Craig Blackmore: I'm going to call the meeting to order. I apologize for starting a few minutes late, but understand there was an accident on I-5 and it slowed things down quite a bit, but we now have a forum. Josh, do you want to say anything to start or…

Josh Morse: Yes. Good morning. I'm Josh Morse. I'm the HTA Program Director. Just a few brief announcements before we start. There are restrooms outside this room, down the hall to the right. In the event of an emergency follow the exit signs and I believe it's downstairs and then out to the parking area. If you're interested in commenting today on the two topics that are open for consideration we have sign-in sheets outside specific to those topics. We also have a list serve sign-up that I encourage you to put your name and contact information on. It's the best way for the program to get information out to you. Thank you.

Craig Blackmore: I don't have any specific comments. Do you have any specific program updates?

Man: No specific updates.

Craig Blackmore: Okay. We're going to launch right in then and start with the HTA previous meeting business. And the first thing we need to do is consider the minutes from the last meeting, which have been available on the web and to the committee members and I'll ask the committee if there are any comments or corrections or concerns about the minutes and I would also entertain a motion to approve and… the minutes are in your blue folders here for your review.

Man: I move to accept the minutes.

Man: Second.

Craig Blackmore: I have a motion to second. Any further discussion? We'll have a vote on approval of the minutes from the September 16th HTCC

meeting. I'll just have a show of hands. All in favor? Six votes for approval.

The second order of business is to have our final binding vote on the draft findings and decisions from the previous meeting and we'll start with the femoroacetabular impingement syndrome draft findings and decision and that's in your blue packet. We've also received public comments, which have also been made available to the committee members prior to the meeting. So I will open the… open to the committee members for any discussion or comments on the draft findings and decisions for femoroacetabular impingement.

I just had one comment I wanted to make based on some of the feedback we've gotten in the public comments on the draft findings and decisions. And that was that there was a concern raised about what was perceived as what might be a change in one of the key questions between the initial drafting of the questions and the technology assessment. And the point was that in the initial drafting the key questions talked about the effectiveness of the femoroacetabular impingement surgery, but didn't specify a comparison group and then in the technology assessment the comparison group was specified that we were comparing to no surgery. And I think in the context of evidence-based medicine you have to compare it to something and so by specifying that we were comparing to no surgery I think that was simply clarifying that this wasn't about comparing one surgical intervention to another. It was about comparing "is the surgery effective compared to non-surgical treatment" meaning anything else—meaning standard medical therapy? And again a concern was raised that by having this really semantic change in the key questions that we would somehow be excluding consideration of case series and there were a number of case series around that topic. And that's really not the case. The case series around femoroacetabular impingement surgery were all included in the technology assessment report. They were all available to the committee members. That was some of the evidence that was considered in our decision making.

In fact, in general case series is one of the weakest forms of evidence. There's a lot of biases that can come into play, selection bias being one, regression to the mean particularly in the context of more subjective outcomes like pain. There's challenges with outcomes assessment in the context of a case

series, challenges with blinding, challenges with placebo effect. So again a case series is usually, in most circumstances, not considered very strong evidence and the committee relies on the best available evidence. So we would in general await trials, controlled trials, particularly randomized clinical trials if they're available more highly. So I just wanted to clarify that. Any other comments on the draft findings and decisions for FAI? So I'd entertain a motion to approve.

Man: Motion to approve.

Man: Second.

Craig Blackmore: Okay. We'll have a vote for approval of the draft findings and coverage decision and just a show of hands all in favor? And six in favor.

Woman: It's actually seven. Seven committee members.

Craig Blackmore: Seven. Thank you. Um, okay, next is the draft findings and decisions for PET scan… are there any comments from committee members regarding the Positron Emission Tomography scans for lymphoma or the public comments we've received on that topic? Okay. If not, I will entertain a motion to approve.

Man: Motion to approve.

Man: Second.

Craig Blackmore: All right. I have a motion and a second. Again, we'll have a show of hands. All in favor of final approval of the draft findings and coverage decision for Positron Emission Tomography in lymphoma? And again seven approved.

Next order of business is scheduled and open public comments on the microprocessor controlled lower limb prostheses. We're actually a little ahead of time. I think what we will do is launch into those, particularly if there is anyone here who signed up to provide comments, and then we'll open to comments from people on the phone if there are any; and because we're a little ahead we might circle back and ask again when we get into that time window. Does that resonate?

Man: Actually we did move beyond the program background, which we could do now. We have a few slides on the program background updates.

Craig Blackmore: That sounds good. That sounds great.

Man: Is that the full screen?

Woman: This? Yes.

Josh Morse: Okay. Thank you. So good morning. My name is Josh Morse. I am the Program Director. Thank you for attending this morning. So as Dr. Blackmore mentioned if you wish to comment and you are on the phone we will ask you at that time and there are sign-in sheets for those who are present.

So briefly I'll go over a bit of the program background and how the program works. Today's topics again are microprocessor controlled lower limb prostheses and osteochondral allograft autograft transplantation.

The HTA program was initiated in 2005 through legislation. It was part of Governor Gregoire's evidence-based health care improvement process. It results in a collaboration across state agencies to review health technologies and determine the best value for the state when it purchases health care. So why health technology assessment? HTA is part of that overall strategy to address the strong link between increasing spending and new technology. The diffusion of medical technology is a key driver of cost increases and where there's a lack of sufficient evidence there's also sometimes a variation in utilization and the program attempts to address that.

Key products include paying for what works is the ultimate outcome through transparency. Topics are published. Criteria and reports are evaluated in an open and public meeting. The technology assessment is written for each topic. Decisions are scientifically based on the best available evidence to address the key questions including is it safe? Is it effective? And does it provide value?

Technologies are selected by the director of the Health Care Authority. Technologies can be nominated from the public or from within the state agencies. A vendor is contracted to produce

the written technology assessment reports. The clinical committee makes the coverage determination and the agencies then implement the determinations.

Evidence for these determinations can come from a variety of sources for efficacy or the question of how the technology functions in ideal environments, randomized controlled trials and meta-analyses may be the strongest evidence. For effectiveness, which is a question of how well technologies work in real-world environments; larger studies, rigorous observational cohorts or population level analyses may be the most informative. Safety is a variant of effectiveness. Larger trials would tend to provide better evidence. Case reports, case series and FDA are also sources of information. Cost information might come from modeled analyses or formal cost effectiveness studies or be based on actual expenditures from modeling or administrative data.

The committee must consider and review the health technology assessment and they may consider other information including information provided by the Health Care Authority or other state agencies, reports and testimony from advisory groups and the public and public comment.

This is a list of topics that are upcoming. In March the committee will review sleep apnea diagnosis and treatment along with bone morphogenic protein. Slated for later next year are stereotactic radiosurgery, robotic assisted surgical devices, upper endoscopy for GERD, and potentially CT/MR for pelvic and abdominal pain and elective C-section. That concludes my comments. Thank you.

Craig Blackmore: Okay. Since we're a little bit ahead of schedule… we try to have the public comments occur when it is on the agenda in case somebody had intended to call in at that time or wasn't here yet. So we're going to jump ahead and do the agency utilization and outcomes and then put the public comment back in at… in roughly the scheduled time period. So Gary?

Gary Franklin: You're really far away. Thanks very much. This is a really interesting technology. It's… thank you. We have some agency data and some thoughts on the report.

Craig Blackmore: Sorry to interrupt for one second, Gary. Committee members, it's in your packet if your eyes are as bad as mine and you have trouble seeing the screen. The slides are in here. Thanks.

Gary Franklin: So we're talking about the microprocessor-controlled lower limb prostheses, MPC for short. The background is that… the hope is that this kind of computerized control of prosthetic functions and now we're talking about lower limb knee or above-knee amputations for the most part. There is a foot MPC, but the evidence on that is almost non-existent. So what we're mostly talking about today is the evidence and your decisions on the knee MPC.

The idea is that better computerized control of prosthetic functions such as control of resistance in the knee, control of stability will theoretically improve balance, gait speed and efficiency. I think the main issues here really relate to "what is the evidence on objective outcomes such as measurement of actual efficiency and oxygen consumption and measurements of actual performance in these studies?" There are a lot of outcome measures that are self-reported related to other aspects of patient preference and patient satisfaction that are important. But the thing that I tried to focus on in here is, you know, what are the objective measures? And it's an important area because the database is basically level 3 and level 4 studies. So the question is which outcomes really are going to carry the day? So the question is, do these MPC prosthesis improve function and more capacity for example in a meaningful way? What constitutes a meaningfully better use of energy and how does that translate into whether it's actually allowing the person to do more in their life and have a better life? These are severe injuries and obviously in the L&I population these are catastrophic injuries for anyone. But when it happens at work we have to pay particular attention to that at L&I.

In terms of the agency medical director's usual look at safety, efficacy and cost, there's not a lot of safety issues with this thing. There is an issue that has to do with it can't get wet because if it gets wet I understand, and others here can speak to it probably better than I, maybe it stops working or something goes wrong with it and so I understand that you actually have to have both a regular prosthesis and an MPC prosthesis most of the time when you have an MPC prosthesis.

Efficacy – we have high concerns because of the low level of data. And cost we have high concerns, which you'll see in a minute. So this is one of the few technologies that we've looked at where the

issue really comes down to… for a huge cost is the added value worth what the patient gets out of it in terms of quality of life, performance and efficiency?

And then is that increased cost of MPC worth the added gain and in whom and for what purpose and under what conditions? So one example is none of the studies are done in vascular… cases with vascular amputations and most of the insurance company's coverage policies exclude the MPC for vascular indications. But I'm not sure that's anything that was dealt with too much in the report or even in our own internal discussions because L&I doesn't see those cases.

Medicaid… Medicare uses and generally most… I believe most rehab units that assess patients for prostheses use a functional scale called the prosthetic functional level assessment and you can see these… there are five levels that are assigned and the question with this kind of a technology is, again, in whom? And I think the feeling among most of the payers and L&I's policy is that you should have a very high level of functioning if you're going to be using this kind of technology and that level of functioning would have to be a K-3 or a K-4. That using this in a… there's a little stuff in the literature that suggests that people that have a K-2 level might benefit from it but the evidence is extremely flimsy. L&I has been focusing its policy on folks that can at least… at least have the ability or potential for ambulation with variable cadence. Typical of the community ambulator who has the ability to transfer most environmental barriers and that it may have vocational therapeutic or exercise impacts that are significant.

So when you're thinking about your decision as to whether to cover it or not, if the decision is to cover we would strongly recommend that you consider which conditions it would be covered under. One which I don't have on here because L&I doesn't deal with it is whether it should be allowed in people with vascular amputations. The database is pretty much non-existent in them. Most people agree that folks that receive this should have very high cognitive functioning levels and very good cardiovascular function. I think that one of the reasons it might not be used in people with vascular amputations is that they have severe cardiovascular problems. So that's just something else to think about. But L&I's coverage policy was done some years ago and we did our own internal technology assessment, which was before some of the studies came out. I think it was in 2003 or

something like that. And our nurses who were heavily involved in these decisions put together, with that technology assessment, a coverage policy and that is that the patient would have to have a CMS functional level 3 or 4 and all of the following: a unilateral transfemoral amputation. Because, you know, worker's comp goals are to return people to work that there had to be a work oriented goal that could be met by this new technology. The client's work requires the ability to ambulate long distances, say 400 yards at varying speeds or over uneven ground or with frequent use of stairs required. In addition, the client had to have demonstrated mastery of the use of a prosthetic knee that had both stance and hydraulic swing control because that's what this… you need to have both of those functions going pretty well in somebody that has descent cognitive and cardiovascular function. And possibly with some other additional performance goals that will be important to meet and that's why you're using this expensive technology. And then there's weight issues. L&I uses a weight of 220. Other coverage policies have other weights as well.

There's no specific, you know, detailed coverage policy. It's basically covered at Medicaid and Uniform Medical. And the foot/ankle system is not covered by any agency.

These are the codes. It's a very complex area. I'm hoping that some of the folks here that have more experience with this can speak to it. But the most important thing here is this… is the average payment per member, which is the third line on this slide. L&I paid for eight of these things. I can't remember what the timeframe was. And it was $101,000 per client for the technology. L&I's reimbursement policies are generally sort of more generous. We're actually in general above the median for commercial payers for everything we pay for. So we're going to be a lot higher than Medicaid and Medicare. We're generally higher than the average commercial payer on those things. So you can look at our payment as being sort of more on the generous side. And then the others have lower per patient costs. PEB was $43,500 for 14 patients and Medicaid was of course much lower. But the average cost for the non-MPC you can see at L&I was about $22,000. So the cost of the MPC is about five times higher than the cost of the regular prosthesis in these patients.

Man: So Gary can I interrupt? I mean there's huge differences here between L&I and Medicaid. You think those differences are

mainly just a function of higher reimbursement or are these different patients? Or are they getting different equipment?

Gary Franklin: I can't tell you for sure. I don't know. Margaret, do you have any idea about that?

Margaret Dennis: I'm sorry, I didn't hear the question.

Man: There's a ten-fold difference between L&I and Medicaid in average patient member payments for the MCP and I was trying to get a feel for is that simply difference in how much they reimburse for the same product or is it a difference in the product itself or is there… I mean…

Margaret Dennis: I believe it is a difference in the reimbursement and the fact that PEB is in the middle between the two indicates that they have a coverage of benefits coordination with other payers for part of their membership. So you're seeing a partial full reimbursement for PEB, full reimbursement for L&I and an under-reimbursement for Medicaid.

Man: But it is interesting that if you look at the reimbursement for the non-MPC prosthesis the very… if you look at the non-MPC reimbursement per patient the variation is much less for the non-MPC than it is for the MPC. So the difference between Medicaid and L&I and the MPC is almost ten-fold difference and the difference in the regular prosthesis is only a four-fold difference on average. So, you know, I think part of it is, you know, how this specific kind of thing is paid for by L&I. But it is a reimbursement difference.

Man: I'm going to let you get to the end of your presentation and then I'm sure everybody will have more questions.

Gary Franklin: And, you know, without going into gory detail here a lot of the cost is not only the equipment, but there's always a lot of add-ons and that's true for the MPC and the non-MPC prosthesis. Perhaps people in the room that are more skilled and knowledgeable about exactly all the little components and all could speak to some of this stuff.

Man: Gary, I have a question about… you mentioned that the… most of these patients that the MPC do have also have the non-MPC as well.

Gary Franklin: I'm sorry, that was called to my attention just before this meeting. I was actually not aware of that. Does somebody else in the room who knows more about this, can they speak to that?

Craig Blackmore: Thanks, Christopher. Let's get through your presentation and then we'll get back into the sort of question and answer period after that just to keep us on schedule. I messed up the schedule. I apologize. Let's continue.

Gary Franklin: Most insurer's do lean towards coverage for the lower extremity MPC, but not in coverage for the ankle and feet MPCs.

So the state agency sum review is that it's a really cost benefit issue. Whether these things are proven or unproven for clinically meaningful outcomes and I would focus on the objective measures as well as the patient-reported perception measures. The high cost and the set cost would necessitate an important view of functional assessment and classification and maybe a careful performance-based assessment in certain centers of excellence if that could be done, and I would certainly defer to the rehab people in the room as to whether that is practical or not. And no evidence to support coverage of the microprocessor ankle foot prosthesis yet.

The kinds of recommendations if you're gonna do coverage… one possibility is non-coverage because of the objective measure studies are pretty weak. The energy expenditure studies really are either non-significant or… on oxygen consumption show something on the order of less than 10% saved energy or no difference in saved energy. So it's that kind of thing I guess I'd be looking at. But if you do decide to cover it we'd certainly… should do it with conditions—functional level 3 or 4, weight, cardio and cognitive issues should be limitations, vascular, non-vascular, a demonstrated knee for a higher performance. That is that you need it because you need it for work, you need it because you have other compelling performance issues.

Sorry, I didn't switch the slide. Anyway, so that's about it. You probably get the picture of what we're saying. Any questions? Yeah, Chris?

Chris: So I'd appreciate it if you could clarify what was brought up by both the reviewers of the report in the cost issue. And what I'm

trying to figure out is the cost of the… what does prosthesis add to the cost… what this joint adds to the cost of a total prosthesis and prosthesis fitting versus a non-MPC joint? And as the reviewers point out the data here… is the data… to get one of these knees we're talking about you have to be either transfemoral or hip disarticulation level amputee. So below knee you don't get one of these. And both reviewers stated it looked like there well may be data on below knee amputees in the comparative data who don't even get a knee prosthesis. So if you have a transtibial amputee and you compare that cost to the cost of anybody over the transfemoral amputation, the transfemoral prosthesis is going to be a lot more expensive and a hip disarticulation even more expensive and more difficult. And I'm trying… I don't understand from the data you gave us what the relative cost of a prosthesis for somebody with a transfemoral amputation would be with either an MPC or a non-MPC joint? Then what is the cost differential? And I couldn't pull that out. And that's an important… that's the whole question here, isn't it? And then the issue of if they actually have to have two prostheses because these are weather dependent or there is some other restriction on the use of them in various circumstances that obviously would have a significant cost differential as well. But can you get at that issue of what is the actual addictive cost of putting in this type of joint into a transfemoral prosthesis as opposed to one that doesn't have this?

Gary Franklin: Well, we tried to get it to the best that we could. Margaret, do you have anything on that?

Margaret Dennis: Yeah. In the evidence report there was a set of tables that listed the various components of the prosthetics and there is one column that is just the microprocessor costs in the… I'm not sure which page it is.

Man: So that's from the technology vendors' evidence report, not from the…

Margaret Dennis: It is embedded… it is our data, the agency data embedded in the technology.

Woman: Page 17.

Margaret Dennis: Yeah, page 17.

Man: Do you want to ask him now or do you want to defer that?

Margaret Dennis: And so there were three tables there; one for each agency showing average costs.

Man: So we're looking now at the technology vendors report on page 17, a table which details cost components for the MPC versus non-MPC prosthetic patients. It's not clear to me from looking at this table if the patient's are otherwise identical in the two groups or if the prosthetic… if the MCP group includes more transfemoral versus the… versus transtibial in the other group. Is that… that's the question that is raised. Can you help us, Margaret?

Margaret Dennis: I don't think that… we did not evaluate the data considering that. So we basically only know this is how much it costs for the MPC… MCP version.

Man: So there's a potential selection bias if you will in that the non-MCP group may have a larger number of less expensive transtibial versus the MCP group might have a greater number of more expensive transfemoral. Is that a fair… potential, we don't know that.

Margaret Dennis: True.

Man: Well I guess I'll also ask the vendor, you know, part of that technology assessment is to look at costs and I think that most people agree that this is much more expensive than a regular prosthesis. Did you have any other sources of information on cost?

Craig Blackmore: Can you just introduce yourself since we haven't heard from you?

Nora Henrikson: Yeah. So I'm Nora Henrikson with Spectrum Research who is the vendor for this. We didn't look at the state data. We just looked at the published literature and we found three studies that were all done in European settings. So… and the trends were similar that the microprocessor prosthetics were more expensive. But there wasn't any published literature that included US data.

Craig Blackmore: Okay. So just to prevent us from getting too far ahead, are there any other questions specific to the data the agency medical directors have brought to us?

Man: Yeah. I have one question about the… both devices being used on one person. When you did your analysis here, your assessment… is there some crossover between these patients where the data for the non-MPC could be… is the same patient as the microcontrolled?

Man: Yeah, I don't know. In L&I those eight patients… a lot of those patients would have had a regular prosthesis to start with and then migrated to an MPC. Now whether… the issue as to whether somebody actually always needs two, a non-MPC and an MPC because the MPC can't get wet… I don't know the answer to that, but that was just brought to my attention today. I didn't realize that before and I'm not even sure that's true. So I don't know.

Man: I had a question just about your statement about the exclusions for peripheral vascular disease. So how do you make that distinction? Is that in the basis of express symptomatology? With a concern about, you know, peripheral vascular disease in relation to generalized cardiovascular disease? Are you making that distinction based on an ICD9 code or on, you know, history of cardiovascular symptoms that would lead you to exclude them?

Man: I'm sorry, were you asking me?

Man: Yeah.

Man: This is an implementation question, right? How would you implement…

Man: Well, no. My impression was from what you said that you were already excluding patients with peripheral vascular disease.

Man: No. What I said was I hadn't actually paid attention to that in my own mind because L&I doesn't deal with peripheral vascular amputees.

Man: Okay. The other agencies?

Man: I'm sure that there may be some of those in the Medicaid population. I don't know about PEB. Steve, do you know if you have any peripheral vascular amputees?

Steve Hammond: [inaudible]

Man: In any case the main point I was trying to make is that almost all carriers have a policy that the patient who you might be considering this in should have fairly high functioning cardiovascular function and fairly high functioning cognitive function and the issue here really is… and almost none of the studies are in vascular amputees. They were almost all in traumatic amputees. So that's… one issue is a lack of evidence in that group and the second issue is do they have enough functionality to actually be able to use one of these things effectively?

Man: I understand the implication. I'm just trying to see where that linkage of peripheral vascular disease and the assumption of cardiovascular dysfunction, you know, how strong that is in your process.

Man: I don't know any more than I've said. I'm sorry.

Craig Blackmore: We'll have more opportunity to ask questions of Gary and his colleagues. But at this point we should move on and we should double back to the scheduled and open public comments. Denise, where are we in terms of public comment? Do we have people signed up?

Denise Santoyo: [inaudible]

Craig Blackmore: So for those of you who are making public comments we ask that you identify yourself and tell us if you are representing any organization or group of people and also to tell us if you have any financial conflicts of interest, if you are paid by an organization that produces a product or if somebody has provided you with travel expenses or not. And we'll start with those who have… we didn't have anybody in advance, right Denise? Or did we?

Denise Santoyo: No, we did not.

Craig Blackmore: Okay. So we will start with the people who are here present and who have signed in and forgive my pronunciation, but first we have Sanjay Perti. We allow five minutes per individual… sorry, three minutes per individual whose here and Denise will give you a warning when you have a minute left. Denise, is that…?

Denise Santoyo: That is correct.

Craig Blackmore: Either of these microphones or that would be fine.

Sanjay Perti: My name is Sanjay Perti. I'm President of Washington Prosthetic and Orthotic Association. I'm also a Clinical Prosthetist/Orthetist in Seattle, Washington. First I want to address some of the comments that came up here in that last presentation. C-Leg technology, which is one of the… which was the first microprocessor knee is not new. It's been around for approximately 15 years. So we're not talking about emergent technology. Some of the newer products, competing products are newer, but that one has been around for 15 years and has been very successful.

As to the comment of patients having… requiring two legs they are water sensitive. If they are submersed in water they would quit working like any electronic device. But simple rain water splashing or anything to that effect would not cause malfunction. It would be a very rare occasion that a person would require two legs. Usually that would be somebody that actually is doing some sort of activity where there is risk that the prosthesis would be submerged. So that would be the one indication that someone would potentially require two legs or use a non-microprocessor knee.

Limits of vascular-related amputations in clinical practice I have not seen in this exclusion from private insurance. You go through a prior authorization process usually and that is a limit that we do not see. It's based usually on functional level and medical necessity.

As to cost on a C-Leg, I did provide a statement that was sent in and I don't know if you guys have that in front of you. But it does go directly to the difference in costs on a C-Leg versus a non-microprocessor alternative. It comes out to between $22,000 and $23,000 for the microprocessor. When you're looking at the cost of prosthetics and all of these charts I think that the financial data is very deceptive to say the least. You're comparing two groups that are very not… there's very little relationship to them. There's a microprocessor group and a non-microprocessor group. The non-microprocessor group by the definition of all the codes included includes anything from a partial foot prosthesis that can be $400 to a transtibial prosthesis to a knee disartic to a transfemoral amputation to a hip disartic. So it includes many, many things. Most of that population is going to be the lower

level amputations and that's why there's many more members and the costs are much lower.

In the microprocessor knee group we are only seeing transfemoral and hip disartic—the higher level amputations. So the costs are much, much higher. So the two groups really have no comparison.

When you were asking about Medicaid and the reimbursement and the differences between them… Medicaid typically doesn't pay for a microprocessor knee as a primary payer. You'd have to go to a prior auth… through a prior authorization process and I don't know of anyone who has actually ever gotten that through. So I would doubt that Medicaid has ever been a primary payer. Most likely there is a secondary payer to Medicare. So you're looking at them paying a 20% portion of that and that's where those numbers are very, very small.

If you look at total costs here and the difference you're looking at 13 people and 8 in L&I and if you look at the cost of that $23,000 difference per person between a non-microprocessor alternative that looks considerably different over a four-year period than the data that was put into the pie charts, graphs and tables. And that's what you really should look at is the difference between a non-microprocessor alternative and the microprocessor alternative.

One last thing. No one talked about safety… reported microprocessors. Significantly decreased stumbles and falls and this has been noted in laboratory research and that is a part of the research that has not been noted. This was an active… in not the laboratory research and that's definitely a huge part of this technology that has not been looked at very indepthly or stated on. Thank you.

Craig Blackmore: I just… I realized you gave us your name and who you represented, but I'm not sure we had a statement as to whether you had any financial…

Sanjay Perti: Oh, um, I probably get my parking paid.

Craig Blackmore: Thank you.

Sanjay Perti: You're welcome.

Craig Blackmore: Next on our list is Carl Enteman(?).

Carl Enteman: Good morning. My name is Carl Enteman. I am a business owner. I have a business in Tacoma and in Federal Way. I've been doing prosthetics and orthotics for 30 years. The reason I'm here today is because I understand there is a huge difference in the reported cost of providing these devices than what I see in my practice. Just last week I wrote up a write-up for an above-the-knee amputee including a microprocessor knee and the cost difference between the prosthesis with and without the microprocessor knee was about $23,000, which Mr. Perte just mentioned. I don't know where the $100,000 for these devices is coming from. I've never been able to add enough codes to one of these things to get it above about $60,000 and the difference between Labor & Industries and most of the other insurances is that the fee schedule for Labor & Industries was set for prosthetics at 25% above Medicare and that was agreed on with quite a bit of research and Labor & Industries decided at that point and at that amount of reimbursement that they were saving money over the previous type of decision making. So the numbers are a little bit higher than you'd find for Medicare and DSHS/Medicaid. But the price difference between a non-microprocessor prosthesis and a microprocessor prosthesis is much less than what was reported. I just did this write-up and there's one code basically for the microprocessor knee and the reimbursement through Medicare is about $23,000. That's a difference. It's not $50,000, $60,000 or $80,000 and I don't know where those numbers are coming from.

Does anybody have any questions on this? As a business owner I'm trying to justify, you know, when I provide these devices for people… there was a statement made that they should only be provided for functional level 3s and 4s, which are very high functional levels. I disagree with that. I think somebody who is at a K-4 functional level doesn't need one of these. Primarily a microprocessor knee is to provide stumble recovery, prevent from falling. Those are for the people who are in the K-2 and low K-3 levels. And I think that that should be taken into consideration that the lower levels; not so much the people who are very strong and very high functional levels they don't need this kind of technology. I don't think it should be ruled out if they have problem with balance and things like that. But I think that whole thing should be shifted to a lower level of function. Thank you.

Craig Blackmore: Thank you. Could I get one of the… seem not to have power out of the… at least one of these power strips. Is there anyone here who has not yet signed up who wishes to comment? Is there anybody on the phone who wishes to provide a comment? Denise… if you're there on the phone we're going to double check and make sure we've got the mute system worked out. Is there anybody on the phone?

So we've gotten no phone comments. So we're going to close the public comment period.

Okay. Next on the agenda is the report from the technology vendor, Spectrum.

Nora Henrikson: So I'm Nora. I'll be giving the presentation. Is it okay if I stay here or should I go up there?

Craig Blackmore: That's fine.

Nora Henrikson: Okay. Is there a clicker? Is this any better? Hello? That sounds like it is working. So I'm Nora and I helped prepare this report. This is our author team up on the screen. And I just want to say… acknowledge Brian Hafner who is our… helped us with this report. You'll also see his name as one of the authors on one of the studies that we looked at. He has gone through our conflict of interest procedures and he was not involved at all in our assessment of the quality of the evidence.

So these are the abbreviations that we used in this report. We… I'm not going to talk too much about this, but I know these will be available publicly. So I wanted to have them up there. We do use MCP for microprocessor-controlled prosthesis and NMCP. So the background of course is this 1.6 million people living with limb loss and that number is increasing. 65% of those are estimated to be lower limb loss, so transfemoral or transtibial amputations. 80% of amputations are from vascular disease as has been mentioned. 20% roughly from trauma; mostly from trauma and then a small portion from cancer or congenital issues.

So of course the burden of lower limb loss is extensive and not hard for any of us to imagine—falls, uneven walking on different types of surfaces, difficulty maintaining symmetric gait, as well as the cognitive and metabolic demands for walking can lead to difficulties with walking at various speeds and can lead to reduced

activities over time. Having one intact limb can lead to joint pain, back pain, osteoarthritis, and obesity related to that reduced activity again. And there are significant community reintegration issues that these individuals face such as returning to work and general quality of life.

So the treatment for limb loss is a prostheses. A lower limb prostheses consists of a socket, which connects to the limb, a foot and a knee if it's a transfemoral amputation and then all the adaptors to connect them together. There are more than 50 prosthetic feet available. One of them is a microprocessor knee as was mentioned and there are about 200 prosthetic knees and about 20 of those are microprocessor. The clinical team uses a lot of different factors when they're recommending their prescription. They are listed here as has been mentioned function is one of the big ones. And so this actually is the same information that's on the slide that Dr. Franklin showed. So we used, instead of the K level, we put it up here as the Medicare functional classification levels. But it's exactly the same information. So 0 is the lowest level and 4 is the highest level of function.

So the technology that we looked at… we were asked to look at in this report was microprocessor controlled lower limb prostheses. A little bit about those – the knees have sensors to monitor and adjust the movements of swing phase when the knee is in motion, stance phase when it's at rest, and then switching between the two. And for the MCP feet they modify the angle of the ankle during the gait.

The potential benefits of these are balance, improved ambulation, safety, stumbles and falls, confidence we think is a pretty big one because if people feel like they're able to move better then they might… that might have impacts on the types of activities that they attempt. And that's consistent with some of the reviews that we looked at. The potential harms are likely fairly similar to a non-microprocessor knee except for that device malfunction if it was submerged in water as was mentioned.

And this is a rapidly progressing field of bioengineering so there's several things that will be emerging over the coming years— powered prosthesis that don't just have a sensor, but have an actual motor in them as well as the volitional ones that are kind of connected to the nervous system somehow. And I don't know

anything more than that. But we didn't look at those in this report.

So this is a picture of one. I just want to say there's a little box there that has a cost in it. This is just pulled from a publically available newspaper article. So we didn't produce this slide at that level. Though you can see there is a socket at the top. I guess there's a pointer here. So there's a socket at the top and then this would be the microprocessor in here and the knee joint and then it goes down and connects to a foot. And then over here is a picture of a microprocessor knee right next to a non-microprocessor knee. You can see they look pretty similar from the outside. And we actually have one here if anybody wants to have a visual aid.

So the microprocessors in these knees perform different functions depending on whether the sensors regulate the stance, the swing or the switching between the two. These are the models that we're aware of that list what they do. Our colleagues on this report were, you know, I think appropriately wanting to drive that point home that they're not all the same. Not all the knees are the same.

So the key questions we were expected to look at… I'll go through them in detail, but key question 1 was around outcomes and measures and clinically meaningful improvement. Key question 2 is efficacy and effectiveness. 3 is safety. 4 is differential safety or efficacy is subpopulations and 5 was the economic considerations.

So the aim of our report was… and the service of answering those questions to systematically review and critically appraise available comparative evidence on these devices. We did decide to focus the report on outcomes that were assessed in real world settings. And that was because we thought the existing evidence in previous technologies has… previous systematic reviews really did support the efficacy of these devices in controlled settings such as stepping down a ramp in a lab or turning, you know, doing some… in an indoor obstacle course, that kind of thing. But we did include those… all those outcomes in our report, but they were in a summary fashion and they weren't… we didn't critically appraise them.

And this is a piece that came out in JAMA right when we were doing the report, which I think provides a nice conceptual

framework of what our choice was around really wanting to focus this work on patients… outcomes that patients experience in real world settings.

So our inclusion criteria was adults who have had transfemoral or transtibial limb loss. The intervention was any microprocessor controlled knee or foot prosthesis and we allowed any comparison. It turned out that all of the comparisons that made it into our review were non-microprocessor knees, but we did allow any at that stage. And again we focused on outcomes assessed in uncontrolled settings. For the study designs we included comparative clinical studies of either outcomes or costs and outcomes and then used those to form the structure of how we answer key question 1 about outcomes. And we used the kind of standard inclusion criteria about English language.

So this is just… it's very hard to see. I'm sorry. This is in the report. This described our literature search process and just shows that we ended up with 12 articles included in the systematic review and then off to the lower right is 12 articles that we summarized their findings.

So looking at the MCP feet. This is going to be a short presentation because we didn't find any studies on MCP feet that met our inclusion criteria. There is one foot that's available and there's a few… the studies… there was like I think two or three studies that did not meet our criteria for inclusion. They were very basic early biomechanical work. And most of the payer policies and such we looked at still consider that an emerging technology.

Man: Can I just drill down on that a little?

Nora Henrikson: Yep.

Man: They didn't meet your criteria because they weren't sort of outcomes in a real clinical setting? Was that the… these were just laboratory studies?

Nora Henrikson: I think I have them here. So in Appendix B we list the ones that we excluded. I'd have to go back and look. One we have does not address the outcomes of interest. So that might have been a biomechanical outcome—like a feasibility type. And then the last

two were the Segal and the Wolf were biokinetic… or kinetics and kinematics, which were not… we didn't include in the report.

Man: Thank you.

Nora Henrikson: Okay. So moving on to the MCP knees. We looked at 12 articles… we included 12 articles. It consisted of a total of 614 people. They were predominantly male, predominantly traumatic etiology, a mean age from 36 to 54, and about… a range of 10 to 20 years since the limb loss. And the function… most of the studies… several of them did use an actual functional level as described by the levels I showed before and some described more qualitatively and all tended to be kind of, you know, at some minimum level of ambulation or activity.

All the studies employed a crossover design, which is within subject design where the person puts on a knee and uses it for a while and then puts on another knee and uses that for a while and then both things are measured. That's probably an over-simplification, but it's kind of a unique design for this area and I can see why that study is used and it can happen over… the knees can be assessed over several months of use, not just one time or day or whatever. But of course the big difficulty here is that the study is really hard to have a blinded study for this because the person is going to know what knee they're wearing.

I think to do a true blinded design here would be… involve some kind of manufacture of a sham knee, which we haven't… and only two studies that were actually the same study population randomized the order of the knee that was put on.

The length of follow-up varied from 7 days to 15 months. The follow-up ranged from… or the lost to follow-up ranged from 100% all the way down to 27% followed up. Nine studies used the C-Leg, which seems to be the most commonly used one as has been mentioned. Two studies the intelligent prosthesis and one study on the adaptive knee. And all of them used various non-microprocessor knees as a comparison.

So this slide describes the level of evidence that we assigned to each of the studies. We had three level 2 studies, which were considered moderate quality. And the other nine were considered low quality, which is a level 3. And then listed there are some of the… a summary of the methodological issues that

might affect how these studies work. So the lack of blinding I've mentioned, a measurement bias. Certainly with a recall bias when you're asking when there's a length of time between the exposure and the… asking the person to assess the device there's a potential for a recall bias. An expectation bias would tend to favor a newer knee possibly. The generalizability has already been mentioned. These are predominantly male, predominantly traumatic etiology. The heterogeneity outcomes measures… I'll talk a little bit about that, but I think this field is still very much evolving and the length of follow-up was… the longest one was 15 months and when you think about a real-life use of this kind of device as somebody such as a young trauma survivor might be using it for a lifetime. So we had some discussion about what would be the appropriate length of follow-up? But I'm pretty sure that the ones included here were short-term. And then the loss to follow-up is likely… is worth looking at. So for example in the Klute(?) and Williams ones, which are both very small sample size 10 of 18 people did not complete this study and 6 of those were for… because they didn't like the microprocessor knee or couldn't use it or whatever.

So the results for key question 1… this starts out as a little bit of a qualitative assessment about what are the expected treatment outcomes. This was kind of our… maybe the beginning of a conceptual model of the… the table describes some ambulation potential improvements as a result of using these devices. Again, it might depend on whether it's a swing control, stance control or switching between them both. Total energy expenditure as measured here is step counts—either step counts or increased physical activity. Global or condition specific quality of life, activities of daily living, and then moving at more globally improved productivity and reduced caregiver burden.

And this table describes the outcomes that actually were assessed in the studies that made it… that we included. So on the left is the objective measures. One study used doubly labeled water, which involved measuring energy expenditure from urine samples that were after a person who'd used the knee in their real life and then another study uses step activity monitor to count steps per day and minutes of activity per day. On the right side is patient reported outcomes that were used—the SF-36 and the EQ-5D. The SF-36 I think is of course the very well used measure that has been… there are population norms for limb loss for that measure

and then the 60 is a calculation based on six questions from the SF-36 and that's often used in cost-effectiveness studies.

There were three condition-specific measures—prosthesis evaluation questionnaire and the 50 question survey by Barry and a prosthetic cognitive burden scale. And then a whole series of individual items around stumbles and falls and preference.

So our conclusions are that there are two methods used to objectively assess MCP use in real-world settings. The majority of the patient reported outcomes are single item measures—the generic instruments, the SF-36, there are populations norms for limb loss and the EQ-5D we didn't find any validity data for this particular population. That's a very well used measure in Europe and there are some articles that suggest a 5% to 10% improvement as the kind of rule of thumb as being a meaningful improvement, but I don't know how that applies to this situation.

The condition-specific instruments – the PEQ three subscales demonstrated some kind of validity and five subscales demonstrated some test retest reliability. The 50 question survey there was no validity data available and limited reliability. And minimally clinically important difference has not been established for any of the condition-specific measures that we were aware of.

So looking at key question 2 around efficacy and effectiveness – these are the data on energy use summarized and I apologize for the busy slide. There's a little bit of method to it in that the numbers that are bolded represent which device was favored because there was just so many outcomes to look at. We thought this might be a good way to represent it visually. Though I hope you can see it's definitely in the report. So the majority of the outcomes around energy use did favor… did go in the direction of the microprocessor knee though the differences were often small and we don't know the cognitive or the clinical significance of those.

Impact on ambulation – at the top is the outcomes instrument, the PEQ and the 50-question survey and the EQ-5D. All did favor the microprocessor knee. An objective measure of impact on ambulation we have one study from one of five people that used the step activity monitor and the results were mixed there. So again the clinical significance is difficult to evaluate.

Quality of life – looking at the SF-36 and the EQ-5D as well as various scales of the PEQ tended to all favor the microprocessor knees. So there is some evidence in the direction of improving for improvement associated with microprocessor knees.

Similar for confidence, activities of daily living and comfort.

Again, same issue with clinical significance, but the direction is similar.

So our summary is that the MCPs are likely associated… the evidence is low or very low for all of these, but there is some evidence that the activities of daily living, balance confidence, comfort and fit and preference are in the direction of microprocessor prosthetics.

So safety – these are all patient-reported outcomes of real life use of these devices in their home or community settings. So the PEQ was a non-significant result with a… but that's a sub-domain of residual… called the residual limb and the only questions around safety fall into that domain. So it includes other things as well. So that one is not significant or roughly similar.

And then the 50-question survey favors the microprocessor knees. The EQ-5D pain was non significant. I don't know that we would expect a difference on pain. And then stumbles and falls – these are all not validated individual items and they were all in the direction of favoring microprocessor knees.

The last study, Jepson(?), was five people and the results there were mixed and that was the one study that was on an adaptive knee. So a different model.

So our conclusions that there's again low or very low levels of evidence that equivalent or improved stumbles/falls improvement on residual limb effects, equipment failure tended to favor microprocessor knees and there's no data around morbidity or mortality with these devices.

On this it's the subgroup analysis… we were asked to look several of these listed here, or all of these listed here. We didn't find any evidence on any of these gender, age, psychological, psychosocial, provider characteristics or payer characteristics. We found two articles that… two articles… paragraphs in two articles that did

some kind of subgroup type analysis both neither of them were particularly testing for interaction or anything that we would like to see. But one looked separately at the lower function. So functional level 2 compared to the functional level 3 people that were in the study. And it was eight and seven people respectively, I believe, and did find that there were… both groups saw improvements in the same direction as far as energy expenditure, satisfaction and safety, but the direction… the magnitude was greater in the functional level 3 group.

Then Seelen – that study did a sort of post hoc analysis of first-time prosthesis users and did find improved SF-36 scores in both the first time and the total group. But there is a high potential for bias with that one and I'll talk about that in a minute.

So our conclusions are that people with lower function level may experience some benefits, very low strength of evidence there and that very low evidence the quality of life benefits extend to people who are first-time users. So looking at the economic questions we were asked to look at costs, both direct and indirects, cost effectiveness, short- and long-term and then ongoing maintenance and replacements. So we found three cost-effectiveness studies. I'll just say that none of these were done in the U.S. and so it's really, you know, problematic to try to transfer that data to a U.S. setting. They were all done in Europe and… but I'll just talk a little bit about some of the trends that we saw.

So the Gerzeli was 100 people with traumatic injury from a worker's compensation database in Italy. I believe it was the National Worker's Compensation Group and they looked at two analyses; one using just health care costs and another using the health care plus greater societal costs like transportation, overnight stays, you know, costs to the patient, and productivity issues. And then the data sources were survey, administrative data, the medical records, expert panel to determine costs and market values of the prostheses and then national fee schedules.

The Seelen study we used 24 people who were receiving care at a rehabilitation center. More than half of them were traumatic amputees. It did use a societal perspective. So a health care plus patient and family costs. And the data sources were patient survey, but it did use the recall of the… for the NMCP. So I believe they asked… I always confuse these two. Yeah, I think they asked… for this one they asked the patients what would… so what

is your quality of life now with this new knee? And then what if you didn't have this knee, what would your quality of life be? So there's some potential for bias there, administrative data and national fee schedules.

And the Brodtkorb study was done in Sweden. 20 people from a prosthesis clinic used a health care cost perspective and considered the data sources were interviews of patients about their use of the C-Leg and hypothetical use of the NMCP. And then the interviews with patient's prosthetists and interviews with manufacturers. So these are really, especially the interviews with the prosthetists and the manufacturers have high potential for bias.

So the trends that we see on these economic studies, the time horizon varies. The Seelen study in the middle there called itself a pilot study. So I think it was, you know, there might be some other work coming out of that group at some point. So they didn't do any modeling. The Gerzeli and the Brodtkorb studies did model out to five and eight years respectively and that was both stated as chosen because of the manufacturer guarantees on length of time that the product is guaranteed.

And so the parameters favoring the microprocessor knees consistently across were the quality of life measures, the productivity measures where they were used, and then, you know, non health care costs. And then parameters favoring the non-microprocessor knees of course were the cost of the device. And I don't know that there is too many patterns besides… born around the health care cost did tend to favor the non-microprocessor knees. Parameters that were not significant were some of the health care around the general care around providing care for these individuals, hospitalizations, transportation, and house adaptation. And then there's… each of them has some potential for bias. So in the Gerzeli study we have the use of expert opinion as a potential for bias, baseline differences in the daily prosthesis use were higher in the MCP group for that one. So they came in with a higher number of hours per day using their prosthesis and again that generalizability issue.

On the Seelen study the SF-36 was assessed retrospectively for a time early in rehabilitation. So when you're looking at the use of these devices over somebody's lifetime or over eight years the

one measure early in the rehab process may or may not be a sufficient way to measure that.

And then on the Brodtkorb study interviews… using interviews as the source data is always… always introduces bias. The MCP group was, as I mentioned, they were people who were already dissatisfied with their non-microprocessor knee and that's why they switched and that's why they were measured. Again, that was the hypothetical assessment of the EQ5 knee. So imagine if you didn't have this knee kind of thing. And then the retrospective analysis of looking back to the time they didn't have their knee.

So all of these were low quality studies. We thought the Gerzeli one we rated that systematically as having the best economic evaluation methods. We found that to be moderate quality. The other two were low quality economic evaluation methods.

So given all that the trends that we found, again there's no studies using U.S. cost data. The European studies suggest that MCP purchase and fitting is more expensive. The European studies suggest that cost-effectiveness analysis using… the more societal perspectives they used and the longer timeframe the more they tend to favor the microprocessor knees and that they are even with the evidence here. There is insufficient evidence to evaluate long-term costs.

So in summary the strength of evidence for all these conclusions is low or very low and the generalizability to the larger population of people with limb loss such as vascular etiology is unknown. The evidence on these knees in real-world settings… I've given all that. Those limitations on the strength of evidence… there really was a consistent small improvement that seemed to be associated with the MCP, but we have… it was very difficult to evaluate if that's clinically significant and there is insufficient evidence to evaluate microprocessor feet, outcomes past one year, and costs in U.S. settings.

And this is my last slide. The limitations of the current evidence… it would be great if there were validated patient-centered measures of microprocessor use in real-world settings including measures of clinical significance. Prospective studies of the effect of these devices on health and function over time so that chicken and egg question has been mentioned. Do these devices actually

improve function? Or are they only given to people with higher function? Those could only be answered with a perspective study. The study participants of more broadly-defined populations would be helpful to see that. That would provide additional evidence and the cost-effectiveness of these devices in the U.S. Thanks.

Craig Blackmore: Thank you. So the way we do this in terms of discussion is a little bit artificial. We have separate blocks for questions directed to our vendor, which would be questions from the committee about specific aspects of the report and then we have our more general discussion among the committee members as we move towards a decision. And what I'm going to propose to do is we just take a few minutes to see if the committee members have any questions specific to what you presented us with and then take a little break and then we'll come back and have a more general discussion. But I also wanted to take a minute and just introduce our clinical experts. I'm actually going to have you introduce yourself. Well, introduce yourself. Your input is going to be valuable here.

Joseph Czerniecki: My name is Dr. Joe Czerniecki. I work at the Seattle VA Medical Center. I'm also a Professor of Rehabilitation at the University of Washington and our Associate Director of our Research Center, which involves prosthetic development and innovation at the VA Medical Center. It's a pleasure to be here. Thank you.

Craig Blackmore: Thank you for coming. The charge of the clinical expert is to really help us to understand the technical aspects of this, which are obviously quite complex. We have the vendor to help us distill the evidence. That's spectrum expertise. But there's going to be a lot of questions here that the evidence doesn't even begin to address and a lot of questions about how the technology is used, etc. that you're going to be quite valuable to help us. That being said let's now go back and see if there are any specific questions the committee has for the vendor report. Committee members, Michelle?

Michelle Simon: I had a question about who… what studies you chose to include and actually one of the public presenters brought up the issue of studies that are in controlled environments versus studies that are in real world environments. I think you did review some of the studies that were also in controlled environments. My question is, if you included those studies in your overall evidence report would it significantly change the outcomes that you found?

Nora Henrikson: No, I don't think so. Is this still on?

Man: Yes.

Nora Henrikson: I don't think so. The reviews that we looked at and the previous technology assessments all tended to come up with the conclusion that there is evidence to support the efficacy in laboratory settings of these devices. Does that answer your question?

Michelle Simon: I'm a little confused. You… so the studies in the controlled environments basically say the same thing as the real-world environments or they do not?

Nora Henrikson: Yeah, they do.

Michelle Simon: They do? Okay. Thanks.

Man: Could I refer you to page 74, Table 17? And about three-quarters of the way down there's the Jepson study. The last row – falls because knee has given way. That's an extraordinary difference and I'm having trouble with those two numbers.

Nora Henrikson: Okay. So that study had five people in it. So there were… so 40% would mean that two people, I guess, had reported a fall because the knee had given way. How else can I help you under…

Man: Well, I'm looking at falls. The numbers are a little bit better for the MCP, but in this row there's… so two falls out of five with the MCP group and no falls out of five with the non-MCP group. Is that a correct interpretation of the two numbers?

Nora Henrikson: I believe so.

Man: The two lines above says there are no falls in the last eight weeks in that group.

Nora Henrikson: Yep.

Man: So one says no falls in the MCP group 3 and the non-MCP. One says, you know, or one person stumbled versus two people stumbled and then the last line says that two versus… the exact opposite of what the first line says. Is that your question?

Man: Yeah.

Man: It doesn't make any sense.

Man: Well, and… yes.

Man: So did people fall or not fall with… more with one knee versus the other.

Nora Henrikson: I will look it up right now.

Man: Can I just ask a question again? This may be a familiar frame, but it's just about trying to understand the labels that gets attached to these studies because, you know, sometimes I think that does color perceptions. You use an assessment of quality in your demean so I'm referring to your table 25 on page 103 for framework for assessing overall strength of evidence and you say that, you know, a quality assessment should be at least 80% to the studies or level of evidence 1 or 2. So am I to understand from that then that if you have one excellent study and four, for lack of a better word, crap studies, then that constitutes a low quality, which by then definition going through the strength of evidence criteria that you would apply in table 26, you know, would actually give you a very low level of evidence.

Nora Henrikson: I'm just catching up with you as far as getting to the page number.

Man: Where are you?

Nora Henrikson: Page 103.

Man: Page 103, yeah.

Nora Henrikson: So could you walk me through that one more time? I'm sorry.

Man: Yeah. Looking at table 25, which makes, you know, you are looking at the quality domain to make an assessment there and… quality at least 80% to the studies are level of evidence 1 or 2. And so, you know, if there for example you did not meet that quality challenge, you know, let's say you had one excellent study and then the cohort that you had examined there was another four poorer quality studies. Then by definition that application and this would actually constitute, you know, that would fail that

quality… the level of evidence over all of the cohort that you are examining. That then when you go onto the strength of evidence criteria would ultimately have to give you a very low strength of evidence because you have one good study and four poor studies. I'm trying to understand the framework by which you are attaching the labels of low quality and very low quality strength of evidence criteria.

Nora Henrikson: That's right.

Man: So… in other words the strength of evidence criteria is a relative judgment based on the overall literature that's available to you from your search rather than, you know, the merits of one study.

Nora Henrikson: Correct. Correct. And I'll… just to… your point is well taken about it… if there was an excellent study; there weren't any in this particular that we assessed.

Man: But the principle of dilution remains the same.

Man: Can I go back to [inaudible] question back on the reviews in the controlled settings, which is like page 40 on your report? You summarize them briefly, but it seems that would still be relevant data. It's not real-world data, but it's data nonetheless on the function of these things and energetics and all that. And did you… going over these reviews, you know, one looks like it says it takes studies from the manufacturer's website and the other one doesn't mention that. Are they high quality reviews? Or were these systematic reviews well done, or are they poorly done systematic reviews? Do you know anything about the quality of them and whether we can rely on their conclusions in any way or no?

Nora Henrikson: So you're on… talking about the Highsmith paper?

Man: The Highsmith and the Work Safe VC paper, yeah. The two of them. The relative quality of them as systematic reviews.

Nora Henrikson: We didn't systematically assess the quality of those reviews. Qualitatively we thought that the Highsmith paper was fairly well done and described fairly transparently. The Work Safe Evidence Based Practice Group report that had the two different versions it was… I think in that one there was a little bit, you know, it wasn't a published in the peer reviewed literature so it had a little bit of a

different format. So I would have to… the quality was probably a little bit less, but I think it was… there were… all these have, you know, were attempts to be systematic.

Man: I had a question about the cost effectiveness studies. Was there any indication of the functional level of the patients that were included in those studies?

Nora Henrikson: Yes. So, on the Broad Corp they were described as generally active. On the Gerzeli it was not reported and on the Seelen study they had a daily use of their prosthesis 12 hours a day. And there was a significant difference between that… between the non-microprocessor users… the non-microprocessor users were at a lower number of hours per day of use at baseline. So those studies were not described in terms of U.S. functional levels. They were more qualitatively described.

Man: Then I have one other question I guess for our clinical expert. Just in terms of the durability of these prosthesis is there any sense that the microprocessor ones last any shorter or longer than the standard prostheses?

Joseph Czerniecki: No. I don't think that there's any significant difference in their relative durability. With the microprocessor controlled knees it's recommended that they go in for an annual sort of "tune-up" to the company and often times the prosthetic firms have a back-up knee, substitute that out while the other one is being maintained or overhauled sort of thing. But, no. And of course I think one of the things we have to be careful of, you know, in kind of looking at all of this sort of data is that we've bundled non-microprocessor controlled knees as a whole sort of family and as you noted there are, you know, a couple hundred non-microprocessor controlled knees and I don't know, you know, and each one of them has unique durability and maintenance and potential problematic requirements. But the next best non-microprocessor controlled knee from a functional perspective is very comparable in terms of its durability/reliability.

Man: So just to follow-up, how long does a knee last? I'm sure there is variability but what's… is it a year? Is it 20 years?

Joseph Czerniecki: Well, you know, it's sort of like, you know, the ads that you see for, you know, a Volvo that's got 859,000 miles, you know, that the manufacturer puts out. I mean effectively you can keep on

replacing parts, add in an item sort of thing. So with many of these for the non-microprocessor controlled knees you can replace bushings, you can replace seals and the hydraulic sort of systems or pneumatic systems. So you're effectively rebuilding it on an on-going basis, but the knee can last a very long time.

Man: Just to follow-up on that question. Sorry about the… what you were saying about, you know, making a comparative judgment of all these knees. From what I'm understanding there and reading through this the main safety benefits to be understood… well, one of the cardinal safety benefits seems to be the ability to switch between swing and stance mode. Am I correct in thinking that? Protection against falls in other words.

Joseph Czerniecki: Yeah. I think the protection against falls feature is one of sort of a stumble recovery mode. With many prosthetic knees if you happen to, for example, trip, stumble, have a miss step where you land on a slightly flexed knee there is basically a catastrophic flexion of the knee and the patient will fall down. With this if it detects a stumble it will actually lock the knee and have a very gradual release of the knee. So effectively you can still stand up if you have a miss step.

Man: But on the basis of the… some of the tables that I… I'm not sure… it was either in the text or in the presentations that we saw that not all knees are the same in that regard being able to actually have that stumble recovery function. The ability to lock the knee. Am I correct?

Man: Yes.

Man: You mean not all microprocessors are controlled or not all knees in general?

Man: The microprocessor controlled knees. They are not all the same in this regard.

Man: No, they don't all do that.

Joseph Czerniecki: Yeah, the C-Leg is relatively unique in that feature.

Man: And that's the one we had much of the data seems to be on the C-Leg.

Man: Yes, the majority of the data.

Man: Yes. I have a question about the processor itself. I can see where it would be somewhat of a lower cost when changing bushings and hydraulics and things that that wouldn't be a real costly thing. But how often do the processors fail and what are the costs of actually, you know, re-implanting a new processor?

Joseph Czerniecki: Yeah. Well, that's actually a really good question and, you know, as a physician prescriber, evaluator and researcher actually the day-to-day sort of maintenance issues are not something that I'm typically familiar with. So, you know, I should probably hesitate to speak to that issue. Obviously the kinds of components and the mechanisms within the microprocessor controlled knees are much more sophisticated. There is, you know, the strain gages and the pylon that function as sensors. There are angular sensors within the knee unit itself. Obviously there are the stance swing transition sort of sensor mechanisms that go into a microprocessor, which then control the flow of hydraulic fluid by the dynamic movement of a needle valve through orifices. So I think there are additional complexities and I'm not sure where and when you might have additional failures within those complexities.

Man: Can we ask one of our presenters how often the processor itself…

Man: Sure. Do either of you two gentleman have a feel for the longevity of a microprocessor?

Man: I have as of yet seen a processor fail. There are points where a knee may reach its useable repair limit where it is basically cheaper to repair… or replace rather than repair. One thing with repaired knees on both non-microprocessor and microprocessor is when you do a repair it's extensive and you get a very short period warranty, maybe 90 days, versus if you replace it you can have a three-year warranty. So at some point with both non-microprocessor knees and microprocessor knees it makes sense to just replace them. Otherwise it's ongoing service, potentially every 90 days versus having a new knee.

Man: Thank you.

Woman: Without randomization to what extent is systematic bias built in all of these toward people who choose who are more active choosing microprocessor knees?

Nora Wilkerson: I think that's a great question. The studies we looked at didn't all address that specifically. In one sense you could look at it as an effectiveness question of often… as I understand the clinical progression is often that people have a non-microprocessor knee first and then they get a microprocessor knee at some point later. But… and not all the studies address that. There was one that did mention that the entry into the study was people who were already dissatisfied with their knee.

Man: It sort of begs the question, is that a bias? I mean if you… if you compare people who don't like their knees to the people that do like their knees that's a bias. But if you compare somebody who has expressed dissatisfaction with their knee between the new and the old technology and they like the new technology I don't know if that's a bias as much as it is a subgroup. Do you know what I mean? I mean maybe those are the people that would benefit that have self-identified. I'm throwing that out there. I don't know, you know, just for consideration.

Man: It would be hard to randomize totally… to blind people. You would almost have to pop… they would know if you switched anything about their prosthesis I would assume. It would be very hard to blind somebody as to which type of knee they had. And these are all experienced users. So they would probably immediately identify the difference and the characteristics and know which one they had. Is that a safe assumption?

Joseph Czerniecki: Well, yeah. I think there's a number of areas where, you know, the blinding could be affected. I mean first of all one has to be recharged. I suppose you could create a sham recharging sort of station where they plug it in and nothing would happen on a more conventional knee. But typically with these microprocessor controlled knees that they are linked to a laptop with the prosthetist and the prosthetist is able to fine-tune the functioning of the prosthetic knee dynamically during gait. So if the patient says, for example, "No, it's not walking fast enough for me. We need to decrease the swing phase resistance," the prosthetist does that interactively. And so, you know, you could never create that with a non-microprocessor knee.

Man: A question again for Nora on this issue of sort of a different… the different knees. And we have issues of sort of potential bias. Like you just pointed out that sort of, you know, that people in these studies sort of know which knee they have and which knee they like before they go in. Most of the studies are experienced users. A lot of them are 10 or 20 years out. And for the comparison knees I guess is there… we've had issues before, technologies, where we've had ROCTs of various sorts, but the comparators may have been relatively poor choices and sort of almost invalidated the study because the comparator was such a poor choice. Is there any… I guess (1) is there any way of… is there any data that really stratifies non-microprocessor controlled knees by energetics and metabolic efficacy and stumbles and falls that leads to… that could point to one or two or three that might be more superior in function; that would be better comparators to a microprocessor controlled… so meaning somebody who wants a different knee than they have doesn't mean they just get a different or a better functioning non-microprocessor controlled. So is there sort of a better gold standard? And is there any sense of what people are actually using as comparators in the studies you read?

Nora Henrikson: Yes.

Man: Does that make sense?

Nora Henrikson: Yeah. I believe most of the… the most common non-microprocessor one is… was this [inaudible] SNS knee. But I have… we did capture that. Do you have anything else you want to say? We didn't do an analysis of the comparison technology in a systematic way.

Man: And the [inaudible] is a swing and stance controlled knee? So it's like a dual hydraulic sort of deal?

Joseph Czerniecki: Yeah. It's a hydraulic controlled knee that basically has both variable swing phase and stance phase resistance based upon its intrinsic hydraulic features and it switches between swing and stance phase, you know, similar to the knee… to the microprocessor controlled knees.

Man: So it's the relatively more sophisticated of the non-microprocessor controlled knee?

Joseph Czerniecki: Yes. That would be a high quality microprocessor.

Craig Blackmore: Any other questions right now for…

Man: Just one more just to… I'm just wondering how much of a learning effort there is in terms of, you know, comfort, use of the knee, etc. From the studies that are available how discernible is that as an effect that you're use or comfort or satisfaction with the knee improves over time? Is there a difference between microprocessor controlled knees and non-microprocessor controlled knees that's apparent? That's a question for both. I think the evidence report and the content expert.

Nora Henrikson: I'm sorry, I didn't listen to the first part because I…

Man: So I'm thinking about, you know, there being a learning effect that basically people get more comfortable in using their prosthesis over time. Is that a discernible effect? And if so is there a difference between the size of that effect in microprocessor controlled knees and non-microprocessor controlled knees?

Nora Henrikson: I don't know the answer to that. That's a great point.

Man: I think it's in the report in the tables. If you go through the months you can see on those outcomes.

Man: So in that point what's the longest we actually have then available and the evidence there for somebody to, you know, to characterize somebody's use of the knee?

Nora Henrikson: A few months. The longest follow-up we have was 15 months and that includes several months use of both… of each knee. And often switching back and forth. So one of the higher quality studies we looked at did, you know, A B, A B pattern… a couple months with each knee.

Joseph Czerniecki: Right. Yeah. I think that has been an issue of how long do you need to wear a microprocessor controlled knee to adequately be able to evaluate its performance? In previous studies that I've been involved with three months was the time period that was sort of recommended by the manufacturer. So we had the patients wearing their microprocessor controlled knee and evaluated their effectiveness at three months afterwards. So that's what we did in our study design. Although I reviewed this

literature, historically, I'm not up on exactly what the time periods were in many of the studies. I think some of them were more brief and some of them may have comparable longer length.

You know, you raise a… I think an interesting and important point about microprocessor controlled knees and the period of adaptation. One of the things that we sort of learned is that, you know, and I think a lot of people sort of feel like, "Well gee if you just provide the prosthetic limb and the optimum prosthesis that the patient will do better. That it is a prosthetic dependent function." However, I think it's important to know that when you have somebody utilize a microprocessor controlled knee ideally they go through an additional phase of rehabilitation and physical therapy so that they learn how to use the microprocessor controlled knee and learn how to use its unique features. Otherwise, what you tend to have is patients revert back to their historical utilization of a prosthesis, i.e. what they did with their non-microprocessor controlled knee and really their ability to take advantage of the features are compromised. So I think sort of a period of motor learning, additional rehabilitation is really advantageous and it helps to facilitate that transition and utilization of the higher quality features. And I think that's also one of the challenges in looking at some of the data. I don't know how frequently that actually occurred.

Man: So I feel us transitioning into the more general discussion. And it's also…

Man: I have one data question.

Nora Henrikson: Could I just… I just wanted to close a couple loops here. So one, the comparison non-microprocessors knees are listed on page 49 and then the other related to the first question around the Jepson article that characterization is what is stated in the article itself. So there's not very good description around what that might mean.

Man: Last question on data. Is there any data on sort of rejection rates of the knee? I mean people who get prostheses and braces and things tend to… if they don't like them they tend to come back and say, "I don't like this." Is there any data on rejection rates on people who get these and come back with them and say, "I want my old knee back," or "I want a different knee. I still don't like this one." Does anybody publish that or no?

Nora Henrikson: Not as such. It would be helpful to have that. I agree. The one study did, you know, eight people dropped out for reasons related to the microprocessor prostheses. The Jepson study did ask, the one with five people of the adaptive knee, did ask if they would prefer to go back and I think two people said they weren't sure. And the other three said they would not return to the non-microprocessor knee. But I haven't seen that captured.

Man: You said that one study six or eight people dropped out because they didn't… run that by me one more time.

Nora Henrikson: Right. I forget which slide it was in but there was…

Man: I heard you say it when you went through it, but can you just run through that again for me?

Nora Henrikson: Yeah, sure. So it was the Kaleigh(?) and Williams studies which were the same study population in two different papers and different sets of outcomes. They started out with I believe 18 people and 10 didn't complete the follow-up and 6 of those it was because of reasons related to the microprocessor knee.

Man: I think two dropped out of the Jepson study.

Nora Henrikson: You're probably right. I would have to double check. The length of follow-up are listed also on page 49. So they are quite variable of why people didn't complete that.

Woman: To what extent are these studies industry funded? About what percent of them? A general estimate?

Nora Henrikson: The one I have at my fingertips are the three economic studies because I… we anticipated questions about that. Two of them… well, one was completely funded by a manufacturer. Another received partial funding and another one did not. And I'll check in my notes at the break for the rest of them.

Craig Blackmore: So let's take about 10 minutes. There's not a clock in the room. I can't have an official clock, but we'll resume here… how about 10:20 we will re-start.

I want to call the meeting back to order. If I could get folks to take their seats, please.

Could I get everyone to take their seats, please? We're going to resume. All right. I'm going to call the meeting back to session. So at this point I'd like to just turn it open to the committee members to see if there are any further questions for either the vendor or more for the agency directors or for our clinical expert. Just take a period of time and see if we can have those questions answered. Anyone?

Woman: I have a question. I had a question about are there centers of excellence in Washington that do fitting and training of these or can we kind of assume that everybody who does it does a good job?

Joseph Czerniecki: That's a really good question. Before Autobach(?), the company that sells the componentry, we'll sell it to a prosthetist and… I hope I'm speaking the truth here. They're required to take a course so that they can actually kind of demonstrate their competency in utilizing it. So it's not something that somebody can just say, "Well, gee, I'm going to fit this and I have absolutely no experience in fitting it." They all have to have a required course to be able to fit it. In terms of the comment about, you know, sort of centers of excellence, there is no private center of excellence.

Woman: So for the C-Leg that's not the Autobach, correct?

Joseph Czerniecki: Autobach is the manufacturer.

Woman: Oh it is? Okay. That's what I wanted to know.

Man: I had a question. If we can get a little more clarity around some of these dollar figures that are being tossed around. Margaret, can you help us out with a better understanding of that $110,000 versus $23,000 dilemma?

Margaret Dennis: Yeah. I'd like to point out that the $100,000 figure was a four-year figure and when we separated our MCP from non-MCP patients we had to… we were not able to discern in one patient which pieces belonged to an MCP and a non-MCP prosthetic. So the… if a patient had any MCP component they were categorized in the MCP category. So those MCP costs reflect the cost of taking care of all the prosthetic knees for an MCP patient over four years including an alternate prosthetic, if there was one, or any

replacements. It could have also… had something to do with whether they were a higher functioning person and using… like wearing things out faster. We have no idea what's included in there. But because of the limitation in claims data that's the way we had to categorize them.

Man: Thank you.

Man: As just a follow-up to that I think one of our guests mentioned the fact that the group included in the non-MCP might have included people with not only feet, but even partial feet and other things. Do we have any concept to whether that's true with that group?

Margaret Dennis: I'm sorry. I don't have the list of all of the prosthetics here, but the categorization was of all the lower limb prosthetics. We just took the microprocessor controlled ones and split them into a separate group. So there could have been foot prosthetics in the other group although I'm sure it was a very small number.

Man: So would it be safe to assume that the vast majority of people in that group would have been a transtibial amputee, that being the most common level?

Margaret Dennis: I…

Man: Partial footer are uncommon and transdermals are relatively uncommon compared to the rest of them.

Margaret Dennis: I didn't do the analysis but I could try and find it out for you and report back. I would assume if it's the most common that's what…

Man: But certainly it's a mixed bag, right? It's everybody who did not have a microprocessor controlled prosthesis and the simple frequency of illness or injury would be that a substantial portion of those are going to be transtibial. So there is at least some selection bias; maybe we don't know how much, but it's there.

Margaret Dennis: Right.

Man: Is that fair?

Margaret Dennis: I would say that's fair.

Chris Standaert: Question for Dr. Czerniecki in the use of these prostheses. So one comment was made about people needing two. If they get one of these they get a back-up leg of some sort. Is that routinely done? And the other question is, when you are fitting people for these are they… are they ever really used as a first prosthesis or do these really go to people who are more experienced users? Is there sort of a standard application for them? Have people demonstrated a need for this… I mean do people consider things about the patient or their prior experience with a leg… a knee before proposing or giving them one of these prostheses?

Joseph Czerniecki: Those are great questions, Chris. You know, so in terms of your first question about the sort of secondary prosthesis, the back-up prosthesis, you know, typically one wouldn't need to have a back-up prosthesis. You get into a little bit of a dilemma sometimes when you have, you know, as you're trying to restore the maximum functional sphere of your amputee patients who want to do many different things, you know, you're constrained if you need to provide only a single limb. So if you have a patient for example who wants to go swimming and they need to use their prosthesis to get to the pool side; well, I wouldn't recommend taking your C-Leg from the changing room to the pool side. It's a damp environment, chlorine in the air. So then you may need a more fundamental, basic prosthesis to enable you to kind of make that transition so that you can participate in recreational swimming for example.

There are some patients that are constrained and needing to use a shower as opposed to a bath and they need to be able to stand up. So they need some kind of, once again, interim prosthetic of some type so they can do those functions.

But in terms of having a back-up conventional limb for typical day-to-day activities that's not really… not typically necessary. And in terms of your question about is this typically a first line prosthetic knee, I mean certainly in my practice it's not the first line prosthetic knee. Some of the criteria that I tend to use are first of all the patient has to demonstrate the ability to be successfully fit with a prosthesis. You know, I think one of the biggest challenges amputees face is getting a comfortably fit prosthetic socket that actually enables them to do things. If you don't have a comfortably fit prosthetic socket you can put whatever componentry underneath it and it will not enable their function. So typically what I like to see is that they've been successfully fit

with a prosthesis, they've demonstrated the fact that they wear their prosthesis for reasonable durations during the day. I like to see them wear their leg for 8 to 12 hours a day. That they are, you know, sort of successful users of a prosthetic limb. Then you sort of try to make a decision about well, okay, now that they've demonstrated a certain functionality with a prosthesis is there something additional that could be gained by the provision of a microprocessor controlled knee? Whether that is expanding their sphere of function so they can walk over more complex terrain, you know, or even be able to expand their community mobility because they have to face ramps or small hills and they're going to be more safe and effective with a microprocessor.

So that's some of the sort of hierarchical thinking that I use, you know, in terms of making a decision about whether to move forward with the microprocessor controlled knee. I have to admit in spite of, you know, my best attempts and our team's best attempt at kind of making the best decisions possible sometimes patients come back and say that they just don't like it. They want to go back to their other knee. And one of the advantages as far as sort of payers go and all of us who sort of help to participate in the payment of prosthetic limbs is that these companies typically offer either a 30- or 60-day return policy. So a patient wears it for a month, they don't like it, you return it and there's no cost incurred. So it gives us a little bit more flexibility to say, "Well, let's go ahead. I think there are some potential goals," and then you can always retreat if you need to without wasting the money.

Man: Is there a difference between transfemoral and hip disarticulation that you've ever noticed in terms of acceptance of these or need for these? I didn't see that brought out in the data.

Joseph Czerniecki: Yeah. Once again it's the, you know, for the hip disarticulation amputee once again I think they have even additional challenges with successful prosthetic socket fitting. But assuming that they've been able to be successfully fit and they have reasonable activity and mobility goals I think there once again I think your inclination is to weigh safety and fall prevention more highly than necessarily expanding, you know, complex [inaudible] ambulation and those sorts of things.

Woman: Your clinical approach sounds very reasonable. Do you have data on if you took that population of people that you see that you assess clinically might go to the next level? Do you have any data

following your decisions about those people and how many of those do well and how many of those do better and how many of those are returned and sort of a practice effectiveness type of…?

Joseph Czerniecki: I would love to be able to answer yes to that question, but unfortunately I don't. You know, we're fortunate in the VA where we're going to be starting a data repository so that we'll be able to, you know, within four or five days have a whole lot more information about what happens in the real world as we prescribe these different components and stuff. But for now I don't think anybody has that data.

Man: I have a question. The gentleman who was the prosthetist who spoke before had alluded to the fact that in his opinion people at level 2 might benefit more than people at level 3 from these because of its potential for preventing falls. Can you speak to that at all?

Joseph Czerniecki: Yeah. I guess my comment is that, you know, I mean we're forced to, as we make decisions, sort of, you know, kind of construct categories. But even within the domain here of saying, "Well, this is a category 2", I mean really that really encompasses a fair spectrum of functional level. So for example I may have a category 2 patient that is moderately heavily reliant on upper extremity ambulatory aids—crutches, walker, to be able to achieve that level of function. And if I… after my evaluation of the patient I don't feel that a microprocessor controlled knee would allow that patient to not be able to use upper extremity aids, I don't see that there is any particular benefit to providing him with a… or the patient with a microprocessor controlled knee. Because they are going to be so reliant on the upper extremity aids that, you know, any added sort of safety effect is essentially irrelevant. But also within that same category you can have patients that might be walking with a single point cane, somewhat constrained in the distance or the complexity of the surfaces that they can walk over where I feel like a microprocessor controlled knee actually would enable them to possibly not use a cane, to be able to expand their sphere of function and in that case I would prescribe one.

Man: But I guess I was trying to get at something different. As opposed to expanding their function I'm wondering about preventing falls. I'm assuming that people who fall more incur a lot more hospital costs and there could be significantly morbid events in their life.

And the implication was that if you prevented falls of these people at level 2, as I'm thinking about it, you might actually achieve more in terms of preventing morbidity than expanding the function of people at level 3.

Joseph Czerniecki: Well, you can expand the function of patients at level 2, right? And so I guess… I think we're talking about the same things because I guess what I'm suggesting is that patients would choose not to walk on complex surfaces or inclines because they feel that they will be at risk. They'll feel unsteady, insecure, they're not going to do those things. I mean you can adapt to an increased fall risk in a number of ways. Right? One of the ways is simply just not to do it. If I feel like I'm going to fall down walking on ice I'll just say, "I'm not going to walk on ice." Right? Or I can say "I'm going to put… I'm going to use crutches or a walker so that I reduce my risk of falls," or "I can augment with a more sophisticated type of knee componentry that will enable me to walk on those surfaces safely and effectively so I reduce my fall risk with those types of terrain." So to me those sorts of decisions are execrably linked—expanding function and enhancing safety. Right? I mean they're linked.

Man: So I want to just turn that over to the evidence vendor as well. You looked at the differentiation between the different levels and the success of the prostheses. Did you find any literature on fall prevention or really safety measures in terms of different levels of function?

Nora Henrikson: So the Hapner(?) 2009 study was the only one that was split out by level 2 versus level 3. And I'm just looking up… I have the article and I was just trying to look up the specific results. It's in the report also.

Man: So that was 17 patients. Right? That's the grand total of the literatures?

Nora Henrikson: Half of those were level 2.

Man: And half of those were… so we basically have eight or nine patients.

Nora Henrikson: Right. Right.

Man: I guess I would have a question sort of in follow-up to Kevin's question in terms of the significance of falls. I think, you know, you can envision a 70-year-old patient falling and being at a high morbidity risk from that whereas opposed to a 20-year-old traumatic amputee could probably fall all day long and never get hurt from it. Is there any sense of the significance of falls in these populations in general?

Joseph Czerniecki: I apologize for not really being up on this data. The fall frequency is pretty significant in people who are lower extremity amputees and I think it's of the majority, like about 50%, will report that they have fallen within the previous year kind of thing. And there have been a couple of publications about the proportion that have resulted in injury and the proportion that haven't.

Another measure that has been used is a measure where they sort of try to quantify the fear of falling in addition to the actual number of falls. Because once again I think the fear of falling is something that constrains people's functional spheres. But I just don't have those numbers off the top of my head like how many result in injury and how severe those injuries are and that sort of thing.

Man: But to some extent, you know, the fall is also… the consequence of a fall is also contingent upon the context of that fall. If you're going upstairs or downstairs, if you're crossing a road then that has a consequence irrespective of one's age group.

Woman: It sounds like the bulk of the research was done on people who were middle aged and younger.

Man: Yeah.

Man: No. It's quite a span of… some of these are mid 70s.

Woman: 70?

Man: Yeah.

Craig Blackmore: Any other questions at this point? Well, we need to make a decision. So we should turn to our coverage and reimbursement determination analytic tool. And the tool is there to help us and it's in your blue packet here. But you've all seen this before. The first couple pages are really a summary of the principles upon

which we operate and that's looking at scientific evidence, etc. I'm not going to go through that in detail.

Second… page 3 of your decision tool lists whether or not there is a national… Medicare national coverage decision. Because our statute requires us to either be in agreement with national coverage decisions or at least… or if not to clarify what the evidence basis is for not being in agreement. And in this case there is no national coverage decision around this topic. There are local coverage determinations, which are provided in here. It looks like there is also information on other guidelines that we might consider.

Then sort of the meat of this is pages 4 and 5 and that's where we as a committee go through and define what outcomes we are interested in in terms of safety, in terms of efficacy and in terms of cost or cost effectiveness. And the first step in the process is for us to determine what outcomes we think are important and the staff has pre-populated the decision tool and what I'd like to do now is starting with safety go through and really decide if we think the relevant outcomes are here for our discussion. So under safety we have mortality and morbidity. We have falls listed as a safety outcome. Fewer negative effects on residual limbs, which I presume would mean that if you're altered biomechanics that might cause arthritis or pain or some other disability on the other side as a consequence of having less function on the affected side if you will.

Other safety outcomes might be if the equipment fails. Are there other safety outcomes that we should be considering in the minds of members of the committee? Okay.

We also have our efficacy or effectiveness outcomes. And, you know, our charge is to really look at outcomes that are important clinically or important to patient's quality of life, welfare, longevity, etc. rather than outcomes that are from a laboratory setting. Though that doesn't mean outcomes from a laboratory setting aren't relevant. So the outcomes that we have to start here are energy and cognitive improvements. And I'm not entirely sure whether I agree with that one. But we can take other people's input. And then improved ability to ambulate, improved quality of life, improvement in ADLs, improvement in balance and confidence, improvement in comfort and fit of the prosthesis, and… I don't know what MCP versus NMCP. I don't

really think that's an outcome. Improved or perceived perceptions by others, quality of life, patient satisfaction and then other outcomes. Are there other outcomes on here that we should be considering, Dr. Franklin?

Gary Franklin: Well I didn't hear one on energy.

Craig Blackmore: There was one energy on cognitive improvements, which I want to talk about.

Man: Those two things I think should be separate—energy expenditure is one thing and cognitive response to all that is a different thing.

Craig Blackmore: Yeah. And what do we think about energy expenditure as an outcome? Is that…? Is that a clinically important outcome in the minds of…?

Man: I mean if you get into distance of ambulation and what somebody can do…

Craig Blackmore: But that's a separate outcome. That's what I'm sort of querying here. Do we really care about energy or do we care what you can do with the energy?

Man: Well, no, I mean improved ability to ambulate may imply you have a better balance, you have better stability, you can handle more terrains. Improved energetic means you can walk farther. I mean they are different.

Craig Blackmore: I like walker farther. Energy can mean how much oxygen you burn, which in my mind is a laboratory measure. Whereas if I can walk further that's real.

Man: Well, no, I think energy can also be a quality of life measure. That if you are exhausted at the end of the day because you've been expending, you know, significant physical effort then that's going to impact upon your ability to see how you might spend the rest of your day, etc.

Craig Blackmore: I was thinking of something different when we talk about energy. When we talk about energy what we're saying is your perception of…

Man: There was that one study that looked at… they used their radioisotope hydrogen and whatever else they gave somebody that looked at actual energy expenditure as an outcome. But the purpose of looking at energy is that it translates into function. So in that sense they are linked, yes. There is one that measured energy and one studied, you know, steps.

Man: It's really an intermediate outcome though. I mean the point is what we're interested in is the patient centered outcomes. Does this make their life better? Albeit because they can walk farther they feel better or whatever else. So I think it's an intermediate outcome that's captured in the later outcomes. I don't think we need to look at it individually.

Man: But the perception, I mean how you feel, is certainly patient-centered outcome.

Man: Yeah.

Man: And maybe that gets to the cognitive to your sense of energy or your sense of how far you can walk.

Man: Some of the energy data was about the same for both. Like the Kirker(?) study they were almost identical. That was on oxygen consumption.

Man: Yeah. The other energy that I saw is in the lab experiments, looking at energetics of the… energy expenditure with… but again the point of doing it would be the translation into function.

Woman: I think one of the reasons for doing that is it is somewhat of an objective measure of something that's otherwise subjective in measure, like how you feel. So, you know, I would make a pitch for keeping it in there.

Craig Blackmore: Okay.

Man: People consider falls… falls are a safety measure. But are falls an outcome? I mean isn't somebody's desire to have a brace so that they don't fall? And therefore they can do more. I mean if you don't fall then you are… some of these studies looked at falls as an outcome measure. They didn't just look at it as a safety measure. They actually looked at it as the outcome of the braces that people fell less.

Man: But you could argue that would come under, you know, quality of life, patient satisfaction because it's referring to falls. It's an embarrassment factor.

Man: But if they measured that as a specific component then…

Man: It's a measured outcome.

Man: …it could be effectiveness or safety or both, I guess.

Craig Blackmore: Okay. So add falls recognizing that it's in two categories. And I'm hearing that we have two components of energy. One is your perception of how you feel, etc. And the other is sort of laboratory measurements, which are an intermediate outcome, but at least they are objective and when you're dealing with non-blinded outcomes objectivity is important. So those are sort of two different aspects. Anything else under efficacy or effectiveness outcomes that we should be considering?

Okay. And then the next category… I'm going to come back to special populations. But next category is cost or cost effectiveness. And, you know, I've got some of the cost components, which would be the initial upfront cost of the purchasing and fitting. That's important. We have total health care costs, which is important from the standpoint of the payer or society. And we might have both short-term costs as well as long-term costs encompassing maintenance, etc. And repeats or add-ons. I guess we might think of that in terms of whether you require two legs instead of one. Anything else under costs that we should consider?

Man: But when you looked at those slides, add-ons were the bulk of the cost of all of those prostheses.

Craig Blackmore: What do we mean by add-ons? Let's make sure we're using that term…

Man: Yeah, I saw that too. I was wondering what that was.

Craig Blackmore: Right. What do we mean by add-ons?

Margaret Dennis: My understanding from talking to an expert at Medicaid is that add-ons are non-optional things like extenders to make the prosthetic your… the correct height for your body.

Craig Blackmore: This is part of the fitting then?

Margaret Dennis: Right. Customization is maybe a better word for it.

Craig Blackmore: Is that your understanding as well from the team out there?

Man: I can give you an analogy. It's like you're buying a car. If you were to go into a car dealership and buy the frame of the car that's the base code. The tires, the windows, the brakes, those are the add-ons. It's everything else that is required for prosthetic use. So that's why it can alter an enormous expense. They are [inaudible] prosthesis that are individually tailored for a specific person.

Man: So add-on is like the socket and the foot and the… those are considered add-ons?

Man: The type of socket.

Craig Blackmore: Okay. Add-on maybe isn't the best term. Really this is part of the prosthesis and the fitting process and the upfront costs is what it… okay. Okay. Thank you.

Okay. And then if we… if we decide for coverage with conditions one of the conditions we might consider is particular populations and we've heard at least some evidence around baseline function as a way of differentiating between populations. Other things we might think about are first-time prosthesis users and we've talked about that a little bit. We really haven't heard anything about gender, but we could consider that. We haven't heard much about age. Provider characteristics we tried to drill down on a little bit. And then patient selection and beneficiary type. Payer beneficiary type, I guess we could consider that although I'm not sure we ever have. And patient selection…

Man: What does that mean?

Craig Blackmore: I don't know what that means.

Man: We have traumatic versus vascular and you have level, I guess. You could look at transfemoral and…

Craig Blackmore: So some patient characteristics might include location of… or type of prosthesis and mechanism of limb loss I guess. And then the other would be the underlying medical condition of the patient—severe vasculo, you know, their functional… their co-morbidities in essence.

Man: I guess the one question I had in that is sort of Mike's question earlier about trying to get at this issue of vascular amputees and is the fact that they are vascular… they have vascular disease, an independent predictor of what to do with them, or is that really… then tie it… capture it already between age and functional level. And so I didn't totally… most of the studies aren't traumatic stuff, but whether… we have to think about it some. So are vascular people distinctly different because they have vascular disease or does it really matter if they are a 30-year-old or a 50-year-old and an 80-year-old vascular path with other medical things? Or is their medical status overall the problem or is the problem just that they have vascular disease? Because there are different people within that category.

Craig Blackmore: Let's table that for the moment. Are there other potential things we might look at in terms of differentiating conditions, in essence?

Man: So can we just clarify this question of peer or beneficiary type? What does that mean and are we actually going to use that? I've never seen that before in any of our decisions.

Man: I was thinking we might not think about that. But…

Man: I would agree.

Craig Blackmore: Okay. Any other outcomes that we haven't mentioned on this list anywhere? Okay. So at this point what we generally do is we sort of solicit volunteers and kind of go around the room and kind of get the committee members to talk about what their thinking is at this point; not necessarily saying I want to cover or not cover or whatever, but just summarizing their thinking about maybe… what the issues are or where they are. To start off our general discussion towards decision making. Is there anybody who wants to kick that off?

Man: Yeah. I mean I really struggled with this review because of a lot of the things that have been mentioned already—that a lot of the studies were done in younger patients with traumatic amputations who'd been using prostheses for years. Whereas an awful lot of the people who get it, that all the patients with a vascular amputation, I mean I'm at the point of thinking for the right carefully selected patients these offer some advantages. It's how you do it. I'm having a hard time anticipating that we can come up with that criteria. I mean from what the clinical expert said here I'm getting a sense of that, but there might be some 70-year-old with a vascular amputation with functional level 2 who still may benefit from this. There could be some young person who just doesn't use it properly, doesn't… that's what's going to be hard. I have a hard time finding objectively what's a patient for whom this would be so much of an advantage over a high end, non-microprocessor knee that would be worth covering and I'm not there yet.

Craig Blackmore: Anybody else want to give us their perspective before we start in?

Man: I think that… based on what I've seen thus far and reading through the evidence, etc. I think that albeit that it doesn't necessarily pass the normal muster of… or the normal quality threshold of evidence that we might seek, you know, the very nature of this intervention and its… in what it is makes it difficult to see, you know, the randomized control trial quality that we would expect. And so we have to content ourselves with looking at alternative levels to what we might normally want. And on that basis I think that, you know, what I'm seeing at the moment is that there is some moderate evidence there to demonstrate some [inaudible] benefits in the right population again. I think the question of baseline functional assessment is an important one, you know, is somebody going to benefit from this? And I'm very cognizant of the parallel that was drawn of the, you know, the patient who's contingent upon… so if you're using crutches, etc., you know, the 68-year-old dementia patient is probably also somebody who is not going to be benefiting from this kind of intervention, etc. So I think that there needs to be some kind of arbiter of baseline functional, you know, threshold to actually demonstrate an appropriate outcome from this intervention. But I think that from what I'm seeing thus far there is a defined group that if we can get at them that may actually benefit.

Man: It seems to me like they do offer safety advantages, as you said. The cost data I find disturbing because it's so muddy. The data from the state I don't know what to do with because it's not apples-to-apples. And so I don't really know what to make of that. We have the European cost effectiveness studies and the data from the vendors. That's what we have, which is something, but the state I don't know what to do with. And I think similarly it seems like there are people for whom this is a better choice and other things. I think we're restricted to experienced users because our studies are [inaudible] that. And it doesn't seem like a rational choice for a first time user anyway, but our data really limits us to experienced users, which is one category we could get at. I'm a bit stuck on the functional level because a number of people have talked about this idea that some people with a relatively low level of function, the level 2, may actually benefit from this. And so saying only people with high function can use them I don't see the data to support that statement. I see it in other policies, but I don't see the data to support that only people who are very high functioning should have one. One study we have says that people who are level 2s may… it's… that's one study on 17 patients. But they may do somewhat better. So it goes back to that drawing a line issue again.

Craig Blackmore: Anybody have a diversion opinion? Thinks we should cover… again, I'm not asking for a specific decision. Anybody have a diversion opinion?

Man: I have an opinion about cost. The one study… was it the Seelen study? The time perspective was just a year and here we hear from the agencies that it was a four-year block of costs that ran up to $100,000 or whatever. So, you know, if it's just within the first year I'm just wondering what… I can see the add-ons of the costs involved in that, but what goes beyond a year on some of these things? And I think we've talked to some of the experts here of what…

Man: What's driving the cost up after the initial delivery of the prostheses. What drives the cost?

Man: I know I've already said something about one other question I think we need to settle is just that, you know, from listening to what you're saying, Chris, about, you know, starting off with a non-microprocessor controlled limb and transitioning to a microprocessor is that, you know, this comes down to cost again.

What are the true costs of that, you know, how much of the fitting, etc. is contingent upon the actual nature of the limb itself? In other words, you know, the socket, etc. that you make. Will that fit both an MPC and a non-MPC or does it have to be, you know, does it have to be adapted? Is there a significant cost in translate from one to the other? I'm asking that because I'm envisioning that some people might actually… might be a more cost-effective just to go straight to an MCP.

Craig Blackmore: I'm going to interrupt. I don't want to get too far ahead. What I'm hearing, I think, is sort of in the cover with condition range. Over here and trying to define what that might look like. But I want to just take a step back and hear if there are arguments on one of the other extremes, you know, this isn't proven or we should just cover this for anybody. Are there people in that space? Or are we kind of all convergent on middle ground here?

Man: I think the evidence shows there's benefit, but I'm having trouble translating that benefit into real-world difference both in terms of expanding function and in terms of preventing morbid events. So I'm… I mean I know that there is some evidence that it does. But I'm still struggling with how much that translates into real-world effect.

Craig Blackmore: Is that a cost effectiveness sort of question? Or is it you're not sure that there's a real clinically relevant benefit? Is that the latter?

Man: Yeah, the latter.

Man: So the relatively short-term follow-up on these things hampers that some, yes, because you can't relate to the long-term safety and hospitalization and morbidity or mortality and other things that might go with… I mean we don't have hip fracture. We don't have this sort of longer term data you would like to sort of say that this really translates into really keeping people safer and out of the hospital down the road.

Man: And I think the evidence says, "Well, maybe there's some benefit," and then we're asked to translate that into…

Man: Yes.

Man: I think the question is a little bigger than that. I think the data on safety is pretty clear. I don't think a lot of us are going to think the MCP is less safe than the alternative. It probably offers some real safety benefits; at least in selected populations. And I think that the data on quality of life improvements and outcomes are real and undeniable in certain selected populations. So it's harder to figure out… can we expand that to these other populations that may potentially benefit? There's just no study in those populations. And so what I'm struggling with is that I think the cost makes a big difference because if I'm thinking about the cost effectiveness of this, if it's really 10 times more expensive to provide one of these then you have an incremental benefit that's small for say a, you know, a diabetic with vasculopath who might actually… it might be better in terms of the safety perspective than the non-MCP prosthesis. But if the cost is ten times as much it's not worth it. That's a big difference than if the reality of the cost data is that it is twice as much. I'm feeling limited in terms of my… the breadth of who I think would… should be offered this technology based on the cost questions.

Man: I mean all we can say at the moment is that it is more expensive. But based on the data that we've had to date is that we don't know how much more expensive.

Craig Blackmore: I think we can put a little bit of boundaries on it. It's probably at least $23,000 and it's probably less than $110,000 over four years.

Man: That's a huge range.

Craig Blackmore: But at the same time it's not $50, you know, and it's not… there's some constraints.

Man: There's probably some outliers too that are sports specific. This is an active group usually that they would… with these studies. These are active people that… in talking to the clinical expert I mean some of these MCPs will go up to $70,000 or something for sport-specific, higher end. So there are those cases.

Man: I think that point of outliers is a great one. When we're looking at a $100,000 number it's eight patients that we're looking at. Can we maybe break that down at all? Do we know, was one patient $500,000 and the rest $20,000? Do we have any information on those eight patients?

Man: Margaret?

Margaret Dennis: I don't have it off the top of my head, but I'll look and see if I have something.

Man: I mean those eight you really get into sort of that range of error and if somebody is, you know, medically compromised, he was somebody who had multi-trauma with all sorts of stuff and they have three hip disarticulations in there with pelvic things. You could go up astronomically on a couple of people and throw the whole thing off.

Man: They are the 1%.

Man: Yeah.

Craig Blackmore: I want to take a step back and ask another question and that is we've been talking about knees. But there are also ankles and feet. I think we're going to deal with those separately. I'm looking for nons.

Man: We weren't presented with any data on ankles or feet though.

Craig Blackmore: Let's see if we can get the feet and ankle kind of out of the way. And then get back to the knee. Where are we on feet and ankles?

Woman: No data.

Man: We have no data.

Craig Blackmore: Okay. So back to the knees.

Man: Can we do anything with the cost data we have from… the only cost effectiveness data we have is European data, which by European criteria it shows relative cost effectiveness.

Man: Pretty good cost effectiveness. One of those studies had the cost per quality at about $3,000, which is dramatic. It's probably better than any intervention in the United States.

Man: The higher one is about 40,000 Euros. So you're in these ranges that are accepted by international organizations. So it's not… but they're…

Man: Those are all, you know, generally active. I don't remember what the term was. It's a specific group that… I mean most of our data comes from that group. Let's face it. So we still bump up against that, "Where's the limit" question and the cost effectiveness…

Woman: Aren't we trying to decide on a special population? I mean it does sound like there is some data and some support. So that's… it's the conditions part that we're trying to figure out right now.

Craig Blackmore: My sense is that we're all pretty close to the covered with conditions land and we're having a general discussion around… not this specific condition, but what sorts of things do we think might be in that equation? And can we even answer that question?

Man: Should we go ahead and move ourselves forward to that point?

Woman: Yeah.

Craig Blackmore: Nods? Alright, let's move forward. Okay, so, we're working our way through the tool and I'm going to start with officially getting feet and ankles taken care of. So, we're going to have two separate sets of voting episodes here, and we're going to start with feet and ankles, and the first voting question then, this is a nonbinding vote, we've reviewed and considered the technology assessment and information provided by the administrator reports, testimony from the vendor, the public, etc., and our question… get our cards. This will be the yellow cards, and the question to be asked is, is there sufficient evidence under some or all situations that the technology is, and this will be a comparison of the microprocessor prosthesis versus non-microprocessor prosthesis. The first question: Is it effective? And your choices are unproven, equivalent, less effective than the non-microprocessor, or more effective than the non-microprocessor, and this is, again, foot and ankle effectiveness.

Man: Who's counting?

Man: Is it 9? 9 unproven.

Craig Blackmore: And then similarly for foot and ankle, is it safe? Unproven, equivalent, less, or more?

Man: 9 unproven.

Craig Blackmore: And then finally, is it cost effective?

Man: 9 unproven.

Craig Blackmore: Okay. Any further discussion at this point on feet and ankles? We'll progress to the binding coverage decision, and our vote will now be whether microprocessor prostheses are to be a covered benefit of the foot and ankle and… so pink cards.

Man: 9 no cover.

Craig Blackmore: And then we are required, again, to determine if our decision is consonant with national Medicare decisions, and there is no national Medicare decision. So, we don't have to address that.

Now, we're going to move to the first voting question as regarding the knee, and this is, is there sufficient evidence under some or all situations that the technology is effective with comparison to non-microprocessor, and I'll note that if you believe there is any circumstance where it is effective, then you should vote yes, whereas if you don't believe there are any circumstances, then you should choose one of the other categories. So, is it unproven, equivalent, less, or more effective than the comparator under some or all situations?

Man: 9 more.

Craig Blackmore: Same question but for safety.

Man: 9 more effective, more safe.

Craig Blackmore: And then the same question but for cost effectiveness.

Man: Okay, 6 more cost effective, 1 equivalent, 2 unproven.

Craig Blackmore: Okay, now in terms of further discussion, what I would like to have, based on our previous conversation, is a discussion around what coverage with conditions would look like, or we could choose that option so that we could then have a vote with knowledge of what that is, and I'd like to have a proposal from somebody, or from the group, to constructive proposal. Denise, if I could get you to take notes and throw them up on the screen and sort of throw out a preliminary straw person or straw dog,

and then we can see and critique. Does anybody want to take a stab at what these conditions might look like?

Man: Well, I'd like to see a discussion based around K… the K levels, because there seems to be some discrepancy between the 2 and the 3 and whether you put a… you can take a patient that is perhaps a 2 and move him into a 3 if we… if we decide on 3 and 4, then is there a gray area where it's a 3, you know, 2+, 3-?

Craig Blackmore: So, why don't we start with the things we're thinking about? Okay, and one of them is going to be the functional level, the K level. So, let's throw K level up there. What other criteria are we considering for our conditions?

Woman: Whether this is a first time use or it's an experienced user.

Craig Blackmore: Okay, so length of… yeah… first time or experienced.

Woman: Other chronic medical conditions.

Craig Blackmore: Okay, so comorbidities.

Man: Cause for amputation.

Craig Blackmore: Cause for amputation distinct from comorbidities, or is that related?

Man: Distinct from comorbidities.

Craig Blackmore: Okay.

Man: I mean if it's trauma, you're going to have someone who has trauma who has lots of comorbidities and someone who has trauma who has no comorbidities. The 20-year-old trauma victim who is healthy or a 70-year-old trauma victim who is not healthy.

Craig Blackmore: I'm just questioning if you care what the mechanism is, if they have comorbidities? You know, is that… which is more important? How they lost their leg or what their underlying comorbidities are? Or maybe its…

Man: That was the question, yeah.

Craig Blackmore: Any other, other…

Man: In the studies we have it categorized usually by trauma or vascular, categorized by comorbidity.

Man: I don't think they're categorized. I mean they're just…

Man: In some studies they are. They tell you what they are.

Man: Yeah, okay.

Craig Blackmore: Other types of categories?

Woman: I think maybe cognitive function might be a good one.

Craig Blackmore: Okay.

Woman: I mean, unless you want to consider that a comorbidity, but I don't think it is.

Craig Blackmore: Well, we can decide that. So, cognitive function, or, it might be physical function, too. I mean, it might be, although then you start to get into the K level, okay. Other thoughts?

Woman: Location of amputation, so we're not talking about lower leg, we're talking about transfemoral.

Craig Blackmore: Or it could be hip disarticulation versus transfemoral.

Woman: That's true, too.

Craig Blackmore: Yeah. Okay, other categories?

Man: Weight thresholds.

Craig Blackmore: Okay. Weight, which might be comorbidity or it might be its own thing, but this has come up several times.

Man: We didn't really talk about that, but actually there were some, there were a lot of, there were some cut points that a lot of the studies used, and I don't know if we should maybe get a little information on that before we move to this next step. Because if it's, if there's sort of a hard stop on, you know on weight, then that's something we should probably include.

Craig Blackmore: Okay, so let's get the list, and then we'll drill down on other factors we should think about.

Man: Does age matter, or is age just counted in comorbidity, or is that not an issue?

Man: Age is a comorbidity.

Man: Age is a comorbidity.

Man: Okay, I don't think of it that way.

Man: I would think it would stay at a functional classification rather than age. There is so much biological [inaudible]there.

Craig Blackmore: I don't think age is a comorbidity.

Man: I don't think age is a comorbidity.

Craig Blackmore: Are comorbidities, cognitive function, and age, can we summarize that as sort of functional capability, although we have to define it anyway, so I'm not sure it matters. Okay, anything else?

Man: Can I ask a question about that? My information and maybe this is my bias where I'm thinking voting is that I think trying to define multiple levels is, to me, I'm not going to be able to do it, certainly not based on the evidence, although there may be something there. I'm more inclined to think that leaving a coverage without any conditions and leaving a lot of these judgments to the prosthetist or people managing is probably far better than me trying to micromanage based on inadequate data and lack of data. So, if we're going to get in, my personal perspective is that, if we're going to get into a coverage with conditions, it has to be pretty simple or otherwise I'm not going to be able, I'm not going to vote in that direction. You know, it has to be pretty, like a Medicare functional capacity level of 2, 3, 4, something like that, or you know, that' sort of where I'm thinking.

Man: So do we go through these?

Craig Blackmore: So, what's the best way to do this?

Man: We can talk about each one, one by one, and see if we have data for them or not, if that helps us. Some of these we have data for. Some we don't have data for.

Craig Blackmore: Okay.

Man: And that might help us.

Craig Blackmore: Okay, so let's go through. So, we'll start with the K level, or, and what do we know? Somebody, summarize what we know about this from the data.

Man: Well, there's good evidence for 3 of the above, and there's not quite so good but still evidence for 2 of the above.

Craig Blackmore: So, the data that we have is for mostly 3 and 4 and a little bit of 2.

Man: Yes.

Craig Blackmore: So, certainly we don't have any data on 0s and 1s.

Man: Can we go back to the vendor for one sec? So, are most of the studies we had talked about in terms of effectiveness, nor, I thought you said that most of them did not actually mention K levels. Or didn't most of these studies that talk about effectiveness and safety, actually they have an exclusion criteria for people below K3, or they don't mention that. I thought you said they didn't mention it in most of them.

Woman: No, almost everybody, I think all the studies, I believe that's on page 49, or no 51, page 51. They all recorded the functional level at baseline.

Craig Blackmore: They were with the one exception of the one with the 17 patients of 2s and 3s. These were all 3s and 4s.

Man: Okay, I heard that wrong.

Woman: Right. So, two studies included people with 2, and then, but only one study did a sub analysis on the 2s, and then of the other ones, they were either 3 or 4, or they were qualitative, you know, assessment.

Craig Blackmore: So, I think at a minimum we could say we don't have any data on 0 and 1 and so we might not want to cover that. I don't know that that's really helpful, but it's a starting point, I guess, and then the 2s, I don't know. What do you people think?

Man: Uh, Blue Cross, they just separate it out. They said functional levels 3 and 4, and level 2 in specific circumstances, which is kind of what we're talking about,

Man: Yeah, I think that's what we are talking about and I think that's what we've heard from our clinical expert is that there are mutations in the 2 category that will have specific characteristics that make them excellent candidates for it. 3 and 4, there may be people where, you know, specific people who wouldn't be great candidates, but the majority would be, and so, I guess I'm envisioning something on the line of 3 and 4, you know, all patients of a 3 and 4 category and 2, if determined to be medically necessary by the treating physician or something along those lines so that you can leave some discretion in that circumstance.

Craig Blackmore: Comments? I see some nods.

Man: I agree with that, and that's what you were saying. That seems very reasonable. For the most part, we have to treat that the treating physicians are going to determine for individual patients whether they will get benefit from this or not.

Craig Blackmore: Comorbidities, functional capacity, potentially including age and cognitive function?

Man: And maybe this is an inappropriate time, but what Seth said, you know, maybe the prosthetist decision at level 2 and maybe 3s and 4s. The point is, is if we have a prosthetist who really feels that somebody with level 4 shouldn't have it, maybe we should leave it all to the prosthetist to make that decision, if they are at least level 2 or higher. You know, but…

Woman: We're not saying they have…

Woman: [Inaudible] I mean is there any incentive?

Craig Blackmore: Did you answer your own question?

Woman: I see. What would be the risk, I guess you could say, of…

Craig Blackmore: You know, I mean I think…

Woman: Maybe a different level of decision maker.

Craig Blackmore: We can, we can decide not to impose any control and basically do cover, just cover it. We can. I mean, we're not going to not cover, and I think we're clear on that. So, we can define the conditions ourselves. We can make broad statements and leave it to the medical directors, or we can empower a subcommittee to define some sort of conditions, and I think what choice we make is dependent, in part, on whether we think there are definable criteria, because that's kind of the bottom line. If you can't say check a box yes or no, if these are all very vague things, then, you know, we're just not, we're not going to get anywhere.

Man: Yeah. I mean, my sense is from the clinical expect, there, a lot of this is just about the personality of the individuals and how motivated they are to do this or that, and that's something that just has to be determined by somebody who is a good clinician. Good common sense. I don't think we can define that.

Woman: And I don't think we're trying to, but I think if we made broad enough inclusion criteria, we're not saying these people have to get this. We're saying they can get this and that the decision is not ours, it is left up to the clinician.

Craig Blackmore: So, I'm hearing at least level 2 and higher, and we're going to, there's going to be a lot of leeway in there, obviously, which is inevitable in a circumstance where things aren't necessarily that objective. First time…

Man: Man my, eyes are bad.

Craig Blackmore: First time versus experienced, how do we wish to address that?

Man: We have very little data on first-time users. These studies are almost exclusively on experienced users. So, I think we can say by data letting first-time users get one is probably inappropriate according to the data portion.

Man: Well, is that going to be a more extensive time course, then? If we have let somebody have one for a couple of years and then they go into their MCP ones, you know, I mean, won't, that will

end up being more expensive, possibly, and that's why I was asking that question before about can there be a transitioning from one to the other, what's the expenses involved?

Man: And we can maybe ask Dr. [Inaudible] again, but I mean, people have to, these are a learning process, getting used to these things, and what's right for somebody, it's not infrequent that you change around things once people start going. So, I mean, the initial prosthesis is a work in progress typically for a while, yes?

Woman: Mhmm?

Man: But you also talked about the fact that people had to relearn, or sometimes, you know, that they couldn't get rid of some of the bad habits, maybe not bad habits, but particular habits that they've acquired with a previous prosthesis.

Man: Right, I mean. You know, patients vary in, you know, sort of dynamic evolution, as they learn how to use prosthetic componentry, and typically we start off with something relatively simple, straightforward, just so that we can understand whether or not that they may be able to tolerate a prosthetic socket, that they be actually able and motivated to function with the prosthesis, and then, you know, we kind of modify prostheses, and the reality is that every time a patient needs to have a new prosthetic socket, which on average is every 18 months or so, 18 months to 2 years, we reassess them in terms of what their immediate functional goals are. So, you may have a patient that has fairly modest functional goals and then in 2 years they have expanded or changed their functional goals, and we prescribe componentry prosthetic feet and knees that try to accomplish those goals. So, all amputees sort of dynamically change throughout their lifespan, and we constantly reassess what's best for them at that point in their careers or evolution.

Craig Blackmore: So, is it worth it for us to talk about performance goals, or is that just something that's inherent in the evaluation and management of the case?

Man: That should be.

Craig Blackmore: So, it wouldn't be anything that we would have… I know in one of the recommendations it's stated that performance goals should

be part of the conclusion, but if that's part of the normal management anyway, I don't think we need to talk about it.

Craig Blackmore: Yeah, I think that's a good question. I think the bigger, in my mind kind of the bigger question, just as a follow-up to that is, is there a circumstance where anybody ever gets an MCP as their first line, as their first prosthesis, or is that something we need to talk about?

Man: I mean, from my perspective, there are uncommon occasions, for example, you know, somebody who is a bilateral transfemoral amputee who you know at the outset, the augmented safety features of the prosthesis plus its sophisticated control features, I think, you know, those patients should get microprocessor controlled knees at the outset. There is no point in wasting time with others, but those are…

Man: But those are very uncommon situations.

Man: It's so long…

Craig Blackmore: So, I mean what's the, I've just sort of polled the committee. Should we include a criterion for first-time versus experienced, or should we leave that to clinical circumstances?

Man: Leave it.

Craig Blackmore: Gary, would you like to address?

Gary Franklin: So, L&I's law, we have to take into consideration a potential for functional improvement in Workman's Comp law. So, we would have to have whoever is assessing the patient, the physician who is assessing the need for this, to assess the potential for functional improvement from getting …

Man: You mean in getting this knee versus another knee?

Gary Franklin: Yeah.

Man: So what about the issue if you just start with this knee? Then the whole prosthesis is a functional improvement, so.

Gary Franklin: I'm only addressing the issue of the potential for functional improvement should, has to be addressed.

Man: I got you.

Craig Blackmore: Okay. So, again, just give me on a nonbinding vote, do the committee members think we should have a criterion for first time versus experienced as our, in our list of …

Man: Before you do that, can I just say one thing?

Craig Blackmore: Yeah.

Man: I guess I'm thinking that my concern and I don't know if it's a realistic one, but it would be that we don't want it to be a knee jerk that everybody that shows up with a lower limb amputation will get an MCP. I think that's, most people feel that's true. So, I don't think it's unreasonable to say something to the effect of a first time, excluded, or this is for experienced users and then have created an exception. You know, with the exception of, certain circumstances determined by the …

Man: Review or whatever you'd say. With the exceptions of agency discretion for that rare circumstance. Yeah, because if somebody really has to prove themselves by being able to use a prosthesis before you really shouldn't give them one of these except in that rare circumstance, then you're almost by definition, it's never the first thing you give them because they have to prove that they, you have to make sure they can fit a socket and get the thing on and off and actually work on them to do something for them. So, if you can't prove that, once you've proved that, this is by definition not your first prosthesis.

Craig Blackmore: Nods? Shakes? Okay. Can I go back? I thought we made a different statement on the first line. I thought we, the statement that we made was level 3 and 4 and 2 under the discretion of the clinician.

Man: Yeah, but what's the difference? I mean, it's always under the discretion of the clinician, right?

Craig Blackmore: Well, okay? I mean if that's the statement you want to make, that's fine.

Man: I'm asking.

Craig Blackmore: I won't approve it.

Man: My assumption is that to get a prosthesis, you have to actually sign an order, an MD has to sign an order for, a physician anyway, has to sign an order for the prosthesis so the prosthetist can't just fit whatever they want without somebody ordering it. Is that correct or incorrect? If you're going to pay for it? Wouldn't you, Gary, don't you guys require a physician order.

Gary Franklin: Yes.

Man: So, by definition, it says physician approval, but if the physician is ordering it, they've already approved. You know what I mean?

Man: I said clinician. I was thinking that the prosthetist was part of this process too, because you've been describing the very complicated process that people go through to look at an individual, look at a lot of aspects of an individual.

Craig Blackmore:: Let's clarify. So, who, what provider makes the decision between, I mean with the patient, that makes the decision between which type of prosthesis, the microprocessor non-microprocessor? Gary or…

Gary Franklin: I mean, under current Washington State Licensure requirements, a prosthetist cannot provide a custom prosthetic device without a physician prescription. So, ultimately, the physician needs to generate a prescription. Now, in terms of practical terms, what happens in the real world, I think that there are some providers that have a moderately high level of expertise in terms of knowledge of prosthetic issues. Others, that oftentimes, it is the vascular surgeon or orthopedic surgeon that ends up being the prescriber who may rely very heavily on the input from the prosthetist, basically, as long as it kind of sounds reasonable, sign off on it, and I think, you know, PM&R specialists tend to be honest with their rehabilitation focus and things, you know, oftentimes be more influential in shaping the prescription along with the prosthetist. So it is more of a joint prescription.

Craig Blackmore: Who's that?

Man: L&I would have to have a request from an attending doctor on this.

Man: Alright. I mean the ultimate person who writes a piece of paper saying this is what somebody should get is the physician. So, since we had up there it said at physician approval or request, that's by definition sort of what happens. The only way to do it is to put an outside reviewer on top of the physician prosthetist. So, if you're going to put a restriction on level 2 in certain circumstances, you'd have to have that level review above the level of the prescribing physician and then go back to the agencies to review that, if that's what you think is appropriate. Does that make sense? Is that what you're asking?

Man: Well, we've been talking for the last 3 hours about the difference between level 2 and level 3 and trying to tease that information out, and this is basically saying we're accepting level 2.

Man: Right.

Man: And I understand the practical implication of what you said, but if I go back to basics, this is a decision to accept level 2 as opposed to trying to appreciate the difference between level 2 and level 3.

Man: I think that the feeling is that the subtleties of which level 2s might benefit from this, and there is at least some evidence that some do, are beyond the granularity that we can come up, and so we were proposing to default that to the physician.

Man: The problem is, I agree with Kevin, because the problem is that you're, you've got a certain group of people in level 2 that are kind of crossing the line a little bit. If you'd just include level 2, you are almost including some of those people from number 1 that are crossing the line. That would be my fear, that there's that gray zone of the lower level number 2s.

Craig Blackmore: So, you think there should be a higher level of review, I mean an agency review, for level 2s?

Man: I guess my statement [inaudible] was just that our sentence before said at physician discretion and the physician is the ordering person, so it makes no sense to say at physician discretion, because they have it anyway.

Man: That's not a barrier.

Man: And so, if you want another level of review, we have to say at agency review for level 2. That's my question. Is that what you're asking for? I'm trying to understand.

Man: I'm not asking really, I'm just trying [inaudible]

Man: What do you think is appropriate?

Craig Blackmore:: I mean, what do we think is appropriate? I mean, should it be all level 2s whose Doc writes a prescription or should there be an additional review process? What's the feeling of the committee? Should we have agency review? Would that be more appropriate?

Man: I think it would be cumbersome, but the…

Craig Blackmore: It's cumbersome, but this is only a handful of people.

Man: It's 8 people a year. It's not that cumbersome.

Man: Yeah, but [Inaudible]

Craig Blackmore: Would that be… I mean, how does the committee feel? Would you prefer that or would you prefer just any level 2 which is what we're saying..

Man: I'm finding myself comfortable with agency.

Man: I find myself agreeing with Kevin. I think that, I really think the data on 3s and 4s while more difficult is fairly compelling. I think that there's clearly going to be some selected 2s, which may benefit, and I don't think it would be unreason… and I guess what I was thinking about when I was talking, when I initially said with the medical necessity, was sort of teasing out the higher level review. I mean, whether if the clinician or physician can make a strong enough argument, the agency, should approve, and it's hard for us to come up with exactly those criteria are. But I think setting a higher standard for the level 2s makes sense.

Craig Blackmore:: We're talking about any 3 or 4, but level 2s only under agency review. Am I hearing that correctly? And is that a better, does that resonate more with the committee? Kevin and [inaudible]. Okay, Denise can we? Okay, and then what did we decide on the first time we're experienced?

Man: Well, we've more or less heard that no one gets a first-time.

Craig Blackmore: So, are we in the same place? You know, you have to be experienced, or there might be exceptions under agency review, again? Is that the..

Group: Yeah. Right.

Craig Blackmore: Do we want to define experience, or do we want to leave that to the agencies to define?

Man: Experienced user with exceptions at agency review.

Craig Blackmore: Right. Comorbidities?

Man: Are they already subsumed at functional level to any point that's worth commenting any further?

Man: Certainly, to some extent but I don't know about to what extent.

Man: I mean that, that's fine. That's a fine bias. I think that's already covered in functional, I'd rather we see a functional assessment rather than ICD-9 categories.

Craig Blackmore: Yeah, I don't see how we can put a limit on this. I mean, I think this is really where the clinician's perspective comes in, and they're not going to offer it to someone who they don't think is going to be able to take advantage of it.

Man: I don't think we can, you know. There are a million comorbidities we can't…

Craig Blackmore: Yeah, alright. Alright Denise, scratch that one please. Comorbidities is dropped, and then how about the cause. We heard that in the agency medical director's presentation. The data that we have is the vast majority of it is trauma, but there is a lot of amputees for vascular pathology. Do we wish to differentiate or not?

Man: The dilemma being that the majority of amputees are actually vascular in origin, and the majority in the study population is trauma, but those 2 categories have excluded, you know, cancer and congenital other issues, but again, I don't know whether you

make a distinction between them and then you put it back up to the functional level. If they're highly functional, it doesn't really matter if they are vascular or traumatic. If they are poorly functional, does it really matter?

Man: I would remove that.

Man: Yeah, I agree.

Craig Blackmore: So, I think I'm hearing, we don't want to deal with causes or conditions. Is that correct?

Group: Yeah, right.

Craig Blackmore: Okay, and cognitive function. Have we touched on that under …

Man: I don't think it's really relevant other than, you know, what we've talked about functional assessment again. I mean, there's evidence that this actually, that the MCPs are tolerated, rather improved one's ability to cognate, because you don't actually have to concentrate on your limb so much so, other than that, I don't really think that there's much of a role here.

Man: I don't know we'd measure it anyway. I mean, I don't.

Craig Blackmore: Okay. Location. We've already talked about the foot and ankle, but in terms of transfemoral versus hip disarticulation.

Man: I don't think we've had any data to be able to tease that apart.

Craig Blackmore: Did the data… we didn't have any data to discriminate. We don't have any data.

Man And both those groups were included at least some of those studies, but the majority of them are transfemoral because that's more common.

Man: But don't we still have to decide if it's going to be transfemoral and above or transtibial or above?

Craig Blackmore: We have already decided against foot and ankle, and that would be the transtibials, right? So, this would just be transfemoral, and if we differentiate between above and transfemoral. And I am hearing, I think, that we're not going to talk about that. Okay?

How about weight thresholds? There were inclusion criteria in the studies, at least some of the studies, if not all of the studies.

Man: Can we hear from our clinical expert about whether there is an issue here or what the issue is?

Craig Blackmore: Let's hear the data first. I mean clarify the inclusion criteria for it.

Woman: Right, so none of the, most of the studies did not report the weight. Of the ones that did, we have an 88 kg mean weight.

Craig Blackmore: That's a mean, but was there an upper threshold that they excluded as an eligibility criteria?

Woman: The Klute Study had an upper, required below 120 kg, which was per the manufacturer.

Craig Blackmore: Per the manufacturer…

Man: So, there's a manufactured specification on weight?

Woman: Right.

Man: So, we may not have to do anything because the manufacturer already says you can't put it in somebody over a certain weight.

Craig Blackmore: Well, we can, I mean people order off label all the time, right? So, we can specify that weight limits, they have to meet the weight limits for the product.

Man: I think you would be in dicey territory ordering use of a mechanical prosthesis when you've received the biomechanical properties of it knowingly. That would be poor form, but…

Man: Yeah, and to do otherwise, you should be assessing probably, you know, if we're making judgments about that, should be based on something like BMI rather than weight, per se, because a large-structured person… you know. I mean the argument is more about the force that will be delivered either to the stump or to the prosthesis itself, just from that…

Man: Is that BMI or is that weight?

Man: No, but what I'm saying is if you're thinking about a BMI… if you're thinking about a weight… it depends on what the nature of the limitation is, and if it's a structural limitation then the question is one of the, you know, forces that are applicable in the end of the prosthesis or the prosthesis is taking. If we're just thinking that there's some kind of benefit to be gained from keeping this with people with a certain weight level because of their cardiovascular morbidities, etc., then that should be a BMI question.

Craig Blackmore: Right.

Man: We could keep it to within manufacturers specifications and you get rid of … for use.

Craig Blackmore: Is that necessary? Dr. Franklin, would you pay for a prosthesis that was ordered for somebody whose weight was in excess of the manufacturer's specifications?

Gary Franklin: As I mentioned earlier, right now with our criteria, that would be 220 pounds, but you know, that wasn't based on much data.

Man: Yeah, where did that come from? Do you know?

Gary Franklin: That's what I just said. I don't think it was based on much data.

Man: We had the same issue. Some of these weight issues may be covered in functional level. Again, you have somebody whose 340 pounds, you know, they have to be an experienced user and be at least a level 2 with a good chance to progress with this, and I suspect that's going to be unlikely, and they probably exceed the specifications of the unit.

Man: I think that, personally…

Man: What if you have a, you know, a 7-foot-3 individual whose unbelievably athletic and loses their limb but happens to weigh 350 pounds. If Shaquille O'Neal loses a limb, is he not a candidate? Probably more because of the manufacturer's specifications the torque is going to be too high, and I think that's a different question.

Craig Blackmore: Do we need to specify that it has to be in the constraints of the manufacturer's weight limits on the prosthesis?

Man: Well, if we're worried about off-label use, it wouldn't do any harm, you know, to come to kind of the crazy stuff like Chris is saying.

Woman: Can I ask the clinical expert, is there much off-label use?

Man: Do people prescribe these for people that are over the limit?

Joseph Czerniecki: We don't. We, I mean rigidly, adhere to all of the manufacturer's requirements, and I don't know. It might be, I don't know. I think this is sort of a shoot from the hip, but it might be worthwhile to either specify that it has to be within manufacturer's requirements or specify what that current body weight limit is. I don't know. What is the body weight limit, currently?

Man: Currently, it's 220. Their new one might be more, but if we were to use it in a way you're going off-label use, we have significant liability if that product broke. So, it's really a safety issue and a certified prosthetist license in our state would be liable if they did an off-use and it failed. So, I don't think that you're going to see what that does.

Craig Blackmore: So, do we leave it on or take it off.

Man: We could say within manufacturer's specifications or leave it off. Either way,

Woman: It wouldn't hurt.

Man: Yep.

Man: It's not going to hurt to put it in.

Man: What's the harm?

Craig Blackmore: Put it in. Weight threshold within manufacturer specifications.

Man: Just say use within manufacturer's specifications so you don't get into other funny issues, I guess.

Craig Blackmore: Okay. Okay, other factors that anyone has? Does this list resonate with people? I mean, we're going to have a vote and without sort of biasing the vote, is this within the realm of what

people were thinking about when they're thinking about appropriate conditions?

Group: Yes.

Craig Blackmore: Okay. I'm going to, we're going to move on. We've already had the first voting question. The second voting question is based on the evidence about the technology safety efficacy and cost effectiveness, and we will make a decision of not covered, covered unconditionally, or covered under certain conditions, and the conditions are as listed. Functional levels 3 or 4, or level 2 only with agency review, should be an experienced user, though exceptions may be made under agency review and the use must be within the manufacturer's specifications. We are using the pink cards, and let me find it, let us vote.

Ten cover with conditions.

Okay. We are required to determine if we are compliant with Medicare national coverage decisions, and there are none. So, we now charge, oh I can't find the right wording. We now charge the staff to draft a coverage and decisions, findings and coverage decisions document for final approval at the next meeting.

Man: Staff will do so.

Craig Blackmore: Well done. It is now 10 of 12, and we are a little ahead of schedule and lunch is not here. What time is lunch?

Woman: 12:15.

Craig Blackmore: Lunch is 12:15. So, we have a little bit of time. I am going to propose that we start the next topic with the agency utilization and outcomes, and then we'll keep the public comment on the timeframe that people might be anticipating.

Woman: Good.

Craig Blackmore: Okay. Let's hear from the agencies.

Woman: Is that the, I can't get my…

Craig Blackmore: I will also thank the public for their input and commentary.

Woman: Yeah, I can't get my computer hooked up.

Steve Hammond: I'm Steve Hammond. I serve as chief medical officer of the Department of Corrections, and I work with the agency medical directors group. This topic is osteochondral transplant techniques. When the subject topic was originally raised for review by the HTA program, which was before my participation in the program, it was raised, I believe, as specifically pertaining to OATs osteochondral autograft transplantation system, which is a proprietary system, which is one type of osteochondral transplantation. We expanded the review to cover that general category. So, by way of background, several techniques for repair of focal full-thickness chondral defects have been developed over the past 10 to 20 years. These include both osteochondral autograft and allograft transplantation. There are various techniques of this transplantation, but generally they involve transplantation of chondral and subchondral bone plugs, either a single or multiple units. When they are transplanted in an array of smaller units, it is sometimes referred to as mosaicplasty. The implants may be autologous or allogeneic. There are other techniques that have been developed to try to repair these chondral defects, including what's referred to as bone marrow stimulation or microfracture chondrocyte transplantation or simple debridement of these defects. The evidence for these techniques is at a fairly early stage of development and leaves many basic questions unanswered, such as what technique is most efficacious in what clinical settings?

So, when the topic was raised and proposed for the program, it was rated of medium concern with regard to safety issues, mainly related to the paucity of long-term follow-up data, uncertainty about long-term outcomes. Efficacy questions were of higher concern for several reasons, as is noted here, one being the somewhat imprecise definition of appropriate indications or case selection, outcome measures are not well developed in this area, and again long-term outcomes we have relatively little data on that. Cost concerns were rated as low because the total cost through the Washington State agencies has been relatively modest, although given some of the aforementioned uncertainties, there does appear to be some potential for overuse or inappropriate application. So, current coverage policy, UMP, PEV covers, L&I covers, Medicaid covers open procedures with prior authorization, arthroscopic procedures are not covered.

In doing the data poll, the CPT codes shown here were used, and this includes open allograft, open autograft of the knee, and then arthroscopic procedures for the knee. We also did look at any accompanying ICD-9 codes indicating osteoarthritis. You can see here that the number of cases has been relatively modest over the past four years, most cases being in L&I. The costs, again, come to a total of just over $1 million for four years. Again, we see varying rates of reimbursement from the agencies and again there is probably some noise in here. Margaret, you know, I look at this $45 per case for Medicaid, and I'm thinking, these are any costs associated with that CPT code in that patient in the four-year period?

Margaret Dennis: Just, that $45 cost is just 2010, and there were only two Medicaid patients in that timeframe, so…

Steve Hammond: Yeah, I can't imagine that that's the cost of the transplantation procedure.

Margaret Dennis: The average Medicaid cost, considering all four years, is $4,000.

Steve Hammond: So, I think that's maybe just a little noise in there, but this gives you a sense of the magnitude of the cost to the state. This divides the number of cases and costs, depending on technique, and we see that just over half of the procedures are open allograft techniques and then the remainder divided reasonably evenly between the other techniques noted. Also, open allografts seem to be slightly disproportionately more costly than the other techniques.

This shows the diagnoses that were associated with these procedures, and they're pretty much as we might expect, and we see that osteoarthritis is not included here, which is somewhat reassuring as to appropriate use of this, as this technique is not indicated in the setting of osteoarthritis.

This shows trends in costs over four years. It's difficult to discern much of a trend, although perhaps some upward trend in the costs for allograft transplantations.

Other coverage – CMS has no national coverage decision. As noted in the vendor report, private payers have somewhat variable and I would say rather complicated coverage policies that relate to what type of transplant is covered, what size of defect is

covered, and so on. The details are in the vendor report. So, looking at risks and benefits of this technology, again, there is some risk, we sensed, related to the uncertainty of case selection criteria and the lack of long-term outcomes data. Benefits, there is also evidence of symptomatic and functional benefit in cases with chondral defects that fail conservative management. Unfortunately, the evidence appears to be of somewhat low quality and somewhat variable in outcome. So, state agencies view summarized, this is an evolving technology with a weak evidence base. Long-term safety and efficacy remain uncertain. There is some potential for overuse or misuse given lack of consensus on patient and technique selection criteria. Our recommendation is to cover with conditions, and these are suggested conditions. For the knee, possibly the talus, age less than 50, absence of osteoarthritis diagnosis, and failure of conservative management. It's pretty straightforward, but if there are questions?

Man: Steve, how'd you come up with those recommendations for coverage?

Steve Hammond: The… most of the data is on the knee. There is, I believe one fair quality study on the talus. Most of the evidence is in younger individuals under the age of 50. I think the vendor can give us more detail.

Man: Maybe I mis-phrased it wrong. What I was really trying to get at was, is it based on evidence-based literature from your perspective, or is it what you've read, or has it come from recommendations from other physicians, orthopedists, or…?

Steve Hammond: It was based on a review of the technology assessment.

Man: Thanks, that's all I needed.

Man: Can we go to slide #7 for just a second. I had a quick question there?

Steve Hammond: Which one is 7?

Man: It's the pie chart. It's about utilization and types of surgeries that are done. I'm curious if there was a time shift from the open to the arthroscopic use of the technology. In other words, is this an evolving technology, or is it becoming more minimally invasive

over time and we simply have, fewer people are done, because it's more recent, or is that just the natural distribution of the techniques?

Steve Hammond: I can't comment on that, but maybe Margaret can help us with that.

Margaret Dennis: On page 30 of the evidence report, there's a trend chart showing allograft and autograft trends over the past four years, and you can see that the allografts look like they are growing over time and the autografts are fairly static.

Man: But, do you have open versus arthroscopy?

Man: Open versus arthroscopy is what I was talking about, yeah.

Steve Hammond: Did you look at that, Margaret?

Margaret Dennis: I'm sorry, what was the question?

Steve Hammond: Trends for open versus arthroscopic procedures over the four-year period?

Margaret Dennis: I may have that in another document.

Craig Blackmore: I might suggest we put that on hold until our clinical expert is here, because I think that relates, in part, to the size of the defect, and somebody will be here that can probably answer that question a little bit better.

Margaret Dennis: I do have another chart, but the... there was no clear trend, so we didn't include it in our data.

Craig Blackmore: Okay. Other questions?

Woman: I have one more question. On your last slide, you say failure of conservative management. Is there a specific bucket that we can call that, or is it just whatever happens to happen?

Steve Hammond: Well, I take that to mean nonsurgical management.

Man: But you don't know how long they had physical therapy or not, or what other interventions were?

Steve Hammond: I believe that varied in the different studies and again, I don't have all of that at my fingertips.

Man: There seems to be a pretty consistent rising trend of, you know, for the allograft procedure, and do you see, or in your assessment, what would cause that kind of trend? Is it the availability of more… tissues or because of the technology changing, because of the users? Do you have any idea why?

Steve Hammond: You know, I really don't, and I'd like to defer that question to our expert.

Man: I think I may be able to help you there. I think that there are commercial… allografts are commercially purchased, so I think there is probably an industry connection between availability and I assume there's something with that, that maybe Dr. Mandt can help with.

Steve Hammond: That's what I was thinking.

Craig Blackmore: Well, I think we may be running out of energy here. Lunch is in the process of arriving. Traditionally, what we do is we have a working lunch to try to keep things moving along. Why don't we resume at 12:30, and we can have a working lunch while we hear the vendor presentation. Or, actually now that I'm looking at the schedule, it says 12:45 on the open and public comments. Why don't we just eat lunch and then at 12:45 we'll do the public comments and then we'll move on to the vendor report.

Craig Blackmore: So, welcome back everyone. Those of you who are just joining us, particularly those of you on the phone, this is the Health Technology Clinical Committee, and we have just reconvened following our lunch break. At this point in the agenda, we have time open for scheduled and open public comments regarding the current topic, which is the OATs procedure. So, I would like to start with any members of the public. Where's Denise?

Man: She's getting the list.

Craig Blackmore: She's getting the list, right? Well, while Denise is going to get the list of people who have signed up on site, and we're going to take the onsite comments first and then we'll call for anyone who is on the phone that would also like to comment. Do we have people who had pre…?

Man: We do have scheduled…

Woman: Yes, we do… two.

Craig Blackmore: Okay, and we're at five minutes on those, right?

Woman: Yes.

Craig Blackmore: So, we're going to start off. We've had two people who have preregistered to give comment, and there's the list. Okay. We'll start off with Paul Just, and if you could, please… it's important to speak into one of the microphones. We're being recorded. If you could just tell us who you are, who you represent, and if you have any financial conflict of interest or were paid either to come here or travel expenses, etc.

Paul Just: I am Dr. Paul Just, and I am Director of Health Care Economics for Smith and Nephew advanced surgical devices division. So, I'm obviously an employee of Smith and Nephew. Could I have the slides please? So, I appreciate the opportunity to make comments today. I want to say first that three leading orthopedic surgeons in the U.S. volunteered their time to review and improve the comments I make here today. They are Dr. Lewis McIntyre and William Beech, chairpersons of the health policy and practice committees of the Arthroscopy Association in North America and the American Orthopedic Society and Sports Medicine respectively, as well as Dr. Brian Cole, section head of the Cartilage Restoration Center and professor of sports medicine at Rush University in Chicago.

In looking at this procedure, one of the most important questions would be, what are you comparing OATs and mosaicplasty to? Really, they are part of a continuum so that when you evaluate this, a reasonable application of the best evidence to meet the needs of your constituents should be the standard applied. Simply rejecting imperfect evidence is not the solution. Now, this morning I heard you say that you're looking for randomized controlled trials, and there are six of them that we can talk about here. As we look at this as a continuum, we see that it goes from palliative therapy to a replacement therapy, total joint surgery. OAT and mosaicplasty are uniquely positioned within this continuum because they're the only surgeries that offer a replacement of pure hyaline cartilage, which is what's necessary

for a joint to function properly. All other interventions, including ACI, result in fibrocartilage or mixed fibrocartilage/hyaline cartilage, which results in an earlier failure, many times, of the joint replacement. So, for many patients, if they don't have an option of OAT or mosaicplasty, they are left with surgeries that may have a suboptimal outcome for them, or where it may not be suboptimal, it may be substantially more expensive than the alternative. When you look at the levels of evidence, outside of spectrum, many of the clinical trials, five of them are called at least level 1 evidence. In spectrum, it's all 2B, but the bottom line is when OATs and mosaicplasty are compared to ACI and randomized prospective trials, you cannot conclude that either procedure is better than one or the others, but you can conclude that they are both very effective. When OAT/mosaicplasty was compared to microfracture, OAT was found to be more effective. What was not included in the spectrum analysis was the randomized control prospective trial of ACI to microfracture, which is relevant because this is a continuum, and many times throughout the report, OAT was compared to ACI. When ACI was compared to microfracture, microfracture had an equivalent outcome at two and five years for clinical outcomes and a superior outcome looking at quality of life.

When we look at something practical, return to sport data, it's highly significant to see from a systematic review that overall return to sports was higher by 36% in patients receiving OAT. So, if we look at that here, and we look at finally the return to sports is about seven months, as opposed to 18 months, it's nearly one year sooner. If we project this out across a model, looking at 50 months of outcomes and how much total time of sport return was allowed, we find 36% higher return to sport play time available in patients who received OAT than received ACI surgery.

Other points of distinction we need to look at, we mentioned hyaline cartilage. Number two, NICE, one of the leading reviewers in the world, does not recommend ACI, and finally, what you can't see hidden behind the way this is projecting is that the Work Loss Data Institute identified how many disability days occur from an open versus an arthroscopic surgery, and substantially more days of missed time occur with an open procedure. ACI is two-stage, requiring an open surgery. So, you are going to see substantially higher disability days. Looking at the costs, therefore, from your data once it's corrected, mosaicplasty is about $11,000 per procedure versus $20-$30,000 for ACI. That would become

probably the best replacement alternative if OAT is not available. That would cost you an extra nearly $300,000 to $500,000 per year for the patients that you have identified. If we finally summarize, we see that in two prospective RCTs, OAT was no less than equivalent to ACI. We find in the procedure that found ACI to have a superior outcome to OAT. The study had significant flaws in that patients are not treated with OAT the way they were in that today. The lesions were too big, and the replacement was set proud. When OAT was compared to microfracture, it was superior. When ACI was compared to microfracture, it was equivalent. So, there is no evidence that patients will gain better benefit from an alternative to OAT or mosaicplasty. Thank you.

Craig Blackmore: Thank you. Next on the scheduled comment list is, forgive my pronunciation, Samir Bhattacharyya(?).

Samir Bhattacharyaa: I'll take it.

Craig Blackmore: So again, if you could just name who you represent, conflict, and then.

Samir Bhattacharyaa: Samir Bhattacharyaa. I represent DePuy Mitek, our sports medicine division of Johnson & Johnson, and I'm a worldwide director of market access for DePuy Mitek. I am really thankful that I'm here. It's a great experience for me, and I'd really like to thank Denise for doing such a great job. So, thank you, Denise.

So, I guess Paul mentioned some of the things that would be kind of duplicate in my presentation. So… basically, we have… we have various, clinicians make decisions based on many factors. For example, size and shapes, which are extensively discussed in the material, in the documentation. However, many other factors, like bone involvement, containment and location are also extremely important. So it's a multifactorial decisions that clinicians take to make a decision which procedure is the most applicable for which patients? The next line basically talks about the treatment paradigm and the continuum of treatment. Without going through the detail of each procedure, we believe that OATs and mosaicplasty is unique, specifically when the lesion is uncontained, and we are talking about the restoration of the subchondrial bone architecture. So, bone is a very important factor here. And, it's a unique procedure when we are talking about mature and hyaline cartilage, as mentioned previously. The question remains to be addressed here that if this procedure is

not done for financing or economics or reimbursement, what's the consequence of not having this option to the patients?

There's a couple of things I'd like to point out on the HTA evidence, that the validity and reliability of the instruments that are used. We found out several documents, several manuscripts and publications that basically extensively discuss construct validity, content validity, and reliability of these instruments. Discussing these instruments with experts who are quality of life experts absolutely confirm that these instruments are reliable and valid.

This slide is probably the crux of the challenge that I am personally facing, and I'm not a clinician so I would definitely like to announce that before. Number one concern is that literature review shows that some of these studies, specifically Goudas and Bently are level 1, and it's not only one literature review but more than one literature review says that, and this is inconsistent with what the findings are from the HTA. Why is there inconsistency? I know it's very transparent what assumptions were made a priority when this HTA was done, but I question the validity of these assumptions. What is the relevance, clinical relevance of those assumptions, and the patient real events of those assumptions? This is definitely very concerning that why this consistency, inconsistency, is there. And, my last slide basically again says that this procedure is definitely effective from literature and it's unique, and patient's definitely benefit from this procedure when done appropriately and to the correct patient populations. Thank you.

Craig Blackmore: Thank you. Is there anyone else who is here with us who didn't have a chance to sign up that would like to speak?

Jack Burg: Dr. Jack Burg is on the line.

Craig Blackmore: Okay, Dr. Burg. We'll have you go next, and if you could please tell us who you are and if you represent anyone, and if you have any financial conflicts, and then feel free to address the committee.

Jack Burg: Thank you, very much. My name is Jack Burg. I'm an orthopedic surgeon in Minnesota, in Minneapolis. I'm a clinical professor at the University of Minnesota. I am past president of the Arthroscopy Association of North America. I do not have any

conflicts, whatsoever, and I will take less than two minutes. I hope that's helpful. I think that the two people before me said it very well. The goal in resurfacing the knee joint is to obtain hyaline cartilage, which is really the cartilage Mother Nature gave us. It has type 2 cartilage, collagen, pardon me, not fibrocartilage. It's the only cartilage resurfacing procedure that can give you this particular type of cartilage, and that's the OATs procedure. Secondly, based upon the Gouda Study, microfracture does not withstand long term stress, and if you look at that particular study at three-year follow-ups, only 52% had good to excellent results with microfracture, as opposed to 93% with the OATs procedure. And then finally, when you look at the cost effectiveness of these procedures in young adults, the OATs procedure is literally a fraction of the cost of the ACI procedure, and I would ask everyone in the room that has children like in my age group, which is 20-32, if one of my children or someone has a brother or sister or a nephew that age, if they had a singular grade 4 lesion at the end of their femur, I would argue that there would be no one in this room that would not want to have their child have an OATs procedure so they had hyaline cartilage instead of fibrocartilage at the end of their joint. And I'm going to conclude, and if there's any questions, please fire away. Thank you very much.

Craig Blackmore: Thank you. Is there anyone else on the phone that would like to speak?

Brian Cole: Dr. Brian Cole.

Craig Blackmore: Thank you. And again, please tell us who you are, who you represent, any financial conflicts, and then go ahead please.

Brian Cole: My name is Dr. Brian Cole. I'm a professor in the Department of Orthopedics and Anatomy and Biology at Rush University Medical Center. My conflicts are I am a consultant for research for Genzyme, Arthrex, and AlloSource, which is a tissue bank, mostly primarily for research purposes, not for any other royalty or other.

Essentially, I have been involved in cartilage repair for over 14 years. Many of the articles that were cited in the evaluation cited are publications from Rush University Medical Center. We have the largest transplant program in the country. We post faculty… tracked our patients following osteochondral allograft transplantation, as well as other cartilage repair procedures. The

levels of research that we have been responsible for have ranged from level 1 to level 4. Clearly, I would like to just point, give you a sort of pragmatic view of this. Much like Dr. Burg has pointed out, the other speakers did a wonderful job dissecting some of the issues with finer granularity. The problem is that if the barrier is a true randomized prospective study to approve or disapprove, this is a condition that is extraordinarily rare in general. The incidents of these procedures, relative to others, is extraordinarily rare. Physicians and patients are no longer [inaudible] to offer accepted procedure because it has really become generally accepted that these are successful operations. In a worst case scenario if one refutes the literature, you would say, well, what about a placebo affect, because there's no true comparison or cohort, and that would be disregarding some of the existing literature. Placebo affects, in general with surgical intervention, never really exceed above and beyond 30%, yet we're reporting success rates routinely in appropriately indicated patients that exceeds 75% at beyond five-year follow-up. The real issue is, these patients have no other alternatives. In other words, knee replacement would be the only remaining option for these patients if you eliminate these options, and if you just want to look at expense, the expense side, every operation these patients get when it comes to arthroplasty has a declining return and a more catastrophic outcome. Two-in-one versus life might be acceptable but going beyond two is actually unacceptable. The other primary difference of these repair procedures are that patients can do things that they otherwise cannot do with a replacement. They can be fully active, return to sport, and would have no restrictions.

I would just tell you that if you spent a day… if any of you had the opportunity to spend a day in my office to talk to the more than 1,000 patients that we have transplanted, and just to see how it has made a dramatic change in their lives, I'm not sure we'd be here having this discussion. I have developed a policy with United Healthcare and developed policies with Blue Cross/Blue Shield in several states around the country following appropriate indication that they can take into consideration all comorbidities that we now know how to respect, such as malalignment, ligament deficiency, and meniscal deficiencies and that's saying if surgeons respect those issues that good and excellent results are achieved predictably better than 75% of the time and just talk to these patients. Just talk to one and you'll see this is a dramatic, life-changing event in the eyes of these patients, and there are no

other options, and knee replacement is not an option, so we have to shrink their world around what their knee can do rather than try to expand their knee to the world and the activity that they would otherwise like to participate in. Thank you, very much.

Craig Blackmore: Thank you. Is there anyone else on the phone who wishes to speak? Okay. We're going to move on then. Next item on the agenda is to hear from our technology assessment vendor. I just need you to be at a microphone. You can sit there or whatever.

Andrea Skelly: Okay. Can everyone hear okay? Alrighty then. I'd like to start by thanking my co-authors on this particular Health Technology Assessment Report and our purpose was to critically summarize the research of efficacy, effectiveness, and safety for osteochondral autograft and allograft transplantation for the treatment of osteochondral defects, and our report focuses on the highest quality evidence available based on a systematic review of the literature. As you've already heard, hyaline cartilage is a very important and unique tissue within the body. It's a hard, white tissue that is comprised of chondrocytes and is within an extracellular matrix, and its primary property is to be a frictionless surface so that when there is articulation of the joints, they can do so smoothly, and it's very resistant to compressive forces. Now, there are a couple of properties that are important to consider. The first one is that it is avascular and, therefore, not having a blood supply it's very difficult to regenerate. Without a nerve supply, it's difficult, sometimes, for symptoms to be manifest early in the development of an osteochondral defect. We also need to consider that what is being talked about here is just not the cartilage surface itself but also the osteochondral unit, which is comprised of not only the articular surface, but underlying that is the bed of cartilage followed by a bed of calcified cartilage and then the subchondral bone plate. Then, beneath that, we get into subchondral trabecular bone. This will be important when understanding the differences between some of the options that are presented as comparators in the literature. The other aspect is that the vasculature and the nerves from that subchondral bone region can extend into that calcific cartilage layer, and that's part of the, what happens in the bone stimulating techniques.

If we take a look from arthroscopic series, one series of over 25,000 patients, suggests that over 60% had some sort of chondral lesion. Of those, about 67% were localized or focal, 29%

osteoarthritic, and only about 2% of osteochondritis dissecans. From that series, the majority, over 58%, were considered traumatic, and 45% of those resulted from sports. In another series of 993 patients, 66% had chondral pathology and 11% were found to be focal, localized with a full-thickness lesion. Causes aside from trauma include repetitive microtrauma, such as it happens in athletes in a variety of different joints. Again, the knee is the most common area, but repetitive trauma to a specific area of the joint causes a problem. Osteochondritis dissecans is an entity that the etiology is a bit unclear. It's probably multifactorial consisting of aspects of patient history or maybe growth disorders, trauma, microtrauma, ischemia, and maybe abnormal ossification. Chondromalacia patellae really is a spectrum of abnormalities which include softening of the surface, swelling and fissuring of the articular hyaline cartilage of the patella, and it degenerates and makes a very unstable structure and then the result is that the abnormal stress then gets transferred to the subchondral bone.

It's most common in women, and its progression to osteoarthritis is suggested in the literature. In terms of assessment, as was pointed out by one of the public commenters, there is an important way to look at the variety of things that go into making the decision, the physical exam. It has to of course include history, whether it is joint effusion, what are the physical demands of the patient in terms of their physical activity? After that is done, then generally there will be a plain radiograph, primarily to rule out osteoarthritis and to check for the alignment with either varus or valgus abnormality, malalignment, and then assuming that there is no osteoarthritis, the next step is frequently then to do an MRI, and the MRI has the opportunity to look at biological information besides location, the thickness and the depth of the defect, and the potential involvement of the bone is important to assess, as well as the integrity of the meniscus, as well as ligaments. The accuracy of MRI overall is about 80… 83% for sensitivity, 94% for the detection of chondral lesions, at least in one moderately well-done study, and that was compared to arthroscopy. And again, the important part of the MRI is to evaluate the integrity of the subchondral bone, which is a factor in what treatments are provided.

Diagnostic arthroscopy is considered "the gold standard," and it allows for the evaluation of the structural components of the cartilage surface. It can't evaluate bone very well, unfortunately,

and so therefore a combination of the MRI and the arthroscopy are generally used to evaluate patients who might be candidates for one of these particular treatments.

Within the arthroscopy, diagnostic arthroscopy, the two most common classification schemes are presented here. Neither was validated formally in the patient population with osteochondral defects. However, they did serve as very important inclusion/exclusion criteria for the randomized control trials. Again, there are a number of potential treatment options from one perspective. Arthroscopic debridement and things like bone marrow stimulating techniques allow for debridement and abrading of the subchondral bone to induce a repair response and then restorative techniques, which include the allograft, the autograft, and ACI. We're going to talk a little bit about those, as they apply to our HTA topic.

So, the topic of the HTA is the osteochondral autograft and allograft transplantation. It should be noted that there is a lot of variability in the terms that are used in the literature and so, for the purposes of the presentation, and we attempted to clarify this in the report, OAT we will use to stand for osteochondral autograft transplantation. OATs is a proprietary name. It's a trademark. OCA we will use for osteochondral allograft, and then mosaicplasty, as its name implies, actually uses multiple plugs and creates a mosaic appearance to the resurfaced area.

In terms of the focus for this HTA, the focus, based on the questions and context provided by the technology assessment program is to look at pressfit dowel or cylindrical types of plugs or geometric plugs of the bone and intact articular cartilage that does not require extensive use of fixation devices, pins, plates, and the like.

Autologous grafting, or autografting, as its name applies takes the tissue from the patient and usually from a nonweightbearing part of the knee, if we're talking about the knee, and so, one or more places of healthy bone are harvested from those nonweightbearing areas and then placed into the defect site, which has been prepared, and the cartilage and the bone, so part of what happens here in the osteochondral transplant is that we're taking both bone and cartilage and obviously, the positive is that it's from the patient's own tissue, so the possibility of rejection is very low. In these areas, the cylindrical plugs are

placed into the defect area. The problem is that if you have a large defect, there is a limited amount of tissue that you can harvest and a size that you can fill. So, that's one of the difficulties with the autograft. With regard to allograft, it's actually… I should have mentioned that allograft is generally, in the literature, intended to be for lesion sizes of 1 to 4 cm^2. Allograft by comparison is intended for larger and deeper lesions and is based on taking tissue from either fresh or cryopreserved cadavers to find a nice match with the curvature of the articular surface is one of its benefits. It avoids the issue of potential donor site morbidity and allows for obviously taking larger or greater numbers of grafts. One of the downsides to this is that the supply may be somewhat limited and some of the preservation of the allograft may pose some issues. There is a small possibility of disease transmission. We did not find anything reported specific to these procedures, and there is a small possibility of failure due to rejection of the bone component.

So, if we, we take a look at the comparators, neither comparator really is for the same indication, as has been indicated by some of the public speakers. Microfracture, the intention is to look at small lesions, less than 4 cm^2 and have a patient that has healthy bone underlying it. Following debridement an awl is taken and create… and holes are created, 3 to 4 mm apart, and that allows then the blood and the bone marrow to create a clot, which releases basically primitive mesenchymal cells that differentiate into fibrocartilage, and it's an inferior wear surface, and it provides some level of repair, but in larger lesions patients have more difficulty after about 18 to 24 months.

ACI is intended for medium to large lesions. It's generally, in the literature, again 4 to 6 cm^2, is what is usually listed, and the indication also suggests that there should be no, or very shallow association with osseous defects.

These are the comparators that are included in the studies. That's why they're here on the slide, not that they are being held up as the ultimate potential comparator for OATs or osteochondral allograft.

Most everybody is already familiar with the key questions. The first question was to identify is there something in the literature in terms of studies, decision-making studies, that would provide a clear definition for patients suitable for this procedure? What are

the expected treatment outcomes, and are there validated instruments to measure the clinically important improvement? What's the evidence of efficacy and effectiveness? What is the evidence of safety, and then is there differential efficacy or safety in a subpopulation, and what are the cost implications?

The scope, basically, we've primarily covered through the other slides. Again, the focus is on the highest quality of study, mostly comparative studies with concurrent controls, whether they're randomized control trials or other comparative studies and full economic studies and published in the English literature in a peer review journal.

Our primary outcomes are patient-reported and clinician-based measures for efficacy and effectiveness, usually around function, safety, donor site morbidities, and issue potentially for autograft and as with any surgical procedure, complications, revisions are also a part of what we needed to look at. In terms of economic outcomes, intercremental cost effectiveness ratios or similar metrics were sought. With regard to the literature, we did a systematic search of the literature and health technology assessment literature as well. We identified 332 unique potential citations. The thing about this particular literature is, while there is a large body of literature, it is largely based on case series. In fact, several case series come from several primary sites, and there were a lot of different reports from the same clinical sites. The primary evidence for the questions, and some are used for multiple questions. We had three reliability studies to look at for key question 1, five psychometric analyses for key question 2, and then key questions 3 and 5 are broken up between autograft and allograft. For autograft, five randomized control trials, seven cohort studies, 15 case series of at least 30 patients, which were only included for safety, were the primary base. And for allograft, there were no randomized control trials and two very poor quality cohort studies and six case series, and we found no full economic studies to report.

So, for key question 1, the overall summary is, there were no specific case definitions that were rigorously applied in the literature. Individualized studies or treatment algorithms basically relied on case series reports as their primary citation. The treatment algorithms that we found were fairly consistent across different, mostly review articles or instructional course materials, and they suggest that again the patient, the treatment be

individualized to the patient and that things like ligament stability and meniscus integrity be assessed, as well as the physical demands of the patient. If we take a look at the primary things that go into those treatment algorithms, again, lesion size and classification, the thickness of the defect were… seemed to be what the decision points were related to.

We looked at the randomized control trial for those criteria that were consistent across them that might point us to what individuals might be most amenable to the OATs procedure, and across the five RCTs, symptomatology, the occurrence of an isolated full-thickness lesion based on either the outer bridge or ICRS criteria of grades 3 or 4 were the most common things for the autograft. For the allograft, we only had case series to go through, and there was really no consistency in which patients might do… were selected for those. Most of them, all of them, were probably retrospective case series and symptomatic lesions were what was most often cited.

Taking a look at the treatment algorithm that we adapted by Cole. It sort of reinforces some of the things that we've talked about in terms of when OAT might be most appropriate in lesions of smaller size and in high-demand patients, if you're looking at the femoral condyle. In lesions that are larger or in higher demand patients, the allograft appears to be what is favored, and allograft appears to be a second-line treatment as an option in any event.

If we take a look at the overall strength of evidence to answer this particular question and we found no validation studies for primary lesion classification schemes, and those studies of clinical decision making specific to either autograft or allograft transplantation. We did find a couple of studies that looked at aspects, mostly of arthroscopy, one which found that there was a potential to overestimate lesion size by arthroscopy when compared to an open evaluation. One clinical study looked at the reliability of the ICRS grading system, but only one looked at agreement beyond chance, and that agreement was fair to slight, and only one study reported on agreement between surgeons, differentiating between two different grades of the outer bridge classification, and that was between grades 2 and grade 3. Most of the studies that… the studies that are included in our report, again is inclusion criteria. It had outer bridge grade 3 or 4.

With regards to treatment outcomes and validated measures and clinically meaningful improvement, the overall strength of evidence is low. Yes, we did find psychometric analyses in persons with osteochondral defects. The primary… the five outcomes measures that we found those four were these. Let me backtrack a minute and say, in order to narrow down the outcomes measures, what we did is we looked at the randomized controlled trials and comparative studies to see which measures were used in those studies, and then from there, look at, of those measures, which had psychometric evaluations, and these were the five that we did find psychometric evaluations for.

Unfortunately, using the criteria that were specified our priority, they did not really adequately test for validity or reliability, and the responsiveness was only done in one study. Only one study looked at minimal clinically important difference. They looked at a pre to post improvement in the IKDC and in the modified Cincinnati Scoring System.

I will also go back and mention that the International Cartilage Repair Society Cartilage Repair Assessment is mentioned in our studies. However, less than 60% of individuals had biopsy and second-look arthroscopy so that this was not considered to be a reliable outcome.

If we take a look at key question 3 with regard to efficacy of autograft versus microfracture, and the patient reported outcomes, we see that on the left-hand side we have one study population in athletes and another study population on the right hand side in children, and in both of these studies at the longest follow-up, the OATs is statistically significantly better than the microfracture technique, and if you consider the minimal clinically important difference of 16.7 point change, it meets those criteria.

Taking a look at the next slide, the clinician-based outcome reported in the one study on athletes, there again was a significant difference between those who had OAT favoring OAT versus microfracture at all follow-up time periods. There is no minimally clinically important difference that we could find for this particular measure. If you take a look at the means represented from those change scores, you see that over time the longevity of the treatment effect for the OAT procedure appears to be maintained using both the IKDC measure, as well as the HSS, the Hospital for Special Surgeries score. For reference, the

Hospital for Special Surgeries scores goes up to 100 and excellent is considered between 85 and 100.

If we take now a look at the other comparator, which is ACI, autologous chondral site implantation, and the patient reported outcomes. The study by Horace provides two of these patient-oriented outcomes. The Lysholm knee scoring system showed that the OAT procedure appears to be favored statistically over the ACI procedure. However, we don't have a minimal clinically important difference, and the percent difference between the two group varied between 5% and 10%. The Tegner activity score, which is basically a measure of physical activity, 10 being the highest in competitive athletes, 0 being those on sick leave or totally incapacitated, there were no statistical differences in that measure.

If we take a look at the two other randomized control trials that reported on either auto mosaicplasty compared with ACI, the one by Dozin is on the top, and they used their own modification of the modified… of the Lysholm score, and a couple of important points to make about this particular study, only 23 of the 44 individuals randomized to receive treatment actually received treatment. This was sort of a two-phase study. The first phase was to do the debridement and then six months later, at sometime point later, then offer then the procedure for which they'd been randomized. And so, during that time period, 14% had improvement after the initial arthroscopy without any treatment. Ten of those 14 went ahead and completed the… out measure, the Lysholm knee scoring system and, so for statistical testing in this particular study, the authors included the data from the people who did not have treatment with the data from the people who did have treatment for their statistical analysis, and they did not come up with a statistically significant difference, although the percentage of individuals with complete or partial success was greater in mosaicplasty. It is a little unclear to what extent that can really be attributed to the treatment itself.

If we take a look at the Bently study, the Bently study was comparing mosaicplasty versus ACI and at 12 months, their application of the modified Cincinnati Rating Scale suggests that a higher percentage of ACI patients had excellent or good results compared with those who received mosaicplasty. I'd like to point out a couple of things about these two studies and about some of the other studies. The Gouda studies used… their patients had

mean lesion sizes of 1 to 4 cm^2. The Horace Study, if we go back, the Horace Study mean lesion size was less than 4 cm, although the range did go up above 4 cm^2. The Dozin Study had lesion sizes less than 1.9 as their mean, and the Bently Study had the largest mean lesion size at 4.6 cm^2. So, this was the study that is most frequently cited as justification for not doing OAT or mosaicplasty in patients with larger lesions. I think…

So, moving on. In terms of clinician-based outcomes, only the Horace Study provided a clinician-based outcome, and there were no differences between the study groups at any follow-up time for that measure.

If we take a look at, again, the only information we have on longevity of treatment effect comes from the Horace Study. This is, again, just a re-graphing of the means related to the change scores you saw in the previous slides. Again, only the Lysholm knee scoring system was statistically different from between the 2 study groups at the different time periods. This gives you an idea of the relative scales for those measures.

With regard to return to preinjury activity, the studies by Gouda looked at return to sports in their two-patient populations, and in these two populations, it's apparent that a higher percentage of individuals receiving the OAT procedure were able to return to sport at their prelevel… preinjury level. At… if you take a look at the children at 4.2 years, of those who were at their preinjury activity level, at the different timeframes noted on the slide there, at 4.2 years, 81% who had achieved preinjury level were practicing at the same level at 4.2 years compared to only 43% of the patients who had the microfracture technique. So, OAT was favored in this particular… there were no other compare… no other literature to compare some of the other aspects asked in the key questions. If we take a look at the summary, then, there are two small randomized controlled trials, one in young athletes and one in children, both of which seem to suggest that there are better functional outcomes sustained after the OAT and that a higher percentage of individuals returned to sport, pre-sporting activity levels compared with microfracture recipients.

If we take a look at the comparator versus ACI, the overall strength of evidence is also low. There were three randomized controlled trials. There was significant heterogeneity across the studies, not only in terms of their protocols but in terms of lesion

sizes and the quality of their methods. The two smallest RCTs do suggest that there may be better function with OAT, but only one showed statistically significant improvement, and that was only in one study measure.

The largest RCT, the one by Bently, we should point out that 94% of these individuals had prior interventions and that although a significantly smaller percentage of mosaicplasty versus ACI patients had good or excellent results. Again, this was very different than the other studies that were represented.

If we take a look then at allograft, there were no randomized controlled trials comparing osteochondral allograft to other treatment options. There were two poor-quality, small retrospective cohort studies, both of which the primary concern with them was confounding by indication, because there were different types of lesions or different severity of lesions treated in the two comparator groups. One study did find that the Tegner scores were insignificantly improved with allograft compared with other treatments, just loose body removal or internal fixation. This is a very small study. The other study did show that the mental health component score of the SF-36 was slightly… was significantly improved after osteochondral allograft transplantation when combined with meniscal allograft, and the comparator here was ACI with meniscal allograft, so not… again, the comparators that we have seen in other studies.

With regard to effectiveness of osteochondral allograft using, again, our focus was on the OAT… like procedure using a pressfit dowel or cylinder. There were six case series. case series are classified as level of evidence for. Three primarily used dowel or cylinder or a geometric plug again without extensive use of hardware. Three used other types of plugs, as well. Across all of them, there was improved function and quality of life following osteochondral allograft transplantation compared to their preoperative status, and one study did look at the longevity of grafts, and 91% of them were still viable at five years, and at both 10 and 15 years 76% remained viable in a moderate-sized case series.

With regard to sort of the summary, in the event that we have no RCTs, we really cannot assess efficacy. With regard to effectiveness, because of the size and quality of the studies, the overall strength of evidence is very low. However, it does show…

they do show or indicate, that there may be a benefit from post… from pre to post in their functional scores, but we cannot assess comparative effectiveness.

If we turn our attention now to safety among autograft individuals, donor site morbidity is one of the issues. If you look at the two RCTs that reported on this, the overall rate appeared to be 10%. We also had three case series of the knee. We had two case series of the ankle and one case series that had both sites. Again, the range from the lowest percent is 2% to 17% for donor site morbidity across these different studies. There were additionally five case series that specifically examined donor site morbidity. Two were in young male competitive athletes, and there was no long-term morbidity reported in those, and the follow-up time was from 12 to 65 months, but this is a very small sample size of 23 patients across the two studies.

In two series, one which had 111 people, the Lysholm scores do suggest that 10% of the individuals may have experienced poor function at a follow-up up to 124 months. The largest case series took a look at whether graft size or number influenced Lysholm scores or Womack scores, and there was no relationship. In terms of an overall look at the safety information, the complication rates from the RCTs, reoperation was more common in microfracture patients. In terms of donor site morbidity, we have talked about that. Infection rates were low. Hemarthrosis was fairly low. Effusion was a greater concern in either microfracture or ACI patients.

Looking at the rate ranges from the case series, the non-randomized studies, revision rates ranged from 0 to 28%. Taking another arthroscopic look ranged from 7 to 38%. Again, infection, hemarthrosis, deep vein thrombosis were all, in aggregate, fairly low. If we take a look then at the allograft, and the case series is all we have to go on in terms of safety, revision and reoperation occurred about 12.5% across studies studies, and graft failure was at about 21% across two different studies; 17% of individuals in one study had subchondral cysts, but my understanding is that the clinical significance is unknown for those. No reports of disease transmission or death were reported in the allograft group, and no reports of death were reported in the autograft group.

So, with regard to safety, infection, DVT, hemarthrosis rates are fairly low. Donor site morbidity ranged from anywhere from 3% to 17% looking across studies, and revision rates from the non-randomized studies were 21% and for safety for allograft, again, no deaths or disease transmission and reoperation rates are given there.

With regards to key question 5, differential outcomes for subpopulations, evidence basically that we're looking for is whether or not in the same patient population both the treatment and comparator are provided and information on different subpopulations is provided. We have very limited information from the randomized controlled trials. They do suggest that age, less than 30 years old, may result in better outcomes for both OAT and microfracture. Data were not presented in these studies with regard to defect size. One study looked at OAT and microfracture and found that there were comparable functional outcomes for the two groups, but those that had larger… larger defect sizes with the microfracture had worse outcomes, but again no data were presented. These were statements from the authors. With regard to defect location, in the mediofemoral condyle, microfracture patients… may have worse outcomes versus other locations, but again there was no association between location outcome for OAT patients, and in the Bently study, a greater proportion of patients who received ACI had excellent or good results versus mosaicplasty in this particular location.

So, with regard to the summary for subpopulations, looking for differential efficacy, safety in any of the subpopulations, limited data are provided from the randomized control trial to truly evaluate differential effectiveness or safety, and indirect comparisons through case series really cannot provide evidence on differential effectiveness or safety.

There were no cost… there were no full economic studies identified, so the level of evidence as we graded it as no evidence.

In summary, the main thing that we experienced is that there are substantial differences across studies with regard to patient populations, lesion sizes, comparators, the outcomes measures used, and a lot of the case series also the patients had concomitant procedures, either meniscal repair or ligament

repair, and so it is very difficult to draw conclusions across studies.

The indications for OAT and mosaicplasty and comparing that with auto… autograft versus allograft appear to be based primarily on case series, and in the majority of studies, all of them included primarily patients who were less than 50 years old. The overall quality of the literature from the methodological perspective is considered to be poor, particularly with regard to the evaluation of allograft and using the levels of evidence that are commonly accepted. So with that… I will end with that.

Craig Blackmore: Thank you. Committee members, questions for our evidence vendor? You've thrown a lot of material at us.

Woman: Yeah. I'm sorry. You may have mentioned this, but you said, 160 of the studies were case series out of 240.

Andrea Skelly: We had… we counted 332 potentially relevant citations. Of those, over 160 were case series, and so from those 160 case series, we could not… we did not include all of them, although a large percentage of them are represented in the data if you look at the data abstractions.

We focused for the autograft on the comparative studies because we have comparative studies. That's the usual paradigm that we follow, and then safety studies because they… safety information, because case series and noncomparative studies may have longer follow-ups or different information. To provide a more complete safety profile, we did include case series, only for safety.

Woman: Okay.

Man: Just a question. Age? I'm just looking because you said you had a table of some of these studies and the age ranges in those studies in a table somewhere. I haven't found it yet.

Andrea Skelly: Yes.

Man: You said people less than 30 do well, and I saw some things in here saying contraindications over age 50 and for certain BMI. I'm just wondering where that data is that would point me to age and are people doing these in people over 50, or if the articles are all, you know. Do you have a table that has the…

Andrea Skelly: Yeah. On page 73 of the vendor report, there is sort of a summary of the population from the randomized control trials, and the age, the mean ages from the randomized control trials. I don't have standard deviations or ranges on them, but these were the mean ages, as well as the mean defect sizes and other things.

Woman: Hello?

Craig Blackmore: Hello. Has somebody just called in? If you're on the phone, this is the HTCC meeting and I would ask that you mute your phones please, so as not to disrupt. Thank you. Questions for the vendor?

Woman: Yes.

Man: So, these are largely younger individuals, and were these studies excluding people over certain ages? Is that part of what was done in them, or are they just happen to all be younger patients.

Andrea Skelly: Some of them did exclude. Now, I did have a table for key question 2 that listed the exclusion criteria, and I'm going to have to take a look at that and see where I have that for key question 1. The inclusion/exclusion criteria are on page 82. And three of the four, excuse me, four of the five studies did put a restriction on age. Actually only two of them formally restricted on age, less than 40 years old, less than 18 years old. Then, the age ranges reported for Dozin and for Bently were 16 to 40 years old, 18 to 45 years old. So, that's what's in the randomized control trials. For the allograft studies, they did not exclude based on age as an explicit exclusion criterion.

Man: You mentioned that some of the data was a little bit cluttered because of the concurrent procedures that were done. Were there any concurrent procedures done in any of the randomized trials? Or was that just in the case series that you were looking at?

Andrea Skelly: Those were primarily in the case series. I would have to go back and look, but I believe most of the randomized control trials were fairly clean. In fact, the inclusion/exclusion criteria for at least a couple of them included ligament deficiencies, meniscal deficiencies and other things… malalignments...

Craig Blackmore: I wonder if you could comment. We have also gotten public commentary here about differences in how your group has graded the randomized trials versus how they've been graded in other… in other systematic analyses. Can you comment on why you are coming up with 2Bs on these trials?

Andrea Skelly: In the… there is still level of evidence 2. We felt that they were not as high a quality randomized control trials, and in the appendices, we have listed the reasons why that these were graded down for the different levels of evidence. For the most part, adequate sample size was one of the criteria for a couple of them. There were some baseline differences between some populations that were not controlled for. Our methodologic… our methodologic paradigm looks not only at study design. A lot of rating study… rating systems look only at study design, and a randomized control trial is a randomized control trial is a randomized control trial. However, from a methodological standpoint, things like whether or not there was a random sequence that was concealed for allocation, whether they state whether there was intention to treat principle followed, whether there was independent or blind assessment of outcomes, whether the co… cointerventions were applied across for both study populations, whether they had complete follow-up with a patient population and control for confounding are all methodological issues that can predispose to bias even within a randomized control trial. So, the different ways of looking at whether a study is a poor quality randomized control trial or a good quality randomized control trial from our perspective methodologically rests on these factors. I cannot speak to the methods that were used in some of the other slides presented.

Craig Blackmore: Thank you. Other questions specifically for the vendor before we get into a more generalized discussion?

Woman: Dr. Blackmore, I would like to point out that Dr. Peter Mandt is now here. He is our clinical expert.

Craig Blackmore: Thank you. In the way… the way we structure this is we try to have an evidence vendor and then questions specifically related to her report, and I think I'm hearing that we were happy now with that and then… then we move on to a more generalized discussion. So, I'm very glad you're here. If you could introduce yourself. The way we rely on a clinical expert is we have the technology vendor who has done the comprehensive literature

review and has summarized that for us, and… but these procedures very often have very specific technical components and indications, and we often have questions about that, and so we're grateful for your presence to help us through some of that. But, if you want to just say who you are and your background, that would be very useful.

Peter Mandt: Of course. Thank you for inviting me. I did my medical school training and undergraduate at the University of Washington and my residency at UC-San Diego, and I did two knee fellowships, one at UCSD and a second one with Dr. Richard Stedman at the Stedman Hawkins Clinic, and as many of you know, the OATs allograft… well, osteochondral allograft studies, a lot of the early studies were done at the University of California San Diego, so I was a part of those as a resident. That was where I first sort of encountered this procedure. When I was doing my fellowship with Dr. Stedman, he's probably best known for being the one who coined the term microfracture, which of course is another method for treating cartilage defects, so I was exposed there kind of at an early time too, and I took a job as the head of sports medicine at Virginia Mason Medical Center where I was for about 15 years, and that's where I had a lot of referrals for patients that were sort of, you know, younger patients with sports injuries that really weren't candidates for arthroplasty.

So then, the osteochondral allograft technique sort of evolved into the OATs allograft, you know, in terminology and equipment. So, I became involved with that, since I had an interest in knee reconstruction and cartilage repair. So, I started developing that special interest and started generating referrals probably in the early 90s or so. So, I've kind of had experience with this over a long period of time. Now, it's not a large part of my practice, or anybody's practice. It's a relatively specialized procedure. So, volume-wise it's not huge, but you know, I've got sort of this relatively unique background for the Northwest area. So, that was why I was… Dr. Chris Wall at the University of Washington was the one who suggested I might want to be a part of this. So, I appreciate your inviting me.

Craig Blackmore: Thank you for being here. One question, which has come up early in our discussion, was the question of open versus arthroscopic repair and when… what the factors might be that determine when you would use each approach.

Peter Brandt: Sure, well, the term OATS, you know, can apply to, as you know, autografts or allografts. You know, generally speaking we use allografts when the defect is larger, and most of the allograft equipment is really only designed to do defects greater than 1.5 cm in diameter, and when it gets to be a plug that large, you really can't do those arthroscopically. You need a large enough incision to be able to put in larger cylinders. So… and the equipment is really not designed to be used arthroscopically either. So, essentially, almost all the allografts are done open. The autografts are smaller, and those are amenable to doing arthroscopic treatment, although… and it depends a bit on the clinical expertise of the surgeon, as well as how large the defect is. Sometimes, it becomes a triumph of technology over reason when you're trying to do three autograft plugs, and so, you know, the results end up not really being that much different whether you do open or arthroscopic, and in someone who is not really experienced with using it, it's better to do it open because you can get a better result if you're not used to doing them arthroscopically. So, you know, it really gets down to autografts and smaller autografts are easiest to do, or easy to do arthroscopically. Bigger ones get to be harder to do arthroscopically, and the allografts are essentially all open.

Craig Blackmore: Thank you. At this point, I'd like to open up a little more to the committee if there's any more questions for the vendor, for our clinical expert, or for the agencies before we launch into our discussion.

Well, hearing none, and this is obviously not the last opportunity to ask questions, I want to turn to the tool, the our coverage and reimbursement determination tool, and again, this is the tool that we use to help us go through the evidence and make our coverage decision. The first couple of pages of this document talk about the principles upon which decision making is made. The second part of the document on page 3 defines whether or not there is a Medicare national coverage decision that would be relevant to us, and the answer is that there are not. There are also some other guidelines from other organizations, including the American Academy of Orthopedic Surgeons, Work Law State Institute, etc. on when… well pertaining to this topic.

The next part of this document is for the committee to delineate the outcomes, which we believe to be of interest around the domains of safety, efficacy, and cost and cost effectiveness, as

well as particular populations or special considerations. So, our first task is to define the safety outcomes that we believe to be relevant and staff has prepopulated this document with a number of them here. Some of these are pretty, pretty obvious or pretty straightforward. Mortality, obviously. Morbidity, particularly pertaining to the donor site in autograft as a safety outcome. Surgical complications, infection, etc. The requirement for reoperation. You could consider that, I suppose, either effectiveness or safety. At least for now we've got that as a safety outcome. MRI findings is on here. I'm not sure… I'm not sure that resonates with me as a safety outcome. It might be an intermediate outcome for effectiveness if the MRI looked better, but again I think our focus is more on clinically relevant outcomes. So, I don't know what the rest of the committee thinks. Personally I don't know that I would consider MRI findings to be terribly important.

Progression of osteoarthritis, rate of graft failure, I would probably put those in effectiveness. Disease transmission from the donor tissue, that sounds like safety to me, and then other adverse events. Any other safety outcomes that are important that we are considering in our decision making that have not been delineated?

Okay. Then efficacy and effectiveness and particularly relevant are outcomes that are clinical that aren't simply MRI findings, for example. So, functional outcomes, obviously, there is a specific point here made about longevity of treatment effects, particularly since a lot of this is dealing with younger populations. Progression of osteoarthritis is arguably one of the most important primary outcomes, and then graft failure would imply treatment failure.

Return to work or preinjury activity or return to sports, obviously important for quality of life and then quality of life is listed here separately. We have differential results between open and arthroscopic procedures. I'm not sure that's a separate category.

Man: It doesn't seem like an outcome.

Craig Blackmore: Right. So that may not fit. Patient satisfaction, obviously, and then are there other outcomes that we think are relevant that… effectiveness or efficacy outcomes that aren't mentioned here that we are including in our decision-making thought process?

Woman: You know, we could consider reoperation, perhaps. I'm not sure that's just safety.

Man: Is that safety, or is that?

Craig Blackmore: I mean, it's sort of in line with like graft failure, and they are related on some level. That might be in both. I don't know if that's just a safety outcome or if that's also an effectiveness outcome. Okay? Anything else?

And then I'm going to, again, jump ahead to cost and come back to the populations. So, for cost, we are going to look at the… both the short-term costs of the procedure, as well as any indirect costs induced, and we're going to look in the short-term, as well as over the expected duration, which is really the patient's lifetime, and we would look from the perspective of the payer, as well as society, and we would consider cost effectiveness.

Then there's the issue of special populations, and this becomes particularly relevant if we do make a coverage with conditions determination and this is where we would start to think about what some of the criteria might be under a coverage with conditions determination so that as we go through our discussion, we can keep that in mind. First would be defect type, which is listed on here, which I think, you know, I think there's sort of the depth or severity of the defect, and then there's also the size of the defect, and I think those might be separate things. So, we're going to go with defect size, and we're also going to go with defect severity or depth.

Man: And location?

Craig Blackmore: And then location is the next point on here, so that would also be important. Gender might be important, I suppose. Certainly, we've heard, we've heard that there is… the data at least is age specific, so we should consider that. The question of whether prior… and I would actually say prior or concurrent other surgical procedures might be important, and that's, I think, two separate categories. Some of these people will have had ongoing problems in prior surgery, and there might be another category who have other injuries about the knee at the same time that might or might not affect the success of the cartilage procedure. I'm

thinking about ACL injury or meniscal injury, and patient selection. I'm not sure I'm seeing that one. Is that… anybody?

Man: Patient selection?

Craig Blackmore: Anybody define anything under patient selection that we haven't already touched on, or have we gotten through that?

Man: BMI popped up in that report somewhere?

Craig Blackmore: BMI?

Man: Yeah.

Craig Blackmore: So we might consider BMI.

Man: I'm just saying it popped up in the report as a variable in some of the studies.

Craig Blackmore: So it's something we might think about. It's not saying we would consider it, or we would keep it. And then payer or beneficiary type. I'm happier not specifying based on that, but I don't know…

Man: I don't see the need for that.

Craig Blackmore: Alright. So that's a pretty comprehensive list, and now we need to work through towards a decision and again I'd like to adopt the approach of having committee members give us their perspective in where we are, not necessarily with an I will… I believe we should cover or not cover, but with a summary of what the evidence tells us and maybe the areas that they see as being key to decision making at this point. So, I will solicit volunteers.

Man: Can I ask one question first? So our vendor broke this up by autograft, allograft, mosaicpclasty, and ACI as a whole separate thing. I assume we're not talking about ACI, chondrocyte, implantation, and are we considering autograft, allograft, and mosaicplasty all as the same thing, or are we breaking them up like the vendor did? She has separate data for them. Do we consider them all as one thing or do we separate them out?

Craig Blackmore: That's our choice. That's why I'm asking. What do you propose?

Man: I'm just curious what people thought about that. The agency seems to talk about them as one thing. This came through as OAT, but that's a trademark name, I think, but it implies all these other sorts of things. So, do we do what the agency does and put it all in one basket of stuff and let the clinician sort of decide when they would use one versus the other, or do we… some of the distinctions seem to be based on different characteristics of the lesions, particularly, or do we, again, do we consider them all as one thing and let the clinicians decide, or do we go through the process of breaking them up?

Man: Given the point of that, there seems to be some dependency on the nature of the lesion, itself, to determine which technique you should use. I think that falls down to the circumstances of the individual patient assessments, and I think we've, that it would behoove us more to treat them as just one entity and then that varies into what you apply to individual patients.

Man: We could view them as one category ourselves and then leave it to the clinician. I just wanted to make that clear before we get talking.

Craig Blackmore: So, I've got one choice is that to say we've got this clump we're going to vote together on the clump and then the individual clinical circumstances will dictate which of the techniques, and then another choice would be to look at them individually. Is there a perspective in the committee that we should look at each of these separately, or are we pretty much all on board with lump?

Group: Yeah… lump.

Craig Blackmore: Okay. I'm seeing lump. That sounds good. And then… I want… if I could get clarity probably in the key questions… and I could get help from Spectrum on this. Where is the… in terms of the ACI, our key questions did not specifically refer to ACI, except as a comparator. Is that how things were addressed from the vendor's standpoint?

Andrea Skelly: The ACI was never part of the key questions. It cropped up as one of the comparators in the literature.

Craig Blackmore: Okay. And the same is true of microfracture?

Andrea Skelly: That's correct.

Craig Blackmore: So we are only addressing this specific family of osteochondral transplantation plug.

Man: Osteochondral transplantation.

Man: Can I ask our clinical expert a question? I think, I'm just trying to get a sense of clinically how this decision process works. So, you know, these are comparators that are equivalent to them from a clinical perspective are OAT seen as comparable to ACI and seen as comparable to microfracture? Like, how is that decision currently made?

Peter Mandt: Well, most of the time it's made based on lesion size. I mean, you know, a microfracture is, you know, another useful tool, particularly if you're in a situation where you run into a defect that's unexpected, you know, during an arthroscopy. I mean, in terms of deciding whether to do an osteochondral autograft versus an allograft, it really gets down to lesion size, and I think that the decision to make… to do an osteochondral allograft based on lesion size has gone from larger to smaller. I mean, the osteochondral autograft, I think the results have kind of shown that multiple plugs start to give poorer results. And also the increased risk of donor site morbidity. So, I mean anything, and specifically though the literature has generally said that anything over two square centimeters is an indication for allograft and anything under is an indication for autograft, but I think, you know, I mean personally I tend to go to allograft or even smaller lesion sizes than that just because of the risk of donor site morbidity.

Man: I guess I'm asking about more in terms of either allograft or autograft as compared to ACI or microfracture. Is that a choice that's made ahead of time and how would you make that decision about whether you're going to do an ACI?

Peter Mandt: I mean, I personally don't do ACI, mainly because I haven't been convinced of its efficaciousness, especially when viewed as, you know, in terms of cost. Many studies have been, unfortunately, you know, I think funded by the company that has the main, you know, interest and benefits from the studies being positive. So, I'm not sure that they are all that good. But, in terms of microfracture, you know, it's… when there's a small lesion that's

sort of an incidental finding, then we'll usually… especially if it's done… found at the time of say another procedure. You're doing an ACL reconstruction and you find a small cartilage defect. Then, we'll do a microfracture, and I tend to do them only if it's, say, under 1 cm or so. And then if somebody still has symptoms down the road, I'll do an autograft or allograft as a second stage in that case.

Man: Thank you.

Man: Yeah, I have a question. As we make our decisions... well, first of all, I would say, it sounds to me like from the beginning we're going to do something… go with coverage with conditions based on at least what Steven had brought out. That's sort of the position where the State's coming from. But, the question that I really am having some problems with is that, if we make a decision not to cover with say OAT or allograft in a particular situation, does that, by exclusion, mean that another alternative procedure that is covered, like microsurgery, which may not be as good, would come in and replace it? In other words, if we get too microscopic in our decision making, are we really just basically doing a disservice to the patient or taking away an option from the physician, and that's part of the problem I have in coming to a decision, and I just want to get an idea from our expert here of whether or not if we took OAT away from some indication that it would just mean that some other procedure would take its place. It's not really a cost-saving maneuver.

Peter Mandt: I mean, I think there's a real risk here. I think because of the way the key questions were formulated, we can't address ACI. If we… if we rule to not cover OAT, then we're still covering ACI, and you know, you could argue that OAT might be better. So, I think in this case, the wording of the key questions may have done a disservice. I don't know. Perhaps not, but I think yes, if we rule for noncoverage of OAT, we will still be covering microfracture and ACI because they're outside of the scope of what we've looked at, and I guess I should ask the direct agency… the medical directors, do they currently cover ACI and microfracture procedures?

Gary Franklin: I think we cover everything but require this procedure before ACI. I think that's what we do, and also ACI is, I believe, hugely more expensive.

Man: It is.

Man: I have a question about natural history. Dr. Just, in the beginning, presented this continuum of disease analogy that talked about this is the beginning of pathology that… that ended up in joint failure, and is that your perception, as well, that this is the beginning, or a type of beginning event that proceeds to joint failure in a high percentage of time? Or is this a pathology that is found in a lot of people and some of them proceed to joint failure over time.

Man: I mean, I… my indications are to do them primarily for traumatic defects. I mean, if you start going chasing, you know, degenerative arthritis and doing OATs allografts or something and, you know, spots of degenerative arthritis, you're just going to get failure around the lesion. You know, normally we do these in traumatic defects or in situations with osteochondritis dissecans. For osteochondritis dissecans, there's really not a lot of other ways to treat it. I mean, you're left with a big… you have a big hole in the knee, and you either live with that hole in the knee, you do a cartilage transplant into it, which restores normal function, or, you know, end up with an arthroplasty. So, you know, I mean not to get too far off the subject but, you know, the comment earlier about, you know, are we going to, is this just going to shift things over to doing other procedures, I mean, that's exactly what will happen. I mean, we were doing, you know microfractures get done at a very large number. Those are done compared to the number of osteochondral allografts predominantly because a lot of surgeons don't do osteochondral allografts. But, you know, the other option is to do a total knee replacement. So, you know, that's going to happen either at an earlier time or as an alternative in treatment to some of these defects. You know, I've had some that were relatively large that, you know, otherwise would have had an arthroplasty. But, you know, these are usually young patients who, you know, in their 40s or 30s sometimes who aren't going to do well with having a total knee replacement, either. So, it would take away a really viable way to treat those patients.

Man: Similar question for the vendor. I mean, is there data on long-term national history of OCDs that you found, or is there… I didn't see any long-term follow-up data on, I mean, 10-20-year follow-up data on any of these procedures in terms of the osteoarthritis

question. But either natural history untreated or natural history after.

Andrea Skelly: From our review, there seems to be a suggestion that there is a potential for progression to osteoarthritis, but a lot of the reports say that the natural history is largely unknown, and we looked, as we were looking to the studies, we looked specifically to see whether there was data on progression to osteoarthritis, and there was very… I mean, we really didn't find anything in comparative studies at all, and I believe there may have been one or two case series that suggested that there was more osteoarthritis in a certain population. There is a large case series by Hangoody that suggests that among athletes, there was maybe more progression to osteoarthritis. The problem is, is we don't know how… what the level of the preexisting osteoarthritis was. So too… within the absence of a comparison group, we really don't know whether the procedure helps or not. The longest follow-up we have from the RCTs is 48 months. The longest we have from the case series is somewhere… well, you know, some report up to 124 months of, but... Again, osteoarthritis is not one that has been well reported.

Man: Can I just ask, and I'm curious with the allografts, do you need to do HLA typing and matching you don't need to give immunosuppressants and…?

Peter Mandt: Well, the articular cartilage itself is relatively immunologically privileged because the cells are buried in the matrix. It's the bone that is what's in danger of rejection. And so, it's impractical to do HLA typing because we're also doing size matching, and if that were the case, then nobody would ever, you know, end up getting a graft match. Bone allografts are used frequently in other areas in orthopedics, and we use them oftentimes in treating tibial plateau fractures where there's a bone defect. Their en bloc pieces are used in spine surgeries, and so what you see is about an 85%, you know, long-term survival rate, and that's based largely upon whether the bone is accepted or rejected and whether or not creeping substitution, which is kind of the method by which the bone is replaced by the host bone over time, you know, ends up being successful, which is kind of the same thing that happens with, say, a spine fusion in which an allograft disk is used. So, yeah, we basically… it's sort of like doing a bone graft and the cartilage is along for the ride.

Man: So, given that, I'm surprised that you haven't done studies at some point, even in lesions small enough to have the OATs procedure done… are you just… is it clear that you get better long-term outcomes with that than with an allograft, because if you use the allograft you don't have to have the host site morbidity problem.

Peter Mandt: Well osteochondral autografts essentially always heal in. The issue, really… unless you get to multiple plugs, and there's technical deficiencies in terms of the gaps between the plugs and so forth that might result in a mechanical inability of the bone to heal, but in one or two plugs that are very well fixated in an autograft, you know, essentially it's always going to heal in. But, then your worry is really more about donor site morbidity. When it comes to allografts, I mean, usually we're using a larger defect. So, I mean, the mechanical problem, I mean the patient usually feels it's usually more than just pain, but they feel like a, you know, a catching or a clunking, or some element of the defect, and if it goes on too long then you end up with a meniscus tear because it's catching on a defect. So, you know, the studies that have been the longest duration have been the ones out of UC San Diego, I believe, because, you know, they were started in kind of the mid-80s, but there were some technical issues there because that was before the advent of the modern instrumentation, and they were essentially all done sort of using hand carpentry. So, you know, there was another variable introduced there besides just the biologic one.

Man: I have a question about, is it the same decision-making process for the patellofemoral lesions, as the condyle lesions?

Peter Mandt: Well, I mean from a size standpoint it can be, but patellofemoral lesions tend to be better tolerated. I mean, it's a… I mean I find… I mean, everybody always in orthopedics has found that the patellofemoral joint sort serve as a bit of a mystery because, you know, you see people who have very significant disease as an incidental finding at the time of arthroscopy and people who have, you know, relatively well-preserved patellofemoral compartments that have symptomatology. So, trying to decide where the symptomatology is coming from, you know, ends up being key. You know, so, you know, I do relatively few in the patellofemoral compartment compared to the weightbearing tibiofemoral compartments of the knee. You know, they are usually either a really large defect on the patella. I have had a

couple that had patellar dislocations, which they sheared off half of the joint surface, and I tried to treat some of those conservatively over time, and they failed, and others with large trochlear defects who start to have mechanical symptoms and so, you know, those can end up being an indication, too. You know, I mean, probably that's less than 5% of the ones that I've done over time.

Man: Thank you.

Craig Blackmore: So, I'd like to get a feel from members of the committee as sort of the big picture of where we are in all of this. We heard from Richard, and what are we thinking? Volunteers to kind of sum up. Seth, thank you for volunteering.

Seth Schwartz: Yeah. I mean I guess I'm similar along the lines of Richard. I think that the data is fairly good in terms of the efficacy of this procedure, and I think we're limited a little bit by the populations that have been studied, which makes it a little harder to think exactly what the restrictions would look like, but I don't… am not necessarily sure that we need to put significant restrictions on this. That's kind of where I am.

Craig Blackmore: How about the other side of the U-table here? Mike?

Michael Souter: I think that it definitely has merits. I'm not so sure that we don't need to put some restrictions on it. I think there are already restrictions that exist in the literature such as, you know, joint instability. I think we should very actively consider the question of degenerative and joint stability, I mean ligamentous instability, etc., and then the whole issue of degenerative disease. You know, that's… I think that we may need to put some limits on that.

Craig Blackmore: Michelle?

Michelle Simon: I guess I have more questions. I'm trying to get a sense of, if this procedure is not done, is it absolutely positive that other procedures will be done, or are there patients for whom nothing will be done, and do we have a sense of whether those conditions that you've talked about are definitely going to progress to osteoarthritis or not? I know one of, in the report, you mentioned… I saw in the vendor report that there was some indication for chondromalacia patellae as an indication for these

procedures, and that's a… lots of people are in that category. At least it used to be a really common diagnosis, and then we really don't know if that progresses to osteoarthritis either. Do we know anything about that?

Peter Mandt: Is that for me? Well, chondromalacia patellae is a difficult diagnosis because in fact, most of my knee professors that have been, you know, that are… have studied this over the years really feel that's not a diagnosis. I mean, it's a description, because chondromalacia means bad cartilage, but it doesn't really mean that they have pain. I mean, we see people with chondromalacia who don't have any pain and vice versa. So, I don't really see that as an indication for doing OATs allografts. I mean, the ones that I do are mostly traumatic defects in the patella. That's why I said there's very few. I mean, if I used that as an indication for doing OATs allografts, you know, they'd be getting done all day long every day, I think. I doubt if very many people do. In fact, one of the university team doctors came to me with patellofemoral pain, you know, and we had a long discussion about this, and she played college basketball at Notre Dame and had an ACL on the other side, and her biggest problem over time has been this one knee with patellofemoral pain, and she had done by someone else a patellar realignment and various other things and still has pain, and you know, her cartilage is thin, but you know, I mean I see people with a lot worse cartilage defects and I just told her, you know, I don't think that's going to be something that's going to fix this problem. I mean, it is, you know… on the one sense, I mean, it would be good if you could… if restrictions could be put. I mean, I think there might be some surgeons out there that might be willing to stretch the indications, but you know, it gets to be sort of an individual decision, and you know, I think traumatic defects, if you look at traumatic defects or osteochondritis dissecans, I mean, those are fairly clear indications. Deciding when a problem is osteoarthritis or something gets to be a little bit more difficult, but, you know, in general, the indication is contained lesions, which means, you know, the cartilage surrounding the lesion is normal. Usually, that's fairly clear cut. You see defined ridges. You know, there's usually an etiology. Somebody had some type of an injury and ended up with a chondral defect. Osteochondritis dissecans is relatively easy to determine on the basis of an MRI or x-rays, and there really isn't any other way to treat that other than an allograft because there's a bone and cartilage defect there. So, I think, I mean, that's, you know, patellofemoral pain isn't really an indication and

chondromalacia is, you know, it's not really a diagnosis as much as a description, but unfortunately it gets used as that a lot, you know, in common terminology.

Michael Souter: I have one more question, again, as well. So, I mean one of the things that we heard from the agency directors was the recommendation that we consider a filter again of failure of conservative management. I mean, how long does it take to arrive at, you know, in your management of these patients? Is this an… clinical intervention that gets… that you do straight off the bat or do you observe somebody? Do you put them through… if we're talking about something of traumatic defects, do you put them in any kind of rehabilitation therapy, etc. before leaping into, and I don't mean leaping in any pejorative sense, but before going to rather a, you know, the decision to do an OATs procedure?

Peter Mandt: Well, probably the majority of the ones that I do are referred to me by outside orthopedists who don't do the procedure, so they've already sort of gone through the gamut of conservative treatment. The problem exists in that… in a large enough lesion, one that's uncontained in particular, which, you know, is usually defined as greater than 2 cm^2, you have a situation in where you have bare bone articulating with the normal articular surface of the tibia and the meniscus caught in between. So, the problem is that if you do nothing and you assume that the bone defect is not going to heal over without some other type of intervention, then it gets to be sort of a race between doing something to fix the problem and ending up with no cartilage left on the tibia and a torn meniscus, which then, you know, ends up being a situation in which the OATs procedure can no longer be done for the smaller lesions.

So, for the smaller lesions under 2 cm^2, you know, I most often treat those conservatively and would do just… and by conservatively I mean it would be a microfracture generally because you usually aren't seeing those lesions until you do an arthroscopy. On an x-ray you can't see them. On an MRI scan you can make a guess, but most of the time they are symptomatic, and generally when there is a traumatic lesion there is some other injury, so we're usually there looking at that and then do a microfracture and see how they do.

Man: I mean, from a nonoperative perspective when you have somebody whose young comes in with a symptomatic knee or even ankle and has a clear OCD on imaging with reactive bone [inaudible] hole in the cartilage, there isn't a lot you do nonoperatively for them, frankly. You know? I mean, you can try to rehab that, but it's not very rehabitable when you have the same issue as the day they came in because they're not functioning.

Michael Souter: Sure, and I accept that, but it all comes down to where you draw the cutoffs.

Man: So, requiring, you know, if somebody comes in and they have, you know, osteochondritis dissecans with a fragment that came out in their knee, I mean, there's no… there's no role for nonoperative care. You go fix that. So, requiring nonoperative care could be a little curious because there are times when they would show up in your office, and it would be inappropriate to do that in a way. At times, it's certainly necessary, but there are other times when it might not be. So, as a requirement…

Michael Souter: I'm not suggesting it would apply across the field. I just want to know just how long it takes to arrive in cases of say, again, traumatic induced injury where it's a minor defect, you know. How long does it take to arrive at the kind of decision to go to an OATs intervention?

Man: One other question on our conditions when I think about is the joint, you know, we talk about the patellofemoral versus femur, and then you talk about joint. We have some data on ankle that she didn't talk about much in the presentation, but they gave us data on ankles, and this procedure is done on ankles. I've seen it done in shoulders, but we didn't get any data on shoulders. So, do we talk about this as a blanket thing? Do we limit it to a given joint? Do we let people do it in ankles and knees? Another thing to think about, because we have some data on that. You didn't talk about the data on ankles in your presentation.

Andrea Skelly: No, and there were no comparative studies on joints other than the knee. There was one comparative study in the talus. It was built as a randomized control trial, but it was not… and the authors eventually retracted their statement, and it was in a very small group… a small… a small group of individuals, and I'm going to have to go back and look at... I've got to go back and find that.

Craig Blackmore: So, I mean, I think I'm hearing, at least in terms of the knee, that there's some feeling that we're in that world of cover with conditions, again, and I'm looking for nods or shakes. Okay. Not sure I have universal agreement.

Woman: It's the conditions that I think are the most controversial.

Craig Blackmore: Well, the conditions are always the problem, right? I mean, that's always the challenge. What about the ankle and the shoulder?

Man: I don't think we have enough evidence to make a decision on other joints.

Man: For the shoulder, we have nothing.

Michael Souter: You know, really for the enclave, I'd consider that we should exclude shoulders and ankles from consideration.

Man: Well, is the pathology different in those joints? I mean, if it's a different pathology, absolutely we should exclude them. If the pathology is identical, we should at least talk about it.

Man: You may run into the same question that if you had an OCD in the talus and you say, well you can't do any sort of transplant, you have microfracture. Maybe you're going to get a microfracture. I mean, they're going to... it's the same question we had before, you're going to do something, because you have a symptomatic OCD in the ankle.

Michael Souter: But we have to be very careful to indulge in any of the intuitive extrapolations. It's that kind of whole road that we do not want to go down, I think, and medicine does tend to do that by default. You know, at present, that's again, what's the agency position on this? Are shoulders covered at this point in time?

Man: I don't think. These are subjected to prior authorization. Shoulders.

Man: We don't allow anything but knees.

Man: You do knees? So, in microfracture in the ankle or shoulder you would allow? Is that what they do?

Man: I don't know about the microfracture. I'm only talking about the transplants.

Andrea Skelly: If you want the ankle one that we have, it was a cohorts… again we classified it as a cohort study because they really did not randomize. It was small. There were 12 people who had OAT. There were 10 that had microfracture and 11 who had chondroplasty. In terms of functional outcomes, there were no statistical differences. The American Orthopedic Foot and Ankle Society Ankle and Hindfoot Scale or the subjective assessment of Merrick evaluation. There were no statistical differences between any of the comparators, but again, a very small sample size for that group. The only… we did not find any comparative studies for the shoulder or other joints.

Craig Blackmore: So who have we not heard from? Kevin, do you want to?

Kevin Walsh: Yeah, I want to respectfully disagree with Seth. I think that, I mean, these studies do show benefit, but when I look at them, I think that they have defined benefit in narrow terms, especially temporally narrow terms. I'm just not convinced. When you look at the Horace Study in slide 24 of the presentation… I'm sorry. I'll back that up, slide 20 looking… comparing OAT to ACI and outcomes. At 24 months, there is very little difference.

Man: Where are you looking, Kevin?

Kevin Walsh: Slide 20 of the slide presentation that the vendor did.

Michael Souter: Page 10.

Kevin Walsh: So, if we're going to limit ourselves to whether this… to up or down on this procedure, and I think we should because while I understand what Richard says, in a lot of other discussions we haven't allowed ourselves to get outside of the context of the questions themselves and think about larger issues.

Man: I just want to look at that study again. I think, you know, one of the things that came out of this was that lesion size there's a big question mark, and I think that, you know, if you look at the mean lesion size, and that's almost 4 cm and this… we're talking about autograft, and I think we've heard very clearly from our expert that you wouldn't do an autograft in that setting anyway, and that was the biggest criticism from basically all the external reviewers

about these studies was that size wasn't really taken into consideration in a couple of those studies that didn't find a significant difference, so…

Man: I understand your point, but you're… the conclusion you're making is, oh well it works, if it's done the right way it works. Well, where's the… prove it.

Craig Blackmore: Well, there's the Bently Study on slide 21. There is also the Dozin Study, which doesn't show much difference. It doesn't show any difference. The Bently Study... I guess this is mosaic. This isn't OAT.

Man: If you look at the study on the previous page.

Man: But the comparison shouldn't be ACI. It should be more microfracture. ACI is still, is a far more expensive and less commonly done procedure than this, and at the moment, as the agency just said, they require a chondrocyte transplant or osteochondral transplant before they allow an ACI. So, saying well, it's no better than ACI doesn't really help us. The fall back would typically be a microfracture, I would think. So, I would go back to the microfracture data, because that would be more commonly done as, they were looking for comparators, and again we don't have any natural history. So, I don't think there's any study on sort of this versus nothing versus just natural history. So, we don't have that data, which would be very nice to have. Natural history data would be great, but I don't think we have it.

Michael Souter: I mean in many ways if you consider that… if you're comparing it against ACI then we're almost duty bound to recommend OAT, because it'd be a lot cheaper.

Man: Also, in the Horace Study, you're taking three different measurement scales and comparing those. Two of the scales were the same and then one of them had what, a 6% advantage of OATs over ACI? On the Lysholm Scale. But the other scales were about the same. So, I can see your point on that, but it was kind of mixed results in that study anyway.

Man: I don't think we know the long-term outcome of any of this stuff, and we don't know the long-term natural history, and the data is not nearly as strong as we would like it to be. Then we've got this added sort of curve ball of we haven't really included ACI in this

and I think I'm of the school that if we think, we should decide if we think it's better than microfracture, and if we think it's the same as ACI, we should support it, because otherwise if we don't, they're going to get ACI, and it's going to be more expensive, and I think probably less safe because it's multiple procedures, and there's even less data. So, I mean it's dissatisfying. I think it would be better if we had data on ACI so we could make ruling on each one, but that's not where we are. But, I guess my perspective on OAT would be that it, at least in the data we have, seems to be a little better than microfracture in young people. We don't have any data on older people and in people with a defined type of lesion and no osteoarthritis, but that's just my opinion.

Craig Blackmore: Who else have we not heard from? Have we heard from you?

Woman: No, I agree with what you just said.

Craig Blackmore: Anybody else? David?

David McCulloch: No, I mean I'm already on the cuff of… what would the conditions be? So for the osteo dissecans. I mean, it should be covered for that and for, you know, I think for trauma in younger people in weightbearing joint of the knee should be covered.

Man: I don't know if it's worth talking… discussing size of lesions because it's something that it's a decision of the physician. I don't think we can get into that.

Craig Blackmore: I don't think we can get into size, but we can get into sort of type. Is it down to bare bone or grade 4, or is it, because I mean, there's a lot of… there's a lot of less severe injuries that hopefully would respond to conservative treatment. Gary, did you have a… can you enlighten us?

Gary Franklin: No, we looked up our L&I policy. We sort of do the… it's suggested the microfracture first, and then this procedure, and then in that kind of order before doing this procedure, we might ask for a microfracture procedure first.

Craig Blackmore: That's your current policy? Is that what you're saying.

Gary Franklin: Yeah.

Woman: But I thought the data showed that that's…

Craig Blackmore: But only for smaller lesions.

Gary Franklin: Smaller lesions.

Woman: But this was better than microfracture.

Man: I think it is.

Woman: In small lesions in some populations.

Andrea Skelly: The Gouda Study in athletes and children does show that on slide 17. It directly compares the OAT to microfracture.

Craig Blackmore: I think we should… I think… my sense is that the majority of the committee is circling around a conditions type of position, and we may not all be there, and it may be that when try to talk about conditions we'll shift around, but I think it would be fruitful to put together draft conditions. Does that resonate with people? I don't want to do that if it's not… can I have some nods or shakes? Richard?

Richard Phillips: I would go along with that, but I'd also say that if we start getting into like… to particulars that we might want to go to a subcommittee to turn it over if we can't come up with something that's very simple and straightforward. I don't want to get, you know, stuck away trying to make decisions, micromanage things that physicians or a subcommittee might do better. But anyway, I agree with you.

Craig Blackmore: Yeah, and I think that's what we'll have to see how we feel and do, yeah, and that's certainly on the table. Okay, and then I think that's where we are with the knee. I'm not sure if that's where we are with the ankle, and I doubt that's where we are with the shoulder. So, I think… I think what I would like to do first is talk about these other joints and then come back to the knee and have it be cleaner. Does that sound fair, Richard?

Richard Phillips: Yeah. I would ask a question. Do we have to make a decision about the other joints, or can we just choose to say no decision because we don't have any data about it, or do we actually have to say a no coverage decision?

Craig Blackmore: I think if we conclude that there's data and we don't have it, or that it wasn't in the scope of the technology assessment, then we should not make a decision. But, if we have the data, it was within the scope of the technology assessment, it's within the scope of our key questions, then we should make a decision, and I believe that the assessment, the tech assessment and the key questions were encompassing of what there is on other joints. Is that correct, Dr. Skelly?

Andrea Skelly: Yes, we looked for other literature on the joints, but again, with 160 case series, if it was in there, it was in case series, except for these ankle, this one ankle study, and then we did use case series that were mostly focused on the knee.

Craig Blackmore: Okay, but I think in, in light of what we're saying that maybe we should do the knee first, and then that will help guide where we go on the other joints.

Man: We could do something… either for shoulder we could not do it, or we could say, you know, other joints at agency discretion and let them decide if they think there's a reason why when somebody really wants an OATs for an ankle whether they would do it, and we could leave it to them.

Craig Blackmore: Let's do the knee first and that will help guide us and then we'll have a range of options on the other joints. So, I'm going to then entertain proposals for what coverage with conditions might look like before we vote on whether we want to do that, and Denise is going to help us out. David, you were thinking along those lines. Can you start us off on what coverage with conditions might look like?

David McCulloch: Yeah, I mean I would base it largely on the page 82 where we have the inclusion and exclusion criteria of the report. It gave the inclusion and exclusion criteria in the five randomized control trials. So, I would say, you know, it should be for age less than 50 or age less than 45 with something, use age, and require that the… in a stable knee, and for traumatic… traumatic reasons excluding degenerative arthritis.

Craig Blackmore: Okay, so we've got age. We've got traumatic lesions excluding degenerative arthritis, and then what else did we hear? We heard…

Man: How about osteochondritis dissecans?

Man: You're going to have to define traumatic somehow, because some of these are sort of repetitive microtrauma, osteochondritis is a very complicated thing in terms of why that occurs. I mean, you could just leave… I mean, I don't know if you have to get into the etiology of the lesion. You could just describe it as for a whatever grade osteochondral lesion, you know, grade 3 or 4 osteochondral lesion.

Man: I mean, I think what's important is that the rest of the cartilage has to be normal.

Man: And that you have to have a focal lesion with the rest of the cartilage normal.

Craig Blackmore: Chronic degenerative disease and all the cartilage is abnormal, then the prognosis is going to be worse. So, maybe absence of degenerative arthritis and then the etiology of the defect is less important. So, Denise you can just simplify that to be excluding degenerative arthritis.

Peter Mandt: Can I make just a quick comment? I mean, many of the… many of the studies, the indication that's commonly accepted, it's described as a contained lesion, you know, meaning that the surrounding area is normal.

Craig Blackmore: I thought we heard from you that some of the larger defects were not contained using Allograft.

Peter Mandt: The implication of contained lesion is that the surrounding cartilage is normal. Now, there are, if there is a lesion that's uncontained because it goes out to the margins of the femoral condyle, I mean, then technically that's not contained, but it still could be a traumatic lesion. So, you know, but the osteoarthritis implies it's an uncontained lesion because the surrounding area is not normal or fades into a grade 4 defect.

Craig Blackmore: I think we're on the same page, we're just struggling for how to put that into…

Peter Brandt: I was just suggesting that terminology.

Man: I don't see that word anywhere in this sort of list of, the word contained, and are people going to know what that means? Because I don't see it in these tables we have. The word contained doesn't appear. They use the Atterberg's classification and other classifications for the depth or severity of the lesion, but they don't use the word contained.

Peter Brandt: Well, I haven't looked at all these studies specifically, but you know, over the years I've, you know, I've kept up on the literature and, I mean, generally… like the International Cartilage Repair Society criteria usually is, you know, allograft is over 2 cm^2, you know, for doing these types of cartilage transplants. They're, usually referred to as contained lesions. Anyway, I mean, whatever terminology you want to use is fine. I just, you know, I just was suggesting that, because that implies that the margins are normal… the surrounding cartilage is normal.

Craig Blackmore: I think your input is helpful so that what we say is clear to the orthopedic surgeons, but, you know, we just have to make sure it's clear to everybody. That's all.

Peter Brandt: No, I understand that. I didn't mean to interrupt, I just thought…

Man: No, no, no, it's very helpful.

Man: We're struggling with the wording. So, I'm looking for the right word. Do you say focal? Do you say contained? Do you say isolated? Do you say it was surrounding normal cartilage? Do you say something that makes it clear that… what you're talking about?

Man: Cigna's got a single focal full-thickness articular cartilage defect.

Man: Say that again.

Man: It's called repair of a single focal full-thickness articular cartilage defect. Does that cover…

Man: Does that resonate with contained?

Peter Brandt: Sure. I mean, you know, there's other synonyms. You know, I mean, the idea… I mean the implication is that you don't want to do it in an area of osteoarthritis where it just happens to have

progressed to full thickness in the central portion of the lesion and the rest of it is on its way. So…

Woman: So, is excluding degenerative arthritis not sufficient?

Peter Brandt: Well, you know, I think, I mean… that's maybe another way to put it, but you know, I mean sometimes it's hard to tell whether it's degenerative arthritis or not, but you know, most of the time you can tell because there's, you know, there's surrounding normal cartilage and then, you know, all of a sudden, there's a grade 4 bone defect.

Craig Blackmore: Well, I mean I think if single focal full-thickness defect is working in a coverage situation for another entity that might be a good way to do it.

David McCulloch: It didn't say full-thickness osteochondral defect?

Peter Brandt: No. Full-thickness articular cartilage defect.

Man: Yeah. It's the cartilage, not the bone.

Man: Single focal full-thickness articular cartilage defect.

Man: You can shorten the second one just to excluding degenerative arthritis, I would think.

Craig Blackmore: Okay, are there other criteria while we tease this one out a little more?

David McCulloch: We just talked about the stability of the knee.

Craig Blackmore: Stability of the knee?

David McCulloch: They excluded people with ligament deficient knees and knee joint instability.

Man: So I need to find that.

David McCulloch: Or do we just leave that, do we leave that up to the orthopedic surgeon. I mean, I'm happy to have the conditions fairly limited.

Man: One group, I guess they excluded knee joint instability. I don't know they defined it, and one excluded a ligament deficient knee.

And do you know how they define knee instability in those studies?

Andrea Skelly: I'll double check.

Man: Off the top of your head.

Michael Souter: Are there accepted orthopedic definitions for knee joint instability, which are reproducible?

Peter Brandt: I mean, well, primarily they are talking about ACL instability, I think, and, you know, in most of the situations, it's been sort of either that you'd stabilize, either you'd stabilize the knee concomitantly with the procedure, or you pick a stable knee. He wouldn't do the OATs allograft and then leave it unstable, in which case, you know, you'd be looking for more, anticipating more problems with the cartilage and menisci, and so, you know, also we'd usually try to not do it in the face of meniscal deficiency.

Man: So, when they talk about knee alignment, some of the guidelines for abnormal knee alignment… what's a normal knee alignment?

Peter Brandt: Well, I mean, you'd define it as somewhere close to a neutral mechanical axis, you know. In a case where I think there might be malalignment, you know, we do digital x-rays that stitch together the hips, knees, and ankles on a single film and then look at where's mechanical axis fall? If you draw a line from the center of the hip to the center of the knee, it should pass, or the center of the ankle, it should pass through the center of the knee, and if it's way off, then they require a concomitant osteotomy. So, you know, some of these chondral defects come… I mean I've had 17 years old with chondral defects because they had such poor alignment and, you know, they're out playing sports and the cartilage chipped off the femur, so we do a concomitant osteotomy and allograft.

Craig Blackmore: I mean, I think this is getting beyond.

Peter Brandt: I'm sorry.

David McCulloch: Remove that fourth line altogether and leave it up to the orthopedic surgeon.

Man: On behalf of the agency medical directors, I'd like to ask a question of the subject matter expert, and that is, that when you get away from traumatic defects in the cartilaginous surface, and there is some underlying disease process that's causing destruction of the cartilage, would you still do this kind of an osteochondral transplantation in a defect?

Peter Brandt: Well, I mean I guess it depends on what that underlying defect is. I mean, if it was malignant, obviously we wouldn't be doing that, but in a case of… the other, I guess, diagnosis, hasn't been brought up yet is osteonecrosis, and you know. I have seen, you know, situations with osteonecrosis and the problem there is that the lesions are a lot deeper, and the surrounding vascularity is compromised. So, sometimes there's no choice. I mean, I had a gal from Bellingham who was like in her like 20s, early 20s, with osteonecrosis of her lateral femoral condyle, and we had to do three OATs allograft plugs, and I think I followed her for about a year and a half until, you know, I definitely saw healing of the plugs. I mean, it was, obviously that's anecdotal. Several of the studies include that as one of the criteria for doing them but that, you know, with the recognition that deeper plugs are necessary and the vascularity surrounding the area is compromised, so in the end the results, you know, maybe not quite as good in that series of patients but, you know, when they're very young like that, you really don't have any other options. I mean, it's either that or a total knee replacement.

Michael Souter: But that's the sort of situation which may be amenable to, you know, application to the agency to review. You know, you can always make an individual case. I do think that we should actually degenerative arthritis, we need to be… add on a little bit more than that, and I think we haven't got malignancy out there. I think we should have, and we don't have rheumatoid arthritis up there, and I think we should have as well.

Craig Blackmore So, you want to say degenerative or inflammatory arthritis, or just arthritis, or?

Michael Souter: Well actually develop degenerative and, yeah, degenerative and inflammatory if that works.

Man: It has to be affecting the joint. If a relatively young person with a spinal arthropathy who has minimal disease and has an osteochondral defect in their knee, it's not from the disease. They

can be quite active, but they can still have an inflammatory arthropathy.

Michael Souter: Yeah, but, this is, um, what you're treating.

Craig Blackmore: Okay. Other criteria?

Michael Souter: Malignancy.

Craig Blackmore: I mean, I hope you wouldn't put a plug in somebody with malignancy. You never know, I guess.

Michael Souter: I don't mean to be surprised by it.

Craig Blackmore: Alright. So should we ask the older people or the younger people on the committee to decide on the age criteria? So, the data in the studies, the sample… I'm sorry, the selection criteria in the studies, we've got basically less than 40, less than 18, 16-40, and 18-45 are the age ranges included in the five randomized clinical trials that we have.

Man: We need to ask too, what that's based on. Is that just based on the incidents of osteoarthritis in our older population, or is it based on anything specific regarding cartilage regeneration and the age categories?

Craig Blackmore: I think it's both.

Peter Brandt: I mean, we tend to go by physiologic age, because obviously, you know, and it's hard to define that because, you know, you see people who are… I mean I did two osteochondral allografts in the last month on other orthopedic surgeons that were in their early 50s, and their knees were both totally pristine, except for these one areas, these single areas, but you know. Somebody who's 60, it'd be very seldom, I think, that we see a situation where there'd be a traumatic defect and we'd feel like we had to do something like this that they couldn't have a total knee, but you know. People get more active as they get older these days than they used to.

Man: I mean, that's my concern. I mean, do you, say you're 41 and you say sorry you can't have it? I mean, that just seems inherently wrong when you're not, basically, I mean it's just a hard cutoff for no good reason.

Woman: And if you've got exclusion of arthritis then that sort of addresses the age issue.

Man: You could say 50, but then you're on the issue of you have a 54-year-old, it's the same thing. You draw a line somewhere.

Man: A 51-year-old. I don't see the point in drawing a line, because the concern is, if the concern is really that they likely are to have other things that are going to make this procedure not an ideal fit for them, and we capture that already, then why do you need age as a criterion?

Man: We're just going by the data.

Craig Blackmore: Bone does heal better when you're younger, and that's… and I'm looking for a nod from my clinical expert over here, but.

Peter Brandt: Well, yeah.

Craig Blackmore: This is isn't simply…

Peter Brandt: It ends up being kind of the same thing, I guess. I mean, you can draw a line at chronological age. I mean, physiologic age usually ends up matching, but I don't think you're ever going to do one on somebody over 60. So, I'm not sure how much you need to put that in there. But, you know, like you say... I mean, there are guys who'll do out there things. I mean, I don't see it so much in Seattle and Bellevue area, but you know, some of the reps tell me stories about, you know, things they see out in rural parts of Washington, and it makes me, you know, scratch my head and think, well, I guess, you know, I hadn't even really thought that somebody would do that. So, I mean, I think, you know it gets down to whether there's osteoarthritis, but, you know, I mean, I wouldn't do one on somebody whose 65 or 70, but in their 50s? I mean, if they're really active and they're otherwise healthy, and their knee is pristine otherwise, then I don't see why not. You know, I've done a number and haven't had any of them fail, but, you know. The larger defects, I mean, there are higher failure rates with those, and there's a lot of different variables.

Man: If we go by our data, though, our data is on younger people. It's on 45. So, if we go by our data, we're at 45ish, and you could. I mean, we could save ourselves some other difficulties and say age

less or equal to 50, put our other things up, and the restrictive to the knee and say other uses outside of this or other use is at the agency's discretion. If somebody has a 51-year-old with a gorgeous knee who is totally healthy, yeah. I mean, the issue becomes, if we don't put age in there, you know, meniscal surgery in 65 years old does not go as well as meniscal surgery in 25 year olds as a group.

Woman: I think that's fair. I have to agree.

Man: But, a lot of people do it.

Woman: I think that's right. If we're guided by the evidence, we really don't have any evidence for age over 50.

Craig Blackmore: We don't have anything over 45, just to be clear.

Man: So, that's fair, but I think, I still struggle with putting a hard stop based on that age. I think if you leave it up to a case-by-case basis for older patients, I don't think that's totally unreasonable, but I don't know. I struggle significantly with putting a hard stop on age.

Woman: I hear you, but that's the reason we're here, and that's the charge of our committee, is to use the evidence to guide the decisions and make these decisions, so.

Man: I agree.

David McCulloch: You could say less than 45, above that at the discretion of the agency. So, you can make your case for a healthy 53-year-old.

Woman: And that probably won't happen that often.

Man: Right.

Man: Again, we're talking about alternatives. You know, you say, okay. So then you got a 51-year-old whose otherwise totally healthy and you say well, either we can do this procedure or you get a total knee.

Man: No, you could do an abrasion arthroplasty. I mean, one of, frankly, going back to the data, you know, one of the arguments for doing these is that they are more viable. They have viable

bone with them and not just fibrocartilage, and so the longevity, theoretically, should be higher. That's the whole rationale here. So, the point of doing them in a 20-year-old is you're putting in healthy bone and cartilage, and you may even get sort of normal regrowth of bone in there and a normal knee eventually, as opposed to abrasion arth… microfracture, sorry. But again, in a 50-year-old you could do a microfracture surgery, but if you have all the surrounding mild degenerative stuff and you do a microfracture and you buy them five or seven years before the whole knee goes, that may be appropriate, actually. So, I don't… I mean our data… I agree with Michelle. We stick with… we're charged with sticking with what our data says, which is this younger population, I think.

Craig Blackmore: Okay, so, age less than 45. Age less than or equal to 45. That's what the data range is on the studies.

Man: Although Steven had recommended less than age 50 on his.

Craig Blackmore: I'm sorry, who said?

Man: Steven had mentioned in his criteria less than 50 from the agencies.

Craig Blackmore: I think our job is to go with the data. Are there other criteria? We have now narrowed this down to age less than or equal to 45, excluding degenerative and inflammatory arthritis at the joint or malignancy and a single focal full-thickness articular cartilage defect.

Man: Sorry, just to complete the age, can we still put in there, would people be comfortable putting in there, or older ages at the discretion of the agency.

Craig Blackmore: Oh, I'm sorry, yeah.

Man: Again, we could just… we could limit it… we could limit this to the knee and then say, older ages or other uses at the discretion of the agency and cover ourselves in ankles or other things, and then we… so that we have some data on ankles but not a lot. There's not a total absence of data on ankle, but not enough to draw a line very well.

Man: They don't do it anyway.

Man: And we could leave it up to the agency if they had a really good case in a 25-year-old.

Craig Blackmore: Gary?

Gary Franklin: Personally, I think that makes it very difficult for us. Your job is to take the data you have and make a decision and to just keep saying, we'll just leave it up to us, that's what we do now and it's a problem.

Man: I didn't say…

Gary Franklin: That's the world we live in right now, and it's a terrible problem, but just on the issue of… I would recommend… when you have some exclusion criteria here, you don't have a… you have the lesion, it's a single isolated lesion or multiple lesions, but I'm concerned about dropping the word traumatic, because in our world, in L&I, it makes a huge difference when somebody comes in with an injury as to whether that lesion is traumatic or as part of kind of whatever else is happening. I guess I would ask…

Man: But you have to decide, I mean, that's a determination as to whether the lesion being treated is related to an occupational exposure, which is different than purely the medical decision on treatment of the lesion. Again, you go to us with osteochondritis dissecans or some other issues that may come up, or osteonecrosis or something which has a much more vague etiology, and I don't think you should leave those out of this. I think this is clearly the treatment of choice for osteochondritis dissecans lesion.

Gary Franklin: If you included that, that's fine, but you left out trauma. There were two things originally.

Man: We took out that line. We took out the line because we put that… we sort of decided not to talk about the etiology.

Craig Blackmore: The committee believes that the data suggests that this is the way to treat isolated defects, whether they arise from osteochondritis dissecans or from trauma, or from whatever. If they are isolated, if it is not in the context of arthritis, then, you know, we're saying that it should be covered whether it's trauma or not.

Gary Franklin: I just wonder what lesions there are that are trauma and aren't osteochondritis dissecans. I keep hearing our expert talking about the traumatic defect.

Man: Well, you could have osteochondritis, you can have, as you said, osteonecrosis. You could have a gross malalignment of a joint either from a congenital issue or a prior trauma that leads to asymmetric wear.

Craig Blackmore: Repetitive microtrauma, which might not manifest as trauma and might just show up as a hole.

Woman: If you look at the Health Care Authority report on page 4, it talks about the osteochondral transplant top 10 diagnosis codes used from 2007 and 2010, and you can see osteochondritis dissecans is 36% of the total, and then we have some acquired deformities, and then there's this vague section on osteochondropathy and chondromalacia and chondromalacia patellae. The bottom four are probably all of the traumatic things, and they only amount to about 12%. So, that's what's currently being used. Do we want to change it beyond that, or limit it beyond that?

Man: It looks like most of them are non traumatic.

Gary Franklin: But I think I'm hearing the…

Man: In the L&I world…

Gary Franklin: …also saying that might be a problem, that it may be being done in some of these cases where it shouldn't be done.

Peter Brandt: I think the idea is you don't want to, you know, you don't want to do them in a case where it's a degenerative etiology so that you end up with, you know, an island of good cartilage surrounded by, you know, a massive area of degenerative arthritis that, you know… so, you ended up having not really done anything for somebody, and it's… I mean, usually those situations are obvious. I mean… you might run into an occasional case where it looks like it's some traumatic injury where it's really degenerative and it ends up you've made the wrong decision and you end up, I mean the patient still ends up still having some time bought, but you know, that ends up not being a definitive treatment.

Man: Question. How often does it happen where you find this at surgery as opposed to making the diagnosis ahead of time. In other words, it seems to me don't you have to have some flexibility?

Peter Brandt: Right, I mean, well you can't really do an allograft without some planning. So, I mean, in those situations, I mean, we haven't really talked too much about this, but you know, trying to decide how you make that diagnosis ends up being kind of crucial, too. I mean, there are occasions when you can see it on the MRI scan, and you know exactly what you're going to find, but you know, to make the decision to do an osteochondral allograft just based on an MRI, especially if the MRI is poor quality, you know, ends up being difficult. I mean, sometimes a diagnostic arthroscopy really changes the diagnosis and the treatment recommendation. So, you know, most… because I have the kind of tertiary referral practice I get referred to a lot of people that already have this diagnosis, and they already have arthroscopy photos in hand and MRIs and so forth.

So, usually if there's a surprise it's that the other guy hasn't really made the appropriate diagnosis, and I'm left kind of trying to sort out what's what here, but if we find one at the time of arthroscopy for say an ACL reconstruction or some other, you know. Somebody's had this injury, and they happen to have an osteochondral defect, and it wasn't really that evident on the MRI, it usually ends up being a smaller defect. So, those are usually amenable to microfracture. So, we'll do the microfracture and then see how they do.

Craig Blackmore: Okay. Is there any other criteria that we haven't discussed?

Man: I still have a question about age.

Craig Blackmore: Yeah.

Man: I'm just wondering why the other policies that we had, very few of them, never mention age other than in their comments.

Craig Blackmore: I think our job is to look at the data and make a decision what the evidence tells us.

Man: I realize that, but there might be a reason why they didn't include age, and I'm just wondering in these studies if the age, you know, what criteria was used for the age cutoff in the studies.

Craig Blackmore: So, slide 80, or page 82. In the five randomized clinical trials, one had an age cutoff of less than 40. One had an age cutoff of less than 18. One is not provided. One had an age range of 16-40, and the final one had an age range of 18-45.

Man: So, we're looking at mostly traumatic events, you know, I'm just wondering if that was the criteria that they used to cutoff, because of the type of…

Michael Souter: But if we're still covering it under the basis of that, if there's a pristine knee and we're treating an isolated injury, and you can appeal to the agency for that, I think that covers all our bases. I mean, that's, if you're concerned about an older individual who has… who is probably going to be relatively rare but who fits that particular category, there's still, you know, there's still the option for the agency to approve that. We all want to kind of limit this from being inappropriately directed towards diffuse disease.

Man: Along those lines, I just have one quick question about, we're talking about a single focal full-thickness lesion. Are there circumstances where there's a trauma to the knee but we're all thinking maybe two cartilage defects that would be amenable to this, or does that not happen?

Peter Brandt: Well, that can certainly happen, and I guess I've seen a few over time, but I mean most of the time it ends up being one lesion. Sometimes, lesions, you know, change such that we have to put in two plugs, but I mean, it's fairly uncommon.

Man: Okay. I guess I was just wondering if it made more sense to say something like isolated full-thickness as opposed to single. I mean, I don't know. You guys feel free to kick me out of this one, I'm just trying to figure this out.

Man: If we go back to our data, do any of these articles talk about multiple lesions being done? They talk about a single lesion, yes?

Woman: One did.

Man: One talked about multiple?

Woman: Yeah.

Man: Which one?

Woman: It's Anders, I guess, on page 148. It discusses it under lesion characteristics, number, location, number of plugs, and it talked about a study that compared, yeah, it comes from patients that had a single lesion versus more than one lesion and that the single lesion performed better, or the people had better Womack scores and Vas pain scores, but that's the only outcome that I see there.

Man: 49?

Man: So, it's 50. Change it to 50.

Man: I would feel better if it was 50.

Man: Because you're 49?

Man: Carson would feel better if it were 50. We can go to 50. As long as it's older than the mean range of the committee, we're good.

Craig Blackmore: I think if we're going to have an age cutoff, it should be based on something, and the most reasonable thing is the age that was included in the data that we have, and if it's 49 in the data, then we'll go 49.

Man: Or we could say less than 50.

Michael Souter: I like less than 50.

Man: 49.95.

Man: Less than 50.

Man: Wait, so 49.6?

Man: No, they can be 49.999 now.

Craig Blackmore: Okay, we're getting there. Do we need anything else on this list?

Man: So, ankle. Are we going to deal with ankle differently?

Craig Blackmore: We're going to get there. We're still working on the list. We're going to deal with ankle.

Michael Souter: The resulting question of one or more isolated or single, because that doesn't make sense as it is. The bottom one.

Woman: And if we're saying one or more, do we need to say anything at all? I mean, isn't everything one or more?

Michael Souter: Did we resolve that?

Man: If we just say a focal full-thickness articular cartilage defect without arthritis and somebody happened to have two of those, they could still do it. Each time, they're treating a focal full-thickness defect. We could leave out the number and we're leaving with the same requirements. It's an isolated full-thickness defect in the midst of a healthy joint, otherwise. So, I suppose you had two of them, you could fix two of them.

Man: I'm more comfortable with one.

Michael Souter: I'm just wondering about somebody choosing to selectively interpret. Oh yeah, that's an isolated one and that's an isolated and that's an isolated one, and you end up with something that's going to...

Man: I like single.

Woman: That's what most of the studies had, single.

Man: I have a question about this, what's the mosaic? Isn't that multiple?

Man: Multiple plugs to fill one hole.

Man: It's a bigger one.

Man: So, it's multiple, it's not for multiple lesions.

Craig Blackmore: It's just that one plug isn't big enough or doesn't fit because of the shape of the defect.

Man: Okay, so it's for a single lesion. That's fine.

Craig Blackmore: Okay, more comments? Okay. I think at this point we should resolve the knee and then we should talk about the other joints. I'm not sure what we're… what are we writing?

Woman: I'm just going to put [inaudible].

Craig Blackmore: Okay. Sorry. So, back to the tool. So, we go through our two voting questions, and the first is a nonbinding vote, and that is around the question of, is there sufficient evidence under some or all situations that the technology is… and we'll deal first with effective, then safe, then cost effective, and it's whether the technology is of unproven effectiveness, of equivalent effectiveness, more effective, or less effective, and that is, the comparison is going to be challenging a little bit here, but I think the relevant comparison is going to be to microfracture. I'm looking for nods, but that seems to be sort of the standard in the absence of this procedure. So, first for effectiveness, do we believe that under at least some circumstance this is more or less effective, etc.?

Man: 1 equivalent, 8 more.

Craig Blackmore: Okay. Then, for safety, again compared to microfracture.

Man: 9 equivalent.

Craig Blackmore: And then finally, cost effectiveness?

Man: Okay, 2 equivalent, 7 unproven.

Craig Blackmore: Okay, further discussion at this point, or shall we proceed? Let's proceed. I think we should give Marie another minute or two to get back for the binding vote. So the question has come up whether we should have the word symptomatic under our conditions. I guess I had assumed they would be symptomatic or we would not be doing anything about them, but I mean it's a legitimate question. If it's not symptomatic, one could argue that it shouldn't be fixed, but if it's not symptomatic, one could also argue that you're doing it to prevent osteoarthritis and you might do it anyway, which is something you found for another reason. Do we wish to comment on that?

Woman: Well, we don't really have any evidence that this prevents osteoarthritis, so I don't think that's an indication.

Craig Blackmore: So, if we're only doing it for symptom relief, then we might want to say, include that. I don't know. Is that one of the criterion in the?

Man: Was there any data on asymptomatic lesions? I mean all these studies had knee pain, I assume.

Man: It would be if you went in for another procedure and then found it. That would be under a symptomatic condition anyway.

Man: Well I guess would there be a condition in which you would go in, say you go do an ACL repair or a meniscal repair and like you said, you find a lesion. You weren't thinking that. You didn't really see it on your MRI. You do a… I mean, you don't know if that's actually symptomatic because you have a meniscal tear. So, you're… these… in my experience is what Dr. Mandt said. These patients routinely will get, they'll go in surgically, they'll see the meniscal tear and they'll see a small defect in the cartilage, and they'll do a microfracture surgery while they're there, but I don't know. Would there be a circumstance where you would inadvertently sort of find one of these in the middle of doing something else with the knee and decide that it actually is too big for a microfracture and they would do an OATs?

Craig Blackmore: Asymptomatic knee?

Man: Well, no. You had a symptomatic knee, but you don't know if the lesion is symptomatic. That's my question. You're getting a scope because your knee hurts.

Man: Feasibly, can we even do [inaudible]?

Man: I think we ought to leave it out personally. I think you can come up with a scenario where you find an asymptomatic patient, maybe a super athlete whose stoic as can be, and you say, oh he doesn't have any symptoms. He might, but the thing is, leave it between the physician and the parents or the patient or whoever. I think that meets everything, and we're probably taking about, you know, less than half of 1% of all the patients, unless I misunderstand the literature.

Craig Blackmore: I think I'm hearing that that's not necessary to include. So I'm going to now ask for a vote based on the discussion and the

evidence. This will be a binding vote based on the evidence about the technology, safety, efficacy, and cost effectiveness, if it is to be covered unconditionally, not covered, or covered under certain conditions and the conditions are patients of age 50 or older… sorry, under the age of 50, but they would only be done on older patients at the discretion of the agencies, and it would not be performed in patients with degenerative or inflammatory arthritis in that joint, or malignancy involving that joint.

Woman: Move the malignancy just earlier in the sentence, excluding malignancy, degenerative or inflammatory arthritis in the joint.

Craig Blackmore: Yeah, great. And then the third condition is that it is to be performed only for a single focal full-thickness articular cartilage defect.

Man: And by transplant, that also means allograft and autograft, correct?

Group: Yes.

Craig Blackmore: But this is only in the knee. Okay.

Man: So, it looks like 10 covered with conditions.

Craig Blackmore: Okay. So, we are required to determine if our decision is in alignment with Medicare national coverage decisions, and there are none, so that is not an issue. So, next we have to consider other joints and joints that were mentioned include the ankle where we have one piece of not terribly rigorous data and shoulder and potentially other joints where we really have no reasonable data at all. So, I can entertain a vote or I can entertain discussion of what conditions might look like. I think we had one proposal the conditions might be the discretion of the agency. Is that the…

Man: I guess I had one issue with this. That the ankle certainly is done, there is less literature, but our literature search was limited to RCTs and comparative studies with concurrent controls, because there are so many studies out there they had to get down to the comparative ones for the knee. But our charge isn't just to look at the evidence only from that kind of data. We don't look at anything else, if there's nothing else. If there's no other data on the ankle… if there's only one sort of comparative study and there

are a bunch of other pieces of data on the ankle we don't know about, we just didn't look for them because they didn't meet our filter, but had we been looking for ankle they would have had to broaden their filter to find more data. So, I'm a little worried we don't have all the relevant data for the ankle, even though it's going to be of relatively low quality.

Craig Blackmore: Dr. Skelly?

Andrea Skelly: Just one comment about that. When we look at the case series, we made a decision because we had comparative data for autograft that we would not include any other for autograft, but we would for safety. For the allograft, we had no such filter, obviously because there were no comparative studies really to speak of. So, that's when we did use a case…

Man: And that's when you picked up the ankle.

Andrea Skelly: No, we picked up the ankle [inaudible].

Man: In a comparative… yeah.

Andrea Skelly: What we did not do is include case series for autograft for efficacy or effectiveness. So, in one sense you're correct. No, we don't have all the case series for the finger or for the elbow or for the shoulder. That's true. If there had been safety data on those in patient populations [inaudible] caught that.

Man: Okay.

Craig Blackmore: So, to clarify, at least in terms of safety, you did not identify any case series other than the ankle and the knee. Is that…?

Andrea Skelly: Maybe let Barbara in case I misspeak, but she did more of the safety aspect. For the autograft, we looked at case series that had at least 30 patients in them to include for safety. Most of them were in the knee. There were two in the ankle, three in the ankle, and there were other joints?

Woman: Not that were over 20 patients. Very small ones in the elbow and the shoulder.

Craig Blackmore: Richard?

Richard Phillips: My concern about taking a vote on it is that a vote not to cover is basically an endorsement of microsurgery or the alternatives to treatment, which is really not the intended effect of what I want to vote on. So, in that sense, I either would want to… my personal point of view, would be to send it on to the agency or not to vote on it and take a stance on it, because I think we'd be… the effect of it would be unintended from what I personally would be thinking. In other words, no data available, don't cover. Those patients are going to get surgery one way or the other, I think, and I think they're going to get the surgery, which should be the decision made between the patient and the clinician.

Craig Blackmore: I mean, I think if it's part of our topic and it was part of the, you know, the technology assessment, and I think that's what we're trying to figure out, then we're under some obligation to vote on it. Now, you can vote for coverage without condition if you think that's appropriate, but I don't think… if the work's been done we have to make a vote.

Richard Phillips: Yeah, and I'll go along with that. I have no problem voting, but that's my concern.

Man: I don't know, this is kind out of task, but I just did a real quick PubMed search, and there are over 30 articles on the ankle, costochondral data that we haven't looked at. I can't say anything about the quality, but there's data there that we haven't heard about, so.

Man: Yeah, that's some of my concern with it.

Craig Blackmore: What else can you tell us, Dr. Skelly? What do we know about those case series?

Andrea Skelly: Some of them were most likely too small. They didn't have at least 30 patients. Again, for autograft, because we made comparative studies we chose to limit the case series to [inaudible] patients. Without seeing the studies that he's looking at and the things that he's looking at, I can't speak to whether they were too small. They could have also… are those autograft or allograft? Are they either?

Man: It looks like both.

Craig Blackmore: So, among the studies that included 30 or more subjects, was that your criteria, or was it 20? The ones that you identified that fit your criteria, what can you tell us about them in terms of the ankle or other joints, if any?

Andrea Skelly: We looked, for those, the case series would be safety only.

Craig Blackmore: Okay, and how many did you find that existed, and what were they like?

Andrea Skelly: Barbara can maybe help me with that.

Barbara: There were three that were over 30 patients.

Craig Blackmore: Is this for the ankle?

Barbara: For the ankle, yes. For the ankle there were three that were over 30 patients.

Craig Blackmore: And is that in a table somewhere in our report?

Barbara: Page 137.

Craig Blackmore: 137.

Andrea Skelly: While you're looking at that the other issue is that the number of case series would say that they did a variety of different sites, but the outcomes were not broken down by site.

Man: So, you're referring to the data table on page 137, which lists re-operation, donor site morbidity, infection for the ankle procedures? Is that what you're referring to?

Barbara: Table 32, which goes across page 136 and 137 breaks down the case series by knee, ankle and combined site. So the ankle are actually the… yes, it is [inaudible].

Man: So, it's a safety data table?

Barbara: It's a safety data table that references the… I'm sorry, I'm wrong there's four. It references the four ankles.

Craig Blackmore: Well, I mean, I think we can, you know, we can look at this one of two ways. One interpretation is that there is no good data, and

we would require more than three case series without controls in order to cover it. The other way to look at it is to say it's a joint and we have data from another joint, and we thought it was sufficient in that joint. What's the difference? A joint is a joint. And I sort of have to leave that open to the committee and what people's feeling is. Would a few case series be sufficient to cover another joint? Is it reasonable to expect each joint to be studied individually, or should we extrapolate from one joint to another, because clearly you're not going to have randomized clinical trials of the thumb, for example, or every other joint in the body? So, I think we can take one of two paths on this.

Man: I guess it depends a little bit on clinically what the disease process is in these other joints that would lead to this situation, and we don't know that. We haven't been hearing about that. So, I mean, maybe we can ask our clinical expert if there's, you know, what the… are there pathologic conditions in those joints that mirror what happens in the knee, or is it just a different joint that functions differently and it's not applicable?

Peter Mandt: Well I think the ankle, I mean, the conditions can be similar. There's osteochondritis dissecans in the talus and there are talar dome fractures that are traumatic. You know, if the lesion is small enough then a microfracture should be sufficient, but there are certainly conditions where the lesions are larger and because the pressures are so high in the ankle, it doesn't do well with lower surface area.

So, I don't personally do ankle allografts, but I do have a partner that does them. Most of them, I think, are starting to transition to doing allografts rather than autografts. A lot of the early osteochondral transfers in the ankle were done using autografts and the problem is that most of the lesions are around the shoulder or the talus. So, we have two articular surfaces, you know, it's sort of that perpendicular ankle so you can't get an autograft plug from the knee to fit into the ankle and have it cover the surface appropriately. I don't know.

But as you say, kind of the osteo… I think the history of osteochondral allografts in the ankle has been sort of one that's, you know, taken off from the positive results in the knee. So, you know, the studies are still early. My partner, Tom Chi, who is an ankle… foot and ankle specialist, you know, has probably one of

the larger series of ones that have been done and his publications [inaudible] clinical applications.

With respect to the shoulder, I think it's a much less common problem. I mean, you don't see osteochondritis dissecans really in the shoulder. There is one other application in the shoulder, though, that is sort of unique and that's a large [inaudible] defect that's come about in chronic instability where the posterior aspect of the humeral head has become deficient and then that contributes to further episodes of instability because of the mechanical deficiency of, you know, losing part of the spherical shape. So, you know, that's been listed as a common reason to do osteochondral allografts on shoulders… well, I mean common relatively speaking because there aren't really that many other indications [inaudible].

David McCulloch: Am I right in thinking that when you take the donor, where does the donor site from the ankle come from, the knee?

Peter Mandt: Well, that's what I was referring to earlier. That, you know, a lot of the earlier studies were using the knee as a donor site for the osteochondral autografts but just the problem being the unique architecture of the ankle is such that in the talus most of the lesions occur on the shoulder of the talus, so you have two articular surfaces that need to be replaced. So, you don't really have a place in the knee where you can obtain a graft. I mean, certainly not without causing additional morbidity. So, you know, I think it's getting to be the more common way to do it is to use an allograft.

David McCulloch: Right.

Craig Blackmore: Other thoughts?

Man: I have one. What's the agency experience with the ankle? Nothing? And you don't allow shoulders anyway, right?

Man: We don't allow ankles or shoulders because there's no data.

Woman: It does seem like this is a little early in this part of this application of the procedure. So, if the data is not there, I'm inclined to not make a coverage decision for it.

Man: I go back to what Richard said, though, that you have one issue that there is the joint-to-joint issue. The ankle is different than the knee. But it's a major weightbearing joint. These things certainly occur, and they're going to do something. You have a symptomatic osteochondral defect in the ankle; they're going to get something. So, I mean the treatment is still there, and I know we have the issue of data, but do you prove every joint? Do you prove every level of the spine for a disk if you're going to… can you only fuse at L5-S1 and not L1-2? I mean, you run into that a bit. They're different. Different outcomes, different everything else, different mechanics, but we don't look at them differently when we cover them, and I…

Woman: Well, we do now. They're already doing that, actually.

Man: By level?

Woman: No, the agencies don't cover shoulder or ankle currently.

Man: No, no, no. Yeah, I know. I know, but for the spine we don't not cover a level, and so I, you know… yeah, I guess you go with what the data is, but do you prove it everywhere, and if you don't cover it, they're all going to… I don't know. Do they do the chondrocyte transplant in an ankle? If they couldn't do the OATs, what would happen? They all do microfractures for 2 or 3 cm defects in the ankle, or they would have to put a plate in or? You know, you get into ankles, what do you do?

Man: Fusion and either back up…

Man: Yeah, you have an ankle fusion. In the ankle, your choices are so poor in terms of what you can do surgically. You can't sort of clean them out. I mean, you're… so that's what I struggle with. The idea of taking that away and saying well then what do you do with a 20-year-old with a posttraumatic OCD in his ankle, which I've seen before? And if you can't do this, then you have a 3-cm or 2-cm OCD in there, what do you do? They're going to get something, and I don't know that.. I don't necessarily like the idea of extrapolating from one joint to another, but I don't know that it's totally unreasonable in this case, and I don't know that this would be, you know… I don't know why I would think this would be an over-utilized procedure. It's pretty rare. People don't usually like to operate on ankles and to scope ankles. So, it isn't something that's readily abused, as far as I've ever noticed, but I

have no data. It's just purely personal observation. So, that's what I worry about.

Woman: I just want to point out that there is no CPT code for anything other than knees.

Man: So, they don't get paid at the moment? Do they bill an unlisted code? They bill an unlisted code and they negotiate for something.

Craig Blackmore: Yeah, I guess what I'm hearing is that there's substantial differences between the knee and the ankle. If nothing else, you have to do a knee procedure to repair the ankle, and I think that it… in many ways joints are the same, but I think in this particular case there are meaningful differences, and we haven't seen any good data, and though I accept the argument that something is going to happen, having something that we don't know if it works isn't necessarily better than having something else that we don't know whether or not it works. So, my feeling would be not to cover other joints unless there's some data that's actually effective in those other joints.

Michael Souter: I would agree. I think this is investigational in other joints.

Man: Absolutely.

Woman: And these kinds of things will arise again, and so we'll… I mean there's no such thing as precedent here, but still. I mean, I think it's worth considering that.

Craig Blackmore: Okay. Other thoughts? I don't want to. Okay. So, back to the sheet. So the first voting question, and we can either lump all joints other than the knee, or we can treat them somewhat separately. My preference would be to lump them. I think people are going to be making their decision the same regardless of which joint we're talking about. So, we'll start with the nonbinding vote on whether the technology, and now we're talking about OATs in joints other than the knee is effective and your choices are unproven, equivalent, and less or more effective, and that's in comparison to again microfracture and…

Man: 9 unproven, 1 equivalent.

Craig Blackmore: Next, is safety.

Man: It looks like 9 unproven, 1 equivalent.

Craig Blackmore: And then, finally, cost effectiveness.

Man: 10 unproven.

Craig Blackmore: Further discussion at this point? Anyone wish to comment?

Man: Just one thing I have to say. So, if we're voting on this, it would be… just to throw this out there, it would be cover, don't cover, or cover with the same conditions that we were talking about from the knee, or?

Man: No, we haven't defined any conditions.

Craig Blackmore: I think we would have a cover with conditions to be specified and then if we elect that we would go back and determine the conditions if people are comfortable with that. Also, we could talk about what the conditions might look like first.

Man: Or do we want to vote on whether we want to separate the other joints out or simply lump them with the knee? It seems like most people don't want to do that. I'm just saying. I'm just trying to figure out what we're actually voting on here.

Craig Blackmore: We've already voted on the knee, and so at this point… there's two approaches. We can either come up with a set of conditions we're comfortable with and then have a vote, and then that set of conditions is binding. We've done it that way, like we did today. Or, in the past, we've done it the other way where you vote on conditions and then you have another vote on what those conditions look like, and we've used either of those, depending on which seemed to feel right in terms of getting to the decision first. My belief is, in this case, we should use the latter approach, because I don't think we're going to end up in the conditions place. If I did think we were going to end up there, then I would advocate we try to decide what those are as a more efficient way of decision making. Okay.

So, based on the evidence about the technology, safety, efficacy and cost effectiveness, not covered, covered unconditionally, or covered under certain conditions, which would then be determined.

Man: 3 cover with conditions, 7 no cover.

Craig Blackmore: The next item is to determine if this is consistent with Medicare national coverage decisions, and there isn't one. So, that's not relevant. We will charge staff with completing a draft of the findings and decision based on our deliberation for approval at the next meeting. Any other bits of business? Then we are adjourned.

Man: Great.