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Health Technology Clinical Committee Public Meeting
March 21, 2014

Craig Blackmore: Well, we have a quorum, so let's bring the meeting together, to order. Well, good morning, everyone. Welcome to the Health Technology Clinical Committee open public meeting. I'm Craig Blackmore, committee chair, and the meeting is now in session. We have a quorum of members, and I will turn it over to Josh for program updates.

Josh Morse: Good morning. I'll do a quick run-through of our, about our program. So, welcome. Today's topics will include, I'll do an overview and today's topics are nonpharmacological treatments for treatment-resistant depression and facet neurotomy in the afternoon. Treatment-resistant depression will be discussed this morning and facet neurotomy in the afternoon. A little background on the program, the Health Technology Assessment program is run out of the Health Care Authority, a state agency in Olympia. The program was created by legislation in 2006 that designed the program to use evidence reports and a panel of clinicians to make coverage determinations of selected medical procedures, tests, and devices based on the evidence for safety, efficacy, and value for state-purchased healthcare programs. Multiple state agencies that purchase healthcare participate to identify the topics that are reviewed through this program and implement the policy decisions that come from the program. They include the Health Care Authority, which operates the Uniform Medical Plan, and Medicaid for the State of Washington, The Department of Labor and Industries, which operates the Worker's Comp Insurance program, and the Department of Corrections. Implementation by the agencies is required by the legislation.

So, the purpose of this program is to ensure that medical treatments, devices, and services that are reviewed are proven to work when they're paid for with state healthcare dollars. So, the program provides a resource for the state agencies that purchase healthcare. We develop scientific evidence-based reports on the medical devices, procedures, and tests that are selected, and we facilitate this committee's work to make determinations based on those facts. So, our overall objective is better health for the citizens of our state. We strive to operate a transparent program to minimize bias, to be consistent, and to be use repeatable processes. The overall process, as shown here in this graphic, the director of the Health Care Authority is charged with the overall selection of

topics for review. We then contract for evidence reviews that are then presented to this committee. The clinical committee makes coverage decisions based on the evidence and other information provided, including public comment, and the agencies ultimately implement these decisions in the healthcare programs.

The principal questions are, is it safe, is it effective, and does it provide value. Again, we value transparency. We publish the topics, the criteria used for selection and review, give reports in draft form along the way, and we conduct open public meetings for these decisions. This is designed to use the best evidence through formal, systematic processes for review of the select technologies, and these decisions are made by this independent committee. The basis of decisions are objective factors in the evidence, including the nature and the source of the evidence, the characteristics of the studies or trials on which the evidence is based, and the consistency of the outcomes in comparable studies. Additional factors might include how recent the evidence was developed, its relevance to Washington State populations, and facts about bias in the evidence.

So, topics that have been reviewed in the past year are shown here, and you can see the bolded topics are the ones that we will be reviewing today. In the future, at the bottom, in May, we will bring proton beam therapy to the committee in public meeting and then the meeting following that is currently scheduled for November and will include thyroid ultrasound for screening and assessment of thyroid abnormalities and neuroimaging for primary dementia, degenerative dementia, and mild cognitive impairment.

There are multiple ways for stakeholders to participate with this program. We have a website, which has a relatively new web address, as shown here. You can join our stakeholder mailing list, which is the most direct way to get updates from the program, or call us, actually. There are public comment periods on proposed topics on draft key questions, on draft and final reports, and on draft decisions from the committee. Anyone is welcome to attend these public meetings. All the meeting materials are posted in advance. We strive for at least two weeks, and anybody may present comments to the committee in public meeting. Anyone may also nominate a health technology for review, and that concludes my presentation. Thank you, very much.

Craig Blackmore: So, next on the agenda would be to finish up business from the previous meeting, and that has two components. First is the approval of the minutes and then second it would be for final approval of the two decisions that we made at that prior meeting. So, first the draft minutes have been distributed to the committee and then made available. So, I would solicit comments on those minutes or motion to approve.

Kevin Walsh: I move to approve.

Michael Souter: Second.

Craig Blackmore: Second? OK. All in favor of approval of the minutes from the previous meeting, if I could just have a show of hands.

Josh Morse: Eleven, or that would be ten. Ten approved, thank you. David's not here.

Craig Blackmore: OK, next is the previous decisions. There were two topics at the last meeting. First was the hyaluronic acid viscosupplementation. The committee made a decision to cover with conditions. The conditions are laid out in the draft findings and decision document, which was distributed to the committee members, and in your packets you will find both a white version and a yellow version. The yellow version contains some suggested additional text for clarify based on review of the actual transcript of the previous meetings, and my thinking here is that the clarity would be useful in terms of implementing the intent of the committee's decision. So, I would like the committee members to review the yellow copy of the decision and either confirm or not confirm that that is consistent with the intent of the committee's decision making. The additional text is highlighted. I have reviewed the transcript of the previous meeting, and I think this does actually capture our intent, but obviously that's, that's just one voice.

Josh Morse: There were lots of public comments in one reference (_____)

Craig Blackmore: Right, which have been distributed to the committee members for review.

Josh Morse: Christine is going to start the phone while you're reviewing this.

Richard Phillips: Do you want us to comment on it at this point?

Craig Blackmore: Either, yeah, I'd like to have comment.

Richard Phillips: My only thing about the, the final statement was that it read that it was restricted to patients who have a contra-, a documented medical contraindication and on down the line. I think also medical contraindication or intolerance. I mean, I think intolerance should be put in that, because there's some patients who really can't tolerate steroids or other things, is that the same as contraindication? I'm not sure, but I think it's more clear for me. I'm not sure what the basis for the confusion was, yet, so, you know, why they changed it.

Chris Standaert: You know, I had wondered about our original language, because I sort of read that and went, could you just say somebody can't tolerate NSAID's and that's a contra-, and then we can do it, and we weren't, it's sort of vague, what we said the first time. I don't know. I don't know, I would think of intolerance the same as contraindication. They can't tolerate . . .

Richard Phillips: I would think so, too, but it's . . .

Chris Standaert: . . . NSAID's.

- Richard Phillips: . . . more explicit. I, you know, I don't know. It's, it almost, by saying, well, how do you know if it's contraindicated unless you try it, you know? I mean for some of those drugs you almost have to have implied that they've tried it in order to say that they can't use it, and yet there's some people who have GI bleeding that you just say, I'm not going to take the chance, you know? They're intolerance to it.
- Chris Standaert: Well, that would be . . .
- Richard Phillips: Is it . . .
- Chris Standaert: . . . that would be a clear medical contraindication, I would think.
- Richard Phillips: Yeah, I would think so, too, but you know, it may be just parsing words, and I don't really, it's fine with me as it is, but I raise my objection.
- Seth Schwartz: Well, there's another issue and that is, how about the person who's tried all these others and still had symptoms. Are we going to allow that person? I mean, they don't have a contraindication to steroids or a contraindication to NSAIDs.
- Chris Standaert: They just failed them.
- Seth Schwartz: They failed it.
- Chris Standaert: Right.
- Seth Schwartz: So, would they be a candidate for hyaluronic acid?
- Chris Standaert: I didn't think that was our intent, was it? Our intent wasn't this is treatment if everything else doesn't work. I thought it was only, our intent was, we allow it if really there is medically no other thing to do for them. That was my understanding.
- Richard Phillips: I agree, and then I think the other thing was, there was a portion of this group that felt it should never be given, so it was really a 5-4 kind of split, or whatever it was in the final vote.
- Christine Masters: One moment please.
- [Recording]
- Richard Phillips: I'll just move that we accept it.
- Craig Blackmore: Is there a second, or further discussion?
- Marie Brown: I'll second.

Michael Souter: I'd like to just check on the use of the word. Are we saying that including all of the following? That means that we actually have to try, or have it documented, contraindication, to every one of those criteria, or do they just want to . . .

[Recording]

Kevin Walsh: I think I have the same question that Michael has. I think this is very restrictive, and I think a lot of the debate that we had was about how restrictive to be. Some people thought totally restrictive and others of us thought not quite that restrictive. If everything else hadn't worked, that it may be an option, and I think where this says it's not an option if everything else is failing. Simply, you could only use it if there are no other options, but not that you've tried them and they've failed, just that there are, that they can't even try other things, and I'm not sure that captures the spirit of the debate that we had. That's, I'm not totally sure about that, but that's my concern about this restrict, this very restrictive language.

Chris Standaert: I mean, we're getting into how, how much we parse this out. I mean, this is very restrictive and I, we had this discussion where, you know, a significant number of people didn't think that it warranted coverage, particularly, and I don't remember there being, well, if nothing else works, you can do this. That's the argument already. That's its standard indication currently, that other things don't work, so you use it. So, if we left that as our restriction, if we say any of the following, then somebody can't tolerate NSAID's you get it because they can't, it becomes a much less restrictive, and you're essentially allowing standard use saying they don't tolerate NSAID's, or we tried Advil, it didn't work. We're going to go with this.

[Recording]

Chris Standaert: Which I did not think was our intent. I thought our intent was to be much more restrictive, personally.

Marie Brown: Restrictive, yes.

Michael Souter: I suppose the implication taken from this is that if you say that you have to, you know, have all of the following, then (_____)

[Recording]

Craig Blackmore: Those of you on the phone, we can now welcome to the meeting. We will let you know of the designated time where it's listening, public input. In the meantime, we're going to try to put you on mute.

[Recording]

Michael Souter: So, my approach to it was just looking at the, you know, following the law of unintended consequences. What happens if we've got somebody who, say for

example, has a contraindication to both NSAID's and nonsteroidals. That's left them, then, the option of physical therapy and exercise, and the presumption then is that one single mode, you know, if it should be enough to sort their problems, that's what we're seeing by effectively, you're limiting the delivery of hyaluronic acid in those circumstances and just given and likely that I think, single therapy is likely to, often completely efficacious on its own circumstances. That's my only concern there is just that we're, by saying that you have to have all of the above then there are some consequences from that.

Craig Blackmore: So it, I think it's a little ambiguous what the all refers to in this statement. So, does the . . .

Michael Souter: That's why I was asking for the clarification.

Craig Blackmore: I mean, either it means the nonsurgical care includes and the all merely refers to this list as types of nonsurgical care or if it means that you have to have a contraindication to all of these. It doesn't, it doesn't, if it said document a medical contraindication to all other forms of nonsurgical care would be unambiguous that you had to have failed all of them.

Chris Standaert: That wouldn't be, that means you can't have any of them. So, there are two ways of looking at this. So, you have the one way that, you just described this, implies that the treatment we're discussing, hyaluronic acid, actually has superior benefit to one of these other choices. Therefore, no, no, no, but that's what you said. So, if well, if they have exercise and we allow them exercise, what if that doesn't work, we should do this. That implies that in some patients, it would be more efficacious than exercise so we should do it. If the idea is that it's no better than anything else out there, it's no better, it's equivalent to giving people Tylenol or Advil or exercise programs, then the only reason for using it is in people who can't access any one of those. Do we have proof that it is, in people who fail exercise, it is better than a failed exercise program? Do we have proof that in people who fail a corticosteroid injection is better than a failed corticosteroid injection? Are these people who aren't going to respond? So, there are two different way, again, there are different ways of phrasing this. This is phrasing it saying it is equivalent to these choices. Therefore, if you can't have any of these choices for medical reasons, it's a reasonable thing to use, as opposed to saying, if these don't work, well, it's, it may well be better than the things that you tried that didn't work, so you can try it. Those are two different ways of looking at the product.

Michael Souter: I'm not certain that I agree with how you are representing what I was saying, that in essence when we are treating people who have got osteoarthritis of the knee we will use NSAID's. We may use corticosteroids, again, as well, and we may use a program of, you know, rehabilitation and physical therapy with that. My point being is that if we embrace this as an all means all to exclude the use of hyaluronic acid in those circumstances, then, you know, we're not truly embracing, kind of, the multimodal approach, which I think may be more efficacious in those times. I don't think we saw any evidence to say that, you

know, hyaluronic acid was any less or more effective in comparison to a combined program using all those modalities together. We looked at pretty much the comparisons where a single, interactions. So, therefore, we should be judging this in terms of single equivalency . . .

Chris Standaert: Right.

Michael Souter: . . . rather than saying that, OK, you have to, you know, fail all of those before you can actually . . .

Chris Standaert: Well, this doesn't say you fail, if you fail all of these you still don't get it, is what, this is what this says. It says you have to have a cont-, you can't have one of them, not that you've failed them, but you can't have it, and, and . . .

Michael Souter: Sorry, take away the fail, but just make it due to intolerance. If, if you've got a contraindication to all of those, that's the only circumstance that you'll get hyaluronic acid.

Chris Standaert: Right, that's what this says, yeah.

Michael Souter: And I don't . . .

Chris Standaert: So, that means that if you can, if you can go to PT and do an exercise program, even if it doesn't work, you can't get the hyaluronic acid is what this would say.

Michael Souter: So, that is what . . .

Chris Standaert: And that would . . .

Michael Souter: . . . I have a problem with. I don't agree with, you know . . .

Chris Standaert: But that would imply, and so there's evidence that in people who fail an exercise program, hyaluronic acid is effective. I mean, that's the question.

Craig Blackmore: No, no, no.

Michael Souter: I think you put words in my mouth, Chris.

Chris Standaert: No, I'm not. So, if this says, if you can't do, you can't have them medically, you have a patient who is in appropriate for exercise, they have heart disease, they have other neurologic things, they can't do an exercise program, they can't take NSAID's, and they can't have steroids, but you can do the injection, that's what this says. What you're saying is that, what I'm interpreting is saying, if you say if they, if we leave it such that they can only do exercise, what if exercise doesn't work and then you're saying maybe they should be able to get the injection. That's very different and what that's, but that's, so how would you, that's how I'm interpreting what you're saying. If you, you're not saying it's a medical contraindication. You're saying they have one choice left, they have exercise.

They have the pool therapy. They have the PT. They have exercise. That's all they have.

Craig Blackmore: So, I think we're . . .

Chris Standaert: So why, by this they wouldn't be able to get the drug whether that works or not.

Michael Souter: And that's the point I'm making.

Chris Standaert: So, what would you like it to say, or what do you think it should say? That it's allowed if that doesn't work?

Michael Souter: Well, I think this is . . .

Chris Standaert: That's what I'm trying to get at.

Michael Souter: . . . this is a problem that we get into when we look at this specific language, which dictates what the medical contraindications of nonsurgical care should be. Now, we're being fenced into this by the use of these terms, and I think that that, you know, I'm looking at the law of unintended consequences, as I said, and in that way, we've become very, we are here now becoming very prescriptive and specific about our definition and our criteria for use in these circumstances, and I'm not certain that that's where our dialogue that we had before was taking us when we were discussing this as a committee.

Seth Schwartz: And I agree with that. I think when I read this, this is basically saying you can't ever use it, because the number of patients in whom you, either contraindication to NSAID's or contraindication to steroid injections, and the contraindication to exercise, is virtually nobody. I mean, you could probably create some, you know, miniscule number of patients that meet this criteria, but this is basically saying, you can never use it, and I don't think that was the nature, the way our debate went. I think we want it to be very restrictive, but I don't think we want it to say nobody can ever get it, which is the way I read this now.

Michelle Simon: I think it might help us to know why this language was changed.

Craig Blackmore: Josh?

Josh Morse: There is one, there was one question that asked if this included exercise and strengthening measures, and that's in your packet, and this was also, the question was also raised by the agencies, as well, is how do we apply this. Does this include just pharmacological alternatives or does it include exercise? So, this was a way to clarify what it included, as far as what the medical contraindications applied to.

Craig Blackmore: So, as I recall . . .

Michael Souter: So, my problem . . .

Chris Standaert: . . . I'm sorry. As I recall, also, the people who, there were, I recall five people who wanted no coverage, so far more, so some of the people who wanted no coverage may be able to clarify their viewpoints here, because what, if you don't say this, if you don't say, it's only for this very small group of people who can't have something else, then you are saying that it is for other people who fail other forms of therapy, which is the standard usage of the drug. We're not, it's not being restricted at all, particularly, saying, that's what I'm, that's what I'm having trouble with. So, if you tell me, I have a patient who has knee pain that can't NSAID's, they have diabetes. I don't want to give them steroids. As far as exercise, they don't work, I can do it. That standard use (_____).

Michael Souter: So, I just have, the, the other viewpoint I'm taking is that, you know, we have a patient who has got, as a medical physician, I can think of a few where they would not be able to take NSAID's.

Chris Standaert: Mm-hmm.

Michael Souter: They would not be able to take steroids.

Chris Standaert: Mm-hmm.

Michael Souter: And now, the only therapy left for them under this plan is physical exercise, and that's it.

Chris Standaert: Yes.

Michael Souter: And I don't agree with that.

Chris Standaert: Again, there were a number of people who thought there was no real proof (_____)

Michael Souter: Well, I accept that, but then that's, that, but this was not brought out in part of that decision, and so if you want to pursue this as a kind of way of capturing the mood at the time, then I would disagree with what we, with the way that we're doing it now, and that should be something that's actually brought out in a repeated discussion and a new vote rather than trying to guess that this would somehow massage the minority at that time who chose to vote in a different direction, but we can't just, you know, make, adopt this language and say this satisfies the dissent of the five at that time who chose to vote the other way. We need to vote on that before I would feel happy with that. I think that, you know, we're looking at fundamentally different, you know, the way this is interpreted, the way this is said, it's fundamentally different from where we were going previously.

Craig Blackmore: So, what I'm hearing is not a lot of satisfaction with the proposed changes to the language. So, in terms of implementation, it may be helpful to the people who

have to implement our decision to keep the word documented before medical contraindication. Does that word cause the same sort of concerns that the other added text does or not?

Michael Souter: I can't speak for Seth, but I would be more than happy if we just simply struck the word all.

Richard Phillips: Yeah, that's, that's what I thought, too. Or put for example. For example would be . . .

Craig Blackmore: Or just, without (_____)

Chris Standaert: So, I, I guarantee you, you're not going to restrict it at all, because people say, they try to, they can't tolerate NSAID's. I don't want to give them NSAID's. As soon as you remove the all, that means as long as they have some in, contraindication to some form of medical therapy, they can have the drug. That's what that s-, this is the difference. If you take out all, you can say they can't tolerate NSAID's, they can have it.

Michael Souter: I'm measuring one set of consequences versus another and I would, I rest, honestly, I prefer striking the word all.

Seth Schwartz: Yeah, and I think, you know, the, it's the contraindication term is different than failure term. I mean, I think if we're saying failure that opens it up to everybody, but since you're saying contraindication, I think that's a clear difference. I mean, I think you can, you can argue that it, that people are going to say, oh yeah, NSAID's are contraindicated. People are always going to work their way around what we say. I mean, that's, we can't change that, but we're, contraindication means a specific thing. It means they can't use it, as opposed to they tried it and it didn't work, or they tried it and they didn't like it, and that's, contraindication is pretty restrictive as it is. So, I, I don't agree with you necessarily that anyone can just use it based on, on this statement. I think if you say it's contraindicated, that's fairly strong. I would agree getting rid of all, I think all is the problem here. I think if you say such as or got rid of that part, I would be comfortable with it.

Craig Blackmore: So . . .

Michael Souter: But, but . . .

Craig Blackmore: . . . just trying to parse out the difference between clarifying language and rehashing the whole decision from the last meeting.

Richard Phillips: Can we put them up on the screen, the two different statements?

Craig Blackmore: Yeah. So, it's the difference between the yellow sheet and the white. So, I'm going to, I am hearing that the addition of the word all in the minds of some of the members of the committee causes some fundamental change to the

wording on the previous document. Now, whether or not everybody is in agreement with whether this captures, you know, whether they agree with it or not, we already went through that and we already had a vote. The intent is really to make sure the wording captures what our decision was, and, and I think what I'm hearing is the word all, perhaps, changes the meeting and, and again, we spent some time wordsmithing this, so I'm going to defer, even though there's obviously a spectrum of feeling among the committee about what, where the sort of bar for appropriate coverage might be. So, what I'd like to do then is to accept a motion to accept the draft, findings, and decisions on the yellow page. So, as amended for clarity except striking the word all. So, it would say nonsurgical care including, I guess it would be, all of, including nonsurgical care, including the following, NSAID's, corticosteroids, physical therapy, exercise. That, that seems to provide clarity without causing differences about whether it is a reflection of previous debate.

Seth Schwartz:

I disagree. I'm, I'm just going to repeat what Chris said. The problem is that if you don't, we have to craft language that, in some fashion, gives the clear message to the orthopedist that just because the patient can't take NSAID's, that doesn't mean they get to have hyaluronic acid. It means they have to go and try exercise first, or, as Chris said, there's no evidence that it's any better than exercise, so why do they get it at all after exercise. If we take out the word all, then basically everybody who has a GI reaction to NSAID's gets hyaluronic acid. They don't have to try exercise. That's reality. So, I, I think that, I understand the, the conundrum that the agency's in, 'cause they're trying to apply the spirit of our decision and they're trying to figure out, well, how exactly do we structure the gate, here, and I see that it's difficult, but if we want to capture the spirit of what we, the discussion that we had and the vote we had, it's not that if you can't tolerate NSAID's you get to have hyaluronic acid. That wasn't the spirit of the decision.

Craig Blackmore:

Well, I think there's a disagreement about the spirit of the decision. So, um, so I guess what we need to do is determine what the committee believes the spirit of that discussion was, since we don't all seem to be on the same page. So, perhaps the, the best approach then becomes to have a vote on the use of all of or not the use of all of, and that would be, that would tell us. So, I guess the first thing, just for, just to be very clear is, first we will vote on the wording on the yellow document, whether or not to include all of, and then we will have a final vote on approving so that the approval vote is sort of clear. Does that make sense from a process standpoint? OK, so what I'd like then is a show of hands, and I'm going to go back to the yellow language. So, I will read it and we will have a vote of yay or nay and the nays will then mean that they are voting for the same language with the removal of the all of. I want to make sure people are following me, because, so what we're voting on now is the first bullet point. Draft findings and coverage under osteoarthritis viscosupplementation will read, restricted to patients who have a documented medical contraindication to other forms of nonsurgical care, including all of the following NSAID's, corticosteroid injections, and physical therapy/exercise, and

then none of the other words on this will be any different. So, I would like a show of hands, people who favor, including that all of piece of the equation.

Josh Morse: I see six raised hands for yes.

Craig Blackmore: It's nice to have a unanimous vote, but we don't always. So, therefore, we will conclude that the use of all of captures the spirit of the discussion we had last week and our current understanding. Now, I would like a vote for final approval of the draft findings and decisions with added text for clarity, which is included on this yellow sheet in the packet. So, could I please have a show of hands for approval of the final decision.

Josh Morse: I see six.

Craig Blackmore: And opposed, just for consistency?

Josh Morse: Five opposed.

Craig Blackmore: Next order of business is the draft findings and decisions for hip resurfacing, and the document has been distributed to the committee members and is in the packet and is posted, and the decision was that hip resurfacing was not a covered benefit. Any discussion on this document before we proceed to a vote? No comments were received. Alright, then I would like a motion to approve.

Male: Move to approve.

Craig Blackmore: Second?

Michelle Simon: Second.

Craig Blackmore: And then all in favor, if I could have a show of hands, please.

Josh Morse: Eleven approved.

Craig Blackmore: OK, next item on the agenda is new business. The first technology for review is nonpharmacological treatment for treatment-resistant depression and first we will solicit public comments. So, do we have any people who registered ahead of time?

Josh Morse: Yes, we do have public commenters signed up in advance this morning.

Craig Blackmore: So, while we are setting up for the people who signed up in advance, if there's anybody here who has not told us in advance, you are also welcome to address the committee. There is a signup sheet, which was outside, it's still outside. Christina's going to go out and get that. We'll start with the people who told us in advance and then we will take comments from people that are here, and then we will go to the phone if there's anybody who has called in who wishes to address the committee.

Josh Morse: Thank you. So, we have four commenters. We've assigned five minutes per commenter. The first is John Neumaier. Yes, please, thank you.

Craig Blackmore: So, for all the people that are addressing the committee, if you could please tell us who you are and if you are representing simply yourself or some organization, and if you could also tell us if you have any financial conflicts of interest related to the topic and if anybody paid for travel or expenses to bring you here, thank you.

Josh Morse: Can you also, I'm sorry, can you turn the microphone on? There's a switch on it. Thank you.

Craig Blackmore: Yeah, the meeting is recorded, so we ask everyone to speak into the microphone and the committee members to identify themselves when they initially speak.

John Neumaier: Thank you. Can you hear me now? My name is John Neumaier, and I'm a professor of psychiatry and pharmacology at the University of Washington, and I practice at Harborview Medical Center. My department is aware that I'm here, but I'm not representing the department specifically, but rather, uh, expressing my opinions. I have 20 years of experience as a faculty member at the University of Washington. I split my time between running a neurobiology research program and caring for patients, inpatients/outpatients, and I coordinate the ECT service at this point at Harborview. I have more than 20 years of experience performing ECT as an attending physician. We gave ECT to 34 patients in 2013. That's not a very large number considering that we have about 2000 inpatient admissions per year. We do virtual exclusively inpatient ECT because of resource utilization at my institution. These people are usually severely depressed, although occasionally we treat people with catatonia, which has failed to respond to the standard treatments and occasionally for mania, although that's infrequent. These individuals have usually failed to respond to a number of medication trials or have not tolerated them and have severe depression. Often, they have either seriously contemplated or recently attempted a suicide attempt, and some have barely survived by the time they come to our service. So, they're severely ill and really quite miserable because of their illness. These individuals often have had depression in the past, rather severe depression, sometimes have had a good response to ECT in the past, and they also are frequently poor or underinsured or under-served in other ways. So, we're taking care of people who have difficulty accessing care in the rest of the community and have often been turned away from other institutions due to financial reasons in relation to ECT.

I just want to comment briefly on my experience with ECT and my understanding of the research regarding ECT. It's considered the standard of care for serious and especially psychotic depression around the world. It has been for many years. The earlier studies were done in comparison to very powerful medicines, such as tricyclic antidepressants or monoamine oxidase inhibitors. These often have serious side effects, as well. My understanding is

that in the report that was prepared for this committee that they focused on research, since 1980. This is curious to me, because that's during a period of time when ECT was already considered the standard of care for many years, and the focus of studies had really shifted towards safety and attempts to finesse the side effect profile rather than to establish efficacy, and I don't think the studies were often designed to establish efficacy, per se, in the more recent era.

Depression is not a homogenous condition. It is very diverse and we have all observed, in psychiatry, people who respond very well to one treatment and not to another, and so we're fortunate to have many treatments available to offer people. I think that we reserve ECT for the most serious cases that we see, and these are people who might stay in the hospital for an extended time otherwise, potentially going to Western State Hospital. We, sometimes, have received transfers from Western State Hospital for voluntary ECT when the people have been able to be discharged from our service, because they had ECT and had been sometimes ill in the hospital for many months, if not more than a year.

I'm going to close my comments by referring to a couple of communications I've received from patients that I've treated. I don't receive thank-you notes or Christmas cards for prescribing Prozac. It never happens, but I do get cards from people who have completed ECT. This card, and I'm not for, to be absolutely clear on people's privacy, I'm going to not read these whole comments, but this card I received in November. It says thank you for saving my life. This is somebody who had had multiple treatments with medications without success, and this card, also somebody who is severely ill and incapacitated by depression said, it is a wonderful feeling to be able to smile and laugh again. One concern about ECT is the stability of the response. I think this is not the right question to be asking, because the analogy may be similar to epilepsy where when one takes the medication for epilepsy, it treats that condition, but it doesn't prevent future problems. I think that the nature of depression and chronic depression is that it can be a relapsing condition and to expect ECT to work on an extended basis in the future isn't realistic and isn't the way depression works, and if people stop their treatments, they will also relapse, due to the nature of the condition, not to the effectiveness of the treatment. Thank you for your attention.

Josh Morse: Thank you. The next commenter is Anna Borisovskaya.

Anna Borisovskaya: Hello. My name is Dr. Anna Borisovskaya. I am an associate professor at the University of Washington, and I currently work in clinical capacity at the Veterans Health in Seattle, Washington. I would like to speak about the . . .

Craig Blackmore: I'm sorry to interrupt.

Anna Borisovskaya: Yeah.

Craig Blackmore: Could you just tell us if you have any financial conflicts of interest.

Anna Borisovskaya: Sorry. I do not have any financial conflicts of interest. The VA is aware that I am here today, but I speak about my own clinical opinion. So, I would like to speak about the ECT and about my clinical experience with it. ECT is one of the most effective treatments in medicine and psychiatry, as evidenced by multiple randomized control trials comparing it to sham, electroconvulsive therapy, and pharmacotherapy, as well as I can attest to its efficacy from my own extensive clinical experience. I have patients who would be dead and would have taken their families with them if not for receiving the electroconvulsive treatment. My (_____) electroconvulsive treatment clinic with some of the most satisfied patients in the hospital. These are patients who have treatment-resistant major depressive disorder, severe schizoaffective disorder, bipolar depression, and these patients have never had anything else work for them, including multiple trials of psychotherapy and pharmacotherapy leading them to lose years of productive life and there is certainly also concern about the fact that these conditions do have symptoms of suicidal ideation and there is evidence that ECT also prevents suicide. Data suggests that at least resolution of acute suicidal ideation within three to six treatments. There is no other treatment that boasts such efficacy. In the (_____) when the suicide and (_____) victims and their families has been fortunately and finally brought to the attention of the public eye, I must point out the need for more effective treatment for severe mood disorders and one of their most troubling symptoms, suicidal ideation.

Further, as a geriatric psychiatrist, I must speak about the particular usefulness of the electroconvulsive therapy in the elderly. The elderly who have a rate of depression as high as 30-40% in the medical and nursing home settings are at very high risk for suicide. Some of the people who are the greatest risk for suicide are males over the age of 85 and older. They often commit suicide by using firearms and are at particular risk. These are also patients who often commit suicide because they are suffering from severe depression, and often these are the patients who do not tolerate the medications and who may be too physically debilitated by depression to wait for their symptoms to improve with medications. I know that, myself, my colleagues, and my hospital, overall, would not be able to provide the superior care that we do without the availability of electroconvulsive treatment.

Also, I would like to speak a little bit about the maintenance and continuation of electroconvulsive therapy. There are some studies that point out that this treatment does prevent hospitalizations and suicide attempts in the patients who continue to receive ECT after the index course of the ECT has been completed, and we have a number of patients for whom nothing else has worked who have been able to stay out of the hospital for years while receiving the treatment at the maintenance clinic at the VA, and I believe that we have saved their lives with this treatment, and I hope that it continues to be available for all the patients in the State of Washington. Thank you, very much.

Josh Morse: Thank you. The next speaker is Farrokh Farrokhi, and Dr. Farrokhi, can you state if you have any conflicts of interest.

Farrokh Farrokhi: Certainly. Thank you, and I have no conflicts of interest. My name is Farrokh Farrokhi. I am a neurosurgeon at Virginia Mason Medical Center. Today, I'm speaking to you on behalf of the national and state organization for neurosurgery on DBS therapy. Can someone else advance the slide, please? Thank you.

So, the, in a setting of background, there are four neurosurgical centers in the State of Washington that perform deep brain stimulation therapy. None of them perform it for treatment-resistant depression outside of research protocol. One center was on protocol, and that study was pulled. The national group, as a whole, is in agreement with the data analysis done by your group that there is insufficient data to render an opinion on whether or not this is effective therapy that needs to be approved. The concern of the national group was that a negative opinion by this group may hamper future advancements, and as you heard from the other commenters, this is an area of great need and DBS therapy has had profound effects in Parkinson's Disease and essential tremor treatment with over 100,000 stimulators placed. So, it has substantial potential. Next slide, please.

I apologize. On the last slide, the only comment in contraindication to your data analysis is, there was a 10% risk of hemorrhage and there are multiple well-proven data streams that show about a 1% risk of clinically significant hemorrhage. So, that's a clerical error in the assessment. So, yes, there is a risk of bleeding in the brain and damage for these patients, but it is at 1%, not 10%. The other complications that make up that 10% risk are device malfunction and infection. Next slide, please.

There have been multiple small trials showing substantial improvement, and I think the passion from the centers that perform this under research protocols comes from the fact that you take clinically-depressed patients and you place a stimulator, see an improvement in their mood and function, and in that exact patient you can turn the stimulator off, and in some cases within minutes to hours, and some cases within days to weeks, have them fall back into their previous depressed mood, turn the device back on, have them come out of their depressed mood. So, that gives the researchers who are doing this work impetus to keep pursuing and figuring out why it is working in those particular patients. Next slide, please. Next slide, please. Next slide, please.

Ultimately, this comes down to recent publications, as early as last month, that show small neural network changes at the area of the implant within a millimeter or two make a substantial difference in the efficacy and the plea is that we need more time and research to figure out exactly where to put these wires to make them work and that it's too early to make a decision one way or another on the impact of this treatment. Thank you.

Josh Morse: Thank you. Our next speaker is Mercy Yule, and if you could please state if you have any conflicts of interest, thank you.

Mercy Yule:

My name is Mercy Yule. I'm a licensed East Asian Medicine Practitioner in Washington State. I have no conflicts of interest. Thank you for giving me the opportunity to present some studies that may be of interest in the treatment of depression that resists pharmacological management. Acupuncture is a safe procedure with few problematic side effects, and research studies on specific conditions are becoming more available. I realize that acupuncture has not been a focus for this committee, so I present these four studies to you for future consideration.

That's good. The first study was published in the Journal of Affective Disorders in 2000. A single blind controlled study of 70 patients with major depressive disorder were divided into three groups. The first group received a standardized acupuncture protocol. The second group received nonspecific acupuncture treatment. The third group was given pharmacological treatment. Treatment was given for four weeks with evaluation twice per week for eight weeks. Here, we see that both standardized and nonspecific acupuncture were found superior to pharmacological treatment when patients were assessed with a global assessment scale. An increase in the graph shows improvement. Here, we see that when patients use the self-assessment tool, the graph demonstrates that symptoms were also reduced more with acupuncture treatment than with pharmacological treatment. Improvement is shown through a decrease.

I'm going to skip the next three slides in the interest of time. To conclude, the author has found that acupuncture did improve the course of clinical depression more than pharmacological treatment. The next study published last year in the Journal of Psychiatric Research was a randomized control trial of 160 patients diagnosed with major depressive disorder divided into three groups. The first group received pharmacological treatment. The second received acupuncture in addition to the pharmacological treatment. The third received electroacupuncture in addition to pharmacological treatment. Treatments were given for six weeks with assessment at one, two, four, and six, and a followup on week ten. This graph shows that the antidepressant effect of paroxetine was augmented by acupuncture and electroacupuncture. Symptoms demonstrated reduction according to the Hamilton Depression Rating Scale. In this graph, MA represents manual acupuncture, the blue triangle. EA represents electroacupuncture, the red square. PRX indicates paroxetine, the purple circle. The word score on the graph indicates the reduction in symptoms. The self-administered self-depression scale also demonstrated lower scores when manual or electroacupuncture were used in addition to pharmacological treatment. The authors concluded collectively, as most antidepressant agents have broad side effects, acupuncture in manual and electrical stimulation modes provides safe and effective treatment in augmenting antidepressant efficacy.

The third study, published in 2009, in Pharmacopsychiatry examined the effective acupuncture treatment on cytokines. It has been suggested that certain pro-inflammatory cytokines play a role in major depressive disorder; 95 patients

diagnosed with MDD were treated for six weeks. The first group received real acupuncture and placebo pills. The second group received placebo acupuncture and real fluoxetine. The third received placebo acupuncture and placebo pills. Patients were evaluated clinically through the Hamilton Depression Scale and CGI, as well as through serum cytokine levels. Both fluoxetine and real acupuncture demonstrated a reduction in pre-inflammatory cytokines. Additionally, the electroacupuncture treatment restored a balance in TH1, TH2 cytokines.

I'm going to skip forward a little bit. There's a lot to talk on the methodology of acupuncture studies, but we don't have time for that, so let's go one more, thank you. Our final study is meta-analysis of 207 studies on acupuncture and treatment of depression, of which 133 are focused on major depressive disorder; 20 of those studies were considered to be good quality according to (_____) Scale. The authors of the systemic review concluded the efficacy of acupuncture as a monotherapy was comparable to the antidepressants in improving clinical response and alleviating symptom severity of major depressive disorder.

To conclude, although the nature of the present review is to consider a specific nonpharmacological therapy for treatment of resistant depression, acupuncture might be considered. Acupuncture can treat major depressive disorder when used alone and can increase the effectiveness of pharmacological treatment, thereby reducing the burden of medication side effects. Thank you for your time.

Josh Morse: Thank you. We had no additional signups this morning, but we do need to check if there's anybody on the phone who would like to comment.

[recording]

Josh Morse: Hello, this is the public comment period. Is there anybody on the phone who would like to provide comment on treatment-resistant depression? I hear no, thank you, Christine, can you mute the phones?

[recording]

Craig Blackmore: Next on the agenda is the report from the Washington State agencies on utilization and outcome.

Charissa Fotinos: Good morning. My name is Charissa Fotinos, and I'm deputy chief medical officer at the Health Care Authority, and I'll wait until the slides are brought up to start. So, we're going to just give the agency medical director comments regarding the nonpharmacologic treatment. We're talking about treatment-resistant depression. Major depression is common with an annual prevalence rate of about 7% of U.S. adults in a lifetime prevalence of about 17%. The diagnostic criteria for DSM-V, which was recently issued, are unchanged from that of DSM-IV, requires five or more symptoms, including a depressed mood or

loss of pleasure for at least two weeks. Usual treatment include pharmacotherapy, psychotherapy, or both, and the standard is to treat for four to eight weeks at maximum tolerated dose to see if there is any change. The graphic just showed a PET scan of a person on the left who's depressed and the right not depressed with much more blood flow seen on the right.

Some definitions that, that might be important as we go through this; traditionally, no response is considered less than 25% improvement in whatever depression score is used initially to rate the depression, partial response 26-49%, responses greater than 50% and remission is generally the term when people get back to the normal level of score with whatever tool is being used to grade the depression.

How common is treatment-resistant depression? The Star*D Trial was one that looked at this. They looked at progressive levels of treatment for patients who were not improving after a series of pharmacologic therapies. After four courses of antidepressant therapy, there was still not quite 40% of people who had not responded. So, at least a third of the time, treatment appears to be resistant. The problem in looking at the literature is that there's not a standard definition or agreed upon definition of treatment-resistant depression. It appears that the researchers and studies are kind of coming to a consensus that a failure of at least two adequate trials of different antidepressants is required to meet the definition, and the other thing that you'll see throughout and hear about later is, there's not a standard definition for what a clinically-meaningful response is. There are some offers out there, but there's not a standard definition.

This just shows a typical course of depression in terms of people beginning on the left side with normal symptoms, as they progress to the full diagnosis of depression. Generally, that's a point in time where people are started on their first therapy. The acute phase is considered to last about six to twelve weeks, and if they have a response and get to remission, then they will continue on therapy for four to nine months and then depending on if they've had more than one episode in the past, they'll generally stay on maintenance and what the, the circles with the drop-off show that really at any time you can relapse or, in the case of the next slide that shows what happens when there is not a response to the first stage. The same kind of curve. You're given the treatment. The person does not respond. A second treatment is tried and similarly, again, a failure and a third time. This is not to say that after the third time everybody improves and responds to depression, but this just shows that the timeframe is much pushed out when folks have treatment-resistant depression.

The four modalities that are being discussed today for your consideration are electroconvulsive therapy, repetitive transcranial magnetic stimulation, transcranial direct current stimulation, and deep brain stimulation, and it's probably worth making the point here that these are interventions, not necessarily other therapies, not psychotherapy, but really interventions that are being looked at. These are graphics of the different types of therapy,

electroconvulsive therapy. Most people are familiar with the repetitive transcranial magnetic stimulation with the magnetic electromagnet. Transcranial direct current therapy is actually a portable thing. You can order them online and sort of self-apply them and use them. So, they are a little bit more flexible in their use, and the deep brain stimulator is implanted.

We chose to ask to review this condition because in terms of safety, there are concerns about the safety of some of these therapies, concerns about the effectiveness across some of these therapies, and the costs were of medium concern, in terms of their cost.

Current FDA status, ECT is approved for major depressive disorder. I'm just going to say rTMS instead of repetitive transcranial magnetic stimulation every time. RTMS is FDA approved, as well, for major depressive disorder. Neither transcranial direct current stimulation or deep brain stimulation are approved for major depressive disorder but transcranial direct current stimulation is approved as a non-significant risk device, and that's probably why you can buy your own on the internet.

Current agency policy, the Uniform Medical Plan, Regence covers ECT, does not require prior authorization. Both rTMS and DBS are considered investigational and not covered. There is not a reference to the transcranial DCS. Medicaid – ECT is covered. Labor and Industries – ECT is covered. Department of Corrections does not have a policy. They review cases patient by patient but they have not treated anyone with either rTMS or DBS.

Center for Medicare and Medicaid Services: There were no national coverage determinations for any of the therapies we are discussing, as of September of last year. The Oregon Health Evidence Review Commission did conclude that both ECT and rTMS should be covered for patients with an episode of major depression who failed at least two pharmacologic treatments. They did not address either tDCS or deep brain stimulation. Group Health: ECT is covered; rTMS is explicitly not covered; neither tDCS or deep brain stimulation are mentioned as options for depression.

Looking at the costs of electroconvulsive therapy over a four-year period, and I don't know if we moved, you can see it on that screen, OK. I can't see it on that screen. I'll turn my back to you. You can see that the four-year period of time, there were 2400 procedures done. Patients, on average, got about 11 treatments. The total cost over that four years was about 1.6 million dollars paid. Average per patient was about \$7300, and average paid per procedure about \$6640.

This is the breakdown of the diagnoses. These are for the patients who are covered by the Uniform Medical Plan, and you can see all of the diagnoses here relate to either major depression or bipolar disorder, either with or without psychosis. The most common reason being recurrent depression that is severe

and recurrent depression with psychosis. So, again, these are all the UMP patients.

In contra-distinction, these were the patients on Medicaid, 134 were treated over those four years, and what you can see that's a little different is that while schizoaffective disorder and simple schizophrenic unspecified disorder were included as diagnoses for therapy in this group, but again, the vast majority were treated with ECT for recurrent depression that is severe.

Breaking it down a little bit, ECT usage between PEB and UMP members, you can see that there are over 200,000 members. Those with depression, about a 9% prevalence if you look across those four years, and then jumping down to the Medicaid patients, quite a few more patients covered, and about 11% prevalence of depression among patients with Medicaid. So, fairly similar in terms of condition diagnosis. This does not break out treatment for resistant depression, just overall, and then if you look at the number of patients who received ECT over that period of time, about one out of every 1000 persons with depression on PEB received ECT and about one out of every 2000 persons on Medicaid received ECT.

This slide highlights the differences in payment between the two, and you can see with the PEB/UMP average paid per patient is anywhere from \$10,000 to \$12,000. Some patients got treatments over multiple years, which is why the overall average was higher, and then looking at Medicaid, the average treatment count per patient and average cost was less. Looking at the overall average treatment for patients for UMP and PEB, it's about 24 sessions, and if you look over the Medicaid population, it's about 4, so a very big difference in terms of treatment.

This just highlights, again, both the difference in treatment, as well as the differences by procedure. Four-year average for PEB/UMP is about \$748, if PEB is the primary \$1200, and looking at Medicaid, about \$158 with \$230 for non-Medicare, and again, this is just sort of a graphic in the difference of payment between having PEB as a primary, Medicaid or Medicare, and/or non-Medicare primary.

We've not had any experience in having anyone that's had rTMS. So, these are estimates that were obtained from different sources, and you can see the cost of rTMS is estimated somewhere between about \$3000, or actually \$2000, and about \$12,000, so somewhere in that mid-range of probably \$8000 on average.

In terms of the evidence summary for ECT in terms of safety, the quality of evidence is low. There is suggestion of some transient cognitive decline in some patients with the autobiographic loss of memory persisting a little bit longer than other symptoms, and it's really difficult from the evidence to determine what the withdrawal rate is, due to lack of benefit. Efficacy during the period of the search, there is low quality evidence that ECT improved symptom scores by 20% and moderate-quality evidence that high-dose and bilateral stimulation are

more effective, and there's really insufficient evidence regarding its benefit and maintenance, quality of life impacts, optimal treatment schedules in terms of frequency per week, or benefits in discreet subpopulations, and in terms of cost, it's reported both as cost savings and more expensive than rTMS, depending upon the study.

For rTMS, safety compared to sham treatment, there was a suggestion of more local side effects compared to ECT. Really, there was no difference in cognitive effects, but also in those studies it showed no difference. There really weren't cognitive effects in ECT. So, it's not really clear that there are a high rate of side effects, and it was not enough evidence to assess whether or not withdrawal rates were higher, due to lack of efficacy. In terms of efficacy, moderate-quality evidence shows it's effective compared to sham treatments, suggesting that the effects may not be long lived, both in terms of response rates and remission rates. Compared to ECT, the quality of those studies is low and again, it depends. Some studies show that ECT is superior. Some studies show that rTMS is, and really there are inconsistent impacts on quality of life and function. In the optimal treatment regimens, differences among subpopulations were not identified. Again, the cost, it depends. Sometimes, it appears to be less expensive than ECT and other times more expensive. So, the evidence is mixed.

TDCS, one systematic review showed that people had more itching, besides there were no serious events, unclear effect on treatment-induced mania and withdrawal rates were similar to sham treatment. Efficacy tDCS versus sham, the low-quality studies were with mixed results. Two meta-analyses and a small randomized control trial suggested improvement in the MADRS scores. When using that with sertraline compared to sham and placebo, there was a suggestion of improved depression scores. In terms of durability, utility, and maintenance, effects on quality of life, there was really insufficient evidence to evaluate those or if there was any difference across subpopulations and weren't able to identify any cost studies regarding transcranial direct current stimulation.

For deep brain stimulation, serious device-related events are possible. Side effects, including bleeding, which we heard about earlier, have included infection, lead fracture, and erosion. There were no apparent changes in cognitive function, and there was overall not enough evidence to state the clear harms with certainty. In terms of efficacy, there were small, very poor quality studies with indeterminate effects on specifically treatment resistant depression relief, the durability of benefits or the changes in quality of life or function and really there was not enough information to draw conclusions about treatment parameters or any particular use across subpopulations. Cost, there is no information available in terms of being looked at in a study.

So, our state agency recommendations: ECT cover with conditions for severe, persistent depression with or without psychotic features after failure of at least two adequate antidepressant trials with or without augmentation. RTMS to cover with conditions, again severe persistent depression with or without

psychotic features after failure of at least two adequate antidepressant trials with or without augmentation. While the evidence does not support it is superiority over ECT, its safety profile is high, and for severe refractory depression, it provides an alternate treatment method. Transcranial direct current stimulation and deep brain stimulation, we propose not to cover those technologies.

Craig Blackmore: So, do the committee members have any questions related to the report, to this agency report?

Richard Phillips: Hi. I have a question regarding the coding that you had up there. I have it on page 7 here. I can't read the slide number, but what I was wondering about was, those are a series of codes. Are they all supportive of major depressive disorder or any one of them could count as that, or is it a particular code that's required?

Charissa Fotinos: As you can see, I don't know if you want to go back. This is, you're talking about the slide with the different diagnoses for the different groups. As you can see, the specificity of coding with ICD-9 gives you a lot of leeway, and so really, these were the diagnoses that were attributed to the patients in whom this therapy, ECT was given. So, it's recognized as really any of those, bipolar or major depressive, so . . .

Richard Phillips: So, would all of those be grouped in this category of major depressive disorders or, I guess what I'm really wondering is, anything we say are we really, really, is there always an out for somebody to use it for one of these diagnoses that, because we aren't really addressing it in this committee or do we, what are we really talking about when we're making a decision?

Charissa Fotinos: I think what you're talking about, really, is, the focus is on treatment-resistant depression, and ECT is, in my experience as a family physician, not a treatment that anybody who administers it takes lightly. It requires a fairly ill person whose tried a lot of other modalities before folks will engage in ECT. So, whatever their underlying disorder is, it is likely that the people who received ECT were significantly ill, had tried and failed multiple efforts or were extraordinarily debilitated by their illness. So, what I believe we're asking you to consider are those most ill patients who have tried a series of pharmacologic agents and psychotherapy.

Richard Phillips: So, if, if we said we don't cover it, there's, I guess I'm still, I'm being a little thick here, but, for example, a bipolar disorder . . .

Charissa Fotinos: Right.

Richard Phillips: You know, if we say we don't cover it for major depressive disorders, does that include bipolar or is it, can they still get the treatment for that?

- Charissa Fotinos: Yes, because what we're, what we're specifically asking you to consider is treatment for treatment-resistant depression and whether that treatment-resistant depression is part of major depression or that is part of depression in someone who has bipolar illness, either of those would work. It's generally, and I'm not a psychiatrist. I don't know about its use for folks who have schizophrenia. You'll see sometimes it is used for that, but really it's treatment-resistant depression whether that's part of a major depressive disorder or depression within bipolar disorder that's severe.
- Richard Phillips: Thank you.
- Michael Souter: And, can you just explain why you think in the Medicare population up to 24 treatments are typical, but in the Medicaid population it's four or five. Is that ...
- Charissa Fotinos: I have theories.
- Craig Blackmore: You know what, I think.
- Charissa Fotinos: I think, and part . . .
- Craig Blackmore: I'm going to, I'm going to just, we're getting, we're moving around a little bit into sort of the clinical realm, and so what I think I'd like to do at this point is introduce our clinical expert, because I think some of these questions might also be relevant to get his perspective and, so, Dr. David Avery, thank you for coming. I'm going to ask you to introduce yourself and give us a little ten-second introduction. We always have a clinical expert participate in our discussions because we're not all psychiatrists who do these procedures.
- David Avery: Is this on?
- Craig Blackmore: It is on. So, we will ask you from time to time to help us understand the clinical context, and we'll direct questions your way. We don't, we don't you ask you for a specific presentation, but we always rely on you for a lot of input. So, if you could just give us, you know, a 30-second introduction. Also, the same about whether you have any conflicts of interest that would be relevant.
- David Avery: Yeah, first conflict of interest. I am on the Data and Safety Monitoring Board for a company that does, is developing a TMS machine that's, also I do clinical work in ECT currently. For 32 years, I was director of the ECT service and director of inpatient psychiatry at Harborview Medical Center and on the faculty at the University of Washington. Currently, I'm professor emeritus from the University of Washington and am in private practice now. If you'd like me to comment on some of the . . .
- Craig Blackmore: I wanted to just introduce you to bring you into the conversation, but I also didn't mean to get Dr. Fotinos off the hook for answering the question, but as we get into some of these more clinical reams, I'm setting you up to participate.

- Charissa Fotinos: I don't know, did you want me to just address the question about why?
- Craig Blackmore: The frequent why, what the difference might be between the (_____)
- Charissa Fotinos: I don't know this for sure, but in my experience in practice treating largely Medicaid patients, access to psychiatry is very difficult. It, it's very hard to find mental health treatment for folks beyond what primary care providers can do. It's out there, but it's very difficult to find. So, I think part of it is perhaps access. What I, reimbursement rates clearly are not favorable at all and so that's not helping but the disparity is, indeed, huge and quite striking both in the number receiving it, as well as the number of treatments.
- Craig Blackmore: Any, do you have any comments on that?
- David Avery: We don't have enough time, actually, for that, but I will say, first of all I was on salary at the University of Washington, Harborview, so I know reimbursement incentive to do ECT, but it was very frustrating because Harborview was the only place where Medicaid patients could access ECT west of the Cascades, and I think there are very few east of the Cascades that offered ECT, and my mission, part of my mission at Harborview was to give Medicaid patients access to ECT, and it, it was, and I, in talking with other hospitals, they cited the reimbursement, lack of reimbursement as one of the reasons they did not offer ECT to their patients. In terms of number of treatments, I was totally shocked by the number of treatments. The average number of treatments for ECT is usually eight or nine sessions, and I can tell you at Harborview Medical Center, we were very close to that. I have no idea where the three or four number per course of ECT comes from. That was a great surprise to me. So, I think our Medicaid patients have really suffered from the lack of availability to ECT over the years, and it would be, and I'll leave you with that.
- Craig Blackmore: Thank you. Any other questions for the agency report.
- Carson Odegard: Yes, I have a question. I have actually a couple of questions, one for Dr. Avery. The difference in the diagnostic codes for schizophrenic or schizoaffective disorders, which rates up there really high in the list, if it's similar to the UMP population, is there a similar code that is up there with the severe depressive (_____)
- David Avery: Yeah, that slide was also confusing to me, because obviously that did not add up to 100%.
- Carson Odegard: Right.
- David Avery: So, some people had multiple diagnoses, presumably, and that was very confusing, but the data indicate that ECT is effective for major depressive disorder. It's effective for the depressed phase of bipolar disorder. There are also data indicating that it's effective in schizophrenia, as well. Schizophrenia,

by its nature, is a more chronic illness and more difficult to treat. So, the remission rates are much lower, but I, I was also puzzled by that.

Craig Blackmore: So, Dr. Fotinos, is that, are we dealing with multiple diagnoses, just for clarity?

Charissa Fotinos: Yes, unfortunately, that's not uncommon as people change providers to have slightly different interpretations of their underlying illness.

Craig Blackmore: Thank you. Any other questions?

Michelle Simon: I just, I had one question about utilization. It looks like in 2012, there was kind of a dropoff across the board in utilization, it seems. I'm just curious about if you have any ideas why that trend would be happening in this state?

Charissa Fotinos: Let me just pull that up.

Marie Brown: There was a major increase and then decrease.

Charissa Fotinos: I do not know.

David Avery: May I comment on that?

Craig Blackmore: Sure.

David Avery: So, Western State Hospital decreased the number of beds. That ended up creating borders at Harborview Medical Center, sometimes eight/nine patients at a time, and typically when a patient in the community on Medicaid needed ECT, I would call the triage nurse at Harborview and say, OK, Mr. Jones needs to have ECT. He'll be coming in. When a bed opens up, call Mr. Jones and basically in about 2011/2012, there were no beds available at Harborview. They're always full and outpatient ECT is not done at Harborview, in part also for financial reasons, I believe, and so those really, and also Medicaid patients often do not have friends or family to bring them to and from outpatient ECT, as required. So, anyway, I think that may be one of the factors involved in the dropoff, because I think, again, Harborview was one of the main providers in the state for Medicaid patients.

Chris Standaert: I have one questions. So, maybe Dr. Avery will help with this, too. So, I don't deal with inpatient stuff, obviously, but I see people with pain and the patients I've had over the years who have been so depressed they've been considering ECT, they have to go through an extensive process to get there that always seemed to take multiple independent psychiatric opinions and there's a, isn't, is there, is that an insurance mandated process, a process within the state licensing that people have to go through, it didn't seem like somebody could just say, oh, these two drugs didn't work, you need ECT. The patients I saw got multiple evaluations to see whether this was appropriate independently, and independently assessed. Is that a standard of care of some sort or is that a, what is that?

- David Avery: Some hospitals require at least two opinions, independent individuals agreeing that ECT is appropriate.
- Chris Standaert: The hospital requires it, or the payers or who requires it, or is that just sort of the community standard that we don't do this unless we know, the people who perform the ECT want independent confirmation. That's what I've never totally understood.
- David Avery: I think it's, it may be just hospitals requiring . . .
- Chris Standaert: Hospital specific.
- David Avery: . . . that, I'm not sure if insurance, I don't believe insurance companies require it.
- Craig Blackmore: Does the state have any such requirements that we're aware of?
- Charissa Fotinos: No and, and looking at the coverage decisions by the, the places I listed, there was no mention that it required second opinion.
- Craig Blackmore: OK.
- Michael Souter: Yeah, just some questions about utilization again, and this is, perhaps, just, I don't know whether you're going to be able to address this, but looking at the treatment kind of averages that we talked about, averages can confuse a lot of perceptions, perhaps, and do you have any sense of what the modal utilization is across all these people rather than looking at the average, you know, what's the modal?
- Charissa Fotinos: Right, I do not. Christine, do you, by any chance have that? We can get that, if that's important. We don't have that at this point.
- Michael Souter: Well, especially when we're looking at significant variability across different populations. I think that's an important question to address, just, you know, like, what's the . . .
- Charissa Fotinos: No, that's a good point.
- Michael Souter: . . . what's the typical pattern rather than just a numerical average. The second question I had was again, and I don't know whether you would be able to address this, based on the, and you may have actually addressed it with your previous answer when we talked about that. There was no, you're not aware of any restriction to bias. I was just wondering what the likely anticipated affect would be of your recommendations for the coverage decision. Are you restricting it to treatment failures, because that will then impact one other question I have for Dr. Avery.

Charissa Fotinos: The reason that the recommendation was delivered as it was is because it's rare, and Dr. Avery would be much better able to answer this, it appears that it's not often the first mode of therapy unless, perhaps, someone is catatonic or so severely depressed. So, if there are circumstances where it would be considered as a first choice treatment, we should know that and consider that. It was not meant to exclude that if it, in fact, is in certain circumstances, the, as it were, first line therapy and . . .

Michael Souter: OK.

Charissa Fotinos: . . . Dr. Avery would need to address that.

Michael Souter: And so that's the following question I have for both yourself and Dr. Avery. In terms of, you know, the practice patterns, you know, rather than your own personal decision, in terms of practice patterns that you're aware of or the State is aware of, you know, what is the, is there a category of patients in whom the ECT is considered a, you know, a first line immediate therapy and, and what kind of proportion is that?

Charissa Fotinos: Just from the State perspective, I don't believe that we have an understanding or really utilize it in that way, and really the focus of this question was treatment-resistant depression, which implies something had been tried. So, slightly different question, but I'll hand it over to Dr. Avery.

David Avery: So, when I saw the focus was on treatment-resistant depression, I wasn't aware that the intent was to restrict ECT use to only treatment-resistant depression. ECT is very effective in schizophrenia, particularly catatonic schizophrenia. People with schizophrenia may also develop signs and symptoms of a major depressive disorder and the ECT is very effective in bringing them out of that major depressive syndrome and their return to their other schizophrenic symptoms.

Craig Blackmore: So, I'm just going to, sorry. I'm going to cut you off for a second. So we, we are constrained in our decision making by the question that is posed to us, and I think we're going to need to hear the evidence report to really understand the boundaries of the literature review before we can figure out if we're only making a decision about major depression or if we're using, getting into some of these other areas. So, I don't want to go off on a tangent until we (_____).

Michael Souter: Sure. I just wanted to get a sense of just the size of the population, though, because if you look at the State rec-, agency recommendations, you know, there's nothing about, you know, the, they're talking about ECT to cover with conditions there, and those conditions are severe persistent depression with or without psychotic features after failure. So, we've, so we're building in the treatment restriction into the State's immediate recommendation. I just wanted to get a sense of what kind of size of population are we talking about here. What does it constitute in terms of the, you know, the categories that we've looked at with these top diagnosis codes.

- Charissa Fotinos: This was not, this recommendation was not meant to address the use of ECT in other conditions where it may be an appropriate first line agent, for instance, in schizophrenia or schizophrenia with catatonia, as Dr. Avery stated. Really, our recommendation relates only to the diagnosis in this context of treatment-resistant depression, but if that language is confusing, we can . . .
- Craig Blackmore: See, see I think, I don't think we're looking at schizophrenia in this. I want to hear from the evidence . . .
- Michael Souter: No, I'm not, I'm not talking about schizophrenia, but I mean, there can be severe, you know, some very severe depressive states and what I . . .
- Seth Schwartz: But then it's not treatment, but, but definition, it's not treatment-resistant if it hasn't had other treatments.
- Michael Souter: Yeah, and, and that's my . . .
- Craig Blackmore: I just want to, I want to table this until we've heard from the evidence vendor so we can understand the boundaries on where they did their evidence review, because that's going to drive the boundaries on which we'll make our decision. I'm not, I just think, I think we need to come back to that when we're, when we have more information. So, I mean are there questions, any other questions regarding this report? OK. I, I think we're ready to move on, and then we'll circle back. So, next on the agenda is the report from, from our, our, our evidence report from Hayes group and Dr. Rogstad. We are ready.
- Teresa Rogstad: Good morning. We've got some abbreviations at the beginning of the slide set. (_____) The little graphic on that STAR*D Trial that was reference earlier. This was a trial designed to test a (_____) treatment algorithm where patients started at step one, they all took the same drug. If they did not remit, they moved on to step two that included seven different regimens. If they didn't remit there, they moved on and there were four steps. As you can see, a little over 38% of patients remitted at that first step at about a little over 30% at step two and then there was a sharp drop. For patients who failed two AD regimens, remission with that third round of treatment was only about 14% and then 13% at the fourth step. So, cumulatively, the trial suggested that about half of patients with major depressive disorder remit after one or two different rounds (_____) treatment and then there's a sharp dropoff. Overall, there's a cumulative remission rate of about 70%, or more precisely, 67%. This is a theoretical number, because it assumes that every patient stays in treatment, which was not actually the case in the trial and probably would not be the case in real life, but this sets the stage for our topic.
- As I said before, there's no established definition of treatment-resistant depression. Generally, it is a growing consensus that it means the patient has failed two previous adequate trials and adequate trial of AD medication, generally assumed to be maximum tolerable dose or (_____) at the time and (_____) from four to eight weeks, as to what constitutes sufficient duration

of treatment. In the STAR*D Trial, it took patients an average of a little over six weeks to reach remission in step one, if they did reach remission, and then (_____). In step two, the average length of time was a little over five weeks.

In 2011, there was an evidence review for AHRQ that looked at nonpharmacologic treatments for treatment-resistant depression and that review included pharmacotherapy, or excuse me psychotherapy, as a nonpharmacologic treatment, because virtually no trials could directly compare any of these nonpharmacologic treatments with pharmacotherapy, the AHRQ review conducted a pooled analysis of 12 RCTs of pharmacotherapy. They weren't able to pool the effects, because there was so much heterogeneity in the (_____) that they pooled data across the pharmacotherapy arms and concluded, based on that indirect kind of comparison, that a change in pharmacotherapy for patients with treatment resistance was more effective than continuing maintaining them on their current AD medication. The AHRQ review concluded that psychotherapy is effective. Another systematic review that came out about the same time concluded the same; however, both of these were unable to determine whether psychotherapy as a treatment for treatment-resistant depression is more or less effective (_____) pharmacotherapy.

There are, of course, some disadvantages to continuing to try new drugs; hence, the development of what are called neuromodulatory treatments. All of these treatments involve some sort of stimulation of the brain. The technologies over on the right-hand side of the slide are not included in this report. In 2009, the (_____) program conducted a report on vagus nerve stimulation, or VNS, for depression and it looked for new evidence on VNS that we didn't find anything that was likely to alter the conclusion so the (_____) and those other technologies in the (_____) circles have very little evidence on them in the literature. So, this report covers ECT, or electroconvulsive therapy, repetitive transcranial magnetic stimulation, rTMS, direct current stimulation, DCS, and deep brain stimulation.

As you've already seen, there are some pretty standard definitions of what constitutes response to a depression treatment and remission. The most commonly used scales, at least in research, are the Hamilton Depression Scale, or HAM-D, and the Montgomery Asberg Depression Rating Scale, or MADRS. These scales have been empirically validated, but the definitions of response and remission are essentially matters of convention. There is no standard definition of clinically-relevant improvement, but possibly accepted definitions of response and partial response might be assumed to imply definitions of clinically important improvement or minimal clinical improvement or (_____). Can you all hear me, or do I need to move the microphone over? I just now thought about it.

Marie Brown:

Yeah, that'd be nice.

Teresa Rogstad: OK, sorry about that. OK, a few studies also measure the impact on quality of life and function and the two most common-used scales were the Global Assessment Functioning scale, which is a psychological problem specific scale. It's recommended in the DSM-IV to be part of the initial evaluation of a patient with depression. The other commonly-used scale was the SF-36, which, of course, is a generic scale. There is a new scale called the WHODAS, or WHODAS. This is actually a disability scale. It's described in the DSM-V as an emerging measure and data are being collected but the WHODAS was not used in any of the studies that we selected for our report. We did not find any standard definition of clinically-relevant improvement or difference according to these functional scales.

So, how do the depression scales relate to the functional scales? They do include some items that relate to function, as you could see with some of the detail that I provided on the HAM-D scale, but these depression scales have been validated against global measures of depression or against each other. They haven't been explicitly validated against quality of life and functional scales. Nevertheless, there is some evidence that as depression scores go down, quality of life or functional status goes up.

This slide presents some of the technical details about these technologies. They all involve delivery of electrical or magnetic electrical energy to the brain. TMS and DCS are completely outpatient procedures, because ECT stimulates a global seizure, it requires an inpatient admission and anesthesia and, of course, DBS is an invasive procedure involving the implantation of electrodes and as has already been mentioned, only ECT and TMS have been approved by the FDA for depression.

Two things I'll point out about the PICO statement, the population was defined as adults who have major depressive disorder or bipolar depression who have not responded to prior adequate pharmacologic treatments, but we did not have an (_____) definition of treatment-resistant depression. Also, psychotherapy as a treatment in patients who had demonstrated medication resistance was not included in this report. It was considered as a potential comparator, though.

The key questions follow the typical pattern. Is it effective? Does the effectiveness depend on the manner in which the treatment is administered? Is it safe? Does effectiveness depend on patient characteristics, and what are the cost implications?

We started our search by looking for systematic reviews published in the last five years and found a recent comprehensive systematic review for each of the technologies. We had to look further back in time to find some data on some of the questions other than that first effectiveness question. We did our last literature search on November 12th.

For ECT and TMS, we considered any randomized trial to be eligible or any systematic review of randomized trials. We did consider observational studies with at least 100 patients for safety data, and we considered any observational study that could shed light on key question #3, the differential effectiveness question. The body of literature is very small for DCS and deep brain stimulation. So, we took any clinical study for those technologies. Our most important exclusion criteria was one that the AHRQ review also followed and that was, we did not include studies that enrolled patient, that did not enroll patients on the basis of some definition of treatment resistance and did not provide enough information about those patients to assume that most of them probably had experienced at least one prior AD failure. We relaxed that exclusion criterion somewhat in order to have some data to answer the key questions having to do with differential effectiveness and safety.

This slide summarizes our search results. For ECT, we found, I believe, it was a total of six systematic reviews with meta-analysis and providing data for various key questions and 11 additional RCTs. For TMS, we identified five systematic reviews and 12 additional RCTs plus three economic evaluations. There were three systematic reviews addressing DCS plus a recently published RCT and then for DBS, we relied on recent Hayes report and found no additional evidence published since that report.

Moving on, I would like to give a little bit of information about the AHRQ report, because it, it had implications for the evidence that was included in our report. We relied on this rather heavily to identify studies of ECT and TMS and used the meta-analyses in the AHRQ report for TMS. An exclusion criterion for that report was any study published prior to 1980 and the rationale was that treatment parameters for these nonpharmacologic treatments evolve over time and the pharmacologic options that are available change over time, too. So, the thought of the AHRQ review authors was that the older evidence is less generalizable to current practice; however, it does create a problem, as has already been alluded to, where ECT, because most of the randomized controlled trials of ECT were published before 1980, there is a problem with that body of evidence, because those trials do not tend to distinguish between treatment resistance as an indication and other factors that just create a very severe situation, such as psychosis or imminent risk of suicide. I do have available, if you want to look at it, a systematic review that was published in 2003 that did capture some of those older studies.

The typical patients in the evidence that we collected had moderate-to-severe generally unipolar, major depressive disorder. Where the information was provided, the patients had typically failed at least two prior antidepressant drugs, sometimes more. The studies were not good about clarifying whether those prior failures occurred in the previous episode or some past episode. If they provided a definition of what constituted an adequate prior antidepressant trial, six weeks was usually the interval that was required. I should also point out that the studies gave very little treatment history other than AD medication. Sometimes, there was information on whether ECT had been tried in the past,

but there was no information on prior use of psychotherapy or whether or not there was any concurrent psychotherapy going on during the trial.

We've organized the slides by technology. So, we're going to go through all four key questions for one technology and then move on to the next. There were only three RCTs published, since 1980, looking at ECT. Two of them compared it with sham stimulation and one compared ECT with a change in pharmacotherapy. They all favored ECT. We considered the evidence to be low, mainly because of such a small quantity of data. That cell to the far right in that first row shows you how the ECT groups and the control groups differed in the degree of improvement that patients experienced. So, what these data tell us was that in these trials, patients who underwent ECT experienced about 7 to 13 points greater reduction and depression score than the patients in the control groups. Because there were so few RCTs that met inclusion criteria, we also looked at a systematic review, the Heijnen review that pulled data from uncontrolled studies. They separated the data between patients who had adequately-documented treatment-resistant depression and other patients where that history was less clear and for the treatment-resistant depression, they calculated a pooled rate of remission of 48%. The rest of the factors that play into effectiveness, the evidence was generally not there or very sparse. We are going to talk about ECT in comparison with TMS in the next section.

This slide is an attempt to provide a little more context for evaluating the results of these studies. This approach was suggested by that 2011 AHRQ review because there are so few head-to-head comparator trials that compare the nonpharmacologic treatments with pharmacotherapy. The AHRQ review authors suggested that if you look at the degree of improvement, just in the pharmacotherapy arms of those pharmacotherapy trials, you could get a sense of the degree of improvement that can be expected from pharmacotherapy and then use that as kind of a benchmark and look at the degree of improvement that is shown in the active treatment arms of these technologies that we're interested in. I've also put data from the STAR*D Trial up there. There is a typo. The remission rate at step three was actually 13.7%. I'm not sure where that 14.3 came from.

So, looking at the data on this slide, there is some suggestion that ECT compares very favorably with pharmacotherapy in terms of the degree of improvement, but of course, these are very indirect comparisons and have to be interpreted with a great deal of caution.

Several different treatment parameters have been investigated with respect to ECT. There was moderate quality evidence suggesting that if stimulation is provided bilaterally rather than unilaterally and at higher doses, then ECT is more effective. Efforts to evaluate the comparative effectiveness of bifrontal stimulation, which is where the electrodes are placed on the forehead, did not lead to any kind of conclusions, and then there was some low-quality evidence from that systematic review I mentioned earlier that captured some of the older data. There was an analysis here suggesting that if the same number of ECT

sessions are administered three times a week rather than once a week, it is more effective. The reason we called that evidence low quality was because there was no quality assessment of the included studies, and there was unsure applicability to the population that we're interested in, also not very much data.

The main safety concern with ECT is the cognitive decline that sometimes occurs during the course of treatment. Two systematic reviews of pretest/posttest studies concluded that such declines are generally transient, although autobiographical memory loss may persist for several months, according to one of those reviews. Efforts have been made to determine whether changing treatment parameters can reduce these cognitive effects, but that evidence is very sparse. It's difficult to evaluate the effect of these technologies on cognitive performance in patients with depression, because depression, itself, has also been shown to diminish cognitive performance. We didn't see any indication of any other safety issues with ECT. So, we considered it to be a generally safe technology. We called the evidence low quality, simply because there were no large case series that could provide reliable adverse event rates. Only one study looked at the withdrawal due to lack of benefit, and actually showed there was a greater withdrawal in ECT compared with sham, but that was just one RCT.

Regarding the differential effect by patient factors, one interesting finding was from that systematic review of uncontrolled studies was that if patients had a well-documented history of treatment resistance, ECT seemed to be less effective than when a treatment resistance was less certain. Another finding that was demonstrated by post-talk analysis of two RCTs was that the effective ECT may not differ according to depression subgroups. Otherwise, there were no data on other factors of interest.

We'll be talking about cost effectiveness when we get to TMS. So, to review, there was low quality evidence suggesting that in treatment-resistant depression, ECT is effective compared with sham stimulation or another pharmacotherapy approach, that's a typo that should be versus pharmacotherapy not psychotherapy. We're not sure of the clinical relevance of the degree of posttreatment difference. No conclusions can be drawn about the effect according to treatment parameters, except that bilateral and high-dose ECT seemed to be more effective. We are left with no data comparing ECT to other active treatments or assessing the durability of the effect or measuring the effect of quality of life and function. ECT seems to be a safe technology. The cognitive decline is usually transient. There were no clear effect modifiers that were identified.

So, for TMS, there's quite a large body of evidence, a lot of randomized control trials comparing TMS with sham stimulation. The AHRQ review conducted a number of meta-analyses. They calculated a weighted mean difference of six points meaning that the difference in depression improvement between TMS and sham was about six points, and the size of the scales being used went up to anywhere from 50 to 72 possible total points depending on the scale being

used. Unfortunately, they did not report pooled remission and response rates. They calculated relative risks instead, but those can be translated to numbers needed to treat, and their analyses suggested that five patients would need to be treated with TMS instead of sham stimulation in order for one patient to respond and six patients would need to be treated in order for one patient to remit. A handful of studies looked at the durability of benefit after treatment with TMS ended and three RCTs suggested the benefits are maintained for two to three weeks, but the findings were inconsistent in studies that look at longer intervals. Of course, it's difficult to say how long the benefit is supposed to last in a recurring disorder.

In studies that compared TMS alone with ECT alone, the results were mixed, and in two studies that compared a strategy of combining the two technologies versus ECT alone, results suggested that both strategies were comparably effective. There were no comparisons with other active treatment.

I've created a slide with some new data that was published after we finished our report. The reason I thought it was important to bring it up is that it does address that area of an uncertainty about the comparative effectiveness of ECT and TMS. Both of these meta-analyses concluded that ECT is more effective. They included the same set of studies. They're a little bit problematic because they lump together studies that compare TMS alone with ECT alone and studies that compared a combination strategy with ECT alone. They also included two studies that were excluded in the AHRQ review, but they did have consistent results.

The studies that measure the impact of TMS on quality of life and function were inconsistent and where an improvement was demonstrated, it was very small.

And here's that slide again comparing improvements with the nonpharmacologic treatment with improvements in pharmacology trials. Unfortunately, we did not have a pooled response or remission rate, so it's very hard to make comparisons. We've presented the range of response and remission rates across the studies, but they don't really allow you to say whether TMS might be better or worse than continued pharmacotherapy. The only treatment parameter that's been investigated is bilateral versus unilateral TMS and the results were mixed.

TMS appears to generally be a safe technology. There is a greater incidence of local side effects, which mainly consists of discomfort or pain in the scalp. Also, one systematic review found a greater incident of treatment-emergent mania but the absolute incidents was very small. Compared with ECT, three randomized control trials detected no difference in cognitive effects. There were no data on other safety issues comparing TMS with ECT. So, our overall conclusion is that this appears to be a safe technology. There is possibly, if we look at the lack of difference in overall withdrawal rates, we might conclude that there is no difference in withdrawal due to lack of benefit between TMS and sham treatment.

A few patient factors have been ruled out as effect modifiers and regarding the other factors of interest, there were no data.

So, we'll talk about the cost-effectiveness studies now. The first one was conducted in the U.S., and it compared TMS with pharmacotherapy. The source trial for the effectiveness data, as well as the economic evaluation itself were sponsored by a manufacturer of a TMS device. The conclusion was that TMS is cost saving compared with pharmacotherapy. There were a lot of reporting omissions with this study, so it was difficult to determine exactly what the inputs were, and it was hard to really evaluate the reliability of this analysis. The other two studies compared TMS with ECT. One was conducted in the U.S. and one in the U.K., and they had a different set of starting assumptions. In the U.S. study, a trial was used that showed a slight benefit favoring ECT and also the cost data that were used in that study showed ECT to be more expensive. So, when an incremental cost effectiveness ratio or ICER was calculated, there was quite a high ratio. The authors also tested the possibility of using TMS initially and then applying ECT for patients who did not respond to the TMS, and that strategy dominated ECT alone, meaning it was both more effective and less costly. Then, we used the data from this study to calculate our own ICER for using that combination strategy versus TMS alone, came up with a fairly reasonable ICER.

Then, if you look at this U.K. study, the data that they were using showed TMS to be slightly more effective than ECT, and their cost data showed TMS to be more costly than ECT. They plotted what's called a cost effectiveness acceptability curve, which resulted in a finding that there's a low probability, 13-22% depending on your perspective, that TMS would be considered a cost-effective alternative to ECT in the U.K. using that 30,000 pounds/QALY as the threshold.

So, to wrap up on TMS, there's a moderate quality body of evidence suggesting that it is effective compared with sham treatment, evidence regarding durability of benefits suggests that it may last only two or three weeks. The evidence that was available to us at the time of the report was uncertain about the comparative effectiveness of TMS and ECT and findings regarding an impact on quality of life and function were conflicting. A moderate quality body of evidence suggested that this is a safe technology. No effect modifiers were identified with respect to patient characteristics or treatment parameters, and the three economic evaluations conducted very different analyses and came to different conclusions that analysis in the Kozel study with the combination treatment is an interesting one that hasn't actually been tested in a clinical trial.

For DCS, we had available to us two systematic reviews with meta-analysis plus one recently-published RCT. The findings favored DCS but some of the pooled estimates were not statistically significant. The more recent and better quality systematic review calculated odds ratios for response and remission and when you translate those to numbers needed to treat, ten patients would have to be

treated for one patient to benefit, and those estimates were statistically nonsignificant. The trial that was published in 2013 randomized patients to four treatment arms and investigated different combinations of TMS and the antidepressant drug, sertraline. Their findings suggested that DCS is effective compared with sham treatment. There were some, there was some additional data not portrayed on this slide suggesting that DCS alone is more effective than sertraline alone.

The evidence regarding durability of benefit was very sparse and insufficient to support conclusions. There were also sparse data regarding DCS as a maintenance treatment and no data regarding quality of life and function. To make an indirect comparison again between this technology and results from pharmacotherapy trials, in this case, it looks like the DCS might not provide an advantage over pharmacotherapy. The two systematic reviews looked at whether the effectiveness varies according to three different types of treatment parameters, and they came to exactly opposite conclusions. So, that did not allow us to form a conclusion about effectiveness, according to treatment parameters.

The main adverse event with DCS is itching in the scalp. No other serious events were reported, except that a handful of RCTs did detect an increase in the incidence of treatment-induced hypomania. Overall, it seems to be a safe technology. One factor, baseline severity, was shown by a meta-analysis to have no association with the effectiveness of DCS, but we had sparse data or no data on other factors.

So, to review DCS, there is a low-quality body of evidence suggesting that it is effective compared with sham treatment. It is generally safe. Indirect evidence suggests that withdrawals due to lack of benefit are not greater or lower in DCS and baseline severity has been shown to not be associated with the effectiveness of the technology. We had no comparisons of DCS with other active treatments or any analysis of the durability of effect or the impact on quality of life and function.

No randomized trials have looked at deep brain stimulation. Five prospective uncontrolled trials all reported improvements in depression after the use of deep brain stimulation; however, one of those studies also included a lead in sham phase where patients thought that they were getting the stimulation and they weren't, and the study found that improvement during that sham phase was no greater than improvement during the subsequent active stimulation phase. There were variable results regarding the durability of benefit and the two studies that looked at quality of life and function were favorable but it was only two studies and there were no control groups. There was no analysis of whether effectiveness varies according to any type of treatment parameter.

There are serious safety issues with deep brain stimulation. We had a narrative review that cited a hemorrhage rate of 10%; however, you heard testimony that that might not be a reliable event rate. There was a systematic review of 546

studies of deep brain stimulation for any indication, and in those studies, over 6500 device-related events were reported, the most common of which was infection, and then over 6500 somatic adverse events. The somatic events included things like speech disturbance and weight gain. There wasn't anything that occurred with a high frequency. There were 11 completed suicides in that data set, and the review authors considered that to be a cause for concern. Unfortunately, this review did not provide per patient event rates. Two other systematic reviews concluded that cognitive decline during deep brain stimulation is minimal and/or transient and in the uncontrolled studies that specifically targeted treatment resistant depression, infection was the only common adverse event. Overall, we considered this evidence to be insufficient because of the lack of controlled data and the lack of large studies that could give reliable adverse event rates. There was really no analysis of effect modifiers in terms of patient characteristics, no cost-effectiveness studies; so, overall, we felt that the evidence for deep brain stimulation was insufficient with respect to all the key questions.

We found seven practice guidelines. Two of them were considered to be good quality, and one we rated as poor quality. Only two of them provided a definition of treatment-resistant depression. One was the ICSI group in Minnesota. They define treatment-resistant depression as failure of three different classes of antidepressant medication and the VA guidelines had a very similar definition in their criteria for receiving ECT.

This slide summarizes the guidelines. They all recommend ECT for treatment-resistant depression. The American Psychiatric Association and the Canadian group have somewhat weaker recommendations for TMS in this population. NICE considers TMS to be appropriate for research purposes only. There were no recommendations on DCS and none on DBS, except in the Canadian guidelines, which described it as investigational.

We were asked to look at four payers, and the only positive coverage policy was a coverage policy for ECT at AETNA. It is covered for medication-resistant depression. The other technologies were either explicitly not covered or we could not find a policy. At the bottom of the slide are recommendations from two groups that serve as advisory groups for patients, the New England CEPAC group favors TMS over ECT, but the Oregon HERC recommends coverage of both ECT and TMS for treatment-resistant depression.

So, here's a summary of our overall findings. The only conclusions that were, or the only issues that were supported by moderate quality evidence were the effectiveness compared with sham of TMS and the safety of TMS. There was also moderate quality evidence suggesting that ECT was more effective when delivered bilaterally and at higher doses. We considered all of the evidence for DBS to be insufficient and there cost-effectiveness studies only for TMS and ECT.

The usual suspects show up in the list of gaps in the evidence, but the bottom half of that slide lists some deficiencies that are very specific to this topic. One

is that we don't have trials comparing these nonpharmacologic treatments with an active treatment. It would be nice if there were trials that compared these treatments with pharmacology or with usual care, however that might be defined. A standard definition of treatment-resistant depression, more uniform reporting of outcomes, and empirically-derived definitions of clinically-relevant improvement in depression would be helpful. Thank you for your attention.

Craig Blackmore: Thank you. Are there questions from the committee members about the content of the evidence report?

Chris Standaert: I'll start. I sort of want to pursue Mike's question, that of the scope of what we're talking about. I'm struggling with this idea that there's no uniform definition of treatment-resistant depression. The state's essentially asking that we make one up, or we define one by saying failure of two drugs, but that doesn't seem to be any standard, except a definition, and you presented a gazillion systematic reviews. When I look through the titles of the articles and things, they, a lot of them are for major depression. They don't talk about treatment-resistant depression, especially with the TMS studies. So, our, and some of these studies look like, when you look at the TMS, it says, well, for shorter durations of depression or less drug resistant depression, but that's, you're varying out of this idea of severe major depression not responsive to drugs, and one, I want to be sure that the studies you just gave us all really talk about patients who have severe nonresponsive depression to standard pharmacological therapy, which I'm not sure that's what you had in there exclusively, and then how, help us with this idea of, if it's not defined anywhere, how did you sort through these studies and how do we start to define the scope of what we're talking about. As Craig said, we can only talk about the reflect, we have to reflect what you looked for and what you just discussed and so we, I need to understand that better.

Teresa Rogstad: Sure. For any evidence that we used for the first key question, which has to do with effectiveness, we selected studies that either enrolled only patients who met some definition of treatment-resistant depression or we could tell from the baseline descriptive data that patients had failed mostly, that patients had failed prior antidepressant treatment, because most of the studies did report the mean number of, mean or minimum number of prior AD failures. So, we feel that the evidence we selected does apply to medication resistance.

Chris Standaert: And so one medication, two medications?

Teresa Rogstad: At least one.

Chris Standaert: So . . .

Teresa Rogstad: At least one.

Chris Standaert: . . . and so the, you also have a thing here saying somebody, one of the, the policies said that a trial of the medication should be at least six weeks.

- Teresa Rogstad: Mm-hmm.
- Chris Standaert: So, if we can do two medications, we're then going to be, are you supposed to treat people for 12 weeks of medications that aren't working who present with this idea of, you know, acute depression and catatonia and, I'm, I'm, I'm trying to, you're man, that's what I'm, you're mandating, that's what I'm curious about. So, so you're saying, so your definition was sort of one drug in what you were looking for. Some sort of treatment for depression that didn't work, pharmacological therapy was your definition.
- Teresa Rogstad: Right.
- Chris Standaert: That's what you were looking for.
- Teresa Rogstad: Right. There are some prior failure of pharmacotherapy.
- Chris Standaert: OK, thank you.
- Joann Elmore: Can I make certain that I'm very clear on your methods, because what you're stating verbally is not what was listed in our documents regarding your methods. In our documents, it stated that your methodology used for this review was to identify existing reviews, and you basically shared with us the existing reviews, and I'm hearing though now that when you pulled these existing reviews, and indeed one of them was an AHRQ, it was a real good review, you only looked at the RCTs that fit this definition that you just stated verbally of treatment-resistant depression, is that correct?
- Teresa Rogstad: I'm not sure I followed the question. The AHRQ review
- Joann Elmore: So, let's go, the AHRQ, basically you gave us a review of somebody else's review, and we want to know, in the AHRQ were they, did they specify treatment-resistant depression because I don't know whether they did or didn't.
- Teresa Rogstad: OK . . .
- Joann Elmore: You list a lot of RCTs, and is it possible that some of the RCTs that you list in some of your tables, they included patients that didn't have what you would define as treatment-resistant depression?
- Teresa Rogstad: We used the same, essentially the same inclusion/exclusion criteria as AHRQ, which was that either the trials and explicitly enrolled patients who had failed at least one prior AD medication or there was sufficient information in the article about those patients that they, you can assume that this was a treatment-resistant population. So, when we looked for studies that were published on technologies not covered by AHRQ or published after the AHRQ review had been published, we took that same approach.

- Richard Phillips: I have a question. In your, one of your earlier slides you had said the ECT was only performed as an inpatient and that rTMS was as an outpatient.
- Teresa Rogstad: Mm-hmm.
- Richard Phillips: And I'm questioning in my mind, are we talking about apples and oranges here. Are they different groups of patients, different levels of depression or, you know, and I'm having a problem putting all this together.
- Teresa Rogstad: Well, ECT has to be performed inpatient because it's done under anesthesia.
- Richard Phillips: Well, that doesn't necessarily mean inpatient, though, I mean, but I understand what you're saying.
- Teresa Rogstad: Oh, OK.
- Richard Phillips: But I'm, I'm talking about is, maybe it's a billing aspect. I mean, can they come in from, as an outpatient to come in for their ECT. I guess that's what I was wondering about. I just want to make sure we were saying the same, that I was assuming that all these patients were identical.
- Seth Schwartz: I don't think you can tease it out, because as Dr. Avery said, you know, the, there's restrictions about how you can bill things. So, you obviously get more money if you bill ECT for an inpatient so they bring them in and make them inpatients. That doesn't imply that the severity of their illness is worse, necessarily.
- Richard Phillips: Well, perhaps our clinical specialist can comment. I'm just trying to figure out if this is, if they're the same clinical group of patients. I guess that's all I want to make sure.
- Seth Schwartz: I'm saying you can't tease it out because of the billing complexity that's thrown in.
- Marie Brown: My question is about the definition of treatment resistant being at least one nonresponse versus what we have here is two nonresponse. When you looked at the articles that clearly studied treatment-resistant, what was there, what was a common definition? Was it at least one or was it two? How . . .
- Teresa Rogstad: Well, it . . .
- Marie Brown: . . . what is the basis for our definition of at least two.
- Teresa Rogstad: At least two was a more common definition than at least one, and back to the other comment about inpatient, Dr. Avery can correct me if I say this wrong, but I think a lot of times ECT is given because patients are in a very severe condition so they're in the hospital because their depression is very severe, but they also generally need to be in the hospital just to get the ECT, so.

- David Avery: Let me just clarify. ECT can be given on an outpatient basis. They do come to the hospital as an outpatient. A friend or relative brings them to and from the ECT because of the temporary memory disturbance and confusion that can occur with ECT. So, there can be, let's say, more moderate levels of severity in patients receiving ECT.
- Kevin Walsh: I have a question for Dr. Avery. Let's go back to slide 21, which was looking at the effectiveness of ECT, and the first row that looks at depression relief versus sham treatment. There's a 7-point improvement on a 54-point HAM-D scale, and for me that's difficult to interpret, because it all depends on what the baseline score was, in terms of how you interpret a 7-point improvement. Is that, do you agree with that, or is there another way to interpret that?
- David Avery: So one fundamental issue is the one that Dr. Neumaier brought up earlier and that is that all the studies prior to 1980 were excluded. Most of the ECT versus sham studies were done prior to 1980 and typically in those studies you see, you know, significantly greater differences between sham and ECT compared to this particular study. I, perhaps Teresa can help me out here in terms of that 18-point drop. That was with the sham?
- Teresa Rogstad: Yes.
- David Avery: I see, yeah. So, that's a, that's a high sham response, and I, and that represents the change score?
- Teresa Rogstad: Correct.
- David Avery: Yeah. So, and yeah, it would be, I don't know what the baseline scores were, but typically . . .
- Kevin Walsh: So, I'm just trying to establish that while there is an absolute 7-point improvement, whether or not that's clinically relevant is unknown because we're not given enough information.
- David Avery: OK, so . . .
- David McCulloch: I think we should get beyond this. ECT is clearly effective. They haven't looked at the studies that showed that. It would be equivalent to saying if we did a similar analysis for the value of panretinal laser photocoagulation for people with bad diabetic retinopathy. You see, there is no evidence, because all the studies were done, very conclusively, prior to 1980.
- Kevin Walsh: I think there's a complication here that you're overlooking and that is that the drug regimens that were possible when ECT was done are completely different than the drug regimens that are used now. So, you're not comparing apples and apples. If you did the same trial today of ECT versus the antidepressant drugs that are used, you might not have the same conclusive results you had before.

- David Avery: May I comment on that?
- Craig Blackmore: In terms of the patient selection. Go ahead, doctor.
- David Avery: Yeah, so the ECT trials were done comparing it with tricyclic antidepressants, and there are a number of studies that indicate that tricyclics, especially for inpatients, are probably more effective than, for example, selective serotonin reuptake inhibitors. Side effect profile may be better, but there's no evidence that our current antidepressant medications are any more effective than tricyclic antidepressants, but I want to answer that other question about the 7-point drop, is that significant. Most of the approved antidepressant medications that, by the FDA, typically show about a 3 or 4-point drop difference compared to placebo, and so that 7-point difference is significant, clinically significant.
- Carson Odegard: Yes, I have a question on some of the sources report so many points and, you know, 1000 points, 600, what, what do we do with that information? How, what are the points?
- Teresa Rogstad: Points on the depression scale, you mean?
- Carson Odegard: No, the total points under the sources. I see 130, or some don't give points.
- Teresa Rogstad: Oh, I'm, oh I'm sorry. That (_____) patients.
- Carson Odegard: Patients.
- Teresa Rogstad: That's patients (_____)
- Carson Odegard: Oh, oh, OK. I was confusing points with the points on the scale . . .
- Teresa Rogstad: Yeah, yeah. Maybe that's not a good (_____)
- Carson Odegard: . . . OK, alright. Those are patients. OK, great. Perfect, OK.
- David McCulloch: Craig, can I ask Dr. Avery, I, I'm trying to get my arms around what rTMS is actually like. I mean, we know with ECT, you said, I mean typically they're given weekly treatments or twice a week treatments for six or eight times and then you look at the effect. With rTMS, I'm told that the beneficial effect is as short-lived as two to three weeks, but I mean, how often is, is that given weekly, twice weekly for an x-number of, I'm just, I'm trying to get an understanding of how to compare. It goes back to Richard's point, are, is rTMS used in similarly-severe depressed patients?
- David Avery: Alright, so full disclosure here. I did research on TMS for 15 years beginning in 1996 and the way TMS was done then and even now is on a daily basis. Patients can be outpatients. There's no memory disturbance, no neuropsychological adverse effects from it. It's on a daily basis and typically it takes, though, about 30 sessions to achieve a good result, so it does take time. The relapse rates, like

ECT, the effect does not last forever. So, typically when it's used clinically now, antidepressant medications and/or mood stabilizers are used to prevent relapse. It does have an advantage over ECT in that because of the lack of memory disturbance it can be used in an ongoing basis for maintenance. So, that is a potential for it.

David McCulloch: Thank you.

Teresa Rogstad: The studies that showed that the benefit lasted two to three weeks did not mean, necessarily, that the patients relapsed at two to three weeks, but the difference between the TMS group and the control group disappeared at that point. So, you know, the control group kept improving over time.

Joann Elmore: Since we're talking about TMS, I'd appreciate a little more interpretation of clinical significance. On slide 44, there's a nice recap of depression relief versus sham of TMS, and the direction of the findings is positive, but, and these are sort of fair to good RCTs, and even though they're fair to good, you give it a moderate quality evidence, probably because they're sham controlled, I'm assuming, and there's over 1000 patients, but just seeing a little arrow and a little plus sign going up, that doesn't tell me, is it clinically relevant and clinically important, and so, to find that, I had to go back to your earlier slide, which is slide 32, and this is where'd I appreciate some interpretation of, you know, what does it mean to have a 6-point change and then you, you talked about, you know, five patients with TMS versus one, in other words, the relative risks versus absolute difference. Can our clinical advisor comment on the clinical significance of these improvements?

David Avery: Yeah. So, I think, again, the antidepressants typically have a 3-point/4-point superiority over placebo. So, it's in the same range of antidepressants. I think it might also be useful to look at effect size and for antidepressants, typically, the effect size is low, like 0.3 or 0.4, and for TMS the effect size is about 0.5. For ECT the effect size is about 0.9.

Craig Blackmore: I'm sorry, what do you mean by effect size?

David Avery: So, effect size is defined as the difference between the active group and the experimental, the experimental group and the placebo group over the pooled standard deviation. It's a commonly used statistical approach that is used and typically an effect size of 0.3 or 0.4 is low, 0.5 is moderate, 0.9 is strong. Perhaps Teresa, the statistician would define this better, but yeah.

Teresa Rogstad: No, I can't add much to it than that, but it does express primarily the strength of the statistical association. It doesn't tell you very much about the, you know, absolute difference in clinical terms.

Joann Elmore: So, back to my clinical question, then, up here on this slide we have WMD in changed scores, depressive severity 5.92 and I heard that there's a 3-point

change score with antidepressants. I'm assuming, is that versus placebo? So, how am I to interpret a 6-point change score versus sham?

David Avery: Clinically, I think that's significant.

Joann Elmore: It seems to me.

David Avery: Yeah.

Joann Elmore: If you're saying that medications only give you a 3-point change score, and this gives us a 6-point change score.

David Avery: Yeah, but again, all that depends on the variants and so forth and again the, the effect size takes into account the variants and the data but anyway, it is, I think, 6-points is significant clinically.

Craig Blackmore: We're due for a break. So, why don't we take ten minutes to a quarter of eleven, and then we will resume with committee discussion.

So, we're going to start off addressing one of the questions that was raised this morning. Do we, do we have a slide you . . . ? So,

Charissa Fotinos: This is a slide that responds to the question about median versus mode or the Medicaid versus UMP patients, and what you can see is that if you look at the mode for Medicaid patients, more patients got one treatment compared to any other number, and that's compared to the mode of PEBB/UMP of 13. More patients got 13 treatments than any other number, and you can see the distribution pattern on the bottom.

Michael Souter: And just having asked the question, I'm staggered at the implications of that.

Charisa Fotinos: As am I. I wouldn't have expected that.

Joann Elmore: Access to care?

Richard Phillips: It makes you wonder if there's not an error.

Charissa Fotinos: Too many numbers.

David Avery: I wonder if it's the Harborview Medical Center billing department or something?

Craig Blackmore: Also a possibility.

Charissa Fotinos: This is state Medicaid claims and . . .

Craig Blackmore: That's what I'm saying.

David Avery: But they're all Harborview.

- Charissa Fotinos: Yeah, maybe Harborview didn't submit it? Maybe. We could hope.
- Craig Blackmore: OK, and then I think we had one other piece of information.
- Charissa Fotinos: Yeah. I, um, this was related to the question of the definition of treatment-resistant depression. When you look at the AHRQ review, they divided their evaluation and review into three tiers. The first tier were studies that looked at a definition of greater than two antidepressant medication failures, two or more. The second tier looked at failure of one antidepressant or more, and then the third tier looked at what they presumed to be treatment failures. It wasn't explicitly mentioned, but that's what they assumed, and so they broke their evidence out into those different groups and my understanding, and I haven't looked at it for a few weeks, is that the recommendations didn't change, essentially based on the tiers that they looked at, in part because there were not great studies that they pulled for quality, and the numbers were small.
- Craig Blackmore: So, let's, let's, can we get that doctor? Like I say, do we have that AHRQ paper? Do we have actual document of the AHRQ systematic review?
- Teresa Rogstad: I've got . . .
- Craig Blackmore: Oh, he's got it right here.
- Joann Elmore: Only some of it.
- Teresa Rogstad: I've got excerpts from it in the binder.
- Craig Blackmore: OK.
- Teresa Rogstad: I, but I think (_____) It's a 350-page document.
- Craig Blackmore: Right.
- Teresa Rogstad: So, (_____)
- Craig Blackmore: So, and anticipating that this is going to be important as we move forward but not at this moment, if I could ask for some clarity about whether or not the AHRQ report identifies differences between these different groups of selection criteria. So, could you try to track that down for us?
- Teresa Rogstad: Well, I, I can tell you that they did, you mean whether there's a difference between studies that selected patients based on one versus two prior failures?
- Craig Blackmore: Yeah.
- Teresa Rogstad: Yes, they did a stratified analysis, and the, the relative risk of remission and response was slightly greater in the studies that required at least two prior failures compared to studies that required only one prior failure, but the

confidence intervals around those relative risks overlapped a lot, and the review authors described them as similar findings, but there was a trend, it appeared, for greater effect in studies that only enrolled patients if they had two prior failures.

David McCulloch: Can I just point out, I hate using the term relative risk. Relative risk is a really weak way of looking at data.

Teresa Rogstad: I know.

David McCulloch: And it exaggerates effect. We want to know the absolute risk reduction, which you can then (_____) and talk about (_____)

Teresa Rogstad: Right, and that wasn't provided in a pooled form in the AHRQ report, but if you like, I can quick come up with some numbers from some of the larger trials and give you a sense of that.

David McCulloch: That would be great if you have the time, yeah.

Teresa Rogstad: OK, sure.

Seth Schwartz: The other question I have before we move forward, well I'd like to put this discussion in some greater context before we start it. Sometimes, when we talk about, when we have to make decisions, like the one that we just talked about for hyaluronic acid, we had all the treatment possibilities in front of us. I mean, we knew that there was physical therapy, there was steroid, there was NSAID, and then the question is, how do we, how do we fall on the question of hyaluronic acid compared to those. That's not what we're doing here. There are other therapies, nonpharmacologic therapies, used for treatment-resistant depression. They were not discussed, and I'm not proposing that they should be discussed but only that there are other possibilities out there. So, it's not that we're making a decision for patients about having this particular intervention or not having it in the context of there being nothing else available. There are other things available. There are other things available that have shown to be effective. So, I just want to make sure that people, that we all understand, we're not painting these patients into a corner by saying no to this intervention. There are other therapies.

Michael Souter: I think that's very contextual, though. I think it depends upon the severity and the presentation and, you know, I think that while you may be able to say that amongst certain patients who will fit a cohort of perhaps, you know, being evaluated and they're not necessarily as desperately depressed as, you know, patient B would be, there are still going to be some patients who by the immediacy and severity of their opinions have limited scope of where to go, and that assumes, again, that we've got all patients who can, you know, take, for example, pharmacological therapies. There are clearly going to be some groups of patients in whom pharmacological therapies may not work by virtue of either their age, tolerance . . .

Seth Schwartz: And I agree with you entirely, Michael, but the literature that we are given to review does not give us the granularity that you just described.

Michael Souter: Yeah, and I'm not arguing with that, but I'm just saying is that I don't, I don't think that we can safely assume that, that all populations covered within the scope of the question will necessarily have an alternative outlet of treatment, you know, as you're suggesting. I think there's a large section that may very well do, but I think we have to be mindful, again, of, you know, at the risk of being repetitive, the law of unintended consequences, small sections of the community who may actually be effected by, you know, by the broader decisions that we might make.

Craig Blackmore: Are there any other questions on any of the information that we've received, so far? OK.

Kevin Walsh: Can I just ask one question to our clinical specialist? I'm just trying to understand how, in the clinical context, you would make a decision of whether you would offer something like rTMS to a patient versus ECT. It seems like ECT is probably more effective, although not dramatically so based on what we're seeing. So, I'm just trying to understand, are we really going to use both of those treatment options for the same patients or is there some clinical selection that goes on amongst those two treatments?

David Avery: Yeah, that's a great question. I think if a person were very severely ill, let's say psychotic, suicidal, there's urgency for having them get out of the depression in the near future, I think that would clearly favor ECT. On the other hand, if the depression were more moderate and let's say it was very important to avoid the temporary memory disturbance of ECT. The person needed to continue working while they're getting treatment, that would clearly favor TMS. Those are, those are some of the factors I would take into account. Those are the main factors, I think.

Marie Brown: Would you use both of them in one patient over a course of time?

David Avery: I think, not at the same time. I think I would see, ECT, again is very important in getting a person out of a depressive episode. There have been some interesting studies done using TMS for maintenance of an ECT response. There may be some overlap between the stimulation therapies in the sense that people who had a history of, in one study people who had a history of ECT response also tended to respond well to TMS. They both have similar biological effects increasing neuroplasticity, increasing brain derived neurotropic factor, etc. So, there are some theoretical reasons why they might overlap, but I guess the scenario I just mentioned would be one in which I could see both of them used on the same patient, getting the person out of the severe depression with ECT and then maintenance with TMS.

- Craig Blackmore: OK. So, let us begin our deliberation process here and we have four fairly discreet different technologies. So, I think we're going to need to consider them all separately and we might as well start with ECT. I think, again, we need to make sure we are clear in our scoping. The topic at hand is adults with major depressive disorder or bipolar depression who have not responded to prior adequate pharmacologic treatments. So, we're not looking at patients with other psychiatric diagnoses for whom these technologies might be considered. They are outside of the scope of our evaluation, and we obviously have some leeway to define what major depressive disorder is and potentially that is a part of our decision. So, I'd like to ask one of the committee members to give us a summary of where they think we are in terms of ECT as a grounding point for the discussion. Any volunteers?
- David McCulloch: I'll give it a go, Craig. My sense is that albeit whether we define treatment-resistant depression as failure of one or failure of two, I think the evidence, if you include all the evidence, is very clear that ECT is effective in this situation. I don't get a sense that it is abused or overused. So, I mean, I'm leaning in favor of, yeah, I mean, I think that should be covered for the treatment of treatment-resistant depression however we define that.
- Craig Blackmore: OK. Does anybody else want to expand on that or have a different perspective?
- Richard Phillips: I would agree with that. I would agree with David on that. The other thing I would question though is that you had said bipolar disorder and in your discussion, and yet on the, in review I say that the typical patient and their systemic reviews and RCTs were patients with unipolar major depression disorder. So, I'm not sure if the data really covers bipolar disorder.
- Craig Blackmore: Well, the search covered bipolar disorder, right?
- Teresa Rogstad: Yes, it did.
- Craig Blackmore: Now, the data may not, there may not be a lot of data on bipolar, but it's part of our scope.
- Richard Phillips: Right, and I guess the question is, I, I, maybe as I was coming into this, my point was that maybe we just don't need to specify and leave that open. Maybe that's the wrong way to go after it, but I, for the very reason you say, you know, we, we don't have all the information that we would like, anyway.
- Craig Blackmore: I mean, I, I think it's important to be explicit on what, what was included in our literature review and so therefore, what's before the committee. Now, there may not be enough for us to tease out different groups, or we may have different decisions about different groups. That's fine, but I just, I don't, I want to be clear that there are other areas where people potentially are using these technologies, and they are not something we've looked at, so.
- Richard Phillips: Right.

- Craig Blackmore: So, we are not able to comment on schizoaffective, or.
- Richard Phillips: And I think that really gets into the issue of coverage with conditions, we just need to define the conditions.
- Craig Blackmore: Well, no. It's outside of the conditions. It's, it's outside of the scope. Our, our decision at the beginning does not apply to these people, no matter what our decision is. We're only looking at major depressive disorder or bipolar.
- Seth Schwartz: I didn't realize, I wasn't, interpreting what we were hearing was that major depression may be a component among other things. The other, excuse me, the other things are not what we were curious about, but most of the literature that's included is looking at the depressive aspects of whatever for the patient, and so that's what we're focusing on. There may be a patient with schizophrenia, but, who is in a major depressive disorder. If we approve it for depression, the schizophrenia is irrelevant, but we're not commenting on the people with isolated schizophrenia.
- Teresa Rogstad: My PICO question is the population of adults with major depressive disorder or bipolar depression who have not responded to prior adequate pharmacologic treatment. So, that's our PICO question.
- Craig Blackmore: There is a, there is a constellation of diagnoses that would fit in the major depressive disorder. We saw all the, but there are some that are on that list that were not included in our literature, and that is the people who have schizoaffective or schizophrenia without this major depressive component, and again, I just want to make sure that we are not going outside of the range. Dr. Rogstad did not do a literature review for the effectiveness of ECT in patients with schizoaffective disorder, correct?
- Teresa Rogstad: Correct.
- Craig Blackmore: So, that's out of our scope.
- Marie Brown: We're assuming that.
- Craig Blackmore: OK, so back to where David has put us, is there anyone who wants to add . . .
- Michael Souter: I would still like to clarify, you know, the, how this entity of treatment-resistant depression is going to be arrived at and implemented, because, you know, it is a term that implies that you've already gone through a stage of therapy, and I think that means, for me, a coverage decision that we want to kind of arrive at is going to be very much dependent on how the State actually implements the decision that we make. It's something of a circuitous argument, but nonetheless, I'm just concerned that if we say the ECT will only be covered in, if you just look at the language that is suggested, ECT would only be covered for severe persistent depression with or without psychotic features, yada, yada,

yada, but after at least two adequate antidepressant trials, in other words, we are implying that definition in there, then that is going to limit ECT until those steps have gone through, and I actually am concerned at the limitation of therapy in those circumstances.

Craig Blackmore: So, so to look at, to try to frame things in the big picture. So, what I think I'm hearing is, you would favor some sort of coverage and you want to make sure that any limits we make on that are not excluding people that might benefit and potentially what was proposed by the medical directors might be too restrictive.

Michael Souter: Yes, I mean, I'm specifically concerned about those people for whom by the severity of their disease, ECT may be a first line therapy. So, suicidal ideation, all those other kind of categories, and again, it's just that if we are focusing on this treatment-resistant depression as a category, then we are in effect already implying that barrier to be there.

Chris Standaert: I think the answer is we reverse the language. So, it says ECT is a covered benefit. We don't say that. We say for patients with treatment-resistant depression, ECT is or isn't covered, and we do that and then we . . .

Michael Souter: And that's fine.

Marie Brown: Good point.

Chris Standaert: . . . do that, and then we say this does not apply to other diagnoses, because I have the same concern you do that we can't restrict it for patient populations in which we didn't study it.

Marie Brown: Who may not be able to take two courses of the antidepressant medication.

Joann Elmore: And then I'm going to propose that we are probably unable to define treatment-resistant depression given the information that was presented to us. I've pulled the AHRQ review. They defined it and categorized all the many RCTs in their review into three tiers. Tier one is, you know, failing two or more prior treatment failures with medications. That's tier one. Tier two is studies in which patients had one or more prior treatment failures, and the third one is sort of everything else where it wasn't stated, etc., and then if you look at the tier one, there are no patients at all that have ECT versus sham. You have no data on ECT versus sham in this tier one change in depressive severity, response rate, remission rate, and so I think we are going to get into sort of a, a fine mess if we try to define treatment-resistant. So, I would ask the group what they recommend.

Craig Blackmore: The group?

Joann Elmore: I mean, I'm not certain we looked at the data for more than two, you know, medication failures, and the data that's presented here in the AHRQ review

shows that there is, you know, ECT, there were no patients at all to draw any conclusions.

David McCulloch: And again, that's because the AHRQ review ignored any studies prior to 1980.

Joann Elmore: Yes.

David McCulloch: Which is when they did those big sham trials and people who failed their tricyclics.

Seth Schwartz: I think we've been in clinical situations like this before where it has not been well defined what, whatever the condition is, and we have trusted clinicians to be able to make that decision, and I think, I don't think any of us think people are overly offering ECT to just a bunch of random patients and this is a situation where I would feel very comfortable leaving it as treatment-resistant depression and not specifying anything beyond that.

Joann Elmore: I would, too, yes. Thank you, I would, too.

Craig Blackmore: So, to be, just to be clear, perhaps to add some data, according to the agency slides, there were 210,000, no, there are 20,000 PEB members with depression and 26 of them got ECT, so that's about 1 in 1000 of the depressed patients, and then for UMP, there were 55,000 with a diagnosis of depression and ECT was performed in 43 of them. So, again, about 1 in 1000. OK, so I'm hearing, I think, some broad support for coverage of ECT, maybe or maybe not with some restrictions around a trial of medication first. Is there anybody who has a very different perspective that they want to share. OK, so it sounds to me like we are not heading to a no coverage. So, the only question would be, is it covered without conditions or covered with conditions and if it were with conditions, what might those look like and one issue is, if we try to define prior treatment, but we think that the way the PICO is written, that might be covered by saying in patients with treatment-resistant depression. Are there other conditions that people feel may be relevant?

David Avery: Have we talked about the issue of medication intolerance?

Craig Blackmore: Sorry?

David Avery: Medication intolerance?

Craig Blackmore: We haven't talked about the issue of medication intolerance, but I think that is not what we're asked to look at.

Teresa Rogstad: A lot of the studies defined failure, intolerance could be a reason for medication failure. So, it is assumed that patients tried previous drugs at a maximum tolerable dose and it didn't work, or they found at least in these trials.

- Craig Blackmore: So, in your PICO, did you only look at papers about people who have not responded, or did you look at people who failed for reasons other than nonresponse?
- Teresa Rogstad: We didn't differentiate.
- Craig Blackmore: So, that is encompassed in your?
- Teresa Rogstad: Yes.
- Craig Blackmore: OK.
- Chris Standaert: Which just gets us back to the definition of treatment-resistant depression.
- Craig Blackmore: So, so again, yeah.
- Chris Standaert: It was very vague, yeah.
- Richard Phillips: So, those patients wouldn't have been excluded.
- Teresa Rogstad: No. That would just be a reason for the failure.
- Craig Blackmore: So, this may, there may be an emerging consensus. I'm looking for somebody to either define conditions that they think would be important or give me a contrary opinion.
- Chris Standaert: I don't know, but beyond saying we're covering treatment-resistant depression, I don't know if we have a place to make a distinction.
- Craig Blackmore: I'm, I'm asking the question, not suggesting. I'm asking.
- Chris Standaert: I don't know of an additional condition to impose upon it other than the straight-up sort of we approve it or we don't approve it for treatment-resistant depression.
- Craig Blackmore: Alright, then we're going to move on. We're going to move on to the, to the worksheet. Alright, so in the back of the section on nonpharmacologic treatment-resistant depression, you will find your decision tool, coverage and reimbursement determination analytic tool, and this tool we are very familiar with and it lays out the criteria that we use for decision making. Is it safe, is it effective, does it provide value, cost effectiveness, and the, it also includes a summary of other coverage guidelines including Medicare, which we have also seen as part of the evidence report. Our staff have prepopulated this document with the outcomes that we consider important in making decisions about safety, efficacy, as well as special populations. So, before we go further, are there other outcomes on here that we are considering in our decision making that have not already been listed? Safety outcomes, I guess I would need to add things like hemorrhage and surgical complications, because, yeah, I'm not, so

surgical complications, device failure, infection. Anything else on here that we are considering in our decision making.

Chris Standaert: I don't know. I mean, it mentioned suicide as a, in the studies on DBS, and they talk about rates of suicide, but I don't know if that's a complication or that's just a, this is a high-risk population we're dealing with. So, I don't, I didn't know quite how to count that one. That's a failure of treatment or that's a complication?

Craig Blackmore: OK, so maybe suicide is an effectiveness outcome, or it could be a safety outcome, and OK. So, that brings us to the first voting question, and that is going to be the yellow, the yellow cards and I think I am short a yellow card. There it is. OK, so what we're to vote on now, and this is a straw vote. It's not binding, and that is do we believe that there is sufficient evidence under some or all situations that ECT is either more or less equal or unproven in terms of effectiveness to, to what? To other, the alternative is basically all the other ways of treating, treating treatment-resistant depression. So, if you think it is more effective under, yeah.

Josh Morse: Eleven more effective.

Craig Blackmore: Safety. Safety.

Josh Morse: Nine equivalent, two more.

Craig Blackmore: And then finally cost effectiveness.

Josh Morse: Eight unproven, two more, one less.

Craig Blackmore: OK, further discussion based on what we've just learned? I'm going to move on to the voting binding question and we are now going to make a decision. So, this is for coverage of ECT in treatment-resistant depression. We're leaving the definition of treatment-resistant depression, yeah, that's what it is for. It's for coverage of ECT in treatment-resistant depression.

Josh Morse: Ten cover, one cover with conditions.

Craig Blackmore: OK, and then we'll just take a quick step back and look at Medicare and these other guidelines and I don't have that slide in front of me. Medicare, I believe, had no national coverage decision. These are practice guidelines.

Josh Morse: It's on the opposite page of your guidelines.

Craig Blackmore: Oops, there we go. OK, so, so we're consistent with some of the private payers, as well as no national coverage decision for Medicare, so we seem to be mostly consistent with other, other recommendations. We are different from the New England Public Advisory Council. They said there was inadequate evidence, but I

think we've reviewed the evidence and we've decided that we thought it was sufficient.

Chris Standaert: (_____) sufficient was nice.

Craig Blackmore: (_____) was nice. OK, next. We go through the same process, and the second technology is rTMS, right? RTMS, so, again I will call on a volunteer to summarize where, where they think we are, yes, where they think we are with respect to rTMS. So, is there a committee member who would be willing to start us on that?

Michael Souter: I'll throw my hat in the ring.

Craig Blackmore: Great.

Michael Souter: I think that what I see in the rTMS data is that it appears to be as equivalent to ECT. I think the, I've got much less concerns about, you know, the acuity of the group. I think this is something that can be looked at more favorably, perhaps, without having to be worried about acute intervention and the concerns about suicidal ideation, etc. So, I think there's room to explore, you know, putting some barriers on there in terms of, you know, treatment trials beforehand, but having just made the decision that we did and leaving it up to the practitioner and given the fact that is probably equivalent in cost to ECT, I'm not certain whether this is actually worth our while to get too particular about it.

Craig Blackmore: I mean, we can, in that syntax, still do that.

Michael Souter: Mm-hmm.

Craig Blackmore: Say in treatment-resistant depression, it is covered in patients who have failed etc., if we wish to. So, other thoughts.

Kevin Walsh: I, I read the studies differently. I think that the relapse rates were equal to the sham groups and that in the studies that looked at ECT and TMS that ECT had lower recurrence rates when you looked beyond a few months compared to rTMS. So, I'm struggling with finding literature that shows it to be, shows it to have a role distinct from ECT. I mean, I'm not saying that there is not one. I'm saying, I don't see that the literature supports it or defines it or proves it.

Michael Souter: I guess I'm looking at the differences in terms of such things as cognitive function, ability to carry on a lifestyle, etc., and those scenarios, and again, I'm persuaded by the point of view that relapse rate is not necessarily the best perspective from which to actually judge the efficacy of this particular clinical intervention.

Kevin Walsh: So, you're saying, based on its lower, on its better safety profile, that's a reason to allow its use.

- Michael Souter: I think it's got an equivalent safety profile, yes.
- Kevin Walsh: So, it has an equivalent safety profile, no benefit, so we should approve it.
- Michael Souter: No, that's not, again, that's . . .
- Craig Blackmore: No differential benefit.
- Seth Schwartz: I think one of the questions is, are you comparing it to sham or are you comparing it to ECT, because I think compared to sham, I think there is data fairly convincingly that it's effective.
- Michael Souter: And that's what I'm wondering, compared to sham.
- Seth Schwartz: I guess I'm saying compared to sham, there is data. I think when you compare it to ECT, it's a little bit less clear. I think ECT probably looks slightly more effective, but not dramatically so.
- Michael Souter: Right.
- Seth Schwartz: I think when we look at the risk profiles, there's, it depends how you define the risks. I think neither of them have a huge risk profile that we're seeing in terms of death or suicide or those sorts of things, but there may be quality of life benefits to this treatment over ECT in selected patients. I am trying to figure, I agree with Michael that it, you know, it seems that these, you, this is clinically used in patients who are slightly less acute than those in whom you might use ECT and yet I'm not clearly seeing any specific criteria that we could use to put conditions upon this. So, I'm just where I am at falling into the same scenario as where we were with ECT.
- Carson Odegard: I think that, you know, one important factor is, like Dr. Avery pointed out that, you know, there are those patients that cannot tolerate the ECT and if you want to get them back to work and you want to make them functional in their scenario, you know, this is, and if the effectiveness is fairly close, it is, I think it's safer. I mean, it appears to be safer than ECT, just because of the anesthesia factor and also the outpatient and the cognitive loss. So, so I think that, you know, the equivalent is just a different, sometimes just a different patient population that you're going to use it for.
- Craig Blackmore: Can I, can I ask Dr. Rogstad to revisit slide 42? So, if, I'm hearing a lot about equivalence, perhaps, and so I always want to make sure if two things are equivalent that there isn't some huge cost impact and why would we pay for something that's substantially more expensive if we have other things that work just as well, but I just want to make sure I understand the cost effectiveness data that was presented. On slide 42, it talks about incremental cost effectiveness ratios and I'm sorry, I'm not clear on which, which procedure is being compared to which and so which is cost effective with respect to the other or if these are cost respective with respect to what?

- Teresa Rogstad: ECT and TMS were compared directly with each other, and the authors used a cost of \$800 per session for ECT and \$75 per session for TMS. They assumed eight sessions for ECT and 15 for TMS. So, according to their submissions, ECT was more expensive and they took data from this (_____) trial, which was a (_____) comparator trial reporting results in terms of changes in depression scores. They combined that evidence with external evidence about utility value and translated that to (_____) and that's how they came up with that incremental cost (_____) ECT versus TMS.
- Craig Blackmore: So, so which is which. I mean, is this?
- Teresa Rogstad: It means, what this number means is that the patients . . .
- Craig Blackmore: I mean, is it . . .
- Teresa Rogstad: . . . with ECT was expected to result in greater QALY gains, but for every quality adjusted life year that you gained, you would pay \$460,000 some dollars to treat patients with ECT compared to TMS.
- Craig Blackmore: So, this is the incremental cost effectiveness of ECT . . .
- Teresa Rogstad: Mm-hmm.
- Craig Blackmore; . . . versus TMS. Alright, that was my question, thank you.
- Chris Standaert: When I look at the, I have the (_____) systematic reviews on ECT versus TMS, and they both say similar things that ECT is, in general, more broadly effective. They talk about it being more effective and more effective in a particular group. So, then one specifically notes psychotic depression is more effective and the other one, the (_____), talks about some (_____) parameters for TMS are not as effective as others, and they mentioned similar things about tolerance and cognitive side effects being better in TMS and in areas where, I don't see things saying TMS is superior. They say, it's equivalent is what they're finding, but on the whole, ECT has areas of superiority over TMS. So, I don't know that it's as effective or more effective than ECT, but it looks like tolerance and side effects are less, and there are some groups where they are equivalent.
- Michelle Simon: On slide 39, I guess I don't know what to make of this, slide 39 says comparing rTMS with ECT and the first bullet point there is 'no overall difference in cognitive effects,' three randomized control trials. So, that kind of goes against what we're all understanding, that there's less side effects with ECT. So, I'm kind of confused about, are those three poor randomized control trials?
- Teresa Rogstad: Are they three, what did you say?
- Michelle Simon: Bad?

- Teresa Rogstad: No, they, all the trials represented are fair to good quality.
- Chris Standaert: Yeah, I mean, I have the (_____) Study right here. It says results based on three studies suggests specific cognitive demand, such as visual memory and verbal fluency were more impaired in patients receiving ECT. It says more, and it says three studies. So, you said three and it's equivalent, but anyway, that's what this study, this, what this systematic review says, which is contrary to that.
- Teresa Rogstad: Right, OK. I'd have to, I'd have to check that out, in the (_____) Study, you said?
- Craig Blackmore: (_____)
- Kevin Walsh: And while we're on that study, I'm just curious, what does withdrawal mean?
- Teresa Rogstad: Dropped out of the study.
- Kevin Walsh: OK.
- Craig Blackmore: Any other comments? So . . .
- David McCulloch: I'm leaning towards thinking we should cover rTMS. My sense is, it's not going to be abused. It will be used possibly for milder patients or for patients who, for patients who are started on it who don't respond then they're probably good ECT. I just feel as if, my sense is, if it's not going to be abused, it, it's another decent treatment option that should be available, and I don't think we should be micromanaging which patients get better versus ECT. I would, my guess is, it would be used for certain patients and let's say they didn't get better and they were really getting severely depressed, they would then try ECT.
- Michelle Simon: I guess, can I say one, on more, I have one other question now talking about nothing abused. Did we actually see utilization data from the State on this?
- David McCulloch: We didn't, and I . . .
- Teresa Rogstad: There isn't data.
- Michelle Simon: There isn't any? Does that mean they're just, it's not, it's not used? So, we have no idea about cost in the State or?
- David McCulloch: So, so, we may well be re-reviewing this in four or five years when you find that the number of requests have been up and up and up and up, but at this point we can't, yeah.
- Marie Brown: So, it hasn't been covered before.
- Chris Standaert: It's covered now or it's not covered.

- Richard Phillips: It's not covered.
- Chris Standaert: Because nobody's, there's no policy. So, it's not being denied. It just isn't being requested. Are there explicit . . .
- Teresa Rogstad: I'm not aware of any requests for it that have been denied. You can specifically ask the utilization review folks, but we certainly (_____)
- Craig Blackmore: Dr. Avery, is anybody doing this in the State?
- David Avery: Yeah, to my knowledge, there are two practitioners, one Dr. Mellman at Swedish Medical Center, and Dr. Dunner on Mercer Island, and yeah, and my understanding is that some insurance companies cover TMS, and, you know, we've seen that data. Yeah, just two in the Seattle area and, as far as I know in this, just two practitioners in the State.
- Kevin Walsh: Can I just ask one more question that I'm, as we look at this more, I'm just trying to, it seems that ECT, ECT is ECT, but with rTMS we're learning there are some differences in whether it's unilateral or bilateral or how you do it, and is, is that something that we need to be thinking about, you know? Is it, is it ineffective if you do it one side and for five treatments versus, you know, I'm just trying to get my head around . . .
- David Avery: I think the number of treatments makes a difference. Clearly, the efficacy goes up with more treatments, and that's where that one cost analysis estimated 15 sessions and larger, multi-site studies indicated probably 30 sessions is necessary for TMS. Yeah, there is controversy about right side, left side and so forth with TMS. I don't know how to advise you about that. There's controversy there. Most of it is high frequency to the left dorsolateral prefrontal cortex.
- Marie Brown: That would have cost implications, though. Sort of like what Craig was talking about. If you have a treatment that usually requires 30 visits.
- David Avery: Exactly, yeah.
- Marie Brown: But we don't have any cost data to see if that's, if it's more expensive.
- Chris Standaert: On our current State agency policy slide, it says rTMS is not covered. So, ECT is the only thing covered by Medicaid, L&I, and Uniform. So, TMS is not covered by any of them is what this says. That's why there are no charges. It's not nobody's billing. I don't think they, no, there's, it's, it says explicitly not covered for Uniform Regence.
- Teresa Rogstad: There was one request in 2012 for TMS through PEB. It was not, it was denied. (_____)
- Craig Blackmore: Go ahead.

- Joann Elmore: I had a question about the definition of response, and it's prompted by Kevin's comment about durability. In all of these RCTs, at what point after applying the technology was the assessment done, and I ask this, because on page 62 in the detailed assessment that's provided, they talk about how just a very, very small number of RCTs actually gave data at the conclusion of treatment. In other words, most of them, they only give you the response rates during treatment, and it seems that there is only a small number, six studies, you know, that give data two to 24 weeks after the end of treatment, and in one of them it, it sort of persists to three weeks, but not at 11. The other one, it persisted for two weeks to three months, but, in other words, we, as a group, have evidence on the impact in its effect at a certain point in time, but we, it doesn't seem as if there's very good data on durability, and I think that's just a caveat in the existing data, and I'm not certain if our vendor can tell us anything to help us in regards to the point in time of assessment that defines treatment effect.
- Teresa Rogstad: It was always at the end of treatment.
- Joann Elmore: OK. Immediate end.
- Teresa Rogstad: Immediate effect, right.
- Joann Elmore: And, of the many, many studies, very few gave data three weeks, or . . .
- Teresa Rogstad: Followup.
- Joann Elmore: . . . followup, yeah.
- Michael Souter: There was the McLaughlin Study that gave duty at six months after a followup, after treatment rather.
- Teresa Rogstad: Would the committee also like some information on risk differences for TMS?
- Craig Blackmore: Sure.
- Marie Brown: You want to use the mic?
- Teresa Rogstad: It might do a better job of leading this.
- Josh Morse: Can you please use the microphone?
- Teresa Rogstad: Oh, sorry.
- Josh Morse: Thank you.
- Teresa Rogstad: Yeah, this is a very quick, quick and dirty, but looking at the RCTs that were represented in our report, the risk difference for response ranged from 0 to 50 points. If you average across the 18 or so studies, it's an average difference of 18 points. Of course, that's not taking into account the size of the studies or

logistical variation or anything like that. For remission, the risk difference ranged from 0 to 37 points, an average of 14 points. I hope that helps.

Chris Standaert: And those favor ECT? You didn't tell us which side goes which way, but.

Teresa Rogstad: Pardon me?

Chris Standaert: Compared to ECT, what is that, favor what?

Teresa Rogstad: I'm sorry. That was TMS compared with sham.

Chris Standaert: OK, sham. OK, nothing to do with the ECT.

Craig Blackmore: OK, so, other comments or should I move along?

Chris Standaert: I guess the only issue would be the circumstances where TMS should not be covered. Should it be a second-line treatment to ECT. Do we even go there, or do we just say yes or no? It's hard. Some of this stuff is hard because of some of the technical issues about how you do it seem to matter.

Craig Blackmore: OK, I'm not compelled to get into technical issues unless I have a reason.

Chris Standaert: No.

Joann Elmore: Right.

Craig Blackmore: OK. OK, so why don't we just move forward with our nonbinding tan cards. Let me get my script. So, these are, is there sufficient evidence under some or all situations that the technology is unproven, equivalent, less, or more effective than other treatments?

Josh Morse: There are nine more and two equivalent.

Craig Blackmore: And second is safety.

Josh Morse: Seven equivalent, four more.

Craig Blackmore: And then finally the cost effectiveness piece.

Josh Morse: Ten unproven, one equivalent.

Craig Blackmore: OK, further discussion at this point? OK, so we're going to move on to the second vote and this is where we always sort of have different ways of approaching things. Can I, can I just get a sort of a straw vote, nonbinding. Are there people who think we're in the no coverage range? OK. So, then we're just down to sort of cover conditionally or cover unconditionally and we can either vote that first or we can try to define conditions first. I think my inclination is to vote first and if people are interested in coverage, then we'll go

down that, or into conditions we'll go down that path. I'm seeing a lot of nods. So, we'll have our vote. This is the binding vote now. Based on evidence of the technology safety, efficacy, and cost-effectiveness, it is.

Josh Morse: Nine cover, two cover with conditions.

Craig Blackmore: So, we will cover patients with treatment-resistant depression. Looking at other coverage decisions that people have made, so some of the private insurers have on coverage policies and the Oregon HERC has coverage, recommends coverage, and CMS has no decision, and the New England CEPAC recommends coverage basically. So, we are, we are saying that the evidence, we think, is sufficient that coverage is indicated and that's based, I think, on both comparison to the sham trials where it seems to be better in comparison to ECT where it seems to be roughly equivalent, and we don't see a big, can't find big cost implications, and it may be that there are clinical circumstances that one might be preferred to the other, and so we're trying to leave people, leave the providers and patients with those options without a compelling reason not to. Is that a fair summary? Alright. Next, next is DCS.

Chris Standaert: We have a common problem with DCS and brain stimulation. Neither one of them are FDA approved. So, do we actually cover something not FDA approved for this when we already just approved two treatments (_____)

Craig Blackmore: Brain, the deep brain stimulator is approved for other indications.

Chris Standaert: But not for, but not for this indication.

Craig Blackmore: We don't, we don't routinely look at whether the technology we're covering is included in . . .

Chris Standaert: I see what you're saying, OK.

Craig Blackmore: It's not an unapproved technology. It's a technology that is approved for other indications. Physicians, providers routinely use things off label and bill for it and get paid for it.

Michael Souter: But I guess Chris is outlining the (_____) which is that there's, you know, it needs a lot of research to be done before, I think, we would consider covering that.

Craig Blackmore: That, that's a different way of framing, yeah. So, so, so you're summarizing, and I think what I hear is insufficient evidence of all three?

Group: Yes.

Craig Blackmore: Any discussion on that or?

Michelle Simon: I think there might be some potential benefit there. So, I think excluding, or including a research inclusion would be . . .

Michael Souter: Well, that's always present, too.

Craig Blackmore: And there's always the opportunity . . .

Michelle Simon: I just want to say it.

Craig Blackmore: . . . to, right.

Michael Souter: Yeah.

Craig Blackmore: OK, then we'll move to our tan cards, and we will look at DCS, and we will say is there sufficient evidence under some or all situations that the technology is unproven, equivalent, less or more effective. So, this is effectiveness.

Josh Morse: Eleven unproven.

Craig Blackmore: And then I would say the same thing about safety.

Josh Morse: Ten unproven, one equivalent.

Craig Blackmore: And cost effectiveness.

Josh Morse: Eleven unproven.

Craig Blackmore: Alright, and then further discussion? Without further discussion, we will move on. So, in treatment-resistant depression, based on the evidence of the technology's safety, efficacy, and cost effectiveness.

Josh Morse: Eleven no cover.

Craig Blackmore: Comparing that to other . . .

Chris Standaert: That was DBS and DCS?

Craig Blackmore: No, that was DCS.

Chris Standaert: Oh, that DCS.

Craig Blackmore: And we're not in conflict with anybody, because there aren't any other decisions out there that have been identified before us. DBS, somebody want to summarize where we are?

Michael Souter: Can we just say ditto?

Marie Brown: Even less.

- Craig Blackmore: So, any further comment?
- Chris Standaert: Just so it goes on the record, there are additional safety concerns with DBS compared to DCS. DCS doesn't, I don't have a lot of safety concerns with DCS, but DBS certainly has safety issues that fall into our consideration.
- Marie Brown: That's true.
- Richard Phillips: What kind of requests do we get for DBS?
- Marie Brown: Do we get any requests?
- Craig Blackmore: I think we heard that nobody is actually doing this in the state for this indication, but there are other centers around the country where people are. Well, there's other indications where it's being used, but there are other centers in the country where people are going and studying it. OK, so is there sufficient evidence under some or all situations that the technology is effective?
- Josh Morse: Eleven unproven.
- Craig Blackmore: Safe?
- Josh Morse: Eleven less safe.
- Craig Blackmore: Cost effective?
- Josh Morse: Eleven unproven.
- Craig Blackmore: OK, and the opportunity for further discussion. We will move on and based on the evidence about the technology safety, efficacy, and cost effectiveness, DBS is?
- Josh Morse: Eleven no cover.
- Craig Blackmore: No cover, and then in terms of other policies, we are consistent with AETNA and Regence. CMS, Group Health Oregon have no policy that could be identified. So, I would say we are consistent with what is out there. OK? It is ten of 12:00, is lunch?
- Josh Morse: Well, we could have another potential agenda item we could move up, which is consideration of questions.
- Craig Blackmore: I think that would be great. So, the final item on the day, and it's actually Hayes. I think your group is, so while we have Dr. Rogstad here, we will jump ahead on the agenda and look at the final item, which is working on the key questions around thyroid ultrasound. So, do we have these in our?
- Josh Morse: These are in the very back of your binder.

Craig Blackmore: It's the very back of the binder, very good. So, we are in the open public comment period on the draft key questions.

Josh Morse: We'll either commence today, depending on the web queue at the Health Care Authority will be online today, or it could be online on Monday.

Craig Blackmore: OK. OK, so is there somebody that can sort of present the background on this to the group or should we just read through it?

Josh Morse: Dr. Hammond may be able to get us started.

Craig Blackmore: Dr. Hammond, can you share with us?

Steve Hammond: The main concern prompting selecting this as a topic is the large increase in diagnosis of thyroid malignancies over the past 30 years with subsequent invasive procedures and surgeries and yet the continuation over the past four years of very low mortality rate related to thyroid malignancies at about 0.5 per 100,000 population. So, the, again the main issue here is whether more widespread use of ultrasound to detect thyroid nodules and lead to biopsy and diagnosis of, for the most part, low-grade malignancies, has led to improvement in health outcomes, as opposed to perhaps exposure to greater risk of harms related to invasive procedures, surgeries, thyroid replacement therapy, radioiodine treatment, and the attendant sequelae of diagnosis of low-grade thyroid malignancies. That is what prompted selection of this topic. I do have one concern about the key questions. What I considered to be the real key question is key question two asking about effect on health outcomes and I'm a little concerned key question one is something of a distraction from the main question. Key question one has mainly to do with the performance of ultrasound in terms of detecting lesions and that is not really the question. We, there's plenty of good evidence that ultrasound is very effective in detecting anatomic abnormalities of the thyroid. The question is whether the use of ultrasound results in improved health outcomes or indeed risk of harms related to unnecessary procedures.

Craig Blackmore: So, I might just jump in as a radiologist. There is a lot encompassed here and it's not explicitly defined in the different categories. So, the first group is high-risk patients who undergo a screening procedure. That's a completely different question and a completely different population from individuals who have an abnormality of physical exam and that is a completely different population from individuals who have an abnormality on an imaging test that's discovered incidentally, and they really need to be treated separately. The key question for the incidental nodules, when do you need to do anything? What are the size criteria? What are the imaging criteria, because we encounter this all the time, and the radiology community is trying to come up with some sort of guidelines, which would not be based on evidence, because there isn't much, but that's a question of, in which patients with an incidentally-identified thyroid nodule should we do anything, and if we do anything, what is it? It's probably ultrasound. The clinical exam is similar in patients with what specific clinical

exam finding should we do anything? Should we do an exam on somebody if they have an enlarged nodular goiter or should we do an exam on somebody with a normal thyroid that has one nodule, and what should that imaging, what should that look like, and should the next test be biochemical or should it be imaging, and then the third group is patients at high risk, is it appropriate to screen and if so, with what, but you can't, you can't lump them, because they, they're completely different.

Chris Standaert: I guess I would reverse the question a bit, too. Is the problem the ultrasound or the problem the biopsy? Right, so once you, so saying you can't, I agree with Craig totally. So, you say you can't do an ultrasound, well that means you can't screen people with it, or, so you find a nodule on a neck MRI, and you have to learn more about it and figure he should biopsy it, and then you say you can't do that. That's kind of weird. You already know they have one, so you've got to look at it somehow, and somebody's going to want to stick a needle in there. If you say you can't biopsy then people are just going to do needle biopsies under CT, which is worse than an ultrasound. So, your, if your goal is to reduce the biopsy rate, which is leading to diagnoses of questionable carcinomas, which are leading to, or cancers that are leading to procedures, the issue isn't the ultrasound. Unless it's ultrasound screening, the issue is the biopsy.

Seth Schwartz: But most of the, I would, I would argue that most of those nodules are not discovered on MRIs, they're discovered on ultrasound.

Chris Standaert: Or exam, well . . .

Seth Schwartz: So, if you don't do the ultrasound to begin with, you don't discover the (_____)

Chris Standaert: Yeah. So, do people do screening ultrasounds of thyroids? Is that something people are doing lots of, just a normal patient whose totally asymptomatic gets a thyroid screened with an ultrasound? I don't know. I've never seen it, but I don't, I don't do that.

Marie Brown: We find them on carotids when people are screening carotid arteries, we find them.

Chris Standaert: Right, and we find them on MRIs when we do MRIs of the C-spine we see them, but then we're stuck. So, it wasn't found on the ultrasound. It wasn't the ultrasound's fault. We found it on the MRI and now we're stuck.

Kevin Walsh: I think, I think Craig was parsing out the, the complexity of this. There are, there are subgroups of patients in whom it would be appropriate to do the ultrasound because of their risk and there's subgroups where it's questionable, because their risk is lower.

Craig Blackmore: Yeah, and, and it's going to be really hard, 'cause it's not, there's not going to be great data.

- Kevin Walsh: And we already know there's no literature to parse this stuff out, probably.
- Michael Souter: Well, so that's what I'm curious about. I mean, who are the groups that are at risk of, you know, of having something there that you actually want to screen for. Who are the groups at risk of thyroid cancer that, you know, there may be a role for in this. Is this, are there any out (_____) total.
- Craig Blackmore: I, I don't know, I don't know the answer to that. I don't even know if we're doing screening.
- Michael Souter: Because obviously, because that, that's the question that's actually in the text here is that ultrasound may also be used as a screening technology in individuals who have no palpable nodule but who are considered to be at risk of thyroid cancer.
- Kevin Walsh: How about all the sailors on that boat that went into (_____)
- Steve Hammond: A couple of groups would be those who have had a history of radiation treatment to the neck and those who have a family history of familial thyroid neoplasia.
- Chris Standaert: So, they get screened?
- Steve Hammond: Or multiple endocrine neoplasia.
- Craig Blackmore: That's actually something we can examine and look at the evidence and maybe make a decision on.
- Steve Hammond: Sure.
- Craig Blackmore: It's much, I mean, it's no less important, but the data is going to be much more difficult to come by for trying to understand all these incidental nodules. I'm not saying we shouldn't try to do it, because I think it's incredibly important, but we're going to struggle.
- Steve Hammond: I think one scenario that's pretty common, the thyroid, examination of the thyroid takes a fair amount of skill and experience, and most primary care providers have some lack of confidence in their neck exams and whenever there's a suspected or even some, any palpable abnormality are suspected, oftentimes the next step is to do a thyroid ultrasound, which leads to oftentimes, depending on what popu-, demographic group you're looking at, sometimes more often than not, you will find a nodule. The question is, does this improve outcomes.
- Chris Standaert: But you, you're, how do you do it, I mean, so you can't tell the primary care providers they can't examine a neck, and you can't tell them when you find a lump on the neck you can't do anything about it. you can't tell them that. That's not, that would be, I mean, you just can't do that, and so they're going to

get an ultrasound or a CT. If they don't let them do ultrasound, they can do a CT or an MRI, because they have a lump and they have got to make sure, is it a lymph node. Is it a thyroid nodule. What is it? Is it something else? You can't tell them they can't work up a physical finding.

Group: Right.

Chris Standaert: And, so you can't do that, and then you can't, you can't say, well I have a nodule I found on ultrasound. The question, the biopsy question comes up, when should you biopsy, and I, I agree with Craig. Maybe there's an issue that you could talk about, when is it appropriate to screen a completely asymptomatic individual with no physical or imaging findings suggestive of a thyroid problem?

Marie Brown: Biochemical.

Chris Standaert: But, you know, who, is this really a problem?

Craig Blackmore: You can define criteria for when to biopsy. I'm just not sure there's going to be any data, and we're going to be stuck saying it's OK to biopsy some of the time and we can't tell you when not to biopsy. So, I mean, I could be wrong. I, I don't know what exists. You know, I don't know what data exists.

Marie Brown: Yeah, maybe there is.

Chris Standaert: I mean, my wife, my wife just went through this. She had a physical exam with a nodule and they found it and as a result she got biopsied, and it, the biopsy was negative, and it was, but it's, you run, you read the literature and it's, you know, biopsy, positive biopsies are 5-20% depending on the population, and that's not small and that's not insignificant, and how do you then restrict the ability of physicians to identify and sort through these things when we don't know the, and that's why I'm wondering where you're going to, how we're going to get there.

Richard Phillips: I think it's going to be hard.

Chris Standaert: Well, I think what you're after is this idea of when is a biopsy really lead to further treatment, not so much when does the ultrasound lead to the biopsy.

Seth Schwartz: I'm not sure that's right. I mean, I'm kind of hearing this a little bit different. I mean, I think the point is, once you get the ultrasound, the whole downstream effect occurs. The question is if, do people with a nodule even need an ultrasound. Now, again, I'm not saying we should or shouldn't do it. I'm saying, I think that's the question. I don't know if there will be data on it, but, you know, is the question so you do a physical examination and you feel a nodule, are there criteria where you could say, well you don't necessarily need to get an ultrasound in everybody. Maybe if the nodule is bigger than 2 cm you get it, or maybe if it's enlarging you get it, or maybe if they have other risk factors. I mean, I don't know what their, whether there are criteria, but I mean, I think

that's the, that's the entry point that they're asking about, because once you get the ultrasound, all the downstream stuff is going to happen, and, but the point is, if getting the ultrasound for a 1-cm nodule is leading to all these risks, you know, there's those patients who get surgery but it's not helping their health outcomes at all then maybe we should say, well you shouldn't get an ultrasound if it's a small nodule, but if it's bigger you should. Now, again, I'm not sure if we, there will be any data to, to do that, but I'm, and I understand, that's the way I understand the question is, should we be doing . . .

Chris Standaert: It's like the PSA. It's like the PSA question.

Seth Schwartz: Yeah, it's like the PSA question, exactly. Right, so I guess what I'm saying is, I don't necessarily agree with what you said, Chris, which is that we can't tell patients, people not to examine the neck. Well, of course not, but we can tell them, you can examine the neck, you may even feel something, but you can't get an ultrasound unless there are certain criteria.

Chris Standaert: So the, but then the issue wouldn't be using the ultrasound as a screening tool, it would be using physical, physical exam as a screening tool for thyroid disease, which would be analogy of drawing a PSA. So you're using the PSA as a marker for prostate cancer, and you don't have any great suspicion. It's a male over 50. They get a PSA. Is that a valid screening test or not. That's a fair question to ask.

Seth Schwartz: No, it's already been asked, and the answer is no.

Chris Standaert: So, what you're asking, huh?

Seth Schwartz: It's already been asked, and the answer is no.

Chris Standaert: No, I know, but that was a fair question to ask. So, but what you're saying then is this idea that it's not the ultrasound. It's not the biopsy. It's actually the physical exam that leads to the concern for something that leads to an ultrasound, is there a way to define when, under physical exam, your findings can, can justify an ultrasound or shouldn't justify an ultrasound. Is that what you're getting at?

Seth Schwartz: Basically, but I mean, I think you flip it. You say, you don't say when should you do an examination. You should say, if you're going to do an ultrasound, what criteria do you need to order that ultrasound, and it may be . . .

Chris Standaert: Based on exam.

Seth Schwartz: . . . high-risk patient, examination which shows a nodule larger than XYZ, or what, I mean, I don't know, I don't know what those criteria are. Maybe there's no way to define them, but I'm saying, I can at least envision that being the question that they want, actually, us to look at.

- Chris Standaert: Right, the exam is a screening tool, essentially, not the ultrasound.
- Craig Blackmore: Under what circumstances will an ultrasound improve outcome, under circumstances the conditions might be a nodule that's growing or . . .
- Seth Schwartz: A 4- cm nodule or what, you know?
- Craig Blackmore: A palpable abnormality, or . . .
- Seth Schwartz: Or voice changes or weight loss. I mean, who knows what it is, but there may be some criteria that you could say clearly in patients with a 4-cm nodule who have lost their voice, an ultrasound or whatever is going to be indicated, because we, you know, they're going to have advanced disease. If it's somebody who is, you know, a 70-year-old patient with a 1-cm barely-detectable nodule, is it going to make any difference in that person's life expectancy or health outcomes, and the answer is probably no. Now, I don't know if we can define this, but I can at least see why it's a valid question.
- Chris Standaert: For the primary care doctors in the group who do this, like I don't do this. Is this something you guys and by exam do you think you could actually build some parameters by which you would then pursue or not (_____)
- Kevin Walsh: No, no. I understand the, I understand the direction of Seth's points, and I think it's a valid to look at the literature to see if there are, is there any, does the literature show us any points that we can stand on or are there none?
- Marie Brown: Especially for a diffuse goiter. I mean, that's what we see so much in primary care.
- Kevin Walsh: Right, you hardly ever pal-, you'll hardly ever palpate a discrete nodule. It, it's almost always a goiter.
- Marie Brown: Mm-hmm.
- Kevin Walsh: And then you, then there's, there may or not be a biochemical abnormality but invariably, that patient gets an ultrasound, and invariably you find something.
- Michael Souter: So, I have one other question related to, again, looking more at the kind of the outcome side, and I don't the answer to this, because I don't do it, but it strikes me as one which I would like answered is that whether or not using ultrasound actually serves to increase the accuracy of biopsy, and I don't know the answer to that.
- Craig Blackmore: I mean, I, I don't know the data as yet, I mean . . .
- Michael Souter: You know, and so does that, you know, so, so if it's improving the diagnostic accuracy of, of, you know, your biopsy tests, which like anything you do has a

failure rate or a certain sensitivity, I don't, again, I don't know the data of that, but I think it would be a useful question to ask.

Craig Blackmore: But I mean, you're, you're increasing your biopsy yield. You're finding more cancers, but then the question becomes what's the clinical significance of the cancers you're finding. I mean, is there indolent thyroid cancers that everybody has by the time their 70 anyway?

Michael Souter: Yeah, so then, then, but then . . .

Chris Standaert: So, we're good at finding it . . .

Michael Souter: . . . you, you can ask the question then about age groups then. You can restrict certain age groups but, you know, but the question still to be addressed, you know, stuck in my head is, is just that, you know, does this improve the sensitivity of, or accuracy, let's just put it that way. Does it improve the accuracy of picking up a clinically-significant disease entity, as compared to just aiming with the nodule that you feel.

Craig Blackmore: Yeah, well the ultrasound is going to find much more and then the question is, finding, does finding more cancer improve outcome? It's the prostate question over again. You can do ultrasound-guided prostate biopsies, and you can, you can have a great yield on that, too.

David McCulloch: Doesn't improve it, though.

Craig Blackmore: But it doesn't improve outcome.

Michael Souter: Yeah, but you can delineate, again, perhaps looking at different groups, as you said, everybody over 70, you may not, you may not care a hoot about that, but if you're 45, you might care a lot more.

Craig Blackmore: I, I, I don't know the data.

David McCulloch: I don't think this committee can help answer this question. I just don't think we can, I mean, the, the various thyroid societies debate and decide and have algorithms about whether it's an incidental nodule or different (_____) if it's this size, watchful waiting or repeat it, and then, it's a whole algorithm that people either follow or don't follow. I, I just can't see that we can legislate through coverage or make recommendations that's going to, that's going to help this.

Craig Blackmore: I, I mean, I, I think we could if the data existed, but I'm very skeptical as to whether or not that data exists.

Michelle Simon: And my concern is if we did somehow put some restrictions on this, folks will still want to find out what the bump is, right? So if they're going to go to a

higher level test, more expensive and more radiation and all that kind of stuff. So, we have to consider that, too.

Marie Brown: Right, and this is a little different than PSA because of that, because when you have enlargement or a lump or even a diffuse goiter, there is a, a level of anxiety that you can't, you can see that, feel that, or see that in a way that you can't, that's not present with an elevated PSA.

Seth Schwartz: I don't think that's entirely true. Most people with a thyroid nodule have no idea they have a thyroid nodule until you tell them, you have a thyroid nodule, you need an ultrasound, you need a biopsy, you need surgery, and they're like, really? So, I don't think it's, I mean, maybe once you tell them you have a lump it becomes more concerning but . . .

Marie Brown: Yes.

Chris Standaert: But once you tell them you have a thy-, they have a thyroid nodule, they say, well, is that a bad thing? Is that a cancer, and then you have to answer that question.

Marie Brown: Right.

Chris Standaert: And that's, that's what leads to this whole thing is that you have to answer that question, and so unless there are things about the exam before imaging that would tell you, there are things on the ultrasound that would tell you that, but then you're getting to the restriction on the biopsy side on that side and not (_____) on the ultrasound side. It's . . .

Craig Blackmore: There is, there is still the screening question, which, which we can address, particularly if there's data. I don't know how common that is, but, if, if we're doing, well, I mean, we could examine the evidence for the use of ultrasound in, you know, people who have had radiated necks or whatever. I don't, I don't know what we'll find. I don't know if there's evidence out there. I don't know if it's a big problem. I don't know. I mean, it's on the list.

Richard Phillips: Is there such a thing as screening with ultrasound, really? I mean, isn't it always because of some abnormal physical finding?

Marie Brown: Carotid artery. There's a lot of ultrasound screening of carotid artery that you find and then you find . . .

Richard Phillips: Yeah, but that's not a, that's not a complete exam of the, of the thyroid gland.

Chris Standaert: Right. That's Craig's category of incidental, you find it doing something else.

Richard Phillips: Yeah, and that's usually done with Dopplers, etc.

Chris Standaert: Which is very common.

- Michael Souter: But there are groups who have familiar risk.
- Richard Phillips: Oh, no, I agree with that. Yeah.
- Seth Schwartz: I think, I think the gist of the concern isn't it, is it not, Steve, the use of ultrasound for things like goiter?
- Steve Hammond: It is, and the, the concern is that we have a, it's been termed an epidemic of over-diagnosis of thyroid cancer and one contributing factor is permissive payment policies paying for ultrasounds basically indiscriminately, and the question is, is there something we can do on the coverage side to help get a handle on this. The discussion has highlighted many technical challenges and doing that. The question is, can we make any headway on this issue through the Health Technology Assessment process. It's a difficult one.
- Chris Standaert: You don't think there'd be data out there on the results of the, on what leads to, indication for biopsies based on ultrasound or other imaging, because that could get at that, and then you have less biopsies. So then, you'd have less diagnoses or you'd have less spurious diagnoses, because you have less biopsies. So, interpret it at the biopsy end not the ultrasound maybe.
- Craig Blackmore: The radiology community is trying to come to some consensus around this, but I, but I don't know that it's a consensus built on evidence. I mean, I haven't looked, but there's a lot of . . .
- Josh Morse: Terri has done some looking.
- Craig Blackmore: Terri has done some looking.
- Teresa Rogstad: Well, I'll just tell you what we know so far. We haven't done an exhausted systematic search, but our sense is that there are studies in which ultrasound is used as a screening tool, both in high-risk populations and on selected populations. They are not very well done. They use the fine-needle aspiration biopsy as the reference standard rather than (_____) confirmation, and they only do, the ones that we've seen anyway, only do confirmation biopsy in the positive results. So, they can tell the sensitivity and (_____) specificity. The practice guidelines all recommend against routine screening but may support it in high-risk populations and then in those patients where a nodule has been detected, either incidentally or through a neck exam, the accuracy studies are better and the authors describe the rationale, just like Chris was saying, it allows you to avoid biopsy if you get focused on findings instead of low level of suspicion. That's what we noted, and we don't think there are any studies out there that actually look at the impact of the (_____)
- Steve Hammond: I think all the guidelines I've seen are by specialty societies, so I think they are prone to bias in favor of more aggressive detection, screening, etc.

- Marie Brown: Right, the biggest question, it sounds like, goiter, the diffuse goiters is where the, is where the escalation has been.
- Teresa Rogstad: Well, also slow-growing nodules that are the papillary form of thyroid cancer, which may never, may never even become (_____), but you don't know, you don't know which type of (_____) you biopsy. So, the rationale behind those is that, to decide whether it makes sense to do (_____).
- Craig Blackmore: I mean, even if you find cancer, you don't know that it's clinically significant. I mean, this is like prostate. Just because you're accurate in finding indolent cancers does not mean you are doing anybody any good, but again, I'm not surprised you're not finding much (_____)
- Chris Standaert: I mean, well, how, another option to focus on the idea of cancer and treatment of, detection of thyroid cancer, and then you get to issues of biopsy and so you start with the area you're trying to screen appropriately for thyroid cancer and then you look at screenings that result in different outcomes. You talk about ultrasound and biopsy as opposed to just looking at ultrasound. Does that make sense, or no? I mean, you're starting the other way. You're starting at the end saying we have thyroid cancer, can we look at, it's a big thing. Can we look at predicted parameters. Can we look at appropriate screening for thyroid cancer. Can we look at biopsy results and when that moves into surgery or that sort of thing? If that's the (_____) . . .
- Steve Hammond: That's the problem we're trying to get at and we tried to frame it in terms of one technology but I would be open to suggestions for a way to make this process have a positive impact on the problem.
- Craig Blackmore: Well, I'm not sure we have solutions for you, but we seem to have had a lot of suggestions. Alright, I think lunch is ready so we will . . .
- Joann Elmore: Can I?
- Craig Blackmore: Yeah.
- Joann Elmore: I want to point out the importance of the discussion we just had and how this emphasizes the need to review the key questions and I'm hoping that this is not going to go forward and we aren't going to fund an evidence review on these questions. I would hope that they come back to us before anything happens, because these are not going to be helpful.
- Steve Hammond: Question two might be potentially helpful, but.
- Joann Elmore: I disagree.
- Michael Souter: Because the answer is going to be no.

Joann Elmore: The, the, I disagree. As currently worded, this will be a mess, and we will be dissatisfied. We may not provide anything helpful to the residents of the State of Washington, and you guys would be out a lot of money for the evidence review. I mean at a minimum, as Craig points out, we need to differentiate, as you're trying to do, 2A has to do with screening ultrasound, totally asymptomatic, you know, healthy person, and 2B has to do with diagnostic ultrasounds, and so as Craig describes, if you're going to evaluate ultrasound, you need to say ultrasound screening and then in screening it's the average population versus high risk and then you have to look at diagnostic, and for diagnostic you have to look at what led to that? Is it a physical exam finding? Is it another imaging, or is it even a blood test?

Craig Blackmore: Is it symptomatic, asymptomatic?

Joann Elmore: Right, and I'm just, I'm intrigued, and I think it's wonderful that you're raising this question. I would love to see us address it, but as it's currently worded here, and you know, saying we're going to break for lunch. What's going to happen with this? I don't want to see this come back in this order. I would like to vote that we not go forward with this review. I mean, I want to, I want to review this, but not with these questions.

Craig Blackmore: We are not officially charged with subjects that we review, but I think we have given a lot of feedback, which, I'm sure will be listened to and we will have the opportunity to provide feedback at multiple points. Let's break for lunch.

Alright, I'm going to call the meeting back to order, since we have a quorum. The afternoon topic is facet neurotomy and we will start off with the open public comment period. We'll start with those individuals who have requested in advance to address the committee, and then if there is anybody who is here but has not signed up in advance, there will be an opportunity for you also to address the committee. There was a signup sheet out front, which is probably now inside. It's right here. So, after we go through this list, there will be an opportunity, if anybody else has not had a chance, and then we will open up the phone line and determine if anyone on the phone wishes to address the committee. I will ask all the speakers that they introduce themselves, tell if you are speaking as an individual or if you are representing an organization and also tell us if you have any financial conflicts of interest, if anybody has paid your travel or expenses, etc.

Josh Morse: So, first is Kevin VorenKamp, five minutes.

Kevin VorenKamp: Hello. Thank you, for allowing me to speak today.

Craig Blackmore: So, we are being recorded. So, we always need to speak into the microphone, etc.

Kevin VorenKamp: Thank you. I am Kevin VorenKamp, and I am practicing pain medicine physician at Virginia Mason Medical Center in Seattle. I have no conflicts to report, and I

have, I will get no reimbursement from my discussion today. I have affiliations with both the American Society of Anesthesiology and American Society of Regional Anesthesia and Pain Medicine, but I'm speaking as an individual physician today. I want to start off by just discussing some of the overall flaws I see with the spectrum report. One glaring one was that there was no physician listed as being involved with the report. I know comments were submitted, expert comments and did not seem to be incorporated into the final draft. There were some methodological flaws with this, and I think the overall idea of looking only at randomized and placebo-controlled trials is a problem for invasive procedures for patients with chronic pain.

Getting to the first where there's no physician involvement, the introductory section of the report showed a glaring misconception of what this treatment is. They commented that there were two types of radiofrequency neurotomy, thermal, or nonpulsed, and cooled, or pulsed, and this is, in fact, incorrect. The cooled radiofrequency treatment is, in fact, a thermal treatment, and that's clearly specified in any of the papers. So, pulsed is a separate entity altogether, but thermal and cooled are both ablative procedures.

As alternative guidance, I want to bring up something that's recently been performed over the past 12 months. There is a multi-society pain workgroup that was put together at the request of the group of carrier medical directors to review all of the LCDs involved in interventional pain medicine. Although this is only in LCDs, essentially the goal is to standardize LCDs across the country, so all of the different carrier medical directors involved. There were 14 societies, including societies in pain medicine, anesthesiology, physiatry, spine surgery, orthopedic surgery, neurosurgery, radiology, and neurology. There were physician representatives for each of these. Facet interventions were the subject of several of these talks that were reviewed. Overall highlights of this, in terms of recommendations for facet RFA are the dual-diagnostic blocks with 80, greater than 80% relief are essential for this to have an optimal outcome. This should be contrast verified, and the technique needs to be one that is going to create an ablative lesion over the nerve. The entire different societies felt all of these technical, both patient selection and technical factors, were required to optimally perform this treatment. We had a portion on physician qualifications that were also edited and added by the carrier medical directors. Essentially, this should be performed by physicians, and this should be performed by qualified physicians.

I'm going to, in the interest of time, focus on one study that does show excellent benefit with the radiofrequency ablation. Dr. Dreyfuss and Dr. Stout, later, will look at some of the other studies that show similar results. So, this was a study published in the New England Journal of Medicine in 1996, nearly 20 years ago. This was a randomized double-blind control trial in 24 patients with chronic pain following flexion-extension injury. This is one of several studies demonstrating good benefit when proper patient selection and procedural techniques are used. This is a schematic of the nerves, themselves, and how the treatment is performed. Essentially, the key to the treatment here, the lesion that comes

out of the radiofrequency cannula comes out proximally along the needle. So, if you were going perpendicular to the nerve, you are not going to be able to ablate the nerve successfully. So, to do it successfully, you need to place it along the course of the nerve.

In this study, they did require relief with dual-diagnostic blocks. They did a standard thermal lesions, and they found median, the mean duration of relief was 263 days versus 8 days and the followup studies showed that approximately two-thirds of patients had complete relief for a median duration of about 420 days. It also showed that complete relief was possible with repeat denervations. Our fluoro image is showing that. This is a different study by Govind with the same setup showing, again, very similar results, median duration of relief 300 days.

So, in summary, facet RFA is an effective treatment when patients are properly selected with correct procedural technique utilized. The multi-society pain workgroup consisting of 14 different societies has put out guidelines and recommendations to how this should be conducted, and the spectrum report does not properly analyze the literature that is out there based on the recommendations listed above. Thank you.

Josh Morse: Our next commenter is Paul Dreyfuss, and he has, a group has pooled their time. We have given them 20 minutes.

Alison Stout: I'm going to start. My name is Alison Stout. I am a physiatrist at Evergreen Hospital. I'm not representing anyone except myself, however, and I have no conflicts of interest. I would like to start by expressing my appreciation for this opportunity to address the committee about radiofrequency neurotomy in the treatment of facet pain. For ease of discussion, I will refer to radiofrequency neurotomy as RF. For RF, high-quality perspective trials have repeatedly shown that in properly-selected patients and by using correct operative technique, RF can achieve outcomes that are clinically significant and enduring and really cannot be dismissed as simply due to a placebo effect, but this conclusion can be obscured, or hidden, by the inclusion of illegitimate studies that relied on poor patient selection and used outrightly sham surgical techniques. Although these studies have the appearance of high-quality RCTs to clinicians without expert knowledge of the precise procedure, they are only evidence of bad practice. They are not evidence of the outcomes of RF when properly performed. By way of analogy, imagine that you've been charged with assessing chemotherapy for breast cancer. Your evidence reviewer, indiscriminately, combines the data on methotrexate, Laetrile, and herbal preparations on the grounds that they are all therapeutic agents that have been used for the treatment of breast cancer. Imagine further that the diagnosis of breast cancer was compromised by accepting a variety of invalid tests, such as palpation alone and mammography without biopsy. The report then concludes that chemotherapy is not effective for breast cancer. Given the methods used, would you really be surprised by those conclusions? Would you accept the

conclusions as valid? Surely not. Yet, this is precisely what Spectrum has done in the case of RF neurotomy.

Regarding patient selection, currently there is wide acceptance of medial branch blocks as the only validated means to select patients for RF. Prior to this, patients had been selected by clinical examination alone, but similar to palpation for breast cancer, this has been shown to be incapable of correctly identifying patients with facet joint pain. Similarly, patients who are selected for RF on the basis of pain relief following intraarticular facet injections have similar problems. These injections, intraarticularly, have never been subjected to controls and have no evidence of diagnostic validity and have no evidence for predictive validity. Low volume medial branch blocks, or MBBs for short, have proven superior for selecting patients for RF. MBBs specifically target only the nerves innervating the facet joints, and therefore the pain that they transmit. They have excellent proven target specificity, and the relief that they provide is a direct simulation of the relief that can be provided by RF. For these reasons, MBBs are widely considered to be the only appropriate selection tool for medial branch RF.

To guard against false-positives, MBBs have to be controlled. Controlled medial branch blocks have become the preferred standard for selecting patients for RF. Controlled MBBs involve blockade of the target nerves on two different occasions, two different visits, using two different anesthetic agents, and having the patient's duration of relief differ according to the duration of anesthetic use. Following an MBB, patients are asked to report hourly pain relief. The higher the percentage of pain relief, the more likely the patient will respond positively to RF. More patients obtain relief from RF if selected after reporting at least 80% rather than only 50% pain relief. Controlled MBBs are imperative, because studies have shown that the clinical outcomes after RF are the worst in patients selected on clinical grounds alone. If the selection criterion is 50% of pain relief following intraarticular blocks or single MBBs, only 33-55% of patients treated will obtain an unconvincing 50% relief following RF. In contrast, when the criterion has been 80% or greater relief of pain following controlled MBBs, 53-60% of patients obtained at least 80% pain relief for at least one year after RF. These superior results are clinically and statistically significant and should not be disregarded.

In summary, high-grade pain relief following controlled medial branch blocks is the optimal method for selection of patients for RF. Selecting patients with less than ideal methods will predictably increase the number of futile RF procedures and dilute the success rate. Regarding the procedural technique, basic science studies have shown that for thermal RF to be effective, in other words, to actually create a thermal lesion that sustainably blocks (_____), the electrode must be accurately placed tangential to the target nerve, and the lesion produced must be large enough to encompass the diameter of the nerve. Techniques that do not take in account the anatomy of the medial branch or that do not produce a great enough lesion are doomed to failure. RF techniques have evolved. Earlier techniques did use perpendicular electrode placement

and often produced smaller lesions. Predictably, studies using these techniques demonstrated poor outcomes. Returning to the breast cancer analogy, inclusion of older treatments known to be invalid, such as Laetrile, would skew any analysis of the effectiveness of chemotherapy. Spectrum's inclusion of RCTs using such outdated techniques in the RF report raises serious methodological and ethical questions. Understanding the importance of appropriate patient selection and usage of validated techniques, we can now examine the literature in a new light. The RCTs of Gallagher, Leclair and van Wijk used both invalid intraarticular blocks to select patients and used improper nonanatomically sound RF techniques. In response to criticism of the van Wijk study, Spectrum stated, "van Wijk studied RF as is commonly performed." Spectrum ignored published letters to the editor by both van Wijk himself and Laclair stating that the selection criteria and RF techniques they utilized were not optimized when compared to current standard, but instead were designed to test the efficacy of RF as it was performed within Canada, Holland at the time, not as it is practiced in the USA, Australia, and New Zealand. Disqualifying the studies of van Wijk, Gallagher, and Leclair leaves only the RCTs of Nath, Tekin, and Van Kleef. The results of these three valid randomized placebo-controlled trials clearly favor RF. In these trials, either single or controlled MBBs were performed using 50-80% pain relief cutoff, accurate anatomic RF techniques were used. Placebo-RF was compared to active RF in a blinded fashion. Followup was for 6 to 12 months. In all three trials, results from active treatment were superior to placebo in regards to pain relief, functional improvement, and secondary outcome measures. Various factors did limit the success rates obtained in these studies, but none of those interfere with comparison to placebo. Collectively, these trials clearly demonstrate the effects of RF for lumbar facet pain cannot be attributed to placebo.

Let us to turn to studies specific to the cervical spine. It might seem that there have been three RCTs on RF for cervicogenic headache, Van (_____), Stovner, and (____); however, none was a legitimate test for cervical RF. In all three studies, patients were selected on clinical criteria only without medial branch blocks, RF techniques were not anatomically sound, and for lack of precise diagnosis, RF was performed indiscriminately. Active RF was compared to sham and predictably, there was no difference between these arms. Since these studies used poor patient selection and invalid technical methodology, the only valid conclusion that can be drawn is that poor patient selection criteria and improper technique yield results that are no better than sham. These trials should not be included in an informed literature analysis.

Of the studies that have used correct selection and ablation techniques for cervical medial branch RF, there is one placebo RCT, and it was already mentioned. A randomized double-blind placebo-controlled trial was conducted on 24 patients with cervical facet joint pain. The criterion for eligibility was complete relief of pain after controlled MBB and no relief with the placebo injection. Twelve patients were allocated to undergo genuine medial branch RF, twelve were allocated to sham RF. The successful outcome was to find complete relief of pain with restoration of ADLs and no need for continuing

healthcare for neck pain. At six and a half months, 8% of the controls versus 58% of the active treatment patients had successful outcome with complete relief of pain. In the active group, the median duration of relief was 263 days versus 8 days in the sham group.

Although this study has arbitrarily been criticized for having a small sample size, it was perfectly designed for the question that it answered. The difference in outcome between active treatment and placebo was so great that the study actually had 100% power to exclude a placebo effect and render the results unquestionably statistically significant. Now, I'm going to turn it over to Dr. Dreyfuss to give additional information on non-RCT data.

Paul Dreyfuss:

Good afternoon. Dr. Dreyfuss, is this still on? I'm from Evergreen Hospital. I represent myself. I have no conflicts of interest. I have been paid by no one to be here today. Sackett has stated, "Evidence-based medicine is not restricted to randomized trials and meta-analysis. It involves tracking down the best external evidence with which to answer our clinical questions." RCTs may be considered the gold standard, but they do not represent all of the available evidence. Dr. Cancado stated in the New England Journal of Medicine, "Carefully conducted observational analyses are at least as reliable as small RCTs and that ignoring the evidence from observational studies is not a viable option." Giving these precepts and given the lack of numerous large, well-performed RCTs to guide and inform us, the inclusion of prospective nonrandomized studies is critical. There are numerous such studies that merit review and consideration by this committee, and they were inappropriately excluded by Spectrum. The effectiveness of lumbar medial branch RF has been demonstrated by no less than eight prospective, nonrandomized trials. These trials provide valuable insight into the effectiveness and external validity of lumbar RF across a spectrum of practices and regions.

There are two prospective studies that selected patients with controlled medial branch blocks using at least an 80% pain relief cutoff and ideal lesioning techniques that warrant special attention. Properly-selected patients based on at least 80% relief of their back pain following controlled MBBs. The study used ideal anatomically sound RF lesioning techniques. Fifteen patients were enrolled. It was found that 60% of subjects maintained at least 80% relief of their pain for no less than 12 months accompanied by a reduction in disability. In the second study, McVicker enrolled patients only if they had complete relief of pain following controlled MBBs. A total of 106 consecutive patients were recruited in these two practices. Ideal anatomically sound RF techniques were used. Success was defined as complete relief of pain for at least six months accompanied by restoration of all desired ADLs and no need for healthcare for their back pain. In these two practices, 53 and 58% of patients had a successful outcome with complete relief of pain. Following the first RF, the median duration of relief was 15 months. With repeat treatments, the median duration of relief was 13 months. These two trials validate the importance of proper patient selection and technique. Together, they demonstrate that 53 to 60% of

well-selected patients obtained 80 to 100% relief of pain for a minimum of one year following properly-performed lumbar RF.

The effectiveness of cervical medial branch RF has also been demonstrated by seven prospective nonrandomized trials. Two studies deserve special mention. Barnsley performed an observational study of 35 patients selected following complete relief of pain with controlled MBBs and no response to placebo injections. The anatomically-sound RF technique was used. Of 35 patients treated, 60% obtained complete relief of pain for a median duration of 44 weeks. In a study by McVicker, two practitioners reported the outcomes of 104 consecutive patients selected on the basis of complete relief of pain following controlled MBBs and treated using anatomically-sound RF technique. The criteria for success, again, was complete relief of pain for at least six months accompanied by restoration of desired ADLs, return to work, and no need for other healthcare for their neck pain. In these two practices, 61 and 74% of patients met this high bar for a successful outcome with complete relief of pain. Relief lasted up to 20 months from the first RF and 15 months from repeat RFs. Together, these trials demonstrate that 60 to 74% of patients can be rendered pain-free for a minimum of 15 months following cervical medial branch RF.

Third occipital nerve RF for C2-3 facet pain deserves special mention. There are three prospective trials that provide insight into the effectiveness of third occipital nerve RF. All studies demonstrated the effectiveness and durability of this intervention. One study specifically evaluated only C2-3 facet RF. In this study, Govind selected patients with controlled third occipital nerve blocks who had complete relief of pain following each block. Anatomically sound RF lesions were performed. Success was defined as complete relief of pain for a minimum of 90 days with full returns of ADLs and no drug treatment for headache. Govind found that 86% of 49 patients obtained complete relief of pain and had a successful outcome. The median duration of relief was 300 days with eight patients experiencing ongoing complete relief; 86% of patients undergoing a repeat RF reinstated complete relief.

In conclusion, all lumbar and cervical studies using appropriate selection of patients and appropriate lesioning techniques have consistently shown positive benefits. Where the data differs is with respect to precise selection criteria, RF technique, and definitions of success. Based on the most rigorous studies using valid diagnostic techniques to select patients and valid optimal RF techniques, over 50% of patients treated with lumbar RF can be expected to achieve complete relief of pain accompanied by restoration of ADLs, resumption of work, and no need for further healthcare for a median duration of 15 months. Some 70% of patients treated with cervical RF can expect to achieve complete relief of pain accompanied by restoration of ADLs, resumption of work, no need for healthcare for their neck pain for a median duration of 17 months. In the event of recurrence of pain, complete relief can be reinstated by repeating the RF. In several studies, complete relief of pain has been sustained by repeat RF for an excess of five years. Such outcomes are unrivaled by any other intervention for back or neck pain. No other surgical or nonsurgical intervention

has been shown to be capable of achieving complete relief of pain accompanied by restoration to normal life and cessation of healthcare for this condition. We would respectfully request that this committee approve the use of thermal RF for facet pain but with conditions, specifically we believe that the use of controlled medial branch blocks with at least 80% pain relief is critical to the success of medial branch RF and should be mandated. Repeat RF should be allowed, but only if substantial pain relief with functional gain occurs for a minimum of six months. I appreciate your time and consideration.

Craig Blackmore: Thank you. Is there anyone here who wished to address the committee but did not have the opportunity to sign up, and finally, can we unmute the phone. We're just going to unmute the phone in just one second. Go ahead. I don't want them to think we're unmuted yet, because we're not. So, is there anyone who has called into the meeting that wishes to address the committee? OK, hearing no response, we will put the phone back on mute and we will close the open public comment period. Next on the agenda is the Washington State Agency Outcome and Utilization.

Gary Franklin: Thank you. This is Gary Franklin, and I've got Lee Glass, my associate medical director with me, because he has spent quite a bit of time over the years working with the community on various guidelines for facet neurotomy, watching patients, tracking our records, etc., etc., and Lee is going to help me if that's OK with you.

Lee Glass: So, there are two procedures that are intrinsically linked in order to obtain a good outcome from facet neurotomy. The first procedure is a diagnostic procedure, the medial branch blocks that have been talked about earlier. Those medial branch blocks are crucial to the diagnostic accuracy that the clinician needs in order to have a successful outcome from a facet neurotomy and as previously mentioned, facet neurotomies typically use radiofrequency energy to ablate the medial branch nerve.

So, this slide shows the anatomy. Every facet joint is innervated by two medial branch nerves, one from one level and one from another level, and the medial branch blocks put a small amount of local anesthetic on the medial branch nerve so that the clinician can then assess whether that has been successful in eliminating pain. There is both art and science to that. Too much local anesthetic is used, it can spread through fascial planes and produce false-positive results, and if the anesthetic is not properly placed, there can be false-negative results.

This slide was shown earlier and further shows the need for accuracy on the part of the clinician in understanding the anatomy and in the conduct of the medial branch blocks. The facet neurotomy is performed after the medial branch blocks are done in cases deemed to be appropriate by using radiofrequency energy to ablate the nerves that were previously anesthetized. I think it bears comment that the Susan Lord article in the New England Journal of Medicine, I think it was 1996, it was mentioned earlier, used very stringent

criteria to determine, using these techniques, to determine who should get a radiofrequency ablative procedure, and in that study the selected individuals had 100% relief of pain with the local anesthetics and had no relief of pain with a placebo injection. That standard, we have not seen in our department being utilized to select patients in this area. More commonly, the selection recommendations have been what you've heard earlier, which is 80% or more relief of pain.

Our department has started approving payments for facet neurotomies in approximately the year 2000, and we produced a log for patients to, after they got a medial branch block to log their relief and duration of pain, and so every 15 minutes they were to put a check mark in a column that my pain is totally gone, mostly gone, somewhat gone, barely gone, not gone at all, and they put checkmarks to show what pain relief they got. They would do that until the pain was back to its normal level and I have seen some very unusual patterns of relief, including a saw-tooth pattern, for which there is no physiologic correlate, and I think that it is very important to understand. There was a comment made earlier about the use of placebo as raising ethical issues, but actually a fully-informed patient who understands that they may receive a placebo injection as part of a way to diagnose a procedure can be benefited by having that done so that the examining physician can be as accurate as possible in reaching his or her conclusion.

Gary Franklin:

Thanks, Lee. I may call Lee back up for a point or two. So, the agency medical directors group, when we picked this topic, felt that the safety issues were of high concern. We've since reduced that to sort of low-medium concern. I'll show you a couple things here in a minute. Efficacy and costs were more of a medium concern.

This is an editorial that was in the spine journal by O'Neill and Owens and what I'm going to mostly talk about today is not the studies that you're going to review or the report necessarily, but some of the methodological issues that, I think, are very problematic in doing this procedure, not the least of which is that I don't think localization is very good at all and, and in addition to that, a lot of the studies actually go, OK, there's this much improvement in pain, but it can be only part of the pain that the patient has in their neck. It's not all of the neck pain, it is part of the pain in the neck or the back, and so that's something to keep in mind here. You know, in an L&I patient with chronic neck or back pain, if you're relieving 20% of the pain, 100% of 20% of the pain, you're not, you don't really have a patient that is really very much better, and I think that is largely what we have seen. This editorial said, "Anesthetic blocks were a valiant attempt to provide objective criteria to diagnose a vague syndrome. However, it is time to recognize that 1) anesthetic blocks are not a valid test to diagnose facet joint pain and 2) the treatment effect (impact on outcomes of neurotomy) and cost-effectiveness of the medial branch blocks are unknown."

This was, I'm not going to go into gory detail here, but O'Neill and Owens, in that same editorial, also did kind of a re-analysis of some of the false-positive

and false-negative information in the Lord article and again, without going into gory detail, felt that like there really was not a substantial concordance, sorry, substantial relationship between whether there was a concordant response or a discordant response on the injection. They felt like, again, there's a lot of non-specificity in all of this, and you'll see in a minute additional information on that.

The RCTs you'll go over here in a minute, but essentially neurotomy versus sham neurotomy, short-term pain relief, four of six RCTs showed no difference. Function, mixed results, and then some other stuff in here that is sort of lower level evidence.

Safety issues, we, again I told you we weren't that concerned about it, but 38% of RF neurotomy, in some studies, have experienced numbness in the area of the coagulated nerves in the postoperative period, but then I found these other two things that were somewhat concerning, Smuck article in 2013 was a retrospective series using pre/post MRI suggesting great disk degeneration at neurotomy levels. I don't know why that would possibly be. It's, it may just be a, you know, a false, a red herring type of finding, but then more concerning to me was this one case report of multilevel cervical facet neurotomies, which within days the patient developed a head drop and EMG evidence of denervation of the paraspinal muscles, and a fixed kyphotic deformity after a few years. Now, maybe this never happens, I don't know, but as a neurologist, this was kind of a disturbing case.

One of the things I wanted to show you was, you know, what it takes to actually pick a decent candidate, even in a randomized trial. So, this was a Nath study in 2008. There were initially 376 patients, which was felt to be, you know, potentially paravertebral tenderness that maybe would respond to a medial branch block and maybe would end up with a facet neurotomy, and they used, I believe, an 80% criteria; 115 of the 376 were negative, 261 had at least 80% relief, but only 40 patients of that entire group ended up in the randomized trial because the rest of them either had too prolonged of a response or strange responses to the control blocks. So, and I'm pretty sure that after you're in practice, the difference between the 376 and the 40 is a lot of movement in there of people actually trying to pick the right patient to do these, to do these neurotomies.

The costs, significant costs are likely incurred for a high rate of true negatives, as in the example I just gave you and, in addition to that, I'll show you in a minute kind of how the costs break down, but a fair amount of the cost is in the diagnostic injection.

There is no good cost-effectiveness data, but one of the studies that is included in the vendor reported, if you look at the second bullet here, I thought was really sort of telling. Overall, no matter how many blocks a patient received, the average number of levels of neurotomy was three, and 60-75% of these were bilateral. In other words, a fair number of these patients are getting, like, four to six neurotomies and, you know, I reviewed a patient, a paper on facet

neurotomy recently for a journal, and one of the statements in that article was, well, you can't really tell where to, you know, exactly where to do it from a clinical exam. You can't really exactly tell where to do it from the x-ray or the anatomic findings. So, it really comes down to prevalence, and that kind of struck a chord me with being an epidemiologist. You, you're doing injections and neurotomies based on prevalence meaning, you know, mostly you're findings on DJD are L4-5 and L5-S1, and I believe that that is partly what is happening here, is that a lot of these patients are getting these, these injections and the neurotomies based on prevalence, you know, three or four neurotomies in a single patient in an encounter.

All of the agencies do prior authorization right now.

As far as other policies, we did find a really obscure CMS National Coverage Decision, but it was a general policy on induced lesions of nerve tracts. So, this was a general policy on nerve ablations for all manner of things and the policy was so old that it didn't have an effective date. So, in that policy they said, you know, you can, you can do some of these things, but it was nonspecific enough to actually apply to this decision. In the U.K., they, in the NICE, National Institute for Health and Care Excellence, they decided do not refer people for radiofrequency facet joint denervation.

Our costs are modest, 4 million dollars over four years, and the average pay per encounter is around \$2500 to \$2700. Again, a lot of these patients, you know, are getting more than one neurotomy. Then, just to break down across the agencies, but again, the total is about 4 million.

So, this was just one curve that we wanted to show you just at L&I. So, at L&I the overall average number of facets treated per encounter was 2.5. This is a slide that shows, you know, which patients got one neurotomy versus more than one neurotomy, and you can see that about a third of patients get more than one and some patients get way more than one or more than two.

This is how it breaks down in terms of the professional services. You can see that diagnostic injections, say at L&I, are about \$778 out of the \$2400. Lee worked on a guideline. Do you want to talk about that for a minute?

Lee Glass:

So, in approximately the year 2000 when, after we had reviewed the Susan Lord article and thought that this might be beneficial for injured workers, I got a group of physicians who were, I think, all of the physicians who were at that time performing the procedure in the Puget Sound area and we met three times and I asked them to develop a guideline. I said, my purpose here is just to make sure that whatever you develop comports with the medical literature, and the guideline that was developed was one that required two differential blocks, so short-acting anesthetic and a long-acting anesthetic so that the duration of relief could be compared to the type of anesthetic to see, make sure that somebody wasn't getting, say a long period of relief from a short-acting anesthetic and a short period from a long-acting anesthetic. Also, this group of

physicians felt that placebo control should not be mandatory but rather should be up to the physician to determine whether to use a placebo injection and at least 80% relief, as I mentioned earlier, not 100% relief. Also, because L&I does not pay to maintain people at a given level of pain relief or function, we say they're at maximum medical improvement and then we pay for any permanent impairment that may exist. We said that the, this interventional procedure needed to be the last thing necessary before somebody was at maximum medical improvement. That was our guideline, and we used that guideline for a number of years until we more formally adopted a guideline with a larger group of clinicians and, but that guideline also followed closely what is shown on the slide. Thank you.

Gary Franklin: So, there are all kinds of criteria out there. You've heard about this already. I'm not going to go through that again. This was the paying log that we used when we were tracking these patients. In our review of our own cases, you know, two-thirds of the cases that had this procedure were still on disability any number of years after that. So, we certainly aren't seeing the kind of results that were just spoken about recently, but then again, if you're only treating part of the pain in somebody with chronic neck pain or chronic back pain, you might not expect to get that.

We didn't see any relationship the doctors who were doing a lot of these procedures and the doctors who were doing fewer of these procedures and vocational outcomes. There wasn't really, this is a soft study. This isn't anything I would break my pic on.

So, in summary, we think that there is low quality evidence for short-term benefit, and it's probably better in the cervical than the lumbar region, but there is no gold standard for the diagnosis and localization of specific pain. Our recommendation is therefore noncoverage or coverage with conditions and that if it is covered with conditions that there should be, like the Lord study, 100% pain relief from the block and no relief from placebo control. If you want to think about, Group Health actually has a criteria where you can do one of these things, you know. You're not going to be doing three or four neurotomies. So, those are our conclusions. I'm happy to take questions.

Craig Blackmore: Questions from the committee?

Richard Phillips: It seems to me that you quote this O'Neill and Owens article that says that there should be no, no blocks done. How are you going to, how do you expect people to be treated then if they can't do a block. I mean, if they come in with chronic pain, if they can't have a procedure, then there's no reason to do a diagnostic block. So I'm not sure I understand exactly what the state's position would be and how these patients should be managed.

Gary Franklin: Well, there's a whole manner of things to treat chronic neck and back pain. This is one procedure, and the key is, obviously, your charge is to figure out whether it's effective and safe and cost effective, and the main points I'm trying to make

are that it looks to me like they are treating part of the pain that if they're doing three or four neurotomies, you know, a lot of these patients, you know, is it really localizing anything and, and so, you know, but the main thing is that there is low level evidence of short-term relief. We're not seeing in the randomized trials the kind of information we heard from Dr. Dreyfuss on these prospective studies. I presume they are prospective. So, I mean, you know, do you do things to people that don't work? They are costing the state a lot of money, and I agree that the safety issue is probably not huge. So, it probably does come down to cost effectiveness and effectiveness. So, that's your job.

Richard Phillips: Well, I'm wondering, too, about the issue of the, is this an issue of appropriateness or is this an issue of indications for the procedure, and I'm trying to separate those two. In other words, do you have, does your data suggest that there is some inappropriate use of this procedure as is, or is it, you know, I guess that's where I'm really coming from. I'm not sure I understand. . .

Gary Franklin: You've got people coming in with chronic back pain and chronic neck pain. You can't really make the diagnosis by pushing on the facet joint. You can't really make the diagnosis because you happen to see something on an MRI scan, because there's not great relationship between what you see on the MRI and where the injections are done.

Richard Phillips: Right.

Gary Franklin: So, then, so you've got somebody with chronic low back pain or chronic neck pain. Then, the question is, do they sub-, can they substantially improve from a very focal injection like this and a neurotomy and that's what we're questioning. We, we don't think . . .

Richard Phillips: OK.

Gary Franklin: . . . that there's much evidence for that.

Craig Blackmore: Other questions? Joann?

Joann Elmore: One comment and then two questions. The comment is that I'm always impressed with the thoughtfulness in which your agency reviews these topics and thinks through the evidence over the years, and I thought it was wonderful how you described pulling together clinicians many years ago trying to think through guidelines, thinking through the care we're providing to the patients in Washington State and gathering standardized prospective data. So, I wanted to just say that that was marvelous that you did that.

Gary Franklin: Thank you. That was, that was Lee.

Joann Elmore: It, it was great. Then, I had two questions. The first is that when you describe the number of procedures between 2009 and 2012, there was quite a drop in

2012, and is that due to change in clinical practice or to incomplete capture of the most recent (_____)

Gary Franklin: We're not really sure, but we did implement, in 2012, new, well your, your other spinal injection criteria, but at the same time we were also reviewing these based on our old guideline, and I think sometimes when you start looking at things more prospectively, things can drop off. It's almost like a sentinel effect. That's my theory.

Joann Elmore: Very interesting. And then my last question is, you described the outcomes of two-thirds of the claims in 2008 to 2013 were still disabled, but what about those that were disabled that didn't have this, what percent remained disabled over time?

Gary Franklin: Yeah, that, I mean, like I said earlier, that's, it's a soft thing, but, you know, the thing, the main thing about L&I, it's all related to the duration of disability. If your disability has been going on for a year or two years, almost anything you do after that time is probably not going to help very much, and so the question is, when are you doing this thing. In the course of the episode of pain, etc., etc. Great questions.

Carson Odegard: Now, when you talk about 20% of the pain, are you talking about 20% of the localization of pain or 20% of the quality of the pain?

Gary Franklin: Well, so again, if you read some of these studies, except for the Lord study, which required 100% relief, which is why, that was one of our conditions, maybe, a lot of the other studies, like Nath, said, you know, you had to have some improvement in pain, 80% improvement from the injection, but it could, it didn't have to be all the neck pain. It could have been some piece of the pain, but that isn't further actually delineated, as to what that means. That was sort of striking to me anyway. Thank you.

Craig Blackmore: Thank you. So, next we have the . . .

Robin Hashimoto: Should I go ahead and get started? Josh?

Josh Morse: We have your slides. Yes, please do.

Robin Hashimoto: Awesome. OK, so my name is Robin Hashimoto, and I am here from Spectrum Research. OK, so you've already heard quite a bit of background about the facet joint. Facet arthropathy is a progressive condition. Because of this, it typically happens in patients who are older in age, and it, of course, can lead to pain that worsens over time. So, the primary physical sign that suggests that pain stems from the facet joint is paraspinal tenderness at the affected joints. In the lumbar spine, symptoms can include axial spine pain, downward radiating pain, and pain that increases with twisting and bending. In the cervical spine, symptoms can include rotating the head, neck pain, shoulder pain, and headaches. Whiplash injuries can also lead to cervical facet pain.

OK, so you've heard also a lot about how patients are diagnosed for facet joint pain. So, a physical exam can be performed to look for paraspinal tenderness, as well as to rule out other pathologies. Imaging can also be used, but really to rule out other pathologies. It can't be used to diagnose facet arthropathy. Currently, the best way to diagnose facet joint pain is to use facet joint blocks, and there are two diagnostic blocks that are most commonly used in the literature. Both of them involve injection of anesthetic into the suspected joint and a positive response occurs if the patient has pain relief following the block. So, medial branch blocks anesthetize the medial branch nerve, which is the nerve that innervates the facet joint and is the one that is targeted during facet neurotomy, and then intraarticular blocks anesthetize the entire joint and as you've already heard, it's been argued that medial branch blocks are better at accurately diagnosing facet joint pain, in part because the medial branch nerves are, themselves, the target of facet neurotomy. It's more of a specific approach, but no studies have directly shown this, in terms of outcomes following facet neurotomy, and this is one of the things that we looked at in the report.

So, diagnostic blocks are best viewed as predictors of how the patient will respond to neurotomy, and there is, of course, potential for both false-negative and false-positive blocks. False-negative blocks can result in a patient being withheld from the appropriate treatment, and false-positive blocks can lead to patients undergoing unnecessary procedures and having inferior outcomes following facet neurotomy. False-positive blocks can result from a number of factors, such as infiltration or vascular uptake of the anesthetic, and as you've heard, the rates of false-positive blocks can be reduced using controlled or comparative blocks by requiring a high level of pain relief following the block in order for the patient to proceed to neurotomy, and also increasing the stringency of the blocks to reduce false-positive blocks will increase the likelihood of false-negative blocks. So, there is a balance that needs to be achieved, and as I mentioned, because there is no gold standard for diagnosing facet joint pain, the effects of different methods of patient selection were evaluated in the report.

So, facet neurotomy is an outpatient procedure. It involves the creation of small lesions, or a single lesion on the medial branch nerve of the affected joint, and the lesions are believed to disrupt pain signals and result in several months of pain relief. Conventional radiofrequency neurotomy was used in the majority of the studies in the report, and this employs electrodes that are heated to 80-90 degrees and applied for approximately 90 seconds to the target nerve, and the techniques for facet neurotomy have evolved, and it has been suggested that better outcomes may result when larger lesions are created, and this can be done using larger electrodes, and this can be done using larger electrodes, higher temperatures, longer lesion times, and by placing the needle parallel to the medial branch nerve. There are other types of neurotomy that are used in the literature. Pulse neurotomy delivers short bursts of radiofrequency energy at lower temperatures, and there is also alcohol ablation and cryoablation. So, if a patient develops recurrent pain following a successful neurotomy

procedure, repeat procedures can then be performed in order for the patient to achieve pain relief again.

OK, so these are the key questions that we evaluated. These were the ones that were posed to us by the State of Washington. We looked at, for key question one, the evidence regarding whether the use of diagnostic blocks to select patients for facet neurotomy improves clinical outcomes following facet neurotomy. Key question two asks about the comparative efficacy and effectiveness of facet neurotomy to other treatment alternatives, and for part of this, we looked at different types of neurotomy, repeat neurotomy, unilateral versus bilateral neurotomy, and neurotomy on single versus multiple spinal levels. We also evaluated the safety of facet neurotomy, as well as whether there was evidence of differential efficacy or safety in subpopulations, and we also looked for evidence regarding the cost-effectiveness of the procedure.

OK, so this just, I'm just going to go over the inclusion criteria we used for the report. For inclusion in the report, studies must have enrolled adults that were being considered for facet neurotomy due to suspected facet joint pain, intervention of interest was, of course, facet neurotomy. Comparators of interest included sham neurotomy, which is essentially a placebo neurotomy. They typically go in and do the exact same procedure, as they would with facet neurotomy, except the radiofrequency generator isn't turned on or the electrodes were maintained at 37 degrees. Other comparators of interest include therapeutic spinal injection and medical therapy. So, the primary outcomes of interest were clinically meaningful pain relief and functional improvement, and we found that a moderate level of clinically meaningful improvement has been defined as at least 30% improvement from baseline levels while a substantial improvement has been defined as at least 50% improvement. Regarding function, there was no clear definition of clinically meaningful functional improvement in this patient population.

So, this just shows the results of our literature search, and as you can see, we ended up including 26 studies in the report. OK, so I'm going to present the results in terms of the overall quality of evidence for the primary outcomes of interest, and the way at which we arrive at the overall quality of evidence is based on our application of grade and AHRQ's recommendations and the four levels of evidence are shown here, so high, moderate, low, and insufficient. So, to do this, we start by grading the quality of evidence separately for each conclusion based on the quality of studies available. RCTs start as high and nonrandomized studies start as low. So then, that baseline quality of evidence can then be downgraded due to risk of bias, inconsistency, indirectness in precision, and publication bias across the studies for that outcome. The baseline strength of evidence can also be upgraded in the case of particularly high-quality nonrandomized studies. So, after taking all of these factors into consideration, we arrive at a final strength of evidence rating and for nearly every outcome for this report, we downgraded the quality of evidence due to risk of bias resulting from methodological flaws in the studies included and for the risk of imprecision the results from very small sample sizes.

So, moving into the results, key question one asks how different methods of patient selection affect outcomes following facet neurotomy. So, again, to address this question, we included studies that compared two different methods of patient selection and then reported clinical outcomes following neurotomy, and I'll just say up front, no evidence was found for this key question for the cervical or thoracic spine. In fact, throughout the report, there was no evidence for the thoracic spine, but for this key question, all of the evidence is for the lumbar spine.

OK, so key question 1A asks about the outcomes following facet neurotomy in patients who are selected by medial branch block versus clinical exam, and we found one RCT of 70 patients that met our inclusion criteria and overall, we found low quality of evidence that there was no difference between diagnostic groups in terms of the percentage of patients who achieved a success composite following neurotomy.

Key question 1B, we asked about the outcomes following facet neurotomy in patients selected by different methods of diagnostic block. We identified one RCT of 26 patients in which patients were selected by either medial branch block or a pericapsular block which, at least to my understanding, is not something that's commonly used. So, this RCT provided low quality of evidence that there was no difference between diagnostic groups at six months in terms of short-term back pain or function. No studies were identified in which outcomes following facet neurotomy were evaluated in patients selected by medial branch block versus intraarticular block.

OK, so moving into key question 1C, this question asks about single versus controlled diagnostic blocks and one RCT met our inclusion criteria. This RCT enrolled 33 patients and reported that at three months followup there was no difference between diagnostic groups in the percentage of patients who achieved the success composite, and the quality of this evidence is low.

Key question 1D asks about the percentage of pain relief required following the diagnostic block, how that would affect outcomes following facet neurotomy. For this key question, we identified one prospective and three retrospective comparative studies, and we were able to divide the results, divide the diagnostic groups up into patients who achieved between 50 and 79% pain relief following the diagnostic medial branch block and patients who achieved 80% or more pain relief following the diagnostic block. Taken together, the results suggested that both pain and function outcomes may be better following neurotomy in those patients who achieved at least 80% pain relief following a diagnostic medial branch block. This was not consistently shown across all the studies, however. The quality of this evidence is insufficient, and this was largely due to risk of bias in these nonrandomized studies.

So, before I move into key question two regarding the efficacy of facet neurotomy, I just want to summarize what we identified for patient selection.

For key question 1A, B, and C, we identified low quality of evidence that patients selected by either diagnostic method that was used resulted in similar outcomes following facet neurotomy. Again, for key question 1B, there were no studies identified in which outcomes following neurotomy for patients selected by medial branch block versus intraarticular block. Key question 1D provided insufficient quality of evidence that pain and function outcomes may be better following neurotomy in patients who achieved a minimum of 80% pain relief following diagnostic medial branch blocks. So, based on these results, when identifying studies to examine the comparative efficacy and effectiveness of facet neurotomy, we did not limit inclusion in terms of type of diagnostic block performed or percentage of pain relief required.

OK, so key question two asks about the evidence of the comparative efficacy and effectiveness of facet neurotomy versus alternative treatments. So, I'm going to start with the lumbar spine and then go into the cervical spine. Again, no studies were identified for the thoracic spine. For this key question, the bulk of the evidence is going to be here for the lumbar spine when looking at radiofrequency neurotomy compared with sham neurotomy. So six randomized control trials met our inclusion criteria, and all of these studies used radiofrequency facet neurotomy. The comparator was sham neurotomy, which as I mentioned before was basically an identical procedure, except either the radiofrequency generator was not turned on or the probe was maintained at body temperature. The studies enrolled between 30 and 81 patients, and patients were followed for 2 to 12 months, and as you can see, a mix of diagnostic blocks were used. So, there was quite a bit of heterogeneity in the diagnostic blocks used. There was also a lot of heterogeneity in the amount of pain relief required for the patients to receive neurotomy. So, you can see that some patients, excuse me, some studies gave a very poorly-defined requirement of a good response following the diagnostic block. Other studies required up to 80% pain relief in order for patients to proceed to neurotomy. In all those studies, patients were blinded to the traffic received, so the patient report pain and function outcomes were, in fact, reported in a blinded manner.

OK, so all six studies reported on back pain as measured by the visual analog scale in the short term, which here was between two and six months. Again, the diagnostic blocks that were used varied as to the amount of pain relief required. Overall, with all the heterogeneity between these studies taken into account, there was low quality of evidence that there was no difference between treatment groups in terms of short-term back pain outcomes. One RCT provided low quality of evidence that there was no difference between treatment groups in terms of pain, as measured by the McGill Pain Outcome Measure. Two RCTs provided low quality of evidence. The leg pain outcomes were better following radiofrequency neurotomy compared with sham, and that was reported between three and six months. One RCT of 40 patients reported low quality of evidence. The outcomes were significantly better following radiofrequency neurotomy. Sorry, that was for generalized pain.

OK, so one RCT also reported the percentage of patients who achieved back and leg pain success, which here was defined as patients who achieved at least 50% pain relief following the neurotomy procedure. When this was measured by the VAS, there was no difference between treatment groups. When this was measured by a global perceived affect, which was measured on a four-point Likert scale with patients reporting complete relief of pain, more than 50% relief, no effect, or increase of pain. Outcomes did favor radiofrequency neurotomy and across the board, the quality of this evidence was low.

In terms of function, function was evaluated by the Oswestry Disability Index and three RCTs. Overall, there was a low quality of evidence that functional outcomes were better in patients who received radiofrequency neurotomy. One RCT reported no difference between treatment groups and the percentage of patients, excuse me, one RCT provided low quality of evidence that there was no difference between treatment groups in terms of function, as measured by the Roland-Morris outcome measure, and one other RCT reported that there was no difference between treatment groups in terms of disability as measured by the Waddell outcome measure.

Looking at long-term back pain and function, one RCT provided results for 12 months following neurotomy and for both back pain and function, as measured by the Oswestry Disability Index, outcomes were better following neurotomy and the overall quality of this evidence was low.

OK, so, and I'm going to talk about, stay with the lumbar spine, and this is the evidence for radiofrequency neurotomy compared with spinal injections. Two RCTs met our inclusion criteria. One of these studies, Lakemeier, which enrolled 56 patients selected patients for neurotomy based on 50% pain relief following a diagnostic medial branch block and then compared neurotomy to patient, then compared neurotomy to therapeutic intraarticular injections. The other study, Civelek, of 100 patients did not provide any details regarding whether a diagnostic block was used and compared neurotomy to therapeutic medial branch blocks. So, two different spinal injections were used here, and they are differentiated.

So, in terms of short-term back pain, there was low quality of evidence from both RCTs. The outcomes were similar following neurotomy and spinal injections. There was low quality of evidence from one RCT that patients were more likely to have back relief success following neurotomy compared with medial branch block therapeutic injections. In terms of function, one RCT provided evidence and showed that outcomes were similar between treatment groups at six months, and the quality of this evidence was low.

In terms of long-term back pain, one RCT provided low quality of evidence that there was no difference between radiofrequency neurotomy and therapeutic medial branch block when measured at 12 months, and the quality of this evidence was low, and then the same study, the same study showed that the percentage of patients who achieved back pain success was higher when they

had received radiofrequency neurotomy compared with therapeutic medial branch block.

OK, so moving into the cervical spine start with radiofrequency neurotomy compared with sham neurotomy, one small RCT met our inclusion criteria, and this one has been discussed before. This is the Lord study. Patients were selected for neurotomy with three medial branch blocks. Two of those blocks used different anesthetics, I believe it was different anesthetics. In those blocks, patients were required to have 100% pain relief. The third block was used with saline, injected saline, and patients were required to have no pain relief. Overall, the results suggest that significantly more patients who were treated with radiofrequency neurotomy achieved freedom from their accustomed pain compared with those who received sham neurotomy, and because of the very small sample size and risk of bias, the quality of this evidence was insufficient.

One study provided evidence for radiofrequency neurotomy versus spinal injections. This one is a little bit different in that patients were enrolled when they had cervicogenic headache. Patients were treated with either radiofrequency neurotomy or anesthetic injection of the greater occipital nerve, and overall the study provided low quality of evidence, but there was no difference between treatment groups in short-term pain.

OK, so key question 2A asked about whether there was a difference in the efficacy or effectiveness of different types of facet neurotomy. We found evidence regarding conventional versus pulsed radiofrequency neurotomy, as well as radiofrequency neurotomy versus alcohol ablation.

So, regarding conventional versus pulsed neurotomy, two RCTs met our inclusion criteria. Both selected patients for neurotomy using a single medial branch block and required at least 50% pain relief following that block. Overall, the studies both showed that there was no difference between treatment groups in terms of short-term back pain or function, and the quality of this evidence was low.

In the long-term, however, one of the RCTs provided evidence at 12 months and showed that patients who were treated with conventional neurotomy did better in terms of back pain than those who received pulsed neurotomy. At the same time, there were no differences in function between the treatment groups at 12 months.

OK, one RCT provided evidence regarding the comparative efficacy of radiofrequency neurotomy to alcohol ablation. Overall, there was no difference between treatment groups, in terms of the percentage of patients who achieved a success pain and function composite outcome.

In the long-term when measured at 12 and 24 months, patients who received alcohol ablation had better outcomes than those patients who received radiofrequency neurotomy.

Key question 2B asked about the evidence of repeat neurotomy, and for this key question we specifically sought out studies in which patients had a successful first neurotomy and then went back and received repeat procedures at the same level. We found case series evidence for this key question in both the lumbar and cervical spine. Overall, we found insufficient quality of evidence, and this is because of the study type that following a successful initial procedure, repeat procedures were likely to be similarly successful.

Key question 2C asked about the comparative efficacy and effectiveness of unilateral versus bilateral neurotomy, and we found insufficient quality of evidence from one retrospective comparative study that showed no difference between treatment groups and back pain success. Key question 2D asked about single versus multiple level neurotomy, and we did not find any evidence that met our inclusion criteria.

Key question three asked about the comparative safety of facet neurotomy compared with alternative treatments, and for this key question, we evaluated safety data from all of the comparative studies that were included in key question two, and these are the only data that we ended up including. We sought out case series that specifically, that were specifically designed to evaluate adverse events for this. In order to get higher quality case series, we required prospective case series to enroll at least 50 patients or retrospective case series to enroll at least 100 patients but no such case series were identified.

OK, so in the lumbar spine, so across the board, safety, there weren't many adverse events reported. For radiofrequency neurotomy compared with sham neurotomy, there was low quality of evidence that there was no difference between treatment groups in terms of treatment-related pain, sensibility changes, motor changes, and undefined adverse events. Somehow this got mixed up, I apologize, but in the lumbar spine for radiofrequency neurotomy compared with spinal injections, in fact it was a medial branch block, there were no cases in either treatment group of infection, motor deficit, or sensory deficit when measured up to six months.

OK, in the cervical spine, there was low quality of evidence from one RCT that there were significantly more cases of procedure-related numbness following radiofrequency neurotomy than sham neurotomy, but none of these cases were considered to be severe enough as to require any additional treatment.

Key question four asked about the differential efficacy, effectiveness of facet neurotomy compared with other treatment options and so we first addressed this key question by looking for heterogeneity of treatment effect. We asked in-studies that included both facet neurotomy and a control treatment, are there

differences in effect between different subgroups, so male versus female. Secondly, we conducted an analysis on a subgroup of studies included in key question Two to determine the efficacy of facet neurotomy in patients selected on the basis of 50% or more pain relief following medial branch block.

OK, so starting with the heterogeneity of treatment effect, one RCT evaluated heterogeneity of treatment effect and this study selected patients using intraarticular injections. Overall, none of the subgroups examined, sex, age, duration of pain, employment status, and not shown here was previous low back surgery, had any differential treatment effect in terms of the composite outcome of success, which is quite a lengthy outcome that they used, many, many parts, and the similar results were found for global perceived effect, pain relief success. In each case, the overall quality of evidence is low.

OK, so next I want to talk about the subset studies that selected patients using medial branch block. So, to lead you up to this, again, in key question one, we did not identify any direct evidence that looked at type of diagnostic block, such as medial branch block versus intraarticular block and how they effected patient outcomes following facet neurotomy. Because of this, we did not place any restrictions on type of diagnostic block for patient selection for studies included in key question two, and this was done in part based on the evidence that we found at the time and based on our correspondence with a clinical expert, Michael Gofeld. However, as you've heard and during the public comment period, it was very strongly suggested that patients should be selected on the basis of at least 50% pain relief following diagnostic medial branch block. So, in order to address this concern, we have provided the results from the subgroup of studies included in key question two, in which patients were selected on the basis of 50% or more pain relief following at least one medial branch block. In the lumbar spine for radiofrequency neurotomy compared with sham neurotomy, there is low quality of evidence from three RCTs of 100 patients. The outcomes were better. Back pain outcomes were better following radiofrequency neurotomy. One RCT provided evidence that at six-months followup both leg pain and generalized pain outcomes were better following radiofrequency neurotomy.

In terms of function, as measured by the Oswestry Disability Index, two studies provided evidence between two and six months followup the outcomes were better following radiofrequency neurotomy. One RCT provided evidence at two months that there was no difference between treatment groups in terms of disability, as measured by the Waddell score.

Long-term outcomes were the same as what I showed you for key question two. It's the same study. Basically, at 12 months both back pain and function outcomes were better following radiofrequency neurotomy.

In the cervical spine, looking at radiofrequency neurotomy versus sham neurotomy, this is the same evidence. Patients were selected using three

medial branch blocks and when anesthetic was injected, they were required to have 100% pain relief. Outcomes favored neurotomy.

In the lumbar spine, one study met this inclusion criteria and treated patients with radiofrequency neurotomy compared with therapeutic intraarticular injections. Patient were selected with a single medial branch block, and as you can see, there was no difference between treatment groups and the quality of this evidence was low.

OK, key question five asks about the cost-effectiveness of facet neurotomy compared with other treatment options, and no studies met our inclusion criteria.

OK, so I'm going to end the presentation by just going over a snapshot of the findings with the strongest evidence and then close with the gaps in the evidence.

So, going to key question two, when you look at all the studies together and don't differentiate in types of diagnostic block or requiring any specific amount of pain relief following that block, overall, though, there are some exceptions, there seemed to be no difference between radiofrequency neurotomy and sham neurotomy in terms of short-term pain. Functional outcomes did favor neurotomy and long-term outcomes favored neurotomy. Again, while all this evidence is from randomized control trials, all the trials suffer from methodological flaws and small sample sizes. We did not identify any data on the comparative effectiveness of radiofrequency neurotomy compared with sham neurotomy.

Still in the lumbar spine when looking at radiofrequency neurotomy compared with spinal injections, again, not placing any restrictions on block type, there was overall no difference between treatment groups and most of the pain or function outcomes, although short-term got pain success following radiofrequency, was better following radiofrequency neurotomy in one trial. Again, this is all RCT evidence and again, all the trials suffered from methodological flaws and small sample sizes. We did find one small retrospective audit study, which I did not show here; 66 patients were included, and there was no information on diagnostic blocks used, and the study provided low quality of evidence that short-term back pain outcomes were similar between treatment groups.

In the cervical spine, first looking at neurotomy versus sham neurotomy, outcomes were better following radiofrequency neurotomy and that should actually read insufficient, my apologies. Again, this is a well-conducted randomized control trial; however, it's very small and did suffer from methodological flaws. No data on the comparative effectiveness of neurotomy versus sham neurotomy was found. We found one RCT, which compared radiofrequency neurotomy to anesthetic injection in the greater occipital nerve for cervicogenic headaches, and there was no difference between treatment

groups. However, in this case, no diagnostic blocks were used and neurotomy was compared to only anesthetic injection of the greater occipital nerve so no steroids were used.

OK, so looking at key question four, we looked at the subgroup of studies from key question two in which patients were selected for facet neurotomy on the basis of at least 50% pain relief following a medial branch block. Overall, there was low quality of evidence, generally in favor of radiofrequency neurotomy over sham neurotomy in the lumbar spine, and this was true for both short-term and long-term pain and function.

In the cervical spine, again, results favored neurotomy. When looking at radiofrequency neurotomy versus therapeutic intraarticular injections in the lumbar spine, there was no difference between treatment groups in terms of short-term pain and function.

So, finally, gaps in the evidence. There were no studies, no comparative studies identified that evaluated the efficacy, effectiveness, or safety of facet neurotomy in the thoracic spine. We did not identify any economic analyses, full economic analyses that evaluated the cost-effectiveness of facet neurotomy compared with other real-world treatment options. We did not find any studies in the cervical spine, which compared different diagnostic modalities and then looked at outcomes following neurotomy. We did not identify any studies that compared medial branch block to intraarticular injections for selecting patients for facet neurotomy. The last time I checked, there is such a trial underway currently, and we did not identify any studies for key question two in the cervical spine, which compared facet neurotomy to intraarticular, therapeutic intraarticular injections or medial branch block. Questions?

Craig Blackmore: Questions on the evidence report? I have a question. So, you've given us a number of small RCTs and given them as low in terms of quality and obviously one of the reasons they are not high, that they are low, is simply the size, but you also mentioned methodological flaws multiple times. Can you just sort of summarize for us the problems that you've identified in these trials?

Robin Hashimoto: Yeah, so typically for RCTs we require, what we want to see is that, is that studies give information on how the random sequence was generated. We want to see a statement that there was concealed allocation and there's, you know, within this there are specific requirements, specific things that we look for. We also want to see that the studies say that data was analyzed according to the intention to treat principle. So, all patients were followed regardless of outcome. We look for independent or blind assessment of the outcomes. We want to see that there are no differences in the interventions, and this typically was not a problem. We want to see complete followup of at least 80% of patients. We want to see adequate sample sizes, and then we also want to see controlling for potentially confounding differences between the treatment groups. So, for this when we apply grade in general, if studies did not meet at least two of these different principles, then they ended up getting downgraded.

So, if the majority of the studies did not meet at least two of those things, then we would downgrade.

Craig Blackmore: So what, I mean, so what were you seeing? Was it that patients were lost to followup? Were they not doing the intention to treat?

Robin Hashimoto: It, it varied.

Craig Blackmore: It varied.

Robin Hashimoto: Um, yeah. This information is in the appendix of the very large report. Let's see, looking at a snapshot, at least in the lumbar studies, most of them gave, several of them did not give adequate statements of concealed allocation or any statements that they followed the intention to treat principle.

David McCulloch: Now, I'm going to inter-, I, I understand that, you know, it's a huge report and some of that is buried in the appendices, but some of these, I would have liked to have seen called out. I mean, if a study does not use intention to treat analysis, it should be thrown out. That's, that's not low-quality evidence. That's not a valid study. So, some of these are I think more major things to downgrade a study than others.

Robin Hashimoto: Mm-hmm.

Craig Blackmore: We, we have these six studies available in the binder here, is that right?

Robin Hashimoto: Yes.

Craig Blackmore: Because I, I think, you know, that's kind of what we're looking at here is there's, there's . . .

Robin Hashimoto: Yeah, and if you put . . .

Craig Blackmore: . . . six randomized trials. They are small.

Robin Hashimoto: Uh-huh.

Craig Blackmore: There's some conflict between them. We're going to have to resolve that.

Robin Hashimoto: Right, right, right.

Craig Blackmore: We're going to have to drill down in some detail to do that.

Robin Hashimoto: So, so in terms, OK, so let's just talk about the three RCTs that use medial branch block, because that's been argued very strongly that those are the, you know, those are the ones to look at. None of them, so OK, all of them provided adequate information on random sequence generation. None of them provided

any statement of concealed allocation. None of them mentioned that they used the intention to treat principle.

Joann Elmore: They may have used it, they just didn't state it.

Robin Hashimoto: Right. Right.

Seth Schwartz: And can I ask a question about how, how applicable that is for this type of intervention where it's actually a shot. It's here, you know, intention to treat is important when you're having people lost to followup for, you know, prolonged use of a medications. I mean here, we either got RF or you got sham.

Robin Hashimoto: Right, but then patients are . . .

Seth Schwartz: So, so how much is . . .

Robin Hashimoto: . . . followed for 2 to 12 months.

Seth Schwartz: Right, I understand, but it's not like they're going to change their group at that point. I mean there's . . .

Robin Hashimoto: No.

Seth Schwartz: . . . intention to treat is almost irrelevant . . .

Robin Hashimoto: No.

Seth Schwartz: . . . if it's an upfront treatment.

Robin Hashimoto: Right.

Seth Schwartz: So that, in my mind, that isn't a reason to downgrade in this type of a study.

Craig Blackmore: Unless there's differential loss to followup.

David McCulloch: Right, because . . .

Seth Schwartz: You know, I'm not, that, that's lost to followup question. I mean, you can downgrade for loss of followup, but that's not intention to treat.

Craig Blackmore: Well, that's fair, but it's, right. So, what proportion were lost to followup, I guess, would be, and how, how do they deal with that? Do they ignore those people or do they include them in the analysis, which would be intention to treat?

Robin Hashimoto: Right. Right, and so, you know, a percentage of patients lost to followup, it varied. Several of the studies met a, you know, had at least 80% followup. Some other ones didn't.

Craig Blackmore: And when they analyzed the data, did they . . .

Robin Hashimoto: Well, and like it said, the intention to treat.

Craig Blackmore: Yeah, but did, what did they do is my, is my question.

Robin Hashimoto: Oh.

Craig Blackmore: So, of the three . . .

Robin Hashimoto: OK.

Craig Blackmore: . . . did they analyze only the patients in whom they had followup or did they analyze everybody that had been randomized to that treatment?

Robin Hashimoto: Right. Haley, can you look into that.

Craig Blackmore: We're going to go on break soon, so.

Robin Hashimoto: OK. Awesome.

Craig Blackmore: That would be something . . .

Robin Hashimoto: That would be something that would be better just to, to check. I'll tell you, yeah.

Craig Blackmore: Further questions?

Richard Phillips: Yes, the question that we're asked to respond to is not whether or not radiofrequency neurotomy works or not or is effective but rather, was the evidence that the use of diagnostic blocks to select patients improves outcomes, and one thing I didn't hear was . . .

Chris Standaert: No, no, we're asked to do both. We're asked to talk about . . .

Seth Schwartz: That's only one question.

Chris Standaert: . . . is do we do (_____)

Richard Phillips: Yeah, so I, I agree that's number two, I agree.

Chris Standaert: Right, both, yeah.

Richard Phillips: I should have said this is, this is question one. You're right, you're right about that and I misstated that, but the real question, I guess, as I'm wondering about this is how the, I lost my train of thought here, the, now you got me thinking.

Let me come back to it, because he dropped, I interrupted my thought here. I don't know about the answer to this question.

Chris Standaert: Craig, this isn't really, so in, I guess somewhat of a thing to throw out to your question about sort of the problems with some of these studies, for some of these, it's a size issue, and so the issues become in randomization and distribution of features, and so the Lord study, a number of very good technical features about the Lord study . . .

Robin Hashimoto: Mm-hmm.

Chris Standaert: When you look at, there's a particular distinction between the two treatment groups in terms of distribution of people who are, litigation or Worker's Compensation are much higher than the control group, and that's not to say that that influences the outcome, but it, it's taken as some by an indicator that randomization, it's so small you don't really get equivalent randomization. When you look at the Nath study, that's a lumbar one, the baseline pain is much higher in the neurotomy group than the non-neurotomy group and they wind up at the same place at the end, and you get a bigger differential drop, but is that a problem with randomization, because you only have 20 people on each arm. It's things like that that start to become problematic, because those are where the debates were on the sides of these studies.

Craig Blackmore: There's a lot of reasons why small studies are bad. You can't account for all unmeasured confounders in the study.

Robin Hashimoto: Yeah, and there, there, I just want to point out, there is a section in the report, it's, it starts on page 135 that talks about the critical appraisal of all the studies. So, there's actually, and it goes in order by key question and then I think it's alphabetical within each key question, but it basically describes each study in a paragraph, and it talks about how patients were selected, the treatments and diagnostic blocks that were used, and then also talks about methodological strengths and flaws, so that's probably a good resource.

Craig Blackmore: You said 135?

Robin Hashimoto: It starts on page 135 and goes to 150, so, and it's in order of the key questions.

Richard Phillips: I recovered from my brain fart here, but I wanted to ask a question. The thing was about the diagnostic testing, was it, what about the patients who had negative diagnostic tests or tests that did not really suggest a need for that. There, there's no implication of what happened to those patients, how they were treated differently. Do you have any record of those?

Robin Hashimoto: I think in general they weren't, they weren't followed. There may be studies where they were followed, but that wasn't something that we were interested in looking.

- Richard Phillips: But essentially don't we need that information to answer that question one? I mean it . . .
- Robin Hashimoto: Intra . . .
- Richard Phillips: . . . I mean, to find out what, how the use of diagnostic blocks affected the outcomes? We have to know what happened to those that had . . .
- Robin Hashimoto: Well, typically patient, oh right. Well, typically those patients didn't receive neurotomy so then they didn't . . .
- Richard Phillips: Well, that's, see, that's the problem. The definition is a little bit recursive. In other words, you don't really go to neurotomy unless you have a positive test, and therefore, you basically obligate the whole, you know, you screw up the whole process. You don't really, you aren't able to differentiate what happens to a negative diagnostic test if you basically just accepted only those who have a positive test.
- Robin Hashimoto: Right, and, and one . . .
- Richard Phillips: And that's the problem I have with it.
- Robin Hashimoto: . . . key question 1A, we did look at, there was one study that looked at the outcomes following the medial, diagnosis via a medial branch block compared with just clinical exam, and there was no difference in that one particular study.
- Kevin Walsh: Were there any studies looking at, at natural history so the patients that did not go on to get, you know, to get the, the RF treatment, how did they do relative to the patients that did get it.
- Robin Hashimoto: Yeah, I, there probably are studies. I am not able to answer that. That's not one of the things that the report . . .
- Chris Standaert: I mean, the thing, I have not seen the answer to that question. It's a good question. I have not seen the answer myself. I think the question they're after with the first thing is not so much, there are people who will do these without blocks and there are treatment paradigms without blocks, and treatment paradigms with blocks and treatment paradigms with different thresholds for blocks and treatment paradigms where they do them then they look and see where was the cutoff. So, she referenced a couple of studies by what Cohen and Derby had two of those studies that looked at sort of, they, they tried to, they did their blocks and they found a threshold of response that might predict outcome, and that's sort of the question we're getting is sort of, if you're going to do these, is there a threshold at which you should draw the line saying you do the block, you move on to neurotomy or you don't, and the standard numbers are 50, 80, or 100, but there's a whole range in there. Some, like the Derby study talks about 7, I think it's 70 or something. So, it's, I think that's more the

question. It's not, do you do the block. I guess you could ask, do you do the block or not.

Richard Phillips: Well, it goes a little back to the question I asked Gary about, you know, when do you do a diagnostic block or not, and if you, and, you now, I'm not talking about the treatments. I'm just talking about how you do the diagnosis. How do you pursue it? I'm having trouble, so . . .

Chris Standaert: That's a hard one because those we just have the inclusion criteria of the studies, which talk about what they look for in the patients in whom they did these, but that's the, that's a big question. When are people, when are they in, when do you go chasing them?

Craig Blackmore: So, I want to try to keep this on specific questions to the report and then we'll take a break and then we'll come back and do a more general discussion. So, specific questions about information presented.

Seth Schwartz: I have one question. It's not really a criticism or anything, it's just, looking at slide #32, really there's one study that compared RF to the alcohol ablation and that doesn't come up a whole lot really anywhere else, but alcohol ablation looked great and I'm curious why, you know, is that used, has that been refuted as being useful? Is there higher harms? Why, is there any information about why that was just looked at then is nowhere else in the report?

Robin Hashimoto: It might be a good question for the expert.

Chris Standaert: I would guess, in part, that alcohol is highly neuro-toxic, and you're putting it in the spine, you know, and you're near all sorts of bad things. They use it for peripheral blocks, but it's tricky when you use it for peripheral blocks, because that's toxic, and if you spill or go over adjacent things. It's not very clean, but I use, maybe, I don't know.

Seth Schwartz: I appreciate your opinion, but I'm curious to know from . . .

Chris Standaert: Yeah.

Craig Blackmore: OK, so, I think we're, we're ready to launch into discussion, since . . .

Michelle Simon: I have one more question.

Craig Blackmore: OK.

Michelle Simon: So, I have a question on the safety data. It looks like you, you made a mention of looking for case series regarding safety and all you have really reported here are these RCTs. I'm wondering, did you look for any other kind of safety data? I know that Gary had presented a couple of studies.

Robin Hashimoto: We did not. We did not.

- Michelle Simon: Because it seems like it's really important for us to get a handle on safety.
- Robin Hashimoto: Right, and generally when we're looking for this stuff, we're looking, we're looking for the highest quality of evidence available. So, that's why we placed restrictions on the type of case series that we were going to include. Otherwise, it would be completely overwhelming with the amount of data available.
- David McCulloch: But with all due respect, RCTs are absolutely the highest standard for comparison.
- Robin Hashimoto: Sure.
- David McCulloch: If I'm looking at safety issues, case series are very important.
- Robin Hashimoto: Right, and we looked for them.
- David McCulloch: You get a bigger number.
- Robin Hashimoto: And we looked for them and we, though, we did, like I said, we didn't find any case series that met specific patient requirements, so 100 patients for retrospective case series and 50 patients for prospective case series, and the studies had to be designed to look for adverse events.
- David McCulloch: OK.
- Craig Blackmore: So, I'm going to, we're going to take a break. Before we do that, however, I want to introduce our clinical, excuse me, our clinical expert who has been sitting over here very patiently. So, it forgive me if I pronounce your name wrong. It's Attaman?
- Jason Attaman: That's correct.
- Craig Blackmore: OK. Thank you for coming. I'm going to ask you to just introduce yourself very briefly but we, we always have a clinical expert here because the committee members are not all people that perform this procedure or intimately familiar with it, and you can help us understand the clinical context and the technical issues, which, in this case, obviously, are very important, and we don't ask for a presentation from you, but questions will come up throughout the course of our discussion and we'll value your input.
- Jason Attaman: And I am happy to answer those questions.
- Craig Blackmore: Tell us who you are quickly, and we'll go to break.
- Jason Attaman: My name is Jason Attaman. I'm a pain medicine physician, board certified and fellowship trained. I practice in private practice in Seattle, Bellevue, and Auburn. I have no conflicts of interest.

Craig Blackmore: Thank you. So, we'll take ten minutes and resume at quarter of 3:00.

I'm going to ask the committee members to resume their seats, and we'll get started. Alright, the meeting is back in session. We have a quorum and, so we will resume with our committee discussion of the topic at hand. It is useful at this juncture to get a starting place for the discussion from one of the committee members, a summary of sort of where we are. So, I will solicit a volunteer, as always, and see who jumps in to summarize the current situation here. Joann.

Joann Elmore: I had a question for the vendor.

Craig Blackmore: Alright.

Joann Elmore: So, I'm not ready to summarize.

Craig Blackmore: Go ahead. Question.

Joann Elmore: I mean, if the rest of the group is ready to move forward, that's fine.

Group: No, no, no.

Joann Elmore: This is a real basic question. The vendor gave a lot of tables and the far right column in many of the PowerPoint presentations was labeled favors, in other words, which intervention is favored in a clinical trial. Now, the, I was pleased to see at the beginning of the, the evidence document slides the definition of a clinically significant outcome, you know, 30% pain relief or 50% pain relief for substantial, but then I was uncertain how you were defining favors to put your little neither or RFN in there, because it could be, it could be one of three things. It could be RFN is just slightly better, or it could be the second option is statistically significant difference that one is favored, or it could be a clinically significant difference. Which of those three were you using to label the column favors?

Robin Hashimoto: So, for, so we had definitions for clinically-meaningful improvement in pain, for those we used that definition, and we wanted to see that at least 30% of patients in the neurotomy group achieved pain relief and that less than 30% of patients in the sham group achieved that same pain relief. Otherwise, we were looking, we were looking at statistical differences, so.

Joann Elmore: OK, thank you, just because some of the differences were small and I wasn't, I'm not certain how to interpret many of those columns, the data.

Michelle Simon: Just another quick question for the vendor. So, that, the study Lord that we've been talking about so much with the small patient size, I was curious when you presented the, the research that you graded their study as insufficient as to quality and I went to look into the section that you directed us to find out why things were graded the way they were, and I find that it was graded at the end.

The study received a class of evidence grade 2. So, I'm a little conflicted about which, what do you mean on that, and it said the study was funded by the Motor Accidents Authority of New South Wales, is that the bias that you referred to earlier?

Robin Hashimoto: No. The risks, so, OK, so it, it, we, we're moving away from giving studies, you know, a level 2 or 1, because it is confusing, but basically RCTs can either be, they can be COE 1 or 2. They can't go below that because they are RCTs and then the risk of bias are the issues that I mentioned before. So, the Lord study didn't provide any statement of concealed allocation, and they didn't have adequate sample size, and so, you know, it could, it could probably argued that the quality of that evidence is low, mean grade. The methodology of doing that is, it's not cut and dried. You have to use judgment, and there's judgment calls going in there, but because of those issues and because of the very sample size, it ended up at insufficient. There were only 12 patients in each treatment group, so.

Kevin Walsh: Could, could I go back and ask you to repeat the answer you gave to Dr. Elmore about the pain improvement differences?

Robin Hashimoto: In terms of how we graded things, or?

Kevin Walsh: No, how you, how you favored things.

Robin Hashimoto: The clinically significant, generally if there was a 30% improvement from baseline in the neurotomy group and you didn't see that also in the sham group or the comparator group.

Kevin Walsh: So, can you go to slide 44 and explain the differences that you're seeing.

Robin Hashimoto: Yeah, just give me one moment.

Kevin Walsh: How that favors neurotomy. Can you pull it up?

Robin Hashimoto: OK, so I can see the confusion. So, in this, so you're looking at long-term back pain, yes? Patients who were treated with neurotomy achieved 63% back pain improvement from baseline compared with those in the sham group had 43%. Yeah, so that doesn't go along with what I was saying.

Joann Elmore: So, (_____)

Robin Hashimoto: Well, OK, so then you could say well, what about substantial pain improvement? Substantial clinically, a substantial clinical difference in, is 50% thank you. So, in that case, patients in the neurotomy group met that while patients in the sham group did not.

- Kevin Walsh: Another way to look at it is that the sham group, the difference between, the difference of improvement between the sham group and the neurotomy group is ten points on a 100-point scale, right?
- Robin Hashimoto: Twelve, but yeah.
- Kevin Walsh: Yeah, OK. Thank you.
- Robin Hashimoto: Mm-hmm.
- Chris Standaert: That's the Nath Study?
- Robin Hashimoto: That is the Tekin Study. That was the one study that provided long-term evidence. Patients were selected via medial branch block.
- Craig Blackmore: So, criteria for clinically-important difference on 100-point VAS is usually . . .
- Robin Hashimoto: It's, it's 30% . . .
- Craig Blackmore: 30?
- Robin Hashimoto: . . . is clinically meaningful, moderately meaningful, and 50% is substantially meaningful.
- Craig Blackmore: But it, but it's not 30%, right? It's 30 points on 100-point scale.
- Robin Hashimoto: That depends on who you ask.
- Joann Elmore: That score, what does that mean to a patient.
- Jason Attaman: Yeah, when we talk about the difference between science and art, this is really an art. It, those values are all over the map in terms of what is 'meaningful to patients,' and it depends on the condition. It depends on even within the same condition and the same treatment, it depends on the study. One study using an anchor-based method using the same treatment, same diagnosis will come up with a different what's meaningful to the patient. So, we have general guidelines, and I think that, that there are differing general guidelines. Some people use percentages, some use absolute points, and so it's difficult. It's a difficult area to really pin down. It's not clean, so that's why you'll get different, different opinions for different conditions and . . .
- Michael Souter: I thought there was some consistency, though, in how people were using the Impact.
- Robin Hashimoto: Right, and that's what we, that's what I was just going to say. We used the recommendations from Impact. So, they said minimally-important improvement is 10-20% improvement, moderately important improvement is 30-49% improvement, and substantial is 50% or more, and that's, yeah.

- Michael Souter: If you look at that, because it's on page 60 of the evidence report.
- Craig Blackmore: So then, the second line up here for function under the ODI, those . . .
- Kevin Walsh: A five-point improvement on a 100-point scale between doing nothing, between a sham neurotomy and a neurotomy.
- Craig Blackmore: I, I think. Isn't that what they're, isn't that . . .
- Kevin Walsh: That's the only way to read that.
- Craig Blackmore: And so that wouldn't even meet the criteria of the Impact.
- Richard Phillips: No.
- Michael Souter: Well, Impact is a . . .
- Seth Schwartz: Impact's about pain.
- Robin Hashimoto: Yeah.
- Craig Blackmore: Oh, it's about pain, right, right, right.
- Robin Hashimoto: We didn't find any, any clear definition of clinically-important functional improvement in this patient population or any even . . .
- Joann Elmore: So, to summarize . . .
- Robin Hashimoto: . . . related patient populations.
- Joann Elmore: . . . so to summarize, we have a lot of columns that may say favor RFN, but this is not a meaningful clinically-significant or validated scale that can help us understand the data.
- Kevin Walsh: That's how I read it. I mean, it does, statistically or numerically it favors one over the other, but the difference between the sham procedure and the procedure is sometimes minimal, which, in my mind, throws some doubt on whether one is really favored.
- Joann Elmore: Does our clinical expert want to comment on the meaning of a five-point difference?
- Craig Blackmore: Let's find out.
- Jason Attaman: I'd be happy to speak to that, thank you. I, I think the issue here, and we're, we're discussing sham versus active treatment. In the majority of these studies, we're actually studying sham versus sham. The location of the needle in these studies had very little, if any, ability to ablate the nerve target. That is the

problem. We had presented that to Spectrum to consider, and it did not seem to make it into their report, but we do know where these nerves are. We know where to place the nerves, the needles to ablate the nerves, and if you look at the images in some of these procedures, especially of van Wijk's study, you can see on his sample images that the needle is nowhere near the medial branch to be ablated. So, while I hope I can help the committee by understanding that while we're debating the quality of the RCTs, the actual procedures done in some of these RCTs are actually sham versus sham.

Seth Schwartz: But that's for the diagnostic block, not the procedure, correct?

Chris Standaert: No, he's saying, he's saying . . .

Jason Attaman: I'm talking about the radiofrequency neurotomy.

Chris Standaert: He's saying the technique by which the neurotomy was done was, was invalid is what he is saying.

Jason Attaman: That's correct.

Chris Standaert: So, is this one of those studies where you feel it was invalid, the Tekin study, or was this done correctly? That's what this study is.

Craig Blackmore: This is Nath, right?

Jason Attaman: Nath.

Chris Standaert: Oh, it was Nath? Oh, this is Nath, sorry.

Jason Attaman: My directive here is not to opine on the evidence but to give some clinical background. So . . .

Chris Standaert: You had just opined on the evidence. So . . .

Craig Blackmore: So, I mean, we, we've heard a lot. We've heard a lot from our, from, you know, the, the various speakers from the public and, and there's this, I think this sense that, that some of the studies used different technique than other of the studies and, and whether that's clear from the evidence report or not, I think we, as a committee, need to acknowledge and understand that people have concerns about it. So, so just for our information, which are the studies where our commenters would believe are representative of, of their technique. What are the names of those. I don't know which ones they are.

Jason Attaman: The majority of those studies were presented to the committee by Dr. Stout and Dr. Dreyfuss. These are the prospective studies.

Craig Blackmore: Yeah, but which ones are they? I mean, I wasn't, I don't have adequate notes from the presentations they gave us.

- Kevin Walsh: Nath, Tekin, Van Kleef.
- Craig Blackmore: Nath, Tekin, and those are the ones that . . .
- Kevin Walsh: And Van Kleef. That's the ones that we were told.
- Craig Blackmore: They used a different technique or those . . .
- Kevin Walsh: They used a better technique.
- Craig Blackmore: Used the worse or the better?
- Kevin Walsh: The better.
- Craig Blackmore: Those are the ones that used the better technique?
- Kevin Walsh: Yeah, Gallagher, Leclaire, van Wijk, we were told, were not of the same quality.
- Craig Blackmore: OK, and so this is the Nath study that's . . .
- Chris Standaert: No, this, this is the Tekin study.
- Craig Blackmore: This is the Tekin study?
- Chris Standaert: This is the Tekin study. I'm staring at the data right now, yeah.
- Robin Hashimoto: Can I just clarify something? So, so the, that's correct, and one of the reasons that we did this stratification here for key question four is that these three studies that selected patients by medial branch block and required 50% pain relief, at least in the lumbar spine for neurotomy versus sham, all of these studies were called out by Dr. Dreyfuss, and I don't remember if I assisted as well, but those being technically appropriate.
- Craig Blackmore: So, this, this one that we're arguing about with whether or not, you know, five points or four points on 100-point scale is important is actually one of the ones that has been identified as using the, the best technique. Is that?
- Robin Hashimoto: To my remembrance, yes, and I'm double-checking on that right now.
- Chris Standaert: The number, the ODI numbers are just that. The control group went from a 40 ODI to a 33.6 at one year and continued to have (_____) continuous number. The radiofrequency group went from 39.2 to 28.0 at one year for the ODI. So, the difference is exactly that, the 11.2 drop versus a 6.5 drop over a year.
- Kevin Walsh: Well, you use the ODI every day. So, if you have two treatments, two different treatments and they produce ODI of five-point difference, is that a significant difference?

- Chris Standaert: My understanding of a clinically, minimally clinically important difference, the ODI is about 13. Target can be anywhere between 10 and 15 or 20, but it's somewhere around that target and so I, the 11 approaches that difference but . . .
- Kevin Walsh: But the difference between them is . . .
- Chris Standaert: Five, no.
- Kevin Walsh: Right.
- Craig Blackmore: So, I wonder, could, well go ahead.
- Michael Souter: I was just going to say, but then just thinking about that, I'd want to be cautious at the difference between them. They're not necessarily be, if there's a threshold that's required to be relevant, do you see what I mean?
- Seth Schwartz: Well, if one's, if one's just over the threshold and one is just under, then theoretically one has met the threshold, but in real terms, does that mean that the one that met the threshold is significantly better than the one that didn't? I, to me it doesn't.
- Michael Souter: It kind of depends on where they are and how big the threshold is. I'm not saying either way, but I . . .
- Seth Schwartz: Right, no, I understand.
- Michael Souter: . . . I've just got that reservation in my mind about it simply looking at the difference between the two.
- Craig Blackmore: Or you could understand it as the number to undergo clinically significant improvement as defined by something. So, it becomes a proportion, which I don't think we know, but, unless I mean, is that in the article? Did they report a proportion with a clinically-significant improvement in the ODI. So, you had another slide here. I think maybe it was 43. There were other outcomes in addition to, this is just the ODI slide, right?
- Kevin Walsh: There was another slide, there was another one that used the Waddell.
- Craig Blackmore: Yeah.
- Kevin Walsh: And there was no difference at two months between sham and neurotomy.
- Michael Souter: Slide 43.
- Craig Blackmore: Slide 43.

- Michael Souter: OK, and then, now I'm curious because I'm looking at slide 46 where there is an RCT six-month followup, the ODI there, and there's, you know, looking at the ODI there between the RFN group and intraarticular injections, but it favors neither. That seems to be a little bit inconsistent with slide 44.
- Seth Schwartz: Right, because the differences seem to be about the same.
- Craig Blackmore: Or it just didn't get a P-value out of it.
- Chris Standaert: Yeah. Their confidence was . . .
- Michael Souter: Was that all it was?
- Craig Blackmore: Yeah.
- Michael Souter: Because they, they don't look that different.
- Craig Blackmore: No.
- Chris Standaert: (_____) The confidence intervals on both of them overlap on this one and the other one.
- Kevin Walsh: Right.
- Chris Standaert: If you have to do the math on them, the competence levels overlap on both of them.
- Michael Souter: I suppose, yeah, OK. I guess the standard deviation's different.
- Robin Hashimoto: Can I answer the question that was asked earlier? So, as it was discussed, there was comments from Dr. Dreyfuss, and he, he called out three valid for lumbar neurotomy versus sham. He called valid versus invalid studies. So, under valid RCTs showing evidence for the efficacy of lumbar medical branch neurotomy in this just subset of RCTs was Van Kleef, Nath, and Tekin.
- Craig Blackmore: So, I, I'm not saying that we should necessarily endorse that division, but I think we need to acknowledge that that's a big concern that's been raised, and it should be something that we consider in our, in our deliberation.
- Michael Souter: It would be useful to know which of these RCTs pertain to those things . . .
- Robin Hashimoto: Those people.
- Michael Souter: . . . yes. I agree.
- Robin Hashimoto: If, if you look at the key question four, the selection by medial branch block.
- Michael Souter: Mm-hmm.

- Robin Hashimoto: For this group. If you go back to lumbar spine neurotomy versus sham, so the previous slides before this one, it's, those are those three studies.
- Michael Souter: Slide?
- Group: 42.
- Robin Hashimoto: Yeah, starting here.
- Michael Souter: I'm on 42. Do you have a page for that Carson?
- Carson Odegard: Yeah, it's actually not a page. If you go into the appendix and then at the bottom of each one of these, you'll see the studies.
- Michael Souter: Is there a page number on that?
- Carson Odegard: Yeah, this is 25.
- Michael Souter: 25.
- Carson Odegard: This is neurotomy versus sham in the lumbar spine, page 25.
- Michael Souter: OK.
- Carson Odegard: And it gives you the (_____) more specific, specificity of the ranges. (_____) the tables anyway. It'll list the studies.
- Craig Blackmore: Any other comments or questions? So, procedurally, I'm going to divide it up based on lumbar and cervical, because that seems to be important. So, right now, we're focusing on lumbar and we'll come back to cervical. Alright, I need somebody on the committee to start us off.
- Chris Standaert: I would like to hear what people think. I mean, I think, in some ways we're looking at two technologies, one of which is contingent upon the other. We're being asked two separate questions, a medial branch block question and do we perceive a threshold for a cutoff if we're going to allow that, and the neurotomy question. Is it, you know, should it be covered based on efficacy, safety, and cost, and if we decide that isn't going to be covered, there's no point in really talking about the medial branch side, I don't think, because that's really the only reason we're doing a medial branch block is to move to a neurotomy.
- Michael Souter: Correct.
- Chris Standaert: So, in some ways you can start to think about it that way, and we have to sort out if we went in order, we can start out whether we think neurotomy is efficacious, and then we could get to the idea of medial branch blocks and decide do we have a cutoff. Somewhere in there comes Richard's question of patient selection. I mean, some of the dilemma, this is, low back pain is

extremely common, but this number of people who really respond to this procedure does not seem to be huge. So, how do you select those patients, but, and starting with that idea of, is neurotomy effective, are we going to go there? If we, if we don't, if that's not chosen to be covered, we don't need to go to the medial branch part, but they're two different questions to think about.

Kevin Walsh: My take on the lumbar procedure is that while there is some evidence that there is some pain relief, even long-term, it does not result in functional improvement. That's how I read it.

Richard Phillips: Could I ask a question of, the one thing that bothers me in this is that the presentation from Dr. Franklin and Dr. Glass was that there was a large number of the patients within this state who get three, four, five, on up, I don't know what the percentage was, but it seemed like 65% got one and then on up, but they were numbered, and that seems to me to get into the issue of appropriateness, which is not what we're talking about here, not what we're going to address here. But the question I want to ask you is that in the literature search, did you find anything that identified patients who got multiple diagnostic studies and neurotomies?

Robin Hashimoto: This was addressed in one of the sub-parts of key question two, and we ended up identifying eight, effectively case series, since it was looking at patients after one versus two, sometimes three, or even more successful neurotomies. So, if a patient had a successful neurotomy and then the pain came back, then they could go on to have another one. Overall, the evidence suggested that patients did similarly well after the repeat neurotomies.

Craig Blackmore: I think that's a different issue. I mean, I think Gary, the data we heard from you all was about multiple different levels, right, not multiple sequential?

Robin Hashimoto: Yeah.

Richard Phillips: And multiple levels.

Craig Blackmore: Maybe both.

Chris Standaert: And repeat procedures.

Richard Phillips: Yeah, so it's a different thing, because the literature says that these neurotomies last for six months or so, is that correct, maybe more, and that the nerve regenerates, or is that wrong?

Jason Attaman: I'd be happy to address that. I think it's important to understand that each facet joint is innervated by two medial branches. So, for those that are not familiar with the procedure, to denervate one facet joint, we need to ablate two medial branches. So, two facet joints becomes three medial branches, just to put the numbers in context. So, one joint is not one nerve. It's at least two nerves, and the second question you asked about the longevity. So, typically, if looking at

the procedures done with proper technique, most of these in the prospective studies, we're looking at an average of, in the low back, roughly around 300 to 400 days. Clinically, my experience shows between one and three years so it falls within the study data.

Craig Blackmore: So, I guess I, maybe I misunderstood a little bit and you can all help me. I thought when we were doing a diagnostic medial branch block, we were going at a single level and, am I misunderstanding and we're doing two levels to ablate to do the diagnostic study on a single facet?

Jason Attaman: I should clarify, that would be two nerves need to be blocked to turn off pain from one facet joint.

Craig Blackmore: So the diagnostic component of this is, you're injecting two different medial bundles.

Jason Attaman: That's correct.

Chris Standaert: So, I don't, our studies, what is the longest followup we have on the studies we're talking about here? I mean, they weren't three years out, so the longest out we have is 12 months, and there's only one that's 12 months, correct? So, then that study is six. The Tekin was 12 months.

Robin Hashimoto: Yeah, all the studies reported between two and six months, it varied, and then one study reported outcomes for 12 months.

Craig Blackmore: So, from the literature, is there some sense of the expected duration of benefit that people report in their studies that were included in the review?

Robin Hashimoto: I believe in the background we have 6 to 12 months, but I think that's probably something that's better addressed by the clinical expert.

Michelle Simon: That Tekin study also found no short-term benefit, but it did find benefit at 12 months. It makes no sense. Page seven.

Craig Blackmore: OK, anybody else want to summarize where we are? Michael, what do you think?

Michael Souter: I thought you'd heard enough from me today.

Craig Blackmore: You're on a roll.

Michael Souter: Oh, dear. Looking at it, I mean, it makes no sense. (_____) I think far from it. I think that there's, you know, there's a lot of concern that this is not an effective intervention across a broad range of patients. There may be subgroups in which this has some degree of effect. I am persuaded more by function assessments than by pain. Pain is such a difficult modality to capture accurately and so much, so many other variables. So many other dimensions of

the patient's character, but at least function is something that offers some objective assessment of whether there's been a reproducible change. So, you know, there appears to me to be some kind of weak signal there, but it's not, again, we're back to our old kind of, you know, problem of the what's, what's clinically significant and what's statistically significant, and we're seeing that kind of here, that barely statistically significant effect in some arenas and some in others. So, I'm, I'm kind of leaning here for certainly . . .

Craig Blackmore: I'm not, I'm not asking you to commit to a position, I'm . . .

Michael Souter: Yeah, no, no . . .

Craig Blackmore: . . . asking for a start of where we are.

Michael Souter: . . . I'm, I'm just . . .

Craig Blackmore: Yeah.

Michael Souter: . . . trying to summarize my, you know, somewhat more fluently than I've done in the past where I look back at the transcripts of how many times I say you and etc., and I'm not doing very well, but I, I think that there's, to me there's a weak effect, but I'm just trying to kind of think in my own mind, just now, how we could possibly identify through that group would be, and I'm finding it hard.

Craig Blackmore: OK. I'm going to call on some others.

Carson Odegard: You know, when we look at the function affect, I know you may want to look at it this way that, you know, Tekin was the long-term guy that got the smallest effect, but yet it favored the neurotomy. That was Tekin. Van Kleef was kind of the middle guy, or no the short-term guy that gave the next level of functional effect favoring neurotomy and then Nath became the middle point of six months giving the most difference, mean difference favoring the neurotomy. So, you had, so we are seeing results here for functional when we take those three studies across the board, it just looks like when we get to 12 months, Tekin's, you know, you go from 15, you go from 4.7 mean difference all the way to 15, or in the short-term Nath, or no midterm 15.6.

Joann Elmore: I would not look at the long-term data in Tekin because they unblinded at a few months.

Carson Odegard: At three months?

Joann Elmore: At three months they unblinded. So, I would (_____)

Carson Odegard: Oh yeah, OK, yeah, mm-hmm.

Craig Blackmore: Michelle, do you want to add anything?

Chris Standaert: So, I'll clarify, too. I don't personally, I don't usually see people with spine pain. I don't do these procedures, I never have. I, their evolution has paralleled my practice lifetime, essentially. Some of the issue with a lot of these studies is the issue that the speakers brought up of patient selection, that if you can find the right patient where this really is the problem where they have a predominance of their pain from one particular joint or two particular joints or a structurally identifiable or a countable number of joints, they seem to be the people where when you really select them out, do relatively well. A lot of people will quote the study by Dr. Dreyfuss, which wasn't included in the report. It was a cohort study, and we see the people who had the procedure, they had a very good response. It was a very small percentage of the people who presented for the study.

Craig Blackmore: Was it a cohort study or a case series?

Chris Standaert: OK, it was a single series. Sorry, so it started with 460 people responded to an ad, then they sort of whittled them down to the 15 who got the neurotomy, and so in those 15, the data, it's, but there's no comparative. It's not a controlled study, and there's no, it has those deficiencies at the end, and it's a small number of this whole thing, and when you look at some of these studies, the Nath study says they treated, as long as one part of the pain was identifiable as being something I could poke on from a joint, we went ahead and tried, and that's where Gary pointed out the Nath study started with 370 people who got medial branch blocks and you wind up with 40 in the study, because they're sort of fishing a lot more. Some of our background noise is this issue of patient selection and the limitations of the study. They're small, the number for whom this works is small. When you go to that Lord study, they really had good results, but boy, they were absolutely finite in the people they did the procedure in. They had 100% relief twice from anesthetic block and no relief at all from saline. The pain was gone, and they had good results in that group. It was 24 people. That's 12 in each arm, very small. So, when you look at those studies, it looks like there's a small people, you can find them, but it's how to do that, and I think that's some of the noise in our studies and the difficulty in pinning down, does this really make a difference, you know? Look at it over populations. It's difficult to pin down.

Seth Schwartz: I think that, that you and Michael are getting at the same thing, and I'm kind of seeing it the same way. I think that when we look at the, you know, all the studies together, there's a lot of noise in those studies, and so it's hard to know, and I don't really find much of an effect. When you filter it a little bit more, you sort of sieve everything through a tighter filter where you have a more accurate procedure, you have more accurate diagnoses, and it looks a little bit more successful, although there is this debate of is, are these really meaningfully different numbers, and then you have the one study where they kind of put it through the tightest filter, which was, again, cervical and not lumbar but, but you know, you can be convinced that those are patients who probably really had this problem, and it seems to be the effective treatment. So, I guess the way I'm thinking about this is, it makes sense to me that, just the face value of

it, is that if you can identify a problem that gets better with a diagnostic procedure clearly, and there is evidence that if you can actually do what you say you're going to do, which is ablate that nerve effectively, if that's where the pain is coming from, that it works. I'm not, I don't find myself doubting that completely. I find what I'm doubting more is, if you've got a patient who, their whole back hurts, are you going to put an injection in one spot and then try to pick out whether their pain is better from that one thing. I think that's difficult. So, there's a lot of noise. So, I guess just to summarize where I am at this point, I, I don't feel comfortable saying this doesn't work, we shouldn't be covering this. I'm more in a situation where I think that if we can define that very, very discreet population in whom we think there's a very high likelihood that it's going to be effective, that that's probably legitimate. What's difficult is that we're not, the filter, even these people testified that it should be, which is two positive blocks with a dose effect, you know, and a duration effect and, you know, the appropriate procedure, and then you have 80% relief of pain. If those the people who are going to get better, we're not, the only study that shows that is the one, is the one study, the long study with cervical. We're not seeing that data for the, for the lumbar folks. So, can we extrapolate that for the lumbar patients and say, that's what the criteria are? And I'm not sure, I think that's what we need to debate, but I'm kind of leaning toward, if we can have as stringent of a criteria as that, is it has to be two blocks where it absolutely works of controlling their pain and a, and a negative control where it doesn't control their pain and, then, you know, then, and then maybe those are the patients in whom we can approve it for. That's kind of where I'm leaning, but I don't know exactly how we structure those criteria.

Marie Brown: That's an expensive diagnostic process, too.

Chris Standaert: Yeah. That's where that gets tricky, too. The second half of our question, though, would be, how do we define who gets a medial branch block in the first place, which gets, just to make it more complicated.

Joann Elmore: Well, I think that's a good point. If you look at the Nath, one of the three supposedly more relevant studies, they started off with 376 patients, then they whittled it down to 261, and then there was 53 that lived too far away and 18 who declined, and the final study was 40. So, how to identify the relevant patients, I think, is really challenging.

Craig Blackmore: Who haven't we heard from? David?

David McCulloch: I mean, I'm, I'm leaning, I mean, it's a, to get, to identify those less than 10% of the patients that might possibly benefit is a pretty complicated and expensive algorithm to get down to. I guess if, if when, I'm saying, we're not going to pay for all the medial branch blocks and proceed with this and that, we're only going to pay for the ones who really meet stringent criteria, I'm leaning towards either saying, this is just not an impressive enough way to improve pain, and it's not without significant side effects and danger that I'm leaning either we should not

cover it at all or we should only cover the tiny minority that go through all those first.

Michelle Simon: I guess my concern is, if we do try to figure out who that tiny minority is, I mean, what, what do we rely on for that. With the study I think that you referred to, the Lord study, you know, by our evidence vendor has been graded as insufficient. So, we don't have a, a lot of great information on that. So, I . . .

David McCulloch: Right, I mean, I, I could easily just say we shouldn't cover it.

Michelle Simon: Yeah, I think I'm, I'm in your camp.

Richard Phillips: I, I think that the, I tend to go along with some of the thoughts I'm hearing that I think we really have to pay attention to what the patients say in these situations. If somebody gets a block and they get a positive effect from it, you know, it seems to me that the common sense would say that you've basically committed to doing something that makes it better. Now, what's the threshold? Is it 80% improvement, 100% improvement? I don't know, but if you then do that, then I, it'd be almost wrong to say, well, I know we said that's about all we can do and you wouldn't even do the neurotomy. So, it seems to me that just common sense would say that this patient should have something done for either nerve block of some kind, one or the other. That's the way I've always done things when I've had problems related to my clinical stuff, the way I was trained, and I think it's probably the right thing to do. One of the things that does bother me is the data that Gary presented, which was the multilevels and I know, I don't want to dwell on that too much, but I really think that's an issue of appropriateness and selection. It's not, you know, we, we, I think these things should, probably should be improved, approved at a single level, maybe two levels, but no more, rather than what we saw before, what he presented. It seems to me that's a separate issue, and I don't want it to really cloud the decision making that we make here, but I don't want to, but at the same time, I don't want to ignore what he says. I think that's important.

Craig Blackmore: I don't know that it's a separate issue.

Chris Standaert: Safety side.

Craig Blackmore: As conditions, if we wish to go that way, we could say a single level will be approved, you know.

Richard Phillips: Yeah, that's, that's really, I agree with you.

Craig Blackmore: I'm not, I'm not proposing that. I'm just, I don't think what you're talking about is irrelevant at all.

Richard Phillips: No, and I, you know, and I, and that comes back from background, I mean, I work with the clinical outcome assessment program. We found out in our, our PCIs the dilatations that are done, it's 15% rate of inappropriate PCIs in this

state based on criteria that were established by the ACC/AHA. So, I know that doctors do the wrong things and for the wrong reasons at times and so, you know, but we have to have some way to police that, and I'd like to be able to help the State with that, but it seems to me we're crossing a means here, and I think one level is probably a better way to deal with it in terms of our, our decision, you know, at least the conditions that I would put on it would make sense.

Craig Blackmore: Well, I don't think, sorry, go ahead.

Michelle Simon: I was just going to say, I like what you're saying but I don't think we have evidence of which level, how many levels. What if somebody's back pain comes from three different facets, and we're only treating one, and then you're not addressing the back pain, and we're paying for nothing essentially.

Richard Phillips: You're probably right about that. We probably don't.

Craig Blackmore: Again, I mean, I think if we believe that this procedure works if you can get total or near total relief from the diagnostic procedure ahead of time, then it seems to me the diagnostic procedure should be targeted at something, and if you don't get relief from that target, you're not a candidate. I mean, I, I think, in my mind it links together, maybe not for others, and I don't want to drive this on a tangent, but I don't see that as inconsistent with the technique that is employed in the trials that we have.

Michelle Simon: You're not restricting to one level. You're suggesting to do as many levels as you like, then?

Craig Blackmore: No, I'm suggesting do a level, because you can't tell if your, if your, if your diagnostic test is positive or negative if you've done a whole bunch of different levels, right? I don't think.

Chris Standaert: When we've talk about the, to get to your point, the safety issue, the vendor didn't state, it's in the report, but the medial branch nerve, so this nerve is a nerve that comes off the nerve root. The nerve root leaves the foramen and comes out, and the medial branch comes off. It sends it one branch up to the particular process to the facet above it and one to the facet below it. That's why that one does half of two different nerves. So, when you only do one joint you do two, when you only do two joints, you do three. That nerve also supplies the multiple, the muscles in the spine, and so the clinical, there is some clinical concern of this issue of Charcot joint, denervated joint, and the issue of denervating the musculature back there, and it's, that's all theoretical. Unfortunately, that's what the Smuck study was sort of getting at. So, it caught people's attention saying that there's increased disk degeneration when you do these. Is that because you're getting essentially a Charcot joint or you're weakening the muscle? What is it? It's one little thing that wasn't in our study, so you can't comment on it, but that's where the concern comes, and when you start thinking of doing five joints bilaterally, you, I mean, you have to start

thinking of the ramifications of what you're doing, and we don't have the number to say it should only be one or two or three. I don't know if two is worse than three, but you start doing the math and you start seeing you're denervating a significant portion, and you're chasing a bigger, the bigger your pain generator you're chasing the harder it is to really cut it down. So, somewhere in there, I don't think it's unreasonable to draw a line on those grounds.

Craig Blackmore: Does anybody else want to jump in at this point? Anybody I haven't heard from? OK, I'm going to try to organize the discussion again and I think, I think from what I'm hearing that we're probably not headed towards a cover without limitations, without conditions. Is that, we're heading down the no cover versus cover with conditions route. I see a lot of nods. OK, so that's how we'll proceed and I think we'll go again with the idea of can we articulate what conditions might look like, and we can head that way unless there's an overwhelming sediment, at this point, in the committee that we should go to a no cover, and I don't know, maybe I could get some subtle nods and shakes.

Kevin Walsh: Let's vote on covering or not and then do the conditions.

Craig Blackmore: OK. We can do that. We've got to do that first, yeah, yeah. I was just, I wasn't quite sure we were there yet, but I'm hearing that might be a good step.

David McCulloch: That might help us get there.

Craig Blackmore: OK, we will work through our tool. So, this is the HTCC coverage reimbursement determination analytic tool and committee members are very familiar with the content of this. It is information to help guide us through the decision-making process. The staff has prepopulated this with Medicare coverage and guidelines, as well as other payers. So, it looks like CMS has no national coverage decisions relative to this. We see that Aetna allows, it looks like one treatment procedure per level per side in a six-month period if I'm reading that correctly, and they have a bunch of constraints on other failed conservative therapy, etc.

Josh Morse: Craig, the medical directors did mention they identified a possibly-related coverage decision on nerve ablation.

Craig Blackmore: They, they did. That is true. It was a decision, I think a general policy from, let's find it. Let's find it. It was a national coverage decision for induced lesions of nerve tracts, which is general rather than specific to the spine and it was a long time ago, and it said that program payment may be made for innervation procedures when used in selected cases concurred in by contractors medical staff to treat chronic pain, and NICE, I believe, does not cover. Then there's other . . .

Richard Phillips: Did we hear earlier that there was a local coverage decision for Noridian here.

- Craig Blackmore: No local coverage decision. That there is one. Is that . . .
- Chris Standaert: The one we heard about was a process by which medical societies are working with Noridian to develop protocols that, outlines of what would become local coverage decisions for all local coverage carriers in the country to consider. So, they're trying to see if the local care around the nation will fall in line with a similar degree of local coverage decisions as a process that's in play, as far as I know.
- Richard Phillips: OK, so we don't have a, a local coverage decision?
- Chris Standaert: I don't know if Noridian has approved the one for facets yet. I'm sure Dr. Dreyfuss knows, as he is part of that process, but.
- Craig Blackmore: Dr. Dreyfuss, does Noridian have a coverage decision that's relevant to . . .
- Paul Dreyfuss: They have a coverage decision on this, and they have allowed for facet RF with the condition of 80% relief from the, following medial branch block with the ability to repeat if there's at least 50% improvement for a minimum of six months with functional improvement. Six other carriers nationwide are adopting the exact same criteria per the new OID report (_____) with all these LCDs to go through a national health CD methodology to avoid the expense and time of an NCD. So, this has now moved forward. There is no contrary decisions to Noridian that is now being propagated across the country. So, I've been part of the (_____) Society in arbitrating this whole effort with my partner, Dr. Baker. So, it's all very consistent in how this would be posed. The conditions are very strict, as they should be.
- Craig Blackmore: Thank you. There are also various society guidelines in here. OK, then the, sort of into the decision-making process, part of the tool, staff has prepopulated this with outcomes that we were considering in our decision making, and we should look at this list of safety, efficacy, and cost outcomes, as well as special considerations and populations and make sure that these are, that there aren't others that we have considered in our decision-making process, which are, which are not reflected in this list. So, I'll ask the committee to look at page 17 and 18 and provide any feedback. I think sensibility means sensory?
- Chris Standaert: Yeah.
- Craig Blackmore: Are there other, well, I guess we, we have talked about potential muscle weakness and the potential for advancement of degenerative change related to denervation as a potential safety outcome that's not, I think, encompassed on here.
- Michael Souter: Just as a kind of question that comes up in looking at this, when thinking about special populations and outcomes, is there, and this may be a question for the clinical expert or Chris to comment on. Is there anything about diabetic patients

given the fact that they would be much more at risk of, you know, Charcot type joint syndromes and others.

Chris Standaert: Not that I've ever heard of or seen. I've never seen data on diabetic patients with this.

Michael Souter: OK.

Jason Attaman: I've not seen that study specifically on a diabetic population. Regarding the concern about Charcot joint in the nondiabetic population, it is certainly a valid concern, but in order for that to occur, we need complete denervation of a joint. We are not completely denervating the joint with medial branch neurotomy. It is still partially (_____) vertebral nerves and also, there needs to be severe microvascular disease as a condition to the Charcot joint, which is not occurring in this specific population.

Michael Souter: Yeah, I was getting at that, hence the question about diabetes.

Craig Blackmore: OK, any other outcomes that we need to consider? I guess we would want to think about return to work. We heard a little bit about that. Oh, here it is, disability. Never mind, that's on there. OK, so again, we're focusing on lumbar. The next step in the process is our first voting question, which is around whether there is sufficient evidence under some or all situations that the technology is either unproven, equivalent, less or more effective than other forms of therapy and, so in terms of effectiveness.

Josh Morse: Five unproven, six more.

Craig Blackmore: And the next would be safety.

Josh Morse: Seven less, two equivalent, two unproven.

Craig Blackmore: No mores, and then finally cost effectiveness.

Josh Morse: Eleven unproven.

Craig Blackmore: OK, further discussion at this point before we continue the voting process? Alright, so we will move on. We will move on to the second vote. So, this is going to be, it's, it's a binding vote to cover or not cover, but if we, if the committee elects to cover with conditions option, then we will have to decide on those conditions by vote, and then we'll have to have a revote to make it official that that, that that's what we've decide. Is that . . .

Seth Schwartz: OK, just to specify, this is for lumbar only, right?

Craig Blackmore: This is lumbar only.

- Chris Standaert: And the choices are cover, no cover, and cover with conditions, and the conditions will be determined later, and there will be a subsequent vote for approval of those conditions if that's the way the committee goes, so.
- Josh Morse: Four no cover, seven cover with conditions.
- Craig Blackmore: Alright, Margaret or Christine or somebody, can I get you to man the? So, we will now discuss potential conditions. We have several templates to work from. We have the recommendations of the various societies. We have the recommendations of the medical directors. We have the inclusion criteria for the various studies and we have a starting template.
- So, is the committee interested in the concept of only covering neurotomy under circumstances of specific criteria for the diagnostic blocks?
- Group: Yes.
- Craig Blackmore: OK. So, I'll ask Margaret, let's get rid of the cervical and do the lumbar, since we're not doing cervical yet.
- Chris Standaert: Can we think about this on two levels because we have, we don't get here unless we do the medial branch blocks and so we can have, we can either set the conditions for neurotomy or we, we, but then apply it also to medial branch blocks in terms of patient population. So, is it only axial low back pain? Is it lacking significant structural problems? What is it? Or we can just set the conditions for neurotomy based solely on the medial branch block response and then set separate conditions on when you can do medial branch blocks. Does that make sense? It's two layers. So, there's two entry points. The entry point is a medial branch block, and then how you get from that to here is the question we have.
- Craig Blackmore: Right.
- Chris Standaert: This has to address. So, we can set conditions all the way around for this. If we only consider it in people then you would only consider medial branch blocks in whom, in people for whom this would apply, but we can set the restrictions on two different levels. We're going to need to address the medial branch block issue and do we restrict that, conditions for that in some way or not also.
- Seth Schwartz: It seems that there were, we've been told at least that there are clinical, clinically, clinical diagnostic procedures or findings that would put, send you down this pathway. I'm seeing head shaking. I mean, there, there was . . .
- Chris Standaert: They vary depending on the study.
- Seth Schwartz: OK.

- Chris Standaert: You know, they're not, there's no uniformly-accepted, we would have to say that, I would think. We have the ability to say that if we want. If we don't want everybody with whole body pain getting this for their low back, we can say that.
- Michael Souter: But if they, if they have to approve affect, I thought we were purely being asked to decide on the merits of facet neurotomy.
- Chris Standaert: I don't think so. I think we're deciding medial branch blocks as well.
- Michael Souter: I'm, then we're getting into a much bigger question actually.
- Seth Schwartz: I mean, here's a look at the, what the agency directors told, you know, put up there. We can start with that.
- Craig Blackmore: So, does somebody, does somebody have a copy of the official key questions?
- Josh Morse: I do.
- Craig Blackmore: What's it say?
- Chris Standaert: What's the first key question?
- Josh Morse: The first key question is one with sub A through F. So, would you like me to read the whole question? With different regions of the spine, lumbar, thoracic, cervical facet considered separately. What is the evidence that the use of diagnostic blocks, i.e. medial branch blocks or intraarticular injections with local anesthetic to select patients for facet neurotomy improves clinical outcomes following facet neurotomy. Consider each of the following: A) Diagnostic block versus alternative diagnostic test, for example physical exam or radiological exam. B) Type of diagnostic block that is medial branch block versus intraarticular injection for patient selection. C) Use of a single diagnostic block versus two or more uncontrolled diagnostic blocks and that is use of short versus long-acting local anesthetics or use of local anesthetic versus saline. D) The degree and duration of pain reduction from diagnostic block. For example, pain relief of greater than or equal to 30% versus 50 or greater than or equal to 50 versus greater than or equal to 80%. E) Unilateral versus bilateral diagnostic block. F) Diagnostic block of single versus multiple levels. That's just question one. Do you want all of them?
- Michael Souter: No, but I mean we, we don't ordinarily have to go through every element of the key questions in order to define, you know, the entity that we're, the problem that we're dealing with.
- Craig Blackmore: I would interpret that key question as being do we think the medial, the diagnostic block is necessary to, as a precondition for performing the therapeutic clause.
- Group: Yes.

- Chris Standaert: But I do think the . . .
- Craig Blackmore: Not, not that we have to define, I, I . . .
- Chris Standaert: Oh, sorry.
- Craig Blackmore: . . . I don't think we've seen that.
- Chris Standaert: But, well, no, there are inclusion criteria for the studies where the entry point is medial branch block. So, the studies all have inclusion criteria and the first thing they get is a medial branch block and then they have inclusion criteria for the response of medial branch block. So, again, we can do this two ways. So, I bring it up because, for example, I don't think people with whole body pain who have low back pain when you poke on them are good candidates for neurotomy. I think it's highly likely to fail in those people. So, people with axial low back pain with very focal pain, that's a different story, and the studies talk about people with back pain, people with radicular pain as exclusions. Dr. Dreyfuss's paper talks about excluding people with significant cervical and thoracic pain, and peripheral joint pain. So, you're really trying to get people who have back pain. They're the ones you select for the medial branch block, and we can put that here so they're included (_____)
- Michael Souter: And I, and I understand that, but if we're, let's just build a conceptual model of, OK, we're going to, we're going to limit the number of injections that one can do. You're going to have to demonstrate an effect of the medial branch block before you can engage in a neurotomy.
- Chris Standaert: Mm-hmm.
- Michael Souter: I think, you know, we can, to some degree, again, we can rely on the practitioner to kind of realize that if they've got somebody with low back pain and they're going to get one, one level to demonstrate the effect of, that's probably not going to be an efficacious intervention and so, you know, the chances are you're not going to get any, you know, key effect from that. So, that's going to be a treatment failure from the get go. There's no chance that you could succeed in that circumstance. Do you see what I mean? So, I think, I think, again, the practitioner has got some (_____) definition there.
- Craig Blackmore: But I think there's, you don't want to have everybody in the world getting a diagnostic block.
- Michael Souter: But how, how many people are likely to do a diagnostic block when they're faced with a complete, in somebody's who's got, you know, complete back pain?
- Craig Blackmore: I don't know the answer to that.

- Chris Standaert: People do, I mean, I can tell you people do but, I mean, that's some, somewhat of the issue and if the procedure is going to be accepted and effective, patient selection is important and so it is important that you find . . .
- Michael Souter: Yeah, but, but they're only going to get as far as the, as the medial branch blocks.
- Chris Standaert: Right.
- Michael Souter: They're not going to get to the facet neurotomy stage.
- Craig Blackmore: That, that still, that's . . .
- Chris Standaert: But it's still a procedure.
- Craig Blackmore: . . . it's a facet injection.
- Chris Standaert: It's not a, you know, just doing medial branch blocks, you know. There, it's, it's an invasive procedure, a needle in your spine, it's fluoroscopy. It's money. It's all those sorts of things to go fishing for the person in whom to do the neurotomy is a significant portion of why Dr. Franklin brought this up is that, that you fish pretty hard to find the people that are there and can you, if you keep it narrow from the beginning, and even simple things like for axial, for the treatment of axial low back pain only or for patients with only axial low back pain.
- Michael Souter: We haven't explored any of that . . .
- David McCulloch: Right, and Chris did the . . .
- Michael Souter: . . . in the discussion with them, Chris.
- David McCulloch: . . . the State's not going to pay for all those fishing things. We're only going to pay for the, the small subset who, who we do find.
- Chris Standaert: So why isn't the patient, the State going to pay for medial branch blocks that are fishing? So, we, we did talk, but every study looked at has inclusion criteria for who gets a medial branch block or who is the entry point. They all have them.
- Michael Souter: None of that was discussed in the evidence review.
- Craig Blackmore: Well, we have it, I mean.
- Chris Standaert: We have it all.
- Craig Blackmore: So, our job is to identify the group of people in whom we think this procedure potentially has benefit. Now, the only . . .

- Michael Souter: For facet neurotomy, yes.
- Craig Blackmore: . . . but the, the only people in whom we believe, the only people in whom we've seen evidence that the facet neurotomy works is the ones who met the very limited inclusion criteria of these research trials.
- Michael Souter: Yeah.
- Craig Blackmore: So, I don't think we're . . .
- Michael Souter: And I'm, I'm not disputing that, but then when we start saying, OK, well whose, who are we going to let, who we should do diagnostic tests on? That's a different question.
- Craig Blackmore: I, I don't, I mean, it, we're only going to do diagnostic tests on people who we think will benefit from neurotomy. Otherwise, there's no point in doing it, and the people that are going to benefit from neurotomy are the ones that fit the criteria for the randomized clinical trials, because we don't know anything about the people who didn't meet those criteria, right? I mean, if the randomized clinical trials excluded people with radiculopathy, then we shouldn't be paying for, for diagnostic medial bundle branch blocks in people with radiculopathy, because we don't have any reason to believe that this study will work on them. We don't know that it doesn't, but we don't have any evidence to drive paying for it. I don't think, I mean, I'm, I'm agreeing with Chris.
- Michael Souter: I'm not necessarily disagreeing with you. I'm just saying that that's an element, which has been absent from our discussions, too.
- Craig Blackmore: Well, we still have time. I mean, we have the information. We have all of the data. We know exactly who was enrolled in these studies. We know exactly who, we have data on benefit, if we believe there's benefit.
- Seth Schwartz: Can you tell us what the entrance criteria were for these studies? Let's use the three, the last three that we think showed effectiveness.
- Josh Morse: So, as Carson pointed out earlier, on page 72 of the appendix there is the, the details on the individual studies. For example, the Nath study is on page 72. I think the Tekin study may be below that or further ahead.
- Craig Blackmore: So, for Nath, for example, it says adult patients with continuous low back pain of at least two years who had not responded previous treatment. Patients had to be able to identify at least one component of their pain, which could be attributed to one or more lumbar zygapophyseal joints. Such patients had to have paravertebral tenderness and obtain at least 80% relief from medial branch block, and exclusion criteria were pregnancy, coagulopathies, malignancy, infection, mental handicap, psychiatric disorder, and the other exclusion was patients with a motor deficit or any other indication for surgical treatment. The next study, the Tekin, that was, that was one of them, age

greater than 17, symptoms greater than six months, continuous low back pain with or without radiating into the upper leg and with focal tenderness over the facet joint, pain on hyperextension, no findings or neurologic deficit, no indication for surgery, no radicular syndrome, unresponsive to traditional conservative treatment, such as bedrest, medication, physical therapy, trigger point injection, and epidural block and experienced the positive response to medial branch block. Exclusions were prior RF treatment, coagulation disturbance, allergy to contrast dye, malignancy, mental handicap, pregnancy. Van Kleef, 20-60 years of age, chronic low back pain greater than 12 months, initial mean VAS score of more than 4, probably on a 10-point scale, I would guess, conservative therapy attempted without success, absence of any focal neurologic deficit, by routine exam stating that they were pain free after block, and exclusions were clinical lumbar radiculopathy or other abnormality, previous back surgery, patients with a known specific cause of low back pain, and they list disk herniation, spondylolisthesis etc., patients with diabetes and patients with more than one pain syndrome.

Craig Blackmore: So, that gets into people, I mean, what, they vary. So, the Nath study is sort of saying if you have some pain we can identify as from this one area of your back, we will treat that one area of pain and ignore the rest, and I think when you look at their numbers, their endpoints are vaguely different between the groups and it's the weakest of them in the results. The other ones are really focused, trying to focus on low back pain and things, symptoms that would be in the facet and that's really what they should have. So, excluding radiculopathy, excluding disk herniation, excluding other potential causes of back pain and not having other pain syndromes, not having chronic neck pain, not having widespread whole body pain, not having other things, because then you're really only treating a little piece of their pain and those are not the people in whom the data really says this works well.

Richard Phillips: If we just said those patients who have facet-related pain, then we . . .

Chris Standaert: That doesn't work, but you only know that by doing the medial branch block.

Craig Blackmore: I think at a minimum we can say greater than 17 years, consistent, the minimum symptoms reported on any of these studies was six months, six, 12, and 24. So, I would say it has to be at least six months of continuous low back pain and they all exclude people with radicular symptoms and neurologic deficit or motor weakness, I guess, and they are all unresponsive to traditional conservative treatments, which is not further defined, and, you know, exclude people with cancer and pregnancy, but I'm not sure we need to go.

Chris Standaert: They'd be excluded from fluoroscopy in the first place. They should be.

Craig Blackmore: And then the other criteria would be whatever we decide in terms of the criteria from the diagnostic block.

Seth Schwartz: Why are you picking six months? It's six, 12, and 24.

- Craig Blackmore: Well, the minimum is six.
- Seth Schwartz: Yeah, and the maximum is 24.
- Craig Blackmore: So, I'm, I'm starting with the minimum. I'm not opposed to 12 or 24, but, but it has to be at least six if we're going to, you know, it can't be three.
- Chris Standaert: What else did you say? I would include the no, no other known structural cause of pain so people with an unstable spondylolisthesis, we think that's why they have pain, it's hard to know, I guess. Known is difficult.
- Craig Blackmore: Yeah.
- Chris Standaert: But a disk herniation.
- Craig Blackmore: And no other syndrome.
- Chris Standaert: No, not that. That's too, that's not, people aren't going to know what that is. So, no acute fracture. So, no other clear structural cause of pain.
- Craig Blackmore: Is six months too lenient. Should it be 12?
- Joann Elmore: Two years.
- Craig Blackmore: Should we put two years?
- Richard Phillips: It's consistent with the literature.
- Joann Elmore: Nath was two years.
- Kevin Walsh: Well, one was six, one was 12, one was 24.
- Seth Schwartz: The other thing was failure of other therapies I think was in there for most of them.
- Craig Blackmore: Failure of conservative.
- Group: Yeah.
- Marie Brown: There was some information, though, about if you, after two years, the likelihood of, was it return to work or whatever, is much, much less, so . . .
- Chris Standaert: Pain syndromes, in general, by the time you get over a year are much more difficult to treat.
- Marie Brown: Right.
- Craig Blackmore: You're done.

- Chris Standaert: Yeah. Yeah, they're much so. I would think two years would be a very long time. You really think somebody has it to sit in them for two years.
- Marie Brown: Early intervention.
- Chris Standaert: Would be too long.
- Seth Schwartz: You have that people's function didn't improve anyways, so.
- Craig Blackmore: Alright . . .
- Richard Phillips: I think that these will be the same criteria for the diagnostic study, too. That's what . . .
- Chris Standaert: That's the idea, yeah.
- Richard Phillips: . . . we're really, really saying.
- Chris Standaert: Then we don't have to go there, really.
- Craig Blackmore: And then the other one is no other pain syndromes.
- Chris Standaert: No other pain syndromes.
- Craig Blackmore: Which, is that, does that have clinical meaning? No other pain syndrome? Would that exclude somebody with neck pain and shoulder pain and?
- Chris Standaert: We have a definition.
- Marie Brown: Symptoms or syndrome?
- Group: Syndromes.
- Chris Standaert: Syndromes. I mean, I would . . .
- Group: Yeah, syndromes.
- Chris Standaert: . . . that would (_____) I would think syndrome would be like fibromyalgia or something that has a name as opposed to, whatever that is, that's a good question, too, but, neck pain, chronic neck pain or whatever.
- Craig Blackmore: OK. OK, is this, does this resonate with people as a starting point?
- Group: Mm-hmm.
- Craig Blackmore: OK, what, where are we in terms of percent improvement and number of blocks?

- Seth Schwartz: As far as the, the number of blocks, I mean, I think that the, we want to believe that the blocks are actually doing what we think they're doing, and I like the, the concept of using the two different anesthetics with different durations of action, essentially acting as a control. I think that we saw that in several of them and that seemed reasonable.
- Craig Blackmore: So, two, two blocks?
- Seth Schwartz: And they had a terminology for it. It was like two controlled blocks or something.
- Joann Elmore: Controlled blocks using lidocaine and (_____).
- Chris Standaert: Well, yeah. Sometimes if it, it (_____) too, differential controlled (_____).
- Richard Phillips: Does it, does it require the same resources to do a diagnostic block as it does to do a radiofrequency ablation.
- Craig Blackmore: Nearly.
- Chris Standaert: You don't need the machine. You just put a needle in with lidocaine. You don't need the machine. You don't need the neurotomy machine.
- Richard Phillips: Right, but don't you have to do it under fluoroscopy.
- Chris Standaert: It's under fluoro.
- Richard Phillips: Or with radiographic. So, you have to do it in the radiology suite and?
- Chris Standaert: Mm-hmm.
- Richard Phillips: So, really the cost there, it's really just the radiofrequency machine is the only difference? I, I was, what I was coming to in terms of cost is there any difference.
- Craig Blackmore: I don't, I mean, is, if you have to do ten blocks before you get your treatment, you may be driving up the cost because you're doing more diagnostic, but . . .
- Richard Phillips: Yeah.
- Craig Blackmore: . . . I don't know what the answer is. The medical directors liked two, so they must not be afraid of the cost of two.
- Richard Phillips: I'm, I'm happy with it. I was just asking the question.

- Jason Attaman: May I comment on that? That is correct. Essentially the same equipment with the exception of the radiofrequency generator, which would need to be in the examination room to answer your question.
- Craig Blackmore: Usually the same operator, too, right? The person who is doing the diagnostic is usually the person who would be doing the . . .
- Jason Attaman: That is correct, yeah.
- Craig Blackmore: Yeah.
- Jason Attaman: I would say nearly 100% of pain physicians would do the diagnostic blocks and the radiofrequency neurotomy. May I comment on the pain syndromes that may include carpal tunnel syndrome? Patients, very commonly, would have something as simple as carpal tunnel syndrome, are you saying that, are you suggesting to exclude medial branch blocks if they have something like carpal tunnel syndrome or headaches? Just my clinical, because pain patients rarely would come in with one single discreet localized pain complaint.
- Craig Blackmore: That would seem to be the argument against doing this.
- Richard Phillips: Well, we're still talking about lumbar here, so I think . . .
- Michael Souter: You can, you can say . . .
- Richard Phillips: . . . there's no carpal tunnel there.
- Michael Souter: . . . no, no other pain syndrome effect in the spine. How about that?
- Craig Blackmore: For lumbar.
- Michael Souter: I would say affect in the spine.
- Craig Blackmore: No, no. I think that's fine.
- Chris Standaert: You don't, you don't want . . .
- Craig Blackmore: We won't, we won't use that same wording once we get to cervical if we're here because then I think it becomes, then it becomes (_____).
- Gary Franklin: Craig?
- Craig Blackmore: Yes.
- Gary Franklin: I'm sorry, so I think what we were talking about what was a short-acting, long-acting, and a saline placebo.
- Craig Blackmore: You want all three?

- Gary Franklin: Well, that, that would be the best, according to Dr. Glass, that would be the best way to do it and then, and then you would want a certain amount of improvement from the active block and no improvement from the placebo block.
- Craig Blackmore: Yeah. So that, so we're saying two . . .
- Chris Standaert: Two different . . .
- Gary Franklin: Long-acting, short-acting anesthesia plus saline.
- Chris Standaert: So, that is the, that is what was used in the Lord site, but that is not what was used in the other studies. A three-block protocol, I think Lord was the only that used that of the studies we looked at.
- Craig Blackmore: We're using Lord as indirect evidence for the lumbar spine. We've already talked about that.
- Michael Souter: I would have thought that if you're actually wanted to pick up placebo effect, you'd get as much chance of that with being able to discern between the short-acting and the long-acting effect. I don't see any reason to add to the expense of the procedure by adding in another block.
- Michelle Simon: That's kind of the point of the long-acting and the short-acting, isn't it?
- Michael Souter: Yeah.
- Craig Blackmore: So, three or two?
- Michael Souter: Two.
- Craig Blackmore: Any threes? Twos? Two.
- Richard Phillips: Why don't we say, well, that's fine. I was going to say at least two.
- Chris Standaert: You can put in the word differential improvement or whatever, because what you're after with the two is that with the short-acting you get a shorter response than with the longer-acting. The longer-acting you get a longer response, not just that you do two different anesthetics but that you actually respond physiologically to those two.
- Craig Blackmore: Temporarily appropriate improvement in pain.
- Chris Standaert: Yes.
- Craig Blackmore: Alright. I need a percent threshold improvement.

- Joann Elmore: 100.
- Craig Blackmore: I'm hearing 100.
- Richard Phillips: I take greater than 80 or 100 are the two choices I would go for.
- Craig Blackmore: I'm hearing 80. I'm hearing 100.
- Marie Brown: 80, 80.
- Michael Souter: Yes.
- Michelle Simon: If you have a long-acting and a short-acting, you should be pretty certain, I would think. It wouldn't be hard to achieve 100% if you give them that, right? Why not say 100.
- Craig Blackmore: Alright, how many 80s? Hands up. How many 100s? Hands up. We've got five to four.
- Chris Standaert: We've got a couple abstentions. 80. Alright. How many levels or sides per intervention?
- Michael Souter: One level.
- Group: One.
- Craig Blackmore: One level. This would be one nerve level, which would be two injections.
- Michael Souter: Above and below.
- Chris Standaert: That's one joint level. Our studies . . .
- Craig Blackmore: That's one facet level, yeah.
- Chris Standaert: . . . are usually more than one.
- Craig Blackmore: This is for the, this is, studies more than one?
- Chris Standaert: Mm-hmm. Do you have the numbers of joints in the different studies? I don't think it should be five by any means, one or two.
- Robin Hashimoto: In the lumbar spine, at least comparing neurotomy to sham, I think one study used more than one but in general, the studies did not report the number of joints that were denervated.
- Richard Phillips: Were they always unilateral or, did it include bilateral? I know it varied from, I mean, in those three studies particularly is what I was focusing on.

- Michael Souter: So, the Nath study, we got between two and six radiofrequency lesions. So, that would be one level to three levels.
- Chris Standaert: Well, if it's the same side that would be five.
- Seth Schwartz: They said it wasn't reported how many levels, but it, that many lesions. Does lesions mean levels, or?
- Chris Standaert: No. If they're contiguous, if you did all one side, six would be five joints. If you did two sides bilateral, six would be four joints.
- Michael Souter: If you've done lesions, you're doing above and below each level.
- Chris Standaert: Yeah, but when you . . .
- Michael Souter: Six would be three.
- Chris Standaert: No, so if you . . .
- Michael Souter: Oh, no. Sorry, you're right, you're right. Yes, you're right.
- Chris Standaert: OK.
- Michael Souter: Yeah. I'm thinking if they're all together, you know.
- Chris Standaert: The Tekin study is L1 to L3 or L3 to L5.
- Seth Schwartz: Either L1 to L3 or . . .
- Chris Standaert: Or L3 to L5.
- Michael Souter: We've got single diagnostic medial branch block.
- Chris Standaert: I would say two. Just by the law of averages that means three nerves instead of two nerves, so it's one more nerve and you cover one more joint, and you probably increase your yield. That's purely theoretical. I don't have data for that one.
- Michael Souter: More pain per level.
- Craig Blackmore: All this time precisely vocalizing and then we just inject everything. Van Kleef it says not reported. Maybe the clinical expert can help us out. How commonly do you do one level versus multiple levels and one side versus both sides? What's the common practice in the community?
- Jason Attaman: The common practice, at least in this region, would be one to three joints per side.

- Craig Blackmore: Two to four injections, or nerves.
- Jason Attaman: Nerves. So, if, if we were discussing joints denervated, it would be two to four. I think more commonly one to two, but it is variable, and that's joints specifically.
- Craig Blackmore: Right, thank you.
- Richard Phillips: Now I take it that means the diagnostic tests have to do the same thing?
- Chris Standaert: We could just stipulate that you can only do the diagnostic procedure, I mean, you can do the diagnostic procedures in patients who would be, who would meet these criteria, something like that.
- Richard Phillips: So, in other words, if you were to do a diagnostic test on, say, two joints or one joint, something like that, you could not do four joints in a, at a radiofrequency neurotomy, you know? In other words trying to be all encompassing. You would never do that.
- Chris Standaert: It would seem odd for somebody to go and do a neurotomy on a joint they hadn't done a medial branch block on.
- Richard Phillips: That's what I would think, too, but I . . .
- Chris Standaert: Yeah.
- Richard Phillips: . . . that's . . .
- Chris Standaert: It's easy to say in here.
- Richard Phillips: . . . the reason I'm asking the question.
- Jason Attaman: Your thinking is correct, at least from other physicians I work with.
- Chris Standaert: You might see people try to narrow the joint level down, do more than one medial branch block and then they're down to one to two joints, I could see that happening with this, but I don't, probably not a massive deal I wouldn't think.
- Craig Blackmore: Six months? Twelve months?
- Michael Souter: How will you know if it's been effective if you start adding it to any frequency less than six months. I think this is of the outcome studies we have.
- Chris Standaert: You should get at least six months of good relief from the procedure or you shouldn't be doing it again.
- Marie Brown: Right.

- Chris Standaert: If you get two months of good relief, why are you doing it again?
- Michael Souter: Well, no, what I'm just saying is if you start adding in procedures any more frequently than q.6 months, then it's going to be difficult to know what your outcome is.
- Craig Blackmore: So, is it six months or is it 12 months or?
- Marie Brown: You mean to start with? You're talking about to start with?
- Craig Blackmore: I mean before you can get another one.
- Michael Souter: Six.
- Craig Blackmore: So, you have documented clinically-significant improvement in pain and/or function.
- Chris Standaert: If you mandate to have relief for six months, how can you do another one at six months, because they should still have relief from the first one.
- Craig Blackmore: Well, that's how this is. It says allowed, they're allowing one every six months if they had improvement from the first round. I'm not saying . . .
- Chris Standaert: For six months.
- Marie Brown: Not improvement for six months, just improvement.
- Craig Blackmore: Clinically-significant improvement.
- Chris Standaert: So, if they get improvement, we have to define a timeframe for how long we think they should benefit from this before they do it again. So, if somebody's better for a week, you're going to do it again in six months? We're going to allow this again in six months? I don't think that's what the intentions are. Studies don't say that. I think requiring benefit for six months before you're allowed to do it again and do a repeat neurotomy is reasonable, and usually a neurotomy a minimum of nine months at 12 months at six months.
- Craig Blackmore: So, I, so how we operationalize that and what do other people feel about that as a suggestion, saying we would allow it every say 12 months if they had six months of improvement the first time? Is that what I'm hearing?
- Chris Standaert: Nine or 12?
- Craig Blackmore: Or nine.
- Carson Odegard: Maybe nine. If they have another six months of pain, (_____).

- Chris Standaert: So, better for six months and then deteriorate. The window of how long these work is somewhere in that nine to, looking at the aggregate data, is somewhere in that window.
- Michael Souter: Do you need to say allowed every x-months if you actually say that you have to have demonstrated improvement for at least six months?
- Chris Standaert: Probably not.
- Michael Souter: I think if you've, if you've got demonstrated improvement over six months and now you've gotten a recurrent need, then you have a right . . .
- Chris Standaert: You can't do it without this anyway because . . .
- Michael Souter: . . . to set the time interval.
- Chris Standaert: . . . you already made it to six.
- Marie Brown: That's right.
- Chris Standaert: Right. Right. Self-evident. So, it would be repeat neurotomy allowed with significant, if significant clinical improvement in pain and/or function.
- Craig Blackmore: At six months.
- Chris Standaert: For six months, yeah.
- Michael Souter: Or you could just say with document of clinically-significant improvement in pain and/or function over six months before repeat injection.
- Craig Blackmore: Do we want and/or function or do we want and function?
- Michael Souter: Sometimes, it depends on what function somebody is capable of to actually trust them, you know.
- Craig Blackmore: I'm asking the question.
- Michael Souter: If they're lying.
- Marie Brown: I think requiring function is reasonable, both pain and function.
- Seth Schwartz: I don't totally agree with that. It is a slippery slope. I mean, what we've seen is pain. We're not seeing a huge improvement in function and, and I don't know that I think pain in and of itself is not an important outcome. I mean, if you have six months of pain relief that, that seems significant. I mean, surely, sure we want you to go back to work, but we don't want you at home, you know, unable, you know, hurting either necessarily.

- Chris Standaert: And we don't know that this would result in a significant improvement on the scales we use, ODI and Rowland and things, because you may be doing it for other reasons. Somebody can't look up, bend over, do other things. They just don't pick that up in the process of those measures, and we don't have a standardized measure to tell us that, so.
- Seth Schwartz: Yeah, I think and/or is probably better.
- Richard Phillips: And/or or just or.
- Seth Schwartz: And/or.
- Marie Brown: And/or.
- Craig Blackmore: Gary and Lee, is this operationalizable, if that's a word?
- Gary Franklin: Yeah, I would think so.
- Kevin Walsh: May I ask a question about the age limitation? The studies appear to have included people who are much older than 17, though their inclusion criteria may have been 17, the actual range was much higher inclusion. Does that make a difference? I don't know if this applies to people who are 18 and older?
- Craig Blackmore: I mean, I guess if we knew that nobody under a certain age had been involved in any of the studies we could maybe make that conclusion, but is that true?
- Chris Standaert: Well, in the neck, we're not on the neck, but it comes up in whiplash in 20-somethings, but I don't, that's a difficult decision.
- Craig Blackmore: Yeah, I don't, I don't, I don't know what the range, I see the mean and standard deviation.
- Chris Standaert: It's typically going to be a degenerative process, which will be older people. It's not 18-year-olds typically.
- Kevin Walsh: And on the flip side, is there an upper age limit? Was there an upper age limit in the studies?
- Chris Standaert: I don't think so.
- Craig Blackmore: Again, my opinion would be that we don't have compelling evidence to deal with anything except that under the age of 18 has issues, because it's pediatric and they weren't included on our trial.
- Chris Standaert: And the issue of improvement in pain and/or function after a differential block, do we really just want pain, or do we really measure function?

- Craig Blackmore: You can be more active and still hurt. That, that's a viable outcome, right? I still have pain but I'm doing more.
- Chris Standaert: But as for that two hours you have lidocaine in you, I guess if you document it some way. I don't know how you document 80% improvement in function.
- Seth Schwartz: And I don't think any of the studies used that. It was just pain. It was pain related.
- Joann Elmore: It was just pain if you're going to be evidence based.
- Chris Standaert: And it keeps it clear because then you have that one form they have to fill out that documents rate of pain.
- Michelle Simon: So, there's some more things to consider. On our, in our report, section 2.5 is indications and contraindications for facet neurotomy on top of page 81, and there is a list of things there, which we haven't even considered for this yet, so maybe we should take a look at that and see if anything is compelling. The top of page 81.
- Craig Blackmore: Cancer and pregnancy and . . .
- Michelle Simon: Oh, it's tenderness over facet joints on palpation, pain on hyperextension, pain non-exacerbated by coughing or sneezing. There's all kinds of stuff.
- Chris Standaert: Is that the appendix, again?
- Michelle Simon: Page 81. I don't think it's appendix.
- Craig Blackmore: Should we say something to the extent of six months of continuous low back pain clinically referable to the facet joint? I mean, that's what they're getting at.
- Chris Standaert: Include the following.
- Craig Blackmore: Six months of continuous low back pain.
- Chris Standaert: Yeah, but it didn't say tenderness over the facet joints, which is on there.
- Craig Blackmore: Clinically-referable to the facet joint. I mean, there's going to be clinical (_____) and we're not going to be able to dictate (_____)
- Richard Phillips: That was my original thought. I thought that physical exam was not a good way to diagnose it, though.
- Michelle Simon: The one study we have shows it is just as equivalent.
- Kevin Walsh: It's just as good.

- Michelle Simon: It's just as good in the one RCT.
- Richard Phillips: As the diagnostic studies?
- Michelle Simon: Jade or something.
- Kevin Walsh: Yeah. Page four.
- Richard Phillips: See, I, I was thinking that was just the one study. I thought, in general, it wasn't as good.
- Kevin Walsh: That was the only study.
- Richard Phillips: Yeah, that's what I mean.
- Michelle Simon: Cohen, 2010.
- Kevin Walsh: Well then there is, there is no more in general. It's the only study we have.
- Richard Phillips: Oh, I see what you're saying.
- Craig Blackmore: Alright, other thoughts on this?
- Chris Standaert: This does mention major mental illness and psychiatric disorder as contraindications, as well. I don't know if we want to go there or not.
- Group: No.
- Craig Blackmore: OK, any other, I kind of want to rush things, but any other? OK, are we happy with this? I'll take a show of hands. Those who are not happy, do you have other suggestions for this list or not?
- Michelle Simon: I still think that patient selected by 100% improvement would be better. That's my feeling. You would know for sure. I mean, it's not such an intervention that we're like, wow, what great results, you know? So, I think requesting 100% improvement is not unreasonable.
- Craig Blackmore: And we tried and we got a vote five to four.
- Kevin Walsh: I agree.
- Michelle Simon: You asked.
- Craig Blackmore: Alright. So, I want to take a formal vote again. This is with the pink cards, and this time we'll be voting for cover, no cover, or cover with conditions as defined in this list.
- Josh Morse: This replaces your previous vote?

- Craig Blackmore: This replaces our previous because now we have an understanding of what conditions would look like.
- Josh Morse: Seven cover with conditions, four no cover. That did not change the previous vote.
- Craig Blackmore: OK. So, we reconciled that with the coverage decisions, and we've already discussed those and, um, we are similar but we believe that the evidence that we have is best reflected in things like the inclusion criteria for the randomized clinical trials. So, where are, where we differ slightly from other recommendations is because we believe that that is the evidence that defines the groups in which it might be effected best. OK, and then we move on to the cervical. Do you have what you need for that?
- Josh Morse: I do, thank you.
- Craig Blackmore: So, cervical. Again, I think we're probably not headed to a cover unconditionally. I might, well let's have some discussion. We need to discuss the cervical. We have one randomized clinical trial, which is, which we've talked about already in terms of the inclusion criteria and there's twelve patients in each arm, and there appeared to be some benefit in the intervention group, although the significance and the magnitude of that benefit is perhaps less clear, and then I guess there is actually two components of cervical that we might need to parse out, and one is neck pain and the other is headache. The, who did the study?
- Chris Standaert: Govind?
- Craig Blackmore: No, the, the New England Journal of Medicine, Long?
- Chris Standaert: Lord.
- Craig Blackmore: Lord, Lord. That, I believe, was specifically neck pain. I just want to double check. Is that?
- Chris Standaert: I think it was below C2-3.
- Richard Phillips: Also, I seem to recall that in the reading that there's the C2-C3 level is managed differently than the other levels, too, just because of the anatomy involving the odontoid, is that correct, or?
- Chris Standaert: And they said they excluded C2-3 from the Lord study because of technical issues, but C2-3 is thought of as the headache source, not so much neck pain. It refers up typically. It's a different procedure. It's the same idea but technically a different procedure.
- Seth Schwartz: I don't think we've seen much evidence for success with headache.

- Craig Blackmore: Does anybody think we've seen much evidence for success with headache?
- Chris Standaert: Did the vendor go look? I know some of the commenters asked that you look separately at C2-3. Did you go look separately for C2-3? Did you find things or did you not? You don't pick up the, the Govind study mentioned it, but that was a nonrandomized trial.
- Craig Blackmore: So, we're going to divide it up. We'll deal first with cervical spine for cervical pain and again, I don't think I'm hearing cover unconditionally. So, our choices are going to be no cover or cover with some set of conditions and the best evidence seems to be this Lord study. Discussion on that? Comfortable with where we are? OK, so let's go to our tan cards and replace. I think we've already dealt with the outcomes on our sheets, and they are pretty much the same, except headache is an outcome for the second part of this. So, the first voting question, is there sufficient evidence under some or all situations that the technology, neurotomy, is effective for cervical pain and, compared to other treatments.
- Josh Morse: Six unproven, five more.
- Craig Blackmore: Safety.
- Josh Morse: Eight unproven, two less, one equivalent.
- Craig Blackmore: Cost-effectiveness.
- Josh Morse: Eleven unproven.
- Craig Blackmore: Further discussion at this point?
- Chris Standaert: We have one tiny study that showed great results with 100% improvement with the triple-block protocol that Gary, Dr. Franklin, was talking about earlier. That's how the study was done. Theoretically, it seems similar to lumbar, but the data is different.
- Michael Souter: I just, logically, don't see a distinction between doing a saline block and doing a short and long-acting again. That's all I'm saying.
- Craig Blackmore: OK, same thing. We'll vote for coverage and if we make a decision for cover with conditions, we'll go back to the exercise of defining those, and then we'll revote. If we come down on either cover or no cover then this will be the final vote.
- Josh Morse: Seven cover with conditions, four no cover.
- Craig Blackmore: So, starting with the list that's already in front of us, I think I would probably change the 80% to 100%, since that's what we have data on. Any other issues on here? We're talking about C3, C4 and lower.

- Chris Standaert: And the word headache comes out, probably.
- Craig Blackmore: The word headache comes out?
- Chris Standaert: He has neck pain/headache. If you put headache in, then you could just do the cervical spine, including C2-3 under the same position. If you left it at neck pain/headache we could consider cervical spine, in general, wouldn't separate out C2-3, because that's where people would be going for neurotomy in the case of a headache.
- Joann Elmore: This is all based on the Lord study, which was . . .
- Chris Standaert: Excluded C2-3.
- Joann Elmore: Correct. It's from C3 and below.
- Craig Blackmore: Procedurally, so let's do that. Let's go, procedurally I want to put this aside and look at the upper cervical spine and treatment of headache. So just, just leave it alone for now, please, Margaret, Christine, whoever's got it and tabling this for the moment, I want to take a new vote on cervical treatment for headache, right? Does that make sense? Is everybody clear?
- Michael Souter: Yes.
- Craig Blackmore: So, for now, we're not looking at neck pain. We're looking purely at headache. So, this would be injection C3 and above. So, we're going to go through our grey, our tan cards, effectiveness. Are you guys clear or are you?
- Joann Elmore: Yeah, in other words, you're talking about the one study with 30 patients.
- Josh Morse: OK, you're voting. I see ten unproven, one less, and that was on effectiveness?
- Craig Blackmore: Safety.
- Josh Morse: Ten unproven, one less.
- Craig Blackmore: Cost-effectiveness.
- Josh Morse: Unproven, 11.
- Craig Blackmore: OK, so now limiting ourselves to what I just said, headache upper cervical spine coverage decision.
- Josh Morse: OK, ten no cover, one cover with conditions.
- Craig Blackmore: So, then we can define the cervical conditions, as they have to be at below the C3 level.

- Kevin Walsh: I would like to ask a question of the people who voted to cover cervical spine. The decision was based on one study, why would you not use the inclusion, limit yourself to the inclusion criteria of that study?
- Craig Blackmore: I mean, I think we're still working on that.
- Kevin Walsh: Right, I'm just throwing that out.
- Craig Blackmore: How do they differ from this? I haven't looked at it.
- Seth Schwartz: The only difference is the use of saline as a negative control.
- Kevin Walsh: Right, they used, you had to have no response to saline.
- Seth Schwartz: And I think as, as Michael said, and I think some of us are thinking, that the duration of effect effectively shows that it's a control.
- Craig Blackmore: Because you're doing another invasive procedure to confirm the diagnosis, and we're not convinced that it's worth doing another procedure I think is the, is the feeling that is coming out. Yeah, go ahead.
- Carson Odegard: (_____)
- Michael Souter: Carson, can you speak into the microphone, please?
- Carson Odegard: Oh, sure. How often do you see this procedure done at above C3 for neck pain, not headaches.
- Jason Attaman: Fairly rarely. The C2-3 joint, in general, is most commonly responsible for the headaches, some upper neck pain also. It does have involvement in neck pain, upper neck pain.
- Carson Odegard: Yeah, that's my question. If we limit it to C3, below C3, we're going to eliminate or not include those patients that have neck pain above that level.
- Craig Blackmore: So, what were the inclusion criteria for the Lord study?
- Seth Schwartz: Those patients were excluded from the Lord study. That's why, and that was, I think, what that decision was based on. There is no data, we saw no data for usefulness of this procedure in those patients with that problem. There may be data or case reports, but from what we saw in the controlled studies, there was no data.
- Michael Souter: And just knowing the, you know, getting into a world of hurt with the (_____) as well.
- David McCulloch: (_____) C2.

- Michael Souter: Well, and vertebral artery and all.
- Craig Blackmore: OK, other thoughts on these conditions?
- Chris Standaert: Well, the question should we use what Lord used is tricky. I have the study here, and they have criteria that are similar to what we have. They have, be seen by a specialist, try conventional therapy without success, and referred by a practitioner, but they said to come in to get the study, which then included the triple block protocol that had to have a block out of their own unit or private radiology practice before coming into this study. So, they were already blocked before they came in the study and then they got triple-blocked again is the way I read it. So, we can't use that as an inclusion criteria, really. They're saying they had already been pre-screened to get blocked before they got there.
- Joann Elmore: Prescreened with the block, and if they are positive, about two-thirds are positive, then they come, and then they get this triple screen, which is placebo-controlled.
- Chris Standaert: Right, but . . .
- Joann Elmore: Then if we're going to go with conditions, I say, according to whatever they did here in order to get in.
- Craig Blackmore: I, I would leave it as it is just because it's simpler and I don't know that we're really adding much other than complexity by doing that parallel to what we've done in the lumbar spine.
- Michelle Simon: I agree. I think it's possible if you do the prescreening you have less interventions on patients than if everybody goes straight to three blocks.
- Craig Blackmore: Well, the three blocks aren't at the same time. I mean, you do one and if it doesn't help then, you don't. . .
- Michelle Simon: Right, but they all have to happen
- Craig Blackmore: . . . do the others.
- Michelle Simon: Don't they all have to happen? You're not, so even in the people if they fail one.
- Chris Standaert: By this, if they fail one of these, you'd eliminate them. One block and they didn't respond, they're out. If they don't have 100% relief, they're out.
- Michelle Simon: Alright, well it's kind of the same thing, then, really.
- Craig Blackmore: I mean, I think it's, it's . . .
- Chris Standaert: (_____) totally get there.

- Craig Blackmore: . . . very nearly the same thing.
- Marie Brown: Yes.
- Craig Blackmore: Less complex. So, you have to have 100% improvement after each of two blocks. So, if you don't have 100% improvement after the first one, you're done.
- Seth Schwartz: And we're talking the C3-4 through?
- Chris Standaert: The C7 facet joint. (_____) No, C3-4.
- Craig Blackmore: C3-4.
- Michael Souter: And how many levels do we do at a time, a single level?
- Richard Phillips: Is that C7-T1? Well, you said C3-4 through C7.
- Craig Blackmore: C6-7 is what they did. C6-7.
- Michelle Simon: Can we do slashes?
- Craig Blackmore: You want to do slashes? OK, do we want to specify the number of levels? That's not on here.
- Michael Souter: That's what is was asking, was it in the study?
- Josh Morse: It indicates not reported in the report.
- Marie Brown: Can we include anything at the time here?
- Chris Standaert: So, symptomatic joints we have, you know, I guess it's only one joint per patient. One person had bilateral (_____) No, I see. They had three, nine, in the (_____) with one joint C2-3 contralateral C4-5 and another patient C2-3 and contralateral C5-6, and another patient C2-3 and ipsilateral C4-5 and C5-6 in one patient and bilateral C2-3 and C5-6 and contralateral C6-7 in one patient. Most of them had one. Two of the 24 had more than two.
- Michael Souter: I suppose my only concern in doing multiple levels in a spine patient is just about what we may be doing to the musculature, the innervation of the musculature again, you know, but I don't know that there's any sound data to kind of base that concern on.
- Craig Blackmore: I mean, I'm happy being conservative and limiting it to a single level.
- Michael Souter: I, I would agree with that.
- Craig Blackmore: So, we said one to two in the lumbar.

- Chris Standaert: So, one level, so you could do bilateral at the same level or one joint?
- Craig Blackmore: One joint.
- Chris Standaert: We can't do bilateral? I'm asking because of what . . .
- Craig Blackmore: I, I would, you know, I think, I think the, the evidence is weak. I would try to keep the invasiveness to the minimum and I would, I don't know. This is the facet level, it's not the . . .
- Carson Odegard: But you're excluding C7.
- Craig Blackmore: We're excluding the C8 nerve root and . . .
- Chris Standaert: C7-T1 facet.
- Craig Blackmore: And that's just the, it's just the inclusion criteria that's in the study.
- Richard Phillips: Does that include bilaterally, the one joint for intervention.
- Craig Blackmore: Not as written.
- Richard Phillips: So, it's, it's one joint unilaterally?
- Craig Blackmore: That's what, that's what that says. Comments?
- Chris Standaert: I don't have an issue with bilateral (_____)
- Craig Blackmore: OK. So, we'll vote again with conditions as specified. Your choices are no cover, cover, or cover with conditions.
- Seth Schwartz: May I ask a just clarifying question, and maybe the agencies need to answer this, but one joint per intervention, is that, is that one intervention in a six-month period or is that different levels within a, because you have different levels, different interventions.
- Craig Blackmore: You get one, and then if it works, you get another one in six, if you get six months of relief, you can have another one.
- Seth Schwartz: The same intervention.
- Richard Phillips: Well, it shouldn't it, in other words, should it read one level specific intervention or should it just be one neck intervention, is that what you're asking?
- Seth Schwartz: I guess that's what I'm trying to ask, yes.
- Chris Standaert: I wouldn't, I wouldn't read this as they can come back a month later and do the joint above and the joint above and the joint above if that's what you're saying.

- Michelle Simon: They could. They could read it.
- Joann Elmore: That's what they did in Lord.
- Chris Standaert: Could you read this, is that how you would read this that you can come back next month and do?
- Joann Elmore: If I wanted to. I don't think it's clear. You said (_____) clear, yeah?
- Michael Souter: So, do you want to change each intervention to each episode of car?
- Chris Standaert: It's the same thing. I can get one next week and another episode (_____)
- Michael Souter: You know, you've got a time limit on it. You can't get it for six months.
- Craig Blackmore: So, we could have a new line that said no spine injection in the previous six months or something along those lines.
- Chris Standaert: You could say before repeat, before further repeat or further neurotomy, I guess so if they miss that time, they can come back in six months and do the level above? That doesn't make any sense either. Yeah, actually that does.
- Marie Brown: That works.
- Chris Standaert: That does it.
- Michael Souter: It's more specific, OK.
- Craig Blackmore: Thank you.
- Michelle Simon: Do you want to say cervical or do you just want to (_____)
- Marie Brown: Change the upcoming, change the other one, too.
- Michael Souter: Yeah, lumbar.
- Craig Blackmore: Staff is charged with changing the other one to reflect that without another vote. So, we're voting, as specified.
- Josh Morse: Seven cover with conditions, four no cover.
- Craig Blackmore: And now there's one other, there's one other aspect to this. We've made decisions about lumbar and cervical, but we've not made an explicit decision about, between C7 and L1. So, in terms of the thoracic spine, I want to go to the tan cards, if I could, in terms of the thoracic spine, is there evidence of effectiveness?
- Chris Standaert: We had no data on the thoracic spine at all.

Josh Morse: Eleven unproven.

Craig Blackmore: So, we're voting unproven, I think, because we saw that the data was basically, there was no data. In terms of safety.

Josh Morse: Eleven unproven.

Craig Blackmore: Cost-effectiveness.

Josh Morse: Eleven unproven.

Craig Blackmore: I believe the cover, the national coverage decisions do not cover or if they do and we conflict it's because there's no data, and so, our final decision on the thoracic spine.

Josh Morse: Eleven no cover.

Craig Blackmore: Josh, do you have what you need?

Richard Phillips: Aren't we good?

Josh Morse: I think we have what we need.

Craig Blackmore: Documentation?

Josh Morse: Thank you.

Craig Blackmore: We've already completed the thing we were supposed to do at the end of the day. So, we are adjourned, thank you, very much.