at the end. Not a lot of attention in
16 that area.
17 So can we classify things based on pain
18 mediators? pH lactate, there is some human data in
19 there that this ischemic like signal may be
20 present. I'll talk a little bit more about it.
21 It's present in incisions and, again, there's human
22 data there. Present in compartment syndromes.

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1 Tourniquet induced pain has this.
2 But I mention that this is present in OA.
3 And if you read some review articles on cancer pain
4 mechanisms, the tumor grows fast, outstrips its
5 vascular supply. Tumor cells love lactate, so
6 they're very good lactate consumers. We need new
7 vessels. When you make new vessels, nerves follow,
8 so that gets hyperinnervated and maybe is something
9 we're talking about for a cancer pain mechanism.
10 So this I think is important. It's my own
11 self-promotion here in pain mechanisms, but
12 recognize that it's present in other clinical
13 conditions that aren't even in acute.
14 NGF, we've studied this. Incisions, it's
15 present in humans in burns. It made the OA trials
16 there for this sort of scenario and is certainly
17 effective and went to bone cancer trials. I think
18 they were held up, but reasonable that this
19 neoinnervation that follows blood vessels is an NGF
20 dependent process.
21 The neovascularization appears. NGF appears
22 to play some role in that. If you do enough

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1 patients, the neovascularization doesn't go well,
2 and you end up holding the NGF trials for dead
3 bone, apparently, or linked, or let's say
4 associated for now.
5 Prostaglandins, we'd say OA, incisions of
6 soft tissue injury, and certainly the dental is
7 strong for prostaglandins. But there's a lot of
8 overlap, and we're going to struggle to do that.
9 So I said I'd show a few of my own slides,
10 and I'll begin with, in acute traumatic pain,
11 monocytes are called to the wound immediately by a
12 change in ReDoc status in traumatic tissue. So
13 there's trauma, and immediately the ReDoc status of
14 the tissue changes, generates peroxide. And
15 according to wound-healing literature that I think
16 I understand, immediately the monocytes and
17 macrophages go into the wound.
18 Macrophages can generate the acid lactate.
19 We've lost blood supply. The macrophages can
20 survive that. They like to generate lactate.
21 Wounds are hypoxic to stimulate neovascularization.
22 Nerves are cut. The yellow ones are cut. The red

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1 ones survive. So the red ones can respond to this
2 example of perhaps a signature for a variety of
3 pain conditions.
4 The difficulty in -- and this may occur in
5 myocardial ischemia in part, so let's be careful.
6 And just one example of that high peripheral
7 mediator, strong peripheral sensitization.
8 So in my opinion, acute and chronic pain
9 diseases share many of the same mediators. In
10 acute pain, trauma coagulation monocyte activation
11 produce a local environment for revascularization,
12 reinnervation, and a hostile environment for
13 bacteria, geared up environment for an
14 immune-mediated response to clean up the dead
15 cells, clean up bacteria.
16 That tissue, that local tissue repair, the
17 surgeons who study wound healing study the skin.
18 That same process is occurring in deep tissue and
19 we think is a very good pain generator. But that
20 repair process when transduced in nociceptors
21 contributes to pain, that process is redundant in
22 osteoarthritis and cancer as well, I think.

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1 So lunch is ready. Let's try two more
2 categories. Treatment, drug A is effective in
3 condition A but ineffective in condition B.
4 Unfortunately, gabapentin sort of became the broad
5 spectrum analgesic. When it came out, we said it
6 was an anti-neuralgic. We use it in total joint
7 replacements, breast surgery, and spine surgery.
8 Cyclooxygenase 2 inhibitors are good in the
9 perioperative period for orthopedic and neurologic
10 surgery. Maybe we get a little separation because
11 they're less remarkable in thoracic and gynecologic
12 surgery.
13 I showed you glucocorticoids look to be a
14 little bit better in laparoscopic hysterectomy and
15 cholecystectomy and less effective when the surgery
16 opens and becomes major.
17 I think Deb brought up in an email,
18 bisphosphonates have fair specificity for bone
19 related pain I think by impairing osteoclast
20 activation, which creates that high acid
21 environment for bone resorption.
22 So we can get some specificity, I think,

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1 because if you study the autoimmune phenomenon, and
2 drug companies have sort of gone okay, we've got
3 this, this and this, these are all conditions that
4 have been approved -- these are all drugs that have
5 been approved in these autoimmune conditions.
6 So if we can talk about acute autoimmune
7 conditions, we can separate ourselves out with
8 these drugs because I think they found very little
9 utility in other conditions, at least they haven't
10 been approved yet. And I think a part of an issue
11 is the pain field has viewed this as inflammation,
12 and that's chronic pain, but it's a specific
13 inflammatory pathway. The rheumatologists
14 capitalized on it and have done a remarkable job.
15 And we, in looking at etiology, aren't so good.
16 Someone asked me one time -- I gave the TNF
17 inhibitors in our incisional pain model. NGF
18 inhibitors worked, TNF inhibitors didn't work. And
19 they asked me what did I do wrong because it didn't
20 work. And I knew that the rheumatoid arthritis
21 patient, at least an acute one, has a totally
22 different response to a group of medications that

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1 acute pain patients do not respond to. So there's
2 a little bit of specificity here.
3 Many acute and chronic disease states share
4 the same treatments. COX-2 inhibitors have broad
5 efficacy, but appear to be stronger in orthopedic
6 related acute pain conditions, and I think Chris is
7 mentioning this tomorrow when he talks about post-
8 operative pain. We've got some specificity there
9 if we want to include autoimmune conditions.
10 This is my last hope. I saved it for last.
11 Tissue injured. So there are tissue-specific
12 responses to acute injury. And I think I'll posit
13 it's always a model that skin responds different
14 than ligament, that responds different than bone,
15 than vasculature that's injured, joint that's
16 injured, viscera that's injured, nerve that's
17 injured, or the dental area that's injured. They
18 respond differently to injury.
19 So I said here, off the top of my head, if
20 someone does a small skin incision on my foot, it's
21 cutaneous injury, it's not too bad. I'm going to
22 have some hyperalgesia if I walk on it. But at

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1 least by my observing others who've had plantar
2 fascia release at that same area, they struggle to
3 walk for weeks and have a pretty significant amount
4 of hyperalgesia, long-lasting and of greater
5 intensity.
6 So we've gone skin, skin and fascia, and
7 let's add bone. But if we do a hip replacement now
8 we've injured skin, and we've injured fascia, we've
9 injured muscle, we've injured ligament, and we've
10 injured bone, and that produces a much greater
11 intensity of response.
12 Pick a different surgery, we injure skin, we
13 injure fascia, we injure muscle. Let's include the
14 peritoneum. I think there's a little bit of
15 literature that if we deep, local anesthesia has
16 high efficacy. And then we injure the viscera, and
17 we don't understand that well.
18 On the acute pain service, sometimes someone
19 will be scheduled for an eight-hour Whipple. It's
20 open and close. You have to be careful when you're
21 rounding because you go and see them, and it's
22 noon, and they're done, and they look great because

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1 they had a 1-hour surgery, not an 8-hour surgery.
2 Less injury here, less retraction of muscle and
3 fascia, but those seem to be components to that.
4 So tissue transduction does -- I guess I'm a
5 little bit self-promoting here -- but does have
6 some specificity, differences in visceral afferents
7 and what they're expressing. Subchondral bone
8 afferents have a lot of the NGF receptor, which
9 made them useful in the OA trials.
10 We have nociceptive markers that are
11 associated with tissue signatures that may not be
12 causal, but I'm optimistic. My favorite is tissue
13 injured.
14 If we want to look at mechanism -- this is a
15 slide a graduate student dug out for me on hip
16 replacement patients. There is pain at rest. In
17 two different studies from the same journal, from
18 different organizations, they did a non-invasive
19 hip surgery, and then the surgeon got permission to
20 extend the skin, to double the size of the skin
21 incision. There was no difference in pain and
22 opioid consumption.

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1 If they did the minimally invasive surgery,
2 different group, versus dividing tendon, muscle,
3 ligament and fascia, they had greater pain and
4 greater opioid consumption with more fascia muscle
5 and ligament injury.
6 So there is evidence, at least I like to
7 think, I'm biased, of tissue specific mediators,
8 receptors and responses. The skin is great for
9 studying heat and mechanical hyperalgesia in
10 rodents, but deep tissue likely generates clinical
11 pain, at least if you'll buy the previous slide.
12 Acute ischemic pain appears to be a muscular
13 pain rather than a cutaneous pain. Someone
14 thromboses, their propliteal artery, they've got
15 cramping in their muscle, usually not complaining
16 about the skin, and changing the degree of
17 cutaneous injury has little effect.
18 Acute pain and repair, it's linked to
19 neovascularization. Repair mechanisms vary with
20 tissue. The repair people are ahead of the pain
21 people. But there's also redundancy. There's this
22 receptor that we think is a pain mediator present

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1 in joint, viscera, muscle, and skin. In the
2 trachea, may mediate some asthma, not pain, but in
3 muscle it may mediate pain, for example.
4 So I already concluded at the beginning of
5 the talk, and now I'll conclude again, can these
6 mechanisms inform classification of acute pain
7 conditions? And the first thing I'll say is, not
8 very easily. The cup is a quarter full. We don't
9 have sufficient information. We need the other
10 three-quarters.
11 In my opinion, my straw, throwing down the
12 first straw of the meeting for Bob's straw man, the
13 best opportunity for pathophysiologic
14 classification may be in the types of tissue
15 injured. Thank you.
16 (Applause.)
17 DR. BRENNAN: Do you want to go straight to
18 lunch? Okay. Fire. Bring it on. Henrik?
19 DR. KEHLET: I think this was a very
20 eloquent talk, and it clearly argued for us to
21 focus on the early acute pain phase.
22 (Laughter.)

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1 DR. BRENNAN: It's so difficult to dissect
2 different acute pain states. Other than time to
3 separate acute and chronic, the pain system needs
4 some really good pathways to work well, to be
5 linked to wound healing, to be linked to alarming
6 systems. And so it can use the same ones in both
7 acute and chronic pain states.
8 Yes, Suresh?
9 DR. SURESH: So Tim, thank you very much for
10 this talk. An other question that will come up,
11 and I think will come up in discussions further, is
12 what happens with acute on chronic pain? Are the
13 mediators going to be different as opposed to the
14 mediators for chronic pain alone? We have a whole
15 group of these individuals who are coming back for
16 surgery, et cetera, and how do we deal with them?
17 DR. BRENNAN: I'm going to say the mediators
18 aren't -- I won't expect the mediators in the
19 peripheral tissue to be profound in chronic pain
20 states. If there's a chronic infection there,
21 you're going to find that. But when we've looked
22 for what are the mediators and trigger points, you

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1 can't find them.
2 I think it's become scarred, maybe from
3 healing, and maybe it's structural, or it's
4 hyperinnervated. I'll throw that out as one of the
5 ways chronic pain distinguishes from acute pain.
6 So I don't think they're there. I think they
7 disappear as neovascularization develops.
8 Yes, Greg?
9 DR. TERMAN: I'm not sure it's relevant, but
10 I'd be interested in a couple of words on
11 allodynia. Your definition of central
12 sensitization sounded a lot more like hyperalgesia
13 than allodynia, just because of responding more but
14 in a normal -- to the normal stimuli.
15 DR. BRENNAN: I think the IASP kind of put
16 allodynia and hyperalgesia on a continuum on that
17 2008 definition. So I think they kind of just said
18 it's all hyperalgesia throughout the spectrum of
19 stimuli. I thought -- and anyone else can comment,
20 but I thought that was the case. And they
21 broadened central sensitization quite a bit. So we
22 could all study central sensitization because once

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1 it gets past the afferent, it's all central.
2 MALE SPEAKER: Thanks for a good talk. I
3 really like the point about starting with tissue
4 injury because since we spent the morning -- I'll
5 admit, and I don't want to throw tomorrow on its
6 head, but I'm having a real tough time with the
7 5 dimensions and trying to fit broad stroke acute
8 pain states into the 5 dimensions.
9 Pat's probably going to be talking after
10 lunch, and I think it's going to be a great
11 follow-up talk to yours, because I'm almost
12 wondering -- and I know it's going to come up on
13 the discussion this afternoon probably, is do we
14 just need to not throw out the dimensions, but
15 completely or at least consider redefining them in
16 terms of acute pain? And I think a good discussion
17 point later today would be is tissue injury
18 actually the first dimension we should start with.
19 I purely conceptualize it in my head, but
20 just wanted to throw that out there because I'm
21 sure that topic is going to come up for
22 conversation in terms of redoing all the dimensions

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1 to fit a better acute pain state. I hear your
2 point, and I think tissue injury should be
3 discussed, and I think that might be a good pure
4 place to start with.
5 DR. BRENNAN: Okay. Noted.
6 Yes. All right.
7 DR. TURK: So if there are no more
8 questions, we'll break for an hour for lunch. One
9 announcement. We've changed the agenda. So at
10 1:00, Patrick will be giving his talk. That will
11 be followed at 1:45 by Steve Bruehl giving the talk
12 he was going to give tomorrow afternoon, but we've
13 upgraded it to this afternoon. Then there will be
14 a coffee break at 2:30, and 3:00 until midnight
15 will be the panel discussion and Q&A.
16 (Laughter.)
17 (Whereupon, at 11:58 a.m., a lunch recess
18 was taken.)
19
20
21
22

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1 AFTERNOON SESSION
2 (1:12 p.m.)
3 DR. CARR: All right. Can you all hear me?
4 The mic is working? What I'm going to do is get us
5 going. We're a few minutes late, but we'll pick up
6 the slack, and we should be back on schedule before
7 long.
8 As you heard this morning, at the end of the
9 morning session, we're switching the sequences a
10 little bit. So it seemed to make more sense to get
11 more foundational work and throw out some more
12 fundamental ideas.
13 I've known Patrick for several years, and he
14 is absolutely an idea person who brings expertise
15 in mathematical modeling and almost philosophy, if
16 you will, to the issue of acute pain and big data,
17 how to manipulate it, and how to data mine, and so
18 on.
19 So I'm very much looking forward to the
20 talk. I had a sneak preview, and I thought it was
21 tremendously thought provoking. So Patrick, the
22 stand is yours.

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1 Presentation – Patrick Tighe
2 DR. TIGHE: Hi there. Good afternoon,
3 everybody. Can everybody hear me okay? Fantastic.
4 My name is Patrick Tighe. I am an
5 anesthesiologist at the University of Florida, and
6 we're going to talk a little bit this afternoon
7 about towards the taxonomy of acute pain
8 conditions, lumping versus splitting and other
9 general considerations.
10 Now, this is a little bit different in that
11 we're not going to be focused directly on pain
12 itself, but really more the organization of
13 information as we look at how best to organize our
14 ontologies or taxonomies.
15 For disclosures, I have no financial
16 conflicts of interest to report. The most
17 important non-financial conflict of interest is my
18 family, mentors, collaborators and colleagues.
19 This is truly a team effort, and there's no way we
20 could have done any of this work even with just a
21 portion of the wonderful support system we have
22 behind us.

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1 The three topics we're going to go over
2 today, first we'll go over the need for ontologies
3 and why this is so important. We'll look at
4 something called schema architectures, which is
5 different ways we can organize how we approach this
6 group to give information about pain. And finally,
7 we'll talk about the potential applications to the
8 actions I mentioned that we've discussed so far
9 this morning.
10 So the need for ontologies, we need these
11 now more than ever. But I'd like to start by
12 defining a few terms, and the first is a
13 vocabulary. Well a vocabulary in this sense is a
14 very specific connotation. It's a list of terms
15 that don't really carry any context.
16 There's no organizational schema to this.
17 Blue, pizza, bubble, beach, red, hamburger, you
18 might be able to infer some similarity between the
19 concept of hamburger and pizza, but aside from
20 this, just a wash. It's a flat listing. There's
21 no organization whatsoever.
22 So how does this differ from a taxonomy?

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1 The taxonomy is an organizational listing of items
2 in tree form. As most of us learned at some point
3 in school, we have kingdom, phylum, class, order,
4 family, genus, species. This is how we organize
5 organisms in terms of some type of classification.
6 Notice this is generally quite linear, and
7 generally a species is a member of single genus,
8 which is a member of a single family, et cetera.
9 There is not a lot of overlap here.
10 So this fits very well into the
11 organizational structures we've tried to use
12 already today, where we take one concept of pain
13 and try and lump it into a single organizational
14 structure whatsoever.
15 This is incredibly helpful. These are very
16 valuable in any types of classification schema.
17 It's typified by a tree structure. And we see here
18 a relatively simple structure. We have one parent
19 and multiple children. But in general, we don't
20 see multiple children belonging to multiple
21 parents. It's usually a one-to-one type of
22 matching going from bottom up.

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1 This differs a fair bit from an ontology,
2 where we look at organizing a multifaceted complex
3 collection of relationships, and I have a wonderful
4 definition here courtesy of Wikipedia. But really
5 what's important is this allows us to interconnect
6 what would otherwise be different conceptual
7 mappings.
8 So now, with an ontology, I can map and
9 define all sorts of pain related concepts, and I
10 can relate it to other domains, such as health
11 policy, or education. And I can begin networking
12 things together.
13 Interestingly, this is the approach that a
14 lot of our computer science and database folks of
15 latched onto because it allows them to have a very
16 robust structure. And when we organize data in
17 this methodology, we can then leverage it, we can
18 do things with it, we can operate on it, and it
19 enables a much stronger sense of research.
20 So what does that look like? Well, we
21 talked previously in taxonomy about a general
22 ontology, or a general tree structure. And we see

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1 here an ontology that were much more different.
2 We still have elements of a tree structure,
3 but we can separate out to a number of different
4 areas, and some of these can actually be
5 interrelated. So there was a discussion earlier
6 about a patient with bone pain from a sickle
7 crisis, and we see here that an ontologic
8 representation allows us to link children together,
9 even across what would appear to be relatively
10 different superordinate settings.
11 So now I can have a method of measuring
12 blood pressure, such as arterial line, and we can
13 also refer to it as the type of site that we're
14 using it. Is that femoral? Is that arterial line
15 in the aorta, or perhaps femoral, or radial, or
16 others?
17 Another important feature of this is that we
18 can take our blood pressure and link it to heart
19 rate. And this is obviously a very dynamic,
20 complex relationship in physiology. But we now
21 have a schema to look at how these two concepts can
22 interrelate with one another.

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1 guess that's okay, too.
2 Thirty minutes later, we were still having a
3 discussion about what kind of blood pressures we
4 wanted, before and after surgery, just after
5 surgery. What if there was discordance? What if
6 we had two measurements within 3 minutes of each
7 other? What if they were different?
8 It turns out that for something that I
9 thought was as simple as blood pressure, it's an
10 incredibly rich representation of concepts that we
11 need to map out. And it's not just for a research
12 purpose, for blood pressure. It's not even for a
13 diagnostic purpose. It's actually so we can enable
14 the operation of our clinical enterprise.
15 Our electronic medical records depend upon
16 an accurate organization of the information;
17 otherwise I don't know what I'm putting down in the
18 record, and I don't know what I'm reading when I go
19 to make a medical decision. So it's even more
20 fundamental than establishing research and clinical
21 diagnoses. It actually enables us to provide a
22 substrate with which to build a research enterprise

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1 It's much more than just a tree-like
2 structure. It enables us to have a lot more
3 flexibility to map what I think a lot of us intuit
4 from our different perspectives of how this
5 constellation of observations of a patient who is
6 suffering from pain, how we can begin to try and
7 niche it out into our own organizational
8 perspective and maybe objectify it a little bit
9 further.
10 Why are they so important now? Well, I
11 would say three simple words, "electronic medical
12 records." We had a research protocol a little
13 while ago that we simply said, hey, we'd like to
14 look at the blood pressure for patients after
15 surgery. And they said, okay, what kind of blood
16 pressure? And we said, well, their blood pressure?
17 (Laughter.)
18 DR. TIGHE: They said what kind of blood
19 pressure? What do mean? Well, would you like
20 their systolic and diastolic? Well, yes, oh yes,
21 systolic and diastolic and mean. From which site?
22 Either arm should be okay. Is a leg okay? Well I

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1 and to build a clinical enterprise.
2 What does that value mean I think is one of
3 the core tenets that we've run into with
4 ontologies. When somebody tells me they're in
5 pain, what does that mean? There's some discussion
6 of validity and such, but this becomes very
7 concrete when we're looking at medical records and
8 other databases.
9 When you say that this patient has acute
10 pain after a total knee arthroplasty, how do I know
11 that you mean a tri-compartmental knee arthroplasty
12 versus a uni-compartmental knee arthroplasty? We
13 have to be very concrete and specific.
14 We also have to be able to roll things up.
15 And this requires us to start defining variables,
16 in some cases by other variables. It's like an
17 algebra of organization. I don't necessarily even
18 need to know what the exact term is, I just need to
19 know what the representations are in some cases.
20 But this enables us a considerable amount of
21 flexibility not just for how we look at things
22 organized today, but how we may look for things

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1 that are organized when we discover mechanisms that
2 we don't know about today -- when we discover new
3 treatments that we don't have a lock on today.
4 These ontologies have shown themselves to be
5 incredibly robust about adapting to those future
6 cases.
7 So how do we actually do this? And I think
8 this is a really fun way of looking at it because
9 it speaks to the quantitative parts of our mind.
10 By the way, the mathematicians and engineers we
11 work with, they love to look at pain research
12 because they can't find really a messier problem
13 that is less deterministic than pain.
14 You know, they talk about airflow over a
15 wing. Well, there are physics to describe that.
16 And heart rate and blood pressure interactions,
17 they're pretty good physical models. When we talk
18 about pain, all bets are off. It's really a very
19 rich collaboration, but they still want to organize
20 it, and I don't blame them.
21 So there is actually an entire international
22 standard for how we organize information. It's

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1 called the Unified Markup Language, or the UML.
2 And the schema simply denotes what that looks like,
3 what does that roadmap look like.
4 So three different domains. First, we were
5 kind of defining an acute pain taxonomy or ontology
6 if we link this up further. We'd eventually like
7 to disseminate this, and this is what Mike is going
8 to be working on this afternoon to get it in print
9 tomorrow. And then we'd eventually like to
10 operationalize this to use in research in clinical
11 and other domains, public policy, education,
12 et cetera.
13 What does our timeline look like? Well,
14 we're doing this today and tomorrow, and Mike's
15 going to disseminate this tomorrow. But this is
16 going to go on and on and on, and we're going to
17 have to -- this is going to be repeated, to some
18 extent, but we're always going to need to use this
19 ontology.
20 This is not a one day event. It's not going
21 to be a recurring one day event. What we do today
22 makes a difference for a very long time. And we

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1 actualize this good, very rich discussion. We'll
2 disseminate this for a publication and other output
3 venues. But really, the operationalized systems,
4 at least in this generation, it's through the
5 electronic medical record systems because then it's
6 in the United States being the common interacting
7 footprint, and we need really big data sets.
8 In one of our recent experiments, we were
9 looking at 144 different types of states for a
10 given pain intensity rating in terms of how they
11 transition. And one of our researchers said, "I'd
12 like to consider just one more step in the
13 sequence." And we went from 144 different states
14 to 20,500 different states with just one more
15 consideration. And if we went up to two
16 considerations, we'd be well over a million.
17 So we're going to need, at some point, to
18 start looking at how we can unify this across the
19 country, hopefully across the world. And that's
20 going to be very dependent upon having an accurate
21 ontology, so that when I talk about post-operative
22 total knee arthroplasty pain, I know that somebody

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1 else is talking about the exact same concept in the
2 exact same context.
3 There are established components of an
4 ontology that are pretty well typified no matter
5 what the domain is. Our domain is in pain, but if
6 you were talking about airplane parts, we'd have a
7 similar ontology, or a similar description of
8 components, and the first is the classes.
9 So this is the general category. In
10 general, as we'll get to later, we might think of
11 chronic pain as a class, and acute pain as a broad
12 class. The objects are those individual instances.
13 So if I talked about a class of cars, an individual
14 instance might be a Porsche 911, which seems like
15 it would be a lot of fun to drive. If we looked at
16 attributes, those are the descriptors of that
17 object.
18 So how do I differentiate a Volkswagen
19 Beetle from a minivan made by Toyota? Well, there
20 are lots of different characteristics, and those
21 are the attributes of those. And we saw in the
22 prior example that we were looking at not just the

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1 value, but also the sites and the types and such.
2 One of the concepts I haven't heard
3 mentioned yet, but I think is a really exciting
4 opportunity, is this consideration of the methods
5 component, and these are things we can do to the
6 construct. I can diagnose pain. I can treat pain.
7 I can risk stratify pain. I can look at pain
8 outcomes. These are things that I can actually act
9 upon the object in question.
10 So with the blood pressure, I can decrease
11 it. With a car, I can drive it and steer it. But
12 we now have a formal mechanism of organizing the
13 methods, the things we can act upon for that
14 construct, and look at organizing that as well.
15 The key, though, at the end of the day is
16 the relationship. And it's not just the one-to-one
17 vertical tree-like structure, but this can be very
18 intricate in networks horizontally as well. A lot
19 of times, we actualize this by looking at the
20 verbiage, so we see blood pressure is a vital sign.
21 It has a site. It interacts with. Those are the
22 key buzz words that are denoting the interaction.

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1 So in your discourse and discussions, if you
2 realize that using the frame, acute pain has a
3 mechanism, oh, well we have a relationship there,
4 and it's worth mapping this out as we move forward.
5 So we'll go over some of these broader
6 constructs. The first is the notation for the
7 schema of classes, simply usually a box, and we
8 have a vehicle. We can actually put specific
9 instances of that vehicle, usually after a colon,
10 or sometimes as a separate line.
11 Keep in mind, though, that we can have lots
12 of different cars, and so in some cases, this ends
13 up being very -- we call them super classes or
14 subclasses. So just because I have an object in
15 this car, I can also redefine car as another type
16 of subclass, and we can go on and on. We'll get
17 later into some discussions about where we draw the
18 line and say, no, this is too much splitting or too
19 much aggregation.
20 The Unified Markup Language organization is
21 very neat, at least according to our engineering
22 colleagues. We have the object name or the class,

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1 in this case up here, which is a car. We have the
2 attributes listed here. Then we have the things we
3 can do, or the methods listed below. So it's a
4 nice organizational approach to mapping out these
5 concepts. We can have a class, and again, it
6 denotes a specific object. Notice the organization
7 is very similar, but we have specific instances or
8 vocabularies.
9 Earlier, we had talked about whether there
10 was a given vocabulary or listing of terms that
11 would fully describe and attribute, and this in
12 that case would be let's look at all the different
13 colors we could paint a car, or all the different
14 engines we could put in a car. And at some point,
15 then you have a menu item of things.
16 That helps a whole lot when we're starting
17 to trade information and make sure that all of our
18 schemas agree with one another, that when I say I
19 have a silver car, I also know that you have a
20 silver car when you say silver, and we're not
21 talking about charcoal grey versus black.
22 The attributes can also take a slightly

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1 different variance here. We can talk about
2 intrinsic properties of the object, and this is
3 more of the philosophical discussion. Those are
4 the physically imbued objects -- or physically
5 imbued properties that are characteristic of that
6 object. There's generally not debate about what we
7 see there. Then there are the extrinsic, the ones
8 that depend on external relationships, prior
9 perspectives, a little bit of opinion, et cetera,
10 et cetera.
11 Very importantly, just as we talked about
12 how objects sometimes need to be reconsidered as
13 classes, sometimes attributes can be classes onto
14 themselves. Confusing, but allows us to further
15 characterize what an engine is.
16 I probably don't need a whole lot of
17 characterizations about color, but I may want to
18 look at a 4 cylinder versus 6 cylinder engine for
19 instance. And I'm going back to the engineering
20 example here because this is concrete. There's not
21 a lot of debate. I think a lot of us have
22 exposures and experience with motor vehicles, so we

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1 can put this into a little different context.
2 We'll come back to map it to pain in a little
3 while.
4 The relationships end up being the last
5 component, probably the most important. And if I
6 had a question of like what was your trip like, I
7 can look at different domains, the food, the
8 people, the hotel, and notice with the vehicles I
9 can talk about the different kinds of
10 transportation you used during that trip. But I
11 can also get circular. I can offer a class or a
12 construct such as parking that ties maybe what the
13 parking was like at the hotel, but also what that
14 vehicle was like.
15 So I'm not going to offer any specifics
16 here, but this is a framework for when we're
17 discussing about acute pain and we have things
18 start crossing into different domains and
19 overlapping, we now have a way of visualizing this,
20 and at least reliably reporting it from one party
21 to another, so that we can at least agree what
22 we're trying to say. And whether that's the right

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1 thing or wrong thing, that's a different
2 discussion, but hey, we have a tool in the toolbox
3 now.
4 When we developed this schema, we also have
5 a concept called "inheritance." And what this
6 means is that each of the attributes share
7 something in similar to the class above it. So if
8 I have a class of cars, that's a subclass of
9 vehicles. We can begin to see that these take some
10 of the characteristics of its parent class.
11 Now strictly, it's supposed to subsume all
12 of the characteristics of its parent class, and
13 then offer some additional ones. But there's lots
14 of ample opportunities for this to be violated in
15 practice.
16 So what we see, again, looking at our
17 relationships is that a bike is a vehicle. A car
18 is a vehicle, and a plane is a vehicle, too. We
19 have a parent or super class. We use these terms
20 interchangeably, and children are subclasses. We
21 have more general as we go up, and more specific.
22 We generally try not to get more general as we go

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1 down. We need to reorganize that if that's the
2 case.
3 Very importantly though, we say, gee, this
4 plane is just a different kind of vehicle, right?
5 There's a lot of -- I mean, cars and bikes
6 generally don't have wings. They generally don't
7 climb, or at least into the air. And so we may
8 have to put in an intervening super class here so
9 that we can further differentiate planes into
10 helicopters, airplanes, jetliners, rockets, what
11 have you.
12 It's an organizational approach, but in
13 doing so, each of those subtypes of planes will
14 still carry the key characteristics of the vehicle
15 as we defined it. Again, it allows us that
16 vertical structure so that we can relate complex
17 relationships to keep the similar things kind of
18 similar, but still niche out so that we can take
19 care of the exceptions where they may be.
20 So how do you know how many classes and
21 subclasses to do? For instance, one of the worries
22 you have is that you could create a taxonomy that

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1 has a heading of chronic pain, and then 10,000
2 different types of chronic pain, each of them
3 incredibly narrowly specified.
4 Actually, that's quite elegant in many
5 domains, but it becomes very problematic if I try
6 to start lumping them together, such as I'd like to
7 look at all the patients with a headache. Okay,
8 there are a lot of reasons to say that headache's
9 not a good grouping example, but I may have a
10 reason to differentiate that from toe pain for some
11 research or clinical question.
12 So having a very flat horizontal structure
13 becomes problematic because I don't have a
14 mechanism where I can reliably cluster things
15 together with any measure of organization.
16 Some folks from Stanford suggested that we
17 should consider the 1 in 12 rule, where if you have
18 an organizational structure where one parent has
19 just one child, this child probably needs to be
20 rolled up into the parent. But likewise, if we
21 have more than 12 subclasses of a parent, we
22 probably need to put in some intervening groups up

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1 here. They don't need to be perfect. And again,
2 they can still cross laterally. But it begins to
3 suggest that when you organize this, it becomes a
4 little more human, human machine interpretable.
5 Another fascinating thing I think that was
6 brought up in the discussions this morning is just
7 what do you do when you have multiple inheritance
8 patterns? And we'll steer away from pain, and
9 we'll go to something a little simpler, wine, and
10 we'll say what if we have port wine?
11 Well, you could easily classify that as a
12 red wine. It is indeed the color red. But it's
13 commonly not a dinner wine, I am told. It's
14 usually used as a dessert wine. So where does it
15 fall?
16 So you could create a separate category, but
17 in an ontology, you just say, you know what, it's
18 got attributes of both. The types of attributes it
19 has are similar. We can talk about the color. We
20 can talk about the taste. We can talk about the
21 typical volume. And while those values will be
22 different, the attributes used to describe them,

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1 the categories of information used to describe them
2 are similar, whether we're looking at either of
3 those two parents. So this allows us again a lot
4 more flexibility in how we consider these concepts.
5 How do we know when we're thinking about a
6 new domain of knowledge whether we should consider
7 this a class or a concept under this framework?
8 Well, Noy McGuinness, again from Stanford, came up
9 with a very nice example. I won't read it to you,
10 but it gives an idea of whether we consider this as
11 a restriction, in other words does it disallow
12 certain other categorizations, or is it just
13 another characteristic that's going to be more
14 universally shared. And that can help us
15 distinguish between the two.
16 Another perspective on how you make this
17 decision is looking at how you would organize in
18 classes here. And again, we'll have all these
19 slides available to look at this in further detail.
20 This allows us to move to the top down,
21 bottom up approach. Now that we have that vertical
22 structure in mind, we can start with the general

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1 concept, broad classes, acute pain versus chronic
2 pain, toe pain versus headache. And do we work
3 down to is TPRV1 versus 2 presence in each of
4 those, and that's the top-down approach. Or we can
5 start with pure mechanisms, or treatments, or
6 method, or any other methodologies we'd like to
7 look like, and then try and aggregate in kind of a
8 bottom-up approach, if you will.
9 Why are we doing this again? Well, it
10 allows us to independently decompose each
11 characteristic. So we can say, well let's look at
12 classes and then specific instances of acute pain
13 for instance here, post-operative, amputation,
14 central traumatic, cancer. And we can separate out
15 the attributes, or I think the dimensions did a
16 very nice job of aggregating many of the common
17 attributes that we may want to flesh out in this.
18 But we also now have this new concept of methods
19 when we say what can we do to that pain.
20 So as we think of new terms, we can start by
21 saying, how would we put those terms into this
22 general framework.

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1 Very interestingly, there's a five-step
2 program for lots of things, that includes making an
3 ontology. And the first test, as the good
4 Dr. Mackay pointed out that's a preamble to this,
5 is try and borrow from somebody else first. That
6 may not be available and commonly isn't, but it's
7 still worth looking.
8 I will say that my interpretation so far of
9 ICD-10 and SNOMED CT, it does some of what we would
10 like, but not quite there. But very importantly,
11 everything we do for the rest of these five steps
12 will probably have to be remapped in some variety
13 back to those other sources so that we can have
14 some type of common language when we're discussing
15 these concepts.
16 After you determine the domain and scope of
17 what we'd like to talk about, so we're going to
18 talk about acute pain today, and we're not going to
19 talk about the environment. We're not going to
20 talk about political landscapes. We've defined our
21 domain and scope to some extent.
22 Then we list in a brainstorming session the

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1 terms for consideration. And a lot of this has
2 already been done it sounds like in the first
3 meeting, where we then looked at different classes
4 and hierarchies, but more importantly attributes as
5 well.

6 So those terms, if you will, would be what
7 we'd flesh out into here. And we just have a broad
8 vocabulary of terms, and we'd start slotting them
9 in, whether they're classes, attributes, methods,
10 et cetera. And there's a lot of discussion, I'm
11 certain, to be had in that framework.

12 Then you start creating specific objects,
13 specific instances, and I think of these as those
14 exemplars that were discussed earlier this morning.
15 We're going to talk about certain subtypes of pain
16 that are universally agreed clusters, if you will,
17 that we kind of look at and say, yeah, I'll agree
18 that there is a subtype of acute pain that may be
19 associated with post-amputation pain. But those
20 are specific objects that are going to carry their
21 own set of characteristics and will probably be
22 hierarchically related in some variety to other

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1 concepts, even if they're just considered a subtype
2 of acute pain.

3 So what does that mean for us today? Well,
4 if we look at our 5 dimensions that were discussed
5 elegantly earlier in our talk, we see that there
6 are very much attributes. We can look at the core
7 diagnostic criteria of a type of acute pain, the
8 features of that pain, the medical comorbidities,
9 consequences, risks, and protective factors.

10 We could offer the opportunity to include
11 additional dimensions or attributes such as the
12 temporal nature. You could consider listing the
13 response to treatment, or you could consider that
14 just as a method. But these are the different ways
15 we can characterize those concepts, if you will.

16 So we'll kind of zoom in here. These are
17 our attributes. And the attributes are then kind
18 of put out there as the terms we'd like, and then
19 we'll talk about the classes. We talked about
20 those exemplar papers here. And there's already
21 been some discussion of subclasses of acute pain
22 that will be the topic of many excellent talks

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1 tomorrow throughout the day. And those are
2 basically soft entries into what we'll see
3 here -- in just a second, I'm sorry -- the objects.

4 I think it is worth discussing whether we
5 should include the methods earlier. Entire lead up
6 discussions to this meeting, there had been some
7 talk about, well, gee, should we have quantitative
8 sensory testing characteristics then as an
9 attribute? Could we look at imaging results, for
10 better and for worse, and their specificity and
11 sensitivity as attributes, or should we consider
12 those as a holdout category of things that we can
13 do on these pain concepts?

14 They're methods. They're things we can do
15 for a patient presenting with a specific type of
16 pain, or not to. It's okay to keep some of these
17 empty.

18 Very importantly, each of these can be
19 lumped and further cut into a separate series of
20 classes onto themselves. So for instance, we may
21 have several different imaging modalities that we
22 may want to separate. We may want to have entire

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1 separate classes of mechanisms for comorbidities.
2 For instance, we may look at psychiatric
3 comorbidities and differentiate those from medical
4 and surgical comorbidities.

5 At the end of the day, this is what we're
6 trying to get to, I believe, in terms of looking at
7 some generally agreed upon subtypes of pain that
8 are going to be comprised of attributes and
9 potentially methods that are used to characterize
10 these objects. And these objects will fall into
11 some organizational structure under these classes.

12 It may be one layer, as has been known so
13 far with chronic pain. We may find that certain
14 types of objects share a large number of the
15 attribute details, such as mechanisms, the expected
16 comorbidities, perhaps response to treatment, and
17 that may serve as an opportunity to develop
18 subclasses for further organization.

19 So again, let's look back. We have
20 determined the domain and scope. We can list
21 important terms for those consideration. We've
22 defined classes and hierarchies for consideration.

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1 We may want to start lumping things together in 5
2 here based on the attributes we have for those
3 classes; again, a kind of overall schema of how
4 this would look like in a UML interface that would
5 be more applicable to electronic medical record
6 system or any database used to flesh out patient
7 specific details for where they fall under these
8 domains.

9 So now we can look at a couple of examples.
10 Let's say we have acute pain and we've decided
11 there's going to be a post-operative pain. We'll
12 have 5 different attributes, or maybe mechanisms.
13 And each of these diagnostic criteria may be a very
14 long list of things that could fulfill it. It
15 could be a dropdown menu. It could be values we
16 enter as integers.

17 We may do certain diagnostic tests to see if
18 it's post-operative pain. I'm not sure what those
19 would be, but you could. You could also say what
20 treatments this is most likely to respond to. That
21 may help us further segment these types of pain.

22 Again, we're going to organize it as super

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1 class and subclasses, the attributes and the
2 methods. We begin to see, well, here are a couple
3 different other subclasses of acute pain that we
4 can look at, and now we get into yet another layer.
5 So we've agreed that there is -- let's just pretend
6 that we've agreed that there's a post-operative
7 pain class based on the acute pain super class.

8 Well, let's call this alpha and beta. Maybe
9 this is thoracotomy and knee replacement. We see
10 that the attributes or dimensions are similar, but
11 the values used to fit in are different. The
12 values here can help us inform how to organize
13 these. We may be able to do that empirically, or
14 we may have to do this quite analytically.

15 Interestingly, the analytical approach is
16 very automatable and naturally updateable and can
17 allow us some objectivity in how we cluster these
18 things together, provided that we have an agreed
19 upon vocabulary or list of possible variables that
20 can be used to specify each of these attributes.

21 Another interesting detail is that despite
22 having two different types of post-operative pain,

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1 we can then further subdivide the treatments, these
2 methods, into their own sets of classes. So this
3 can become a little bit recursive, which is a
4 little confusing, but it also allows us
5 considerable flexibility so that we don't have to
6 know about all the treatments today. We just know
7 how we would characterize the treatments.

8 I don't have to know about all the different
9 types of post-operative pain today, or even all the
10 other subtypes of acute pain today. I just need to
11 know how we would characterize them, and that it's
12 okay to interrelate them to other disciplines as we
13 move forward.

14 Again objects, and here we have methods as
15 classes. We're allowed non-linear relationships,
16 so that we can give ourselves considerable
17 flexibility and allow us for overlapping.

18 I want to make sure I'm very clear on this
19 point. I am not suggesting that this is a
20 wonderful idea or the solution to all of our ills.
21 This may actually lead to a much messier definition
22 than we would like. But I think it's very

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1 important to recognize that the capability exists
2 and would fit in very well with other ontologic
3 structures used in other healthcare domains for
4 folks trying to link very difficult concepts where
5 they say, well, this is what we see and this is
6 what we're able to measure, but there's this
7 underlying truth of probably a lot more
8 complicated.

9 These non-linear confusing relationships are
10 an intervening step that allows us to take our
11 current concept map and still link it to some
12 future, better but unknown concept map that's
13 hopefully coming tomorrow or next decade.

14 So we've gone over the need for ontologies.
15 They're very important. This is how the United
16 States is rolling out its electronic medical record
17 system. At the end of the day, it's all about
18 where your data objects live and what they actually
19 mean when we talk about a blood pressure or an
20 acute pain episode.

21 The schema architectures I think are a nice
22 way for us to codify this as we have discussions or

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1 you're trying to get somebody else to say, oh, this
2 is what I mean, or this is how I would organize
3 this. I think it's a very nice, universally
4 accepted method that you can take to your hospital
5 folks, to your IT vendors, and say, look, this is
6 what we want to do. And instead of it being a
7 two-year project, hopefully it's something a little
8 more expedited because you've already taken the
9 initial intake steps.

10 We can readily apply this to the work that's
11 already been done. The concept mappings I think
12 are very clean. The dimension structure fits into
13 the attribute structure very well.

14 So even if we don't use any of the schema, I
15 think it's very important to take at least this
16 terminology back to your home institutions and say
17 this is what we'd like to do based upon what we've
18 agreed upon and this action team. Can you help us
19 with this? And they'll recognize that, hopefully,
20 and say yes. And we're four steps down the road
21 rather than having to try and figure out what each
22 other means.

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1 So thank you all very, very much for your
2 time. Appreciate it.
3 (Applause.)
4 DR. CARR: Thank you very much, Patrick.
5 So as we alluded to earlier, we will be
6 having a panel on the discussion of how or if the
7 AAPM dimensions should be modified, but in order to
8 continue to give and provide more thought and
9 context to support that later introduction, we've
10 moved up Steve Bruehl's talk from tomorrow
11 afternoon to today.

12 Steve played an integral role in CRPS and in
13 the whole scientific leadership of formation in an
14 evidence-based fashion of the AAPM dimensions.
15 Steve is a professor of anesthesiology at
16 Vanderbilt, and I'll turn the podium over to Steve.

17 Presentation – Stephen Bruehl
18 DR. BRUEHL: Thank you. Patrick, that was
19 excellent. I now understand on a much higher level
20 what we did with AAPM.
21 (Laughter.)
22 DR. BRUEHL: I guess we didn't do too badly.

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1 All right. So the reason I was moved up is
2 we were realizing, as we were listening to some of
3 the questions this morning and kind of what are
4 task is here today, that going over some specific
5 examples of Dimension 1 and the issues involved in
6 that might actually help focus our attention in a
7 more productive way.

8 Because as you can see already, there are
9 all these different directions we can go of on.

10 And at the end of the day here, we want to have a
11 plan for how to proceed with something that is
12 tangible and useable. And what I'm going to do is
13 talk about the Dimension 1 only, okay, not to say
14 that it's more important, but this is something
15 where we can actually validate what we're doing,
16 whatever we come up with, and I want to show how
17 you go about validating it.

18 I was telling somebody at lunch -- and you
19 will see in a sense that the emperor has no
20 clothes, and I will admit that right off
21 there -- just by the nature of what we're trying to
22 do, there are inherent problems in doing that and

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1 trying to take an empirical approach to proving
2 that we're doing something right. But I will
3 explain some of those ins and outs, and hopefully
4 that will help.

5 I think based on what Dan mentioned earlier,
6 this is all about constructing reality. We are
7 going to define what X condition is. That's our
8 job, and we have to do it as well as we can. But
9 that's really what we're trying to do is define
10 these conditions. Nobody else is doing this, or
11 they're not doing it the same way we are doing it.

12 According to what Patrick just said, I think
13 what we're going to be talking about here primarily
14 are the attributes, which would be the diagnostic
15 signs and symptoms that go with the objects, which
16 in this case would be a particular category of
17 chronic pain, is what I'm talking about here.

18 So, two issues to be considered. These are
19 just the conceptual issues here. One is validity,
20 and this is simple question, are we measuring what
21 we think we're measuring. The other one is
22 reliability. Can we measure the same thing over

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1 and over again and get essentially the same result,
2 either over time or across individuals?
3 Now, while these are independent constructs,
4 they do interact somewhat because you can't have a
5 valid diagnostic category that is not also
6 reliable. You have to have reliability for it to
7 be valid.
8 However, you could have an extremely
9 reliable set of diagnostic criteria that are
10 totally meaningless because they are not in any way
11 reflective of the way reality is. So we have to
12 keep in mind we need to in an ideal world
13 demonstrate both of these.
14 Now, I'm going to start out talking a little
15 bit about reliability. There are a couple of
16 different types that we're concerned with here.
17 One is interrater reliability. And this is if we
18 have the same patient seen by two different
19 physicians, would they both come up with the same
20 yes or no response to individual criteria within
21 our set of diagnostic criteria. And the second
22 related question is, would they come up with the

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1 same categorical yes/no answer as to does this
2 particular patient have this disorder. It's just a
3 dichotomous decision.
4 So it's kind of two levels of interrater
5 reliability. And then we've also got test/retest
6 reliability, and this just means over time, if we
7 were to make the diagnosis over a period of several
8 days, would this end up with the same result each
9 time. And would that dichotomous decision end up
10 being the same on each of those instances.
11 This can either be within one diagnostician,
12 and that would be what's sometimes referred to as
13 intrarater reliability. Or this could also be
14 across multiple clinicians.
15 This would be the situation where you've got
16 somebody comes into my clinic for a specialty
17 evaluation. I do it. I say you've got X disorder.
18 I send them back to the referring physician, and
19 the referring physician now is thinking, all right,
20 they say you have this disorder, now I'm going to
21 evaluate this, will I come up with the same
22 decision. So when you've got referrals, this is

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1 actually a real issue.
2 One aspect that's really important -- and
3 this ultimately comes down to wording. And I love
4 the people I've worked with on AAPT, but I have to
5 say that there have been varying levels of
6 appreciation for the importance of how things are
7 worded. Tiny wording changes can totally alter the
8 intent of things. They can totally change whether
9 they can be operationalized or not.
10 There are a couple of examples here, and
11 this is a real example from the IASP criteria for
12 CRPS. This was from the 1994 criteria. It said,
13 "Evidence of changes in skin blood flow."
14 Now, in one sense, that seems very clear
15 what that means, but when we say this person has to
16 be assessed, what does that really mean? Do I have
17 to get a Doppler, laser Doppler measurement to be
18 able to decide that? Is that something where I can
19 just look at the color of the skin? Do I need to
20 use an actual thermogram to quantify digital
21 temperature really finely? If so, over what area?
22 So there are all these layers of issues,

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1 kind of like the definitional issues that Patrick
2 was talking about a minute ago with blood pressure.
3 So ideally, we want to specify as clearly as
4 possible how you would assess these things.
5 Another hypothetical example, if we just say
6 progressive distal sensory abnormalities, well,
7 that's great except what are you including in that?
8 Positive signs? What about negative signs? Would
9 you treat those the same way? Would pain related
10 abnormalities be considered part of the sensory
11 abnormalities, or is that separate?
12 So how those are worded is going to have a
13 big influence on whether two people could agree
14 that that sign is present. So the wording is
15 important.
16 Also, let's say in a set of criteria we've
17 got four different specific criteria, and in some
18 cases it may be you have to have all of these to
19 get the diagnosis, but frequently there's kind of a
20 Chinese menu approach. You have to have at least 3
21 of these 5, or 3 of these 4, or whatever it may
22 be. Those are called decision rules. It's how you

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1 come to that dichotomous decision as to whether a
2 person has or meets the diagnostic criteria.
3 Now, obviously, if you have a rule that says
4 3 of 5 criteria have to be met, that's very
5 straightforward. It would be easy to have two
6 individuals agree on that. But in some
7 cases -- and I've actually seen some instances like
8 this in the older psychiatric manuals where there
9 are very complicated decision rules.
10 So you have to have criterion A. We've got
11 a list of five things for criterion B. You have to
12 have at least two of those. And criterion C, you
13 only have to have if you have less than 4 symptoms
14 in B, which makes you think a lot. And the more
15 complicated you get in those decision rules, the
16 less likely it is that two people are going to
17 agree that a given patient has the diagnosis. So
18 wording matters.
19 When we're talking about test/retest
20 reliability, we do have to consider the context of
21 the situation and would clinical features or those
22 diagnostic decisions be expected to be stable over

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1 whatever time period we're assessing them over.
2 Now, with acute pain, if we're comparing
3 day 7 to day 21 post-op, in many cases, we would
4 expect that there would be pretty dramatic changes
5 in those features over that period of time. So in
6 that context, test/retest reliability may not be
7 very meaningful. But if we're talking about two
8 evaluations in a given day or from day 1 to day 2,
9 we'd expect a fair level of consistency there.
10 I think the main thing to remember here is
11 criteria that can't lead to people making the same
12 diagnostic decision, both within a person over time
13 and between providers, really is not going to be of
14 very much use clinically if it can't do that over
15 brief periods of time get those same decisions.
16 So you can test this. There are different
17 ways of doing this, and these can either be focused
18 on the individual criteria themselves that we're
19 trying to operationalize, or it could be focused on
20 the overall diagnostic decisions.
21 One way of doing this simply and cheaply are
22 vignette studies. So an example of this might be,

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1 we would do a videotape of an actual patient being
2 examined, where it's done in a way where you could
3 actually see exactly what the clinician is looking
4 at. You can hear all the questions being asked.
5 You can hear the responses.
6 So we've got a standardized evaluation, and
7 now what we do is we hand clinicians our diagnostic
8 criteria and say, use these criteria based on the
9 information provided here on this video to tell me
10 whether this patient has X disorder. And you get
11 multiple people to do that. And that is one simple
12 and cheap way of finding out whether you have
13 reliability in those diagnostic decisions, or even
14 in those individual diagnostic criteria.
15 Now, the problem with that is that it
16 doesn't necessarily generalize well to real-world
17 clinic settings where you can interact with the
18 patient, get more information, redirect things. So
19 it has some utility, but I wouldn't want to rely
20 solely on that if I had the resources to do
21 something more than that.
22 But I think vignette studies could be useful

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1 for fine tuning wording before you do the expensive
2 studies, which we would call a field trial. And
3 this is where you've actually got real clinicians
4 with real patients sequentially doing evaluations
5 of the same patient, ideally over a couple of days,
6 so you can get at this both within individual and
7 between individual reliability issues.
8 So these are very doable studies. They can
9 be done on any particular condition. All you've
10 got to have to do this is some money, some
11 clinicians to do the evaluations, and you have to
12 have a draft set of criteria, or what is most
13 likely to be happen is we're going to have our
14 AAAPT-1, which are the consensus based/literature
15 based criteria. That would be what we would test
16 with this. And we might discover that some
17 particular aspect of this condition, the way we've
18 worded it is very unreliable.
19 Well, that tells us we need to alter those
20 criteria, improve them to address that problem.
21 And then if we do that with the vignette study, now
22 we can test it in the field trial and see if it

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1 works very well.

2 So not to bore you with statistics, but I do

3 want to mention a couple of things. And I have to

4 say, I saw this large -- it's in Europe. But it's

5 a government-funded study, huge study, and they

6 published this thing on test/retest reliability,

7 and they were reporting correlations.

8 That is a huge no-no because correlations do

9 not factor in that you're going to get agreement by

10 chance to a certain degree. So what we want to use

11 is something called kappa, which is kind of like a

12 correlation for dichotomous variables that would

13 factor in chance agreement. You're going to get an

14 inflated value if you're looking at correlations.

15 There's also something called the intraclass

16 correlation coefficient, which mathematically is

17 interrelated with kappa, but it can handle the

18 ordinal, interval, and ratio variables. They all

19 are kind of ranged just like a correlation would

20 between zero and 1, and higher is greater

21 reliability. And the gold standard in the

22 literature seems to be somewhere around 0.6 or

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1 is the origin of that?

2 Who defines it? Are we taking something

3 that came up with a consensus group that you read

4 somewhere and that's how you've defined it? It may

5 be perfectly acceptable to do that, I'm just saying

6 to think about, as you're creating these, where

7 you're getting the information you're basing those

8 diagnostic criteria on.

9 How do we measure that syndrome? How do we

10 measure the components, the clinical features of

11 that syndrome? Sadly, in many cases, and I'm sure

12 this doesn't apply to any of you, but there's a

13 situation where you will literally get the

14 response, "Well, I know it when I see it." Based

15 on what? "I just know what it looks like."

16 So it's like a gestalt. Maybe a little hard

17 to pin down exactly what they're looking at,

18 although I think that any clinician who says that,

19 you could probably work with them to put on paper

20 exactly what that means.

21 Finally, if you come up with this definition

22 that defines X disorder, will everyone agree on

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1 higher is acceptable. Obviously, the higher it is,

2 the better.

3 Now, I want to move on to talking a little

4 bit about validity. This is where the hard part of

5 this whole project comes in. So our question is,

6 do the criteria we come up with reflect what they

7 are supposed to reflect? So if we are targeting X

8 condition, whatever that is, do the criteria we

9 come up with accurately reflect that condition?

10 Conceptual issue, and I hate even having to

11 talk about this because it makes my head hurt. So

12 what is X pain syndrome? What defines what that

13 is? Take a step back from the way you normally

14 practice because you probably apply labels all the

15 time without really thinking always how you get to

16 that decision. But step back.

17 Where did you get the idea that these

18 particular features are what indicates a patient

19 has X? And what is that actually based on? Was

20 there anybody that ever proved that that was the

21 case? Was this your training? Was this some

22 consensus you've seen in the literature? So what

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1 this? Well, they probably won't because, as I said

2 at the beginning of this, we are constructing

3 reality and people have different realities. They

4 may not like what we come up with, but we have to

5 do something.

6 Now, the problems are that pain is

7 inherently subjective. Maybe Sean's imaging

8 research suggests there are some ways of

9 objectifying pain, but in normal circumstances

10 we're not going to have a means of doing that very

11 well. And because it is subjective and because we

12 don't know pathophysiology very well for most of

13 these conditions, we don't really have a gold

14 standard to use as our reference point for saying

15 that this set of criteria is good and this set is

16 bad. There is nothing independent of the

17 subjective pain itself.

18 I also have here noted this in quotes here,

19 "fuzzy boundaries." That's kind of my way of

20 thinking about what Patrick was talking about a

21 minute ago about the different classes, and how

22 closely or how far apart they are. Because you may

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1 have classes that literally overlap. They share so
2 many common features that if you were to map it
3 out, it would look like they really are not very
4 distinct. In this context we're talking about
5 certain chronic pain conditions.
6 An example I was actually involved in years
7 ago was migraine headache versus tension type
8 headache. Are they really two different types of
9 headaches? They overlap clearly a little bit.
10 They both involve head pain and may even share some
11 other characteristics in common, but are they
12 really different?
13 In some sense, in an effort like we're doing
14 here, what we're doing is we are arbitrarily saying
15 here's the dividing line between this condition and
16 that condition, and we're going to write our
17 criteria to make sure that there is a clear
18 dividing line. Now the reality underlying that may
19 be that those conditions do in fact overlap, but
20 that's something that we can actually test in
21 certain types of research we might do.
22 So because of the subjectivity and lack of a

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1 gold standard, any pain syndrome, whether it's
2 acute or chronic, is really at best going to be a
3 syndrome that is a construct, which we are assuming
4 exists. We have created something that we hope
5 reflects an underlying construct. And you cannot
6 show absolute validity for these constructs. The
7 best we're going to be able to get is relative
8 validity, relative to some reference standard we
9 pick.
10 There are several types of construct
11 validity that may be relevant; content validity,
12 that is are we actually doing a good job capturing
13 whatever the domain is that should be reflected by
14 that condition.
15 Now, this is the one place where patient
16 input may be particularly valuable because they may
17 be able to help inform what types of things they
18 consider important in somebody who has this type of
19 condition. So it's like are we measuring
20 adequately that whole domain that we're interested
21 in.
22 Internal validity, I'm not using in the

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1 sense that statistical design people would talk
2 about it. I'm talking about the validity of the
3 internal structure of the criteria. So if we've
4 got a diagnostic category and we have 4 different
5 diagnostic criteria within that, are the way that
6 the signs and symptoms are broken out across those
7 4 criteria valid? Do those subgroupings make
8 sense? And I'll give you an example later of
9 exactly why that issue is important in a pragmatic
10 situation.
11 Concurrent validity. So we pick a gold
12 standard. We don't have an absolute gold standard,
13 but we can pick something that is our surrogate for
14 that, and we can see do our criteria match up well
15 with that.
16 Convergent validity, I remember this phrase
17 from graduate school. I always liked it. The
18 nomological net. It sounds so mysterious. And
19 what it's talking about is we have this construct
20 we can't really measure that's floating in space
21 here, and around it we have all these things we can
22 measure, and we have expected associations between

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1 those measurables and what that underlying
2 construct is.
3 So the specific example that I would give of
4 this is in the ACR fibromyalgia criteria, they
5 don't explicitly talk about doing quantitative
6 sensory testing to look at degree of temporal
7 summation, which is an index of central
8 sensitization.
9 Now, theoretically we would expect
10 fibromyalgia to have a lot of central
11 sensitization, and we could measure this, but it's
12 not part of the diagnostic criteria. So that would
13 be an example of convergent validity, somebody
14 who's showing a high level of temporal summation
15 and getting the fibromyalgia diagnosis.
16 Finally, we've got discriminant validity,
17 and this is when we have two -- in this case, let's
18 say we're talking about two different acute pain
19 conditions, and we've got diagnostic criteria for
20 each. The question is, can we reliably distinguish
21 between those two conditions? And if we can't,
22 then we've got a real problem because it would

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1 suggest that maybe the objects in our class are not
2 two objects but rather a single object.
3 So if we have to pick a gold standard, what
4 do we use? If you go look at the literature on
5 people who have tried to validate diagnostic
6 criteria previously, they're really a pretty
7 limited number of features.
8 Now, pain is not like something like
9 Alzheimer's disease where you can do an autopsy and
10 look at the plaques, and look at their clinical
11 signs and symptoms before they died, and make a
12 direct association.
13 We have these, what I call sometimes the
14 bronze standard, or tin standard, or something a
15 lot less valuable than gold, but it's all we've
16 got. Now, we might use whatever the current
17 consensus based diagnostic criteria are.
18 So when we developed the CRPS criteria that
19 were adopted by the IASP in 2012, what we used were
20 the consensus based 1994 criteria. We also could
21 use just this fairly vague term of usual method of
22 diagnosis.

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1 Now, as loose as that sounds, that was
2 actually the gold standard for validating the
3 fibromyalgia criteria that are used even today.
4 It's a pretty poor gold standard, but really it was
5 all we had at the time to do that.
6 We've also got expert clinician diagnosis,
7 which is probably not really much different than
8 usual method of diagnosis honestly. That's what
9 they used doing the DSM for psychiatric disorders
10 in the version 3R. And then they can use
11 previously published diagnostic criteria, so DSM-4,
12 DSM-5 were evolutions based on the previous
13 version. That was the gold standard they used. So
14 we do have some gold standards we can use for
15 research.
16 Now, if we're trying to do empirical
17 validation, there are some statistical pattern
18 recognition techniques that may be useful when
19 applied in certain ways. And these would include
20 things like principle components analysis, which is
21 similar to factor analysis, cluster analysis,
22 latent class analysis, and classification and

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1 regression tree models.
2 Some questions that we might address, some
3 things we might do using those types of techniques,
4 one would be to identify groups of statistically
5 similar patients based on patterns of clinical
6 features. So let's say that we are interested
7 in --
8 Somebody throw out an example. What's a
9 pain condition, an acute pain condition you'd be
10 interested in? What? Fracture pain? Okay.
11 So you've got fracture pain and we get multi
12 sites, and we see fracture patients, and we start
13 systematically collecting data on the types of
14 symptoms they report, the objective signs that they
15 exhibit when you examine them, maybe in this case
16 x-ray results or other kinds of objective testing
17 like that. And what we do is we have then this big
18 database of features that might be associated with
19 fracture pain.
20 Now, what we're interested in is what is the
21 core of this. Is there something we can narrow
22 this down to, a set of core features that are

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1 prototypic? So now what we do is we use one of
2 these techniques like the principle components
3 analysis, and you can even use cluster analysis for
4 this, to try to narrow that down.
5 What you'll see is, it will tell you which
6 of those large set of features you're looking at
7 hang together. Which things tend to covary?
8 Because when they covary, that suggests that there
9 is some underlying construct that it reflects, and
10 that's really what we're interested in, is that
11 underlying construct.
12 So we could use that type of approach to
13 narrow down our domain from something really broad
14 to something that may be more clinically practical
15 and narrow that really represents the core of
16 whatever that pain condition is.
17 Now, we also could identify groups of signs
18 and symptoms that cluster together within a given
19 patient population, and this is for the individual
20 criteria.
21 So in this case, rather than looking just at
22 throwing a whole bunch of features into an analysis

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1 and seeing what comes up, we have more -- we may
2 have a draft set of criteria for example that have
3 certain signs and symptoms split out a certain way,
4 and we can use these types of pattern recognition
5 approaches to determine whether that way we've
6 broken it out is actually supported by the way the
7 data appear in a real-world data set. Because if
8 what we have in our criteria match up with the way
9 things really are in the real world, then we've
10 done a good job of reflecting that.

11 Finally, we want to show in some cases, and
12 this is the fuzzy boundaries issue, are two
13 conditions distinct? So we literally use cluster
14 analysis on a large sample of migraine and tension
15 type patients, and it was very simple.

16 We told the program -- we said, give us a
17 two cluster solution based on the signs and
18 symptoms we did. And then through everybody else,
19 we have a group the computer says is one type and
20 another type, and we've said, okay, how many in
21 each group actually got a diagnosis of migraine
22 versus tension type? And sure enough, it's about

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1 90 percent accurate in both groups.

2 So it really supported the idea that these
3 are different statistically distinct subtypes of
4 headache. You can do that with any two conditions.
5 It's particularly useful, though, when you've got
6 conditions that you wonder whether they may
7 overlap.

8 Common validation questions. Do the
9 criteria that we've proposed have concurrent
10 validity relative to some existing reference
11 standard? So this might be whatever the field
12 considers the best set of consensus criteria. It
13 may be some professional organization's criteria
14 that's listed on their website. It could be
15 anything you pick.

16 The other question is, do revised criteria
17 improve discriminative validity relative to
18 existing criteria? So you'll notice on that second
19 question you don't have to know absolute validity.
20 All we're trying to say is when we change things,
21 can we do a better job than we did before in
22 discriminating two groups?

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1 How would we do this? If we're looking at
2 categories of things, how do we know we've done a
3 good job? Well, you've got the obvious thing of
4 overall accuracy. It's a simple number or
5 percentage. It really is not very informative
6 because nothing is ever 100 percent accurate. And
7 when it is not 100 percent accurate, it's really
8 good to know why it was inaccurate. Was it false
9 positives? Was it false negatives? What was the
10 proportion of those?

11 So what we're really interested in primarily
12 are sensitivity and specificity. Sensitivity is
13 the true positive rate. Specificity is the true
14 negative rate. So true positives would be that
15 they actually have the condition that we're
16 interested in studying, and true negative is
17 somebody who clearly does not have that condition
18 and are we accurate in making that judgment.

19 Positive and negative predictive power,
20 these are actually the probability that if I make a
21 diagnosis that somebody has the condition or
22 doesn't have the condition, the probability that

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1 that is going to be accurate.

2 The problem with that, while it's a nice
3 idea, is it's dependent on the base rate of the
4 disorder in the population, and frequently we don't
5 know that very accurately. So it's subject to a
6 lot of swings in magnitude depending on what
7 assumptions you make.

8 However, there's another option called
9 positive and negative likelihood ratio that can be
10 directly calculated from sensitivity and
11 specificity that gives you a number that can be
12 interpreted in a fairly similar way, so that's
13 probably preferable.

14 So a couple of things to point out here.
15 Now, sensitivity and specificity are interrelated.
16 If you change the wording of your criteria, you
17 change the decision rules, both are going to be
18 affected, generally in opposite directions. So if
19 I have a set of criteria that has 4 possible
20 criteria that they could meet and we say as a
21 decision rule, you have to have 2 of these 4 to get
22 the diagnosis.

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1 How does that differ in sensitivity and
2 specificity from if we say, you have to have 3 out
3 of 4? What we can do, if we want to do it
4 elegantly, is we can plot sensitivity versus the
5 specificity on what's called a receiver operating
6 characteristics curve, and it will allow you to
7 find the cutpoint that will give you the optimal
8 balance between sensitivity and specificity;
9 somewhat arbitrary, because you have to decide
10 what's more important.

11 In a clinical situation, generally, we are
12 most concerned about not missing diagnoses, so we
13 have to put a high priority on sensitivity. We
14 don't want to over-diagnose people who don't have
15 the condition, so we have some concern with
16 specificity, but relatively it's probably a little
17 lower than sensitivity.

18 In a research context, you might argue that
19 specificity is a little more important because we
20 really want to make sure that everybody we get into
21 our research samples absolutely does not have other
22 conditions, and there are ways of altering the

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1 decision rules to do that.

2 Have you ever heard where receiver operating
3 characteristics came from? This is from World
4 War II radio operators. It was something they come
5 with then, which I didn't know for a long time.

6 I'm going to spend the rest of this talk on
7 the very specific example of complex regional pain
8 syndrome, showing how we use the approach I just
9 told you about to modify criteria in a way that we
10 hope has improved them.

11 Now, truth be told, we did not do
12 reliability testing. This was totally unfunded
13 effort, just did not have the resources to do it.
14 We were depending on the good graces of the people
15 that were collecting data for us. So we were able
16 to look at some of these relative validity issues
17 but not really the reliability issues.

18 So we started with just a rational approach
19 looking at the criteria that had been published by
20 Merskey and Bogduk in 1994 in the IASP taxonomy
21 that has already been discussed some today. That's
22 when they were fighting, right?

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1 So criterion 1, presence of an initiating
2 noxious event are cause for mobilization. It
3 actually says in the footnote, you don't have to
4 have this to get the condition. My question is,
5 well why include it? It doesn't add anything to
6 the diagnosis. I think that was a compromise I
7 would guess.

8 Number 2, continuing pain, allodynia, or
9 hyperalgesia, which is disproportionate. So any
10 one of those is enough to get it. So in theory,
11 you could have no allodynia or hyperalgesia and
12 have some continuing pain that you judge is
13 disproportionate, and that would meet that
14 criterion.

15 Number 3, this is the one that's the biggest
16 problem, evidence at some time. Now, when you say
17 at some time, if we take that at face value, that
18 means I don't have to see this when I examine you.
19 You could just come in and tell me that your arm
20 used to swell really badly, and you sometimes got a
21 cold arm and then it turns warm for no reason. And
22 I examine you and everything seems totally normal.

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1 That still meets that criterion.

2 The other thing is, it lumps together things
3 that on the face of it are very different, edema,
4 changes in skin blood flow, undefined how I should
5 assess that, or abnormal sudomotor activity.
6 Again, not defined how I should assess that, but it
7 all has to be in the region of the pain, and then
8 there's an exclusion criteria at the bottom.

9 So the question is, do the criteria
10 adequately capture the core defining features of
11 CRPS? Is the structure of the criteria optimal?
12 That is those individual criteria like criterion 2
13 and 3. Are the layouts of the signs and symptoms
14 reflective of what happens in the real world? Are
15 the diagnostic decision rules good?

16 The reason we're concerned with these is
17 because that will influence the sensitivity and
18 specificity. And in this context, when we're
19 talking about sensitivity, we're saying how well do
20 the criteria identify the CRPS positive cases.
21 Specificity is how accurate are we in identifying
22 the non -- screening out the non-CRPS cases.

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1 For the content, the domain questions, we
2 went to the literature, and you could very quickly
3 see that there were several features in the
4 diagnostic criteria I just showed you that do
5 appear in the literature a lot: allodynia,
6 hyperalgesia, skin temperature or color changes,
7 sweating changes, and edema.
8 However, if you look at the literature, you
9 will also see very frequently mentioned a bunch of
10 other signs and symptoms that were not included in
11 those criteria I showed you. So trophic changes to
12 hair, nail, and skin, tremors, dystonia, and so on.
13 The question is, were those criteria, as I showed
14 you before, adequate, or were we missing key
15 features of the disorder?
16 So what we did was a multi-site study. For
17 rare conditions, in particular like this, you have
18 to use multiple sites to do this. And I would
19 anticipate anything we do in this effort would
20 require multiple sites as well.
21 We ended up with 123 patients who all met
22 those 1994 criteria for CRPS I showed you, and they

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1 required symptoms. Do they provide different
2 information?
3 Well, what we saw with this just looking at
4 simple frequencies was that there were some
5 parallels. These are the signs here, symptoms on
6 the right. And you can see in red are the things
7 that were most frequent. So color changes were the
8 most frequent sign and symptom; same for decreased
9 range of motion. And then in blue, those that were
10 the least common were nail and skin changes.
11 So the rank ordering was similar across
12 signs and symptoms, but you'll notice the absolute
13 numbers for signs are always quite a bit lower than
14 what we got for symptoms. What we took from that
15 was that signs and symptoms both are reflecting
16 real phenomena, but some of those features of CRPS
17 are labile, and they may not be showing it on the
18 day of clinical exam. And that would account for
19 it being more common as a symptom than a sign.
20 So our interpretation of this was that both
21 provided meaningful information, but they weren't
22 totally redundant.

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1 all underwent a standardized evaluation of signs
2 and symptoms related to CRPS using a structured
3 database form. There was an instructional video
4 that showed how to do the exam or the different
5 aspects that were covered on there, as well as
6 instructions for how to do the different
7 components.
8 You can't read this, but this is just an
9 example. For signs and symptoms, they were all
10 coded, symptoms here, signs down here. Symptoms
11 are all yes/no, signs all yes/no, but within each
12 broad category, such as temperature asymmetry, you
13 could specify cold, warm, or labile.
14 So it was just laid out like this in a very
15 easy to use way. The reason we did the dichotomous
16 choices was to enhance reliability because it's
17 easier to make a yes/no distinction than it is to
18 get agreement on fine gradations of something like
19 that.
20 Internal validity. Does it make sense to
21 include both objective signs and subjective
22 symptoms in the criteria? The old criteria only

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1 Is the grouping of signs and symptoms in
2 each criterion supported by the data? Well, you
3 look at number 3 again here, so the question is
4 this evidence at some time for edema, skin blood
5 flow changes, or sudomotor activity changes, is
6 that too low a threshold to say that all you've got
7 to do is have one of those? Is it too easy to get
8 the diagnosis?
9 So we used principle components analysis to
10 identify groups of signs and symptoms that seemed
11 to have underlying common relationships. They
12 covaried together. And what you'll see here is
13 that we got 4 relatively independent factors when
14 we examined those signs and symptoms that we
15 collected.
16 We had one that we called the sensory
17 factor. This was basically allodynia and
18 hyperalgesia. This was very similar to what was in
19 criterion 2 that I showed you. There was a
20 vasomotor criterion.
21 This is a component of criterion 3, but it
22 wasn't the whole thing because what actually

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1 happened was a little surprising, was that the
2 sudomotor measures, the sweating changes and the
3 edema were linked together, but they were separate
4 from the vasomotor.
5 So really, criterion 3 in those criteria I
6 showed you statistically broke out into two
7 separate factors. And then we've got the
8 motor/trophic issues. They lumped together, but
9 they were separate from all the others. And this
10 is not even assessed in those criteria. So that
11 suggested there was a problem.
12 So our conclusions were that those IASP
13 criteria from 1994 are not really internally valid,
14 and that it's a real problem when we combine
15 vasomotor, sudomotor, and edema all into one
16 criterion because it can lead to over diagnosis by
17 making it too easy to meet that threshold. And it
18 suggested a revision was needed. And what we
19 wanted to do was to revise based on the findings of
20 these studies.
21 What you'll see is -- and this is
22 overlapping study. It's not exactly the same

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1 patients, but it's a lot of the same ones;
2 117 patients meeting those diagnostic criteria, and
3 then 43 patients who had non-CRPS neuropathic pain,
4 judged to be non-CRPS based on expert clinician
5 opinion. These were things like PHN or diabetic
6 neuropathy, as well as other specific neuropathies
7 where the cause was known and it didn't seem to be
8 CRPS.
9 The idea was simply that if the CRPS
10 criteria could not be used to discriminate between
11 these two groups, they really were not going to be
12 very useful. That was the basic idea of this, is
13 that CRPS patients should look different than these
14 other type of patients because they have a much
15 stronger loading of autonomic features and some of
16 these other things that you don't always see as
17 prominently in other neuropathic pain symptoms.
18 So we got the same standardized measure of
19 signs and symptoms. And what we ended up with was
20 sensitivity was great, as you would expect because
21 of the way we did the study, but specificity was
22 not. It was only 0.36, meaning that the people who

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1 had non-CRPS looked very much like those 1994
2 diagnostic criteria, so they were very likely to be
3 misdiagnosed. Now, because of that over-diagnosis,
4 this number gives us a reason to say we need to
5 revise things.
6 We just point out AAAPT, we could do exactly
7 the same process. So we come up with our first
8 version of the criteria here, then we start
9 collecting data, and then we can play around with
10 revisions to those criteria based on the problems
11 we see. And then we can compare our new proposed
12 criteria to the first version of the criteria to
13 see if we're actually helping things or hurting
14 things. So the process is very similar.
15 For the CRPS example, one change we thought
16 of, just based on looking at the results of all
17 this, was requiring the presence of objective signs
18 was going to be useful because it really didn't
19 make sense to allow patients to essentially
20 diagnose themselves, because it was really -- they
21 didn't have to have any clinical features when they
22 came in, patients could just read on the Internet

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1 what CRPS was and come in and say I've got these
2 things, and that's the diagnosis.
3 We also thought it was important to include
4 motor/trophic changes because they weren't covered
5 at all, but in the historical literature they were
6 clearly considered part of the same syndrome. We
7 wanted to break out vasomotor features from the
8 edema, sudomotor features, so we have two separate
9 criteria.
10 We proposed these, and then at a consensus
11 meeting, we went over all the data, discussed it,
12 made a few minor revisions, and decided to proceed
13 with testing the revised criteria that we came up
14 with.
15 They are called frequently the Budapest
16 criteria. The clinical criteria are what you'd use
17 in normal clinical circumstances. The first thing
18 is continuing pain that's disproportionate to any
19 inciting event. The key thing there is, it's
20 insisting that the patient has to be painful,
21 because you actually get people who look like they
22 have CRPS who say it doesn't hurt, which does not

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1 seem to be the same thing. So that was included
2 there for a reason.
3 Then we've got a symptom block, and in that
4 symptom block we've got these 4 areas that came out
5 from the principal components analysis. And what
6 we said based on the findings of our study was that
7 if you have 3 or more of those symptom areas,
8 you've got the diagnosis. Well, take that back,
9 you meet the symptom portion of the diagnosis.
10 Now, we say for signs, you got the same
11 4 categories: sensory vasomotor, sudomotor, edema,
12 and motor/trophic. And for this, you have to have
13 at least two of the categories positive on exam the
14 day that they are seeing you.
15 We also decided for research purposes to
16 make an explicit recommendation for an alternation
17 to the decision rule if you're doing research
18 studies and you want to narrow it even further to
19 make sure you don't have any false positives. So
20 what we did is it requires 3 or more sign
21 categories, and that's to increase specificity.
22 What you can see here is -- and this is not

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1 the original data I showed you. This is a totally
2 separate study. We replicated the effect we got
3 before, which was that the IASP 1994 criteria are
4 very sensitive but had poor specificity. The
5 Budapest clinical criteria continued to be
6 extremely sensitive but increased specificity quite
7 a bit. And the research, as intended, we knew it
8 would drop sensitivity but it did in fact increase
9 specificity.
10 So this tells us that the new criteria are
11 not perfect, but the numbers would say that they're
12 better than what we had before. And keep in mind,
13 this was all done in the absence of having any
14 objective gold standard.
15 The IASP taxonomy committee finally agreed
16 to adopt this in March of 2011, and it was adopted
17 by the IASP board. It is now on their website.
18 It's official. And now the clinical trials are
19 using this as their diagnostic criteria because it
20 is better than what was out there before. It kind
21 of filled the gap.
22 Take-home point of all of this, if you

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1 remember one thing as you're trying to plan out
2 your AAAPT criteria, the wording matters, and it
3 matters a lot. What I've been recommending to the
4 AAPT groups as they have written their criteria, is
5 play some mental games with yourself.
6 So you have a set of criteria you're
7 thinking about, pick a patient who's very extreme
8 on this end, a patient who's extreme on this end,
9 and a typical patient. Try to apply the criteria
10 to that patient. Do you get the results that you
11 intended?
12 So what you're probably going to find, if
13 you literally take those words as they are written,
14 is you're going to discover some problems with the
15 way that things are worded. You're going to
16 exclude people you didn't mean to exclude, or
17 you're going to have criteria in there that are
18 meaningless because everybody has it.
19 So, anyway, just play around with it. You
20 really have to put some thoughts into the words
21 that go into these. So that's it.
22 (Applause.)

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1 DR. CARR: So we're actually just about in
2 the same time slot as we originally planned, except
3 what we're going to do is move the group discussion
4 until after the break. We're right on time for the
5 2:30-3:00 break. Then we will reconvene, and I
6 will invite Patrick and Steve to join the other
7 panelists so we can have an unfettered discussion.
8 So thank you very much, and we'll see you in
9 30 minutes.
10 (Whereupon, at 2:32 p.m., a recess was
11 taken.)
12 Group Discussion
13 DR. CARR: Good. So as we're walking in,
14 let me remind people, we just shuffled around the
15 schedule because we had speakers who were scheduled
16 either later after this panel session or tomorrow
17 that really had things to say that were relevant to
18 this overriding beginning question, which is how
19 should the AAPT chronic pain dimensions be revised
20 to provide a framework for acute pain, and whether
21 that is taxonomy, diagnostic criteria?
22 For those of you who just wanted a memory

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1 jogger, I had listed the headlines, but we have the
2 people who struggled and wrote these out here with
3 us now.
4 So the opening question might be, is there
5 anything missing? There's a few questions we can
6 ask. One would be, if you pose a question saying
7 CRPS is to chronic pain as X is to acute pain, is
8 there an X, is there a condition that we're
9 troubled at our inability to diagnosis or place
10 into a crisp compartment?
11 So I'll start with this question. Sir?
12 DR. MCLEAN: The one thing that I would say
13 is that I think that we -- at least it seems to me
14 that it would be helpful before going into
15 discussion to come to some agreement on the goals
16 and the priorities of the goals. Because I think
17 we could easily have -- you know, what the goals
18 were will really influence what the best criteria
19 is.
20 At least my concern is that if one person
21 has, pedagogy first, and another has ontology
22 first, and another has diagnostic criteria first,

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1 and we don't have any sort of prioritization of
2 those, that we could end up going in lots of -- it
3 could become a little circular or unclear. So at
4 least that's my thought.
5 DR. CARR: I think that's a great point.
6 Let me take a few more questions from the floor,
7 but I'm tempted to ask you, Dr. McLean, what would
8 your goals be? Before we do the next question.
9 DR. MCLEAN: I would say my own bias is that
10 the most important thing for us that we can
11 contribute right now is to make sure that two
12 people studying the same condition or testing a
13 drug on a condition are actually studying the same
14 condition.
15 So creating a common diagnostic criteria is
16 number one, and then I'm not sure about other goals
17 after that. But again, that's just my thought, and
18 I'm glad to go with whatever the group's thoughts
19 are.
20 DR. CARR: Well, let's spend a few minutes
21 talking about that. What is our goal? Roger, and
22 then there was another question. Kristen. First

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1 of all, hear from Roger, and then Kristen.
2 DR. FILLINGIM: Yes. So I'm certainly
3 limited by coming in with ideas of what the goals
4 of this meeting are based on what the goals of our
5 earlier meeting with AAPT were. And I think
6 essentially there are two primary goals. One is to
7 develop a framework that working groups can
8 systematically use to develop diagnostic criteria
9 for acute pain conditions and to decide what the
10 acute pain conditions are to which that framework
11 will be applied. That's very much what we did.
12 DR. MCLEAN: And the framework being the
13 dimensions?
14 DR. FILLINGIM: Yes.
15 DR. MCLEAN: Yes.
16 DR. FILLINGIM: If you follow anything close
17 to what we did, it would be the dimensions.
18 Although, I guess this group could decide that
19 doesn't work at all, we're going to come up with a
20 framework that's not that at all, but a framework
21 nonetheless.
22 DR. MCLEAN: But do you think that

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1 the -- and this is truly a question, will those
2 dimensions depend on what the use is or what the
3 goals are in terms of the use or the product?
4 DR. FILLINGIM: You mean how you want the
5 diagnoses to be used?
6 DR. MCLEAN: What are the priorities for the
7 diagnostic system in terms of its utility or
8 application?
9 DR. FILLINGIM: I think that's for this
10 group to decide, but I think it's for clinical use
11 and for research use, to improve clinical care and
12 to enhance research as you've talked about.
13 DR. MCLEAN: Yes.
14 DR. FILLINGIM: There's a clinical trial of
15 X, that everybody who is studying X is studying the
16 same thing.
17 DR. MCLEAN: I thought that this morning,
18 the example of creating the classification systems
19 and then creating diagnostic criteria that everyone
20 would use and try to get everyone to use them was a
21 good example of where there's a tension there.
22 For example, if there's just a goal of

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1 coming up with diagnostic criteria for
2 fibromyalgia, based on something that everyone can
3 agree on, then saying, okay, we're going to call it
4 musculoskeletal versus central nervous system, you
5 run the risk of pissing off whoever those people
6 are in the different camps.
7 They're less likely to use it because you're
8 sort of going beyond the evidence and experts'
9 opinion to say, well, my best guess right now is
10 that it's this category or that category, without
11 even meaning to. But just being agnostic, but
12 saying, oh, for now we're going to lump it over
13 here; you could still potentially -- so there are
14 these tensions.
15 DR. TURK: Can I add to that point?
16 DR. CARR: You can add, then I'm noticing
17 there's Kristen, Chris Wu, and Rosemary. So we're
18 all going to get our say.
19 DR. TURK: This is just a clarification.
20 When the working groups in the AAPT come up with
21 their criteria, they're encouraged to send these
22 out to relevant organizations, to relevant people,

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1 to people who might disagree, to try to see if they
2 could get input and potential buy in from them.
3 So we're well aware when you have a working
4 group of 5 or 6 or X number of people, you're not
5 always representing everybody out there. But the
6 goal, the hope is to go back to the other groups,
7 other individuals, other organizations if you know
8 that this is a disease that's covered in the
9 neurology area to make sure that we have the
10 appropriate people.
11 So they may not agree, but at least the
12 mandate was that they should, to the extent
13 possible, go back to relevant groups, relevant
14 individuals and not to -- to try to increase the
15 buy in. Of course, they could always come up with
16 a disagreement.
17 DR. CARR: Steve, why don't you add?
18 End of Day Wrap-Up
19 DR. BRUEHL: Keep in mind -- so those are
20 excellent questions. This is a multipurpose
21 project. It's clinical. It's research. And Bob
22 wanted me to make sure to keep things on track

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1 here.
2 There are tangible things we have to come
3 out with this. One is what are the dimensions
4 we're going to use, and the other is, start to at
5 least move down that road of thinking about what
6 the different buckets would be that we need
7 different core diagnostic criteria for. So if we
8 come out of this at the end of the day tomorrow
9 with those two things, we're good.
10 Now, to answer your question, some of these
11 things that have been raised, part of the reason
12 for this was the hodgepodge, if you look across
13 different diagnoses, there are criteria out there
14 for some of these; now, maybe less so in acute pain
15 than chronic pain.
16 But chronic pain, it was a mess, using all
17 different formats, some of which like TMD
18 explicitly included psychosocial factors, which are
19 known to have a major role in how those play out;
20 other conditions that clearly had a role of
21 psychosocial factors with no acknowledgement at
22 all. And it's just everything was very different.

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1 The idea was to parallel DSM and put
2 everything on a level playing field so that we're
3 covering the same bases for every major disorder.
4 And it's not going to be an exhaustive list of
5 everything that might be diagnosed for acute pain,
6 but the major conditions that are the largest
7 problem areas or most prevalent.
8 So that's what we want to be thinking about
9 is these dimensions, of these five that are up
10 there, a good parallel for what would be
11 appropriate for acute pain.
12 Do we need to add a separate dimension that
13 addresses clinicity issues, or temporal issues, and
14 risk for chronification, and that kind of thing,
15 kind of like was discussed earlier, or are there
16 things that we are totally forgetting that may be
17 so important they should be a dimension? Or is
18 there a dimension on here that is irrelevant for
19 some reason to the topic of acute pain?
20 So be thinking about that. And the
21 discussion, don't be afraid to challenge. Now is
22 the time to think a little out of the box,

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1 challenge things. But we do have to, by the end of
2 the day tomorrow, narrow this down to actually know
3 what those dimensions are.

4 DR. DWORKIN: So Sam, the only thing I want
5 to add is we've had two precedents that we've
6 really drawn on. One is Steve's work with CRPS,
7 and the other is psychiatry and the DSM-3, 4, 5.

8 I think it's accurate that for both of those
9 previous efforts, research was the initial
10 objective, using the criteria in research studies,
11 clinical trials, drug applications. And then
12 second was educational. And it's only once you
13 have the education occurring that you then get
14 widespread adoption in the clinic.

15 So at least using those two efforts as
16 precedents, DSM and CRPS, I think the order of
17 objectives would be sort of what you were saying,
18 which is clinical research, education, the clinic.

19 DR. CARR: So let's go -- and Kristin, you
20 had a comment?

21 DR. SCHREIBER: Actually, yeah. My comments
22 were exactly on the things that everybody's been

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1 talking about. So it occurs to me that -- I mean,
2 it's really great to have the framework of chronic
3 pain here. However, there are some really
4 important differences that I think impact the
5 prioritization of how we frame what's going to be
6 number 1, 2, 3.

7 Firstly, I think the most prominent is that
8 it's not as much of a mystery the diagnosis. In
9 most cases, I think, for acute pain, we kind of
10 already know what the diagnosis is, and so not as
11 much effort or emphasis needs to be put on that.

12 Probably more prominent should be how are we
13 going to treat it quickly because we don't have the
14 luxury of seeing this patient over many months and
15 working on the diagnosis. We have to kind of see
16 it right away, figure out what treatment is going
17 to be best for them.

18 So I would argue for it being a little bit
19 more oriented towards being able to figure out what
20 treatments will be helpful, and then
21 individualizing. So that's where, as I mentioned
22 before, the 4th and 5th, and maybe then if we said

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1 there's a 6th, which is a time component, that
2 those would be increased in prominence in the acute
3 pain framework. That's just my two cents.

4 DR. CARR: Thank you. Chris Wu?

5 DR. WU: I think those are excellent
6 comments. One consideration is the core diagnostic
7 criteria, if that were to be removed, or if there
8 was an argument against removing it, instead of
9 relating it to the pain itself, would it be more
10 appropriate to direct it to the underlying
11 diagnosis that led to the pain, which is frequently
12 true in acute pain diagnosis.

13 That seems to somewhat differentiate it from
14 a chronic pain diagnosis, where the diagnosis is
15 intrinsic to the pain itself; whereas here we talk
16 about the diagnosis being intrinsic to the
17 underlying mechanism that led to the pain.

18 I think that carries some important
19 treatment connotations. For instance, if we had
20 bone pain from a fracture, trauma versus metastatic
21 lesion may lead to different expected treatments
22 and functional prognoses. So it's a way of

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1 somewhat distancing ourselves from the first
2 dimension, or at least modifying it to this
3 context.

4 Does that seem -- can you build from that?

5 DR. SCHREIBER: I guess I definitely wasn't
6 saying take out the first three. You know, I just
7 think maybe less prominence. I don't know if we
8 can turn it on its head. But as someone mentioned,
9 the first thing that people will look at is the
10 first one, and then ignore the rest, and then maybe
11 we haven't served our purpose.

12 DR. CARR: Now Chris, and then we'll
13 continue around the room.

14 DR. WU: Based on what I've heard, so we're
15 interested -- the purpose of this is more, for what
16 Bob says, initially for research, clinical
17 research, and then we want to organize -- I mean, I
18 don't want to use the diagnostic ability so
19 everyone's on the same page. I understand
20 Kristin's concern about the clinical use of this.

21 I'm not sure -- are we allowed not to use
22 the 5 dimensions? We might come up with a

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1 different system. But ultimately, I think the
2 challenge is that we have to serve multiple
3 customers here, and that will be very difficult, I
4 think, potentially in this current format that we
5 have.
6 DR. CARR: Rosemary?
7 DR. POLOMANO: So I think I have to digest
8 those dimensions a bit. But for me, for acute
9 pain, to replace the thinking for the core
10 diagnostic criteria, it's really about the pain
11 event. So it's really about surgery, trauma,
12 procedure.
13 It's not about the diagnostic criteria,
14 isn't as much about the symptoms and the signs.
15 There are certainly supporting data. So I would
16 just encourage us to think about this
17 situational -- not necessarily temporal, but
18 situational or event stimulus for the pain.
19 The other thing is that when Patrick was
20 talking -- so Patrick you can give the right names
21 to what I'm saying in terms of the leveling. But
22 when you think about if the strategy for

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1 practice -- and, again, I think this has to be
2 useful for practice.
3 If you think about the strategy for practice
4 as pain prevention as a strategy, if someone is
5 having surgery, you would have that opportunity to
6 look at the mediators for pain and the modifiers
7 for pain, and address them preoperatively.
8 But if it's a trauma patient or it's a
9 patient who develops something, when you can't see
10 them before they have their pain event, then those
11 kinds of strategies or frameworks of thinking for
12 mediating and modifying pain are going to be
13 different with each acute pain type based on the
14 nature of it.
15 So it makes it more complex than thinking
16 about everybody, preventing chronic pain for
17 everybody and looking at these modifiers because
18 you have the opportunity. For acute pain, you
19 don't always have the pre-event opportunity, but
20 you certainly have the post-event opportunity for
21 understanding these mediators and modifiers.
22 So whatever model we do, the sequence of the

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1 pain has to be -- or how the pain is situated has
2 to be part of the dimensions.
3 DR. BRENNAN: I had written down injury, but
4 I like your event as broad as one of the criteria.
5 DR. POLOMANO: So an infectious event would
6 be herpes zoster. I mean, I think you can
7 actually -- for all of the acute pain I was just
8 thinking as everyone was talking, you can fit some
9 kind of event to it.
10 So maybe it needs to come first, and then
11 maybe the dimensions, these dimensions will serve
12 us well. But the common medical
13 comorbidities -- so I just want to say again -- I
14 think really needs to be thought of in terms of
15 mediators and modifiers for pain. Depression.
16 DR. FILLINGIM: Let me just say, first of
17 all, my feelings won't be hurt if you get rid of
18 all of these components of the framework.
19 (Laughter.)
20 DR. FILLINGIM: And let me be clear, when we
21 developed AAPT, we always intended that there would
22 be an acute pain taxonomy, but we didn't take that

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1 into consideration at all when developing these.
2 These are fully intended to serve chronic pain
3 conditions and chronic pain conditions alone.
4 The process I described might be
5 informative. Some of the other characteristics of
6 the taxonomy might be worth considering. But I
7 think acute pain, as you're pointing out, is in
8 many ways a different animal, and you may need your
9 own dimensions.
10 DR. POLOMANO: And I think you can align
11 these dimensions with more relevant but similar
12 dimensions that address, in concept, almost
13 something that's the same.
14 DR. CARR: Okay. Paul, Bob, Mike, and then
15 Srinii.
16 DR. DESJARDINS: [Inaudible -- mic
17 off] -- and I don't know what turns these off
18 spontaneously, but I'll go back to them when I need
19 to.
20 DR. CARR: When the value of the comment
21 declines.
22 (Laughter.)

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1 DR. DESJARDINS: Oh my God, it's off
2 already.
3 (Laughter.)
4 DR. DESJARDINS: I found it easier to think
5 about this when I started thinking about the kinds
6 of questions one might want to ask. And it became
7 obvious in the context, from my preparation looking
8 at orofacial pain, there is never pain that shows
9 up in the face in this area that's acute that isn't
10 already tagged with a diagnosis.
11 So I like, Patrick, your comment of whatever
12 the working diagnosis, let's start there because
13 your job is not to define how dental pulpal pain
14 comes up. There are criteria for doing that.
15 So the predictors, and again as a clinical
16 pharmacologist looking at how I would use this, a
17 system that could help design -- and I think I'm
18 saying something a little bit different from what
19 you were saying, but similar.
20 A system that might help me look at who is
21 not having a -- predict who is at risk for not
22 having a smooth recovery, what are those factors

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1 that I need to be thinking, in particular, how am I
2 going to treat this differently than how I would
3 treat every other oral surgery patient?
4 The other piece that I think innovators have
5 learned, and again my last comment, is that perfect
6 is the enemy of a good enough. And I think if we
7 can have diagnostic criteria and a system that's
8 good enough to launch, it will be improved, and it
9 doesn't need to be perfect.
10 It will not be perfect for everyone, but if
11 we agree out of the box that it's good enough now,
12 then we're going to make some progress. And I
13 think we've learned that in innovation in many
14 different fields. So thank you.
15 Dan?
16 DR. CARR: Any comments? We'll continue
17 then. So Bob, you had a comment?
18 DR. DWORKIN: Yes, okay. My first comment
19 is regarding having a dimensional framework. And I
20 wanted to make reference to an article by Elena
21 Kramer in 2007, writing on whether or not DSM-5
22 should include dimensions still. And 25 words that

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1 she wrote might be helpful here for somebody who
2 thinks we shouldn't have dimensions.
3 She says, "Every categorical diagnosis can
4 be made dimensional by using symptom count, symptom
5 duration, symptom severity, degree of impairment,
6 certainty of diagnosis, consensus of multiple
7 diagnoses." And then she goes on to cite a couple
8 of specific examples that show the clear benefit to
9 a dimensional approach.
10 We have not talked about genetics or
11 epigenetics, but I think that a comment was just
12 briefly made that when we go on rounds and we see
13 the patient with acute pain, we know what the
14 diagnosis is, and I couldn't disagree with that
15 more.
16 I think if we knew what the diagnosis was
17 every time, then every time we saw a patient, we
18 would be able to prescribe the right treatment and
19 it would work. Instead, I think we kind of figure
20 out what some of the possibilities are based on
21 what does and doesn't work. So I think we can't be
22 glib about knowing.

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1 Last is the piece about acute and chronic
2 pain. They're both pain. And I thought that
3 excellent discussion about with the boxes and the
4 methods of steering and braking that Patrick led is
5 very useful.
6 For those people who might be passionate
7 about how chronic and acute pain might be
8 connected, I think if we design two different
9 systems to study them, it will make them much
10 harder to connect. And I think there's a strong
11 advantage, and I would strongly support that we
12 adopt the same basic framework that was used for
13 the AAPM.
14 DR. CARR: Thank you.
15 Let's see, over in the back and then Srin,
16 do you still have a comment? Okay, back, Srin,
17 Mike, Mark, Henrik, and Santhanam.
18 MALE SPEAKER: Well, I think the diagnostic
19 part really dramatically varies depending what it
20 is. So if someone presents with the first onset of
21 right lower quadrant severe pain, there's a pretty
22 good differential diagnosis there. And it could be

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1 anything from an ovary to appendix. So a wide
2 range of things and the diagnostic criteria that
3 lead you to come up with a diagnosis really matter.
4 If they had imaging that demonstrated a
5 lesion that required surgical exploration to
6 determine what type of lesion it was, and they had
7 zero pain beforehand, and they have an incision,
8 they had surgery, that's pretty easy diagnostic
9 criteria.
10 So those seem like very different things.
11 They're both acute pain, but they're really quite
12 different. And the emphasis on kind of the context
13 in which the pain occurs really, really is what
14 matters the most.
15 If that person having surgery had
16 pre-operative pain that was in the exact same area
17 where they're having their pain, they're quite
18 different than the person who didn't have pain
19 beforehand.
20 Then sometimes even if we know the
21 diagnosis, the type of pain the person is
22 experiencing could be quite different. My example

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1 is rib fractures. Someone has a rib fracture,
2 sometimes it's very specific point pain right where
3 the rib is fractured. Sometimes it's a generic
4 kind of pleural hemithorax kind of pain. Other
5 times it's very much intercostal neuralgia like.
6 Those are all related to that rib fracture and that
7 rib trauma, but they're three very different types
8 of pain.
9 So there's a lot there, and the diagnostic
10 criteria may be really important for one and not so
11 important for the other. But it seems like the
12 context is what we need to really lay out first.
13 DR. CARR: Okay, I think, Mark, that you
14 were next. And we'll do the best we can, but
15 everybody who has something to say will be called
16 on.
17 DR. SCHUMACHER: Right, thank you. So
18 again, struggling with the 5 domains but wanting to
19 retain the structure as mentioned, I had discussed
20 this briefly with a few folks during the breaks, is
21 that potentially the last three, and maybe if you
22 added tissue site, maybe plus or minus visceral

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1 involvement -- so the idea that possibly the last
2 three represent modifications or modifiers, and
3 depending on their weight, if you have strong
4 evidence, that could then kind of jump the queue to
5 solidify your diagnosis.
6 So I look at the rest of those as perhaps
7 the flexibility we're looking for in terms of
8 coming up with the value of a diagnosis or not.
9 And it could also integrate other aspects that have
10 been mentioned about genetic testing or all this
11 other, which becomes more the precision medicine as
12 time goes on.
13 So not fully thought out, and not to be made
14 overly complicated, but it just seems like these
15 are modifiers to the primary issue. Thank you.
16 DR. RAJA: So I was trying to think of what
17 is so unique and different about acute pain
18 compared to chronic pain. And many of you have
19 talked about an acute event or injury initiating
20 the pain. And Tim, in your discussion you clearly
21 indicated that the mechanisms for injury to -- or
22 pain resulting from injury to, say, muscles and

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1 tendons, or bone, or neuro, may be very different.
2 So somehow, I'm looking at this dimension,
3 and the nature of the tissue involved in this
4 injury process resulting in acute pain doesn't seem
5 to come out. And maybe that's something that needs
6 to broaden into this dimension for acute pain.
7 DR. CARR: Mike and then Henrik.
8 DR. KENT: Sure, thanks. So I'm also
9 struggling with the 5 dimensions, but I agree with
10 Bob in terms of adapting some format. I'm just
11 wondering, initially, we were talking about let's
12 see how well the 5 dimensions fit, and then talk
13 about buckets. And I think we've had some comments
14 about events, focusing on tissue injuries.
15 I'm wondering by having that slide up there
16 if we've just become cognitively locked, not to the
17 dimensions but the words of the dimensions.
18 In the form of high school football, I was
19 just wondering if more of a chalk talk type
20 scenario, should we just bring the slide down and
21 actually start from what Pat was talking about, the
22 objects, start talk a little bit about do we want

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1 an event, do we want to talk about tissue injury,
2 and then just start -- not start fresh, but start
3 fresh and just start listing dimensions. And then
4 put the slide back up and see how similar or
5 different we are, just as a way to move forward a
6 little bit.
7 DR. CARR: So we're all okay taking them
8 down? So can you just take the slide off for a
9 moment.
10 DR. KENT: By the way, I did not play high
11 school football.
12 (Laughter.)
13 DR. CARR: So Henrik, you've now had a
14 chance to absorb a lot of these comments. What do
15 you think?
16 DR. KEHLET: Well, first of all, the
17 diagnostic, I think when you look at the post-op
18 pain literature, we still see a lot of studies
19 where it's just pain and it's rated. It should be
20 diagnosed exactly in relation to anatomical
21 function; I mean, movement associated pain. That's
22 the first thing.

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1 Then I think we should use Tim's proposal
2 because you elegantly showed transduction mediated
3 pain, inflammatory, mechanically, ischemic,
4 et cetera, et cetera. That goes into the
5 diagnosis.
6 When it comes to the comorbidities and risk
7 factors, again, it's really important to have
8 pre-injury pain at the site of injury or pain at
9 other places in the body. It's crucial. Opioid
10 using before the injury catastrophizes and also
11 assessment of the nociceptive function, if it
12 possible, at least before operating. Are these
13 high pain responders or not? That's extremely
14 important.
15 But the most important is really what is the
16 consequence of the acute pain. And if you have 8
17 on your best scale after tensile operation, it
18 doesn't threaten your life. If you have 8 after a
19 colonic section, it may threaten your life. So we
20 need to have the functional consequences of the
21 pain assessed in detail; in detail.
22 DR. CARR: Thank you very much.

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1 Any comments on that comment?
2 MALE SPEAKER: Dan, I don't know if it's
3 premature, but I just want to follow up on that,
4 and we discussed this during the break, and that is
5 this concept of defining what high impact acute
6 pain would be.
7 There's an analogy to this because we took
8 this on in the National Pain Strategy, and one of
9 the working groups there, the population research
10 working group for the NPS, under Michael Van
11 Korff's leadership and Ann Scher, we worked
12 together to define high impact chronic pain.
13 We recognized that the driver from this was
14 the HRQ data, which shows that in our country,
15 1 percent of the patients utilize 23 percent of our
16 healthcare resources; 5 percent of our patients
17 utilize over half of our resources. So there's a
18 small sliver of people that are accounting for the
19 big impact from a societal burden.
20 Apropos, Dan's use of Gertrude Stein's, "For
21 a difference to be a difference, it has to make a
22 difference," one thing this group could come out

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1 with is something that defines that group of people
2 that really make a difference.
3 We defined high impact chronic pain in the
4 National Pain Strategy as chronic pain associated
5 with substantial restrictions of participation in
6 work, social, and self-care activities for 6 months
7 of more.
8 One could readily come up with a definition
9 here of high impact acute pain and be able to use
10 that to separate the people that Henrik just talked
11 about, those two groups of people, one whom you
12 know might have a high pain score, but they're not
13 going to go on to have high impact chronic
14 pain -- high impact acute pain, the other one, who
15 would.
16 So I would put that forward as something
17 very tangible this group could define.
18 DR. CARR: Well, if I could add a comment.
19 I think, to me, that is an attractive idea because
20 in the daily world of practice, we already now have
21 many clinical pathways that are established that
22 work pretty well for most people and do not need

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1 continual observation and monitoring by physicians.
2 There are nurse-led pain services that do
3 absolutely fine.
4 So it would be possible to invest a lot of
5 time and energy and thought into elements that are
6 not really problematic, that no one really is
7 interested in improving because they work pretty
8 well.
9 So there might be some starting point to
10 begin with, what Henrik has mentioned and what
11 you're saying, that we should be concerned with
12 improvement and where are the areas for improvement
13 the vexatious high cost small minority or the ones
14 whose life is at risk. So we should stratify our
15 own efforts according to the importance of the
16 target.
17 I don't know how that's -- it's somewhat of
18 a departure. It's a little bit different than the
19 chronic pain or the AA. But how do the AAPM people
20 feel about that? Dennis or Bob?
21 MALE SPEAKER: Well, so Dan, Sean, I'm not
22 sure how that maps onto diagnostic criteria. If I

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1 very high here, low on this and high on this, that
2 patient is going to be a problem.
3 So we would hope that however these
4 5 dimensions are laid out, that that would allow
5 you to do exactly what Sean and everybody else has
6 kind of mentioned about those high burden patients
7 or high-risk patients, those patients that are
8 difficult to treat effectively.
9 I keep hearing this idea of wanting to use
10 these criteria to predict. We want to know what's
11 going to happen -- we want to profile them, know
12 what their course is going to be, and based on that
13 knowledge of what's likely to happen, be able to
14 intervene early before they ever get there. And I
15 think that could be captured if you pick the right
16 dimensions, and I think that's what our task is,
17 isn't it?
18 Just so you know why I'm standing up here is
19 because I want to get -- we've got 45 minutes left,
20 officially, and I wanted to start taking some notes
21 if people want to throw out some suggestions for
22 dimensions. And one thing just before I forget

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1 want to do a clinical trial of shingles pain or
2 acute post-operative pain following herniorrhaphy,
3 I need to have inclusion/exclusion criteria. And
4 even if those types of acute pain don't have a high
5 societal impact, is this going to provide me with
6 guidance in doing a clinical trial?
7 So I hate to sound like a broken record, but
8 I think of most things in terms of their
9 implications for clinical trials.
10 DR. BRUEHL: Segue from that. So thinking
11 about the -- I'm not going to call them
12 Dimensions 3 through 5, or 2 through 5 as we had
13 them up there before, but what was mentioned
14 earlier, I think about creating dimensionality out
15 of these other dimensions.
16 So instead of just categorical yes/no does
17 the patient have this, those issues of who is the
18 high-risk patient, if we structure it right in
19 Dimensions 2 through 5, simply assessing each of
20 those areas, you would have -- like an MMPI profile
21 where you've got dot, dot, dot, dot, 5 dimensions,
22 and you've got certain patients, if they're here,

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1 this.
2 So back to the issue on Dimension 1, two
3 things. One is, we are not diagnosing disease,
4 okay. So while the pain, acute pain may be due to
5 pancreatitis, we are not creating diagnostic
6 criteria for pancreatitis.
7 I'm just telling you what the parallel is in
8 the chronic pain. Now, you could choose to do
9 differently. But in the chronic pain setting, we
10 were going to just say that whatever group
11 specializes in pancreatitis has their certain
12 criteria.
13 So these are pain criteria. So what we
14 would say is, make reference in the diagnostic
15 criteria, has been diagnosed with pancreatitis
16 according to blah, and then you got your pain
17 characteristics. And I agree with the comment
18 earlier that some conditions, there's going to be
19 very little to describe the pain other than just
20 it's intense. There aren't a lot of other
21 characteristics.
22 I want to go back to Trip's comment earlier

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1 about diagnosing acute neuropathic pain versus
2 non-neuropathic pain. Clearly, there are
3 differences in presentation between certain types
4 of chronic pain conditions.
5 When you're coming up with that Dimension 1,
6 which really does need to be about making that
7 dichotomous diagnosis, that's where you want to
8 capture whatever those differences are that when
9 you see a patient, you would go, this is an
10 indicator that X is going on. In this patient, I
11 can see this pattern. They've got Y going on.
12 So that said, I'll go back to Dan to answer
13 questions. But pretty quickly here, let's try to
14 get to just brainstorming at least some
15 possibilities for the 5 dimensions or however many
16 you've got.
17 DR. DWORKIN: Temporal trajectories.
18 DR. BRUEHL: Temporal trajectories.
19 Dr. Wu?
20 DR. WU: Essentially, maybe we could just
21 not even worry about whether it's 1, 2, 3, 4 or 5,
22 but just like temporal trajectory, event,

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1 diagnosis. Maybe this is not a dimension.
2 DR. BRUEHL: Okay. Put that on the table
3 for now. There were a couple of others. I'm sorry
4 you said the temporal --
5 MALE SPEAKER: Trajectory.
6 DR. BRUEHL: Temporal trajectory.
7 MALE SPEAKER: Steve, I'll put in -- I put
8 locations, organ or tissue.
9 DR. BRUEHL: Okay.
10 MALE SPEAKER: All one.
11 MALE SPEAKER: What about organ system
12 involved?
13 DR. BRUEHL: Would that fall under
14 locations, organ system all as one?
15 MALE SPEAKER: Are we at the level of trying
16 to say like characteristics is one, or should we
17 say more things like quality and intensity? I'm
18 not sure quite what layer to go to with this.
19 Whether just characteristics is -- or whether we
20 should get more granular than that at this point.
21 DR. BRUEHL: I think that's a good broad
22 term, and we don't have to decide what those

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1 mechanism, all the things we've been talking about,
2 characteristics.
3 FEMALE SPEAKER: Inciting event.
4 DR. BRUEHL: I'm just going to call it
5 event. That could be a disease. It could be
6 whatever.
7 FEMALE SPEAKER: Preventable or not
8 preventable.
9 DR. BRUEHL: What?
10 FEMALE SPEAKER: Preventable or not
11 preventable.
12 DR. BRUEHL: Okay.
13 FEMALE SPEAKER: It's like a trajectory.
14 DR. BRUEHL: Because what is preventable?
15 The pain?
16 FEMALE SPEAKER: Like because we're saying
17 some things are going to fall in one category
18 versus the other. Some things will already be
19 going on, and some things are going to be something
20 that's happening in the future.
21 DR. BRUEHL: So preexisting or not?
22 FEMALE SPEAKER: Yes. At the time of

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1 characteristics are, and that may vary from
2 condition to condition. But you're talking about
3 pain qualities in some way. Yes.
4 MALE SPEAKER: How about modulating
5 conditions? Very broadly and you could subclassify
6 different domains of modulating conditions.
7 DR. BRUEHL: Okay. And when you're saying
8 modulating conditions, are you talking about
9 medical conditions, psychological state, what?
10 MALE SPEAKER: All of the above, so you'd
11 have to have subclasses to describe the cohort of
12 things that could modify the presentation.
13 DR. CARR: Did you have functional
14 interference?
15 DR. BRUEHL: Not yet.
16 MALE SPEAKER: And I think you want to have
17 the degree of trauma, or degree of inciting event
18 that caused the acute pain, so you can say the
19 event and degree.
20 DR. BRUEHL: Okay. Quantified somehow.
21 MALE SPEAKER: Correct.
22 MALE SPEAKER: I know this is not mentioned

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1 about trying to look at events, but in terms of
2 diagnosis, but I think we have to finally link this
3 up with some kind of ICD-10 that Sean talked about
4 in the morning. That's very critical as well,
5 because that's how you finally put all this
6 information back into the electronic medical
7 records.
8 So I know it's not what you're doing right
9 now, but I think ICD-10 is something critical that
10 we need to talk about.
11 DR. BRUEHL: : Put that in the parking lot.
12 I don't know -- could I just say I don't
13 know what the degree of the event -- what does that
14 mean?
15 MALE SPEAKER: Can you give an example?
16 MALE SPEAKER: Yes, so essentially, I mean
17 it could be a skin abrasion that can cause acute
18 pain. Or you could have a huge fracture of 10
19 bones that's causing the event. So what Tim talked
20 about, Tim Brennan talked about, the degree of
21 injury, which kind of tissues are injured would
22 make the degree of the acute pain mentioned --

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1 MALE SPEAKER: Wouldn't that go under the
2 organ tissue system?
3 DR. BRUEHL: Okay, let me ask, is that
4 extent? For example, like we had the incision
5 example earlier, where a small incision and a large
6 incision didn't make a difference. But if we're
7 talking about multiple bones versus one bone, does
8 that make a difference, and is that a way to
9 objectively quantify something like this? Is that
10 kind of what you're talking about?
11 MALE SPEAKER: Can I just say in that regard
12 as someone who studies acute and chronic pain after
13 sexual assault, most rape survivors who show up at
14 the emergency department in the United States have
15 moderate to severe pain in four or more body
16 regions. And the great majority of it is not in
17 areas where they were physically traumatized, so
18 the stressed induced type analgesia, and we see it
19 in BC [indiscernible] and so forth.
20 So I get very nervous about this extent as
21 because stress-induced type analgesia doesn't seem
22 to obey those rules.

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1 DR. BRUEHL: Okay, so --
2 DR. TIGHE: As a contrary point, though, I
3 do like that model [indiscernible], inflammation,
4 and sepsis. We're talking about high impact pain,
5 where you can have poison ivy all the way to a
6 septic event that can lead to the same mediator
7 threatening the life of the organism.
8 So there are parallel models in other
9 disease states that I think it's worth considering
10 for extent. I don't know how you quantify that,
11 though, in pain.
12 DR. KEHLET: So I want to go back to Kumar's
13 parking lot again, the ICD-10, just for one reason.
14 DR. BRUEHL: I've got to put it down here.
15 (Laughter.)
16 DR. KEHLET: Okay. But it is Kumar's
17 parking lot, by the way. The important thing to
18 realize is the ICD-10 also gives us criteria for
19 whether the operation was done arthroscopically,
20 laparoscopically. Those things are going to matter
21 a lot in terms of predicting your pain and your
22 management of pain.

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1 So if we take that out of the equation, how
2 does that help? I mean, an event is an event, but
3 then the intervention, especially post-surgical, is
4 going to be completely different if it is
5 laparoscopic versus an open laparotomy.
6 MALE SPEAKER: Then that is one issue. So
7 we at some point would have to start thinking about
8 how you characterize the event. It kind of gets
9 back to the classes and subclasses and all that.
10 So if you've got surgery as the big class,
11 and then you have -- I'm blanking on examples right
12 now, but you've got something like -- you've got
13 lumbar surgery, and now you've got microdiscectomy.
14 You can narrow it down more and more.
15 DR. BUCKENMAIER: Well, I kind of like this
16 idea of looking at organ systems and maybe
17 percentage involvement because this idea of ICD-9
18 breaks down the trauma. And certainly, a soldier
19 with a polytrauma is very different.
20 MALE SPEAKER: You have to use the mic.
21 DR. BUCKENMAIER: I'm sorry. I'm not used
22 to using a mic because usually most people ask me

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1 not to.

2 I think this idea of a soldier with

3 polytrauma as opposed to an isolated trauma, we see

4 very big differences just like the scale of

5 surgery. The analogy that was used was

6 laparoscopic cholecystectomy versus an open

7 cholecystectomy. Certainly, more tissue is

8 involved in an open cholecystectomy, more organs

9 involved than with a laparoscopic.

10 So I would agree that my concern as an

11 anesthesiologist for these two patients would be

12 different from a pain perspective. And that's

13 certainly the case in actual trauma, where you're

14 dealing with a 3 or 4-limb amputee with multiple

15 system involvement as opposed to somebody that has

16 a light injury, they've just lost an ankle.

17 DR. TIGHE: So one comment on the ICD-10.

18 It does allow us both procedural and diagnostic,

19 and it does allow a roll up. It in itself is

20 ontologically organized. However, I don't think

21 it's designed to encompass all of the dimensions.

22 So it may be useful as an entry for a triggering

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1 event or something similar, but I don't think it's

2 going to encompass some of the other domains.

3 The other issue is that many of our patients

4 will come in with multiple diagnoses. We keep

5 track of 50 simultaneously. So then you'd have to

6 keep track of are we looking at primary diagnoses,

7 the first 10, the first 50? What if they resolved?

8 So it does get a little bit tricky. I don't think

9 we can just say we'll include ICD-10, but it does

10 carry a lot of value if appropriately

11 contextualized in this.

12 MALE SPEAKER: But for event, should we -- I

13 mean, do we need to go back even further from

14 laparoscopic pain after choly? Back to

15 Dr. Brennan's talk, do we need to go back even

16 further to the tissue, that's not organ system but

17 the tissue that's involved, a bone versus parietal

18 pleura, versus lung tissue.

19 A good example that Brett gave is you

20 compare visceral pain. Well, that's not a

21 diagnosis, but pain after gall bladder isn't really

22 a diagnosis either but it's very specific.

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1 So are we getting stuck on focusing -- are

2 we equating event to diagnosis, or do we need to

3 take a step back further as the group -- is there

4 any capability to be more of a tissue injury,

5 whatever that etiology is, inflammatory,

6 neuropathic? Just a thought to throw out there.

7 FEMALE SPEAKER: Could I just comment on

8 that? In many surgeries or injuries, there's going

9 to be multiple tissues involved, so that just sort

10 of messes up that as an organizing principle.

11 MALE SPEAKER: But I don't necessarily think

12 it does mess it up as an organizing principle

13 because I don't think you need to start -- I don't

14 think Dimension 1 needs to start at the peak of the

15 pyramid.

16 So if I have a femur fracture and I get it

17 fixed, it's bone pain. They probably cut through a

18 nerve, it's nerve pain, muscle. But that all plays

19 into a classification system not necessarily to

20 lead to the diagnosis, but to classify the complex

21 array of that acute pain experience. So it's

22 complicated, but I think it's essential.

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1 DR. BRUEHL: I'm thinking what you just said

2 there, those different aspects of the injury, to

3 me, all would be tapping into, kind of jointly into

4 the degree or extent and the organ system issues.

5 I think those are -- it sounds like what

6 everybody is saying is that that is pretty critical

7 to understanding how seriously we need to take pain

8 for a given patient because there are clearly a lot

9 of differences, and some would be very low extent

10 and low severity, and all that, and others very

11 high, who were probably the ones at high risk for

12 complications on down the road.

13 So I think it's important to look at all

14 this. I'm not sure how it's going to be organized,

15 but it's great. Keep throwing them out.

16 DR. BRENNAN: Steve, is keeping it early on,

17 Steve and Roger, keeping it broad early, and then

18 catching tissue differences that may occur, as Mike

19 points out, further on down the line an approach

20 that fit with your previous work? If it starts

21 really broad, it will catch a contusion with or

22 without fracture that are very different.

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1 DR. BRUEHL: Are you saying that the way the
2 criteria that we would propose or worded would be
3 broad or specific?
4 DR. BRENNAN: Keeping it broad at the --
5 DR. BRUEHL: Dimension 1 level.
6 DR. BRENNAN: Not at the level, but just if
7 we end up with 7 dimensions, the broader they are,
8 the more likely we're going to --
9 DR. BRUEHL: Yes, that's good. I agree.
10 DR. FILLINGIM: And I wanted to get back to
11 this event thing, and there's a lot of focus on
12 tissue. But as Sam points out, there are other
13 aspects to the severity of the event from the
14 psychological meaning of the event, be it motor
15 vehicle accident or sexual assault, where the
16 tissues involved in the event seem to be far less
17 important than other aspects of the event severity.
18 But that could still be -- so the way these
19 dimensions will play out for different conditions
20 will be sort of coded differently, or the way it
21 gets filled in will be somewhat different. So that
22 relates to the broadness. So these dimensions need

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1 to be broad enough to incorporate that kind of
2 variability across conditions.
3 MALE SPEAKER: There's no evidence
4 that -- if we're talking about neuropsychiatric
5 sequelae or disorders of the brain or nervous
6 system, as a population, that more trauma equals
7 more outcomes. PTSD rates are just as high among
8 people discharged from the emergency department as
9 they are among those admitted.
10 There's just this huge variation there, so I
11 think that's really important to keep in mind, that
12 greater tissue injury outside the OR has very
13 little to no correlation with risk of
14 chronification across [indiscernible].
15 DR. BRUEHL: Can I just ask, are there
16 protective effects? Some people -- like they both
17 have similar injury, both have PTSD, one gets
18 better and one goes on to have a horrible
19 outcome --
20 MALE SPEAKER: We know in the emergency
21 department, expectations of recovery -- Roger and I
22 have a paper working on that, that we know that you

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1 know comorbid psychological symptoms, those types
2 of things, the things that we would expect from the
3 pain literature.
4 DR. BRUEHL: Okay. And that's under
5 modulating conditions as we have it up here, right?
6 Yes.
7 Steve, then we'll do Bernie.
8 DR. RAJA: One aspect in acute pain, which
9 has significant therapeutic implications that needs
10 to be brought in, it may come under Dimension 5
11 that was in the chronic pain, and that is prior
12 comorbidity and therapy.
13 For example, a patient on 100 milligrams of
14 methadone pre-op because of a drug abuse issue
15 post-operative after surgery is a totally different
16 acute pain patient than one who has never seen
17 opioids before. So somehow building that into the
18 acute pain taxonomy is probably important.
19 DR. BRUEHL: That sounds kind of like
20 the -- for chronic pain, it was common medical
21 comorbidities, but I think maybe for acute pain, it
22 is more the condition existing prior to the injury

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1 that we're talking about in the event here. It was
2 ongoing at that time, right? Yeah.
3 Steve?
4 STEVE: I would say -- I know we're talking
5 about surgery in like big traumas, but if we take
6 acute pain, extensor tendinopathy like elbow pain
7 let's say, it's a big difference if it's a work
8 related versus sport related, you know, those types
9 of things. So more of the context, I think maybe
10 that's within that Dimension 3.
11 DR. BRUEHL: This is like psychosocial legal
12 context.
13 STEVE: But it also can have a physiologic
14 effect too. Yeah. And that could also be
15 protective because if it's work related, but they
16 have a strong relationship with their boss and a
17 positive outcome about their job, that's a better
18 outcome. So yeah, I think that whole context of it
19 with the injury.
20 DR. BRUEHL: Okay. And you said medical
21 also? Is that kind of primarily bias, or
22 psychosocial, and legal?

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1 STEVE: No, in an underlying context. So
2 again, was it work related, was it while they were
3 running.
4 DR. BRUEHL: Okay.
5 MALE SPEAKER: And I think event is -- one
6 thing about event is it's kind of a shorthand for
7 that.
8 STEVE: Yeah.
9 MALE SPEAKER: You know, which doesn't
10 capture all of it, as you're pointing out, like
11 work related or not. But a lot of it we know --
12 STEVE: Then you take a deeper dive in it.
13 MALE SPEAKER: Like when you say a rape
14 versus car crash versus this, you learn a lot about
15 it.
16 STEVE: Yeah.
17 DR. BRUEHL: So this is the context of the
18 event, or I guess it would be the context of the
19 pain, too, because the event and the pain are kind
20 of inextricably linked in here.
21 DR. FILLINGIM: Well, but it sounds to me
22 like a combination of the event, is this a work

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1 related injury or a sports injury, but then also
2 sort of modulating modifying factors that are
3 present, that might be around the event, but might
4 be completely independent of the event. These
5 people are independently wealthy, and so they don't
6 need a settlement. So it's sort of combination of
7 the event as well as --
8 STEVE: Maybe those are --
9 (Crosstalk.)
10 DR. FILLINGIM: -- factors.
11 STEVE: -- interrelated do you think?
12 DR. FILLINGIM: Yeah.
13 STEVE: The modulating conditions and the
14 context.
15 MALE SPEAKER: Steve, I'm not following.
16 The prior conditions and comorbidities, are you
17 talking about prior pain conditions and pain
18 comorbidities?
19 DR. BRUEHL: No.
20 MALE SPEAKER: You're talking about medical
21 or --
22 DR. BRUEHL: Well, opioid use. I don't

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1 know, does it go beyond that? Other medical
2 conditions.
3 MALE SPEAKER: Because I think they're
4 distinct concepts, right. Like there's the
5 comorbid medical conditions, and then there are
6 pain comorbidities.
7 DR. BRUEHL: Yeah.
8 MALE SPEAKER: And I think that they're very
9 distinct here.
10 DR. BRUEHL: Do you have a preferred way to
11 word it that would be clear?
12 MALE SPEAKER: Well, I didn't know what
13 you -- but you made it sound like that was coming
14 from some -- like you have talked about this
15 before, prior comorbidities, that this was part of
16 your past taxonomy work.
17 DR. BRUEHL: No. This is talking about
18 conditions, comorbidities present at the time of
19 injury, of the event.
20 MALE SPEAKER: I think that when we talk
21 about pain specifically, does the chronic
22 overlapping conditions become very important?

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1 DR. BRUEHL: Right. So prior chronic pain
2 would be a context that's --
3 MALE SPEAKER: But even more than just
4 chronic pain. I mean these chronic overlapping
5 conditions, what we would call centralized pain. I
6 mean, much to the chagrin of some in the room, we
7 would call it centralized pain. Those I would say
8 are important, and there are ways to assess that.
9 MALE SPEAKER: So do you think that's
10 comorbid or a modulating factor?
11 MALE SPEAKER: It depends on what you're
12 treating the person for that day. So I would
13 say --
14 MALE SPEAKER: Ankle fracture.
15 MALE SPEAKER: Yeah. I mean, I think that
16 is a comorbid condition.
17 MALE SPEAKER: So I mentioned before about
18 how I'm not as good a diagnostician as some other
19 people, and I find that treatment informs my
20 diagnosis more often than I wish.
21 I don't know how that would be codified in
22 this listing, whether it was response to initial

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1 treatment or yes or no, or whether you know a WHO
2 3-step approach failed or succeeded. But in some
3 way, I think that building in a response to
4 treatment might be helpful.
5 DR. BRUEHL: I think that makes some
6 rational sense. What it implies is the diagnosis
7 isn't static but it's a feedback process. You make
8 a diagnosis initially, and maybe that would be
9 blank at that time. You try some things, and then
10 you would have to revise the diagnosis, at least
11 that dimension based on their response. And under
12 extreme circumstances, maybe their lack of response
13 would change your diagnosis.
14 I guess it's open to the group as to whether
15 that makes sense to do that. So response to
16 treatment, so it would not be available at the time
17 you make the initial diagnosis, though.
18 MALE SPEAKER: Well, it would be because
19 most -- very few of us, even those on the front
20 line, aren't necessarily the first responder.
21 DR. BRUEHL: Okay.
22 MALE SPEAKER: So something might have been

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1 done.
2 DR. BRUEHL: Okay. I'll put it down here.
3 MALE SPEAKER: For example, it would have
4 the ability to identify a condition that was not
5 easily treatable if you broke the treatment down
6 and it didn't work, and you found that no treatment
7 most of the time.
8 DR. BRUEHL: Okay.
9 FEMALE SPEAKER: I don't know exactly where
10 this would fit, but I think it's probably
11 important. And this sort of gets to like -- or
12 hopefully it would capture the times when the
13 diagnosis is uncertain and is potentially much more
14 serious, like you just had surgery now you have
15 abdominal pain, and it might be an anastomotic
16 leak, or your lung may have collapsed, or I don't
17 know,
18 Where would we -- would that be under
19 context maybe? I kind of feel like pain is almost
20 always worse for people when it represents
21 something unknown to them. If they know, oh, well,
22 I'm having pain because of X, this acute pain

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1 because of X, they're not as concerned about it,
2 we're not as concerned about it.
3 So I don't know. I'm not necessarily saying
4 anything. I'm just throwing out a question.
5 MALE SPEAKER: Could I comment on that, too?
6 DR. BRUEHL: Sure.
7 MALE SPEAKER: So what Robert or Bob said I
8 think has relevance here. Previous experience with
9 the same or similar conditions or treatments is
10 very relevant to the current diagnosis and
11 treatment. So it may not be the response in the
12 emergency room or the vehicle, but I've had this
13 before; or even more telling, I've had this
14 condition before but this is worse, or this is
15 different. These can be very telling. I don't
16 know how you're going to categorize that.
17 But I did have another comment, and that
18 goes to the utility of these different criteria.
19 Because while the criteria may apply to the
20 clinician in the diagnostic and therapeutic
21 setting, they also apply to the clinical
22 investigator in the research setting, but for

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1 different reasons and different uses.
2 So that's why I like the idea that Tim had
3 of using broad categories here. And then when we
4 write this up, what we include here for the
5 clinician in ruling out or in certain diagnoses may
6 be exactly what we want to rule out of a clinical
7 trial because it would confound the evaluation of
8 therapeutic response.
9 So that's the next step I think, which is to
10 take these broad criteria and say, what is the
11 utility for each of the two major purposes?
12 DR. BRUEHL: Right. And keep in mind, just
13 for terminology, these are not only the criteria,
14 these are the dimensions that we would be looking
15 at. But yes, I agree. Steve?
16 MALE SPEAKER: And I just want to say one
17 quick thing. In practice, Dimension 1, assuming
18 it's actual diagnostic criteria, that may indeed be
19 as far as some people go.
20 I think what you have to think about this,
21 though, is that each patient, if this was done
22 thoroughly, covering all 5 dimensions, you would

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1 have a really nice description of everything you
2 need to know about that patient that is relevant to
3 the pain. That's kind of what we want to end up
4 with at this, because that could be used to plan
5 treatment, track treatment, et cetera.
6 I'm sorry, go ahead. Dan?
7 DR. CARR: I was just going to say in trying
8 to think of categories, I'm not wedded to this, but
9 thinking about population based, you might have
10 event, host, environment, pathophysiology, and
11 impact. I'm trying to span with broad terms the
12 concepts that people have talked about in the last
13 hour. So it would be event, that is pain event,
14 host, environment, pathophysiology.
15 DR. BRUEHL: I'm sorry, event, host --
16 DR. CARR: Event. The next one would be
17 host, like in public health, you speak of host
18 factors for vectors, so host meaning patient.
19 Environment. Pathophysiology. And impact.
20 So I think those are broad. I don't think
21 of things that people have brought up, like your
22 points Henrik, I think they could fit in here

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1 somewhere to try to make a foundation for the most
2 comprehensive and potentially most granular.
3 DR. BRUEHL: What's the last one again?
4 DR. CARR: Impact.
5 DR. BRUEHL: Impact.
6 DR. BRENNAN: I think impact relates to
7 consequences that -- functional consequences that
8 Henrik brought up.
9 DR. BRUEHL: So we have the functional
10 interference up here.
11 DR. CARR: I would say functional
12 interference -- instead of impact, functional
13 interference.
14 DR. BRUEHL: Yeah. All right, I'll add also
15 impact there.
16 Yes?
17 MALE SPEAKER: [Inaudible - off
18 mic] -- degree of the physical injury, we talked
19 about. It could be physical injury. We can say
20 skin, muscle, bone, nerves, and vasculature, and
21 visceral organs is actually they may present
22 differently. And we need x-ray for one, we need

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1 physical exam for the other one, or just
2 differential diagnosis for visceral injury.
3 On the next line after degree of the
4 physical injury, we have pain processing, a
5 spectrum or host dimension, personality,
6 catastrophizing, pain experience, influence of the
7 second person, like a family member or a surgeon.
8 That's a very big influence, the way that the
9 experience the pain or define the pain.
10 Response to medication or basically response
11 to opioid is another thing. That depends on
12 genetics, all the side effects that the patient may
13 experience. It could be too good. It could be no
14 response at all. I mean, oftentimes we get called
15 because patient has too good response to opioid
16 rather than not responding to opioid.
17 Functionality or mobility is I think the
18 ultimate thing that we get worried about the
19 patient that has severe pain and is not moving,
20 rather than a patient defining like severe pain but
21 continue to move and continue to function. That's
22 like kind of putting it in summary.

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1 DR. BRUEHL: What do you mean when you say
2 pain processing?
3 MALE SPEAKER: I mean the same thing as
4 Dr. Carr said, host. Pain processing is that the
5 same pain in two different persons may actually be
6 realized differently or expressed differently.
7 DR. BRUEHL: So how would we put that if it
8 were to be part of the dimension? Because it has
9 to be clear to people who weren't sitting in this
10 room talking about this. Are we talking about pain
11 sensitivity or -- to the extent that we can assess
12 that.
13 MALE SPEAKER: Pain experience is one good
14 way to put it. The patient had a bad experience
15 with the pain in the past.
16 DR. BRUEHL: Okay. So we had here previous
17 experience with the same condition.
18 MALE SPEAKER: Or any condition that is
19 painful.
20 DR. BRUEHL: Any pain. Okay. So previous
21 pain experience.
22 MALE SPEAKER: Yes.

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1 DR. BRUEHL: Okay.
2 MALE SPEAKER: If we follow Dan's proposal,
3 before the event, we had pre-event risk factors,
4 and we repeat ourselves. It's clear from the
5 scientific literature that catastrophizers,
6 anxiety, and those things, the pre-operative
7 opioid, or pre-injury opioid treatment, how is your
8 nociceptive function before the injury, are you a
9 pain sensitizer, expectations; and then pre-injury
10 pain in the area where you have the injury versus
11 pain in other places in the body. It's easy. It's
12 easy.
13 DR. CARR: So would you accept those under
14 host? Those are host.
15 MALE SPEAKER: What?
16 DR. CARR: Those are the factors of the
17 host, or the patient.
18 MALE SPEAKER: Yes, but that's pre-event
19 risk factors.
20 DR. CARR: Yes, which would also include age
21 and gender, for example.
22 MALE SPEAKER: No, it doesn't matter. You

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1 cannot change it, and it doesn't matter.
2 DR. BRUEHL: I'm going to play devil's
3 advocate here. So here is a pragmatic problem. So
4 the patient comes in, let's just say has surgery,
5 and you're seeing them after surgery. And now
6 they've developed this pain, and you're diagnosing
7 it. And it says you're supposed to identify their
8 pre-event catastrophizing.
9 How do you go about knowing what happened
10 before this ever developed, if they had never not
11 been assessed for that specifically.
12 FEMALE SPEAKER: Well, I think in that
13 situation, it wouldn't -- I mean, it would be nice
14 to know what it was, but it wouldn't really matter.
15 You would look at whether they were catastrophizing
16 right then, and see, oh, the host is
17 catastrophizing. So therefore, I may need to
18 employ a different strategy.
19 DR. BRUEHL: Okay.
20 MALE SPEAKER: Those are different
21 measurements, too. I mean, the pre-event pain
22 catastrophizing evaluation will have a different

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1 outcome. Those 26 points will be different than at
2 the time of the pain itself; that's for sure. So
3 you have to deal with what you have.
4 MALE SPEAKER: You would think.
5 MALE SPEAKER: But part of this exercise is
6 to help for future scientific trials of analgesics.
7 And we have to have enriched analgesic trials in
8 the future. That means that we have to stratify
9 exactly for these pre-event, well-known risk
10 factors so that we can focus on the relevant
11 patient groups and forget about those who are
12 irrelevant and they are easy to manage.
13 DR. BRUEHL: So really, instead of saying
14 pre-event risk factors, if we just call it risk
15 factors globally, it does not sound much different
16 than what we had in the AAPT dimensions. That is
17 Dimension 5 I think, yes.
18 Roger?
19 DR. FILLINGIM: And I think just like in
20 chronic pain, if we just met them, we don't know
21 what their premorbid risk factors were. We can
22 rely on their history or other factors. So just

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1 because some of this stuff is difficult on the
2 ground doesn't mean it's not important. And there
3 will be circumstances, certainly more so with acute
4 pain trials, where we can actually gather
5 information before the pain starts.
6 DR. RAJA: Still I like the concept of host
7 and host risk factors. And although Tim's didn't
8 want to consider immune function as an important
9 thing, I can think of a scenario where a patient
10 with acute zoster with an HIV who has low immune
11 function will have a much more intense acute pain
12 than one with normal immune function. So host risk
13 factor with immune function as one of the modifiers
14 may be important criteria.
15 DR. BRUEHL: So the host is physiological
16 conditions potentially. It's psychological
17 potentially. Social potentially, in a sense,
18 because it's the interactions with the environment.
19 FEMALE SPEAKER: Experience.
20 DR. BRUEHL: Experience too.
21 MALE SPEAKER: It's experience, too,
22 absolutely. I like the term host.

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1 FEMALE SPEAKER: [Inaudible -- Off mic].
2 DR. BRUEHL: Oh, sorry. I'm trying to leave
3 space. So we added risk factors, which would be
4 the far left. Then we have the event, the host,
5 which is the patient. We have the environment. We
6 have pathophysiology and impact.
7 Pathophysiology, Tim, in this model with
8 pathophysiology, would that be the TRP V1
9 [ph] -- what level are we talking about if we're
10 talking about pathophysiology there would you
11 think?
12 DR. BRENNAN: I think if it's broad enough,
13 it can go to any level you'd like to because I
14 think in some of these disease states, we might be
15 able to take it to that. I think in an autoimmune
16 condition that's associated with pain, it can go
17 down to a molecule in a biologic. So I think as
18 broad as we can keep it --
19 DR. BRUEHL: Okay.
20 DR. BRENNAN: -- so that we can get it to
21 the receptor if we need to.
22 DR. BRUEHL: And this is the pain

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1 pathophysiology, not the associated disease
2 pathophysiology.
3 DR. BRENNAN: No. We still have some that
4 will eliminate pain based on biologics. So I think
5 in the future, it will be valuable to be broad in
6 that way.
7 DR. TIGHE: I think also if we keep it
8 broad, we can always narrow later within that
9 domain. We can subclass and such, so we don't have
10 to have an absolute definition at this stage. We
11 give ourselves some wiggle room in the future.
12 MALE SPEAKER: Just to think out loud and
13 play devil's advocate for a second, I wonder
14 whether event, host, environment, pathophysiology,
15 where people using this system wouldn't know
16 whether, okay, the host factor, that could be
17 the -- well there's no characteristics in there in
18 terms of diagnostic criteria, although they could
19 be like let's say that we're going to have core
20 diagnostic criteria.
21 DR. BRUEHL: Separate from that.
22 MALE SPEAKER: Separate from that, so it

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1 would be an additional dimension. And then if it
2 was host -- so if the person had a history of high
3 catastrophizing, I guess that could affect the
4 pathophysiology of the pain as well as be a
5 characteristic of themselves, and it could be
6 related to their environment if they catastrophize
7 because of some psychosocial situation.
8 Again, these terms may well be as good as
9 any. I'm just trying to think about future users
10 and them knowing what goes where, and if there's
11 any terms or other things we should consider that
12 might be more self-evident.
13 DR. BRUEHL: We can break down into these
14 categories and rename them, just use them
15 conceptually to lump together things. I think
16 that's totally fine.
17 MALE SPEAKER: And we need an acronym, too.
18 DR. BRUEHL: Bob is working on that tonight.
19 DR. CARR: Well, just to clarify, though,
20 for pathophysiology, we could by convention put
21 different things in different compartments. But I
22 was trying to respond to Tim's challenge to keep

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1 the things broad. And pathophysiology, to me,
2 could include your very good point about which
3 tissue, which tissue type was affected. What was
4 the location? What are the putative mediators of
5 that particular configuration?
6 DR. BRUEHL: So I think mapping -- and we're
7 not locked into this, but I was just thinking, I
8 can't do it right this second, but it may be
9 worthwhile listing the event, host, environment,
10 pathophysiology, impact, and then mapping the other
11 things that we've said here onto that. It would be
12 valuable to do that.
13 Would you mind if I take down the paper in
14 order to write on another one?
15 MALE SPEAKER: Go right ahead.
16 MALE SPEAKER: There's a charge.
17 DR. BRUEHL: Well, I mean, is anybody
18 actually reading this and relying on this to make
19 some comment right now?
20 Knox, go ahead.
21 DR. TODD: You're welcome to go to the next
22 page.

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1 DR. BRUEHL: Okay.
2 DR. TODD: But there is a charge.
3 (Crosstalk.)
4 DR. BRUEHL: That's right, I didn't realize
5 it was a post-it note.
6 DR. TODD: So one of the things I've been
7 thinking about in listing to the conversation, and
8 perhaps this is just a contextual factor, Sean and
9 I were talking about rapid learning systems and how
10 users would use this information to modify our
11 healthcare systems.
12 So as a patient comes in, private pain
13 becomes public assuming it's not an overt injury,
14 and there's a transaction between the patient and a
15 clinician or a caregiver. How do you quantify the
16 caregiver characteristics?
17 The content perhaps of communication around
18 an acute pain presentation that I think are
19 impactful, and knowing some of that data would help
20 us modify our treatment systems. Is there a way to
21 measure, perhaps, caregiver gestalt about prognosis
22 for outcome, or is there a way to measure degree of

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1 certainty or confidence in the outcome that a
2 caregiver might have? And use that information
3 then to feed back to the system to modify where
4 there might be improvements.
5 I'm impressed there's some literature in the
6 emergency department that looks at the content of
7 communication and how little we know about that
8 content of communication, and how powerful it could
9 be. As a clinician, that's appealing to me, but
10 I'm not sure how practical or feasible it might be
11 to capture it.
12 DR. CARR: Maybe that could be environment
13 of care. So it could still go into one of those
14 categories.
15 DR. TIGHE: I think more broadly that also
16 points to the access of the patient to certain
17 treatment modalities depending upon the healthcare
18 setting, and that is going to influence the
19 experience that you aggregate within this domain.
20 If certain therapies just were not available
21 or were not culturally used in that healthcare
22 setting, would you consider that in a broader

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1 environment or would you have a special subheading
2 for healthcare setting?
3 DR. CARR: Maybe if there is a difference, I
4 don't know, but maybe change environment to milieu.
5 DR. TODD: But it would be interesting to
6 see it captured in some sense, whatever bucket it's
7 put in.
8 MALE SPEAKER: Just for the sake of
9 parsimony, event might be tucked in under core
10 criteria. So for example, post-operative pain, the
11 core criteria is that it occurs within 72 hours of
12 an -- I'm just making this up.
13 DR. CARR: Good point.
14 FEMALE SPEAKER: And then 2 and 4 could
15 those be combined?
16 DR. BRUEHL: The more we combine the better
17 because seven is unwieldy.
18 FEMALE SPEAKER: Two and 4 together, you
19 mean?
20 MALE SPEAKER: That could just be one of the
21 criteria that [inaudible – off mic].
22 DR. BRUEHL: Okay. So that takes this off.

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1 Sorry, 2 and 4 you're thinking, risk factors.
2 FEMALE SPEAKER: Most of the risk factors
3 are sort of applicable to the host [inaudible – off
4 mic].
5 DR. BRUEHL: They would be characteristics
6 of the host. Yes, that would make sense. So host
7 patient, to me, for lack of a better way to think
8 about it, it's kind of like if I draw a circle
9 around the patient, it's everything inside that;
10 except for pathophysiology because we've broken it
11 out..
12 DR. DWORKIN: So I was thinking about
13 exactly that, Steve. So host is the moment before
14 the event, and pathophysiology occurs
15 right -- starts right after the event.
16 DR. BRUEHL: Right after. Okay.
17 DR. DWORKIN: So host is right at the event,
18 and pathophysiology is after.
19 DR. BRUEHL: And risk factors were present
20 at the time of the event, so it would make sense to
21 combine that.
22 DR. DWORKIN: So they're host.

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1 DR. BRUEHL: Yes.
2 DR. DWORKIN: Exactly.
3 MALE SPEAKER: And then, Bob, let's say two
4 folks get in an automobile collision, and one
5 person -- they have the same -- we'll just
6 hypothetically, the same level of pain. One is way
7 less active because of that pain, really markedly
8 drops their activity.
9 Is that part of pathophysiology because it's
10 occurring after? You know what I'm saying, in
11 terms of, let's say, just behavioral response.
12 DR. DWORKIN: So to me I think that's
13 something different. I think that's kind of
14 impact, but functional impact.
15 MALE SPEAKER: Okay. [inaudible - off mic].
16 I think impact is fine. Yes, it works.
17 DR. DWORKIN: Though, I think a lot of us
18 believe that the kind of functional consequences
19 could exacerbate the pathophysiology and that those
20 2 dimensions could be in a loop.
21 MALE SPEAKER: [Inaudible - off mic]. I
22 guess in this time frame maybe we could just say

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1 impact.
2 FEMALE SPEAKER: We lost our temporal
3 element. [Inaudible - off mic].
4 DR. BRUEHL: That goes last. It goes last
5 because that's the only place I have to put it
6 unless it fits --
7 (Laughter.)
8 MALE SPEAKER: The only thing I'll say about
9 temporal is it doesn't imply a longitudinal
10 evaluation, and so often we're making these
11 diagnoses cross-sectionally. So we may or may not
12 be in a position to -- like if I'm in the emergency
13 department and it's two hours after something, I
14 may say, oh, I'm going to diagnosis him with this,
15 I'm going to trial this medicine or new
16 intervention. But I don't really know over that
17 two hours has it been temporally or --
18 DR. BRUEHL: Well that gets at a little
19 confusion I have about the concept. So the
20 temporal, the way we talked about it earlier, to
21 some extent was talking about for a given disorder
22 what was the evidence on risk for chronification

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1 and maybe the factors that would be relevant to
2 chronification. So it had to do not necessarily
3 with a snapshot of where they were in the temporal
4 course necessarily, or maybe not just that, but
5 also going forward what was likely to happen.
6 Now, was I misunderstanding that or is
7 that --
8 DR. TIGHE: So I would interpret it to mean
9 the anticipated temporal features.
10 DR. BRUEHL: Anticipated.
11 DR. TIGHE: How long will this hurt? How
12 long am I going to be at a decreased level of
13 functioning?
14 DR. RAJA: I think it relates to the
15 pathophysiology. For example, a temporal cause
16 after an amputation in terms of pain would be very
17 different from a skin incision. So there is a
18 relationship between the pathophysiology and the
19 temporal cause.
20 DR. BRUEHL: Which also relates to the
21 severity of the event, right.
22 Deb?

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1 MS. GORDON: Yeah. No, I'm kind of mixing
2 up in my mind, too, the temporal and kind of the
3 nociceptive burden. If you have a procedure, so I
4 mean there's a liver biopsy, that's very different
5 than a laparoscopic liver procedure versus an open
6 liver procedure. So it's tissue trauma and the
7 time of the event, and I don't know how to fit
8 them.
9 DR. BRUEHL: But that's part of the event
10 characteristics. We haven't moved this over there,
11 but the locations, organ system, tissue, all can be
12 used to index the degree or extent. And I think
13 that all kind of fell under part of the event if
14 we're doing it the way we'd originally talked
15 about.
16 Yeah?
17 DR. CARR: So the temporal component has
18 been mentioned. Are there other characteristics of
19 the pain itself that are part of -- you know, the
20 sensory qualities of the pain? And this is a
21 different temporal feature, but fluctuations in
22 pain; the kind of bodily extent of the pain, is

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1 that incorporated?
2 DR. BRUEHL: It's not. On our list over
3 here, we had pain qualities. Temporal could be
4 considered a quality unless we're talking about the
5 predictive risk issue, where it's not really
6 a -- well, it's kind of a different -- it seems to
7 me like a different thing.
8 MALE SPEAKER: I think it serves a dual
9 purpose. I mean, it serves a classification
10 purpose and a diagnostic purpose, like you said.
11 So moving away from a diagnosis where I had
12 procedure what pain's going to look like, you think
13 about right upper-quadrant pain, left
14 lower-quadrant pain, ruptured AAA. Those have very
15 distinct temporal characteristics before they show
16 up to the ER, but their management and
17 trajectory -- and that aids in the diagnosis, but
18 their trajectories afterwards and how it is
19 characterized goes into classifying future risk.
20 So I think it serves a dual purpose. I
21 don't like making things more complicated. My
22 preference, we put it in core criteria, but it

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1 might just apply to two different dimensions.
2 DR. BRUEHL: To put the temporal under core
3 criteria or the risk?
4 MALE SPEAKER: The diagnostic component of
5 the temporal I think is a core criteria. If you're
6 talking about in terms of risk and classifying for
7 chronic pain, I think an argument could be made to
8 put it into another dimension, modulating factor,
9 pathophysiology.
10 MALE SPEAKER: Sorry. Go ahead, Deb.
11 MS. GORDON: Well, I'm just thinking there's
12 another aspect with the temporal stuff, kind of
13 like Brett was talking about with that rib
14 fracture. When you see somebody who comes in with
15 a fresh chest trauma, they look very different than
16 they do two or three days later when that injury
17 blossoms and then they have to get reintubated. So
18 I don't know how that fits in there, but I do think
19 that you go through different phases.
20 MALE SPEAKER: I'm wondering whether or not
21 it might be better to not have this host as the
22 moment before, again, just to sort of throw out

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1 ideas. Because you could say, well, let's say how
2 I respond -- Roger and I are both in a car accident
3 together. He thinks he's going to be fine
4 tomorrow, and I think, oh, my life's over. I'm
5 never going to recover from this, I'm never going
6 to get better, I'm catastrophizing.
7 So is that, yes, it has a lot to do with how
8 we were the moment before, but it really has to do
9 with characteristics of what our presentation is
10 like? So maybe if we were just like, you
11 know -- characteristics or something that would
12 describe characteristics, but it wouldn't so much
13 distinguish the pre-event or the post-event. I
14 don't know if that's --
15 DR. BRUEHL: That was really only to try to
16 explain why pathophysiology was separate, which I
17 don't -- instead of calling it pathophysiology,
18 talk about putative mechanisms or something, then
19 we kind of avoid that issue just by relabeling it.
20 And then we don't have to necessarily say.
21 Because I agree. Catastrophizing three days
22 after an injury, you have no idea what they were

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1 doing before or at the time of the injury, but if
2 they're catastrophizing three days later, clearly
3 that is an important thing to know in terms of --
4 (Crosstalk.)
5 MALE SPEAKER: These modulators -- these
6 risk stratification things, I'm trying to think
7 what category they'll go in.
8 DR. BRUEHL: Yes?
9 FEMALE SPEAKER: What Henrik was saying
10 before is like for some cases, like when you are
11 trying to do research, you do want to know about
12 the pre-operative or pre-event risk factors. So
13 what if we just didn't specify a time and we kept
14 it really general?
15 DR. TIGHE: So one point that Trip had
16 brought earlier that I think is apropos to this
17 discussion, he had talked about the polytrauma
18 patient, multiple sources of pain.
19 One of the trends recently in looking at
20 temporal dynamics of pain, also in the broader
21 temporal dynamics of anything, is to consider
22 there's a spatial temporal issue. So we're not

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1 looking just at changes over time, but changes in
2 location as well.
3 I think that's especially apropos again to
4 the polytrauma patient where you may have
5 differential rates of recovery of different types
6 of tissue injury. You may also have continued
7 evolution on a patchy framework.
8 I think it's very hard to characterize
9 today, but I think as time goes on, that will allow
10 us access to a broader source of information. It
11 may simply be pain radiation patterns, but it could
12 also be differential qualities of recovery over
13 time at different locations.
14 DR. BRUEHL: So the Dimension 3 that was up
15 here a minute ago said pain quality to start with,
16 temporal may be there. Spatial we're adding. But
17 those all seem to fall under the same category to
18 some degree.
19 There are different levels of temporality.
20 One is, is the patient's pain worse in the morning?
21 Is it pulsatile? Does it ever remit? Is it
22 constant high? Is it constant low? I mean, there

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1 are all these different patterns that may be
2 relevant, may not, I don't know.
3 Then we've got the temporal prediction issue
4 saying what is the risk for the future? To me,
5 that aspect of the temporality seems to fit under
6 the risk discussion in Dimension 2, but I'm just
7 throwing that out there to see what people think.
8 MALE SPEAKER: [Inaudible - off mic]. Where
9 is catastrophizing and expectations and all?
10 DR. BRUEHL: That's under host. I'm
11 thinking of that as all inside that circle around
12 the patient.
13 MALE SPEAKER: [Inaudible - off mic]?
14 DR. BRUEHL: No, we've gotten rid of the
15 timing issue on that.
16 MALE SPEAKER: I made a list a couple months
17 ago that when I would see a patient, I go back in
18 the history and see what happened in the past, and
19 now I have to get involved with this patient. I'm
20 going to read you the list that I made.
21 History of pain, history of pain medication,
22 history of drug dependence. I said Cures because

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1 in California we have Cures. It's a program that
2 we go look at the drug history of the patient.
3 History of anxiety and depression. History
4 of chemo. I mean, patients with chemo, oftentimes
5 they come, they have severe pain compared to the
6 same. Pain with previous surgeries. Duration from
7 the last surgery.
8 I mean, if you had a surgery a month ago and
9 now coming for the second surgery, the pain
10 definitely out of control or most of the time.
11 Allergy to pain medication. Side effects from pain
12 medication. This actually defined that person or
13 host.
14 Pain out of the surgical site. If they have
15 a surgery and they're complaining of neck pain,
16 shoulder pain, or back pain or something.
17 Barriers, like extreme age, psychiatric illness, or
18 neurological disorder, culture differences. And
19 emergency surgery is another one that oftentimes we
20 deal with the uncontrolled pain.
21 So these are lists that may be helpful.
22 DR. BRUEHL: It sounded like not all, but

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1 most of those could be categorized under these
2 labels that we had before. What we need to do is
3 take some of these broad categories we initially
4 came up with and make sure they all fit under
5 something here.
6 Just so I don't forget, I'm going to go
7 ahead and stick under Dimension 2 the chronicity
8 risk. We can move it later, but I just want to
9 make sure that that's still a point that's kind of
10 not absolutely clear.
11 All right. So what that leaves us with is,
12 let's see, 3, 4, 5, so we have 6 dimensions, if I
13 counted right. All right.
14 FEMALE SPEAKER: [Inaudible - off mic].
15 DR. BRUEHL: Maybe, yes. Yes?
16 MALE SPEAKER: Where is temporality?
17 MALE SPEAKER: Still thinking about the AAAPT
18 interventions. Where do common features appear
19 here? Because, for example, that would be an area
20 where one could report response to pain treatments
21 or pain medication. Is there a common features in
22 this?

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1 DR. BRUEHL: There is not, and that is an
2 option is we --
3 MALE SPEAKER: Why?
4 DR. BRUEHL: -- we can call it common
5 features and re-categorize things as that, if it
6 makes sense. So as it stands now, in case you
7 can't read it -- and I'm just going to make a note
8 here about the common features.
9 All right. So what we're got is core
10 criteria plus the event, characteristics of the
11 event. So this would be what you would use as your
12 primary way of determining does the patient have
13 this condition, is just following your Chinese menu
14 thing up here for Dimension 1.
15 Dimension 2 is risk factors, host, patient
16 internal, just anything in the circle around that
17 patient, which might include the risk for
18 chronicity as well.
19 Dimension 3 is pain qualities, spatial
20 qualities, temporal characteristics, timing maybe
21 with regards to the event, that kind of thing. And
22 that's something I guess we didn't specifically

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1 talk about, but how long it's been since the
2 surgery, and when you're doing the evaluation and
3 diagnosing that's probably relevant.
4 Dimension 4 is environment. I'm not
5 entirely sure what we mean by that. I mean, I can
6 certainly see some of these things like the legal
7 and work related issues, family, all that.
8 MALE SPEAKER: [Inaudible - off mic].
9 DR. BRUEHL: Environmental context.
10 DR. CARR: And milieu of care.
11 DR. BRUEHL: But is this the external?
12 Because we've already got the host here, which is
13 kind of the internal environment. Is this the
14 external environment context?
15 FEMALE SPEAKER: Yes.
16 DR. BRUEHL: Okay. Probably not a good
17 label for it, but we'll --
18 DR. CARR: So we have milieu of care.
19 DR. BRUEHL: Should I write that down, Dan?
20 DR. CARR: Yes, I mean I thought that Knox
21 made a very good point to that --
22 DR. BRUEHL: Milieu.

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1 DR. CARR: -- what's this interaction,
2 what's the social thing?
3 DR. BRUEHL: Plus it sounds very fancy, so I
4 like it.
5 DR. CARR: Yes, we love it.
6 (Laughter.)
7 DR. CARR: One other comment is just that we
8 have the world's authorities on the whole series of
9 impact to publications, but we also have Paul who
10 first authored a great recent paper on acute pain
11 trials.
12 So there may be some role to kind of
13 thinking about what did that review of acute pain
14 trials show, and could it be mapped onto this
15 system. In other words, is there some gap that
16 we're not thinking of or how does it fit together
17 with the literature.
18 MALE SPEAKER: [Inaudible - off mic].
19 DR. BRUEHL: I'm sorry, somebody else had
20 their hand up first.
21 MALE SPEAKER: Oh, that's fine. Hi, Mark.
22 What about functional consequences? It's been --

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1 DR. BRUEHL: Impact.
2 MALE SPEAKER: That's the impact?
3 DR. BRUEHL: Yes.
4 MALE SPEAKER: Because --
5 DR. BRUEHL: So I should clarify that.
6 MALE SPEAKER: Yes, because you could tie
7 that to many of these topics that we've
8 talked -- you know, specifically what's the
9 functional impact of the psych issue, the opioid
10 tolerance, the prior history of chronic pain?
11 It seems that often those are discussed in a
12 clinical context, one after the other, and can have
13 a -- direct care, that's really important. Thank
14 you.
15 DR. BRUEHL: Rosemary?
16 DR. POLOMANO: So again, some of these fit
17 into some common buckets. So for the risk factors,
18 the biological or getting the precision science in
19 there with genomics, psychological, social, and
20 environmental. And also for punitive mechanisms, I
21 like that better than pathophysiology because acute
22 pain isn't always pathologic. I mean, right? It's

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1 not.
2 I like the punitive mechanisms because you
3 can use the same thinking because it's not really
4 just biological mechanisms. There are punitive
5 mechanisms. PTSD I think is a punitive mechanism.
6 And that might be a risk factor for pain, but it's
7 also a sustainer or -- so again, in category 5,
8 those same buckets of biological, psychological,
9 social, and environmental might hold true.
10 I'm thinking we had talked, and Mark had
11 mentioned, about education, because I really think
12 Dan and I just got done doing an evaluation of the
13 medical licensing exam, the USMLE, and we'll have a
14 publication coming out soon. But it was woefully
15 or dreadfully disappointing in terms of the amount
16 of questions and competencies.
17 I'm just wondering if we think a little
18 farther. We've got research that we're thinking
19 about. We've got practice. And we think about
20 education, and we think about the competencies.
21 And I think the big competency is the nature of
22 pain, the core competency, the coming out with the

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1 nature of pain coming out in here, which would be
2 5, and to kind of cross-link that. And then the
3 assessment of pain competency, which really falls
4 into 2 and 4. So to just not lose track of the
5 educational competencies that we've defined.
6 DR. BRUEHL: Yes, that's a good point.
7 I'm sorry. Brett, you've had a question for
8 a while, right?
9 DR. STACEY: Yes, this is pretty brief
10 but --
11 DR. TURK: This is the last question.
12 DR. BRUEHL: What?
13 DR. TURK: Last question.
14 DR. BRUEHL: You're sure? Two, that's it.
15 We'll get to you two, and that's it.
16 DR. STACEY: My thing is about trajectory.
17 People on post-op day 2 who have expected amount of
18 pain after an event are quite different than people
19 10 days out, who, as Henrik pointed out, the group
20 that have recovered have minimal pain if they kind
21 of overdo it versus the people for now whom pain is
22 quite different.

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1 It's almost a different thing. They have
2 the same insult, the same injury, the same initial
3 start, but were on the wrong trajectory. Those are
4 different. I don't know how you kind of say here's
5 an expected trajectory, here's someone who is off.
6 Somewhere you have to look at healing and
7 expectations.
8 Is it all just three? Is that just that?
9 DR. BRUEHL: I would think that would fall
10 under the temporal because you're always going to
11 be judging whether it's appropriate pain or not by
12 how long out it's been from the injury and --
13 DR. STACEY: So we use the same diagnosis on
14 post-op day 2 and on post-op day 25?
15 DR. BRUEHL: That would depend on whether
16 they meet the core criteria. And they could all
17 meet the core criteria. That is, they fall in the
18 bucket, but be qualitatively very different in the
19 specifics, and that's what's captured here,
20 hopefully, if we've done our job right. But I'll
21 add trajectory here to Dimension 3 just to make
22 sure somehow we address that.

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1 DR. TIGHE: It would also pertain to the
2 context of the events at the time. So somebody who
3 is in 10 out of 10 pain but doing their ninth lap,
4 that's a different event than somebody's 10 out 10
5 pain lying still in bed. So the context is key
6 there as well.
7 DR. BRUEHL: Okay. And we've got one more.
8 MALE SPEAKER: Sure. I'm still just trying
9 to rectify event in my head for this specific
10 reason. If I have right upper-quadrant pain, is
11 acute visceral right upper-quadrant pain the event,
12 or is acute cholangitis the event? Or is the
13 inflammation of my hepatobiliary system leading to
14 pain signaling the event versus I just broke my
15 ankle? Is the event I just broke my ankle, or is
16 the event that the bone's broken and the inherent
17 macromechanisms that are associated with that?
18 I think this might be -- and I think this is
19 probably the answer -- maybe not the answer, but a
20 lot of good discussion tomorrow where we have
21 processes such as acute post-procedural pain, I
22 know what happened, versus orofacial pain, which

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1 can be a fracture, an abscess, some other syndrome.
2 Acute visceral pain, it could probably be 500
3 different diagnoses.
4 So in my mind going in tomorrow I'm
5 struggling with event, so hopefully I will work it
6 out tonight.
7 DR. BRUEHL: Well, and I think event was a
8 short -- if I recall correctly, now, event was a
9 shorthand way, in a sense, of also getting at the
10 extent of the tissue trauma.
11 MALE SPEAKER: [Inaudible - off mic]. Well
12 in the context lots of things. But it
13 doesn't -- event's under core criteria, and it
14 doesn't always have to be present. You know, there
15 may be certain types of pain for which there is no
16 event.
17 DR. BRUEHL: That's true.
18 MALE SPEAKER: But for certain times, it's a
19 sine qua non.
20 DR. CARR: Can I just as a comment, I'm
21 actually optimistic about that because I'm thinking
22 back to you know being taught how to do history in

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1 physical, and when you write it up and hand it in
2 to your preceptor, there's a part called history of
3 present illness. And, generally, people get that
4 right. You don't wind up giving the history of an
5 irrelevant illness. I'm optimistic that that can
6 be dealt with, but it's a good point.
7 MALE SPEAKER: All right, that will do it.
8 DR. RAJA: [Inaudible - off mic].
9 DR. BRUEHL: Yes, right. Yes, onset very
10 broadly -- I'm just going to put that in quotes.
11 It could be all kinds of things. All right. I
12 guess that's it, right, for now.
13 MALE SPEAKER: [Inaudible - off mic].
14 DR. BRUEHL: Yes, we will. Yes. I know the
15 cartoon you're referring to.
16 (Laughter.)
17 MALE SPEAKER: Could you please restate the
18 homework.
19 DR. BRUEHL: Think about these things. Come
20 up with a solution. Be brilliant tomorrow.
21 (Whereupon, at 4:51 p.m., the meeting was
22 adjourned.)

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