Transcript for April 12, 2000 Meeting

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BIOFEEDBACK THERAPY FOR THE TREATMENT OF URINARY INCONTINENCE

HEALTH CARE FINANCING ADMINISTRATION
Medicare Coverage Advisory Committee
Medical and Surgical Procedures Panel

April 12, 2000

Baltimore Convention Center
Baltimore, Maryland

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Panelists

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Alan M. Garber, MD, PhD

Vice-Chairperson
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Voting Members
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H. Logan Holtgrewe, MD, FACS
Kenneth P. Brin, MD, PhD
Les J. Zendle, MD
Bruce Sigsbee, MD (Not present)
Linda D. Bradley, MD
James P. Rathmell, MD

Arnold M. Epstein, MD
Temporary Voting Member
Lisa Landy, MD

Consumer Representative
Phyllis E. Greenberger, MSW
Industry Representative
Marshall S. Stanton, M.D.

Non-Voting Guests
Michael Risager, MD
Diane Smith, RN

Acting Director, Coverage and Analysis Group, HCFA
Hugh F. Hill, MD, JD
Executive Secretary
Constance A. Conrad, RN

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P R O C E E D I N G S

MS. CONRAD: Good morning, and welcome panel chairperson, members, guests and temporary voting members. I am Connie Conrad, executive secretary of the Medical and Surgical Procedures Panel of the Medicare Coverage Advisory Committee. The panel is here today to provide advice and recommendations to the Executive Committee regarding biofeedback treatment of non-neurogenic urinary incontinence in adults. At the conclusion of today's session, panel members will be asked to vote on two questions. The answers to those questions will constitute this panel's recommendation, which will be submitted to the Executive Committee when it meets on June 6th. When the Executive Committee ratifies the panel's recommendations, it will officially transmit that recommendation to HCFA. HCFA will then act on that recommendation and will enact its coverage policy within 60 days of receipt of that recommendation.

For the purposes of today's panel, Dr. Lisa Landy, standing member of the Durable Medical Equipment Panel, and a noted expert in the field of urinary incontinence, received an appointment to temporary voting status. Dr.

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Landy's expertise will enhance this panel's deliberative process.

In addition, we welcome Dr. Michael Risager, carrier medical director for with Trailblazers Health Enterprises, in the state of Maryland, and Dr. Risager has not come in yet, and we also welcome Diane Smith, a urotechnology consultant and continence specialist, as nonvoting guests.

The following announcement addresses conflict of interest issues associated with this

meeting and is made part of the record to preclude even the appearance of impropriety. To determine if any conflict existed, the Agency reviewed the submitted agenda and all financial interests reported by the panel participants. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employers' financial interests. The Agency has determined that all members and consultants may participate in the matters before this panel today.

With respect to all other participants, we ask in the interest of fairness, that all persons making statements or presentations disclose

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any current or previous financial involvement with any firm whose products or services they may wish to comment upon.

And now I would like to turn the meeting over to Chairman Alan Garber, who will ask the panel members to introduce themselves.

DR. GARBER: Thank you, Connie. I would like to ask the panel members to introduce themselves. I am Alan Garber, professor of medicine at Stanford University, and also work with the Department of Veterans Affairs.

DR. HILL: I am Hugh Hill. I am the acting director of coverage and analysis at HCFA, and I'm sitting as the designated HCFA representative to this panel.

DR. ZENDLE: I am Les Zendle. I am a geriatric medicine specialist and the associate medical director for Southern California Permanente Medical Group.

DR. BRIN: I am Ken Brin, a practicing cardiologist, with the Summit Medical Group, in Summit, New Jersey.

DR. HOLTGREWE: I am Logan Holtgrewe, a urologist from Maryland, on the faculty at Johns Hopkins.

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DR. McBRYDE: Angus McBryde, professor of orthopedic surgery at the Medical University of South Carolina, in Charleston.

DR. MAVES: Mike Maves, with Georgetown, and I am vice president of the American Academy of

Otolaryngology.

DR. LANDY: I'm Lisa Landy, a practicing urogynecologist in Tucson, Arizona.

DR. RATHMELL: I'm Jim Rathmell, anesthesiologist at the University of Vermont.

DR. EPSTEIN: Arnold Epstein, chairman of Health Policy and Management at the Harvard School of Public Health.

MS. GREENBERGER: I'm Phyllis Greenberger, executive director of the Society for Women's Health Research, and am the consumer representative.

DR. BRADLEY: I am Linda Bradley, director of hysteroscopic services in the Department of OB at the Cleveland Clinic Foundation in Cleveland, Ohio.

DR. STANTON: Marshall Stanton, cardiologist with Medtronic, in Minneapolis.

MS. SMITH: I'm Diane Smith, nurse practitioner. I am a continence specialist at the

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WOCN, which is the Wound Ostomy and Continence Nurses, in Philadelphia.

DR. GARBER: Thank you. I would like to thank the panel members for the work they have done in preparing for this meeting, in reviewing the evidence before you that we asked you to review before attending, and thank you in advance for your comments, and especially to the HCFA staff who it is clear have put in a tremendous amount of effort in compiling the materials that we have before us.

I would like to just take a few moments to discuss the Executive Committee report that you should have received entitled Interim Recommendations for Evaluating Effectiveness. There is a little bit of history to this document, and we all believe it's crucial for us to have a common understanding of what the document contains in order for us to proceed with the panel deliberations.

The Executive Committee first met after two of the panels in the Medicare Coverage Advisory Committee had met, and the Executive Committee decided it would be worthwhile to provide some guidance to the panels on how to go about their tasks of evaluating evidence regarding the health

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care technology, whether they be treatments, diagnostic modalities, preventive intervention that they are studying. The Executive Committee wanted to insure that there would be transparency in the processes that the Executive Committee used in making their determination, that there would be consistency between panels, from one panel or from one meeting to another, and that the panel deliberations and the evidence supporting the deliberations would be of the highest scientific quality.

So the Executive Committee felt it would be worthwhile to give the panels some guidance about the panels' analysis that they would expect to receive. Now, one thing that's important for you to know is what the Executive Committee is. The Executive Committee ultimately has the responsibility to decide to ratify or not, and forward to HCFA or not, the results of the deliberations of the panels, or you could say the recommendations of the panels, but the recommendations are essentially in the form of answers to a series of questions.

So the executive committees and panels are not in the business of making coverage

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decisions; that's a role for HCFA. What we do is advise HCFA, and the Executive Committee was seeking to give guidance to the panels about what form they would expect the recommendations to take, and the processes that would be used in order to reach a determination.

Now, the executive committee viewed the document that they produced and unanimously approved, by the way, as basically an interim document that's subject to change; it's a work in progress. What that means is, this is an untested set of recommendations the Executive Committee has made and in fact, we are the very first panel to operate since these recommendations have gone into force by the Executive Committee, and the Executive Committee recognized that some of the provisions within the document may be difficult to implement, but they felt they were necessary to alleviate uncertainty about various components, and they were

expecting some feedback about how well these recommendations work.

And in fact, as you will see, this panel will follow all the operational recommendations of the Executive Committee, but if we've got some question about whether it would be feasible with

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more advance notice and so on, or whether some performance recommendations need to be acted upon and which may not be feasible under the circumstances, that's information that the Executive Committee really needs to have.

Now, although the Executive Committee was perhaps somewhat tentative about some of the details of their recommendations to the panel, we should be clear that the major principles behind these recommendations are not really subject to significant debate, and I think I reflect the deliberations of the Executive Committee accurately when I say that. A lot of the discussion within the Executive Committee had to do with details, what the general principles of the approach were, and I believe were uniformly acceptable, and that's why I want to spend particular time on that.

One other aspect about why these are interim is that we are not in the business of trying to tell HCFA what they should do. And as I said, we are not making coverage decisions; we are answering the questions posed to us. The nature of the questions and how we answer them might change after HCFA releases its rules regarding the procedures for coverage determinations, and are one

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of the processes we use as advisory bodies to provide HCFA insight of the regulations and laws that they may issue. So, these are provisional in that sense as well.

The report before you, as you know, has two parts. Basically, the Executive Committee's report has a set of recommendations that concern the general approach to evaluating evidence, and the second part is operational, and as I alluded to earlier, it may be the operational aspects of the Executive Committee report that will be difficult to implement in the future, and could not be fully implemented before this meeting.

The evaluation of evidence is really critical and it will determine how we go about our discussions and make our determinations today. Essentially, the Executive Committee report divides the issue of evaluation into two components. One is that the panels must determine whether the scientific evidence is adequate to draw conclusions about the effectiveness of the intervention under consideration. And that's how we are directed in the document, to act. The panels must determine whether the scientific evidence is adequate to draw conclusions about the effectiveness of the

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intervention in routine clinical use in the population of Medicare beneficiaries. All right. And in most technical evaluation processes, I believe this is the most difficult determination, whether evidence is adequate.

I think it's fair to say that HCFA would not be coming to us for advice about what the evidence says if we had a set of very well designed randomized control clinical trials clearly demonstrating effectiveness, without any major design flaws, and if the set of trial results were all broadly consistent, i.e., consistent in terms of showing efficacy or effectiveness for the intervention under study. I would suspect that we will be dealing with interventions where the evidence is a bit murkier and there is a judgment call. At the same time, I would hope that they don't bring us questions where there is no evidence whatsoever.

So we as a panel will be asked to evaluate adequacy of evidence, recognizing that there is going to be considerable room for disagreement and for discussion and debate. And I won't go through the details of what makes evidence adequate or not, but I think the fundamental

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principle is if the set of studies falls short of the ideal, can we draw the conclusion that the treatment is or is not effective, without being, without having considerable uncertainty because there may be bias in the study results one way or the other that make it impossible to determine whether the treatment really works.

So that's the difficult task that our panel, and every panel, I believe, will have to grapple with. And we are very fortunate in having Deborah Zarin here today, from the Agency for Health Care Research and Quality, who will discuss some of the issues in evaluating evidence and what constitutes good study design.

The second component of the evaluation of evidence is assuming that the evidence is adequate, how effective is the intervention under study? And the Executive Committee has not given us the very simple option of saying it's effective or not; it's a considerably more complex task that we're given here for the situations where the interventions under study are, have adequate evidence.

And this criteria, and I will read from the document, concerns the size of the health

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effect. Evidence from well designed studies, meeting the adequacy criteria, must establish how the effectiveness of the new intervention compares to the effectiveness of established service and medical items. We're asked to make a statement about the comparative effectiveness of the intervention under study, to assign it to one of seven categories. Now, in fact, we could have come up with 14 or 21 categories without too much difficulty, we could have narrowed it down to three or four. The Executive Committee felt that the seven categories that are in the document best capture the full range of possible outcomes of the medical evidence in terms of effectiveness, without being unduly complex.

Now as I say, no panel has yet applied these recommendations and we may in some situations decide it's too difficult to assign to one of these seven categories, that maybe three or four would be better. We may decide that we want to give a more finely detailed description of comparative effectiveness, that's something that may well be subject to change.

So, that's the broad principles of how we will operate and as you think about how we

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approach this task, you should recognize what this

is not, this is not a discussion, should we cover or should we not. We are asked to evaluate evidence, and to say what the evidence says. This is not a discussion of cost effectiveness or cost. Cost is not part of our charge as a panel or the Medicare Coverage Advisory Committee as a whole.

This is not a discussion of how important the disease entity that we're considering is, about the toll of the illness, or about whether there should be coverage for some treatment of the illness because the illness is so important. I hope that HCFA always brings us questions where the health condition is important. I think all of us who've had any personal experience as providers or family members, know that incontinence in particular, can be a devastating problem and I think we can start with that as an assumption that we're all working from, that this is a very important problem, and our task is not to determine how important the problem is, but to determine whether there is enough evidence to conclude whether these treatments we are considering work, and if we do determine there is enough evidence, what does that evidence say.

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So, our task of evaluating evidence alone, I would suggest, will be difficult enough. And the other issues, although they are interesting, such as the burden of illness, those are interesting and important questions, they are not really what our deliberations are about today and tomorrow.

The process of evaluating evidence is not the same as making a best guess about whether something works based on literature. It's about deciding whether the evidence meets a high enough standard to draw conclusions. And I like to think of my colleague, who is a bone marrow transplantation expert, who firmly believes that for several indications, bone marrow transplantation is a highly effective procedure. Yet, he is a very firm believer in carrying out randomized control clinical trials of bone marrow transplantation in those situations. And the reason is, although he thinks it's better, he also recognizes that there is considerable uncertainty

about whether it truly is better, and that he could be proved wrong in a well designed trial.

In fact, many people would argue that if you are sure that one treatment is considerably

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more effective than the alternative, it would be unethical to perform a randomized control trial. So we are not saying, what do you think works better, or how much better do you think it works, what's your best guess. We're saying, is the evidence strong enough for you to be sure of the conclusion that you draw. That's our task.

Let me turn now to the operational aspect of the Executive Committee's recommendations, and I am not going to discuss these in any detail, but let me just tell you about the general thrust of the operational recommendations. These recommendations are based on the collective experience of a number of individuals who have participated in evidence evaluation processes through their professional societies, through their other activities, through participation in evidence based practice centers and so on. And I think that the Executive Committee felt very strongly that the work of the MCAC, the work of its panels should really be the standard to which others should aspire, and that meant that the process should not only be open, transparent and consistent, but that it should be of the absolute highest scientific quality.

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That meant the preparation of very high quality evidence reports that summarize the body of literature, the evidence that the panels will use; that the discussions conducted by the panels would be focused on the questions at hand and conducted at a high level; and that the panels would explain their reasoning and each member of the panels would be prepared to explain why they voted on each question as they did.

There is an extensive review process that the executive committee asked for, which we have implemented partially for this panel meeting, not entirely. The review process that they recommended includes both internal and external review, and I believe that we have come very close

to meeting their requests for the internal review. And we have two panel members, Dr. Lisa Landy and Dr. Les Zendle, who are essentially the internal reviewers from the panel of the topic at hand.

There is one constraint that this process works under that doesn't apply to every professional society or group that evaluates evidence, and that is timeliness. And I think everybody pays lip service to timeliness, but we are particularly aware in our deliberations that

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HCFA needs our advice in making coverage determinations themselves, that the public is waiting for answers about these questions, and a lot hangs in the balance. So it's incumbent upon us to make this process work as quickly as possible, and our goal is to have the highest quality product in a very short duration of time. And of course, the time that we take is undoubtedly going to be too long as far as some people are concerned, but we're trying to strike a balance between very high quality and timeliness of the report.

So that's what the Executive Committee report said. We realize, this Executive Committee, that there may be ambiguities, there may be things said that aren't entirely workable. That's something that we'll find out through our deliberations over the next couple of days. But I know that the Executive Committee has high expectations for the operations of our panel, we are dealing with some difficult questions and in a very real sense, our work will be precedent setting.

Any questions from the panel? Les?

DR. ZENDLE: Yeah. Alan, I wondered if

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comments are made either by panel members or the public about coverage issues, will they be ruled out of order, or how will you handle those?

MS. CONRAD: We will ask them to stop speaking and proceed with the rest of their topic. We will ask them to stop; we will interrupt them.

DR. ZENDLE: So comments should be limited to the evidence --.

MS. CONRAD: Exactly.

DR. ZENDLE: -- and not to whatever subsequent decision by somebody else about coverage, what effect that might have.

MS. CONRAD: Correct. And I have notified all speakers and organizations that the issue at hand is not Medicare coverage, it is not coding issues, to please address the scientific evidence.

DR. GARBER: Any other questions or comments from the panel members?

MS. CONRAD: Okay. It is now my pleasure to introduce Hugh Hill, the acting director of coverage and analysis group in the Office of Clinical Standards and Quality. He will discuss an overview of evidence based methodology.

DR. HILL: Well, it's my -- I was going

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to say a little bit about the history and how we got to where we are, but Alan's explanation was so good I don't need to try to gild that lily, so let me just shift into what we're going to do to talk a little bit about evidence based medicine and methodology. And it is my great personal pleasure and privilege to introduce to you Dr. Deborah A. Zarin.

Dr. Zarin comes to us from a sibling agency; she's the director of the technology assessment program at AHRQ, the Agency for Health Research and Quality, in the federal Department of Health and Human Services. Dr. Zarin oversees a comprehensive national program which performs assessments of diagnostic and therapeutic interventions in order to glide -- guide clinical and policy decision makers. It's infrequently a glide, certainly a guide. Prior to this, Dr. Zarin was medical director and the director of the Office of Quality Improvement and Psychiatric Services for the APA, the American Psychiatric Association, and in this capacity she directed the APA's practice guidelines project, and was co-director of the APA's practice research network. Dr. Zarin is a nationally recognized expert in evidence based

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medicine, clinical decision making, practice based research and practice guidelines, and she has published more than 50 peer reviewed journal

articles focusing on these issues. She graduated from Stanford University and received her doctorate in medicine from Harvard Medical School; she is also board certified in general psychiatry as well as in child and adolescent psychiatry. We feel very privileged to have her help with this panel this morning. Dr. Zarin?

MS. CONRAD: Excuse me just one minute. Could we have Megan Cohen contact Dick Coyne in the back of the room? Sorry about that.

DR. ZARIN: What I was asked to do today was to tell you everything you need to know about clinical epidemiology in 30 minutes or less, so if I start talking too quickly, someone should tell me.

Clinical epidemiology has been, the working definition I use is really the systematic extraction of data from clinical studies to draw valid conclusions, which is what we're all trying to do. I guess the slide is going to stay cut off on the left, but it may be that nothing important is on the left.

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The main question that I was asked to address is, why is methodology important. Basically what this panel and what the MCAC in general is trying to do is to implement evidence based medicine, which is decision making based upon data regarding the likely impact of different treatments on specific outcomes for specific populations. In order to do that you need to evaluate the evidence, which is what Dr. Garber was just talking about.

Just for orientation, there are really for this purpose, say three types of studies. Studies designed to evaluate the therapeutic effect, to evaluate a diagnostic test, or to evaluate screening tests. The latter two can be considered similar. We're going to focus for my talk on studies evaluating therapeutic effect.

There are really three steps that this panel is going to end up observing or participating in. One is, the systematic review; how did you find the studies that you will be evaluating, how do you evaluate the individual studies, and how do you evaluate the group of studies, the study

synthesis.

Study review really, for the purpose of this talk, I'll just leave it at, it's important to specify how the studies were selected. And obviously you would like them to be selected in some rational comprehensive way that's free from bias, so that you're not seeing certain studies, say those with a positive outcome, and you're leaving out studies that might have a negative outcome. Okay.

So let's focus most of our time on how do you evaluate the individual studies, what are the key things? What you're really asking is does this work, does this intervention under discussion work? That really involves two questions. Did it work in the study group, in the experiment that you're reading about? That's really an internal validity question. The next question is, will it work in the relevant group? That was the question Dr. Garber was addressing in terms of, will it work in the Medicare population, or whatever subpopulation is of interest to you. Those are really two separate but obviously related questions. Okay.

To look at did it work in the study group, there are key issues really, design, patients, treatments, time frames, outcomes, analysis, so I'll make very brief comments about these. But this is to give you an overview of the kinds of issues that are important. Okay.

Did it work? The first question is, compared to what? Turns out, this is a very important question. There's different kinds of studies; you can have an experimental treatment versus placebo, along with standard treatment versus placebo, because you're really comparing the experimental to some standard treatment. You could have the experimental treatment versus standard. And what I left out, which would be nice, would be experimental treatment versus standard, versus placebo, a three-armed study. But really always underneath it, the question is, did this work compared to what?

Why do you need the compared to what?

Why can't you just say did it work? This is really the question of why do we need a control group at all. Sometimes you might feel like, I know what happens without the treatment, why can't I just look at your treatment and not worry about another arm of the study, either a control group that as they said in the impact report, implicit or explicit.

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First is, there are contextual factors. You might know that it works, say in your practice setting or somewhere else, but you don't know how it would have worked in the setting where the experiment was taking place. It has to do with factors of the patients, the setting, other issues that might be going on. There are recall reporting guides. If you depend on, say, just case reports, obviously people are more likely to publish either the very positive cases or the very negative, depending on what the issues are.

And there are placebo effects. And by placebo effects, I realized after I made the slide that I was really lumping a few different kinds of things. One is, what would happen with no treatment, which is sort of the natural history of the illness or the disease process. The other is, what would happen with a placebo which includes both the sort of paratreatment issues; so if you give a treatment, you're also perhaps, say it's a drug study, drug A versus placebo. You're meeting with the patient once a week, there's some sort of counseling, they have to come to the clinic, they're getting cared for. There's various factors that might in fact be important in influencing

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whether that patient has better outcomes at the end.

And then there are other less well understood but clearly documented effects of placebo. And in fact, there are people who say, who have reported that placebos, for example in a drug study, the more side effects, the stronger the placebo response. There are people who have reported placebo responses from surgery, for example sham surgery, that kind of thing. So there are clearly a bunch of things going on that might

lead you to, if you didn't have that placebo arm or the no treatment arm, would lead you to not understand the difference between what's happening in the experimental arm and this placebo or control arm. Okay.

Is the standard that you're comparing it to appropriate? This is a very important question. Is it in fact what the real alternative would be? If you're comparing a new experimental treatment, for example, to something else, did the person who did the study pick an alternative that is in fact the alternative that makes sense? And you can get into other issues about that, which has to do with, was the standard given in an

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appropriate manner or was it perhaps given in a suboptimal manner? There are biases that can creep into a study design that way.

The next big question is, who are the patients? A study needs to be very explicit in its report in saying what the eligibility criteria are. Otherwise, when you evaluate the study and you're asking, did it work, you have to say, did it work for whom, and you have to be able to know whether the patients in the study -- you basically need to know who they are.

The next issue with patient selection is, you want the patients in the different arms of your study, the experimental and the various standard or comparison arms, to be as similar as possible. Clearly, randomization is the best way to insure similar groups. However, in randomization, details are key. You'll hear somewhere along, you know, in some of your panel deliberations, debates about was there blinding, was randomization concealed, various things like that. Certain things that can essentially undo blinding have to do with side effects, the way placebos were given, et cetera. And there are documentation of how different suboptimal methods

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of randomizing to overestimation of the effect of a treatment. So details are very important there.

Nonrandomized observational studies, which are probably a lot of the kinds of studies you will end up considering, there are many

potential biases in terms of influencing how the patients essentially got into each of the treatment arms, because someone wasn't, they weren't randomized. For example, clinician decisions, I think in the MCAC Executive Committee report, refers to an evaluation of a surgical procedure where perhaps only the healthier patients were referred by their clinicians to get the surgery because they were worried about referring the less healthy patients so that in fact, the surgical patients might have been healthier to begin with than the nonsurgical patients. Obviously, the opposite can occur. If it's a very risky procedure, perhaps only the patients who are more severely ill, closer to death, would be referred. So there are all sorts of selection biases.

Patient decisions. I'll give you a couple of examples in a second where, especially if it's an observational study where it's things that the patients are in control over, either requesting

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a treatment or something that they do on their own like taking certain vitamin, the patients might make decisions that you might be able to guess about which way the bias goes, and you might not be able to.

Let me just run through, to give you pause, two recent newsworthy issues where nonrandomized studies, in fact including big ones, have led to results that are discrepant with new large randomized control trials. The first is hormone replacement therapy in heart disease, in fact in secondary prevention of heart disease. I prepared this slide yesterday, but coming in this morning on NPR I heard yet a new report about this. And basically the story is that there were several large well done observational studies of secondary prevention of coronary heart disease, showing a large benefit of hormone replacement therapy. A meta-analysis of 30 of these showed a 35 percent reduction in risk, with up to 89 percent for those with a severe coronary heart disease.

Recent randomized control trials have shown no benefit and in fact, as reported this morning, possible risks for some groups of patients. This is frightening to me, because in

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fact these were very well done studies and if you read the reports of the observational studies, there's discussion in the reports, could those results be due to patient selection bias, could it be sort of healthy life style factors, patients who go to get hormone replacement therapy are also more likely to do other things that are good for them.

And the conclusions, although you know, there were always the people who were saying caution, unless it's randomized we can't believe it, there were a lot of people who were saying well, no, the size and the effect is so strong and it looks so consistent across studies that it must be true. It looks like it's probably not true. Vitamin E and heart disease, basically a similar kind of story.

And just to -- these were over, you know, several large studies, well over a hundred thousand individuals involved, good follow-up documented end points. These were very well done studies. They did as they could to control for known risk factors for heart disease in this study. And again, the results seemed to, in the two large randomized control trials, are showing different results than in the observational

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studies.

So this is an example where methodology is important and even when you do it as well as possible, lack of randomization can be a problem that, it's not always possible to control. We don't know all the factors to control for, is one of the issues, or we don't know how to control for them. Okay.

Another issue to consider is characteristics of the treatment. Was it described appropriately, meaning basically, did what work? You might say certain treatments, a pill, they took the pill, and all they do is say the dose and how often it was given. Other treatments might have many more aspects to them: How often was the patient met with, what exactly happened, was this the appropriate treatment, do you understand what the treatment is that was, that's being studied?

Another issue is time frame, and this is

an important issue that needs to be considered. The first is, how long was the treatment being given for, meaning what's the time frame of the actual study? Was this a treatment that is given once, like surgery? Is it given over a month, is it given over two months, what's the time frame of
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the study?

A related but different issue is how long was the follow-up? For example, if it's a treatment for an ongoing or chronic or incurable condition, is it meant to be given chronically and if so, when did they decide to end the study? Or is it meant to be given for a certain period of time and then stopped, and then it's very important to ask what happens when the treatment stopped. And that has to do with, when was it appropriate to measure the outcomes.

Outcome measures. What was measured? How are we agreeing to decide whether this treatment works? Basically the reliability of the outcome measures, and there you get into blinding of the rater, and depending on how subjective or objective the measures are.

Validity of the measures. In part, what I mean by that, if they're intermediate measures, are they in fact related to the real measures of importance which might be more -- you know, some measure of morbidity or mortality, but also, are they relevant? If it's sort of a quality of life measure, are these the measures that the patients and their clinicians care about?
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And then statistical analysis. Again, I'll leave it at saying details matter a lot, that you know, very well done studies can be analyzed in ways that would make the inferences invalid. I will just mention the issue of power, especially for negative studies. Was the study, did it have enough patients, were the measures such that it would have been able to detect a meaningful difference.

And then there's an issue I'll mention of dropouts, you'll hear a lot about that. If you have for example assigned patients to experimental versus standard treatment arms, what do you do

about people who -- there might be a lot of people who drop out of the experimental arm. What if all the people who drop out drop out because it wasn't working? And if you only measure the percent, you know, the percent benefit in the people that finish the trial, that's going to be really an overestimate of the effect, because in fact, an awful lot of people in whom it didn't work left and said forget it, I'm going down the street and I'm getting some other treatment. Okay.

That was did it work in the study that we're reporting; now, this is the external

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validity, will it work in the relevant group? Again, let me remind you, compared to what? This is another, there's an external validity issue of the comparison treatment. Was the comparison that was chosen in the studies you read in fact the real comparison in the real world? You have seen drug studies where a new drug is compared to quote-unquote a standard drug, but in fact you might realize that in your day-to-day clinical life, that quote-unquote standard drug is no longer what anyone uses, and something else is what they use. So in fact, the real life decision isn't the experimental drug compared to that standard, it's something else. And then you're left not really knowing how it compares to what the real alternative is.

There is external validity issues in the treatment, in other words, how it's given. If it's a provider dependent treatment, say surgery, you know, are the surgeons who participate in the study better at the procedure than other surgeons would be? Another one of the issues of the treatment might be dose intensity. What were the frequency of clinical appointments in the study, and is that what maybe accounted for some of the issues,

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et cetera?

And then of course there's patient issues. It might have been studied in 25 year old healthy male volunteers but you're trying to figure out if it's going to work in 65 year old men with various comorbid illnesses who are on other medications, et cetera.

So all of these are very critical in determining, will it work in the relevant group. And there is no, none of these issues have answers. I mean, this is really clinical judgment, carefully thinking about what the issues are.

Let me just mention briefly, that was sort of up to now was really how do you evaluate individual studies. Okay. Now, what do you have when now you have 10 in front of you and you have to synthesize a group of studies? Just to give you a sort of menu here, in general, research syntheses can be qualitative, which is basically a narrative, preferably a critical narrative saying there were five studies and here's comments on each one of them. They can be quantitatively synthesized, for example, at a meta-analysis. In essence a meta-analysis is saying, okay, we have for example, five randomized control trials of this study, each

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with 100 patients; let's act as if those were 500 patients in one study, and look at the results that way. And there is obviously, details are important in all of these in terms of the validity of the analysis.

Decision analysis is a method of really looking at a series of steps. For example, if you're evaluating a screening program and you're trying to show a health benefit, well, you can't really show a health benefit of screening without knowing what's going to happen when you get the results of screening. And all sorts of things can happen with the results of screening, so you get a very complicated set of steps in decision analysis, as a useful way of sometimes showing that.

Finally, obviously, you have all seen and heard about cost effective analysis, which can use any of these other methods, but is also trying to answer the question, what's the cost per unit of health benefit that I would get from doing this intervention.

The issue in answering the question, was this an appropriate synthesis, is was the appropriate technique chosen, meaning, did the technique match the question you're trying to

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actually answer. And was it done appropriately,

was the report of this synthesis sufficient to let you know whether it was done appropriately. Were the assumptions valid, were there sensitivity analyses. There's a whole set of questions, but this is sort of a run through of some of the key ones.

So, that was probably less than 30 minutes, and I hope that's helpful.

MS. CONRAD: Thank you, Dr. Zarin.

DR. GARBER: Are there any questions from the panelists for Dr. Zarin? Yes.

DR. STANTON: More a comment than a question. I think that in the introductory -- it was a very nice presentation and the presentation and some of the introductory comments that were made, I think adequately emphasize the importantness of randomized control trials. But I have a little bit of a concern, though, that it is setting a tone, and that we need to be cautious about setting the bar too high, because a lot of the criticisms that were made about different trials, including randomized control trials that were just made, are valid.

But if for example, the randomization

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methodology is not set forth in the methods portion of the paper, does that mean we're going to somehow lessen the impact of that study? Because I think if we look at many papers that are published in excellent journals such as New England Journal, or JAMA, we'll find that the randomization methodology often is not spelled out. And so, I think we have to be careful, because that was pointed out a couple of times in the TEC assessments that were done.

I'm afraid also that we're going to lead to very few therapies that come before this committee ever passing muster if we have the bar set so high that we're looking at the ultimate randomized control trials as being our gold standard, and this doesn't really reflect reality, because I think if we look at the different therapies that are practiced today, we will find that very few of them would pass that muster if we brought it before the committee, and had to validate that with randomized control trials as

were just described.

DR. GARBER: Thank you. Let me just make one brief comment. I think these are very important points and this is exactly what the panel

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will need to grapple with, but let me just say though, that our questions do not concern the therapies or interventions that are not before us. And we can tell HCFA, not as panelists but as individuals, you might tell HCFA you should cover because other existing therapies don't meet these standards. But our question is really not about the currently covered therapies or things that may have disseminated to widespread use before. Our question is, is there adequate evidence that enables us to make comparative effectiveness statements.

And if the answer is no, if we prove the answer is no, that's the answer, and it's irrelevant whether interventions that have been adopted in the past did not have to meet the same standards. That is a legitimate question to raise with HCFA, but it's not the question that we as a panel will be dealing with. We will be looking at these interventions, in this case interventions to treat incontinence, and asking whether there's adequate evidence.

And I think we will, we may have differing views among the panelists about whether nonrandomized studies are adequate in this

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context. One of the reasons the Executive Committee did not make blanket statements about that is that everything tends to be situation specific. That is, we have to look at the specific studies and decide whether the randomization was adequate, the study design was adequate, and so on, presumably on a case-by-case basis.

I'm sure this is probably more appropriate debate for the Executive Committee to take on, but I think in mind that we should not be so naive as to think that our recommendations, our evaluation of the literature and our statement we make about that, I think will carry a lot of weight in HCFA's decision, so I think we should not be naive about that.

DR. GARBER: I agree with that completely and we are after all, a coverage advisory committee. It's simply that we are not making recommendations about coverage, we are making determinations about evidence. That's our task. Thank you for those comments. Any other questions or comment for Dr. Zarin?

MS. CONRAD: Okay. Let's proceed with today's agenda topic, biofeedback for the treatment of urinary incontinence. And we will start off

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with Mr. Perry Bridger, who's an analyst in the coverage and analysis group.

MR. BRIDGER: Thank you. As many of you are well aware, urinary incontinence is a significant health problem for the Medicare populations. For example, prevalence of urinary incontinence in the above age 65 Medicare population is estimated to be near 35 percent for females and 20 percent for males, with rates even higher in hospitalized older adults and those in long-term care institutions.

Urinary incontinence affects individuals' quality of life and often leads to other comorbidities, isolation and depression. Frequently, patients do not report this problem to their families, care givers and health professionals, and urinary incontinence has remained an under reported and under studied condition.

In the following two slides, I have outlined for you several of the treatments which exist for the management of urinary incontinence. These include behavioral treatments, PFES, pharmacologic therapy, bulking agents, sacral nerve stimulation, and surgery. In general, which

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treatment option to pursue for the different types of urinary incontinence is dependent upon specific patient indications, comorbid states, cognitive function, and the willingness and ability to participate in treatment.

The Medical and Surgical Procedures Panel of the Medicare Coverage Advisory Committee will review the evidence and make recommendations to HCFA about two of these treatment modalities,

biofeedback and PFES. Today the panel will hear testimony and review the scientific evidence regarding the use of biofeedback as an adjunct to PME. Tomorrow the panel will hear testimony and review the scientific evidence about PFES. Currently, coverage for biofeedback therapy is subject to varying local policies and PFES is not paid for by the Medicare program.

For the purposes of this meeting, biofeedback therapy is defined as a therapy that uses an electrical or mechanical device to provide the patient a visual and/or auditory evidence of pelvic floor muscle tone in order to increase the patient's awareness of the musculature and to assist the patient in the performance of PFMEs. The panel has had the opportunity to read the

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technology assessment, evidence and other materials related to biofeedback.

After the public comment and scheduled commentary presented here today, the panel will be asked to vote on a sequence of questions regarding this therapy. These questions are directly related to the scientific evidence regarding biofeedback, and comments made today should be directly relevant to this topic. Dr. Ken Simon, during the HCFA presentation, will more fully address these questions, the points to consider and the categories of effectiveness.

I will now briefly outline these for you. The first question we are asking the panel to discuss for biofeedback therapy is the following: Is the scientific evidence adequate to draw conclusions about the effectiveness of biofeedback in routine clinical use in the Medicare populations with the following three indications: Stress incontinence, urge incontinence, and post-prostatectomy incontinence.

In answering this question, the panel should consider the following points: The adequacy of the individual study's design, the consistency of results across studies, their applicability to

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the Medicare population, and their applicability beyond research settings.

If the evidence is adequate to draw

conclusions about biofeedback, and the panel votes affirmatively on question 1, the panel will move on to question 2, which addresses the size and direction of effectiveness. Therefore, question 2 asks: If the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effect of the addition of biofeedback to PME compared to PME alone?

When answering this question, the panel is asked to place the size and direction of effectiveness into one of the following seven categories: Breakthrough technology; more effective; as effective but with advantages; as effective and with no advantages; less effective but with advantages; less effective and with no advantages; and not effective. Please remember that Dr. Simon will elaborate on these points more fully during the HCFA presentation, and you will have the opportunity to discuss them as well during your deliberations.

We thank the panel members and all of you for making an effort to participate in this

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meeting regarding biofeedback and PFES therapy for the treatment of urinary incontinence. We look forward to your deliberations.

MS. CONRAD: Thank you, Perry.

Well, it seems like we are running a little bit ahead of schedule, but that's good.

DR. EPSTEIN: Can I get a clarification on one issue?

DR. GARBER: Yes.

DR. EPSTEIN: It strikes me that the key operative word here is adequate, is the information adequate. Can somebody guide me on what adequate should mean problemistically? I'm really serious. That seems to be the nub of the matter here intellectually. Can anybody tell me how to operate that word?

DR. GARBER: I think that you won't get a numeric statement, but it's essentially a burden of proof issue, the burden of proof that has to be established by the intervention, i.e., that the evidence is sufficient for you to be confident that no further study is really needed to determine whether it's effective. Now you might still think

that you need more evidence to be able to quantify the effectiveness, but in order -- you have got to

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be comfortable in saying there is enough evidence to assign this at least in broad terms to one of the categories in question 2, although I would suspect that none of us believe you have to be precise about that assignment in answering number 1.

So with respect to the questions about the, that Dr. Stanton raises, for example, you might ask, going back to the postmenopausal hormone replacement studies, was the evidence adequate based on the observational studies? And I think as we gained more experience, what many people would say is, if you think there's a reasonable chance that a well designed randomized control trial will show something different, then the existing observation studies don't meet that standard.

Now in the Executive Committee document, there is an example of an observational study design that would clearly be considered adequate. That is where the prognosis from the illness is so certain that, for example, something that's uniformly fatal within a month or two months, if you just have an observational study that's showing that people who receive the treatment lived for a at least a year, we don't need the randomized

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control trial to determine effectiveness.

But there are several factors that Dr. Zarin had mentioned that can cast doubt on whether an observational study would be truly conclusive, or a randomized control trial that has less than ideal study design would be conclusive. That's not to say that you always need a randomized control trial, but there is a judgment call here about whether the observational studies are sufficiently well designed to remove any serious concern that might account for the results.

DR. RATHMELL: I would also like to clarify. I want to be very clear about the question that we're being asked. We are not being asked whether or not there is adequate evidence to support the effectiveness of biofeedback. We are being asked if there is adequate evidence, and now

I'll quote. Here's the question in the technology: Does adding biofeedback to PME -- now biofeedback by the definition of the process, includes PMEs -- and we're being asked if adding biofeedback results in a greater improvement in health outcome, okay?

It's very important because none of the panelists have any of the evidence, and I

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understand there is a large body of evidence looking directly at the effectiveness of biofeedback versus control, okay? So it's very important, we're looking at a very very small subsection and we have been given the evidence only on a small subsection. So we can't answer the question about whether biofeedback is effective; all we can do is compare it to PMEs, a very very specific question.

DR. GARBER: Yeah. Thank you for that clarification. And let me emphasize that the question posed is in a sense deliberate, because our entire set of classifications for effectiveness are based on comparative statements, and as Dr. Zarin had mentioned, what you compare it to is critical in analyzing the data and making the determination. Yes?

DR. RISAGER: Just a procedural point. I wonder if speakers could announce their names as they speak. We can't see up here what your names are.

DR. GARBER: Yes, thank you. Les Zendle.

DR. ZENDLE: In response to the first question, about what's sufficient, one of the

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issues about relativity, I guess, is that if a disease is very rare, you might not need as much evidence to be convinced that something makes a difference than if a disease is very common. And mainly because you would never be able to get as much evidence as one might want, because the disease is rare. But if it's very common, then there really isn't a reason why the evidence can't be obtained to a higher bar, as you said.

I know that there are rare diseases with fatal, quickly fatal outcomes, that I'm not going

to expect, because I would be expecting something that's impossible, as much evidence about as something about a common disease.

DR. GARBER: Any other questions? Dr. Landy.

DR. LANDY: I had a point to clarify. I thought we were supposed to answer two questions, one being first, efficacy of biofeedback, and then go on to question 2, if that was determined yes. I think the confusion is, the body of the technical assessment only addresses question 2.

DR. GARBER: Well, we can discuss what the report -- you're referring to the report, the TEC report?

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DR. LANDY: Yeah, I think that's where the confusion came up. But I think we are actually supposed to answer two questions.

DR. GARBER: Well, they are sequential questions, as Perry just said. If the answer to the first one is yes, the evidence is adequate, then we deal with the second. The report, I believe, does address both questions. I think the tables have a lot of commentary about adequacy of each individual study, as well as some of the statements about adequacy. Did I understand your question correctly?

DR. LANDY: I was just clarifying, because I think Dr. Rathmell felt that we were only supposed to answer the second question.

DR. RATHMELL: This is Dr. Rathmell. Our technology assessment doesn't look at biofeedback versus control, except tangentially. There are many additional studies that look at biofeedback versus control, like a waiting list control, various control groups. And so I don't think we can answer the question as to whether there's adequate evidence, as to whether biofeedback versus control, but biofeedback versus the PMEs alone, that's all we can assess, that's

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all the technology addresses.

DR. GARBER: Yeah. I think that the question that we were posed by HCFA is the one that the evidence report attempts to answer. I'm not sure that it's, the question is -- I see. This

question does not spell out that it's compared to PMEs alone. Is that your concern, that HCFA's question doesn't state that?

DR. RATHMELL: HCFA's question does very specifically say that what we're comparing to is PMEs alone. So I would say, that's the only question we're addressing. Versus someone sitting on a waiting list and doing nothing, they are not instructed in anything, we are not answering that question.

DR. GARBER: That's correct.

DR. McBRYDE: This is McBryde. But I'm reading this, voting question for our committee, and it says, is the scientific evidence adequate to draw conclusions about the effectiveness of biofeedback in routine clinical use, da da, and that is the first question. Your comments are exactly pertinent, so we have to decide on that before we can go any further, it seems to me.

DR. GARBER: Well, I have to apologize.

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I actually have different drafts of the questions in front of me, and I'm not sure which is the final one. And we do need to get this resolved, because it sounds as though operationally, our question has to be the comparison to PMEs. I thought that's what we were dealing with, but maybe Hugh can clarify.

DR. HILL: I think there is going to be some more said about this on the HCFA presentation on this subject, but the question we planned to ask you in sum that you will be presented later, was: Does the addition of biofeedback as adjunctive therapy to PFME provide improvement in treating incontinence? We understood it to be the combination of the two.

MS. SMITH: I would like to make a comment. They are absolutely right. If you look at the preliminary paragraph of the technical report given to the panel on biofeedback, it says biofeedback itself is not a treatment for urinary incontinence but can be used as an adjunct to PFME. And the second paragraph says, the objective of this technology assessment is to determine whether adding biofeedback as an aid to performing PFMEs results in a greater improvement in urinary

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incontinence as compared to PFMEs alone.
DR. GARBER: Well, it sounds as though we're all in agreement, and there was one version at least that did have the incorrect language. But let me just make sure that we have agreement from Hugh and the panelists that we are comparing the combination to PME alone.
DR. HILL: Perhaps it seems to be incorrect because we may have made a nonarticulated assumption. We regard that as first tier therapy, and this is as an addition. The question is about the addition to the first tier therapy, so does that --
DR. GARBER: Yeah. As well as we're all operating on the same assumption. I think there were definitely some versions of the question that left out that that was the explicit comparison. I understand what the confusion about. The way Dr. Rathmell stated it before, the way it was just stated, is the question we're dealing with.
DR. RATHMELL: Just to be very clear, and it's important, because when we get to part two, if we get to that second question, we have to put it in a category, is it as effective but with advantages, or as effective with no advantages.
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Now we are going to be asked to make a judgment versus other treatments that are out there, okay? We may not be able to do that, but that's okay. That's why it's so important to understand what we're doing.
DR. GARBER: Oh, absolutely. And let me also add that one of the difficulties that we will face in dealing with question number 2 generically, not just with regard to this technology, is we'll have to have a discussion about what those other things are. So we will deal with that as appropriate.
MS. CONRAD: Okay. Let's proceed with the individual presenters. Let me caution you first of all, please stick to the topic, please stick to the time limit. And as we said before, no pleas for Medicare coverage or codes.
And the first speaker is Joey Spauls Smith.

MS. SPAULS SMITH: Good morning. Members of the panel, ladies and gentlemen, there is a handout of the transparency available to members of the panel if you would like that for reference. I have no conflict of interest with anything.

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My name is Joey Spauls Smith. I am a registered nurse from California and have been a certified biofeedback therapist for 12 years. This summary of data is done as a practicing clinician in a routine clinical setting specializing in behavioral continence therapies. It is not a randomized and controlled study, nor is it strict research. It is carefully collected data from patient verbal reports, patient completed diaries, pad counts, pad rates, and EMG reports.

The number of patients was 54, most having had poor results with verbal instruction of PME and attempting to do it on their own. Excluded were patients having fewer than three sessions and noncompliant patients. The types of urinary continence addressed were stress, urge, mixed, and post-prostatectomy. The biobehavioral model used included biofeedback with PME, twice daily requested use of EMG, biofeedback home trainer, use of urge protocol, timed voiding, reduction of bladder irritants, and physiological quieting only.

The results were that of the 41 patients with stress, urge and mixed urinary incontinence, 34, or 83 percent were successful, meaning success

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defined as greater than 90 percent in reduction of leakage. The number improved were 6 of the 41, or 15 percent, improvement being defined as less than 90 percent reduction in leakage. And there was one unsuccessful patient, or 2 percent. Of the post-prostatectomy urinary incontinence patients numbering 13, 9 of those were successful, or 69 percent, again, having 90 percent or greater reduction in leakage. Four, or 31 percent, were improved, and everyone was successful. So of the 54 patients, 43 were successful, or 80 percent; 10 were improved, or 18 percent, for a total of 53 patients having success or improvement, or a total

of 98 percent, with a 2 percent no success rate of one patient.

The conclusions are that in this group of patients, PME alone without biofeedback did not work for them, yet with biofeedback all but one had symptom improvement. Biofeedback is effective and in this case, the work was done in a routine clinical setting as opposed to a strict research study. Biofeedback is the accepted way to do PME, as Dr. Kegel did it in the late 1940s, and I believe that the Blue Cross/Blue Shield TEC report is flawed, and I believe others will be discussing

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that. Thank you.

DR. GARBER: Thank you.

MS. CONRAD: Next on my list is Mary Cate Upton. She has not reported to me, so I am not sure if she is even in the audience. Okay. How about Diane Newman?

DR. BRADLEY: Connie, I would just like to ask, are we able to ask the presenters questions about evidence presented?

MS. CONRAD: Yes, you may, but could you hold the questions until the open panel deliberations, because these folks are really given strict time limits. Is that all right?

DR. ZENDLE: May I make a suggestion? I actually think that although their time limit should be their presentation, that it might be more relevant to ask a question about the presentation right after the presentation, if it is flexible that way.

MS. CONRAD: Go ahead, Dr. Zendle.

DR. ZENDLE: I don't have a question.

DR. HOLTGREWE: I have a question of the last speaker. When you treated post-prostatectomy incontinence, what was the interval of the onset of your therapy following the procedure?

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MS. SPAULS SMITH: With most of these patients, it was at least a year.

DR. HOLTGREWE: Thank you.

DR. BRADLEY: Could you also define the age of your patients?

MS. SPAULS SMITH: Yes. The age range was between 38 and 87 years of age.

DR. BRADLEY: And male, female?
MS. SPAULS SMITH: I do not have that breakdown. It could be retrieved. By far, mostly women.
DR. BRIN: What was the low percentage that would still put someone in the improved category? Was that 10 percent or 15 percent?
MS. SPAULS SMITH: Usually at least 25 percent reduction in leakage.
MS. CONRAD: Is that it? Thank you. Miss Newman?
MS. NEWMAN: I'm sorry. I only have one copy of my full presentation. I am going to give a summary because of the time frame, and I gave it to Connie so that she will have to copy it for you.
My name is Diane Newman and I am an adult practitioner in private practice in Philadelphia, Pennsylvania. I'm also a visiting

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professor at Rutgers, the State University of New Jersey, College of Nursing. I have an appointment to the Food and Drug Administration's GI neurologic panel.
I would like to acknowledge the assistance of Dr. Andrew Fantel on this presentation. Dr. Fantel is a urogynecologist who is in private practice in Long Island, New York. Dr. Fantel has been funded by NIH, NIA, and conducted clinical trial RCTs, of which the most famous is bladder retraining, and biofeedback assisted pelvic floor rehabilitation treatments in persons with urinary incontinence. Dr. Fantel and I both provide behavioral treatments in our practice.
Dr. Fantel and myself were the co-chairs of the 1996 Agency for Health Care Policy and Research urinary incontinence in adults panel. We were also a member of the 1992 panel, so we were with that panel looking at that work for I guess a total of seven years. Neither Dr. Fantel nor myself have any financial involvement with manufacturers of any products being discussed here. However, I do provide and have provided consultations to individuals, insurers, facilities,

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institutions, who want to start nonsurgical

behavioral treatment for urinary incontinence.

Dr. Fantel and myself would like to submit this presentation for the consideration by the Medical and Surgical Procedures Panel. I want to thank the HCFA members who have assisted me in doing this. The title of my presentation is Efficacy of Pelvic Muscle Rehabilitation for Urinary Incontinence, the Issue of the Use of Biofeedback.

The Agency for Health Care Policy and Research has published two clinical practice guidelines, this is the only topic they have done two on, on urinary incontinence in adults. There may be a third attempt to redress these issues as the Agency, AHCPR is now called the Agency for Health Care Research and Quality, and has commissioned Rand to determine the need for updating the 1996 guideline, and I'm involved in giving them information on the behavioral end.

These guidelines were developed by a panel of UI experts, selected through a thorough exhaustive review of health disciplines, clinical expertise, and consultation with professional organizations. And the following slide shows

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everyone, and I know another individual on our panel, Dr. Whitmore, will be speaking tomorrow.

But this was the first panel, this was the second panel, and as you can see, there was a combination, I always say it was Noah's ark, doctors, nurses, all the experts in the field, consumers, and also therapists.

The second panel did something different. We went out to exhaustive review. We had consultants of experts in the field to look at this. We also had technical specialists to look at this. We also sent it out to 56 outside reviewers, which included HCFA, to determine what they thought of the guidelines and whether it was efficacious.

The panel rated the strength of evidence supporting each recommendation based on the following criteria, and we were told to do this, and we had to give it a rating system. A is a recommendation that is supported by scientific evidence from properly designed and implemented clinical trials providing statistical results that

consistently support the guideline statement. A rating of B was a recommendation supported by scientific evidence from properly designed and implemented clinical series that support the

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guideline statement. C is the recommendations that are supported by expert opinion. It is important to remember that these ratings represent the strength of the supporting research evidence and not the strength of the recommendation itself.

Urinary incontinence is a significant problem with both young and old adults. I want to stress, it's also seen in young women. That's very important, I think. Statistics are that one out of three women post-child birth experience stress UI. Its impact is felt in associated health care costs and quality of life.

The panel attempted to try to clarify behavioral treatments. The 1996 guideline outlines the application of pelvic muscle rehabilitation, which includes behavioral modification, bladder retraining specifically for those patients with urge incontinence and overactive bladder, PMEs and the use of methods to enhance the rehabilitation of the internal pelvic floor and bladder muscle.

Based on the database evidence, the panel made the following recommendations: Pelvic muscle rehabilitation and bladder inhibition which are the interventions, using biofeedback therapy which is the method, are recommended for patients

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with stress, urge and mixed UI. The strength of this evidence was A. Since that recommendation, there have been additional evidence based research supporting the strength of the level of evidence.

This is Dr. Bergio's study in JAMA, which I don't think is in the TEC report. This is an RCT where she compared behavioral treatment using biofeedback to what is considered the standard of treatment for urge and overactive bladder, drug therapy. She also had a control group. She showed that there was an 81 percent reduction in UI episodes in the behavioral treatment group.

A second study by Wyman and Fantel compared bladder retraining to PMEs to combination

therapy. They also found that the combination therapy had significantly fewer incontinent episodes compared with the older two groups.

A third RCT -- oh, I have to stop.

DR. ZENDLE: Can you just quickly go through your slides just real quick, so we can see them?

MS. NEWMAN: Okay. The third RCT was published in JAGS last year and this was done at home by the individual, and again, they had a

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control group, mostly women, mixed UI, with a good biofeedback behavioral treatment had a 75 percent improvement in the treatment group.

DR. GARBER: Are there some questions from the panel, just very briefly?

DR. EPSTEIN: Yes. Just very briefly, are there any data that address the issue that we're addressing?

MS. NEWMAN: Yeah. Our feeling, and you can read my report, is there's no such thing as pelvic muscles alone. Kegel talked about biofeedback. There's no such thing as doing a Kegel and PME alone. I want you to show me where the data is. You either use verbal, mechanical, you use some method of feedback. Biofeedback is a methodology, it's not an intervention. The pelvic muscle rehabilitation is the intervention. And if you go to your basement in the library, you'll see Dr. Kegel had a perineometer, which is a biofeedback device.

DR. EPSTEIN: There are a couple studies in the literature that we were given, one in particular that I recall.

MS. NEWMAN: Which one?

DR. EPSTEIN: I'll have to pull it out.

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It was the one that I think had three arms, they compared PME, PME and feedback, and control. What was the PME arm if it doesn't exist?

MS. NEWMAN: It basically was a commission explaining with digital exam, tactile biofeedback, how to do it, then using a mechanical device. But there is -- you know, that's what Dr. Fantel and the panel felt, there is no such thing, which is why this is fascinating. You have

to utilize something, it's an internal muscle, to show the individual how to contract it.

DR. HILL: Were the results equivalent with the various means, mechanical versus digital versus verbal?

MS. NEWMAN: Well, the thing is that it's shown that when you use more mechanical, where the feedback is more visual, as opposed to a finger, you know, tactile, if you can see it and see what you're doing, the biofeedback that's used in the mechanical devices has shown increased improvement.

DR. HILL: So the data does break that out?

MS. NEWMAN: Yes. I mean, the issue is that one of the statements of the TEC report is

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that alone, we didn't compare alone and with biofeedback. There's no such thing as alone. Kegel never said alone.

DR. GARBER: Thank you.

MS. CONRAD: Has Mary Cate Upton come in? Okay. Let's proceed with the industry. John Spurlock, with Hollister.

DR. SPURLOCK: Good morning. Thank you for the opportunity to speak. Before we get started, I did receive travel expenses from Hollister, but that was really the only support that I've ever received from Hollister. I've not received anything in the past and I don't have any financial interests in Hollister as a corporation.

I'm a solo urogynecologist from Bethlehem, Pennsylvania. I have been practicing urogyn since 1994. I am employed by St. Luke's Hospital in Bethlehem, Pennsylvania, and I am the director of the Continence Management Institute at St. Luke's. I am also an assistant professor of OB/GYN at Temple University in Philadelphia, and I direct a urogynecology fellowship at St. Luke's Hospital. I do have some handouts of some of our data, so I will give these out now, and I also have the overheads that match these.

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I also brought along an article from Dr. Bump from 1991, in the American Journal of OB/GYN, and I apologize, I didn't get a chance to

make copies of these, but I will make the copies at lunch time and bring them to the panel. In which he really tends to clarify the whole issue of talking about it, versus active intervention, which we call biofeedback.

And as many of the previous speakers have mentioned, Dr. Kegel 60 years ago did in fact have a vaginal probe that he placed into the vagina to help the patient get that biofeedback and make sure they were contracting the right muscle.

Our patients come with a variety, a mixture of problems. Many of them come with urinary urgency, that feeling like they have to hurry up and go. And our mix is about 90 percent female and about 10 percent men. Most of the men are post-prostatectomy. They also come with a feeling of frequency, a feeling like they have to go every half hour to an hour. Nocturia, which is just nighttime frequency, getting up -- some of our patients get up six times at night to empty their bladder. And also, stress incontinence.

Now we do treat pelvic prolapse and also

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stress incontinence with surgical intervention if necessary, but about 60 percent of our patients come with mainly urgency, frequency, nocturia, and a mild stress incontinence. And we treat these patients with a combination of biofeedback and electrical stimulation.

Now, the mechanism of this problem is really a bit of a mystery. My feeling has always been that there is a weakness of the small muscle of the pelvic floor that helps one to hold urine, but it may also be an overactive bladder or either a motor or sensory urge incontinence from an involuntary detrusor contraction. However, we don't tend to do urodynamic testing on our patients before we recommend treatment such as biofeedback, because in our experience from many years ago, only about 10 or 20 percent of the patients had actual detrusor instability, an actual contraction of the detrusor that was involuntary. We tend to go more on history and physical exam and again, using the examining finger to feel the strength of the pelvic floor.

The problems with this therapy is that

it's very difficult to ever have a pure controlled group. As soon as -- and some of the other

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speakers have elaborated on this -- as soon as you place anything into the vagina or the rectum, you are already doing biofeedback in a sense. And so even if you don't have the patient hooked up to a computer screen where they can visually watch their contraction, you are already placing something in there that helps them to focus on the pelvic floor.

The other problem is that many patients have tried what they call Kegels that they were given from a previous five-second description, you know, go home and stop your flow, something like that, which actually is worse than nothing at all. Stopping the flow midstream probably gives them a voiding dysfunction, it probably doesn't strengthen the pelvic floor.

So, the other problem is, how many treatments are enough? We see about a 10 percent improvement with each treatment, and I know that's kind of difficult to quantify, but when we get out around seven to nine treatments, we see about a 75 to 80 percent overall improvement.

And I do apologize. We tend to combine biofeedback and pelvic electrical stimulation, because we do see such a rapid increase in

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improvement. We see a 75 to 80 percent improvement with those sessions, so being out there in practice, I really don't want to waste the patient's time, I don't want to bring them back for a session of one thing and then six months later, bring them back for a session of another thing. So the data here is a combined treatment.

Our first slide, and I went back and looked at this data, and it does not have a control group. This is just pure patient satisfaction. These patients are given a survey before they start our treatment, and they are asked to rate from the beginning, it was overall satisfaction, so this was some of our earlier data from January of '97 through October of '99.

And it was 475 patients who basically came with a variety of problems, urgency,

frequency, nocturia. And after they had completed, this was about, the average was about seven sessions of treatment, they were asked to rate in their own words, were they satisfied. And again, 78 percent felt that their problem was improved, 82 percent felt that they were satisfied. Could we have the next overhead, and this will correspond to the second page.

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We then felt that we really weren't asking enough questions when the patients were finished, so in addition to the one on the left, the blue slide, and the one on the right, the kind of orange one, has it improved and are you satisfied, we asked about their specific problem. Frequency, has your urinary frequency improved? And 68 percent felt that -- there was a 68 percent improvement in their frequency, 67 percent improvement in their urgency, and a 71 percent improvement in their leaking. And again, we asked the patients themselves to rate this. If we could have the last slide?

And this was our most recent data, and this was really just our last four months. I wanted to go back and bring you our most recent experience. 59 patients who were treated, and they had an average of about seven sessions. And again, an 88 percent improvement in frequency, a 78 percent improvement in urgency, and a 93 percent in leakings, either stress incontinence or urge incontinence. And 92 percent were satisfied with these results.

So, I would like to stop, and if there's any questions?

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DR. HOLTGREWE: Without urodynamics, how can you be sure of what type of incontinence you're treating? We all know there's a variety of reasons for pelvic floor insufficiency and unstable bladder. Without urodynamics, out of the 475, how do you know which is what?

DR. SPURLOCK: Well, it's a good question. We have often debated this issue about pre-urodynamic testing and as I said, we are only finding -- in the literature they tended to say upwards of 50 percent of patients were having a

detrusor instability. But in the old days they used to use carbon dioxide to do the urodynamic testing, and the carbon dioxide gas would get into the bladder and combine with the water in the bladder, the urine, and produce carbolic acid. And that would irritate the bladder, and I think that may have been why there is such a high incidence of detrusor instability or motor urge.

What we found is that on our patients, and this was five years ago, that only about 10 to 20 percent of patients with urgency had motor urge. Most of the patients -- in other words, detrusor instability, they could actually demonstrate a contraction on urodynamics. And the

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other question that I would have is, does it really matter what's causing their urgency frequency nocturia if 80 to 85 percent are getting better with the treatment?

So by just a good history about the urgency, the frequency, how many pads are you using, do you feel like you have to hurry up and run to the bathroom, you're not going to make it in time, and then doing a careful pelvic exam and feeling the pelvic muscles, which is what we're trying to strengthen. If we find that those pelvic muscles are very weak, then doing urodynamics before we start treatment, we have not found to be that helpful, because the outcome is the same.

If they have a severe prolapse, or a severe stress incontinence where they're wearing three or four or five pads a day, this type of therapy does not improve that that much. For those patients who are probably going to go on for surgical management, we will do a preoperative urodynamics to try to elucidate the type of incontinence that they have. But for some therapy like this, a benign therapy that doesn't involve medication, doesn't involve surgery, we've always felt that urodynamics was an expensive procedure

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that really didn't answer that many questions for us. That was, again, just our personal experience. Yes, sir?

DR. ZENDLE: Maybe you can help me with what may be an issue we all have, and that's what

are we talking about when we talk about biofeedback? It seems like in looking at some of the studies that are quoted, that sometimes it's just an education with a person, and giving verbal feedback based on examination, and then sometimes it's with an EMG and sometimes it's with a pressure sensor of some kind, and our -- what's your definition? And it seems then we could have something that's very simple, a biofeedback device, all the way to something with lots of bells and whistles and music and whatever. How do you then define in the study, what is biofeedback?

DR. SPURLOCK: I will attempt to answer it from my own personal experience. For 10 years I practiced general obstetrics and gynecology, and I was as guilty as the next person of, when a patient would come in and mention incontinence, I'd put my hands over my ears, and then when they would drag my hands off my ears they would say, well, what can I do about it? And I'd say, well, just go home and

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when you're emptying your bladder, squeeze the muscle that helps you to stop it, and do that, you know, 30 to 100 times a day when you're driving or something, or some silly thing like that. And I thought I was doing something, and the patients of course would all come back and say that they didn't notice any improvement, they were still having a problem. And then I would tell them, well, you know, get some pads or live with it.

And then I went and did a fellowship and learned a lot more about biofeedback and pelvic floor therapy, and I began to realize and actually went back and read Dr. Kegel's article. And I realized that he was not just verbally telling someone what to do, but he was either having a finger palpating the muscle of the pelvic floor and asking them to pull up, to pull up on that muscle like they are trying to hold their urine, or he was placing a balloon, it looks like a condom catheter, in the vagina, hooked up to a tube, hooked up to a monometer, and he asked the patient to squeeze the pelvic muscles. And to me, that's what biofeedback is. Biofeedback is not the stuff I was doing 15 years ago.

DR. ZENDLE: But some of the studies

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that we're comparing are called exercises alone without biofeedback. It says eight weekly sessions with a trained therapist. Now, to me, that's not just giving verbal instructions. They must be doing something during that time, but it's distinguished from say an EMG biofeedback.
DR. SPURLOCK: Yeah. I think the instruction would just be explaining, not doing --
DR. ZENDLE: Forget about just instruction. Let's talk about these sessions.
DR. SPURLOCK: Okay. The next level I would say would be actually placing a probe or some type of device into the vagina, or the rectum in post-prostatectomy men, it's placing a device that can sense pressure into the vagina or the rectum. In our case, it's hooked up to a computer screen and the patient can see and hear how well they are squeezing that probe. And then over time, over weekly sessions, they can see their progress in terms of being able to squeeze that muscle stronger and longer.
DR. ZENDLE: Couldn't that be done without the machine?
DR. SPURLOCK: I guess the only other way to do it would be for the person with them to
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put a finger in the vagina or the rectum. Most of our patients are not intimidated by being able to sit in a comfortable chair like a Lazy Boy chair and be covered, and insert the probe themselves and watch the screen. I think that many of, or some of our 70 or 80 or 90-year-old patients are a little bit intimidated by having a finger in the vagina, of the examining person, trying to teach them how to squeeze the right muscles. So I think -- does that answer your question?
DR. ZENDLE: Well, I guess, then, you would say that they probably wouldn't do as well?
DR. SPURLOCK: Yes.
DR. ZENDLE: And I guess, where is the evidence for that?
DR. SPURLOCK: Again, it's just my personal experience as a clinician out there in the field doing it, and you know, I have to see these elderly ladies every week, and I know they are

willing to do the biofeedback using the small probes and things like that, where they get the automatic feedback. They don't seem to do well with just talking about it or showing them one time with an examining finger. They don't seem to do very well.

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In a very small study, and I apologize, I didn't bring it, we were going to plan to present it. We had 20 patients randomized to just talking about it, just explaining how to do it, and then 20 patients who had the probe in the vagina. And within a few sessions of just the talking about it, all of the patients in the talking group wanted to be in the active group, in the probe group, because they weren't getting better with just talking about it. But it was such a small series I didn't bring along the data, but just about everybody in the 20 who were just the talking, wanted to have the active.

DR. GARBER: Let me interrupt for a moment please. A lot of the questions are going into areas that will be part of the subject of the open discussions. So let me suggest to the panelists that if you have questions for the presenters that you want to ask immediately after their presentation, limit them to very specific questions about their slides rather than the general discussion that will come afterwards. And let me ask the presenters to please stay around for the open panel session so that we will be able to ask you questions again later. I'm afraid that

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some of these questions may turn out to be repeated in various forms in each of the presenter's talks, and we do want to stick to the schedule as closely as we can.

MS. CONRAD: Next is Dr. Michel Boileau. We're going to rearrange the schedule just a little bit, and after Dr. Boileau's presentation, let's take our break at that time and then we'll keep all the professional organization presentations together. And the first presenter on the list of professional groups is Dr. Roger Dmochowski. Okay. Dr. Boileau, would you state for the record if you have any conflict of

interest?
DR. BOILEAU: Definitely. Good morning. My name is Michel Boileau. I'm a urologist in private practice in Bend, Oregon, a clinical professor of urology at Oregon Health Sciences University, a chairman and cofounder of Deschutes Medical Products. You probably assume that I am a proponent of PME with biofeedback because I'm a principal of a medical production company. Actually, the opposite is true.
I became a founder of Deschutes Medical Products because I was a proponent of this
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treatment. When I entered private practice 13 years ago I was a urologic oncologist. It quickly became apparent that urinary incontinence with its consequences would become a significant part of my work. 13 years ago, about all we offered was pro-Bhantine or surgery. But even today, most people who start medical therapy quit because of poor results or side effects, and less than 20 percent stay on therapy for six months or longer. Most patients do not want surgery, considering conservative treatment such as PME their first choice.
I was only vaguely aware of PME with biofeedback, but my interest led me to a course taught by Dr. John Perry. With new knowledge, I attempted to incorporate this treatment into our practice, but my colleagues were resistant because of expense related to space, staffing, equipment, time constraints, poor reimbursement, and economic conflict. Why would a surgeon promote nonsurgical treatment? But I was convinced that this treatment should be an integral part of multimodal therapy for urinary incontinence.
All of us would agree that correcting, that exercising muscles makes them stronger, but
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biofeedback does much more. It facilitates contraction, relaxation, the ability to convert between those two states, strength, and endurance. Still, someone argued that biofeedback is unnecessary and you know, it's hard to prove common sense.
If I am to believe the technology

assessment, we would need a randomized control trial to prove that runners who train regularly run better than age match controls who don't run. We know that many people exercise correctly and effectively because of tools such as EFX, with its pulsometers and its preprogrammed protocols that provide motivation. In the case of incontinence, multiple studies have shown with assisted biofeedback and PME, have shown strikingly consistent and excellent results.

In some of those studies, the non-biofeedback patients also seemed to do well. But careful reading will show you that many of those patients had intensive coaching, repeated vaginal exams to assess strength, and even regular EMG assessment to monitor progress. On the other hand, if we look at studies that used only verbal or written instruction, the results are clear.

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In 1999, Bump and his colleagues reported that 51 percent of their patients were unable to correctly contract pelvic muscles, and 25 percent demonstrated a technique that worsened in contacts. They concluded that verbal and written instructions are not adequate and that vaginal pressure biofeedback can prevent technique failure.

Another clinical factor influencing any exercise program is compliance. The average time spent brushing one's teeth is ten seconds, but SoniCare's simple two-minute timer encourages compliance and more effective brushing.

PME with biofeedback has also been shown to enhance compliance. Some of the reasons for poor compliance with a PME program include inconvenience, scheduling conflicts, and repeated embarrassment. So it seems that the factors necessary for long-term success are correct technique, compliance, and long-term maintenance.

In 1992, we founded Deschutes Medical Products to develop a comprehensive biofeedback assisted program that would allow women to treat themselves conveniently and privately, provide durable results because of compliance and long-term

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maintenance, and reduce the need for surgery or

medication.

The fruit of our efforts was the Persist treatment system, which has won five national and international awards. The system included the video for instructional motivation, a journal and workbook for education, motivation and self assessment, and a trainer with a pressure sensor that inflates to fit each person uniquely, multilevel protocols to identify the exercise effort, and feedback of strength and endurance.

We then proceeded to test our hypothesis, that a self-directed treatment system can be as effective as in-office treatment in many cases. The 55 self selected incontinent women who entered the study ranged in age from 25 to 81 years. We measured self assessment scores, voids per day, leaks per day, and severity indices for stress and urge incontinence. The trial lasted 16 weeks. There was a 79 percent response rate, 43 percent cure, 36 percent showing 50 percent or greater symptom improvement. All correlations showed statistically significant improvement, and there was no significance to age differences. The elderly did as well as the young.

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These results were strikingly similar to those referred to earlier. The study will be published in Wound Colostomy and Continence Nursing in July.

It might interest you to know that 11 separate Blue Cross carriers have approved the Persist system on the basis of medical necessity but still, accessibility remains a problem. Two weeks ago, the FDA gave Deschutes Medical Products clearance to market and sell Free-A, a nonprescription over-the-counter version of the Persist system, to help women with stress and urge incontinence. We regard this development as a tremendous advance, allowing many more patients access to treatment. It will provide significant cost savings when compared to alternatives, especially surgery and long-term drug use.

PME with biofeedback works. Just ask the patients. Having dry pants is not a placebo effect. By taking a comprehensive approach, using in-office therapy when needed, and including self

directed home based care, we can simplify and broaden access to treatment, preserve privacy and alleviate embarrassment, provide durable results, reduce the need for surgery and medication, and we

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can significantly decrease the cost of treating our Medicare patients who suffer from urinary incontinence. Thank you.

DR. HOLTGREWE: Could I ask a question? In the 55 patients you presented, did you make any effort to define the pathophysiology involved in the incontinence with urodynamics? In other words, who were you selecting to treat in this group.

DR. BOILEAU: These women were self selected. It was only the history. This was an attempt to see if women could select themselves to present for therapy and then self treat.

DR. GARBER: Thank you.

MS. CONRAD: All right. Let's take a 15-minute break, really, 15 minutes. See you back here at 10:35.

(Break taken at 10:21 a.m.)

DR. GARBER: We wanted to be very sure that we're all working with the same definition. This is the definition of biofeedback that's repeated that's used for the assessment and for purposes of our deliberations today, what you see on the screen.

MS. CONRAD: Okay. Our missing individual speaker has been found, Mary Cate

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Upton. Following Miss Upton's presentation, we will proceed with the professional groups with Roger.

MS. LECROY: Actually, I am Cheryl LeCroy. I am speaking in place of Mary Cate Upton. I am the clinical coordinator for the Virginia Continence Center, a division of the Virginia Urology Center in Richmond, Virginia. This is a 26 urologist practice.

MS. CONRAD: Excuse me. Do you have any conflicts of interest?

MS. LECROY: Not at all.

I have been performing biofeedback for the last five years. Patients see me in a nurse run clinic beforehand and do a lot of verbal kind

of things with them where we discuss behavioral modification and Kegels, and try to talk them through it. If they continue to have problems, they are referred for biofeedback.

Utilizing the MOS 36-item short form health survey, or SF-36, which is a quality of life survey, a five-year study of quality of life and treatment efficacy was performed. All patients are asked to complete a survey pretreatment and in follow-up at six months, and then yearly.

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The total number of patients that we utilized biofeedback on is 313; the total number of female were 250, and 63 were male. Average number of sessions per patient is 3.97, with a range from one to nine sessions, depending on the patient.

Our total number of patients participating in our survey was 206, 152 of which are female, and 54 are male. Average age is 63.5, with a range of 20 to 90. As far as diagnoses treated, for women, 39 percent are mixed incontinence, 31 percent are pure urge, 16 percent pure stress, 7 percent were frequency, and 7 percent were dysfunctional voiders. For males, 32 were post-prostatectomy and four were post-TURP; this accounted for 60 percent of my male population.

Average number of times patients responded on the survey to having urinated per day initially was 9.3, which had been reduced now to 5.9. Number of daytime incontinence episodes was initially 2.9, reduced now to 1.2, five years out. Number of times urinating per night was initially 2.8, now 2.3. Our number of nighttime incontinent episodes, initially 0.9 is now 0.7. Average number of pads worn per day before biofeedback was 2.4,

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and is now 0.9. And our patient satisfaction with quality of life after biofeedback is 72 percent, at five years out.

In conclusion, biofeedback is a successful, cost effective, and efficacious treatment option for patients with incontinence. Thank you.

MS. CONRAD: Thank you very much. Panelists? Thank you.

DR. ZENDLE: Can I ask you, which biofeedback device you used?

MS. LECROY: I used the Hollister equipment, using a vaginal probe, which gives an electromap of use of the accessory muscles.

DR. ZENDLE: Thank you.

DR. GARBER: Thank you.

MS. CONRAD: Dr. Dmochowski.

DR. DMOCHOWSKI: Good morning. I am Roger Dmochowski. I am a urologist at the North Texas Center for Urinary Control, I also have a clinical appointment at the Uniformed Services Medical School at Bethesda. I was the data manager and facilitator for the American Urologic Association's guidelines on stress incontinence that were published in mid-1997, which specifically

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looked at surgical therapy for the treatment of stress incontinence in healthy females.

I am going to present to you our position statement, that of the American Urological Association, and this position statement was essentially created by a subcommittee of members that included experienced nurses and clinicians dealing with incontinence on a daily basis, as well as urologists and urogynecologists with a specific interest in incontinence as a key frame and focus of their practice.

We did also in our recommendations strongly utilize the criteria that was set forth by this panel and HCFA for purposes of levels of evidence and also degree of treatment effect.

So, I will give you our verbatim position on biofeedback and then I'll amplify a few points. With respect to biofeedback, there is much confusion regarding use of this term when in effect, most investigators are really referring to biofeedback assisted behavioral modification. This makes it extremely difficult to evaluate the effectiveness or relative noneffectiveness of biofeedback as it is classically defined as an isolated entity. Although there does not appear to

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be an overwhelming consensus based upon objective data for the use of biofeedback in the treatment of urge and/or stress incontinence, the committee

would like to recommend a program of behavioral modification as effective in the treatment of urge and/or stress incontinence.

Behavioral modification should be subsequently defined to include toileting assistance; bladder retraining, which is educational instruction in volitional changes in voiding habit with verbal prompting and specific scheduling patterns; also, to include pelvic floor muscle exercises, the old Kegel type exercises; and also volume of oral intake modification as well as other dietary changes that may be necessary for specific patients.

Further, on the basis of expert opinion and based somewhat on results that are expressed in the literature, our committee would like to go on record as recommending a tabled biofeedback within such a program of behavioral modification. Treatment sessions are recommended no more than once weekly not to exceed a total of 10 sessions in one year. The selection of the frequency and total number of treatments is obviously arbitrary and is

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based upon expert opinion of our subcommittee.

The committee also recommended that further research in this area be done, specifically to include trials of biofeedback alone versus behavioral modification with biofeedback assistance; number two, a comparison of the various biofeedback roots, vaginal, rectal pressures, EMG monitoring, both including frequency and the ideal number of sessions to deliver those treatments; and finally, number three, the utilization of the aforementioned techniques, coupled with chronic maintenance biofeedback in the home setting.

Our conclusion is that based on our literature review, we believe that biofeedback represents an approach that will produce results that would approximate a value between a level three, as defined by HCFA, which is as effective with advantages, and a level four, as effective but with no advantages. So somewhere between a level three and level four, we feel the evidence based on randomized control trials and evidentiary based literature search, would place this specific intervention as between a level three and level

four intervention.

I would like to amplify our comments

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about the utilization of biofeedback within a graded program. We feel very strongly that behavioral modification is crucial to the treatment of patients with chronic urinary incontinence, biofeedback being one component of that behavioral modification program that I previously described.

Several of the panel members have commented on problems with the literature, and one of the problems with the literature is that it really in many cases, when we look at specific questions of biofeedback versus just PME, pelvic muscle exercises without biofeedback, the definitions are not well stated within the literature and in many of those circumstances, those patients receiving pure PME and/or biofeedback are doing it within the context of a larger incontinence delivery care system, a center of excellence type concept. It is very important that we consider that in analysis of the data, as we really can't extrapolate for an isolated component of that intensive global therapy for the patient and make any sense really of the data without including that concept of, again, this global approach to incontinence.

We would like to ask the Committee

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specifically if they have questions of us. I can certainly comment specifically on articles that we used heavily in our evidentiary search. They very much closely resemble articles that you relied on heavily, and I would like to compliment Dr. Lefevre on his technology assessment; it's a very good assessment of the literature, specifically what we were admonished to do, which was to keep our data inclusion relative to randomized control trials. I think the point was made by Dr. Stanton that there is good data in other types of objective trials, but in terms of randomized control evidence, I would strongly recommend to the Committee that they look at references 2, 3 and 8, which are references that specifically deal with methodology and analysis of pooled study data for making the analysis of whether biofeedback alone, or with or

without PME is effective therapy.
Yes, sir?
DR. GARBER: I just wanted to ask a brief clarifying question. It sounds like the AUA did a very very thoughtful job, and I commend you on that. And what I wanted to be sure of was how you would, or to what extent the AUA recommendations or conclusions apply specifically

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to the question of PME plus biofeedback, versus PME alone. You went through it all quickly and I think you may have said it, but I didn't quite catch it, so could you just elaborate on that point?
DR. DMOCHOWSKI: Yeah. I mean again, if you look at our summary recommendation number one, where we have in bold type, I think you see that we specifically feel that biofeedback alone represents between a level three and level four intervention. However, we feel that it may approximate higher degrees, at least a level three, solely a level three, if it's included in a global continence care delivery system, because I think it's very important that the coaching, the volume intake modifications, the other behavioral therapies that are instigated as part of a global continence care program, really devolve and give substance and draw sustenance, if you will, from the isolated biofeedback.
Again, many of the panel members have asked specifically, what about biofeedback versus biofeedback with PME, and there is data on both sides of the fence. And specifically, if you'll look at references, Berghmans' reference, which is reference number two in our literature survey,

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versus Weatherall's reference, which is reference number eight, they use the same data to come to different conclusions, and the different conclusions are based on methodologic differences. Berghmans used a stratifying type analysis, whereas Weatherall used much more of a meta-analysis, using numbers of patients and explicit outcomes.
So, we view it in the context of a global approach. As an isolated therapy, we would have to rate it between a level three and level four intervention, which I think is what you wanted

us to do.
DR. GARBER: Thank you. Any other questions from the panel members?
DR. STANTON: Do you see biofeedback as being something that is, that you recommend being used right at the onset along with PME, or is it something that's added for difficult cases, and if so, why?
DR. DMOCHOWSKI: Well, I will speak for myself and also for our review of the literature, and also for what we do in our continence care system in patients who elect conservative therapy. And I think it's important to keep in mind that we are dealing with a symptomatic disease and we have

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to present our patients with options. And we as urologists have been very self critical of ourselves over the last two decades because a woman with incontinence who presented to a urologic clinic in the 1980s was either offered pro-Banthine or surgery.
And let's face it, we realized with our experience with PTH that patients want a few more options. And especially when you're dealing with a non-life threatening, but significantly quality of life threatening disease, which urinary incontinence is, patients want options to therapy. So we integrate in my practice and in the practice of many people who contributed to this, biofeedback assisted PME intensely very early in therapy in those patients who elect a behavioral component to the overall therapeutic approach.
Behavioral therapy is not of interest to some patients and that's an individual patient's choice, but I think it should remain a patient's choice. It should not be mandated that a patient can't have that as a component to their therapy based on reimbursement or whatnot.
So, I think your question to wit is, do we use PME alone or with biofeedback, we use an

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initial trial -- on my initial assessment of the patient, the patient has an assessment, a digital assessment of the pelvic floor musculature, which is what PME is, and an instruction on how to contract those muscles. And then there is

intermediate training sessions that are done with more intensive type biofeedback type monitoring.

And we have, our session now, this is totally arbitrary, is a four to six week time cycle. Quite frankly, it's dependent upon the patient's insurance reimbursement or the patient's ability to pay, although we do as much free service as we can, especially in the elderly. In our Medicare population specifically, which is covered by Trailblazers, we do not receive reimbursement for biofeedback, so we do biofeedback as a service to our patients because of quality of care issues. And also quite frankly, the patients appreciate it and it's good press for us. So we do it out of service to patients.

I do not think that PME in and of itself, a coach sitting there with fingers in the vagina, is as good as instrumental therapy, utilizing patient assisted observation of their pelvic floor contractions. That is my personal

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opinion. Again, there is some data, especially if you look at Weatherall's meta-analysis, that would suggest that my statement is true, but I'm speaking for my own self now, and the AUA's position is as expressed in bold on your paper.

DR. GARBER: Thank you.

MS. CONRAD: Next we have Lindsey Kerr, and after Dr. Kerr, Cyndy Feldt.

DR. KERR: Good morning. My name is Lindsey Kerr. I am a practicing urologist in Colchester, Vermont. I'm fellowship trained in incontinence and urodynamics, and I'm director of the Vermont Continence Center. I am here today to represent the National Association for Continence. I have given you all a handout, and you also received in your packet prior to coming here a two-page summary of our position.

I have no financial ties to any industry represented here. I don't think they even bought me a cup of coffee this morning. I have been NAFC's national spokesperson for approximately two years now, and in that role I do interact with patients, corporations, industry, insurance groups, government and other regulatory agencies. I've also advised the last AHCPR guideline presentation

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done in 1996 on incontinence.
Now we've been asked to provide testimony today on the efficacy of biofeedback therapy for urinary incontinence using evidence based methodology, and although many technologies and pharmaceutical interventions can easily be evaluated using this technique, biofeedback for incontinence is not one of those that can be easily looked at in this way. And I'm sure having now reviewed the literature, probably many of you would agree with that statement.
I'd like to take a few moments to put the problem and my organization in perspective for you, because we are a consumer advocacy group. I'm not doing studies to present here today, and I certainly am not representing a physician organization, before I get to address the literature directly.
NAFC is a national 501.C(3) not for profit organization that was chartered in 1982 as help for incontinent people. We are dedicated to improving the quality of life for individuals impaired or troubled by incontinence. The success of our 17 year old organization is reflected in the size of its membership, numbering approximately
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128,000 across North America and beyond. The readership of our publications, the quarterly quality care newsletter, its now annual resource guide, and the quarterly COS affiliates bulletin, and our subject specific educational pamphlets, is estimated to reach about 250,000 people because of its known shelf life.
Urinary incontinence was conservatively estimated by the AHCPR in 1996 to affect approximately 15 to 30 percent of community dwelling adults, and at least half of the individuals confined to nursing homes. That translates to 13 million Americans, 85 percent of whom are women. In studies done by Kimberly Clark and Neal Resnick, of the Brigham and Women's Hospital, find that the figure may actually be closer to 25 million, when we take into consideration those with temporary or periodic incontinence.

In the spring of 1999, NAFC worked with the Alliance for Age and Research, and presented before the Special Senate Committee on Aging, data that supported their work that there were four critical areas for health concerns for seniors. They were Alzheimer's, loss of vision,

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osteoporosis, and urinary incontinence. We know that urinary incontinence is very expensive, to the hue of, the University of California Berkley has estimated it to be $27.9 billion; 85 percent of that is direct cost. Nursing home care, where most patients end up because of incontinence, half the patients do, that's 39 to $43,000 a year, and two-thirds of that is paid for by Medicare and Medicaid.

During our 17 years of work in public education, NAFC has utilized consumer research to determine our priorities for advocacy. Our primary purpose of this research is to assess the behavior patterns and attitudes of the organization's ever expanding newsletter readership base. And while individuals participate in each one of the surveys we've done, and there is a summary of that in the first page, our trend data is certainly considered to be meaningful.

A total of 98,000 of our consumers were surveyed through a mailing from the quality care newsletter. 1,837 returned completed surveys by the survey deadline, accounting for a 1.9 percent return rate. There was no monetary incentive given for completing the survey, nor was a postage paid

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envelope included. Responses were substantial enough to allow for a degree of accuracy within plus or minus 2 percent at a 95 percent confidence interval. Answers from those responses, and they're summarized on printouts of slides, reflect the attitudes, demographics, experiences, of 95 percent of our general readership.

Data was cross tabulated by the following categories for condensed responses. We looked at gender, age bracket, household income bracket, category of health care insurance coverage, diagnostic category, type of treatment pursued, treatment satisfaction, type of health

professional consulted for diagnosis and treatment, management products and devices utilized.

You have to keep in mind when you look at our survey results that the pool of potential respondents was a newsletter based group, not the American public at large. There was an opportunity for non-response error, and each of the surveys we have conducted since 1986 exist independently of each other, although we do talk about them in toto.

The average age of the respondents was 67 years. Women to men in our readership, the

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ratio is 2.7 to 1; in the survey it was 2 to 1. 54 percent of the respondents described their health as being good, compared to 67 percent in 1986. Continuing to be of significance to NAFC is the overall level of consumer dissatisfaction with treatment measures. Six years ago, 35 percent of our respondents registered dissatisfaction to treatment outcome; three years later that had jumped to 62 percent, with no significant difference between men and women with respect to the responses. This year, our survey from 1999, again, there is a high level of dissatisfaction with treatment outcomes, 64 percent.

NAFC in 1986 commented on how diverse treatment options were becoming. Now three years later, respondents are disclosing greatest interest in conservative treatment measures. Approximately half of all women and men rated nonsurgical, noninvasive, nonprescription drug avenues of treatment as their number one most helpful treatment that they have undergone in the past five years.

Our overall results do demonstrate how positively people feel about their outcomes with conservative measures. 52 percent of all men and

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40 percent of all women rated these treatment modalities at the top of their list. PME was considered the most helpful treatment, and clearly our readership believes in the utility of these treatments.

Stating that, only 3.3 percent of all respondents considered themselves cured following

their most helpful treatment, and only 8.6 percent overall explicitly expressed that they had been very pleased with their outcomes. It appears that there is a large gap between outcome of objectives of consumers and what really is available to them.

Although we have had the opportunity to review the literature in support of noninvasive treatments for urinary incontinence, NAFC readership base has actually allowed us to reflect on what consumers of these modalities appreciate and what they dislike. We did not separate the use of PME from that of exercise within the context of biofeedback. We will plan on this in our next survey. Quite frankly, we find this separation arbitrary and nonsensical because biofeedback does incorporate PME, and as far as we can tell from the review of the literature, PME was probably taught within the context of at least some initial

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biofeedback.

Time is a precious commodity. We don't think that clinicians will have adequate time to instruct patients well and adequately in PME. Bump and Bo have both demonstrated in their patient reviews that instruction alone is not adequate. 25 percent of the patients end up worsening the incontinence, and a third of them end up not being able to identify the muscle appropriately.

We agree that more funding should be made available, and special attention paid to improving the quality of the studies performed. Our members certainly deserve no less. Thank you.

MS. CONRAD: Panelists? Thank you, Dr. Kerr. Cindy Feldt. The presenter following Miss Feldt is Catherine Dubeau.

MS. FELDT: Good morning. My name is Cynthia Markel Feldt. I have been practicing as a physical therapist for 14 years and am currently practicing at Mayo Clinic in Jacksonville, Florida. I am a specialist in the treatment of urinary incontinence. I am here on behalf of the American Physical Therapy Association, the APTA, which represents nearly 69,000 physical therapists, physical therapist assistants, and students of

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physical therapy. I have no current or prior

financial interests in any manufacturer whose products are under discussion today.

You have in front of you the testimony that I am rendering. You also received a prior statement that included our review of the literature that should be in your packet. The Agency for Health Care Research and Quality, the AHRQ, formerly the Agency for Health Care Policy and Research, the AHCPR, is a lead government agency charged with supporting research designed to improve the quality of health care, reduce its costs, and broaden access to essential services. The clinical practice guidelines on adult urinary incontinence published in 1996 by the AHCPR established an algorithm for the evaluation and management of urinary incontinence and primary care.

The AHCPR guidelines state that PME intervention using biofeedback is recommended for patients with stress, urge and mixed urinary incontinence. The AHCPR gave an A rating, the highest rating possible to the strength of evidence supporting this recommendation, and you heard about this earlier today by Miss Newman. The AHCPR

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criteria for an A rating are scientific evidence from properly designed and implemented controlled studies, providing statistical results that consistently support the guideline statements.

Because these guidelines were formulated by a neutral government agency comprised of health care research experts, the APTA strongly urges the Medical and Surgical Procedures Panel to weigh the findings of this report heavily in its deliberations regarding utilization of biofeedback for treatment of urinary incontinence in the Medicare population.

As you are aware, another assessment of the literature has been done. At the request of HCFA, Blue Cross and Blue Shield Association completed a technological assessment of the use of biofeedback in the treatment of urinary incontinence. Some remarkable contrasts should be noted. For example, while the AHCPR clinical guidelines were based on a review of the literature by a panel of leading health care and research

experts, the Blue Cross Blue Shield TEC assessment was authored by one individual. While the AHCPR assessment was performed under the auspices of a neutral government agency, the Blue Cross Blue

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Shield TEC assessment was done by a health insurance association, many of whose members are for profit organizations. The Blue Cross Blue Shield Association's assessment reviews research articles which compared pelvic muscle floor exercise, PME, to PME plus EMG biofeedback for the nonsurgical and nonpharmacological treatment of stress, urge, or mixed incontinence.

The issue at question today is whether the use of EMG biofeedback confers an added benefit and produces a significant result over the sole administration of PME to justify its use in certain populations with UI.

The Blue Cross Blue Shield assessment identifies a number of clinical studies. It then attempts to critique their outcomes, significant differences between treated and control groups based on the rigor of each study. In its analysis, the assessment concludes that of six controlled studies that were identified, in which the above comparisons were made, two reported a significantly greater improvement in the biofeedback plus PME group as compared to the PME group alone. Of the three trials with randomized group assignment, one reported significant improvement in the biofeedback

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group.

Of the two trials that were judged least prone to bias, neither showed a significant benefit of biofeedback. But of the four trials with potential biases identified, two showed a benefit of biofeedback, one found no significant difference, and one did not report on statistical significance.

It would be ideal if the literature available studied the precise parameters and the precise population under the precise conditions. Unfortunately, that is rarely the case in clinical research and it is not the case here. The studies available investigated a variety of parameters, and did so under differing conditions. It is important

though, that as the stakeholders in the effort to determine the most reasonable coverage guidelines that we are careful that our pursuit of a preference for one kind of evidence not be transformed into an impassable barrier. It is important to view the available in aggregate, analyzing the components but not losing the perspective of the overall scientific and clinical picture that is created by the parts.

Burgio in '98 found PME plus biofeedback

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to be superior to pharmacological intervention. Bump in '91 found that 41 percent of women could not do sufficient voluntary muscle contraction of the pelvic floor, an integral element of any effective urinary incontinence treatment program. Berghmans in '96 found that patients who received PME plus biofeedback make larger improvement quicker than if they received only pelvic floor exercise; in other words, biofeedback enhances early improvement and recovery.

Burns in '93 found biofeedback to be better than the control group, and PME superior to the control group. The study was criticized because the control group did not receive pelvic floor exercise, and because PME plus biofeedback was not compared to PME alone. However, a profile finding which was overlooked if not deemphasized by the TEC assessment, was that the strength of the pelvic floor musculature in the biofeedback group was significantly greater than in the group that received PME alone. Moreover, the study suggested that the reduction in urine loss symptoms may be due to a multifactorial approach on biofeedback, pelvic muscle and behavior techniques, including education on anatomy and bladder function.

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The foundation's multifactorial approach is education, and biofeedback is a critical and effective tool in educating the patient in ways of gaining control of and strengthening the muscles of the pelvic floor. Both PME performed with the direction of a professional therapist, and PME with biofeedback, require the patient to actively participate in the treatment. The addition of feedback supplies the patient with visual and

audible information indicating the strength of the muscle contraction, and the degree in which the exercise is being performed properly.

The APTA believes that it is imperative that Medicare heavily rely on the medical research of experts of the AHQR, a neutral government agency, rather than the opinion of a single health insurance organization, when making such an important decision. Thank you.

DR. RATHMELL: Can I ask you a question quickly. Excellent. Very very good and thorough, and you talked real quick; it was hard to keep up.

MS. FELDT: Sorry.

DR. RATHMELL: But the question I want to ask you is, does it have to be an electronic device that provides the biofeedback? Can we go

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back to Kegel's original pneumatic device?

MS. FELDT: You mean the pressure versus electronic?

DR. RATHMELL: Exactly. And is -- tell me why you think electronics is better, if you think it's better.

MS. FELDT: I don't believe there's any solid studies out there comparing the pressure perineometer versus the EMG perineometer for us to make that kind of a comparison. I prefer the EMG because I understand the muscle function better, and I'm looking for the muscle function. And that's what I do as a physical therapist, versus the pressure, which doesn't give me that indication.

So I can't analyze situations such as, I'm looking for how fast does the muscle come in, how quickly does a muscle relax, how long can they sustain the contraction. Those indications tell me if I've got more of a neurological overlay with the muscle or if I just purely have muscle weakness and atrophy. I also look at the indication with function, and I find that pressure perineometers don't allow me to do as much in functional positions because of how the devices are created.

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As a physical therapist, my specialty is function, so I worry about can they do the things that they did before with leakage. So if a

person's condition is that they're having problems getting up and down out of a chair, and I just do a pressure perineometer lying down, or just a digital lying down, they can't necessarily transfer that over to the sit to stand regimen. So I use the combination to try to help them with the functionality of it.

MS. CONRAD: Thank you.

DR. ZENDLE: I'm sorry, I have another question. On page 4, you say Berghmans' '96 found that patients who receive PME plus biofeedback made larger improvements quicker than if they received only pelvic floor exercise?

MS. FELDT: Yes, sir.

DR. ZENDLE: I just want to make sure that you were referring to the same paper, the one in Neurology and Urodynamics in October '95? I'm sorry, '96?

MS. FELDT: That's the only Berghmans article I am aware I referred to. I would have to go back. I don't have that in front of me.

MS. SMITH: There's two Berghmans. The

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one Berghmans is, that she's referring to, was actually a research study done by Berghmans, and the one that you're thinking about is the one in our technical assessment, which is a review of studies. So actually, Berghmans is a researcher, and Cindy is absolutely right; that's what the Berghmans '96 study did find, was that patients who received PME with biofeedback actually got better quicker, and that was actually the point of Berghmans' study in '96.

DR. RISAGER: Except, he omits the fact that the long-term, over full period of treatment, showed no difference.

MS. FELDT: Any other questions? Thank you.

DR. GARBER: Thank you.

MS. CONRAD: Next we have Catherine Dubeau, and following her, Barbara Woolner.

DR. DUBEAU: Good morning. On behalf of the AMDA, I'd like to thank the panel for the opportunity to speak to you this morning. My name is Dr. Catherine Dubeau. I'm a geriatrician who has been doing incontinence research for the past

10 years and has been a long-term care medical director for six years. I have no financial conflict of interest to talk to you about this morning.

I'm here to represent the American Medical Directors Association, which is a national professional association committed to the continuous improvement in the quality of patient care by providing education, advocacy, information and professional development for medical directors and other physicians who practice in the long-term care continuum.

The AMDA position on biofeedback is that although incontinence is extremely prevalent in the long-term care population, there is insufficient evidence to support biofeedback for incontinent long-term care residents, and our conclusions are based solely on the long-term care population. Therefore, if the MCAC decides to provide coverage, we would be interested in helping MCAC identify those long-term care residents who based on available research may be likely to benefit from biofeedback.

I would like to take a moment to explain why incontinence in the long-term care population is different than in community based populations. The long-term care population has the highest prevalence of incontinence of any population known, with at least 50 percent of persons in long-term care affected. However, this high rate often leads to denialism by residents and staff that incontinence is normal in this setting. The target population in long-term care is one that is often immobile and cognitively impaired. 76 to 83 percent of incontinent persons in long-term care have dementia and they are also more likely than their continent peers to have impaired mobility, depression, stroke, diabetes, and Parkinson's disease, with at least one-third having multiple such conditions. Thus, both the assessment and treatment of incontinence in long-term care are more difficult, and translation of any behavioral therapy or biofeedback outcomes from community dwelling older persons is unreliable.

Furthermore, current regulatory mandates regarding incontinence in the long-term care setting focus on documentation and care planning, rather than on process and improvement, and individualization of care planning is limited. Furthermore, incontinence care in this setting is provided largely by unlicensed staff, which are certified nursing assistants, and current

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administrative costs provide a negative incentive toward incontinence care in this setting, since it is currently cheaper to simply diaper patients than to provide the prompt in voiding that we know will help them.

Lastly, data on the quality of life impact of incontinence in long-term care is just emerging. Although we long assumed that this had a negative impact, we now have some evidence where we have shown that social engagement is actually worse in incontinent persons compared with dry persons in long-term care when you look at persons with moderate ADL impairment, and that social engagement improves when residents become continent.

The AMDA position on biofeedback is based on a literature assessment. And unfortunately, when you turn to the literature, other than case reports that are not randomized, there are no specific studies specifically addressing PMEs or biofeedback for the treatment of incontinence in long-term care.

If we look to a study that may be applicable, the best is a randomized control trial of biofeedback in home-bound frail elderly that was published by McDowell and all in 1999 in the

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Journal of the American Geriatric Society. What they looked at was a home care population that was frail, having subacute medical problems. They were old, with a mean age of 77. They were very incontinent, with a base line of four episodes a day. And at least a third required regular care giver assistance, and over half of them required an assistive device for ambulation. What they looked at in this population was a comparison of home based biofeedback using electronic device in the setting of a multifactorial strategy to prevent

urge and stress leakage, and they compared this to a group who received only social visits.

What they found was the control subjects had a median 6 percent decrease in their incontinence, while the intervention subjects had a 75 percent reduction. They found that better outcomes were associated with stress as compared with urge incontinence, and in terms of outcome predictors, failure was more associated with male gender and the need to ambulate with an assistive device.

This is however, despite being a very well designed and executed study, does not address the question of whether the addition of biofeedback

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to a comprehensive multifactorial behavioral strategy makes any difference. Furthermore, it was highly selected, in that they could enroll only 29 percent of those who initially assessed for the trial. And finally, they excluded persons with mini-mental scores less than 24 percent and therefore, did not represent the cognitive impairment we find in long-term care.

In terms of potential target populations for biofeedback and behavioral therapy in long-term care, I have summarized in the handout some potential target populations, including those with uncomplicated stress and urge incontinence, patients who are not cognitively impaired, incontinence severity that is at least moderate to severe, and a treatment program that involves organizational management, staff support, ongoing feedback to staff and residents, and resident acceptance. Thank you very much for your attention and I will be happy to take any questions.

DR. GARBER: Thank you.

MS. CONRAD: Thank you, Dr. Dubeau. Miss Woolner. The next scheduled speaker is Dr. Geoff Cundiff.

MS. WOOLNER: Dr. Garber, Ms. Conrad,

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members of the panel, guests, I am Barbara Woolner on behalf of the Continence Coalition, which is a group of, an alliance of the Society of Urologic Associates and their Wound Ostomy Continence Nurses colleagues. We represent more than 7,300 nurses,

and neither the Continence Coalition nor I have received funds or any financial support for our presence here today. I do personally provide workshops for professionals teaching biofeedback techniques, and I have done that since 1991.

As evidenced by our prior position statement and utilization parameters that we submitted to HCFA earlier, the Continence Coalition strongly supports the judicious use of biofeedback for stress, urge, and mixed incontinence, within a framework of a structured behavior modification program.

Biofeedback for pelvic muscle rehabilitation is a standard of care in the community. Literature supporting its use has grown 10-fold in the past 10 years. Many excellent clinical studies are never published, and randomized control clinical trials of biofeedback of this type of design are severely limited due to lack of funding. Aside from that, the design of

these types of trial overlook some of the qualities that makes biofeedback so effective.

In biofeedback sessions, therapist interactions to promote high expectations of success motivate patients to make their own physiological changes. This is the cornerstone of biofeedback use in clinical practice. The Continence Coalition respectfully requests you to consider all of the available evidence today in your deliberations.

Biofeedback is a necessary component for many women and many male patients in rehabilitating the pelvic floor muscles. The Kegel exercises, which are historically used for biofeedback, show very clearly changes that are made in pelvic floor muscle activity with biofeedback over a period of time. Here, early stages, awareness and function changes, and later on, phase of regeneration and phase of restoration. These were published in 1948 by Dr. Arnold Kegel. And if you review the literature, Dr. Kegel never did PME without biofeedback, it was standard.

Many individuals are able to contract pelvic floor muscles correctly. However, there are many who cannot. Biofeedback is crucial in aiding

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these patients in their attempts to reeducate poorly functioning muscles. Bump found that 40 percent of the women in his study were unable to perform an appropriate pelvic muscle contraction with standardized verbal instruction alone. We believe standardized verbal instruction, which is very common in practice, is very suboptimal.

In my own personal practice, we found an even higher number of our patients unable to identify the pelvic floor correctly. 51 percent of 216 women we evaluated for incontinence were unable to identify or recruit their pelvic muscles. Further, 65 percent had either abandoned the exercises or were performing them incorrectly with no benefit at all.

This is an illustration of a gentleman post-prostatectomy. In the first section here, you see inappropriate use of abdominal recruitment, along with pelvic muscle contraction. The green represents pelvic muscle contraction and the pink line abdominal accessory recruitment. Within this same visit, within a matter of seconds with verbal coaching from the biofeedback therapist, the patient is able to experiment with his own muscle and eventually to identify and isolate a, albeit

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small, pelvic contraction. Immediately with reinforcement of this correct response, he says aha, he has an aha moment, this is what you're talking about. The next contraction is very efficient, although he sort of blows his remaining oxygen supply to the muscles and can't do it very well after that. Within a few weeks of exercise based on what this patient is actually able to do, he's back in the dating game. This is very very prevalent in the reason we use biofeedback the way we do today.

In the 216 people that we evaluated, we had statistically analyzed by Vital Research in Santa Monica, California. These patients were all seen in a private urogynecology practice. Of the 216 patients, their mean age was 59.9 years of age; they ranged from 27 years of age to 90. They were seen in a range of two to five biofeedback visits, a mean of 3.242 biofeedback visits. The inclusion

criteria was mixed, stress, urge incontinence as determined by urodynamic testing. The patients had been seen for two or more biofeedback visits and they all attended a three-month follow-up. The exclusions were quite a few, and I'm not going to go through that extensively now. However, we did

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do urodynamic testing on all the ones that we included in study.

Other diagnoses such as fecal incontinence, urinary frequency was not included in this group, although those patients are also well identified as being receptive to biofeedback assisted PME. The primary diagnosis of these people, 45 percent had mixed incontinence, 18 stress, and 30 percent urge. Prior treatments included surgery, PMEs with or without biofeedback, medication, and a considerable number were on hormone replacement therapy. We offered them PME alone, biofeedback in a behavioral program, medication, surgery, or the ability to do nothing about their problem.

The ones who accepted the behavioral treatment, they were highly educated in the method of lower urinary tract function. We used voiding diaries, dietary and fluid management, bladder training, and pelvic muscle rehabilitation. At three-month follow-up, we did another manual examination, using the same modified scale that was used in the initial examination.

This is an example of a patient who cannot identify the muscle without biofeedback.

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You see a clinician points out a very very minimal change in muscle function on EMG. With the appropriate changed N scale here, the patient is able then to see the magnification of this muscle exercise, identify it with her own receptive responses and make changes over the long run which produce effective pelvic muscle contraction and corresponding symptom reduction.

These group of patients reduced their leaks by overall, 81 percent, pad use by 58 percent. Change over time of their pelvic muscle rating was statistically significant with inter-rate of reliability of 89 percent. The EMG

changes themselves increased over time in terms of amplitude duration of a sustained contraction and repeatability of short quick contractions.

And we believe that the addition of biofeedback to this group of women significantly improved their ability to properly recruit pelvic muscle function. We stand on the fact that biofeedback is a standard of care in the community, that it is necessary for some patients, and we request that your attention be directed in a positive manner. Thank you very much.

MS. CONRAD: Thank you, Miss Woolner.

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Okay. Next, speaking will be Geoff Cundiff, and the next speaker will be Alfred Bent.

DR. CUNDIFF: Good morning. My name is Geoffrey Cundiff. I'm associate professor and director of the division of gynecology at Johns Hopkins Medical Center. I also sit on the research committee of the American Urogynecologic Society. Dr. Nicolette Horbach, our president, will be with you tomorrow. On behalf of the American Urogynecologic Society, I'm pleased to provide testimony on the utility of biofeedback in conjunction with PMEs for treatment of urinary incontinence. I do not have any financial association with any company providing biofeedback and in fact my patients who received biofeedback receive it from our physical therapy department.

The American Urogynecologic Society is a 21 year old nonprofit organization whose nearly 1,000 members have a special interest and expertise in the field of urogynecology and reconstructive pelvic surgery. Our membership includes gynecologists, urologists and allied health professionals, many with fellowship training who practice in academic and clinical practices. The mission of the society is to promote research and

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education in the specialty, and to improve the quality and delivery of health care to women with pelvic floor disorders. Many of our members were instrumental in the development of the first AHCPR clinical guidelines on urinary incontinence and in chairing the panel of experts for the 1996 revision.

One area not addressed in the assessment that our society feels would be helpful for the panel to know, and has been alluded to some before, and that is the history of PMEs, commonly known as Kegel exercises. Dr. Arnold Kegel is famous for his work developing resistance exercises to restore the pelvic floor muscles. In 1948 the literature barely addressed exercises for regeneration of muscle function and therefore, Kegel decided to experiment with various means of exercising pelvic floor muscles. After 15 years of study and research, Kegel concluded, and I quote: "Only exceptional women would continue to exercise long enough to produce results on a mere instruction to do so. Many women, in addition have no awareness of function, and unless provided with some way of knowing whether or not they are successful, soon become discouraged or are unwilling to make even an

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initial attempt at exercise."

Kegel, recognizing the inadequacy of exercises alone, developed the perineometer, an early form of feedback, that gave a visual readout of the strength of muscle contraction. Kegel's research demonstrated a 90 percent reduction in urine loss with PMEs using a perineometer.

As the technology assessment prepared for the panel suggests, clinicians use biofeedback to improve the patient's ability to perform PMEs. Our members have seen patients increase the effectiveness of pelvic floor exercises, leading to greater improvement and self control of incontinence. While the assessment dismissed several studies based on biases and statistically insignificant results, clinicians often place value on clinical results of studies, rather than exclusively on the design of the studies in determining the benefits and applications of therapeutic interventions.

Dr. Zarin already referred to randomized clinical trials as the gold standard, and we've spoken about some of the limitations. Certainly, they can also suffer from design flaws, including the lack of external validity, inadequate power,

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and an outcome measure that is not valid or does

not completely capture the benefits of an intervention.

The American Urogynecologic Society feels the improved outcomes applied by the assessment charged to the panel is an incomplete means of deriving the success of biofeedback with PMEs. Specifically, we believe that it is possible to draw conclusions about the effectiveness of biofeedback from the present literature, and that there are also some added benefits not touched upon.

As the assessment reported, two of the six controlled trials reported a statistically significant greater improvement with biofeedback added to PMEs. Burgio reported 92 percent cure for those treated with biofeedback and PMEs, compared to 55 percent of those given PMEs alone. In randomized trial, Glavind reported a 91 percent versus 22 percent three-month improvement in pad tests.

Shepherd also used a randomized trial in allocating 22 women with stress incontinence to either PMEs or PMEs with the perineometer. 91 percent of those with biofeedback were cured or

improved, compared to 55 percent with PMEs alone. The assessment dismissed this last study as statistical tests were not performed. However, this response is similar to those of Burgio and Glavind.

Prior evidence based reviews also support the use of biofeedback. You have already heard about Weatherall, who performed a quantitative analysis of five randomized clinical trials, and concluded that biofeedback may be an important adjunct to PMEs in the treatment of genuine stress incontinence. Our society feels that the 2.1 odds ratio for cure with biofeedback combined with the exercises is significant and validly support the author's conclusions.

Now speaking to the effectiveness with benefits, that is, we see this as not only effective but also having benefits. And these are benefits that are unique to biofeedback. Awareness of the pelvic muscle is critical to success and the biofeedback device is one method of teaching

patients how to contract the pelvic floor muscles. Some patients will do fine with verbal instructions but others will not. Many patients have difficulty identifying the pelvic floor muscle groups when

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given verbal instructions.

You've already heard about Bump's study, that found that 25 percent of subjects given verbal instructions actually performed a technique that was counterproductive. Burgio and Engel agreed with Bump's findings and Kegel's theory that many patients had difficulty identifying and controlling, as well as coordinating the function of the pelvic floor muscle group. When verbally instructed in pelvic floor exercises, patients may perform them ineffectively, which may be detrimental. With biofeedback, these exercises are performed with simultaneous sensory feedback given to the patient to help facilitate awareness of the state of muscle contraction.

Feedback learning, as described by Trias, is considered essential for learning new motor skills. And I quote: "The ability for comparison between kinesthetic experience and the observed response is often absent during attempts at learning healthy muscle exercises without biofeedback."

Glavind and co-workers revealed an indirect benefit of biofeedback in patients continuing exercises, versus the dropout rate that

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accompanies the use of exercises alone. 89 percent of the biofeedback group did their exercises regularly, versus 50 percent in the control group. While the assessment saw this dropout rate as a potential source of bias, it speaks to an important benefit of biofeedback, and that is improved compliance with therapy.

One of the more common reasons given by patients for discontinuing therapy is inconvenience of repeated therapy. And recent studies have suggested that this compliance can be facilitated by supplementing hospital based biofeedback with an inexpensive personal pelvic floor trainer that can be utilized in privacy and at the patient's convenience. Long-term benefits are not published

yet, although you heard about some of that this morning.

In summary, the American Urogynecological Society believes the use of biofeedback offers the possibility to control and correct contractions of the pelvic floor muscles and to visualize the strength and duration of any contractions. Biofeedback treatment of urinary incontinence is an efficacious management method that yields significant therapeutic benefits and

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low risk for selected patients. Thank you.

MS. CONRAD: Thank you. No questions?

DR. CUNDIFF: Everyone is tired out at this point.

MS. CONRAD: Dr. Bent. And the final presenter after Dr. Bent will be Dr. Perry.

DR. BENT: Good morning. I'm Alfred Bent. I'm a practicing obstetrician and gynecologist here in Baltimore. I am in charge of residency training at Greater Baltimore Medical Center. I have a program in fellowship training in urogynecology and reconstructive pelvic surgery at Greater Baltimore Medical Center and University of Maryland. I have been program director on a number of occasions for ACOG in the management of urinary incontinence, and have worked with them on several other projects related to incontinence.

On behalf of ACOG, an organization representing more than 39,000 physicians dedicated to women's health, I do appreciate the opportunity to address the Medical and Surgical Procedures Panel of the Medicare Coverage and Advisory Committee on the subject of biofeedback.

I received a summary of the technology assessment provided by Dr. Frank Lefevre, director

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of special assessments, just last week. It appears that the assessment provided by this summary has concluded that biofeedback does not provide additional benefit to PMEs alone. I wish to view some of the studies on which this decision or conclusion was reached. You have already heard a number of these, so I'll try not to reiterate too much.

Both the Agency for Health Care Policy

and Research guidelines in 1996 and the first international consultation on incontinence, cosponsored by the World Health Organization in Monaco in 1998 have recommended behavioral techniques as first line management of stress, urge, and mixed incontinence. The Monaco conference went on to recommend a therapy consisting basically of three sets of eight to 12 slow velocity maximum contractions sustained for six to eight seconds each, performed three or four times a week, continued for up to 15 to 20 weeks. A person with specialist training should assess the patient to be sure the correct voluntary pelvic contraction is maintained and performed.

Interestingly, the AHCPR in 1996 also stated that the intensity of the exercise performed

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influenced functional and physical as well as psychological outcomes, and the protocols seemed to yield a reduction in urinary incontinence. As we have heard, Weatherall in 1999 concluded that the odds ratio in the study she looked at showed that biofeedback combined with pelvic floor muscle exercises compared to pelvic floor muscle exercises alone showed a 2.1 odds ratio. These were the same five studies that Berghmans analyzed in 1988 and concluded that there was no benefit. Which one do we really look at or believe?

Of the analyzed studies, Glavind, as we've just heard from Dr. Cundiff, showed a significant improvement in the biofeedback group, while Berghmans in 1996 in his own study, showed that there was no difference in treatment when you added biofeedback to pelvic floor exercises.

It's interesting that the protocol or the decision or the statement presented to HCFA considered the studies that showed improvement to be flawed. One of the coauthors of the 1998 Berghmans study is Dr., or Professor Kerri Bo, who is very well published in the area of pelvic floor muscle exercises for stress incontinence, and who herself usually does not look at biofeedback as a

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means of treating or teaching these patients. The thing is, if you have Dr. Kerri Bo teaching you how to do these exercises without "formal biofeedback",

you could probably learn very quickly, because of the way she knows how to do it and how to instruct properly.

A more recent publication by Berghmans and just published in 2000, has decided to take another systematic review of randomized clinical trials, and there were 15, and concluded in this study that there were too few studies to evaluate the effectiveness of pelvic floor exercises with or without biofeedback. Meanwhile as we've just heard, the older studies of Burgio and Shepherd have been excluded in the consideration presented to HCFA.

There was only one study on urge incontinence, and that was by Burton in 1998, and it basically showed no benefit basically from biofeedback added to pelvic floor exercises. The AHCPR when they analyzed this study thought that there was a strong selection bias in this study, and there were groups who definitely had a difference in terms of severity of incontinence.

Recently, Hirsch in 1999 studied 33

patients treated with electromyography controlled biofeedback home training for six months, and showed improvement in 85 percent of these patients, although urodynamic parameters did not change. And that's the usual, the urodynamic parameters very seldom change with this therapy. The number of patients asked to enroll was 67. He only acquired 33 patients.

The principle is that it's very difficult to recruit patients for this therapy, and it's even more difficult to keep them in the program without positive and continued reinforcement. The real world practice is a far cry from randomized controls, or blinded study protocols, where we have highly trained and motivated individuals instructing and interacting with patients. It may be inappropriate to extrapolate results from a research setting to our clinical practice.

In the real world, patients are most often managed by a clinician with no other really good backup in terms of nursing support services. Someone has to show the patient how to do the

exercises and must provide this continued positive reinforcement reaffirming the process. This

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someone is generally not the physician, it's usually left to allied health personnel.

In studies that are performed to look at these things, the study personnel have protocols to follow, they have assigned time to spend with the patients, and a detailed script on what to say and how to say it. Unless we can provide trained personnel to handle patients, it's difficult to provide any better than a handout on how to do the exercises.

One of the great difficulties in hiring personnel to look after incontinent services is the lack of reimbursement provided by many carriers. The greatest and most consistent reduction in incontinent episodes is provided by multimeasurement biofeedback as indicated by the AHCPR. We don't know the maximum amount of benefit to be obtained or how long it should be done, but perhaps up to 15 or 20 weeks of treatment. The normal physician's office has a great difficulty in providing this approach.

I feel, and the ACOG feels that the use of biofeedback to assist training will allow appropriate use of pelvic floor muscle exercises directed by a physician or trained personnel, and

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it will most likely result in greater compliance for these patients, and a decreased frequency of dropouts. Thank you for your attention.

MS. CONRAD: Thank you, Dr. Bent.

DR. RATHMELL: One question, right to the point, Dr. Bent. Dr. Lefevre's study actually concludes something different than you told us just a minute ago. He says, quote: "It is not possible to draw conclusions from this body of evidence on whether the addition of biofeedback to pelvic muscle exercises results in improved incomes as compared to pelvic muscle exercises alone."

DR. ZENDLE: Outcomes, not incomes.

DR. RATHMELL: I'm sorry.

DR. BENT: We would hope to overcome this difficulty in interpretation. It's just that the report reflected a negative bias, and I'm

obviously trying to --
DR. RATHMELL: But his conclusion says there's not enough evidence. Would you comment on that? Do you feel there is enough evidence? Do you conclude something different than this?
DR. BENT: I feel that there is evidence; there is probably not enough evidence to conclude without any question one or the other. I

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feel that in practice we are able to teach our patients in the clinical setting that's hard to reproduce in the study setting. That's the issue we're dealing with here. It's very difficult to apply the clinical to the study setting. There may be the need for further study to look at specific how to do this in a very large number of patients. The studies out there, if you look at the studies you want to look at, conclude ineffectiveness. In clinical practice, we see this effectiveness. Most of the time, however, we do use biofeedback to help do this.
I think it would be an error to conclude that it therefore should be dropped because it may not work.
DR. RATHMELL: But remember, the position we're in is to assess the adequacy of the evidence. That's what we're here to do, so that's why I posed the question.
DR. BENT: Well, I just want to make sure you look at all the evidence, both positive and negative.
MS. CONRAD: Thank you, Dr. Bent. John Perry.
DR. PERRY: Thank you. I've asked my

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colleague and friend Linda West to help me with the mechanics of the presentation here. As unaccustomed to public speaking as I am, I get a little nervous. I'm a psychologist. I am the inventor of the EMG vaginal sensor in 1975, this device that is responsible for most of this evolution, and I have a quarter century of personal involvement in its promotion. Also, since 1994, 100 percent of my income has come from royalties on the EMG sensor. I hold the highest credentials in the field of biofeedback, certification as a senior

fellow of the BCIA. And in addition, the AAPB, the biofeedback society, received a grant from Vaughn Technology, a biofeedback manufacturer, to cover my travel expenses here.

In summary, the review is based on a very selective literature review. The cited papers actually contradict the conclusion, and the academic objective is of debatable value in the real world. The panel's objective, as you know, is seeing whether biofeedback adds to improvement compared to PMEs alone, but that's not as simple as it seems. It's very narrow, and it's particularly interesting to compare that with the objective used for tomorrow's presentation, which is to determine

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whether pelvic floor stimulation improves health outcomes.

The problem with that limited objective is that the continence therapy, as you've heard from previous speakers, is already typically staged. People always start with PMEs and progress to biofeedback. The regional policies call for that.

Now it says the evidence is not sufficient to demonstrate an additional benefit. Is there a benefit to PME alone? The report claims that there are several controlled trials of PMEs and that collectively these trials establish the effectiveness of PME. But they, in spite of claiming there are several, they only cite two, Wells and Burns.

Now here's Wells in '91, 79 percent symptom improvement, but her PME alone group wasn't PME alone, like most people think. She actually had seven monthly vaginal palpations with verbal feedback, as well as sensory feedback for the patient, and seven monthly EMG evaluations which I have circled from her Table 5, before and during the course of therapy. This isn't PME alone.

And Burns, the other one, the PME alone

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group actually included two EMG evaluations with my sensor, pre and post-treatment, which undoubtedly had some influence on the effectiveness of her so-called PMEs alone.

If you want to look at what PMEs alone

really do when you've got verbal instruction alone, we've got very good evidence, just came out this past month. 27 percent symptom improvement with handouts and written instructions.

Now looking at the stress incontinence studies that Blue Cross did examine, the first studies had no significant differences between them, but from the point of view of a person skilled in biofeedback quality review, there are several problems. One is that the quality of the biofeedback work that was done in these groups was extremely poor. Burns used an untrained therapist to bring his improvements down to 61, and she used EMGs, which brings her PME alone up to 54. Berghmans, he used a stim electrode and you just can't do that and get good results; that's what brings his PME group up is that vaginal palpation an verbal feedback. That wasn't PME alone, so that's no comparison either. And finally, the quality issues from a biofeedback perspective with

the Italian study are they only had six sessions, six weekly sessions of perineal, that's surface biofeedback, and they compared that with 13 weeks of PMEs.

Well, okay, the other three studies in that group, found significant differences, but reasons to exclude them. Burgio, 81 percent, he considered that to be an excellent study. Her PME group got very high results because they got vaginal palpations and verbal biofeedback. Glavind, 91, excellent study. It says there's a potential for bias, but it doesn't say that there is. Shepherd, 83 to 25, excellent. And Shepherd, by the way, is the only one that used home trainers like Arnold Kegel did.

Urge incontinence, Burton is cited as finding no significant differences, but you have to read much more closely to the original text. Burton called his control group behavioral treatment. It included 11 urge patients who got bladder training and only three stress patients who got PME alone instructions. And Burton technically does not qualify for inclusion in the TEC report. One that did was Burgio, and she had much better results.

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So look at the levels of what the literature shows. Verbal instruction, 27 percent symptom improvement. Add palpation and verbal feedback, 51 to 60 percent. Add EMG testing, 54 to 77 percent. Add formal biofeedback training, 80 to 94 percent.

The question that was raised about the benefits of adding biofeedback to PME alone, but historically, PME alone results from subtracting biofeedback from Kegel's original program. This is Kegel's biofeedback device, and I have one down here if you want to see it. Kegel's patients were required to keep records and actually to write down the millimeter scores that they obtained with this device.

In summary, the entire report is not, is an evaluation not of technology but of research design. Examination of even the cited papers contradicts the conclusion. And in any case, real-world decisions must be based on the best available evidence. And in our opinion as experts in biofeedback, biofeedback ranks as a breakthrough technology. I thank you.

MS. CONRAD: Thank you. Panelists? Okay.

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DR. GARBER: I just wanted to thank the public speakers for their comments. I hope I'm speaking for the panel in finding all of your comments very informative, and I'm sure that they will be very helpful in our deliberations, both the information and the perspectives that you provided.

MS. CONRAD: Thank you also.

Before we break for lunch, a brief comment from Perry Bridger please.

MR. BRIDGER: I just want to alert the panel to a couple of items. Connie has another copy of the questions, and we have added some language to more precisely define the question after the discussions this morning. I'm going to read the first part of the question, the rest remains the same.

Question 1 reads: Is the scientific evidence adequate to draw conclusions about the effectiveness of biofeedback as an adjunct to

pelvic muscle exercises in routine clinical use in the Medicare populations for the following three indications: Stress incontinence, urge incontinence, and post-prostatectomy incontinence? And you will consider the following points when answering these questions, and Dr. Simon will

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elaborate again on these points.

Secondly, I just want to alert the panel that in your blue folders that you received this morning, there are copies of the slides that both Dr. Simon an Dr. Lefevre will present to you this afternoon. Thank you.

MS. CONRAD: Thank you. Well, it's 12:04. Let's try to make it at 1:15, please.

DR. GARBER: You will make it at 1:15, or we will start without you.

(Luncheon recess at 12:04 p.m.)

MS. CONRAD: Okay. Continuing on, HCFA is now going to do a brief presentation, and the presenter is Ken Simon, M.D.

DR. SIMON: Greetings, Mr. Chairman, panel members and guests. Continuing our dialog today on the topic of urinary incontinence with the focus on biofeedback in particular, I would like to begin with the definition that we use for the purposes of our discussions today: Biofeedback, by definition, is a therapy that uses either electronic or mechanical device that relays visual and/or auditory evidence of pelvic floor muscle tone. This is done in an effort to improve the awareness of the pelvic floor musculature and to

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assist patients in the performance of PMEs.

The first layer therapy for behavioral treatments form the basis for when treating with urinary incontinence, and the behavioral treatments that are available include toilet training, bladder training, and PME. Now in order to determine whether a patient is an eligible candidate for behavioral treatments in the treatment of urinary incontinence, it's suggested that one, they be compliant, that they be motivated, and demonstrative that they are cognitively or mentally intact.

Kegel's exercises have been the mainstay

of therapy since the 1940's, and early on he added the perineometer, and used in conjunction with the exercise, is to provide a more objective and exact means of measuring pelvic floor muscle strength. Through the use of the exercise therapy, it enhanced the voluntary control of the skeletal muscles and did require that patients perform these exercises several times a day and for several weeks duration in order to derive benefit from it.

With this as the backdrop the question that we raise is: Does the addition of biofeedback as an adjunctive therapy to pelvic floor muscle

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exercise provide improvement in treating urinary incontinence, as opposed to pelvic floor muscle exercises alone?

With that as the question, we then formed use criteria, developed criteria to form a framework by which we would then embark upon an evidence based literature review. There are several criteria that we chose and we felt that, one, full-length peer reviewed articles that report on the outcomes of treatment for urinary incontinence using biofeedback in conjunction with some of the behavioral techniques that were previously mentioned should be included. And there should be an adequate description of the patient population, which includes the categories of incontinence. It should include patients with documented evidence of stress incontinence, urge incontinence, mixed incontinence, or post-prostatectomy incontinence that was diagnosed either via urodynamic testing or by physician diagnosis, and the methods used in determining the diagnosis should be clearly outlined.

There should be a concurrent comparison group of patients treated with pelvic floor muscle exercises without the aid of biofeedback. And it

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should also include an adequate description of the course and delivery of treatment, which should include the length of treatment as well as the number of sessions.

The objective measures of health outcomes would be those that we would expect to see in most of the studies that are in the literature

and it should contain the percent change in incontinent episodes usually contained in the patient's diary, should outline the percent decrease in the volume of urine loss using the standardized pad test. There should be information regarding the percentage of patients that are dry upon completion of the therapy. And there should be information regarding the percentage of patients who have sustained at least a 50 percent reduction in incontinence.

With the assessment question and the parameters of our evidence based review, we then submitted that information to one of the evidence based practice centers. Dr. Frank Lefevre, from the Blue Cross Blue Shield Association Technology Evaluation Center, will present the TEC assessment on biofeedback.

Dr. Lefevre is an assistant professor of

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medicine as well as, he holds an appointment in the department of preventative medicine at Northwestern University, and at this time will provide the assessment for biofeedback.

MS. CONRAD: Thank you, Dr. Simon.

DR. LEFEVRE: I want to thank you for the opportunity to present the results of our work on this subject, and I would like to start by saying first of all that my expertise is in the area of reviewing of literature and systematic reviews and technology assessment. I'm an internist by training and I am not particularly an expert in incontinence or urology, but again, I do have expertise in reviewing literature.

Secondly, I want to make the point that I want to acknowledge the collaborators on this work from Blue Cross, and also the extent to which we worked with HCFA. Unfortunately, in the report that you got, sole attribution was given to me but in reality, this was not a one-man project. It was a collaboration among the members of TEC, as well as among the consultants that work with the TEC program and clinical experts that we have with our program. And particularly, Naomi Aronson, who's a PhD and the executive director of the TEC program,

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had very substantial input into this project. And

also Ted Speroff, who's a methodologist from Vanderbilt University, who also works with the TEC program, had substantial input, especially into the methodological aspects of this project.

I was asked to give a little history of TEC, because many people may not be aware of what TEC is, and I wanted to first bring you up to speed on what TEC is and what we do at TEC. TEC was founded in 1985 by the Blue Cross Blue Shield Association, and the association is the umbrella organization for the Blue Cross Blue Shield plans. It provides support services for the plans in areas such as credentialing, certain types of quality assurance activities, as well as technology assessment. And TEC has been in existence since 1985, as I said, and since that time has produced over 400 full-length technology assessments, making it one of the oldest and most active bodies in the area of technology assessment.

There has been a significant evolution of TEC since it was founded. During the period from 1985 to 1993, it was purely a proprietary organization, where the products of TEC were disseminated only to the Blue Cross plans. In

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1993, TEC partnered with Kaiser, and in essence went public in 1993, partnered with Kaiser and at the same time offered their product to outside subscribers, such as health plans and HMOs, whereas they can subscribe to the TEC program and receive the TEC products. And most recently, the latest enhancement to the TEC program was in 1997 when TEC was named one of the 12 AHRQ evidence based practice centers. This has given us the opportunity to participate in larger evidence based projects that are entirely in the public domain.

This slide just gives you a general idea of some of the relationships that TEC currently has. And still, the Blue Cross Blue Shield plans are the main clients of the program, but Kaiser is also a major partner with us, as well as subscribers. There are many subscribers to the TEC program, and they range from what we call executive subscribers, who pay a premium in order to have involvement in the entire TEC process including the selection of topics that are reviewed, all the way

down to purchasers of individual assessments, who can just simply buy one assessment if they're interested in that particular assessment. And finally, our relationship with AHRQ, which has been

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in place since 1997. Between the Blue Cross Blue Shield plans, the Kaiser Permanente program and the subscribers, the TEC program reaches a total of 120 million covered lives.

Now, a major priority of TEC is to maintain the scientific integrity of its products. The TEC mission, and this is an explicit and overt mission, is to produce rigorous, high quality scientific assessments of medical effectiveness. And TEC does not make coverage decisions, and this is a crucial aspect of our orientation. The goal of TEC is to provide the plans and the subscribers with the best available evidence on these technologies in order to assist the plans in making these very difficult health coverage and health policy decisions. In concert with that, TEC does not consider costs. Except for the special case where we've done a formal cost effectiveness analysis, costs are not at all a part of our assessments; we are entirely focused on evidence of effectiveness, and this is what we will be talking about today.

Next, the TEC program has what we call TEC criteria. These TEC criteria are sort of a set of rules for which we can judge evidence against,

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and this gives us an anchor for which we can hopefully achieve a standardization and a consistency when we're reviewing diverse technologies. I think this is very analogous to the document that the Executive Committee has produced. They've sort of given you a set of rules for what kind of evidence is acceptable, and set the bar for where they want this evidence to reach. And I think that is a very helpful and crucial aspect of doing assessments such as this, to have that kind of anchor.

And finally, the TEC program has a medical advisory panel, and this consists of 18 experts in the field of technology assessment and clinical research, some of which are Blue Cross

Blue Shield plan directors, but the majority of which are independent of the Blue Cross system. And this medical advisory panel has the authority for the final approval of all TEC assessments that are disseminated, including the current assessments on urinary incontinence. These have been through the medical advisory panel process and they've been approved by the medical advisory panel.

So again, that brings us to the objective of the current assessment, and this has

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been stated many times today. I won't bother to go over it again, but I will again emphasize that what we will be looking at, in concert with what HCFA is looking for, is the adequacy of evidence. And regarding adequacy of evidence, you want to be concentrating on, is the evidence consistent, is it of high methodological quality? And if the evidence is adequate, then we will be looking at, what is the magnitude and the effect of this evidence?

I think it is useful to go over a little bit of the background of the treatments for urinary incontinence. And this has been, again, stated many times, but I think it does bear reiterating, because if it's not understood exactly why we're setting up the assessment like we are, then it engenders a lot of confusion and people don't understand why we're making the conclusions that we do. So again, let's look at the different options for behavioral treatments, and some of these are listed here. And the point is, there are many different types of behavioral treatments, and these may involve combinations of these treatments or may involve one in particular by itself.

Now when we're talking about PMEs, PMEs

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is a heterogeneous collection of treatments. It can vary from simple verbal instructions by a physician to contract the muscles all the way up to focus intensive one-on-one sessions with a trained therapist. Now biofeedback is one of the variations in PFMEs, and PFMEs can be done with or without biofeedback. Now that's been a subject of debate today; can you separate out biofeedback from PFMEs? And I think the answer to that question

really depends on how you define biofeedback. If you define biofeedback the way that we have defined it, where we're talking about a mechanical or electrical device that relays visual or auditory information back to the patient, you can. You can separate out what PFMEs alone versus what is PFMEs with biofeedback. And if you're going to broaden the definition of biofeedback to include verbal feedback, therapists who use digital palpation of the pelvic muscles, it may be somewhat more difficult. But we came up with this definition of biofeedback a priori, and this does allow us to separate out what is PMEs with or without pelvic feedback.

I would also point you to the AHCPR guidelines, which have been cited many times today,

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and on page 36 of the AHCPR guidelines it's stated that PFMEs can be done with or without biofeedback. And they also have definition of biofeedback which is interesting to look at, varies slightly from ours, but I don't think it includes the whole range of options that have been discussed today.

Now, behavioral treatments are considered the first line therapy for most individuals with incontinence, and there's not really any controversy about this. There is evidence for effectiveness of PMEs alone. We did not do a comprehensive systematic review on this, but there is a body of evidence looking at PFMEs alone versus control, and there is evidence for efficacy. There is also evidence for effectiveness of biofeedback assisted PMEs. Since biofeedback is an add-on to PMEs, you would expect that if PMEs work, then biofeedback assisted PMEs will work at least as well as PME alone. But the controversy in this area is, what is the contribution of biofeedback to the effectiveness of biofeedback assisted PFMEs?

Now, when AHCPR in 1996 stated that biofeedback assisted PFMEs are effective, they were

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saying that biofeedback assisted PFMEs are effective as opposed to control. And we have no disagreement with that. And the TEC report is not

at all in disagreement with the AHCPR report, and I would like to emphasize that very strongly, because I think if we don't understand that point, then we are still not really clear about what we're doing here. AHCPR did not address the contribution of biofeedback to biofeedback assisted PFMEs. Also in the AHCPR report on page 38, there is also a statement to the effect that more controlled trials are needed to assess the contribution of when biofeedback actually contributes above PFMEs. So there's no disagreement there. We are looking at a different question and I feel that this is the important question. This is the area of controversy, and this is, I think, the important question that needs to be answered.

New, how do we approach answering this question? We approach it by doing a systematic review. What is a systematic review? A systematic review is an evidence based method for determining treatment effectiveness. This is generally considered by most experts in the field to be the best available method for determining treatment

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effectiveness from a body of literature. And there is a formalized methodology for doing the systematic reviews.

This has evolved over the last two decades, and going back to the early 70s, the Cochrane collaboration, starting in Europe and England particularly, first promoted the idea of doing systematic reviews of medical literature in order to determine effectiveness, in order to reconcile conflicting studies and confusing data. The Agency for Health Care Policy and Research, it was formerly known, has done extensive work in doing systematic reviews of effectiveness back when they were doing guidelines such as the urinary incontinence, and similar guidelines. And they published a manual in 1996, which was actually my first introduction to a formalized methodology for doing these reviews. This was published by Steven Wolf. And finally, the Annals of Internal Medicine has a very excellent series on doing systematic reviews, published in 1997 and 1998, a series of six to eight articles which describes in detail the methodology that should be used when doing this

type of effectiveness review. And this was edited by Cindy Moreau, from the University of Texas at
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San Antonio, and Deborah Cook, who is from Scotland.

And this is the methodology that we follow when we do these reviews. The basic steps of the systematic review are listed here. First of all, we develop a problem formulation, and this is where we worked with HCFA to develop our problem formulation. We had done previous assessments in the area of urinary incontinence, but when we did this update to our assessments, we wanted to make sure that it met HCFA's needs and met the needs of the MCAC. So we worked with them on the problem formulation and that involved, what were the patient indications, what was the treatment, and this gets back to what was the definition of the treatment? You heard Dr. Zarin this morning emphasize how important that is. You have to define what the treatment is. So we defined what biofeedback was, and then we went forward and looked for studies that used the biofeedback as we defined it.

Thirdly, we defined, where are the outcomes that you look at. Where are the most clinically relevant outcomes in this field that we're going to abstract and that we're going to
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consider important and relevant to our decisions on effectiveness? And finally, the fourth aspect of the problem formulation is, what is the comparison group? There always needs to be a comparison group that we're comparing the technology with.

The second step of a systematic review is to develop study selection criteria. And it's very important to emphasize that both the problem formulation and the development of study selection criteria are done a priori; these are done before we review the literature. And the idea is, we make the problem formulation and then we ask ourselves, what types of studies can answer this question? And derived from that, we come up with a set of article selection criteria and then we systematically search the literature using multiple databases, using hand searches of relevant

bibliographies, and consultations with clinical experts, in order to try to capture all of the relevant literature that meets this article selection criteria.

Next step is to abstract the relevant outcome data into evidence tables as you see in our report, and finally, to put the data together, to synthesize the data either qualitatively or

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quantitatively.

So, for this assessment, again, to go over briefly the problem formulation, and this is similar, identical to what Ken had previously outlined. The patient indications are the three indications here, stress incontinence, urge incontinence, post-prostatectomy incontinence. The intervention is the addition of biofeedback as we defined it to PFMEs, and the comparison group is PFMEs alone.

I think the outcomes of this assessment bears a little discussion. And because these are not ideal outcomes, and this is not really a criticism of this study but it's a criticism of the state of the field and the outcome measurements in the field, what is the outcome of interest that we're concerned with? The outcome of interest is a reduction in the frequency and/or severity of urinary incontinence. So how do we measure that? The most common way to measure that is patient recorded incontinence diaries, and the second way of measuring that, specific for stress incontinence, is a standardized pad test. For the diary measures, basically the patients keep a record of their frequency of incontinent episodes

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over a specified period of time. That might be a day, that might be two days, or that might be a week. The standardized pad test involves putting a patient through a standardized series of maneuvers that are expected to induce incontinence, such as jumping jacks, squatting, things like that, and then measuring the weight of the urine loss on an absorbent pad.

Now, derived from these measurement instruments are the reported outcomes that we're going to be focusing on for this assessment. And

the most common outcome that's reported is a percent change in incontinence, and this is a comparison of the pretreatment level of incontinence versus the post-treatment level of incontinence, and looking at the percent reduction in the frequency of incontinence. Also, you can look at the percent of patients improved, which the International Incontinence Society has defined improvement as a greater than 50 percent reduction in incontinence. So the percent of patients improved refers to the percent of patients who have achieved at least a 50 percent reduction in incontinence. And finally, the percent of patients who are cured, who no longer have any incontinence,

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is also a relevant outcome.

Now I go through all this because I want to make the point that there is a lot of potential variability in these measurements. First of all, you would probably expect that there would be a lot of inherent variability in incontinence in general. It may vary from day to day depending on such things as activity level, fluid intake, and probably many other factors. And added on top of it, the patient recorded diaries are relatively a subjective measure and may also be prone to a high degree of variability themselves. And this may lead to the potential of measurement error, and this is not an insurmountable problem, but I think it's an important problem to remember as we are looking at the outcomes of these studies.

So to review, the key question again, for patients with stress incontinence, urge incontinence, or post-prostatectomy incontinence, does the addition of biofeedback to PME result in greater improvement in health outcomes, as compared to PME alone?

The study selection criteria, as Ken had outlined, I think the most important point here is that we required a concurrent control group, and

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this was done because we felt that uncontrolled trials would never be adequate to answer this question. There were too many other potential factors that might impact on the outcomes in an uncontrolled trial that we would not be able to

separate out, and therefore, we would require that only trials with a concurrent control group could possibly answer this question. We didn't require these studies had to be randomized, but we did require they had to have a concurrent control group.

Our search results resulted in eight articles that met the study selection criteria, and six of these were for treatment of stress incontinence and one each were in the categories of urge incontinence and post-prostatectomy incontinence. So right away we see that the bulk of the discussion here will be on stress incontinence, that evidence on the other two categories is very sparse.

Of the six controlled trials, there were a total of 321 patients, with a range in the studies of 22 to 135. This is a relatively small body of literature, especially if you look at it in relation to the many, many patients who have

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urinary incontinence. Of these six trials, three of them are randomized and when we reviewed methodological quality, we identified potential biases in four of the six.

I want to talk a little bit about these potential biases and really say what we meant by this, and these actually were supposed to be arrows, but I guess they'll suffice, whatever they are. But our approach to assessment of potential biases in these studies is to first of all look for those broad areas of bias that have been empirically associated with an over estimation of treatment effect in prior literature, and there have been a number of such biases identified. And particularly for this assessment, we would be looking at selection bias and attrition bias, both of which have been associated with an over estimation of treatment effect in prior literature.

When we talk about selection bias, we're really referring to the comparability of the groups. And in the two studies here, the Burgio study and the Ceresoli study, in which we've identified a potential for bias, these are nonrandomized studies. In a nonrandomized study, there will always be a potential for selection

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bias.

As far as attrition bias goes, this refers to the number of patients that dropped out of the study or withdrew from the study, and how these patients were handled in the analysis. And for the purpose of this assessment, we required that if the studies had a greater than 20 percent dropout rate, and the dropout rate was not balanced between groups, and the studies did not account for this dropout rate in the analysis, we identified them having a potential for attrition bias. We identified two studies here which had that potential for bias.

The other type of bias we would look for would be particular types of bias which may be particular for the clinical context we're looking at. And here measurement bias is listed, and I left that in parentheses because since all the outcome measures are potentially prone to measurement bias, we have to keep that in mind although, again, this is not a criticism of the study, it's a feature of the outcome measures that are used in this field.

And the last type of bias we looked at was performance bias. Now performance bias refers

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to the intensity of treatment given between groups. And since biofeedback is an add-on treatment, if you simply add on more treatments or more sessions to a base line set of PMEs, there's a potential for performance bias in terms of increased contact with the therapists, increased training effects, and other nonspecific effects which follow from a therapeutic encounter with clinicians. And some of the studies controlled for performance bias, but some did not. And we identified three studies which potentially had performance bias present.

Now the other thing I want to say about bias is, when we say potential for bias, we're not saying that the study results are due to bias. We're saying that there is a potential there and we cannot exclude that bias may have had an impact on the effects we had seen. In the ideal most rigorous designed study, the idea is to make the

study impervious to bias, so there's not a chance that there's any bias that may impact on the treatment effect. And what we're saying is, there are some methodological shortcomings which open the potential for bias. We can't say whether the results are due to bias for sure, but we can say

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the potential is there.

Let's look at the outcomes for these studies, and we'll go look at two outcomes, and this is a simplification of the table in the full assessment of Table II. And this is the outcome of percent change in incontinence, which is leaks per day. And of the six studies, there were four of them that reported on the outcome measure of leaks per day, and of these four studies that presented data on leaks per day, one of them showed a statistically significant difference between groups, and that was the Burgio study with a 76 percent improvement in the combined group, versus a 51 percent improvement in the PME alone group. The Shepherd study, which showed a rather large difference between the two groups, 83 percent versus 25 percent, did not perform any tests of statistical significance. And the other two studies, the Burns study and the Berghmans study, showed no differences in the rate of change in incontinence.

So we have of the six studies here, of the four studies which reported on this outcome, two of them were positive, one which was statistically significant and one which appeared to

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be significant but did not report any statistical testing, and two which showed no difference.

The second outcome that we can look at is the pad test. And again, you can look at the percent change in incontinence on the pad test in the same way as you look at the frequency of incontinence. Here there were three studies that reported on this outcome measure, one of which showed a statistically significant difference, and this was the Glavind study. It showed a 91 percent difference in the combined group versus a 48 percent worsening in the PME alone group. The other two studies, Ceresoli and Berghmans, showed

no difference in the groups of interest on this outcome measuring.

So what can we say in summary from this body of data on -- okay. Before I go on to the next slide, the summary of body of data on stress incontinence, what can we say in summary? Okay. There are six studies and three of them report a statistically significant difference in favor of biofeedback. Three of them report no difference between the groups. Another way of assessing the results is to do what may be called a sensitivity analysis, by grouping the studies by certain

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measures of quality or by certain factors of methodological interest.

And one way we can do this is by separating them into randomized study and nonrandomized study. So if we look at the three studies which were randomized, two of them showed no difference, one showed a difference. If we look at the three studies which were not -- I'm sorry, I may have said that wrong. Of the studies that were randomized, two showed no group differences and one showed a group difference. Of the studies that were not randomized, there were two of them which showed a difference and one that did not show a difference.

We can also look at the presence or absence of bias. There were studies that we did not identify any potential source of bias, and both of these did not show a difference between the two groups. In the four studies in which there were potential biases, two of them are positive and two are negative.

Okay. Going on to the other categories of incontinence, urge and post-prostatectomy incontinence, again, there was very sparse literature in this category. There was one study

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on urge incontinence of 32 patients which showed no group differences between the two group, 79 percent versus 82 percent. And similarly for post-prostatectomy incontinence, one study of 30 patients which showed no significant group differences.

So, our overall conclusions are listed

here. And what can we say? We can say that some studies report a benefit for biofeedback plus PME over PME alone, but some do not, so this is not a consistent finding. What are the explanations for this inconsistency? First of all, I've listed three here and there may be more, but I'm going to put forth three possible explanations.

First of all, there may be no benefit to the addition of biofeedback, and the difference seen in the positive studies may be resulting from bias. We cannot exclude that possibility. We cannot say that's the reason why the studies are positive, but we cannot exclude it either.

Secondly, there may be a benefit to the addition of biofeedback, but the negative studies underpowered to detect this difference. None of these studies reported power calculations, and they were all relatively small studies. So given the

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relatively small studies with high variability in the outcome measures, it may be very possible that you need much larger studies to detect a difference that may be there.

A third possibility, the addition of biofeedback may benefit a subset of patients. These might be patients who are not able to correctly perform PME's. This has been alluded to several times; several of the speakers have said that this is a patient group that they've applied biofeedback to, or a patient group that would be expected to receive benefit from biofeedback. And this makes sense. I mean, patients who can't do the PMEs on their own, it's certainly possible that biofeedback may help them in doing that and may aid them in doing that. However, none of the studies have addressed this particular population, so there is absolutely no literature, there's no evidence to assess this question, and so we have no ability to say from an evidence based perspective, whether or not this is true.

And finally, among these three possibilities, the available evidence is not adequate to distinguish which may be true.

I would like to make a couple more

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points about prior systematic reviews that were

mentioned previously as well, because I think it's very interesting to compare our TEC report with other similar systematic reviews that have been done in this field, and there have been two that have been mentioned.

First of all, Berghmans in 1998 did a systematic review of controlled trials similar to what we did, for stress incontinence. Came up with a total of six studies, four of which were identical studies to what we have. They came up with two studies which we did not include, and we came up with two studies that they did not include, because of slight differences in our selection criteria. What did they find? First of all, they did an assessment of methodological quality that was much different from what they did; they did an overall assessment of methodological quality, and they made a cut point of what they considered sufficient methodological quality or not. And of the six trials, only two of them met what they called sufficient methodological quality. So overall, their assessment was that this was not a high quality body of literature. And of the two studies which met their criteria for sufficient

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methodological quality, both reported no group differences.

Now the Weatherall study which has been alluded to, was a follow-up study to the Berghmans study. And what Weatherall did was, he took the studies that were included in the Berghmans review and he attempted to quantitatively combine the results from these studies in a quantitative meta-analysis. And he first looked for an outcome measure that was consistent across the studies and could be combined. And the outcome measure that he used was percent cure. And the percent cure was only actually adequately reported in three of the studies of the total studies in the Berghmans review, so his meta-analysis only applied to three of the studies. And if you look at the three studies that were included, it was that Berghmans study from 1996, the Burns study from 1993, and the third study was the Glavind study, all of which are included in our review. And two of these three studies have an odds ratio for cure which is very

close to one; Burns an Berghmans had an odds ratio of 1.5 and 1.8, with confidence integrals of 0.5 to 4.3, and 0.4 to 8.0. The Glavind study had an odds ratio of 4.8 for cure, with a very wide confidence

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integral of 1.1 to 21. When he combined these three studies, he came up with a combined odds ratio of 2.1 with a 95 percent confidence integral of 0.99 to 4.4. So this was a combined result that achieved marginal statistical significance.

And I think it's also very important to realize that this result is pretty much entirely driven by the results of the Glavind study. This is a potential flaw in meta-analysis, that you don't take out potential flaws in the study. And the Glavind study reported a very high odds ratio for the cure rate, whereas the other studies did not. So I think it's important to understand that, and we're keeping these in perspective.

So I think that our conclusions as we put them forth here, we firmly stand by the conclusions that the evidence is not adequate to determine whether the addition of biofeedback to PFMEs has a benefit. I think there is certainly room for legitimate scientific debate as to how we performed the systematic review, and when people are critiquing our study and looking at the ways that we did our study, it should be looked at in that light. Were the methods that we took to perform this systematic review valid methods and if

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not, where did we fall down? Was our article selection criteria wrong, was our setup of the problem wrong, was our definition of biofeedback wrong? And I think we certainly welcome that kind of scientific debate in hoping to resolve this difficult issue. Thank you.

DR. GARBER: Thank you, Frank. Les?

DR. ZENDLE: Well, this has been a very interesting day. It's hard to believe we have already been here for six hours; it's gone pretty quickly. I want to thank and congratulate the presenters and the organizers of this. I've learned a lot.

After today -- you know, I went over the questions myself beforehand and I have listened

very carefully to what people had to say. And I have no problem accepting the AHCPR '96 guidelines, and I have no problem agreeing with the clinicians who feel that some patients do better with feedback and PMEs than with the exercises alone. And I actually think it should be made available to those patients who are so identified, especially if a guideline is being followed that tells you which patients it works best on and which form of biofeedback and what the regimen should be.

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But I have to agree with the TEC assessment that there isn't sufficient evidence, scientific evidence of sufficient quality really, to conclude that adding biofeedback to the exercises is better or not better than doing the exercises alone. And I guess the only other point I would make is that the statistical definition of what's enough evidence isn't really a matter of opinion, it's a scientific matter, that science has already made agreements as to what is scientifically relevant, and I don't think this meets the magnitude of that.

It does leave me with one important question, though, and that's why hasn't there been more research in this area? It's not like this is a rare problem, and it's not like these are mild symptoms. This is a common problem that is a major life disruption not only for the patient, but for families and for society. And it's shocking to me actually that there are so few patients that have been looked at in a rigorous way and therefore, we can't reach conclusions with statistical validity. And I'm not sure who's to blame for that, but it's just a question that I'm left with and frustrated with.

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DR. GARBER: Thank you. Before we proceed with other questions and comments from panelists, I think Ken Simon had a few other things to add to finish off the HCFA presentation.

DR. SIMON: In our review there were articles that did not specifically address the assessment question but did meet some of the inclusion criteria, and these were excluded from the assessment. However, we did review the

articles and include them in the panel's review, so the panel does have the articles available.

There is a sequence of questions, however, that we would like to pose to the panel. The first question is, is the scientific evidence adequate to draw conclusions about the effectiveness of biofeedback as an adjunctive therapy in routine clinical use in the Medicare populations for the following three clinical indications: One, stress incontinence; two, urge incontinence; and three, post-prostatectomy incontinence?

As you ponder over that question, there are several points that we would like you to also consider when reviewing the evidence. Is there evidence that the studies do not over or

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underestimate the effect of the intervention? Are the results of the studies consistent or are they contradictory? Are the results of the studies applicable to the Medicare population? Do the studies permit conclusions about the health outcome of the technology? And are the results likely to apply in the routine clinical setting?

If the answer to the first question is yes, then we would proceed with the second question, which is, if the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effect of the addition of biofeedback to PME compared to PME alone?

That goes back to the categories of effectiveness which were brought up and discussed earlier in the day. There are several different gradations of effectiveness. When we talk about breakthrough technology, we're really referring to an intervention that has such an overwhelming impact on the health outcome that it becomes the standard of care. More effective refers to those interventions that have a significant impact on the health outcome compared to the existing therapies. As effective but with advantages refers to those interventions that are as effective as existing

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therapy, however there are additional advantages; there may be fewer side effects, maybe more tolerable to the patient, things that are

preferable to patients. As effective with no advantages refers to those interventions that are as effective as existing therapies, however they offer no advantages, but are clearly better than doing nothing. Less effective but with advantages refers to those interventions that are less effective than existing therapies, but they do have advantages such as, again, there may be fewer side effects or more tolerable for patients. Less effective and with no advantages refers to those interventions that are less effective than existing therapies that offer no advantages but are better than doing nothing. And lastly, not effective refers to interventions that are either not effective at all, or clearly may be harmful to patients and are much worse than doing nothing at all.

So in summation, does the addition of biofeedback as an adjunctive therapy to PFME provide improvement in treating urinary incontinence as compared to PFME alone? Do the studies from the evidence based review permit

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conclusions about the health outcome of the technology?

Is the scientific evidence adequate to draw conclusions regarding the effectiveness of biofeedback as an adjunctive therapy in the Medicare populations for the following three clinical indications: One, stress incontinence; two, urge incontinence; and three, post-prostatectomy incontinence? And if the evidence is adequate to draw conclusions, what is the magnitude of the overall health effect of the addition of biofeedback to PME compared to PME alone?

I'd like to thank the panel for the opportunity to present this information before them and thank our lead analyst, Tony Norris, for all his hard work in this effort.

DR. GARBER: Thank you. Now we move into the phase of open committee deliberations and at this time only panel members will be recognized to speak, although panel members may direct questions to public speakers or other members of the audience. I ask the panel members to bear with

me if I don't see at first when you raise your hand. Some of your faces I can't see at all, so if I see your hands, I may not know whose it is. We'll try to work it out. If it looks like things are getting a little too chaotic, maybe we'll ask you to stand when you have a point to make or a question to ask.

As I mentioned at the outset, two panel members were designated as reviewers, Les Zendle is one of them, Lisa Landy is the other. Les, I assume that was your opening statement. And I would like to ask Lisa to speak before we open up to the entire panel to ask questions and make comments. And when we get into the general panel deliberations, I hope that we will adhere fairly strictly to the questions that HCFA asked of us, and let me just propose that all of our comments and questions be oriented around that, and hopefully we will reach some consensus one way or the other fairly quickly on at least the aspects of the questions they have asked us. Dr. Landy.

DR. LANDY: Yeah. I had some opening remarks. Some of them are kind of reiterating what's been said already today, but I kind of want to summarize things.

The first one is, the task set before us is a very specific one, and it's to answer a series of efficacy and additional benefit. The MCAC committee has helped us and set forth guidelines for us as panel members specifically to follow, and these guidelines were set up to assess new technologies and compare them to established practices. And we're to use evidence based medicine as the foundation for our decisions.

And as we can see from today's presentations, multiple presentations, that there are several levels of evidence that we can consider and weigh appropriately when we answer these questions. We've heard today from representatives of multiple professional societies and specialty organizations presenting their consensus statements regarding efficacy of this behavioral intervention.

The 1998 NIH consensus statement

recognized the efficacy of behavioral intervention and specifically biofeedback. There are guidelines of practice that we all use when we practice in this field based from the AHCPR guidelines which recommend the use of behavioral interventions, including biofeedback, as first line therapy. We also heard presentations of a technology assessment which confirmed biofeedback efficacy, and then

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focused on answering the question of whether there is additional benefit achieved from biofeedback over PME alone.

I would like to summarize some of these key points that come out of today's presentations before we go into our discussion, and use this as a launching point for our deliberation. One of the points is that biofeedback is not a new technology and that the guidelines that were set up to do is to compare to established practice. Biofeedback is a very well established practice. And that goes back to the issue of why is PME alone chosen as the standard for comparison? In the original presentation by the statistician, there was the question of choosing appropriate standards. And I think we should keep that in the back of our head when we look at all this information and data.

From 1948 on, when PME was introduced, Kegel himself recognized the need of using a device to assist and be adjuvant to the PME alone. And from the very beginning of therapy in this area, a device or perineometer, or some kind of intervention was utilized. So it has always been a part of established care and standard to use some form of biofeedback method. It really isn't a new

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technology.

And we have been given evidence from multiple sources, the Bump study in 1991, Kerri Bo's study in 1990, and most recently, the Sampselle study, 2000, showing the drawbacks of doing Kegel exercise with just verbal instruction, and I think that was brought up very clearly.

In 1992 and 1996 updates, the AHCPR guidelines for treatment was more developed, and this was a panel of experts in the field, who came up with these guidelines and recommendations, and

they came up with these guidelines based on strong scientific evidence, rated their evidence, and this is akin to our task set before us today. Their job as panel of experts back in 1996 was very similar to what we are being charged with today. And they felt that based on their review and the strength of evidence, they've made recommendations regarding pelvic muscle rehabilitation and bladder inhibition using biofeedback therapy as recommendations for treatment of these patient groups. They specifically did not sort out biofeedback and remove it from the formula. And I think there is something flawed with that whole question of taking away a therapy that's always been part of the

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treatment from the very beginning.

The technology assessment has come to certain conclusions. I think in our discussions, we can critically analyze the data. Like they said, the AHCPR guidelines specifically did not address the issue of whether the addition of biofeedback to PME is more effective than PME alone, and I think it specifically was avoided as to not take that out of therapeutic treatment modalities. We have to treat people, because we treat people in this area with multimodality treatment.

Since then though, the question has come up and been the focus of several evidence based reviews. In de Kruif and van Wegen, one in 1996; Berghmans in 1998; and the meta-analysis by Weatherall in 1999, as well as the current technology assessment, all of them with varying conclusions.

I would like to make a point too. This panel was initially charged with addressing the issue of efficacy of biofeedback as an incontinence intervention, and now we are being asked to compare it as an adjunct therapy to PME versus PME alone. Now the question is asking about efficacy as an

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adjunct to a therapy, and this is an important distinction when looking at the literature. And when we reviewed this before we came here, we may not have looked at the literature in quite the same way as this nuance brings up. But for the question

at hand, those studies comparing PME alone to biofeedback and PME are the ones we really need to critically review.

And we have to look at them for comparison of groups, methodology, and outcome measures. And while analyzing the data, we need to keep in mint that the PME alone groups show variability between the studies as to what the treatment intervention was in those groups, and consist of interventions other than PMEs, and that may influence the results of the data. And that brings me back to the issue of, did we select an appropriate standard to compare it to?

So that -- in one of the presentations by Dr. Perry, he gave us some slides and I think we critically need to look at those, but he brought out some of the potential information about methodology, about the PME alone group.

So, I thought that was a good launching point now for us to open up discussion.

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DR. GARBER: Thank you, Lisa. Arnie?

DR. EPSTEIN: Even without the prompting by Lisa, I was thinking the same thing, that the final slide you brought out, you actually brought out two, but the final one was particularly interesting to me, where you talked about the 25 percent, 50 to 60, and 55 to 70 percent, and he had very little time when he did that, and I wonder if we could give him two minutes to get him to expand on where those numbers came from and the strength of the studies behind them?

DR. PERRY: I didn't really get the question.

DR. GARBER: I think Dr. Epstein is asking if you can show us the last slide, is that correct, or the second to the last?

MS. SMITH: He means this one, the levels of PME where you compared the written instruction from Sampselle, Berghmans in '96, and Burgio, where you had 27 percent, then 51 to 60 percent.

DR. HILL: We have it in our handout.

MS. SMITH: We have it in our handout.

DR. EPSTEIN: Yeah, and I was really -- I have the handout and I have the visual memory,

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and I didn't have the Sampselle study that I can recall beforehand. It's partly because of that but also partially because I think it makes potentially an interesting case, and I wonder if you can take the talking points that you would have used five minutes for but were forced not to, and now take them.

DR. GARBER: Not five minutes though. Let's keep this brief.

DR. PERRY: The Sampselle study is especially interesting because they avoid all the problems with contamination and really did do PMEs alone. They just had a handout, here it is, a one-pager and you know, this is your education. And I'm amazed, you know, really the differences between us all come down to one thing. TEC wants to use a rigid definition of biofeedback and a catchall definition of PME alone. It's interesting because it was sort of the other way around back in the guidelines where they used surgery, clear; drugs, clear; everything else is behavioral, including stim. Does that answer? So, you have a really rigid category of biofeedback, and a catchall category of everything else counts as PME alone, and when you do that, you get nonsignificant

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results.

DR. LANDY: A comment I'd like to make. I think the importance of sorting out the PME alone group is that if it truly is an intervention, then what you're looking at is the result of an intervention, as opposed to how we clinically use the descriptive term of PME alone. And when clinically applied, most clinicians in this area would do some form of verbal instruction, written instruction sheet and send the patient home, and that's truly what the studies are not comparing. The studies are comparing one intervention to another, so that PME alone is not really a good standard. The best standard we have are looking at the studies with, comparing a waiting list control group, because that most represents what we see clinically, because those are people who on their own, at some point in their association with a physician were taught or told to do Kegel

exercises, or they read it in a magazine article, and that's what they're doing on their own. And that best represents the result we get with PME alone clinically.

DR. GARBER: Ken Brin, did you have something?

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DR. BRIN: I had a question for Dr. Lefevre and Dr. Zarin, if she is still here, which has to do with the number of patients that we would need to achieve the power, the number of patients we need to show statistical significance. By looking at Dr. Lefevre's, I'm not sure what number slide it is, but it's biofeedback plus PME versus PME alone, the one at the bottom of page 8 of the handout. The total N of patients studied comes to 298 and if we exclude those where data isn't recorded, we only have 204 patients. If you look at the last column, the efficacy of PME alone, which we're already questioning the degree of informal biofeedback in there, is almost 50 percent. So in a meta-analysis of 200 patients where one of the interventions has a 50 percent efficacy, what type of efficacy do you need in the other arm of the study in order to prove that that in fact is efficacious? Are we talking about needing to show that there is a 90 to 95 percent success rate in that column? What is the power that would be needed, given these numbers?

DR. RATHMELL: Could we frame it a different way, the way you would really frame a research question, which isn't what power would you

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need, because that's going to be what it is. How many patients do you need? If you were to for instance, take the best designed study, with an estimate of population variance, and do a power analysis, like you're going to do a study, how many patients would you need in each limb? I'm sure you did that as part of your TEC assessment.

DR. BRIN: Well, you need one of the two. You either need to say what percentage improvement you have, or with that patient population, what percentage of improvement is necessary. So the two go hand in hand, and you can answer either side of it.

DR. LEFEVRE: Well, that's a little bit hard for me to answer because it depends both on the variability and the expected difference between the groups. On the variability we have a fairly good handle on, but we don't really know what the expected difference between the groups would be. So depending on what expected difference you're going to set, it would determine, I mean, your number of patients would vary. Our methodologists did fool around with that some, but I really would not be doing justice to try to reconstruct his numbers.

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But I would also say, one thing is that in some of the studies, particularly if you look at the Burns study for example, in which they did three groups, this is where they had the three groups with the biofeedback plus PME versus the PME, versus the waiting list control. And the outcomes there were 60 percent improvement in the biofeedback group, 54 percent improvement in the PME alone, and 6 percent improvement in the waiting list control. And these were statistically significant differences. So that study was probably adequately powered to detect a potential difference of that magnitude.

There's one other study that is similar to that that we will talk about tomorrow, where Bo, a Bo study that looked at four groups of patients, two of which were PME and a waiting list control, and had a difference of 60 percent in the PME group versus 10 percent in the waiting list control, again, a statistically significant difference, and there was probably adequate power. Now these studies were not, there were not power calculations done and again, I can't really reconstruct the numbers off the top of my head. But the potential in these studies would have approximately 30 to 40

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groups of patients, we're talking about 50 percent difference, 60 percent versus 10, that seems to be adequate power.

So if we're talking about large differences, you know, 40 to 50 percent in a group of patients of 30 to 40 with these type of measures, that would be adequate power, but

differences less than that, I can't really say.
DR. GARBER: Arnie?
DR. EPSTEIN: Yeah. There are a couple of numbers I keep in my head. If you're looking at differences in means, it obviously depends on how variable your population is. If you're looking at a proportion, like the proportion of people who improved or stopped, whatever, if you think of the baseline proportion being 50 percent, sample size of about 380 gets you plus or minus 4 percent. So keep that in your -- when you're talking about a sample size of 22, it's plus or minus a very large number.
DR. GARBER: Marshall?
DR. STANTON: I had a question for Dr. Lefevre also. I'm struggling with one of the questions we have to answer, which is the adequacy of the evidence, before even moving on to any

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others. And one aspect that's weighing heavy on that is the variability of the published results. One of the things -- you listed three possibilities. There's another possibility that I would like you to comment on and that is, it could be that the control limb, the PME, may have varied between the different studies that were assessed. When you went over the studies that met the criteria, did you look to see how much difference there was in how the PME was done and particularly, could that have been contaminated by some types of biofeedback that may have lessened the difference in some of the studies, and had zero types of biofeedback that would have had an effect?
DR. LEFEVRE: There was a lot of variability in the PME, in the delivery of PME. This is one of the problems with this body of literature. And this varied from -- some studies such as the Burns study, which I just alluded to, the three arms, where they gave the patients a videotape and written instructions, okay? So they gave them a videotape, written instructions, and then had follow-up visits; that doesn't appear to be biofeedback. This is the study that had a 60 percent improvement in that group.

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Then there's other studies that had the

verbal feedback, where a trained therapist would be working with the patients on a one-on-one basis, using digital palpation of the muscles, and then you know, giving verbal feedback. And if you call that biofeedback, then that's a contamination effect.

Now this is a problem when you are trying to compare studies across studies, when you're trying to compare studies to each other, the variability in the delivery of the PME is a very big problem. This would limit our ability to quantitatively synthesize this data. Within a study, as long as the two arms are balanced as to the type of PME they got, and then the biofeedback is added on, it's not a particular problem within a study. It's particularly a problem when you're trying to compare studies across the body of literature.

DR. STANTON: Well, it is a problem within a study, because it can narrow the difference. If the PME incorporates some very effective, quote, biofeedback, that's not the mechanical biofeedback that we're talking about here, that's raising the gold standard of the

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control. I'm just trying to sort out, why was the variability, like you were trying to sort out also.

DR. LEFEVRE: I mean ideally, you would like a study where the PME is identical in the two groups, and then biofeedback was an add on. If you look at the Burns study, that's pretty close to what they have. That's where they gave the videotapes, or they gave the written pamphlets, and then they taught the group biofeedback in the other group. The studies that use verbal feedback and compared to biofeedback compared, you can make that argument that you're comparing, you know, verbal feedback to mechanical feedback, and that could be a potential problem, and the baseline PME may actually vary. So there were a mix of those types of studies. And ideally, the best study would be the exactly the same PME in both groups. And there were some studies that came close to that, particularly the Burns study.

MS. SMITH: The one problem with the Burns study, however, is that the PME group was not

PME because there was EMG testing of the PME group, and during that EMG testing it basically, not only measurement of muscle occurred, but patient reeducation could have occurred. So she was

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actually testing a modified form of biofeedback.

DR. LEFEVRE: Well, we don't know that for sure. The EMG was meant as an outcome measure. It was meant to test the muscle strength pre and post, and it was a tool to be able to measure the muscle strength. There may have been -- I mean, you could -- there are some times when you have a test like that that has a treatment effect, you can hypothesize that that may be true, but I'm not sure that we can say for sure that that is true. The EMG not meant as a training, it was meant as a tool to measure muscle strength.

MS. SMITH: As someone who actually was there when she presented the original data in 1991, I think I have some reason to say that. The other thing is, I'm very familiar with her protocol because I reviewed that during the time that she was doing her study, so I'm very familiar with that. And it is a criteria that has not been brought out in the literature, and as a technical expert, I think that should be a very important point. You would not be aware of that because you don't have that ability, that backdrop.

DR. LEFEVRE: Again, it's possible. I don't think I can say from the evidence in the

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report. I can't say. It may be possible.

DR. GARBER: Let me just make one quick comment. Apart from the specific issue at hand, this is about the use of information and data that are not publicly available. It is very difficult for us as a panel and for any other panel to rely on information that is not available in the published literature. In the future we may be dealing with unpublished data in some forms, but let me caution that we may all have some detailed personal knowledge of some aspect of the study that does not appear in print, but there is no way to really incorporate that information fairly, because we don't have a systematic way of including all such information. And I think that there will be

situations when we will want to rely upon unpublished information, but we have to have very clear criteria about how that will be included.

And I appreciate the comment that there are features of the study that do not appear in the print version. That is undoubtedly true of every single study that we will publish, that we will review. But our deliberations should largely stick to what's in the published literature and what has been described in print, because we just don't know

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how things work in every study in that level of detail. Furthermore, as any of us who participate in studies know, two of us participating in the same study may have entirely different perspectives about how the interventions were administered, particularly if it's a multisite study.

So I'd just like to caution us about the use of information that's not in the published literature. Dr. Maves?

DR. MAVES: The only thing I would say, and it actually adds on to that point in a way though, is that it seems pretty clear from the testimony that we heard this morning that in point of fact, and I think this is Dr. Lefevre's point, is that there seems to be some elements of biofeedback inherent in a PME program de novo. I mean, I guess the amount of biofeedback may well be in the eye of the beholder, but I think it does make our task here more difficult.

If you look at Dr. Perry's slide that we talked about, if you take a look at PME alone, his conclusion is that it's about 27 percent effective, and if you add biofeedback, he says that should be 80 to 90 percent effective. It seems to me as an ear, nose and throat specialist far removed from

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this problem, that one should be able to tell the difference between 27 percent and 80 to 94 percent, just taking those values at face value.

But I think in point of fact, the thing I'm wrestling with is, I don't know where we are on his chart, but we're someplace up here, trying to really clearly distinguish, and I'd be happy for Dr. Lefevre to kind of give us some background, because that is the tough problem. What really is

the control group? Is it really pure, and I think you mentioned this, you know, just give them a sheet of paper coldly and say this is PMEs, go home and do them, as opposed to a program of biofeedback. But I think that's one of the reasons, at least for me, I am kind of wrestling with that problem.

And I think it's a very difficult one, and everybody here has given good testimony that the biofeedback helps. I sort of have been kind of conversely worried that if that's the case, should we then conclude that the PMEs alone don't work? I don't know what your conclusions were looking at the data, or if you have any opinion on that.

DR. LEFEVRE: Again, we didn't do a systematic review of the data on PME effectiveness

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alone, so I would not try to make any kind of comprehensive evidence based assessment of that. The two best studies that I'm aware of were the ones I mentioned, the Burns study and the Bo study, which had PME group alone versus the waiting list control. Both of those studies, improvement in the PME alone group was 60 percent, okay?

There are a number of other controlled studies which are cited in the TEC report, again, which show a benefit to PME. And I can't come up with a number to put that on, and I think the issue of what PME is, of course that's a big question, because PME has many, many levels of variability, and I think there is evidence in the literature that the intensity of PME is related to the outcome effect. There are studies that have compared different intensities and certainly different outcome effect. I don't think that we're disputing that.

But I think, again, in a peer study comparing PME by whatever definition you give, and where PME is equal between two groups, and then biofeedback is added on, that kind of study has the potential to isolate the effect of biofeedback apart from what the baseline PME is. So I think, I

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agree that's a tremendous problem in this literature, because there is no standardized definition of what PME is. And there is even

studies that show the combination therapies of, for example, PMEs plus bladder training is better than PME's alone. So there is all these different variations in PME, and it's really hard to say, what is the efficacy of PME, because there's no standardization.

So we try to look at studies which can isolate the effect of biofeedback, given some background level of PME, which varies across studies. But again, with studies, you would hope that you might be able to isolate the effect of biofeedback.

DR. LANDY: I think the other factor is, the studies that we have to look at don't allow us to factor out the subgroup of patients that might benefit from biofeedback. And we do know from other studies, like Wyman, 1998, that any structured intervention program with education, counseling and frequent patient contact, is going to show a certain percent improvement over a control group without those interventions. And the factor here that we don't have is, we have the

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numbers of PME and biofeedback, PME alone in the control group, but we don't have any way of factoring in who might benefit and who might not, other than putting someone through a program of PME alone, and then applying biofeedback to those failures.

The problem we have with that clinically, and that was actually shown by Glavind, 1996, there was a high dropout rate in the people in the PME alone group. There was lack of, less compliance, and we lost some motivational factor there. And I think if you start to apply that concept clinically, a lot of patients are going to go untreated.

DR. GARBER: Dr. McBryde has had his hand up.

DR. McBRYDE: I just need things even a little bit simpler than the ENT person as an orthopedist, but to me what I'm left with is that whether it's in a study or across studies, or meta-analysis or whatever it is, I'm left with the fact that our definition of biofeedback is clean and it's an unclean definition of PME, and that's

kind of my way of looking at it. Although certainly, that excellent report that Dr. Lefevre worked on, it doesn't make a definitive, something in my mind, as to biofeedback as a successful adjunct. But I don't know how we are going to get around the fact that the definitions are different in studies and across studies.

DR. GARBER: Let me just interject a comment about the messy control group. The messy control group, based on words that I've read, is actually much more the rule than the exception. Every trial that I have ever looked at that had a usual care group as a control, which is a very large number of trials, had something relatively undefined in the control. And typically, if you think of things like multiple risk factor intervention trials, the usual care group would get some of the intervention that the intervention group does.

So in other words, if you were interested in intensive blood pressure management, you couldn't ethically conduct a trial denying the usual character of blood pressure treatment. And the trials are designed in those circumstances to pick up a difference, if you want to find out whether more intensive use of the intervention works. And what that means is to ask a very pure question, and we just heard how difficult it is to ask a pure question in this context, to ask a pure question, what would it be like to use no biofeedback whatsoever, might not be possible, but you may have some hints.

And what is typically done in these trials is that you see if the more intensive intervention actually works better, if you have greater effectiveness. Because if your hypothesis is correct that the intensive intervention is better, you will get a positive result, even with the messy control group. Now it means you probably need a larger study in order to detect the difference; you will be relatively underpowered as compared to the so-called cure question of no biofeedback whatsoever.

But this is a problem that we will

confront every time, and I think we have to ask, what are really the consequences of having the messy control group? And I would contend the major consequence is you will tend to understate a difference and you will tend to be underpowered. Yes?

DR. HOLTGREWE: I think one of the things that we have to bear in mind is that

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incontinence is not a disease, it's a symptom. It's like headache. Headache can be due to a sinus infection, brain tumor or eye strain, and there are a variety of anatomical pathophysiological conditions that bring about incontinence, a symptom.

One of the things we're discussing here is post-prostatectomy incontinence, which is totally different in its cause and its pathophysiology from stress and urge incontinence in the middle aged or older female. And very honestly, as far as biofeedback and muscle exercises in post-prostatectomy incontinence are concerned, the literature we have on that subject is just pitiful. There is no way anyone that has a bit of scientific experience could make any conclusion from our existing literature.

So I think that right off the bat, I think we have to exclude post-prostatectomy incontinence from our deliberations, because there just really is inadequate information. Like Dr. Garber said, there's really only one study out there. So I think we have to remember, we're not talking about a disease, we're talking about symptoms of multiple diseases, because there are a

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variety of anatomical defects that cause this, so I think we have to bear that in mind, but I really feel very strongly that post-prostatectomy, the data is just hopelessly inadequate. And that's as a urologist, by the way.

DR. GARBER: Well, I wonder if it would be helpful at this point, we could look at the specific questions, and with Dr. Holtgrewe's comment, maybe we could start with just a question of the adequacy of evidence for the third indication. We do have three indications here,

stress, urge and post-prostatectomy.
DR. HOLTGREWE: Is a motion appropriate?
DR. GARBER: Well, we're going to vote at the end of the day, but the question is, should we have further discussion of the post-prostatectomy.
DR. HOLTGREWE: Well, I feel very strongly that we have inadequate information to make any kind of decision. I'm not saying that biofeedback in conjunction with PMEs wouldn't work in post-prostatectomy incontinence; I'm simply saying we have no evidence that it's good, bad or indifferent. We just don't know.

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DR. GARBER: I think I jumped the gun there. We will have to wait until the end of the day even to take up that question. We can still have discussion though, about all of those points.
DR. ZENDLE: What do you want to discuss?
DR. HILL: This isn't a great discussion issue, but I just wanted to ask the point. Maybe the biofeedback isn't so much in the eye of the beholder as in the cerebellum of the receptor. The reason people dropped out, maybe I'm making a wrong assumption, but I just didn't know why they dropped out. We don't know if they dropped out of the studies because they got better or they weren't getting better or for some other reason, and I don't see how the dropout rate always goes in one direction, and maybe I can get a response on that. I thought I was hearing sort of the underlying assumption that the dropout rate suggested a unidirectional bias.
DR. LANDY: Both of the treatment groups initially got the same treatment in the Glavind study. He gave two to three sessions of instruction and PME, then added four weeks of biofeedback training, and the dropouts were in the

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period of time in that initial -- actually, I'm not sure at what point in time they occurred, but it happened at a greater rate in the PME alone group.
DR. GARBER: I think Hugh's point, though, is that a priori, you can't say with

unbalanced dropout rates, which way the bias goes. And in point of fact, even with balanced dropout rates, you can't say a priori which way the bias goes in.

DR. LANDY: Yeah.

DR. GARBER: Just one methodological point that I think both Frank Lefevre and Deborah Zarin had touched upon. This is why most high quality randomized control trials use an intention to treat analysis, and they would include the dropouts, the outcomes among the dropouts, and attribute those to the group of initial assignment. And to the extent that studies don't do that, there is a fairly widespread consensus that if you don't analyze that way, that is, you either remove the people from the analysis, or if they cross over, put their outcomes in the other group, that that is incorrect.

And there is pretty universal agreement, you should use intention to treat, count the

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outcomes among the dropouts, according to the initial therapy. Now there's obviously a problem if the dropouts are lost in follow-up, and trials invest a huge amount of effort to find out what happened to those people. But I think the general point is true, that there is a potential for bias, unless you knew everything about those individuals, you can't say for sure which way the bias would go, if there is a high dropout rate.

We do have the option at this point, if we think that we might be ready to vote on some questions fairly soon without further discussion, we can move up to the next session of public presentations. Does anyone on the panel object to that? We have to make sure we get the public presentations. Yes, Marshall?

DR. STANTON: Yes. I guess I would like to, since we're ahead of schedule, it's sort of an interesting little side issue that was in one of the articles that I don't think has gotten any discussion, and I'm interested in the opinions, particularly of the urologic specialists, but anybody. I think it has no discussions because it wasn't listed as one of the clinical outcomes because it's more of a physiologic outcome.

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And this was in the Burns article where they looked at change in pelvic muscle activity by EMG, and it was interesting that although the clinical outcome was very similar in the biofeedback and the PME groups, it was only the biofeedback group that had the improvement, or the biofeedback had improvement in the EMG at the end of the assessment. And it struck me as being interesting because it's a physiologic measure, which is different than a clinical outcome, but I felt it was interesting and I am just interested in other peoples opinions.

DR. GARBER: Any comments?

DR. RATHMELL: Dr. Lefevre, you actually commented as an intermediate outcome; can you just reiterate maybe two sentences?

DR. LEFEVRE: Yeah. I think, you know, the orientation that we take is that primary health outcomes, which are outcomes that are experienced by the patient, should be the primary outcomes. If those outcomes are lacking, we'll then look for intermediate outcomes and attempt to say, is this intermediate outcome linked to true health outcomes and if we can make that link, then we will accept it as an acceptable outcome. However, if there are

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true health outcomes, we would always assume those as primary outcomes.

DR. RATHMELL: So in other words, if you were still incontinent and had the same rate of incontinence despite the increase in muscle strength, who would care, right?

DR. STANTON: Well, one of the interesting things might if you had a long-term outcome, it might be different. Because not many of these studies, I think only one went to six months, most of them were eight or 12 weeks, and is there a long-term outcome? We're not going to be able to answer this question, but you can speculate that those people who had a physiologic change had a better long-term outlook, but there's no evidence.

DR. ZENDLE: Isn't there one study that showed that there was actually an earlier effect with biofeedback that disappeared at 12 weeks, or

eight weeks?
DR. STANTON: The effect didn't disappear; the other group caught up.
DR. ZENDLE: Okay. The difference disappeared. And so if the physiologic -- if the long-term outlook were going to be better, you

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would expect it to go the other way?
DR. STANTON: Except I was thinking long-term like a year, something like that.
DR. GARBER: I saw somebody else? Okay.
Connie just informed me of a very important fact. The refreshment stand closes at three. Our original schedule had us beginning our break at three, so I would like to propose that we break now, and resume with the open public commentary at three o'clock. Thank you.
(Break taken at 2:50 p.m.)
DR. GARBER: We are about to resume.
MS. CONRAD: Okay. We are going to take the next few minutes, maybe as many as 30 minutes, to allow anyone in the audience to approach any of the microphones, there's two aisle microphones, one podium microphone. This is the opportunity for those who forgot to ask for speaking time, or who were too late, or who just all of a sudden remembered something that they would like to mention to the panel members. So at this time, if you wish to, first come, first serve, approach the mike, state your name, your affiliation, and address the panel. Yes, ma'am.

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MS. PALUMBO: My name's Mary Val Palumbo. I'm a nurse practitioner from Williston, Vermont. I represent the Continence Coalition, and my organization noted that HCFA had placed a consumer representative on the panel. 52 patient letters were sent to the consumer representative that mainly address quality of life improvement. I do believe that the Medicare population is interested in quality of life and that should not be left out of the debate, and I think that this is a vital piece to your deliberations. I'd like to read an example of one of the letters.
I am very pleased to write in support of

my experience with the biofeedback treatment for urinary incontinence. My story is simple. I had major surgery for prostate cancer and I know that I would not have done the prescribed exercises which helped me regain control of that bodily function without the visual understanding that came from biofeedback that I received. It was very difficult to focus on the muscles involved simply because of verbal or even written instructions, and I would suspect that I would not have continued without the ability to see in my mind's eye the computer screen and the effect that each subtle sequence produced.

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Furthermore, I hope that any committee evaluating this procedure will take into major consideration the terrible emotional impact that this invasive surgery places on the patient, and that the assistance and support provided by the biofeedback is an essential and integral part of the overall healing of the patient, both physical and emotional. Thank you.

MS. CONRAD: Thank you. We have a total of 30 minutes, there are 27 left.

MS. FELDT: I appreciate being able to address the panel again, due to the time constraint on my verbal testimony earlier this morning and a notice in the Federal Register that stated a March 22nd deadline, the American Physical Therapy Association submitted written comments to HCFA so that comments could be available to the panel prior to this meeting. I have, however, received information that the members of the panel did not receive our written statement, but did receive the TEC report. What I would like to is to insure that you have access to this information, so we are going to hand out our position papers so you may use them in your deliberations later. Thank you.

DR. HILL: Sorry. I have to speak up

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here. We have these deadlines for a reason. Anything that you want to submit subsequently, we can take into account, but throwing copies of -- I know that we asked presenters to give us transcripts and their written statements so that the record would be complete, but I think we do have to limit the actual handout to that which was

submitted by the deadline.
MS. FELDT: Sir, it was submitted by the deadline. It was submitted by March 22nd, and I am under the impression --
DR. HILL: Well, if we received it by March 22nd, it was included.
MS. SMITH: No. It is part of the catalog of items that was available to the panel. But what Cindy Feldt is talking about is that the panel members received in hand the TEC report, and had to request other things that were part of the catalog items, so that's what she's talking about.
DR. HILL: Yeah, I'm sorry; that's correct. That's like some of the excluded articles, and some of the other things. If the panel members has asked for them, they would have been distributed to them.
MS. FELDT: So if I would have submitted
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this morning along with my written testimony, it would be accepted?
DR. HILL: No, because what we asked for with your written testimony was a transcript, which you did give us, and it was appreciated.
MS. FELDT: Thank you.
MS. CONRAD: Yes, sir?
DR. SAND: Hi. I'm Peter Sand, from Northwestern University Medical School, and I'm the secretary treasurer of the International Urogynecological Association. And one thing that came to mind in listening to the deliberations and the discussion that's always impressed me about biofeedback is that in some of the literature that you're looking at, which has an international base, the discussion came up earlier this morning about applicability of studies. And while prospective randomized or prospective controlled trials are very useful, I think we also, to make the waters even more muddy, we had to consider that in different countries we see different outcomes and different results.
Those of us who are familiar with Karri Bo's work, which was discussed earlier for example, recognize that Karri has been able to maintain
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populations of women in pelvic floor therapy with

biofeedback, whether this is manual or auditory biofeedback, or both in the case of the study I'm referring to, for periods of two years and beyond with near a hundred percent compliance. This just doesn't happen in the U.S. We don't have these kinds of patients. We don't have these kind of medical systems that allow us to have continued follow-up. And so I think when we start to look at these studies, I would ask the panel to consider and perhaps even weight the applicability of these studies to a U.S. Medicare population, which is what I think we're supposed to consider.

The other thing, and the other issue that I don't think we have good data on unfortunately, but it seems to be very clinically relevant to myself and my peers, is compliance. We talk about compliance in control trials, we try to track this and report this, but in clinical practice it is very clear that compliance improves with the intervention and the strength of the intervention, and obviously if there's biofeedback, and there are visits associated, and there's what we like to call in our office the coach effect, in which you have to report to the coach on a regular

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basis, you're more likely to be compliant with your pelvic floor exercises. And so inherent in biofeedback and in that intervention is hopefully improved compliance through needing to report, needing to be assessed, whether it's with electromyographic assessment or whether it's with pneumatic assessment, you need to be assessed for your progress, and the change not just in your incontinence episodes but in most programs the change in pelvic floor muscle strength.

And this hasn't come up. I don't know how you quantify it, but I think it's an interesting thing to consider when we look at the benefits or the enhancement effects of biofeedback. Thank you very much.

MS. CONRAD: Thank you.

DR. PERRY: My name is John Perry. I would just like to build on one of the things that Dr. Sand just said with respect to biofeedback and Europe. One of the problems is that Europe was very slow in showing an interest in biofeedback,

and I think this can be shown most clearly in the fact that the American centered Association for Applied Psychophysiology and Biofeedback just celebrated its 32nd annual meeting last week in

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Denver, whereas the European Biofeedback Association just celebrated its fourth annual meeting. So the research in biofeedback that comes out of Europe relatively, I'm looking for a polite word, young, and does not show the polish and experience with the technology that the American studies show.

I'd also like to make a very brief comment with respect to the question of why isn't there more research. And the problem is that almost all of the things that are done in biofeedback are not patentable and there is no industry behind them. Biofeedback companies are typically under, I don't know what the numbers are, but we're talking about very small companies, run by a half dozen dedicated people, and there's simply no incentive for them to fund the kind of research which we all agree would be wonderful to see. In this respect, biofeedback is extremely different from drugs, and research is quite different because there isn't that kind of money behind it.

MS. CONRAD: Thank you. Diane?

MS. NEWMAN: I didn't get enough time this morning. You know, Dr. Landy brought up a few

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important things. Number one, you asked why we -- first of all, I'm surprised we're comparing PME alone with PME and biofeedback, but you asked why there's not more research. It's because the standard of treatment is with some type of biofeedback. And that is what we have all been doing for almost 20 years, so I don't think you're ever really going to see research alone.

Now I was part of the investigators in the Sampselle article which is one of the references in my outline. That was published in January. That was a five-year study which was a research utilization study, and it was in the AUA Journal, and what it showed is we took what was in the clinical practice guidelines and tried to put

it into clinical practice. And we took life style changes with caffeine, fluid, we took bladder retraining, and we took a handout on tables. And we went to 21 public private women health centers around the country. We surveyed 1,800 women. Only 132 went into treatment, and basically there was very little improvement, but -- as far as decrease in incontinent episodes. By the way, 42 percent of these women said they had some urinary symptom.

But what's important about what we did,

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and again, Dr. Landy brought up, we didn't just do pelvic muscle alone. We also did caffeine reduction, fluid management, bladder retraining, and so, the effect may have been from caffeine. Caffeine reduction does act as a bladder irritant, so to say that you have PME alone, there is no such thing. And when we did try to do it with just our handout, it didn't work. Thank you.

MS. CONRAD: Thank you. Yes, ma'am?

DR. WHITMORE: Hi. I'm Kristine Whitmore, a urologist and director of the Pelvic Floor Center in Philadelphia, Pennsylvania. I have been treating women mainly for the last 13 years with urinary incontinence. I really appreciate the difficulty you're charged today with utilizing a new form of evaluation of the literature, making it evidence based. But in order to obtain any kind of an outcome without bias, it seems to me and in my experience, and having participated in clinical trials, that you have to measure the pelvic floor muscles before and after PFMEs. That therefore marries biofeedback and PFMEs. And I thought that one of the charges today was to figure out what the efficacy of PFMEs are.

And the second point: If the studies

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truly are messy according to the current proposed system, what right do we have to use the proposed evaluation system of the data as evidence based, which appears inconsistent with the clinical efficacy that has been shown through groups of expert panels who have demonstrated by guidelines there is efficacy. And I really question the efficacy, a true value of everything that we're trying to do, by answering these questions.

Please also consider the patient. There are a lot of patients out there that may be denied their therapy because of our inability to answer all the questions, and keep an open mind as to the difference between PFMEs and biofeedback.

DR. ZENDLE: Can I ask a clarifying question? I'm not sure who I'm asking, but a couple times it has come up that handing out a sheet of instructions or giving verbal instructions is not PMEs. I agree, if you give somebody a pill and they don't take it, you can't count them in the pill taking group. Is anybody using that definition, that PME alone only means giving a sheet of instructions?

DR. LANDY: What we're saying is that is the clinical situation that is the most common

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scenario. That is PME alone in the clinical setting, not in the study design setting. And we have seen and done research on the drawbacks of verbal instruction alone, and the lack of efficacy of that. But that more represents what happens clinically in practice than what we're looking at in these controlled randomized trials.

DR. ZENDLE: Is there a standard of PMEs that would include more than giving verbal and written instructions, that would include the measurements that were talked about?

DR. RISAGER: Excuse me. You referred to a clinical practice of just handing out paper. I think one of the reasons why there may not be that much in the way of studies is because what people do out there, certainly speaking about our area here in Maryland, is urology and neurology groups, when women come in complaining of stress incontinence, or whatever, generally they're well organized groups; they have a nurse who is particularly skilled, and she takes the patient in hand and will teach them pelvic floor exercises. She does hand out sheets of paper, but actually teaches, changes -- there is the other bladder training pieces as well. And this is certainly the

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five years I have been in Maryland and dealing with urologists, this is the standard of practice.

So what I'm seeing here, there are

various types of standard of practice, pelvic floor exercises meaning one thing in Maryland, another thing in your neighborhood perhaps.

MS. SMITH: Well actually, I think you're all saying the same thing. When the nurse takes a patient and then gives specialized instruction, she is most often using biofeedback to deliver that specialized instruction. That has become the clinical standard, and I think I can say that as a technical expert. I am very well aware of what happens in the field of nursing and continence.

The other thing that that means then is that you really have to realize that biofeedback is not, you're not going to have 50 million patients in a randomized control trial because it is considered the standard of urologic nursing, and for many urologists considered a standard way of treating mixed, urge and stress incontinence when it's originally presented.

DR. ZENDLE: Could you distinguish the different kinds of biofeedback, from the bells and

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whistles to the more simple?

MS. SMITH: Yes. The most common form of biofeedback that you are actually seeing clinically being used is an EMG type of biofeedback. There is also a manometric form of biofeedback that is given in home trainers, that is also given in some more sophisticated pieces of equipment, that usually give you the option of doing manometry versus EMG. But actually, EMG biofeedback is the clinical standard.

And what's interesting about that is actually the studies that have shown efficacy, for example like the Burgio study in JAMA, and even if we look at Burns, they were using EMG perineometry. So they really were using what has now become the clinical standard.

You know, Magnus Fall, we're going to focus on pelvic muscle electrical stimulation tomorrow, he has a very interesting article that's in your packet, where he goes through the pros and cons from his standpoint, and he's considered basically an expert in electrical stimulation. He goes through and he describes the pros and cons for

FES. And one of the things that was fascinating to me about his work and that article in 1998 was that

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you could really say that's very similar to biofeedback. He actually says that the reason there aren't huge amounts of study in PFS, for example, is the same probably, because it has become the standard.

If most centers, most urologists, most urogynecologists, most nurses who are doing these interventions behaviorally with patients consider biofeedback the standard, that's why they basically don't look for extreme efficacy in a randomized control trial, because they have accepted this as the standard way of basically teaching PME.

The most interesting article was passed out to you this morning, which is Bump, which I think was also described, I hope in the TEC report, I'm not really sure. But in 1991, he used urodynamic measures to visualize an effective PME exercise. He actually was able to show with urodynamics whether or not a woman could inhibit the flow of urine from the bladder by doing a correct PME. And what he really showed with that, it was just by his brief verbal instruction, and you're talking about physicians instructing the patient while they are doing urodynamic studies, and have done a previous physical exam of that

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patient, that most women could not perform them correctly. And what the addition of biofeedback is is really giving a different type of physiological response to the patient about their muscle structure, and that's why it basically is more effective.

And what Lisa's been trying to say, what a number of the other of the presenters have been saying, is that brief verbal instruction is the alternative standard that is given. You know, when clinicians who are in this field talk about PME, that's what they mean. They mean that the patient was given a piece of paper and they basically said, look, try these exercises, they might work for you. If you're really going to have a structured exercise program in the United States, you're getting biofeedback.

DR. RISAGER: I would like to emphasize what I said before, which was, PME is being done in the physician's office and they are being given biofeedback through one-to-one training by a nurse. They are not as a rule, at least in our bailiwick, getting there biofeedback mechanically.

DR. GARBER: Let me just ask if there are any more public comments. We sort of glided into -- yes?

DR. BOILEAU: One last one, sorry. I'm Michel Boileau. I'm a practicing urologist and the founder and chairman of Deschutes Medical Products. I think it's important for the panel to realize, I'm sure you do, that incontinence in these patients is potentially a devastating lifelong problem, and that treatment, particularly biofeedback and PME, is more than just the six to eight weeks that they come in for their initial assessment, their training in how to do correct exercises and initial strengthening of the pelvic floor muscles. For these patients to really be successfully treated, they need maintenance therapy, and biofeedback does enhance compliance. But the patients also need a tool or an avenue, whether it is regular follow-up with their therapists, that they can go back on a regular basis and be treated, or whether it's a home trainer that they will be able to return to at will, but they need some mechanism or tool to help them utilize this throughout their life if it's going to be really a successful therapy.

MS. GREENBERGER: I would like to say something. As the consumer rep, I think I'd like to speak to the consumer. First of all, I'm puzzled as to why we would have all these public comments and patients, and the letters, which I did receive and read, and then sort of ignore it because it's not scientific evidence in the research that we're getting. So I think that, I mean I'm concerned that all these people have weighed in, they are professional organizations, the advocacy organizations and the patients, and it seems that up until the last couple comments they were sort of being disregarded.

Secondly, I think it's clear, and this is not unusual in terms of women's health, that there hasn't been a whole lot of funding for good clinical trials in this area. And it's not that long ago that we really started talking about a condition like this, so it's probably not surprising that there aren't -- there isn't great freight research.

So I think that -- and I also think that we've had a fair amount of discussion about the confusion of the definition of what pelvic exercise really is and whether that does, ipso facto, include biofeedback. So I, this first question is sort of a nonstarter. I mean, we're not going to

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be able to evaluate this if we're looking at scientific evidence, but if we're looking at people who are getting the treatment and giving the treatment, it's a totally different question. So I'm not comfortable answering this first question with the word scientific in it.

DR. GARBER: Thank you.

DR. HILL: I think we have one more speaker, if we have time.

MS. CONRAD: No. Phyllis, let me address the comment that you made about disregarding position papers and some of the information that's come in to HCFA. Nothing has been disregarded. Every piece of paper, every word is read, it's carefully considered, and will be considered in any coverage determination process. What we did at the request of the Executive Committee recommendations is limit the amount of material that was mailed to the panel members. But everything we have is available to them and there are stacks of papers, it is all catalogued and available.

MS. GREENBERGER: I know it's available and I've read it. That's not my point. The point is that using the word scientific negates the

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public testimony, because the research trials are not consistent with the public testimony. So I'm not saying that we disregarded the information, I read it, we all did, I'm not saying we didn't.

But under these circumstances, at least

as a consumer, I'm not a doctor, so I'm sitting here listening, and I have read everything, that we can't make a determination about these on the basis of scientific literature, which I think this question is asking us to do. Apparently there aren't enough trials, they're not good enough, they haven't been funded, and they don't illustrate what I think is really happening out there in terms of treatments. So my confusion or question is, if we have to answer this question based on science, and science translates to clinical trials, we've got clinical trials that apparently aren't giving us the science that we need to make the decision, but we've got everybody else saying that this is what works and this is what people want. So my question is, how do we answer this?

DR. GARBER: Maybe I could just quickly address that, Phyllis, because I think you raise very important points. The testimonial information, the consumer letters, the opinions of

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other expert groups are important information. Our panel is once again, let me emphasize, not making coverage determinations or coverage recommendations. We have been asked to deal with the scientific evidence to see whether it's adequate and if we agree that it's adequate, to say what it shows. That does not mean that all the other evidence or information, including the testimonials, doesn't matter. But we do have a set of well defined questions to address, and the panel has to decide which evidence is applicable to the questions and to determine whether it's adequate. And that in no way says anything negative about the value of other forms of information.

Now, you could say that you believe that our panel should not be being dealing with these questions, that they are too narrow, that the adequacy analysis of evidence criterion is too narrow, and you are certainly entitled to that opinion. What I can tell you though is this was an issue of absolute unanimity among the Executive Committee, that that is the task of the panels, and I believe that had HCFA's concurrence. So we have a well-defined task, I believe, and so the real question is what information do we use in carrying

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out our task? And let me emphasize again, the other kinds of information that we have are important and should be reflected at some stage in the coverage process if not in this particular context.

I think we have one other public speaker.

MS. CONRAD: This is absolutely the last one.

MS. DEGLER: Good afternoon. My name is Margaret Degler. I'm a urology nurse practitioner and a program director of a continence clinic. And I just want to point out, the first question that I understand was on the table for months was, was biofeedback more efficacious than PME? Now I understand for the past seven hours this question has changed around at least three times today, but what we have heard for over seven hours is the clinical efficacy of biofeedback assisted PME. And in any scientific study, when there is such efficacy in the control arm versus the placebo arm, it is unethical to continue that scientific study. And how can we, after hearing all this evidence, say that there is not enough evidence based medicine to continue biofeedback as the standard?

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MS. CONRAD: Thank you.

DR. GARBER: Okay. Back to the open panel deliberations. Let me suggest that we deal with the questions in order, and would it please the panel if we were to deal with stress incontinence, urge incontinence, and post-prostatectomy incontinence in order, or in any particular order? Yes, Logan?

DR. HOLTGREWE: Alan, perhaps we could reverse the order. Because I think of all of the data that I've look at and we've all looked at, that clearly, the post-prostatectomy incontinence, first of all, it's a different problem, it's a different disorder, it's due to a surgical procedure, the consequences of a surgical procedure, and out of all the things we're going to discuss, there is, I think least evidence available on post-prostatectomy incontinence and the value of biofeedback and even PMEs, or a combination

thereof.

Now, having said that, I certainly don't want anyone to think that there isn't in my mind any place for this. I just don't know, and I don't think there's a compelling body of evidence that has been presented that available in the literature

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today in any way suggests that we know for sure that this is of value. So I think this is the least documented of anything we have, so I would propose and if a motion is in order, I would move that we strike it, and we state that we have inadequate information on this to draw any conclusions. And if a motion is in order, I would so move.

DR. GARBER: Is there a second?

DR. EPSTEIN: Second.

MS. SMITH: I would like to bring something out. I gave Connie Conrad a copy of an article in a recent journal of the Lancet, in January, 2000, there was an article with a fairly good end that showed that men prior to prostatectomy, radical prostatectomy, were given biofeedback, and then those men were given biofeedback again post their procedure. And there was a control group where the men who were just receiving the procedure of radical prostatectomy, and it showed that there was an efficacious benefit in using biofeedback to train those men. In other words, the men who received biofeedback pre and post had incontinence for less of a period of time than the men who basically just had the procedure

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alone.

So, I do think there are some other things in the literature that should be considered. The problem is the idea of using biofeedback in post-prostatectomy in the whole gambit of doing behavioral therapy is a relatively new one, and I think that there are studies that are coming out. There's also an abstract that's going to be presented in AUA that has similar results. So I think there is some evidence to suggest that there might be some benefit there.

The other comment I want to make is that generally thinking about it, with the exception of

what you were telling me before, Dr. Holtgrewe, is that many people consider the type of incontinence that men experience post radical prostatectomy to be of a stress type incontinence. There is evidence in the literature for stress incontinence in women and you may want to extrapolate that into stress incontinence in men post radical prostatectomy. I think this is a relevant clinical point and should be something that the panel should consider.

MS. CONRAD: Excuse me. Before we go any further with this, I have a piece that I have

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to do to comply with the Federal Advisory Committee Act, so if you will just bear with me.

For today's panel meeting, the voting members present are: Michael Maves, Linda Bradley, Kenneth Brin, Arnold Epstein, Logan Holtgrewe, Lisa Landy, Angus McBryde, James Rathmell and Les Zendle.

I must state for the record that a quorum is present, that no one has been recused because of conflicts of interest. And now at this time, Dr. Garber can take over the panel discussion again. Thank you.

DR. GARBER: I'm not sure that taking over is quite the right word.

DR. HOLTGREWE: Let me respond to that statement. We would all welcome an effective therapy for those men who have the misfortune of having incontinence after prostate surgery. But I really feel we must confine our thoughts, comments and opinions, and our decision, based upon current peer review literature, which on this particular topic is very, very, very meager. Now hopefully in the months and years ahead, we'll have additional information at which point in time, other decisions can be made. But I'm quite conversant with the

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literature that exists, and I just don't feel that based upon this and the material we've been sent here, that we really have enough information to make a decision whether this is good, bad or indifferent. We simply cannot tell from the existing body of peer reviewed medical literature, which is what I think we must confine our decision

upon at this point.

So I say again, I think that this is different from stress incontinence and urge incontinence in men and women who haven't had a prostatectomy. Of course women don't need to worry about having a prostatectomy. But I really do believe that we have inadequate information to make a decision. You just can't scientifically say we know that biofeedback is of any value in this situation. Maybe it is. We need to find out, and we hope there are studies, and they will hopefully be soon on the horizon and available to us. In the meantime, I don't see that we can decide.

DR. GARBER: Les?

DR. ZENDLE: For the purpose of efficiency, could we vote on a motion that sort of added the words, any of the following three indications? Because if that get voted down, it's

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silly to then separate it out, if a majority feel that none of these meet the criteria. Now if they feel any of them should, they should vote yes, and then we'll have to divide it up and see which ones, but it seems to me that that's unlikely.

DR. GARBER: Well, it seems to me that we have a motion that's been seconded. And either, I guess the motion could be withdrawn or it could be amended, but we have a motion. Let me ask. I thought I heard somebody second it.

DR. EPSTEIN: I was going to second it, but I decline to second that motion in that Les has as an alternative. I think it will be more efficient and drive us more quickly to where we need to go.

DR. GARBER: This really gets well beyond my meager knowledge of Robert's Rules. So as I understand it, we have a motion that was seconded and the second was withdrawn, and therefore, the motion does not stand.

Now Les has a motion.

DR. ZENDLE: I move that we vote on question one with the understanding that we're adding the words, the Medicare populations for any of the following indications. If there is a yes

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vote, then we'll have to separate them out, but

we'll see what happens.
DR. LANDY: I thought we were supposed to address each of those individually.
DR. EPSTEIN: I think he's saying if none of them are going to win, then why do we have to drag ourselves three times over the same coals?
DR. LANDY: Because they are different issues.
DR. GARBER: That's part of the discussion on his motion, but I haven't heard a second.
DR. EPSTEIN: I second.
DR. GARBER: Okay, there's a second. Now we can discuss it. Dr. Landy?
DR. LANDY: I am very confused about the motion. Can you clarify it, because I'm under the understanding we were going to address each of these independently.
DR. ZENDLE: We will, if my motion passes, that we say that there is scientific evidence on any of these, then we will address them individually. If we don't, then there is no reason to address them individually.
DR. LANDY: So, if you can clarify what

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an affirmative vote is versus a negative vote?
DR. GARBER: Do you want to restate your motion?
DR. ZENDLE: If you believe that there is scientific evidence to draw conclusions about the effectiveness of biofeedback as an adjunct to PMEs, blah, blah, blah, in any of these conditions, you should vote yes. If you feel there is no scientific evidence in any of these, you should vote no.
DR. LANDY: Thank you.
DR. HILL: HCFA is interested in why you vote, so under either rubric, whether you divide them out issue by issue or take on overall vote like this, we would still very much like to hear what's the thinking behind the vote on a per indication basis.
MS. CONRAD: May we have a show of hands please, those for, in favor of the motion? Is this unanimous?
DR. LANDY: No.

DR. GARBER: Actually, I think I may share some of the uncertainty about what the motion is. As I first understood you to propose it, Les, you're asking for the panel to decide en block if

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maybe none of these conditions meets the adequacy questions.

DR. ZENDLE: Or any of them.

DR. GARBER: Okay. So anyway, there's first going to be a determination about whether any at all meets the evidence, the adequacy criterion. You're proposing we do that en block, ask that question and if the answer is yes, then we proceed individually among each one.

So the motion is not to make a determination about adequacy of evidence but about the procedure that we will use; is that correct?

DR. ZENDLE: No. If the majority of the panel doesn't vote yes on my question, we're done.

DR. GARBER: Okay. So you want to go directly to the evidence determination?

DR. ZENDLE: Of any of them. But granted, if the majority feels that there is evidence for any of them, we have to go on to see which ones they think there's evidence for and which ones they don't. Maybe it's not efficient.

MR. WHITE: I'm John White, and I work in the coverage group with Dr. Hill.

DR. HILL: Temporarily he is serving as parliamentarian.

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MR. WHITE: Just in terms of parliamentary procedure, if Dr. Zendle has made a motion which was seconded to modify the question, you should vote on whether or not to accept that modified question. That really should be the first order of business. And then depending on what happens there, then you should decide to vote yes or no. But you do have that motion to modify the question which has been seconded. You've had deliberations about that motion, but you still have to vote as a whole group whether or not to accept that modified question.

DR. GARBER: Thank you. That explains my confusion, I think, because it's really a two-part thing that you're talking about, and

you're leaping to a changed question and asking for a vote on that.

DR. ZENDLE: I didn't realize there was a motion on the floor that I was asking an amendment for. I thought it was a primary motion.

DR. EPSTEIN: Les, I'd be willing to withdraw my second if you withdraw your motion. I think we might move more quickly going right in the order as suggested.

DR. ZENDLE: Yeah, it's proven not to be

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very efficient, so I withdraw it.

DR. EPSTEIN: I can always tell when I back a losing cause.

DR. GARBER: Okay. It sounds like we are going to do things in order since we rejected Logan's motion by lack of a second to start with the post-prostatectomy.

So let us first deal with stress incontinence, unless there is an alternative proposal on the table.

Is the scientific evidence adequate to draw conclusions about the effectiveness of biofeedback as adjunct to pelvic muscle exercises in routine clinical use in the Medicare population for stress incontinence?

Discussion?

DR. ZENDLE: Call the question.

DR. GARBER: Okay. An affirmative here means that the evidence is adequate for the indication.

DR. RATHMELL: For the parliamentarian, I'll second the motion that we call the question.

DR. GARBER: Okay. Affirmative means the evidence is adequate and a negative means that the evidence is not adequate. All in favor, or all

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answering yes?

I count two.

Okay. All who answer no?

(Drs. Bradley and Landy voted in the affirmative; all other panelists voted no; there were no abstentions.)

DR. GARBER: Okay. I do have a procedural question that I seek the panel's guidance on. You are asked to explain your votes.

Would you rather do that at the end after we have done all these? Okay. Anybody disagree with that?

Is there a motion to address question 2, the same question, except for urge incontinence rather than stress incontinence?

DR. ZENDLE: So move.

DR. BRIN: Second.

DR. GARBER: Okay. All who answer yes, meaning that the evidence is adequate, please raise their hands. All those answering no.

I believe that's unanimous.

(All panelists voted no.)

DR. GARBER: Number 3, the same question except with regard to post-prostatectomy incontinence.

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DR. MAVES: So move.

DR. ZENDLE: Second.

DR. GARBER: All answering yes? All answering no? I believe that's unanimous.

(All panelists voted no.)

DR. GARBER: Now, what -- Logan, do you have a comment?

DR. HOLTGREWE: Personally, I voted no because I feel the available current peer review literature does not adequately confirm that biofeedback in conjunction with PMEs provides any advantage over existing other therapies, and particularly muscle exercises by themselves. In other words, simply stated, there's inadequate peer review literature to support the position.

DR. GARBER: Before we proceed, let me just explain one thing. We take very seriously the obligation to explain the votes, we don't want to put anybody on the spot, so let me suggest that if you have a reason for voting yes or no and if the reason has not been given, that you do take responsibility to give your reasons here openly, so that we at least can collect all of the reasons people gave on both sides of each of these questions, and so that this will be entirely

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transparent, why people voted as they did.

So, not everybody has to explain how they voted, but I hope that all the reasons you

used in reaching your determinations are expressed by at least one person.

DR. HILL: If I may, if you perceive a difference in the three indications, would you please also explain that to us?

DR. GARBER: Okay. Les?

DR. ZENDLE: I wanted to say what my no vote is not, and it is not that I do not feel that this should be covered or that it should be provided to patients. My no vote was that I don't feel the scientific standards of evidence have been reached by the common definition of statistical significance. But that does not mean that I don't think that there is some use to this technology or that it should be provided. I do feel that there are appropriate indications that don't require a scientific evidence standard, but that is not what this group has been asked to do.

DR. GARBER: Jim?

DR. RATHMELL: I feel very strongly that the peer review literature, there is a paucity there, and the technology assessment was very well

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done, and it really does pretty much agree with systematic analyses that appeared earlier as well as the recent meta-analysis. And the question, the big problem that I have here is the question that we have answered is not the efficacy of one intervention versus the other, it's -- or two interventions that are standardly used, biofeedback versus the PME. It's this arbitrary distinction between what constitutes the two, and trying to draw a very discrete line through this of biofeedback versus PMEs alone. And I would agree with what the AHCPR had done, lumping all the behavioral treatments together and saying that they are very effective, and that would be the outcome that I would favor. But the question we have been asked is about the adequacy of the scientific evidence to divide these two very discrete things, and it just isn't there.

DR. GARBER: Arnie?

DR. EPSTEIN: Yeah. I'll go off the reservation a bit, and use this as an opportunity to make a comment for the record, which will at least be read if not used by those who come after

and make the more important decisions about coverage. I think there is a difference -- from

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the beginning this morning when I asked you the question about adequacy, this has hung on the word adequacy, and adequacy depends often on who and for what purpose. If you're a scientist, you define adequacy conventionally as there's only a 5 percent chance that you will say something is true and it's not, or sometimes a 1 percent chance. If you happen to be a policy maker, which is different than a scientist, adequacy is often .5. I think I'm better off going this way than that way, since I clearly have to go in one direction versus the other.

When I reviewed the information that I have available from the scientific literature, and we've all commented on its adequacy or its inadequacy, it seemed to me that Dr. Perry may have had some version of it right. Probably written training does something, a little bit. Probably if you do more than training and get a nurse to reinforce it with or without digital reinforcement, you get more, and maybe even get more with some biofeedback, although I don't know.

I would say that if I was forced to bet on this like a policy maker is on the 50-50 level, I would probably bet you'd get something, but not

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at the 95 percent where scientific adequacy is. So for me, it is easy to, one, vote no on the question, which I did, and then at the same time comment here, urge HCFA to consider the fact that this may very well be an efficacious therapy, and they should consider that in their decision making, lest they be penny wise and pound foolish.

DR. HILL: Dr. Epstein, can you tolerate a question?

DR. EPSTEIN: Yeah, as long as I get a chance to respond.

DR. HILL: I heard you say .5 percent, and we've used that figure when we talk about P values. Then you talk about 95 percent, and I want to know if that's the mirror or how you got that.

DR. EPSTEIN: I think two different ways. If you're a scientist and you're trying to

say this exists, the classical scientific proof is at P .05 or P .01, which means that there is only a 5 percent chance or a 1 percent chance that you're going in a certain direction and in fact it's wrong. That's the sort of classic Type A error. If you are like a policy maker, like HCFA is in this condition, where you either have to encourage its use or discourage its use, then for some policy

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questions, not every one because it's more of a subtlety, you really make a decision, do I think I'm more likely to win this way or win that way, and then your P value is .50. And all I was drawing with the analogy here is if you wanted me to take my best guess. If someone said you're going to make 20 bucks or lose 20 bucks, do you really think you're better off with biofeedback, I'd would probably put it on yeah, you probably, are. But if someone is going to say are you sure, adequacy, then I'm back to a 95 percent. Does that clarify it?

DR. ZENDLE: You went from percentage to a point. The point is, it's 5 versus 50 percent?

DR. EPSTEIN: Thank you.

DR. GARBER: I don't have a very clear view at the end of the table. I thought I saw Dr. Bradley's hand up.

DR. BRADLEY: I think you also wanted the yes answers also. I voted yes on the issue because probably like an orthopedic or ENT, the question is whether someone is pregnant or not, pregnant and virgin or not virgin. And looking at it in black and white, the data that was shared at the end of the morning by Dr. Perry, looking at

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what we would now consider a very archaic method of instruction, as you mentioned in terms of just handing out something, talking with the patient, obviously in real life this millennium is no longer being practiced that way, and then looking at the other studies that we have available to us, the definition of just basic instruction often is muddy. But I think if we just look at the very pure definition of PME with written instruction or handouts given, and then add on all the other things that biofeedback does when it come to

enhancing the patient's perception of body parts, the kinesthetic or the subtleties that the patient is able to determine by having the biofeedback, that it does add in my mind a positive benefit or is an adjunct to PME. And that testimony from patients, and just the actual procedure itself, I think it does make a difference in terms of patient outcome, and I am very comfortable with my decision and vote, again, using the very basic definition of written instruction and handout, and I think the other method does add to patient care.

DR. GARBER: Thank you. Maybe I could take this opportunity to make somewhat of a general comment. I didn't have the opportunity to vote and

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therefore, I don't have the obligation to explain my vote, but I did want to address a point that Dr. Perry raised, which I think is a very important one. And he pointed out that companies manufacturing equipment don't have the money to support clinical trials, and I think that's likely to be true in a number of contexts, and it's a very unfortunate circumstance. There are some areas for a variety of reasons why trials either can't be performed or won't be performed because there is no interested party with the money to pay for it.

And I think what the panel has done here is just addressed the adequacy of evidence, and Dr. Perry's statement is not really about whether the evidence is adequate, but whether it's really feasible to put together adequate evidence, and that's an important message, and I have to say that just speaking as an individual, I hope that HCFA takes that into consideration. Our panel is structured to give a clean answer to a clean, or we thought clean question. But it would really muddy the waters to say that evidence is adequate when it isn't, solely because it's difficult to conduct well designed trials. That does not mean that HCFA should ignore that fact.

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There are situations when the trials can't be done and I think that HCFA should exercise some discretion in deciding to cover in some circumstances, when we as a panel say that the evidence is simply not adequate. So I don't think

that those considerations should be ignored. It is a sad truth that it is not always feasible to conduct well designed studies, and HCFA has the responsibility to decide whether to cover or not in those circumstances.

But we've spoken about what the evidence said, we have not expressed an opinion about whether it's feasible to get better evidence. That's not really part of our role, although we are certainly welcome to comment on that, if you think for example it just wasn't feasible in this area to conduct studies. Les?

DR. ZENDLE: Well, I guess this is sort of related to that. If I were asked to vote whether handing out a written instruction sheet or giving verbal instructions on the PMEs was useful, I would say there is pretty good evidence that it's not, and that there needs to be more than that to be considered. My understanding is that we were including, we were not limiting the PME group to

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only those people that got sheets of paper or verbal instructions, but it was a broader group, and if there is a way of separating that group out, I think if we were able to look at that evidence, we would see that there is a difference.

DR. BRADLEY: Most of the studies, I think unfortunately in terms of inclusion criteria, as Diane has mentioned, it's just not very clear in terms of what's actually happening. So much of what we actually do, we just incorporate it into clinical practice. We are incorporating a lot of -- it becomes the standard in terms of the issue of some of the subtleties of biofeedback, however you want to define it, whether it's hands in the vagina, whether it's a visual analog, whether it's bells and whistles, somehow that's being incorporated, and very few of the studies just look purely at just written.

I mean, if we had six studies or eight studies that purely said we handed out a handout and just said read it and do it, and then add on whatever instrument or instrumentation is used, we would end up with the kind of data that Dr. Perry has talked about. But the studies at least as far as I've looked, as I have read them and listened to

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discussions, so much else is -- there's a lot of little fine things that are happening sort of off record.

DR. ZENDLE: Which is why AHCPR did not separate out the different kind of biofeedback, and I agree with that.

DR. MAVES: Alan, in my no vote, I think it helps just to corroborate that. I think I feel a little bit the way both of you did, and I'll try to explain that. I was presented with the difficulty of making an incremental decision when essentially you have a continuum of evidence. And the interventions, if I can sort of take a look at pure PME, and I was looking at the categories of effectiveness, I suppose it would fall somewhere in the five or six category. If we looked at biofeedback, I think I would agree with our colleagues from the AUA, it's somewhere in the three to four. The problem I had is that when you went back to the literature, when you looked at what documentation did you have to make that decision, it just simply wasn't there.

DR. LANDY: I didn't get to explain my yes vote, and part of it is my interpretation of the question is different. I read this question,

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is the scientific evidence adequate to draw conclusions about effectiveness of biofeedback as an adjunct to PMEs? Biofeedback is always used as an adjunct to PME; it's never been used any other way. So to me the question was really effectiveness of biofeedback and there is a wealth of information on the effectiveness of biofeedback as a therapy.

DR. HILL: May I ask a hopefully clarifying question? If you assume arguendo HCFA's definition for the purpose of the question when we asked the mechanical and electrical device as biofeedback, as distinct from other kinds of biofeedback.

DR. LANDY: Yes, I still answer that.

DR. HILL: Is that first line therapy, is that's what's always done, and would that change your vote?

DR. LANDY: Yes. And no, that would not

change my vote. I think if you worded the question, and that's very similar to the original question we got, but if you worded the question biofeedback, does it confer additional benefit, then I would have more trouble based on the data answering the question. But the wording of it is

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biofeedback as an adjunct to PME. That's how it's always used, that's how it's studied in the literature, and all these case controlled studies, and randomized control trials are looking at biofeedback as an adjunct to PME.

DR. HILL: She's right. That's a word game in there.

DR. McBRYDE: McBryde. I'm probably saying the same thing just in my own words, and that is that I believe that biofeedback as described by all of you is efficacious and I think it's being used and being used in practice settings all over the country, and for the most part it's mainstream, which makes a little bit of this vote almost after the fact, because it's kind of a done deal. I voted no though, because given the rigid, the shotgun standard for PME, and kind of the rigid definition of biofeedback, and looking at the literature and correlating those things, you have to say no, and that's why my vote was no. Perhaps the future will tell a different story, if indeed there will be more.

MS. GREENBERGER: I obviously can't vote, and I think I made my position, but I just want to say, this is really uncomfortable. I mean,

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there's so much confusion about the question, whether biofeedback has been used, as Lisa said.

And I know we're not supposed to be talking about coverage, but let's face it, this is about coverage ultimately, and this is a big issue that's been going on at HCFA, and I am involved in other diagnostics, and other issues, where again, there aren't large enough clinical trials to make determinations on the scientific evidence and yet in my case, since this is the group that I represent, women don't have access to these diagnostics because they don't have large clinical trials, and it's because they're not drugs and

they're not manufactured by the drug companies, they're just are unable to support them.

So I just, I want to go on record also saying that since my group is the Society for Women's Health Research, I understand research, I understand the importance of peer review scientific research, and I am not for a moment discrediting that or overlooking the importance of that. But I just think in this case and in other cases I am familiar with, we don't have the scientific research for other reasons and because we don't have it, we may ignore an efficacious treatment for

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people, and I think that's a real problem. I don't know how to get around it. I know you've got to have the research, but I would hate to see a treatment that works and that people are supporting, both patients and providers, ultimately not be available.

DR. ZENDLE: But sometimes when research isn't done, treatments are made available that actually cause harm.

MS. GREENBERGER: I know, but this is not one of them. And what may happen is that people will be put on drugs or have surgery, and they will have more invasive and more problems, when they could have had a less invasive and an easier treatment. I'm aware of that, and generally speaking you're right, but in this case, I think there is a lot of confusion about separating this from the traditional therapy and that makes me, I would hate to see people not being able to use this because of this decision.

DR. ZENDLE: And I wanted to make clear that I was not voting on a coverage issue. If I had been, my vote would be different.

DR. LANDY: I think there is a big problem with the question, and what was put forth

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to the panel to answer, is what I'm getting from this discussion, and that people may have addressed this topic differently.

DR. ZENDLE: How would you word the question differently?

DR. LANDY: Well, I think the first set of questions we got a month ago, the first question

was effectiveness of biofeedback in routine clinical use, just determining effectiveness of biofeedback as a standalone therapy. And then the second part of the question was, comparing the effect of adding biofeedback to PME alone. And answering that in a two phased question I think would discern and weed out part of the feelings of what we're discussing here. And I think it would give maybe HCFA a little more information to make their decision with.

DR. RATHMELL: Just a comment. I think that if we were to adopt one question that we could answer today, it would be exactly what's in the technology assessment. And it's very clear and it's better worded. For urinary incontinence patients, does adding biofeedback to PMEs result in greater improvement in health outcomes than the use of PMEs alone? That's very clear. We may not be

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able to make that decision, but that's what the technology assessment does, that's what all of the discussion today did. The written question is more nebulous.

DR. GARBER: I think the written question was supposed to be interpreted as corresponding to what you just read from the assessment.

DR. RATHMELL: I think they were supposed to be the same thing.

DR. GARBER: Yeah. I think the panel's deliberations, and I hope if any of you who disagree will correct me now, have worked on that assumption, that it's a comparison of PME plus biofeedback to PME alone, not a comparison of PME plus biofeedback to placebo or something like that.

DR. ZENDLE: Or inadequate PME.

DR. GARBER: Right.

DR. ZENDLE: Could we clarify the motion then?

DR. LANDY: Can we answer question 2?

DR. GARBER: No. The procedure is that if it's no on 1, we cannot go to 2.

Well, if nothing else, I think this

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illustrates the importance of framing the question

very carefully, and this is something that we will always face, but it's what is the comparison that we're making? Is it between two treatments, is it between a treatment and a placebo? What's the standard of care, what's a relevant question, and in fact, the questions come from HCFA, they do not originate with any member of the panel. I'm sure that HCFA would appreciate our input to make them reasonable, but since they ultimately will be making coverage decisions, I assume that the phrasing of the questions is in part dependent upon reimbursement issues. So something that we may not feel is clinically the most important thing might turn out to have a great deal of relevance to their reimbursement decisions, so we have to depend upon -- well, they have to exercise their judgment in formulating the question and we have to do the best we can to answer them.

DR. HILL: I had a couple closing remarks since we are at the end here, if I may. I just wanted to say real briefly what's going to happen next. As Allen said this morning, this is not a coverage decision. HCFA has the responsibility of deciding whether or not this

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treatment modality is reasonable and necessary within the meaning of the statute that Congress has given us. We hope that this panel will follow the Executive Committee's recommendations in this regard and explain its conclusions in writing. In addition to the opportunity to explain the vote, statements that any of you care to submit can be sent in and they will be considered by us in our decision making about coverage.

And so, Miss Smith, if you want to send that article in at that point, that gets to be included in our subsequent deliberations, even though we couldn't allow it to be handed out here.

And then there will be a summary of this that we will try to compose and get Alan to look at, and that will be part of the record as well, and that will go the Executive Committee on June 6th, where they will look at it and hopefully ratify it and pass it on to HCFA, and that will be the basis of our making a coverage decision on this.

Despite the questions about the question, despite the disagreements about the procedure, this has been very helpful to up us and it will go a long way towards giving us what we

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want, which is an evidence based decision about coverage. Thank you.

DR. McBRYDE: Mr. Chairman?

DR. GARBER: Yes.

DR. McBRYDE: I just want to say, this question number 2, if the evidence is adequate to draw conclusions -- it was, wasn't it -- what is the size -- it doesn't say positive or negative -- if any, to the overall health effect of addition of biofeedback and so forth. That might be next time rephrased differently too, because that implies you should go ahead to number 2 whether it's positive or negative, as long as you draw a conclusion, whether it's no or yes.

DR. GARBER: That's correct. If you conclude that the evidence is adequate, you go to number 2 even if the evidence shows that the intervention under study is worse than whatever it's compared to. Number 2, you proceed to number 2 after you've made a determination of adequacy.

DR. McBRYDE: Did we proceed to number 2?

DR. GARBER: No. We concluded that the evidence was not adequate to make any conclusion

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for or against.

DR. McBRYDE: I know I'm confused. I thought we did conclude that it was --.

DR. GARBER: Not adequate.

DR. McBRYDE: Well, that's a conclusion.

DR. ZENDLE: We did not conclude that there was evidence that it's not efficacious.

DR. McBRYDE: That's not what the question says. It doesn't say do not go to number 2 if you vote. Am I crazy? I don't think so. But at any rate, I think that can be phrased a little better.

MR. COYNE: As I recall, the presentation by Dr. Simon had a decision tree on it which may have helped clarify the very

understandable question by Dr. McBryde. But I believe the intent as clarified by the description was that it, that there not be necessarily a progression to number 2 if indeed a finding of an inadequacy was first arrived at in number 1.

DR. McBRYDE: So that should be reflected here too.

MR. COYNE: I agree editorially, that's a very valid point. Thank you.

MS. CONRAD: Okay. To conclude today's

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panel meeting, I would like to announce the proposed schedule for future meetings. The tentative dates, and I mean tentative, for June, are 14th and 15th, and secondly, October 17th and 18th, and I emphasize, these dates are subject to change.

For continuing information, you may visit our web site at https://www.cms.hhs.gov/mcac/default.asp. I would like to ask the panel members to please linger for a few moments. Perry Bridger and Sue Gleeson wish to distribute some evaluation forms, and if you would just take a moment to complete them, that will make them happy.

DR. GARBER: At this point I would entertain a motion that this meeting be adjourned.

DR. EPSTEIN: So moved.

DR. MAVES: Second.

DR. GARBER: All in favor?

MS. CONRAD: Thank you very much.

(The meeting adjourned at 4:30 p.m.)

Transcript for April 13, 2000 Meeting

Please Note: This transcript has not been edited and CMS makes no representation regarding its accuracy.

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PELVIC FLOOR ELECTRICAL STIMULATION FOR THE TREATMENT OF URINARY INCONTINENCE

HEALTH CARE FINANCING ADMINISTRATION
Medicare Coverage Advisory Committee
Medical and Surgical Procedures Panel

April 13, 2000

Baltimore Convention Center
Baltimore, Maryland

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Panelists
Chairperson
Alan M. Garber, MD, PhD
Vice-Chairperson
Michael D. Maves, MD, MBA
Voting Members
Angus M. McBryde, MD, FACS
H. Logan Holtgrewe, MD, FACS
Kenneth P. Brin, MD, PhD
Les J. Zendle, MD
Bruce Sigsbee, MD (Not present)
Linda D. Bradley, MD

James P. Rathmell, MD
Arnold M. Epstein, MD
Temporary Voting Member
Lisa Landy, MD

Consumer Representative
Phyllis E. Greenberger, MSW
Industry Representative
Marshall S. Stanton, M.D.

Non-Voting Guests
Michael Risager, MD
Diane Smith, RN

Acting Director, Coverage and Analysis Group, HCFA
Hugh F. Hill, MD, JD
Executive Secretary
Constance A. Conrad, RN

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P R O C E E D I N G S.

MS. CONRAD: We have a quorum, we are going to begin. Good morning, panel chairperson, members, temporary voting members. I am Connie Conrad, executive secretary of the Medical and Surgical Procedures Panel of the Medicare Coverage Advisory Committee. The panel is here today to provide advice and recommendations to the Agency regarding pelvic floor electrical stimulation for the treatment of nonneurogenic urinary incontinence in adults. At the conclusion of today's session, panel members will be asked to vote on a series of questions. The answers to those questions will constitute this panel's recommendation, which will be submitted to the Executive Committee when it meets on June 6th. When the Executive Committee ratifies the recommendation, it will officially transmit that recommendation to HCFA. HCFA will develop a coverage policy within 60 days of receipt of that recommendation.

For the purposes of today's panel, Dr. Lisa Landy, standing member of the Durable Medical Equipment Panel and noted expert in the field of urinary incontinence received an appointment to temporary voting status.

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Dr. Landy's expertise will enhance this panel's deliberative process.

In addition, we welcome Dr. Michael Risager, carrier medical director for Trailblazers Health Enterprises in the state of Maryland, and we welcome Diane Smith, a urotechnology consultant and continence specialist, as nonvoting guests.

The following announcement addresses conflict of interest issues associated with this meeting, and is made part of the record to preclude even the appearance of impropriety. To determine if any conflict existed, the Agency reviewed the submitted agenda and all financial interests reported by the panel participants. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employers' financial interests. The Agency has determined that all members and consultants may participate in the matters before the panel today.

With respect to all other participants, we ask in the interest of fairness that all persons making statements or presentations disclose any current or previous financial involvement with any firm whose products or services they may wish to

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comment on.

Okay. Let's start with presentation of questions by Perry Bridger, analyst with the coverage and analysis group.

MR. BRIDGER: Good morning. Thank you, and I apologize to those of you who were here yesterday and heard similar remarks. As many of you are well aware, urinary incontinence is a significant health problem for the Medicare populations. For example, the prevalence of urinary incontinence in the above age 65 Medicare population is estimated to be near 35 percent for females and 20 percent for males, with rates even higher in hospitalized older adults and those in long-term care institutions. Urinary incontinence affects individuals' quality of life and often leads to other comorbidities, isolation and depression. Frequently, patients do not report this problem to their families, caregivers and health professionals, and urinary incontinence has

remained an under reported and under studied condition.

In the following two slides I have outlined for you several of the treatments which exist for the management of urinary incontinence.

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These include behavioral interventions, pelvic floor electrical stimulation, pharmacologic therapy, bulking agents, sacral nerve stimulation, and surgery. In general, which treatment options to pursue for the different types of urinary incontinence is dependent on specific patient indications, comorbid states, cognitive function, and the willingness and ability to participate in treatment.

During this two-day panel meeting the Medical and Surgery Procedures Panel of the Medicare Coverage Advisory Committee will review the evidence and make recommendations to HCFA about two of these treatment modalities, biofeedback and pelvic floor electrical stimulation. Yesterday the panel heard testimony and reviewed the scientific evidence about biofeedback and today the panel will hear testimony and review the scientific evidence regarding the use of pelvic floor electrical stimulation. Currently, pelvic floor electrical stimulation therapy is not paid for by the Medicare program.

For the purposes of this meeting, pelvic floor electrical stimulation is defined as the use of a nonimplantable electrical device that delivers

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variable rates of current through the pelvic floor with the intent of strengthening pelvic floor musculature.

The panel has had the opportunity to read the technology assessments, evidence tables and other materials related to pelvic floor electrical stimulation. After hearing the public's comments and scheduled commentary presented here today, the panel will be asked to vote on a sequence of questions regarding this therapy. All of these questions are directly related to the scientific evidence regarding pelvic floor electrical stimulation therapy, and comments made today should be directly relevant to this topic.

Dr. John Whyte, during the HCFA presentation, will more fully address these questions, the points to consider, and the categories of effectiveness. We will now briefly outline these for you. In response to yesterday's comments regarding these questions, we have clarified question 1 to make it more precise. Connie has a copy of these questions, which she will distribute to the panel, and we will provide to the public at the end of my comments copies as well.

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The first question we are asking the panel to discuss for pelvic floor electrical stimulation therapy is the following: Is the scientific evidence adequate to draw conclusions about the effectiveness of pelvic floor electrical stimulation compared to placebo, pelvic floor electrical stimulation compared to PMEs or alternative nonsurgical techniques, PMEs and pelvic floor electrical stimulation compared to PME alone, in the Medicare populations for the following three indications: Stress incontinence, urge incontinence, and post-prostatectomy incontinence.

In answering this question, the panel should consider the following points: The adequacy of the individual study design, the consistency of results across studies, their applicability to the Medicare population, and their applicability beyond the research setting.

If the evidence is adequate to draw conclusions about pelvic floor electrical stimulation in these cases and the panel votes affirmatively on question 1, the panel will move on to questions 2, 3 and 4, which address the size and direction of effectiveness. Therefore, question 2 asks: If the evidence is adequate to draw

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conclusions, what is the size, if any, of the overall health effects of pelvic floor electrical stimulation compared to placebo for the treatment of urinary incontinence?

When answering this question, as well as questions 3 and 4, the panel will be asked to place the size and direction of effectiveness into one of the following seven categories: Breakthrough

technology, more effective, as effective but with advantages, as effective with no advantages, less effective but with advantages, less effective with no advantage, and not effective.

Keeping in mind these categories, question 3 asks: If the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effects of pelvic floor electrical stimulation compared to PMEs or alternative nonsurgical techniques for the treatment of urinary incontinence?

And finally, question 4: If the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effects of the addition of pelvic floor electrical stimulation to PMEs, compared to PMEs alone. Please remember that Dr. Whyte will elaborate on those points more

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fully during the HCFA presentation, and you will have the opportunity as well to discuss them during your deliberations.

We thank the panel members and all of you who have made efforts to participate in this panel meeting regarding biofeedback and pelvic floor electrical stimulation. We look forward to your deliberations.

MS. CONRAD: Thank you, Perry.

DR. STANTON: Alan?

DR. GARBER: Yes, Marshall?

DR. STANTON: Yes. Before we head into the discussions for today, I think there's a couple points that are very relevant that need to be discussed. When I was reflecting on yesterday's deliberations, I think there were a lot of excellent points that were made regarding the burden of proof for conclusive scientific evidence and comparing that with the evidence that's necessary for pointing towards possible improved outcomes for beneficiaries. I think Dr. Epstein's points, vis a vis, P equals .05 versus P equals .5 were particularly poignant on that regard. In clinical practice, our treatment decisions for patients are made by physicians based on his or her

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assessment of the literature and not on a meta-analysis that requires achieving a P value of

less than .05. If the latter were the case, then I think that few treatment decisions would be instituted in clinical practice today.

At the conclusion of yesterday's session, Hugh Hill made some points thanking the panel for assisting in an evidence based process for coverage decision making. These are not his exact words but it certainly was the tone and the point that I took away from his comments. All of this for me raises a lot of concern regarding the weight that this panel's vote is going to play in the coverage decision making process and I think again, as I said yesterday, we should not be so naive as to think that this vote will not play a major role in that decision process.

The process as it is presently designed ignores expert testimony, it ignores public comment, and it ignores the views of the panel's consumer representative. And I asked myself why they should even bother presenting their views. HCFA has convened this panel of experts here who have invested much of their own time and yet the questions that are posed leaves the panel too

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constrained to be of any practical use. As a nonvoting member, I sensed the obvious discomfort of panel members yesterday in being forced to vote one way on a specific question while stating their opposite true beliefs about the therapy that was discussed.

If this new high standard of multiple randomized control trials all having to have the same positive outcome is to be the bar against which all new therapies must clear to obtain coverage, then I fear there are going to be dire consequences. A national noncoverage decision means that no Medicare patient can get the therapy. There is no room for patient appeal. Future clinical trials of that therapy are going to be very unlikely in that scenario. This will stifle the development of new technologies, and I think it's worthwhile for the panel to note that new technologies that come to the market won't be ready for this type of assessment for many years after they achieve regulatory approval.

I see ourselves going down the same road

today and that we went down yesterday, and I have a lot of concerns about that.

DR. GARBER: Okay. Thank you. It's a little bit off the agenda, but I don't think we have a better place to put it, so with the indulgence of the panel I would like to set aside a little time if other panelists would like to comment. Yes, Linda.

DR. BRADLEY: I am very happy that Dr. Stanton had these comments over dinner, and just thinking about this whole process yesterday, I left extremely frustrated. I understand that the Executive Committee needs to set standards, but I think either the bar is so high or if you're doing the limbo, it's so low that you just cannot get under in order to make a decision to move forward.

And I think I have the same feelings. I'm not sure why we have all these people convening here if their testimony both from patients, patients' letters, practicing physicians in the specialty, people who have spent collectively centuries of personal time studying this, and we really are not able to include their personal expertise because of the lack of potential scientific rigor, I think the hurdle is extremely high, and I just am so glad that these comments, I couldn't have said it anymore eloquently. But I also hope that we don't leave today with the same spirit that we left with yesterday. And I would love comments from others that we haven't talked with directly. This is a very frustrating problem.

DR. GARBER: Les?

DR. ZENDLE: If our job had been different, if we had been asked to make recommendations on a coverage decision, I think we would have done it differently, and I think the comments from the public and the professional organizations and the clinical experts would have been quite relevant. I guess because I have been involved in looking at evidence purely from the scientific point of view in reaching a conclusion, and then taking that to decide how you're going to implement that in the real world, that I can separate the two.

I think that it's not unreasonable to decide to cover something even if there isn't scientific evidence, or evidence to a scientific level that it is more effective than other things. But in that case, you have to give some other reason to cover it. And what I don't want to see happen is to have things covered because somebody says there is scientific level of evidence and not say the real reason why it might be covered,

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whether it's a more efficient way of doing it, or it's the standard of practice, those are all valid reasons to cover something. But personally, I like separating what is a purely scientific rationale from other reasons to cover something.

If HCFA, and I guess HCFA is acting under what it perceives were the congressional instructions were, if they decide they want to change what we do to make recommendations on coverage, then I can do that and I would be happy to do it, and I would have reached a different conclusion yesterday. So, I think we do have to get some -- maybe HCFA and Congress and whatever, have to take another look at this to decide what the best way to do this is. But I didn't have any problem with yesterday just looking at the scientific question and reaching a conclusion. I agree though, that if I thought that was going to be, without any kind of other input, the coverage decision, I would be uncomfortable too.

DR. GARBER: Hugh?

DR. HILL: Thanks. A couple of responses. While I appreciate the comments and do acknowledge that they are about coverage and not necessarily about specific evidence on a specific

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case, I do appreciate hearing them. Let me assert to you that we have not ignored expert opinion, public opinion, consumer opinion, that those were all taken into account in the design of the process, that industry and other stakeholders wanted us to go to an evidentiary basis, an open transparent process for scientific evidence as the basis for making coverage decisions, and this is a part of that. And I hope that the panel did not ignore the presentations of experts, the public and

consumers yesterday.

If by not acceding to or agreeing with them we are regarded as having ignored them, that seems a bit extreme. I hope we took them into account. And I didn't hear us asking about whether or not the technology had met the bar of a national randomized trial, and we certainly don't intend to stifle new technologies. But on a hierarchy of evidence we hope that there's some agreement, and there has been in the design of the process, that some sorts of studies are more reliable and the results of those studies are more predictably reproducible than other studies. And hopefully, we can use that hierarchy of evidence and the suggestions of the Executive Committee to try to

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make rational decisions about what we should cover and we shouldn't. And that's why we focus on evidence and your comments about the evidence.

We haven't set the hurdle extremely high. I disagree with that specifically and emphatically. We wanted to hear about it and we did hear about comments about other evidence, and all sorts of things that might be regarded as evidence by some people and not by others were available to you. If you think that the apocryphal story or the odd case report, or the letters to the editors in the journals are evidence and you want to decide on that basis, we want to hear about that. And as you noticed yesterday, we wanted to know what's behind your vote, the thinking behind your vote.

I'm sorry you're frustrated with voting. We think we need that for clarity, but we always want to know the thinking behind it, and we hope you felt like you had adequate opportunity to express your reasoning.

DR. GARBER: Maybe I could just add a brief comment on two points. The first is, the comments of the public speakers, and as I said yesterday, I was personally very grateful to the

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public speakers, because I think that the presentations of the public speakers by in large really did address the questions the panel was posed, and although I didn't ask the panelists if

they were influenced by the public speakers, I got the very clear sense that the panelists took those comments very critically, and the fact that the panelists did not vote the way that some of the public speakers might have wanted them to vote should not be construed as meaning that the panel ignored their comments. I personally found the comments very helpful and it doesn't, the fact that one votes the other way doesn't make that testimony worthless or in any sense less valuable. I think that was a very important part of yesterday's process, whatever the outcome of the voting was. And I hope that we continue to have public commentary of this high quality and I would suspect that in many cases it will turn out to be decisive. So I was not, did not have the sense that that was just an exercise that we went through; I thought it was extremely valuable to our deliberations.

The other point that Marshall raised, which I would like to say a word about on behalf of

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the Executive Committee, is about the standard of evidence and in clinical practice what the standard of practice is. We are not making coverage decisions but as you correctly pointed out, we as a panel are making recommendations that will be an important part of coverage considerations. And by widespread practice, the level of evidence that is used to make coverage decisions is entirely different from what is used in the clinical setting, in the doctor to patient relationship, because in the doctor-patient one-on-one setting, all kinds of individual factors come into play, things the physician, the patient know that aren't fully reflected in the literature, and we make our best guess every day about what's the best treatment, and here making the best guess is absolutely appropriate.

Now I'm not going to comment on how HCFA should make coverage decisions. I don't really know the answer to that, but what I do know is that when it comes to coverage, you use a different standard of evidence. That is what is done around the world, it's what is done by different organizations in the US. A coverage decision is

not the same thing as a one-on-one patient-doctor
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treatment decision. They are clearly related since coverage is a way to enable the doctor to apply a treatment and have it covered by insurance, but the standard of evidence by standard of practice is different. And that is something that the Executive Committee unanimously agreed to as a concept.

Now, it is entirely possible that the panel set the bar too high for the evidence standards yesterday. HCFA and the Executive Committee did not say specifically what kinds of studies would be needed because they expected the panels to come to a conclusion in each context and you did reach a conclusion yesterday rightly or wrongly, and there was a strong majority on these questions.

Now, that doesn't mean that you have to use the same standard in every case. As I said yesterday, we're feeling our way through this process. But I don't think that it would be appropriate, at least from the Executive Committee's point of view, to say the best guess should be the standard of evidence, that is, what we happen to think is best regardless of the quality of the evidence. That's why such a big
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point was made about evaluating adequacy of evidence. Jim?

DR. RATHMELL: I guess this would be a segue into today's topic. My discomfort is very very specific. Yesterday we considered a technology called biofeedback and we were posed a very narrow question comparing one type of control versus the technology itself. And today we are considering a different technology, the electrical stimulation and yet, we're looking at the efficacy versus many different controls. I feel as though we were steered into a very narrow decision, where there was much more information about that technology available, and if we were really supposed to look at the scientific evidence about that technology, we should have looked at everything that was available. Very similar to what we're doing today, versus placebo, versus

other types of controls.
There's much more information about biofeedback that we ignored, to the point where when we were asked a question, the question was so narrow that the majority of the testimony that we heard, and the allusions or the references to a body of literature that wasn't in the technology
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assessment, we had to ignore. But I was left to vote opposite my feeling about the technology without really knowing the scientific evidence, and this is a scientific panel, and I really would have liked to have access to all of the scientific evidence about that technology.
DR. GARBER: Hugh.
DR. HILL: Thank you, Dr. Rathmell. We, as you pointed out, we're learning in this process, and this is the third meeting of a Medicare coverage advisory panel, and the first one of this panel. And one of the discussions that we had internally was how specific to be. We acknowledged and intended yesterday's question to be very specific. And we've learned in the first couple of panels that if we are not very specific about questions, if it's vague or if we're just sort of going to have a discussion about a technology, the information we get back may not be as useful to us in a scientific sense. So, would you extend your remarks and comment a little further about how you would strike that balance?
DR. RATHMELL: Well, let's just be very specific. Can you address why today we have three questions posed about a technology versus other
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control groups, and yesterday we were posed only the third question, which is the additional benefit of adding that to PMEs? This is very specific about this. Why do today's questions differ so much from yesterday's questions, and why were the first two components of the question posed today left out of yesterday's question and technology assessment?
DR. HILL: In some cases the answer to that will be historical, because of the way the requests have come in or the questions have developed. Sometimes the questions will grow

nationally out of our own review of the evidence and what we think can be usefully asked. But in this case, perhaps we can, if you don't mind me asking the analysts who were involved in this, to comment on why there is a difference. John, is that appropriate.

DR. WHYTE: It's a very reasonable question. On the issue of biofeedback, we made the decision to view biofeedback purely as an adjunctive therapy, so in that context we would have to look at PME and biofeedback compared to PME alone. That was not the same assessment that you will hear about today.

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One question did deal with pelvic floor electrical stimulation as adjunctive therapy, but based on many of the requests that we received as well as data we had looked at, there was also an understanding that pelvic floor electrical stimulation could be used as a primary therapy and not as adjunctive. So given that, we then had to look compared to placebo, and compared to other therapies, nonsurgical therapies. But that was not the case in terms of how we interpreted the use of biofeedback. I hope that answers your question.

DR. RATHMELL: It does, except that we heard extensive testimony yesterday about how biofeedback was inextricable from the way that PMEs are practiced in this day and age, and so I was left with the feeling that an artificial distinction had been drawn that couldn't be drawn. It's impossible. There's a continuum between PMEs where a pamphlet or videotape is given to the patient and no further instruction or interaction with the patient, and an electronic device at the other even of the spectrum, that is hooked up to the musculature, and there is extensive interaction with the patient. So there is a continuum and yet, we tried to make some distinction that's impossible

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to make from the daily practice in this day and age. And from the literature alone, it was impossible to make either way, but yet we made it yesterday, and were forced on a decision that had an artificial boundary.

DR. GARBER: Michael Risager?

DR. RISAGER: I need to differ from the previous speaker. I believe we had ample literature and ample resources. One thing that struck me after yesterday was the, here's something that appears to have a place. It's amazing how with 13 million people with stress incontinence who have been treated for years with some form of biofeedback, whatever you use to monitor, to assess the, to develop the musculature, why there have not been better studies. It amazes me. So I think we, I feel we did the right thing to have a clear and precise objective. I would with respect, suggest that we go on, and rather than compare and agonize about the today's, yesterday's proceedings compared to today, let's go on and do today what we have to do, and then learn from that. In short, I think we did the best we could yesterday.

DR. GARBER: Ken?

DR. BRIN: I share a lot of the

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discomfort that has already been raised, but I also recognize that this is a new process and that we're blazing new grounds. I think a lot of my level of discomfort will be assuaged when I see what the end result ends up being. We were asked a very very specific focused question. I believe we answered appropriately, given the question we were asked. The question then arises, how that will be used by HCFA to determine coverage? If it's used with all of the comments that have been made, such as the fact that the baseline comparison is giving biofeedback as part of the standard of care, and that's factored in there, I think we will be very comfortable that our advice was used appropriately. If in fact the outcome is different, there will be some concerns. And I think we should just move on and then watch what the end result of the process is, because it's a new process.

In my own area of cardiovascular disease, stinting is an adjunct to coronary angioplasty. For certain lesions, there's never been and there never will be a good double blind, or certainly not double blind, but randomized study of stinting and nonstinting, because it's standard

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of care. And if a panel were convened to take a look at stinting as an adjunct, it probably would have to make a very similar decision, because the studies haven't been done and won't be done. And if the outcome of that were, well, stinting won't be covered, that would be a different issue. I think we need to see what the end result of our deliberations and advice is, as passed on by the Executive Committee, and as coverage decisions are made by HCFA.

DR. GARBER: Thank you. Arnie?

DR. EPSTEIN: I think I can articulate with some difficulty, but I think I can do it profitably, what makes the discomfort level of some of the individuals so high, and set that in relief for people from HCFA to consider. I'm going to flip for a moment into the coverage decision. I could imagine many, but at least two ways that people might think about coverage decisions. One is, we're only going to cover procedures where there is clear scientific evidence indicating the procedure's effective or efficacious, you'd like both.

The second runs orthogonal to that. It says, in the face of broad consensus from medical

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experts that a procedure is effective, we will cover it absent evidence that it's not effective, so long as the clinical downsides are minimal.

We have -- I can think of both of those approaches being a reasonable approach for coverage. What makes everybody uncomfortable is that the scientific question that we've been asked is designed to lead to the former approach as opposed to the latter approach. We could have been asked two questions: Is the scientific evidence adequate to show that the procedure works? Answer, no. Is the scientific evidence adequate to show the procedure doesn't work? Answer, no. We didn't get asked the latter question, which makes everybody worry that when we get to the coverage decision, we're going to take method A and as opposed to method B, and I think that's what the discomfort level is all about.

MS. GREENBERGER: I think -- I would be astounded if the coverage decision went the other

way. It would be historical precedent frankly, if we came out with the results that we did yesterday and that HCFA decided to cover this. So I think what you're saying is correct, but we're left with the decision that we made yesterday.

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I also think that perhaps we should ask why there aren't, why there haven't been clinical trials. And I heard a lot of good reasons yesterday that people told me that haven't come out, that perhaps they would like to share, if they're able to. And I think this is going to be the case. Dr. Stanton said there are a lot of new tests, diagnostics and therapies unfortunately, that cannot be, that nobody can afford to do mass clinical trials. And I understand that we need to have the scientific evidence; we can't do a procedure or have a diagnostic that we don't know for sure that it works.

But this particular one we're discussing, and certainly the one yesterday, I mean, this is not something that's going to be dangerous. And clearly, I think the clinical evidence has shown, and still we have confusion over other whether we're even asking the right question. If this is standard practice, then it's being used anyway. So I think the question -- I mean, I don't know what the procedure is now at this point, but I just think that the way we answered this question is going to ultimately result in a noncoverage decision, and I think that

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for all these people out there that have been covered by this or have been treated in this manner, not to be covered now I think is outrageous.

I also think that we're changing the question. My understanding, and correct me if I'm wrong, that the question today was changed again. I was told by some people in the audience that it was changed again. The testimony from the public is given to us now so that we don't have time to read it. And I'm just very uncomfortable with the whole process. I think this committee took indicate years from congressional mandate to actuality, and you would think that we could do a

better job than taking so many years to put this together.

DR. HILL: Your comments are reinforcing our perception of the importance of the questions, the critical nature, the central nature of the questions that we ask you, and I hope that you will give us your thoughts after this, and we will pass them on to the Executive Committee and they will form a part of our discussions about how we modify this process as we go along.

MS. GREENBERGER: We would like to write

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a letter, some of us, to the Executive Committee, if we may.

DR. GARBER: Diane?

MS. SMITH: I just would like to say, I think the problem really was the question, and I think that was because of the misunderstanding of those posing the question, and I think that that is a central issue to why almost every person who voted no then said, but if I had to made a coverage decision, I'd say yes. And that's because, if the question had been, if biofeedback has efficacious applicability in doing pelvic muscle reeducation, does it? You would have several studies that were thrown out that would have shown that compared to a waiting list or a placebo effect, overwhelming it has efficacious evidence, significant efficacious evidence, better than some other continence therapies that are routinely reimbursed.

So I think that is really a very valid point and should really be considered by HCFA when they are making their coverage decision, that the question was narrow enough to achieve a no, because the evidence simply was not there because the people doing that research never even assumed that you would ask that kind of a question, because the

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common practice is to think of using biofeedback to teach pelvic muscle reeducation. That is in all of the professional literature, urology, nursing, gynecology, physical therapy, and this is very important.

Even Dr. Garber said, I don't have a vote, but I want to make a statement about coverage. He said, I think that there is evidence

for coverage. And I think that's very important, and should be part of what people are considering when they are making this decision. And I think that it's unfortunate that biofeedback was the first therapy to be looked at in this manner, because it actually isn't new technology which would -- there are examples in urology which is new technology, which there is some clear scientific evidence perhaps, that could have given the panel a level of comport, you know, to play around with appropriate questions. Biofeedback, because it's been around for so long and because it has become a standard of care, it's just inherently difficult to make that type of a question stick.

So I was uncomfortable also, but I really wasn't depressed. Of course, if you know me, you know that I never get depressed. And the

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reason was because every no was punctuated with a yes, in my mind. Every no was punctuated with a yes for coverage, because they said clearly as a physician today, I am voting no because of the question. If I had to tell you if I wanted my patient to have this, I would say yes. And that's what I heard.

DR. GARBER: Before I recognize Les, Diane, I do want to correct a statement you made, or else a statement I made and didn't mean. I don't believe I ever expressed an opinion about coverage. But what I did express an opinion about was that I hoped very much that HCFA would include other information such as the public testimony in making their coverage decision. And if you ever hear me making a recommendation about coverage from the chair, consider me to have a ministroke, and strike it from the record.

MS. SMITH: Really, to me of course, it seemed like a very positive statement.

DR. EPSTEIN: Give some balance to the record.

DR. GARBER: Thank you. Les.

DR. ZENDLE: I think if we had been asked to make some decisions about coverage, then

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there would have been some other questions that we might have wanted to go into, like for example, how

much biofeedback is needed. Because don't forget, when HCFA is going to decide whether it's going to cover something, it means that they're going to pay somebody to do something. Now, if something that costs $50 is as efficacious as something that costs $10,000 dollars, I hope that HCFA won't use our tax dollars to pay for the $10,000 thing. That's a different question, which would require lots of different kinds of information. So I guess that's why I was comfortable yesterday with not having to address the coverage issue.

I would hope that when HCFA does address the coverage issue, they are going to have to look at some of those other things and take that into consideration. I don't personally know how they will do it, but I guess I'm okay with the fact that they didn't ask us to do that.

MS. GREENBERGER: Let me ask a question. What are we doing here? If this is, the decision that we came to yesterday, are they going to look at it and say, well, they didn't think there was enough scientific evidence to prove that it was efficacious, but we're going to cover it

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anyway?

DR. ZENDLE: Yeah. They do it all the time, and other insurers do it too.

MS. GREENBERGER: I find that hard to believe.

DR. GARBER: Let me just make a comment about this. There were extensive discussions about the role of this panel. We don't know all the details about how Medicare is going to make coverage decisions and as I mentioned yesterday, they are formulating their set of rules. So I assume this is a work in progress from their point of view as well, and I hope you will comment on that. But they are asking for very specific kind of information from us, and the fact that they said that this panel will not make coverage decisions indicate they want a particular kind of evaluation from us. And since we are not making coverage decisions, it would seem it's incumbent on them to include other kinds of information in their decisions.

And again, if they happen to make a

coverage decision when we say as a panel that the evidence was inadequate, that doesn't mean that we were ignored. It's just that the information we

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provide is one component of their decision making about coverage, it may or may not be decisive. We don't have experience with this process to be able to say anything about how it will be used, it will be a guess at this point. But the fact that the coverage decisions might not go the way one would predict on the basis of the panel deliberations, does not mean that the panel's deliberations were pointless.

MS. GREENBERGER: But if you flip it -- I mean, let's say it was an invasive procedure that could have some danger attached to it, and the committee decided based on the research that this was not efficacious and could have possible negative results, you wouldn't expect HCFA to cover it then, would you? I mean, how do you make the distinction between a decision based on everything that we have said here today and how they're going to get that information, and a decision based on something that we really think is not a good idea to cover? So I don't understand how it's going to be translated.

DR. GARBER: Well, let me just give you an example based on other organizations that do similar kinds of analyses. It may be that the

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literature is not clear on just routine reading; until a study is done, we can't be sure whether the evidence is adequate. And a massive amount of time went into this evidence report that we were given. And they may conclude on the basis of an exhaustive review that the evidence is inadequate. For example, a disease may be very rare, so it's absolutely infeasible to do well designed studies, you simply cannot recruit enough patients to have adequate statistical power. It would be very reasonable for any coverage body to decide the evidence is inadequate, but it will never be feasible to study this adequately, and the preponderance of evidence supports making this available, and therefore, they make a coverage decision. And that can happen sometimes.

Now obviously, if our panel concludes there is clear evidence that a treatment is harmful, then it would be shocking if HCFA made a decision to cover, but I suspect that the disparity between what the panel concludes and what the coverage decision will be will revolve around this issue of adequacy of evidence. They might decide it would just not be feasible to get adequate evidence in a particular area.

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DR. HILL: We had hoped that this kind of discussion would occur in the context of the Executive Committee's meetings. I appreciate hearing all this. I hope that we will be able to move on to the agenda today and get an answer to the questions that we've asked, and invite you all to send in these good comments, appear before the Executive Committee at it's June 6th meeting. I'm sure they would be pleased to hear and take into account your comments about how these panels should be functioning. In the design of the process, that was the intention, that the Executive Committee would have some oversight.

I understand that some of this is necessary, but I'm hoping that it might be possible before the day runs too far and too long into our agenda, to go ahead and address the specifics.

DR. GARBER: Thank you. Logan, and then Marshall.

DR. HOLTGREWE: I think we have a substantial body of work to do today, and I wonder if we shouldn't press on and do it rather than to constantly revisit what we did yesterday by a substantial overwhelming majority. So I would certainly think we ought to press on with our

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duties.

DR. GARBER: Thank you.

DR. ZENDLE: Can you just confirm that the Executive Committee will have the transcripts of our meetings, of our comments? We don't have to repeat our comments, do we?

DR. HILL: No. That will form a part of the record that they have. But they will be focused on the outcomes in deciding whether or not to pass that on, ratify and pass that on to HCFA.

So, if there's some point that you particularly want to emphasize, or some argument that you want to elaborate how this process should be undertaken, I encourage you to go ahead and send that in. Not only do we want to look at it, but the Executive Committee will too.

MS. CONRAD: Thank you. Appreciate your tolerance. Let's proceed with the open public comments, the scheduled speakers. And the first scheduled speaker is Margaret Degler, who will be followed by Dr. Peter Sand.

MS. DEGLER: Good morning, panel members of the Medical and Surgical Procedures Panel. My name is Margaret A. Degler. I am a nurse practitioner, duly certified in geriatrics and

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urology nurse practitioner. I have absolutely no financial gain from being here today from any of the parties that are here today. I am in practice at Geneto Urinary Associates, Limited, a urology practice in Reading, Pennsylvania, as the continence director of a nonsurgical program for urinary incontinence.

The information that I'm going to share with you today is from my typical routine clinical setting. What I have done is extrapolated data from the age population 65 and over from the dates of January 2nd, 1998, through December 31st, 1999. The total number of patients that I have seen for electrical stimulation in that time frame was 106. The question that we are all here to answer today is, is the scientific evidence adequate to draw conclusions that functional electrical stimulation is efficacious in this patient population? As an expert clinician in this area, I can absolutely say yes, the clinical basis is there. Is the scientific data there? We are going to hear from some of the principal investigators from the studies that were reviewed in the TEC report later today.

I share with you now the findings of the

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106 patients whom I saw over those two-year time period for electrical stimulation. Of the 106 patients, 15 were male; of those 15 male, 13 were post-prostatectomy, two were Parkinson's disease.

Of the female, the majority was combined stress urge incontinence, and there were a few simple stress or detrusor instability patients. That data was extrapolated from urodynamic studies that clearly indicated whether there was detrusor instability, sensory urgency, or combined stress detrusor instability components.

In terms of percentage of improvement, of those 103 patients, in the 95 to 100 percent category, there were 19. In the 76 to 94 percent category, there were 20. In the 50 to 75 percent category, there were 32. And in less than 50 percent, there were 35. If you look at those statistics, over 70 percent of those patients aged 65 and older were significantly improved by the use of electrical nerve stimulation.

And to that, I call your attention to an article which you have by Magnus Fall, Advantages and Pitfalls of Functional Electrical Stimulation. And in the Advantages and Pitfalls, he bullets some particular areas of interest. He refers to this as

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FES, functional electrical stimulation. On page 4, with the pitfalls of functional electrical stimulation, it is interesting that the first pitfall he notices is treatment tradition as one obstacle. The clinician using FES for incontinence is trained to use drug therapy or surgery, FES is an alien principle, and the physiologic rationale may be difficult to accept, not having had the opportunity to learn the mechanisms of action in more detail.

In terms of the positive advantages, he notes, for FES, this method has a firm physiologic basis. A variety of lower urinary tract dysfunctions are accessible to FES. Many research groups at many centers have consistent, similar and favorable results as reported above. It is very difficult to believe that the great number of patients treated in different clinical environments in a number of different countries would respond so favorably had the treatment not had good efficacy.

Next he states, FES is a cheap nondestructive method with very few side effects. In standard external electrical stimulation, no irreversible surgery is involved. As with drugs,

there is no general influence on the receptor
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systems because of specific peripheral activation of complex reflexes. The cost of one year of treatment equals that of one year of conventional drug therapy, and FES has a potential curative effect; drugs do not provides that unique effect.

In closing, I would like to read excerpts of a patient letter, one of my patients that was sent to the panel. This is a post-prostatectomy individual and he has given me permission to read this today. I Glen Hostetter, was diagnosed as having prostate cancer April, 1997. I had a radical prostatectomy done on July 23rd, 1997, followed by 33 treatments of radiation therapy training, in January of 1998. A few months after the therapy I began to have urinary incontinence. My doctor prescribed numerous medications which were not helpful.

MS. CONRAD: Time.

MS. DEGLER: He then referred me for electrical nerve stimulation, and with that I had a welcome success. I strongly urge that the treatment for incontinence be continued.

And to answer the question on a clinical basis, yes, functional electrical nerve stimulation does have efficacy in this patient population.
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Thank you.

MS. CONRAD: Thank you. Dr. Sand. And the following speaker will be Dr. Whitmore.

DR. SAND: Thank you. Good morning. Thank you very much, Miss Conrad, for the opportunity to present before the panel. I am Peter Sand. I am an associate professor of obstetrics and gynecology at Northwestern University Medical School, and the director of the Evanston Incontinence Center. My travel and expenses here today were supported by EMPI Corporation. I've participated in numerous clinical trials using US stimulators and international stimulators over the last 15 years.

I want to talk to you and establish that there is consistent objective data to support that PFES is effective in the treatment of genuine stress incontinence, and there is a study that has

shown that PFES is also successful in resolving detrusor instability in the Medicare aged population, as well as having a long-term efficacy and durability.

The uncontrolled trials, while not as scientifically rigorous, are certainly useful to evaluate the subgroups that aren't of value by

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randomized control trials. And they are certainly available to us; there are more than 200 such studies in literature, and may be valuable as evidence if we have established the placebo effect in the controlled trials. And certainly, these are very valuable to evaluate the long-term effects that can't be effectively evaluated in randomized control trials because of practicality and expense.

Long-term efficacy and durability, I've selected four papers that were rejected from the TEC analysis because they're uncontrolled trials, but they are available to you and are in the bibliography. And in the notes of my presentation, those references are also listed. These trials clearly show at one to six years, significant durability and long-term efficacy with continued use of the device. And if there is time later on in the discussion, I would like to address some of the long-term efficacy and even cure of patients with the use of PFES. In a report that I report that I've highlighted by both Krajl and Lukanovic, in more than 300 patients, women specifically over 65, we also see that this is quite effective, specifically applicable in the Medicare

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population.

Now, I wanted to pose a challenge to the panel or a question to the panel, to look carefully at this picture, to look carefully at the TEC report. This is an excellent, excellent review that Frank has but before you. But I would contend that when we look carefully at this, we have to really examine the question that, did the TEC report show that four sham control trials that we're going to discuss today were conflicting, like the two faces on this picture? Or, is there one unified opinion that stimulation is significantly

better than placebo in the treatment of genuine stress incontinence and detrusor instability?

It's very very difficult to do controlled, good controlled trials. We have to realize though, when it comes to electrical stimulation, that different stimulators are available to us that have different parameters, and I wouldn't think to necessarily use the same stimulator or the same device to treat different conditions. It's just like surgery; I wouldn't use one surgery to treat all the conditions that I face as a practicing urogynecologist. We use different operations in specific different indications.

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When we look at the four sham controlled trials that were reviewed in the TEC study, our study, the first in 1995, was a multicenter, sham controlled, random and double blinded trial, 52 women, 35 active, 17 sham. These data were evaluated on an intent to treat basis, which isn't quite what's stated in the TEC report. And while there may be some unbalance in the enrollment of subjects to the two groups despite the blinded randomized process, this on balance would tend to favor the sham group, in that the patients in the sham group had more incontinence episodes and thus, they had more opportunity to improve.

Nonetheless, pad test data and voiding diary data which were highlighted in the TEC report showed significant improvement or cure with the active device compared with the sham group. In addition, all symptomatic subjective scales were significantly improved with the active device compared to the sham device, leading us to conclude that clearly, PFES with this particular device was effective in treating genuine stress incontinence.

With a similar device with similar stimulation parameters, which is key, Yamanishi, in the Japanese study, looked at just a four-week

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trial. Again, this was randomized and this was not recognized in the TEC report. This is a randomized, one-to-one block randomization, sham controlled double blinded trial of 33 patients; again, 20 active, 13 sham -- excuse me, two-to-one. 45 of the active patients were cured

while only 13 percent were, excuse me, were in the sham group. He showed significant changes in pad tests and voiding diaries.

In Luber's study, using a US device, he showed no significant benefit in treating patients with genuine stress incontinence.

MS. CONRAD: Time, Doctor Sand.

DR. SAND: In a similar study, Dr. Brubaker showed, in 60 patients with stress incontinence, no significant difference. Yet in the 61 women she treated with detrusor instability, there was 50 percent resolution of detrusor instability.

I'm sorry. I'll quickly go to conclusions. The Sand and Yamanishi papers support genuine stress incontinence as more effective than the placebo sham. The Brubaker and Luber study, which used the same device, do not support this conclusion. It was a different device. A device

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that we used that is very effective for the treatment of detrusor instability, but not useful in the treatment of genuine stress incontinence. I believe that there is adequate evidence to support the efficacy of PFES for the treatment of women with genuine stress incontinence based on the objective placebo controlled sham studies that are listed in the TEC report. These are also effective for Medicare patients, and it's been shown in our control trials to be a durable long lasting therapy.

MS. CONRAD: Thank you, Dr. Sand.

DR. LANDY: You said different device, bud why is a device at issue when the frequencies --

DR. SAND: With electrical stimulation devices, thank you, Lisa, there are different devices that have different pulse parameters, different frequencies and different duty cycles. Then there's also the protocol that's used. We've shown in animal studies, in dog studies, that I can make dogs incontinent, using most available commercial stimulators, if we don't allow appropriate rest cycles. This is well known in the physical therapy literature.

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So we can't just look at this literature. I don't mean to divide the literature, but we can't look at it without that clinical insight. And Frank and I had some discussions yesterday. I mean, that's not possible, for an internist and a statistician; he did an excellent review. But we have to look inside of those data, and understand.

So Karl and Linda, in their studies, used one device, that we don't use for genuine stress incontinence, and they showed it doesn't work for genuine stress incontinence. I think it's an excellent stimulator for detrusor instability, which is tough to cure on urodynamic testing, and hopefully we can talk more about that. That device does that. The other device that we used in our studies, very similar to what Yamanishi used, those devices work for stress incontinence. Things aren't as they seem. So I think we have very strong objective evidence, and we'll hear more about some of the information from uncontrolled trials later by the other speakers.

DR. GARBER: Arnie?

DR. EPSTEIN: Yeah. I'm an internist who knows a bit of statistics, so I'm really going

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to need your help.

DR. SAND: Well, please. I don't mean to insult the people who graduated in the top 10 percent of my medical school class.

(Laughter.)

DR. EPSTEIN: Can you just clarify to me the types of devices that you think are effective, the types that are ineffective, and any evidence you have that the distinctions that you make are broadly made in the community?

DR. SAND: I think these differences are well recognized in the treatment community.

DR. EPSTEIN: Do you have any evidence for that assertion?

DR. SAND: What community use is, I think I would find that evidence in the over 200 uncontrolled trials. Probably the best evidence, and a lot of us I think draw upon the cat studies done by Magnus Fall some 30 years ago. Fall -- let me not start to list the coauthors, because I'll

forget them, but basically Magnus Fall showed that frequencies of 5 to 10 hertz were most effective in treating detrusor instability, whereas frequencies of 50 hertz were most effective in treating genuine stress incontinence. Unfortunately, when that

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information was given to biomedical engineers who wanted to create one stimulator to treat all, many of these stimulators showed up with frequencies of 20 or 25 hertz, which significantly diluted our literature unfortunately, because you couldn't just average those frequencies. So that's a problem in our uncontrolled literature and clinical teaching.

In addition, the concept of having a duty cycle that allows for a rest period that's twice as long as the active stimulation period is crucial. Then there is a lot of debate as to the actual pulse duration, which range from anywhere, in devices built in the United States, from .1 milliseconds to 2 milliseconds, what's ideal? And I'm not a good enough electrical engineer to really understand those principles.

But those three things, as well as the amperage, the duration of treatment, can have profound differences in how effective a device is. I don't know if that makes it any easier.

DR. EPSTEIN: Well, I understand that there are different dimensions by which, that lead to efficacy. I think one issue here is whether these different dimensions have been codified into distinct groups of instruments, and whether the

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broad, when HCFA reimburses this, or we judge the evidence, is there any way to tease these out?

DR. SAND: You know, I think the greatest problem with trying to tease that out is that you make a decision based at one point in time with current devices, which have been sort of frozen by the economic freeze of nonreimbursement for these treatments. Clearly, the best parameters with a stimulator are also individual to a patient, and I don't think we have the best device yet. Certainly, looking at some of the international devices we've tested that aren't available here, I think they are better than what we use and have available of FDA approved devices in the States.

So, that's a real loaded question.

DR. GARBER: All right. I'm just going to have to remind you, in asking questions of the public speakers, try to distinguish those that need to be answered immediately, directly, relevant to their current presentation, and you can ask questions of them again in the open committee deliberations period. I just bring this up now because as you know, we're not quite on schedule. Marshall?

DR. STANTON: I can save mine for the

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open period.

DR. SAND: Thank you very much.

MS. CONRAD: Kristine Whitmore, and the following speaker will be Karl Luber.

DR. WHITMORE: Good morning. Thank you for allowing me a brief time to speak with you. I am Kristine Whitmore, clinical associate professor of urology at Hahnemann MCP University in Philadelphia. My expenses to this function were supported by EMPI Corporation.

The question is, is there scientific evidence adequate to draw conclusions about the effectiveness of PFES or PFS in routine clinical use in the Medicare population? Unfortunately, urinary incontinence affects many people; public awareness is recent. Many patients don't tell and doctors don't ask. Few funds have been allotted to do studies that show adequate evidence. However, many guidelines have been established to help a large segment of society with conservative therapy. The objectives of this talk will be to provide an overview of the published guidelines for the treatment of urinary incontinence, discuss pelvic floor stimulation parameters and treatment protocols, and review appropriate patient selection

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criteria for PFS, for which you have been afforded an outline.

The American Urological Association had an ad hoc committee to suggest broad guidelines for the management of urinary incontinence. Behavioral therapy was recommended as first line of treatment, and PFS was included in the guidelines for both stress and urge incontinence. Subsequently, when

asked to assess PFS on a scientific evidence based only evaluation, the answer was that there was not evidence to draw conclusions about efficacy.

Now I'm sure you have all been provided with the AHCPR guidelines to review prior to this meeting, which convened in 1992. The recommendations were for behavioral therapies as the first line of treatment. It was updated in 1996 and levels of evidence were established to assess the quality and amount of evidence, consistency of the findings among studies, clinical applicability of the evidence, and evidence of harms and costs. Subsequently, the AHRQ then asked TEC to do an unrelated scientific evaluation, which showed the question could not be answered with statistical certainty.

The first international consultation on

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incontinence sponsored by WHO, showed that behavioral therapies are recommended as a first line of treatment, and PFS is included in the guidelines for the management of the frail disabled older people, a population which is not unlike these of Medicare.

There was an AUA update series published in 1999 by Dev Lightner, which recommends conservative treatment of urinary incontinence as first line, behavioral therapies are recommended as first line, and PFS is included in the guidelines as a behavioral therapy for both stress and urge incontinence.

The NIDDK launched a promotional public awareness campaign, Let's Talk About Bladder Control. Many organizations included here, or more, showed PFS is included as a behavioral treatment option.

In conclusion, the guidelines recommendations concur, begin with the best and least invasive treatment option. Not all behavioral therapies are created equal. Behavioral therapy is safe and effective. The primary goal of therapy should be patient satisfaction and patient motivation is required.

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Question number 1 leaves us with a dilemma, clinical versus rigorous scientific

evidence. Can I agree that there is statistical certainty? No. I'm a clinician and follow the AHCPR clinical guidelines. Yes, there is clinical evidence. Thank you.

MS. CONRAD: Thank you, Dr. Whitmore. Karl Luber. Following Dr. Luber will be Dr. Antoci.

DR. LUBER: Good morning. My name is Karl Luber, and I would like to thank the panel for the opportunity to share some information with you on our experience with electrical stimulation. I present to you with no conflicts of interest with any device developer, corporation or professional organization. My position currently is as the director of the division of urogynecology and reconstructive pelvic surgery for the Southern California Permanente Medical Group in San Diego. There I am responsible for delivery of care decisions for a very large group of women with urinary incontinence. I also co-direct a fellowship in urogynecology and reconstructive pelvic surgery at the University of California at San Diego.

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What I would like to do this morning is just very briefly talk to you about -- I'm not getting this to come up, will you help me out? Thank you very much -- about what we have learned about the efficacy of electrical stimulation in the treatment of women with genuine stress urinary incontinence. And my comments and all patients that I'm going to present on today are patients with genuine stress incontinence, that is, genuine stress incontinence consistent with the International Continence Society definitions.

Very quickly, the background information on functional electrical stimulation, in the early 1960s there were some anecdotal trials. Connie, I'm getting asked to stop here. I don't know if that's --

MS. CONRAD: I've got you timed.

DR. LUBER: Thank you very much. And then in the 1970s, these clinical trials, anecdotal trials went on to look at animal studies, where we learned the theoretical mechanisms of electrical stimulation and how they work. In the 1980s we saw

a number of open ended clinical trials. And then all of this information drove folks in the early '90s to look at doing RCTs. The reason it drove

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us to doing RCTs and the reason I very strongly feel that nonrandomized, noncontrolled trials are not of particular value in making these decisions, is that there is a huge confounding effect of electrical stimulation, not a simple placebo effect. In other words, if I'm asked to carry an anal plug around in my rectum for a half an hour a day, or perhaps more as happened in many of these trials, there's a darned good chance it's going to affect my ability to contract my pelvic floor, consistent with what I think a lot of us felt, if not voted on yesterday, with the effects of feedback on the pelvic floor musculature. So I think that uncontrolled trials in electrical stimulation are not of a particularly large amount of value to us in making decisions.

We set out to try to understand whether electrical stimulation as recommended by the manufacturers was an effective treatment for genuine stress incontinence. The study design was a prospective randomized double blind control trial done within our facility, a single center, and supported by a Kaiser Foundation grant. The inclusion criteria and exclusion criteria I won't dwell on, as we have to move along quickly. I will

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share with you that the treatment parameters we used were identical to those used in the studies that Dr. Sand described. We used a two-to-one rest to work cycle, we used 50 hertz for our stimulation, so there's really not a huge difference there. As far as the amplitude, I believe it was two million amps; I frankly would have to review my own paper to look back at that, which was the manufacturer's recommendation at that time.

We randomized people, and I show this to demonstrate to you that the randomization was consistent with what you'd expect. I know you don't need to do this; if it's randomized, you're going to assume that everybody comes out equal. But as you can see, there was no statistically

significant difference in the number of patients enrolled, dropped out, age, previous surgeries, or other potentially confounding variables. Results from our trial demonstrated that the subjective improvement and cure, as well as objectively cured groups showed no statistically significant difference.

Now when I first presented this, I was castigated by my colleagues and told, you just want

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to do surgery, you don't want to show that this works. The truth of the matter was, we embarked upon this trial with the bias that this was going to work. We wanted to demonstrate the efficacy of this, because we wanted to extend this therapy throughout our organization. And it in a sense blew up in our face and I wasn't very happy with that. But you know, once again, I had to go with the information that came to me from the trial, I had to be honest about the outcomes that I was looking at.

Based upon this trial and frankly based upon my interpretation of the other trials, we made the conclusion that functional electrical stimulation was no more effective in approving or eliminating the symptoms of stress or genuine stress incontinence than was the daily retention of the control probe. Functional electrical stimulation may be of value in conjunction with a physiotherapist who uses it to help patients as we say, jump start their muscles, that is, to teach them an awareness of where that musculature is, and then go on to help them to learn to contract those muscles. But as a standalone therapy to take home, we could not support its use.

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MS. CONRAD: Time please.

DR. LUBER: It's all yours. There are hundreds of thousands of operations done for genuine stress urinary incontinence in the United States each year. We need to seek alternatives that are nonsurgical to help these women. There's no question about that. But in our zeal to embrace and learn about these techniques, we should be careful not to initiate a process which would establish a standard of care for which there are

not adequate scientific underpinnings. And I frankly believe that that's where we are. We may find with adjustments and changes, and redesign, that electrical stimulation is of value. At the current point, we do not have the data to support that. Thank you very much.

MS. CONRAD: Thank you, Dr. Luber.

DR. STANTON: A quick question. I may have missed this if you said it at the beginning. Were these results published?

DR. LUBER: Yes, sir. These results were published in the Journal of Neurourology and Urodynamics, and that's in the TEC report, sir.

DR. BRADLEY: What was the treatment time? I may have also missed that. How many weeks

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of therapy?

DR. LUBER: 12 weeks of therapy.

DR. BRADLEY: How did you assess compliance in that study?

DR. LUBER: The device itself has a compliance meter in it. In other words, the patient would have to be sneaking to turn it on and leave it without using it, but we can download the daily use of the device to demonstrate efficacy.

DR. BRADLEY: And what was the compliance?

DR. LUBER: 87 percent. It was surprisingly good. Thank you very much.

DR. GARBER: Thank you.

MS. CONRAD: Dr. Joseph Antoci.

DR. ANTOCI: Good morning. I'm Dr. Joe Antoci. I'm a community practice urologist in Connecticut, and I have no financial conflicts in being here today. I would like to submit to the panel written documentation of what I'm going to say.

It was first shown in animal studies dating back to 1895 that bladder contractions could be inhibited by cutaneous and rectile stimuli. In modern times, human studies have continued to

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support the observation that PFS inhibits bladder contractions. Janus showed in 1979 that true physiologic responses could be recorded on urodynamic evaluations in patients undergoing

pelvic floor neuromodulation. Tanago and Schmidt's work, published in 1988, demonstrated that electrical enhancement of the tone of the external sphincter suppressed the detrusor and improved bladder storage. In his 1991 paper, which is referenced in HCFA's TEC assessment, Dr. Magnus Fall elucidated the principles of PFS. He worked out the optimal energy levels and pulse configurations that would inhibit detrusor contractions.

In 1997, de Grote described the neurophysiologic pathway that accounts for these consistent observations. Basically, PFS prevents the pudendal nerve from telling the brain that the bladder is filling, and therefore the brain does not send the message to the bladder to contract. It's also been noted by Fall in his '91 paper that PFS is a useful tool in facilitating PME training.

HCFA's own TEC assessment indicates that PFS is better than placebo and equal to alternative therapies in the majority of studies evaluated.

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This TEC assessment also focused on studies published since 1980 but ignored previous work, including 24 other PFS studies performed from 1967 to 1979, which encompassed data on 793 patients. I was able to retrieve data on 38 studies published from '68 to '98. A total of 1,375 patients were treated with PFS and 863, or 62 percent of those, were improved.

In this day and age, cost is always a factor. The cost of PFS compares very favorably to alternative treatments. When HCFA Connecticut covered PFS, the rate was $84 for a six-week treatment period. Modern day anticholinergics such as Ditropan, Excel or Detrol, cost anywhere from 90 to $180 per month.

Although the panel is not considering implantable neuromodulation technology, it is noteworthy to note that the total patient cost, for instance, for a Metronics Inter-Stim device is $25,000. The Inter-Stim literature also notes that there is a one-third reoperation rate on these patients. Compare then the 67 percent patient improvement rate at $25,000 per patient to the 62 percent patient improvement with PFS at a fraction

of the cost.

In summary, we know that PFS works, we know how it works, we know that it's a useful teaching tool for PME, we know that it's better than placebo, and we know it is equal to alternative therapies. And ladies and gentlemen of the panel, this is a critical point: As all clinicians who treat incontinence know, there is no single therapy for all incontinent patients. Patients need options and choices.

Finally, please consider the following in your deliberations: When a body such as Medicare does not cover a given treatment, that effectively dissuades health care providers from offering that treatment to their patients. That is tantamount to denying patient care. Thank you very much.

MS. CONRAD: Thank you, Dr. Antoci. We are going to move along with the industry presentation. Deborah Jensen, representing EMPI, followed by Francie Bernier.

To try to pick up a little time, we are going to try to not schedule a morning break. Just leave the room as you need to.

MS. JENSEN: Good morning. My name is Deborah Jensen and I'm the vice president of regulatory affairs, clinical research and quality assurance for EMPI. EMPI is a medical device manufacturing firm based in St. Paul, Minnesota, that specializes in devices to assist patients with functional disabilities, including the Inova PFES device for the treatment of incontinence. EMPI has been involved in the manufacture and distribution PFS devices since 1991, and we are grateful for the opportunity to discuss the place of PFS therapy in the treatment of incontinence patients of Medicare age before today's panel meeting. We trust that the panel members will listen carefully to the evidence presented today.

Clearly, the task of the panel to qualify whether conclusions can be drawn regarding the scientific evidence supporting this technology, and then quantify the size of the health effects for this technology, is not an easy task. But it

certainly is an important one for the beneficiaries who could benefit from this treatment option but are currently not able to access this therapy as a result of the national noncoverage policy.

It is clear from the scientific literature that there is not support, or sufficient evidence to say that this therapy has no benefit

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for any beneficiary. Rather, it is our opinion and the opinion of several clinicians presented today, that there is scientific evidence to draw conclusions about the effectiveness of PFES in routine clinical use for the Medicare population.

I would urge the panel members to consider the following point: PFS is a technology that has been around for a long time. EMPI's Inova PFES device received FDA clearance in 1991. In these past nine years, EMPI has made the development of scientific and clinical evidence to support the safety and efficacy of this therapy a constant goal through the support and sponsorship of four separate clinical trials.

The first, a randomized placebo control trial of stress incontinence subjects, published in 1995 by Dr. Peter Sand, demonstrated the statistically significant improvement when compared to placebo. EMPI subsequently completed two treatment optimization studies that evaluated the effect of treatment frequency on patient outcome when PFS was used to treat stress, and then urge and mixed incontinence. These were subsequently published by Dr. Richardson in 1996, and Dr. Siegel in 1997. Both of these trials documented with

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statistical significance that improvements were seen in incontinence symptoms in patients from their baseline values.

Most recently, the encouraging results for a PFS study in post-prostatectomy incontinence patients pointed out that this therapy also holds promise for this group of patients. Publication of the results of this trial is pending.

Concurrent to the development of scientific evidence to support this technology, EMPI has developed relationships with health care providers in the private health care peer community

in an effort to determine the place of PFS in the care of patients suffering from incontinence. As evidenced by the reviews of this technology undertaken by such prestigious independent expert groups as AHCPR and the World Health Organization, PFS does have a place in the continuum of care.

This place has been further substantiated by the over 300 private health plans in the United States that are providing reimbursement for this technology. Collectively, three of the largest plans, Aetna U.S. Health Care, Blue Cross Blue Shield, and United Health Care provide coverage for over 40 million Americans.

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This information provides strong support that the clinical community and a significant number of private health plans have determined that the support for PFS is sufficient for it to be a standard of care, and that it has a place in the treatment of incontinence patients. Thus, they have answered the question put before the panel regarding the effectiveness of PFS affirmatively.

At this point in time, I would like to yield the remainder of my time to Dr. Kristine Whitmore, so that she may further discuss the adequacy of the scientific literature. Thank you.

DR. WHITMORE: Thank you. We are going to go on to the treatment parameters and protocols. The evidence is adequate. The study design underestimates the effect. Randomization in the RCTs limit the dose response, ala, we cannot get to maximum intensity, so for stress incontinence we cannot produce a muscle contraction, and for urge incontinence it's hard to obtain maximal stimulation to cause an inhibitory effect on the bladder.

For stress incontinence, we'll talk about treatment parameters. The scientific literature supports a production of an involuntary

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muscle contraction. Magnus Fall, of course, has many papers that have established that a frequency of 50 hertz is achieved at maximum urethral closure pressure. There is variable intensity, zero to 100 milliamps, to maximum muscle recruitment. This is done to produce a contraction, often seen as an

anal wink. There is a duty cycle or work-to-rest ratio of one to one or one to two, five on, five off, five seconds on, ten seconds off. Usually 15 minutes treatment two to three times daily will produce up to 120 contractions per day. Initial treatments are usually six to eight weeks.

There is also support for urge incontinence, during which we want to achieve a reflexive bladder inhibition. The most common frequency is 10 hertz. Maximal intensity has to be achieved, usually to the point of discomfort, and then backing off to a sensation tolerable to the patient. The duty cycle is usually one to one. There are 15-minute treatments, two to three times a day, and initial treatments are as short as four weeks.

There was a question asked about utilizing the same parameters among various studies. For the randomized control trial by

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Yamanishi in 1997 for the treatment of genuine stress incontinence, did use a frequency of 50 hertz, did achieve maximal intensity level by urodynamics of maximal urethral closure pressure. Had a number of contractions, 15 minutes, 120 a day. 15 minutes two to three times a day of treatment. The treatment period was four weeks, and the objective cure rate was 45 percent.

Additionally, Richardson, 1996, stress incontinence treatment. Utilized a frequency of 50, visualized pelvic floor muscle contractions as maximal intensity. Compared daily versus every other day treatment protocols. Used 15 minutes of treatment twice a day for 120 contractions, or 60 contractions per day. The duty cycle was one to two. Treatment was 20 weeks. And the objective cure rates, daily, 22 percent and every other day, 53 percent.

Let's switch to urge incontinence. Brubaker, 1997, utilized 20 hertz frequency, lower frequency. Digitalized pelvic floor muscle contractions at maximal intensity. Had 20 minutes twice a day of treatment. The duty cycle was one to two. Treatment was eight weeks. And if you pull out the urge incontinence portion of her

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population, the estimated cure rate is 50 percent.

Another optimal treatment protocol for urge incontinence, Siegel et al, 1997. Again, low frequency, 12.5 hertz. Pelvic floor muscle contractions were visualized at maximal intensity. There were 15-minute sessions twice a day. The duty cycle was one to two. 20 treatment weeks, and objective cure rate, 28 percent.

In conclusion, the final question then to number one, clinical versus rigorous scientific evidence, can I agree that there is statistical certainty, no. Since I am a clinician, however, there certainly is clinical evidence. Thank you.

MS. CONRAD: Thank you, Dr. Whitmore. Francie Bernier. And the next group of public presenters, the professional organizations, I have been asked to rearrange a little bit, so the first speaker for the professional organizations following Ms. Bernier will be Nicolette Horbach. Thank you.

MS. BERNIER: Good morning. My name is Francie Bernier, I am a nurse from Colorado. Over the last nine years I have offered continence care to my patient, mostly women, and I am now a clinical consultant. My trip has been sponsored by

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Hollister so that I may speak to you about the use of electrical stimulation.

The question you've been charged today is, is there adequate clinical evidence to support the use of electrical stimulation in the treatment of urinary incontinence? The answer is yes. For the over 20 million Americans who suffer from urinary incontinence, there are few treatments that offer little risk or side effects except a conservative management program. Pelvic floor therapy includes a variety of interventions, to include behavioral modifications, biofeedback directed PMEs, and intercavity or surface electrical stimulation. The integration of these options into a continence program has created a multimodality approach for the treatment.

Up until recently, medications and surgery have dominated the continence care. Surgical risks include morbidity and mortality. Additionally, these procedures may not cure

incontinence and have been known to worsen symptoms in some cases. The surgery failure rate has been reported at about 30 percent.

The AHCPR guidelines have encouraged the use of the least invasive or the intervention with

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the least risk, such as behavioral modification, as the first treatment option for those that suffer from incontinence. The significant side effects from medication, such as dry mucous membranes of the mouth and eyes, constipation, headache, and visual disturbances, and general malaise, have compromised their use, especially in the elderly.

Electrical stimulation is a successful treatment modality for the treatment of incontinence. This option has been effective used to retrain the pelvic floor musculature in those with weakened or atrophic muscles. Additionally, the effect of electrical stimulation on the bladder and voiding symptoms has been shown to decrease or eliminate the symptoms associated with urgency and frequency.

The use of electrical stimulation is not new to the medical community. In Europe, stimulation has been used to treat incontinence for many years and historically it's been reported and traced back to 1895. Over the years, the increased use of electrical stim has been applied to technology which now uses internal sensors or surface electrodes to directly provide stimulation to the muscles and nerves. Electrical stimulation

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has increased use in the medical and rehabilitative communities over the years. The application of specific frequencies of electricity to muscle causes a chemical response which has been demonstrated to relax a spasming muscle, or recruit muscle tissue in order to reeducate a muscle dysfunction.

It is the standard of care for specific cardiac conditions in which the heart muscle is experiencing an arrhythmia, such as in ventricular type of cardio, or in a cardiac arrest. The electrical charge of a cardiac muscle can calm the tachycardia and set the heart muscle into a normal sinus rhythm. Additionally, when applied to the

cardiac muscle during an arrest, the application of an electrical stimulation will recruit and reeducate the electrical conduction system of the cardiac musculature to contract and function efficiently.

Used in rehabilitative medicine, electrical stim again provides a calming sensation to the muscle in spasm, or can reeducate a flaccid muscle. In a recent interview with Dana Reeve, the wife of Christopher Reeve, she reports the daily application of electrical stimulation had kept her

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husband's large skeletal muscles in a completely functional state. His muscles are reported to be in the same condition they were in previous to his spinal cord injury.

Fall's study, which has been referred to this morning, conducted research using low frequency of 5 hertz to obliterate bladder spasms in cats. When the same frequency is applied to those who suffer from urge incontinence, the results have been duplicated. A vaginal electrosensor or surface electrodes can deliver the application. This stimulation is applied to the pudendal nerve, which then induces a pelvic floor muscle contraction. The induced passive contraction causes initiation of the inhibition reflex and directly stimulates the sacral afferent nerve fiber.

Additionally, when applied to the pelvic floor at higher frequency, electrical stimulation causes activation of the somatic nerve to the striating muscles of the pelvic floor. Efferent stimulation of the periurethral striating muscles and leading to the ani, cause an increase in urethral closure pressure. By encouraging the patient to contract the pelvic floor muscles when

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the stimulus is active, helps the incontinent patient identify, recruit and coordinate pelvic floor muscle movement. This reeducates the patient and the pelvic floor, and decreases urine loss associated with stress and urge incontinence.

This increased benefit can move a patient closer to becoming successful in their biofeedback training. A significant reduction in

incontinent episodes, from 41 to 72 percent, has been reported in electrical stimulation for stress and urge incontinence. The long-term efficacy of treatment has been reported in up to two years following.

Various settings have been proven successful to treat the different types of incontinence. These settings have been accepted as the standard of care and range from 5 to 12.5 hertz for urge incontinence, 20 hertz for mixed incontinence, and 50 and 100 hertz for stress incontinence. Most recently, a study evaluated stimulation of 200 hertz; it has received FDA approval to induce a pelvic floor muscle contraction, and has improved voiding in those who suffer from nonobstructional urinary retention.

The use of this therapy should only be

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applied when indicated. After careful assessment as to the muscle function, the decision to apply electrical stimulation should be when the pelvic floor musculature is determined to be weakened as documented by digital exam and a pressure monometry of less than 10 centimeters of water with no endurance to the contraction.

Additionally, when the symptoms of urge incontinence is impacting quality of life, the application of electrical stimulation has been included so to reduce the symptoms. Although a lack of a perfect randomized controlled study has yet to be done, this evidence is clear. The results specifically demonstrate that electrical stimulation can normalize urodynamic parameters in those who suffer from urge incontinence.

In those with stress incontinence, electrical stimulation has not demonstrated the same in some cases. This may be due to the anatomic defect which exists within the lower urogenital system. However, during proper continence reeducation sessions, the patient is instructed how to reuse the pelvic floor muscles during exertional activity which precipitates the incontinent episodes. These would then normalize

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the parameters that are evaluated for stress incontinence.

Exclusion to the therapy should include those who have a pacemaker implant, a copper IUD, those who suffer from mental confusion, during pregnancy, and in the presence of a pelvic malignancy. Additionally, this treatment should be withheld during episodes of acute urinary tract infection, any episode of vaginal bleeding or vaginal infection in women, and in the presence of fecal impaction. The use of electrical stimulation should only be considered after careful assessment has been made to evaluate for the presence of these contraindications.

The number of visits may not exceed 12 visits for most patients. In most cases, improvement in symptoms can be seen within the first few weeks. However, most patients require reinforcement of the new behavior and as with any rehabilitative program, the chance of symptoms returning, if the patient does not comply with the program.

Also, the elderly often require more frequent visits than the younger population, as the rehab process seems to take more time in that

group.

The patient's response to electrical stimulation is very positive. Those who were previously frustrated by the inability to contract the pelvic floor muscles report great satisfaction in their awareness and spontaneous performance of pelvic floor exercises. This is often experienced immediately after the first session. Once the patient is able to contract the pelvic floor musculature and reuse the pelvic floor, there is a decrease or elimination of urinary incontinence symptoms.

As we face the decisions about electrical stimulation, please consider the patient. Incontinence is a symptom of another medical problem. The studies you have evaluated have judged the outcomes but have not measured value in all of the factors which affect results. Recognizing how each patient differs in their presentation, I am asking you to be aware of the variability within the patient population. These studies come to their conclusions from the

technical report and the consistency of the results are dependent upon too many variables which have not been considered.

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The value of muscle reeducation process as well as the calming effect this treatment option has on the bladder should be available as a treatment for those who suffer from incontinence. Electrical stimulation offers no risks. It is cost effective by decreasing the number of office visits required to achieve a continent status and improved quality of life. Thank you.

DR. GARBER: Thank you.

MS. CONRAD: Okay. Nicolette Horbach. And the following speaker will be Julie Pauls, Dr. Julie Pauls.

DR. HORBACH: Good morning. I am Dr. Nicolette Horbach, associate clinical professor of obstetrics and gynecology at George Washington Medical Center, a practicing physician in northern Virginia, and the current president of the American Urogynecologic Society. I have no financial disclosure to report. On behalf of the AUGS I am pleased to provide expert testimony on the need to provide insurance coverage for PFES for the treatment of urinary incontinence.

Urinary incontinence has been estimated to affect over 20 million Americans, the majority of whom are women. As surgery is not always

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appropriate or effective treatment options for all types of urinary incontinence, the availability of noninvasive treatment alternatives is a major concern for urogynecologists and their patients.

The American Urogynecologic Society is a 21 year old nonprofit organization whose nearly 1,000 members have a special interest and/or expertise in the field of urogynecology and pelvic reconstructive surgery. Our membership includes gynecologists, urologists, and allied health professional in academic and clinical practice. The mission of our society is to promote research and education in the specialty, and to improve the quality and delivery of health care to women with pelvic floor disorders. Many of our members are fellowship trained and national and international

leaders in the field of urogynecology.

Our members were instrumental in the development of the first AHCPR clinical guideline on urinary incontinence, chairing the panel of experts for the 1996 revision of the urinary incontinence guideline. The NIDDK, the NICHD, the NIA, the NINR, and AHRQ continually fund research conducted by our members. Because of our society's efforts, NICHD now has a urogynecologist on staff

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to coordinate the expanded research in this field.

PFES is a therapeutic modality indicated for the treatment of urgency and urge, stress, and mixed urinary incontinence. The therapeutic effect of pelvic stimulation rely on electrical activation of nerves. Detrusor inhibition is mediated through low frequency stimulation of the sacral afferent and potentiated by pudendal nerve stimulation. Electrical stimulation of the urethral musculature is via higher frequency activation of the somatic nerves to the striated muscles. Thus, the treatment of urinary incontinence with PFS involves the, physiologic coordination of both bladder and urethral function.

There are two reasons that providers use pelvic floor stimulation as a treatment modality. One reason to use PFS is to neurally inhibit inappropriate bladder contractions. Another reason is to hypertrophy the skeletal muscle for the treatment of stress incontinence. PFS involves an electrical probe that provides the contact surface for transmitting current to stimulate specific nerves.

The effectiveness of the pelvic floor electrode will depend on its size, shape and

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material, as well as the critical parameters of pulse amplitude and duration, wave form, frequency and duty cycle. The study parameters that the technology assessment relied upon in evaluating the effectiveness of PFS were not adequate and therefore, did not yield consistent results.

The first question that the technology assessment posed to the Medical and Surgical Procedures Panel relates to the efficacy of pelvic stim in reducing incontinence. Although the

technology assessment provided to the panel concluded that electrical stimulation does not meet the appropriate criteria for establishing its effectiveness in the treatment of urinary continence, a report by Aetna in 1996 determined that PFS is effective in treating urinary incontinence. Two randomized placebo control trials provide evidence of the efficacy of PFS in the treatment of urinary stress incontinence.

Yamanishi conducted a four-week double blinded trial comparing electrical stimulation to placebo treatment in 44 patients with stress urinary incontinence. Efficacy of pelvic floor stimulation therapy was judged using several outcome measures, including the number of

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micturitions and leakage episodes, the number of pad changes, degrees of disturbance in daily activity, and patient impressions. There was a significant decrease in the daily frequency of pad change and disturbances in daily activities in the active device group compared to the sham device group. Also, there were significantly more cured or improved patients for frequency of leakage and pad tests.

In previous assessments, Blue Cross and Blue Shield Association discounted the findings reported in the Yamanishi study because their results were, quote, inconsistent and conflicting, unquote, with other studies. However, Blue Cross Blue Shield report failed to identify any flaws in the methodology of this study, nor were complaints issued about the reliability and validity of these results.

Although the technology assessment discounts the Sand report for, quote, sufficient methodologic quality, unquote, an independent review by MedTap International summarized the study as a multicenter prospective randomized, double blinded trial comparing 35 women receiving PFS to 17 women receiving a sham device. To determine

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treatment efficacy, Sand and the other investigators conducted urodynamic testing accompanied by a pad test, and subtractive phystometry (phonetic) before and after device

use. After 12 weeks of treatment, the patients using the active device had significantly greater improvement in weekly and daily leakage episodes, pad testing, and vaginal muscle strength, when compared with the patients treated with the sham device. The pad test also showed that stress incontinence was improved by at least 50 percent in 62 percent of the patients using PFS, compared with only 19 percent of patients using the sham device.

In the largest randomized trial, Brubaker compared PFS to sham device in 146 women with stress incontinence, detrusor instability and mixed incontinence. This study utilized multichannel testing, testing, urinary diary, and assessment of quality of life, to determine the efficacy of pelvic floor treatment. After eight weeks, 49 percent of the women with detrusor instability who used the active electrical device were cured.

Despite the concerns regarding study design, the 1996 AHCPR clinical guidelines on

urinary incontinence concluded, research indicates that PFES can significantly reduce urinary incontinence in women with stress incontinence, and may be effective in men and women with mixed, urge and stress incontinence. Treatment using stimulation requires monitoring by a health care professional to determine effectiveness.

The technology assessment also asked the panel to compare the efficacy of PFS as compared to PMEs or alternative treatments. If a patient can spontaneously perform PMEs, she does not need PFS. However, as with all areas of weakened or poorly enervated skeletal muscles, PFS augments strengthening of muscles. This approach has been used in other parts of medicine for many years, including orthopedics and physical therapy.

The third inquiry of reference in the technology assessment questions the addition of PFS to PMEs to improve outcome above those obtained from PMEs alone. As professionals treating urinary incontinence with the above treatments, AUGS feels that this question was the result of lack of knowledge or understanding regarding application of the two modalities. PFS for stress incontinence

contracts the same muscles as a correctly performed
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Kegel exercise.
The advantages of PFS are twofold. The correct muscles are always contracted, and voluntary compliance to exercise is not required. Electrical stim and PMEs are used for different people. Women with muscles that simply have mild disuse and atrophy can exercise without any device, and women with more moderate disuse and atrophy need additional treatment. Thank you.
DR. GARBER: Thank you.
MS. CONRAD: Julie Pauls, and the following presenter will be Mikel Gray.
DR. PAULS: Thank you. Good morning. My name is Dr. Julie Pauls. I'm a physical therapist and an assistant professor at Texas Women's University at the Texas Medical Center in Houston, Texas. I am here on behalf of the American Physical Therapy Association, representing its almost 69,000 members. And I have no current or past financial interest in any manufacturers whose products may be under discussion today.
And Connie, I have asked that you distribute my testimony, and ask that it be put in the permanent record of this proceeding.
To the question of the day, is the
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evidence adequate, the APTA responds that yes, there is adequate clinical evidence to support the use of PFES in the care of urinary incontinence. And we believe that, because the Agency for Health Care Quality, formerly the AHCPR, is the lead governmental agency charged with supporting research design to improve the quality of health care, reduce its costs, and broaden access to essential services. The clinical practice guidelines that we've discussed and were updated in '96 established an algorithm for the evaluation and management for urinary incontinence. These guidelines state that PFES has been shown to decrease incontinence in women with incontinence, and that it may be useful for urge and mixed incontinence as well.
These guidelines were given a B rating as mentioned earlier, which is the second highest

rating available. And they based this on the scientific evidence from properly designed and implemented clinical studies that support the guideline statement. Because these guidelines were formulated by a neutral government agency comprised of health care research experts, the APTA strongly urges this panel to weigh the findings of this

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report heavily in the deliberations regarding Medicare utilization of PFES for incontinence.

As you are aware, another assessment has been done. At the request of HCFA, Blue Cross and Blue Shield association completed this technology assessment we've been discussing. Some remarkable contrasts exist that should be noted. For example, while the AHCPR practice guidelines were based on a review of literature by a panel of 16 leading health care experts who are experts in urinary incontinence, the Blue Cross TEC assessment was authored by one individual with input from other reviewers. While the AHCPR guideline was performed under the auspices of a neutral government agency, the technology assessment was done by a health care insurance organization, many of whose members are for profit organizations. Thus, the APTA has some concerns with the way this assessment presents the PFES studies and the results thereof.

We believe that with respect to the efficacy of PFES compared to sham PFES or placebo, this assessment contains inconsistencies and misrepresentations of those data. It is on the basis of these and other concerns that we would caution the panel against formulating any

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recommendations solely based on this assessment.

In reviewing the study by Sand, PFES compared to placebo, the assessment offers a good deal of conjecture without any justification for statements it makes. For example, the assessment suggests an increase in leakage in the placebo group would have been statistically significant if the sample size was larger, but then suggests that if this increase had been found to be significant, it was not biologically plausible. In other words, the assessment first hypothesizes that a situation might exist, and then declares that it is not

biologically plausible.

The assessment goes on to explain that this biological implausibility occurrence might instead have been due to an artifact, due to instability of the measurements of incontinence, in this case the use of patient diaries, a point the assessment fails to make in criticizing other studies that use the exact same methodology.

None of these statements in the assessment are supported by quantifiable methods and more importantly, none disprove the profound clinical results of the Sand study, namely that PFES is superior to sham PFES.

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In the Joe Laycock and Jerwood study, the assessment places emphasis on the findings that the percent of patients cured was not statistically significant. It also emphasizes that the percent of patients showing greater than 50 percent improvement was not reported. The assessment chooses to downplay, if not ignore, the profound finding that the PFES group showed significantly, up to two times more greater decrease in the grams of urine leakage compared to the placebo group. Anyone who's suffered from urinary incontinence will tell you that decreased leakage is absolutely significant. And this study demonstrated how much difference PFES can make.

In its summary the assessment concludes that the body of literature does not support strong and consistent evidence that PFES reduces the frequency and severity of incontinent episodes. It bases its conclusion on the observation that the studies investigated different parameters of PFES, and that the administration of the interventions varied. While it's true that the studies did investigate various parameters such as frequency, duration, intensity and location, as we've discussed earlier today, the literature clearly

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shows PFES to be superior to placebo.

However, studies by Kerri Bo in Norway, and Olah, while confirming these findings, also suggest that the positive effects of PFES may be similar to that obtained from a structured PME program. But there is considerable difference

between no effect versus no better than. The important issue here, which we feel is missing from the assessment, is whether it is appropriate, worth the extra time, equipment and effort to employ PFES, while other less expensive ways can frequently but not always accomplish the same thing. That conclusion is missing. We read instead that PFES is ineffective. Clearly the assessment draws a conclusion that it's not supportable by an objective analysis of the literature.

PFES has been shown to be effective, and is particularly useful, and this is the critical key, please underline it in your papers, it's particularly useful intervention for those patients who are not capable of a voluntary muscle contraction. For these reasons, PFES is a valuable adjunctive intervention and should be covered under the Medicare program. With the increased frequency

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of urinary incontinence in the aging American public, the APTA believes that it's imperative that Medicare rely heavily on the medical and research experts at the AHRQ, the neutral governmental agency.

In closing, the APTA urges this panel to adopt a recommendation for utilization of PFES for the treatment of incontinence at a level three category of effectiveness. We do so because number one, clinically, there is adequate evidence to conclude that it's effective. Secondly, because its efficacy is supported with valid and reliable scientific literature recognized by a panel of experts. And thirdly, probably most importantly, because of the profound benefit it can provide to your beneficiaries who suffer from this condition. Thank you for your attention.

DR. GARBER: Thank you.

MS. CONRAD: Thank you. Next is Mikel Gray, with Alfred Bent on deck.

DR. GRAY: My name is Mikel Gray. I am representing the Continence Coalition today. My travel to this meeting was not financed by any of the manufacturers or any manufacturer at all. I have no existing, nor do I have any previous

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conflicts of interest or financial relationship with any of the manufacturers involved today. My titles are assistant professor of urology and nurse practitioner with the department of urology at the University of Virginia. I'm also associate professor of nursing at the University of Virginia.

I want to first limit my comments, and I also want to take Miss Conrad's advice, and be a little supplemental to some of the comments that are already made. Therefore, I'm not going to spend significant time talking about PFES as model therapy in the management of stress urinary incontinence; that has been discussed previously. I am going to focus on the use of PFES in the management of urge urinary incontinence, particularly detrusor instability, or motor urge incontinence.

So, I think the first thing that I must say to you is, and to remind you that when you talk about PFES for urinary incontinence that is indeed a broad topic. Its application for urge urinary incontinence and the physiologic response to urge urinary incontinence, its application to stress urinary incontinence are two completely different

things.

There are several possible therapeutic benefits to electrical stimulation as you know, and there has been evidence presented today, and I will not again repeat that evidence, that electrical stimulation in the low hertz frequency range, using duty cycles of one to one or generally one to two, is effective in the inhibition of bladder contractions. There have been two particular randomized studies that have reported the usefulness of transvaginal electrical stimulation for the treatment of motor urge urinary incontinence.

Smith, in the Journal of Urology, randomized a group of 38 women with urge UI and urodynamically documented detrusor instability to treatment with either an anticholinergic medication or maximal electrical stimulation using an intravaginal probe. Outcome measures for this particular study are point on relevant to the

questions we've been asked to address. That is, he looked at the number of pads used within a 24-hour period, he looked at the frequency of urination reported on bladder log or voiding diary, and he also looked at the number of UI episodes within a

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24-hour period.

In this particular study, cure was defined as complete oblation of urinary incontinence, and discontinuation of pad usage, both a scientifically relevant and a clinically relevant outcome. Improvement was defined as at least 50 percent reduction in pad usage and UI episodes, as well as a drop to 10 or less voiding episodes over a 24-hour period.

Based on these particular outcomes 22 percent of the 38 subjects were assessed as cured, and 50 percent were improved by stimulation, yielding an overall improvement rate of 72 percent. Now these rules were reported in the report as comparable to that achieved by pharmacal therapy.

However, in the author's discussion, there is an important point that must be made, and that is to say that individuals who were treated by PFES were able to avoid the bothersome side effects of anticholinergic therapy. There is good documentation in the literature that up to 82 percent of patients who were started on an anticholinergic therapy, specifically Ditropan and media release, will discontinue therapy within one

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year of starting because of intolerable side effects. And when we look at scientific evidence and balance that against clinical relevance, I would point out that there are no side effects associated with anticholinergic therapy that are specific and relevant to PFES.

Therefore, Dr. Antoci's point is well taken, that there must be alternative treatments for urinary incontinence, particularly for urge urinary incontinence.

What can we take away from this study? We can take away that the efficacy is comparable to that achieved by pro-Panthylene, a specific anticholinergic. We can also take away the lesson

that these patients were able to achieve these comparable results without any cholinergic side effects.

A second study is that of Brubaker in '97, who reported on a randomized trial, a transvaginal stimulation versus an intravaginal sham probe. This particular group included 121 women who completed the study. 61 of those particular studies had urodynamically proven detrusor instability, motor urge urinary incontinence. The outcome measures in this

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particular study included subjective perceptions of improvement, objective comparisons, and pre and post-treatment urodynamic testing.

The most interesting and the most provocative finding in this is that among those with urodynamically proven detrusor stability, motor urge urinary incontinence, 49 percent reverted to stable detrusor function, were cured following the treatment course, as compared to 6 percent who used the sham device.

It is unfortunate, and I certainly would acknowledge that there is a limitation in this study, because there was insufficient bladder log entries in order to measure that as an outcome. However, if you look at what she reports, which is adequate subjective improvement, you will find that there was a 35 percent adequate subjective improvement, while only 17 percent of those on the sham device achieved similar results.

In this particular study, chi square analysis was used to analyze that. The statistical significance, the P value unfortunately failed to reach statistical significance, although if we apply the .05 rule talked about earlier, it would have achieved statistical significance, but she

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used a .01.

There are uncontrolled trials that I believe are relevant. Again, I would urge the panel and I submit to you that when you look at the preponderance of data, the uncontrolled trials are helpful as supplemental to the controlled trials, although I agree with the comment that the controlled trials must form the basis of your

judgment. However, again, I submit to you that the uncontrolled trials can prove valuable as providing adjunctive information.

Primus and Kramer in 1996 used transvaginal and transrectal electrical stimulation in a group of 75 patients. They were diagnosed with urgency and/or urge urinary incontinence again, urodynamically documented. This particular study I'm pointing out, and I believe it's notable because it includes 51 women and 24 men. In many instances there are significantly greater data on men; in this case, there's significantly greater data on women, and what data we do have on men should be pointed out as well.

30 of these particular subjects had neuropathic basis for their hyperactive detrusor contractions; that is, they had detrusor

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hyperreflexia owing to multiple sclerosis. 45 had idiopathic detrusor instability. Following three-week of treatment with maximal electrical stimulation of at least 15 sessions, 59 percent experienced both urodynamic, objective, and subjective improvement. Follow-up was done, and it showed that the improvement persisted for approximately two years within the majority of the idiopathic group, but the neuropathic group unfortunately had a relapse of symptoms approximately two months after.

Jonnasen in 1990 also provided a trial that was uncontrolled. Again, subjective evaluation showed a 65 percent improvement, 67 percent subjective improvement. Ericson in 1989 again showed similar things. And finally, one of the first trials was done by McGuire, who showed a 75 percent achievement rate of complete continence, and 15 percent were reported as improved, using strictly urodynamic criteria.

Can we say that there is adequate evidence that PFES is effective in the management of motor urge urinary incontinence, particularly detrusor instability proved motor urge urinary incontinence, using the strict ICS definition? I

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submit the preponderance of data shows that there is.

There is also an advantage that has not been adequately discussed in my opinion over pharmacal therapy, for patients who are intolerant, and I am not arguing that all patients are intolerant. That is fortunately a smaller proportion than it has been because of recent advances in pharmacal therapy. Nevertheless, of the many patients who prove intolerant of the side effects of anticholinergic therapy, transvaginal, transrectal electrical stimulation using specific parameters is effective. Thank you very much.

DR. GARBER: Thank you.

MS. CONRAD: Dr. Bent. Dr. Perry on deck.

DR. BENT: Good morning again. I am Alfred Bent, a practicing obstetrician and gynecologist up the street at the Greater Baltimore Medical Center. I've been program director for ACOG for a considerable length of time, so I represent ACOG today, the organization of 39,000 physicians dedicated to women's health. I appreciate the opportunity to address the panel. I have no financial interest in the products being

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discussed and have traveled at my own expense the 12 miles downtown.

I did participate in two studies using the Hollister device which was provided to us. We were not funded. In fact, I think we spent more money to try to do the studies than we received. However, we are of the opinion that there is adequate evidence to conclude clinical efficacy of electrical stimulation. We heard about the AHCPR guidelines from 1996 that determined electrical stimulation may be helpful in mixed urge and stress incontinence, and that it was most likely helpful for stress incontinence. For stress incontinence, the studies have been presented and I don't need to repeat them. I have summarized them in my previous submission to you.

Brubaker's study did not show efficacy. There's a question regarding the parameters. Sand and Yamanishi showed efficacy. Luber did not, although in Luber's study, most patients had either refused or failed PMEs as a form of therapy.

I would like to spend a little bit of

time discussing the study that was presented in some detail in the report to HCFA, and that's the Karri Bo study, which composed patients who were

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treated by PMEs, electrical stimulation, vaginal cones, and a control group. Once again, I probably am showing my bias, but Professor Bo is known for her rejection of electrical stimulation therapy and formal biofeedback techniques, and it does show that result in her study, in my particular bias. She does discuss the use of PFMEs, however, by a trained physical therapist through a structured program, although that's not considered formal biofeedback, and we discussed that yesterday.

Although the average age of the patients in the Bo study was 49.6 years, the report to HCFA stated that this study was generalizable for the Medicare population. The mean age in the Yamanishi study from '97 is 63 years; it seems to me that's a little bit more Medicare age than 49 years.

The biases in the Bo study do need some clarification in my opinion. The PFME group performed their exercises daily, had training in groups once a week with a physical therapist, had an audiotape with verbal guidance for 12 contractions to use at home, and kept a training diary. The electrical stimulation patients were seen monthly and were observed by the physical therapist receiving their stimulation therapy,

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probably through one-way glass. Oh, sorry.

They used their devices for 30 minutes daily. The compliance was 93 percent in the exercise group compared to 73 percent in the electrical stimulation group, which is not surprising considering the extra stimulation in terms of contact that the PFME group received. The baseline stress pad test for the exercise group was 36.6 grams and that for the electric stimulation group was 56 grams. So, I suppose you could say there's a bias in starting there in terms of what they're starting with in their pad test results.

A statement was made in the report that there was a 78 percent improvement on the pad test for those patients receiving exercise therapy compared to only 13 percent in the electrical

stimulation group. This figure wasn't really found in the Bo study, or at least I just didn't see it or read it, and it look like it was derived by comparing baseline pad test measurement and the change that occurred after therapy. Well, for the exercise group, the change that occurred was 30.2 grams less and their baseline was 36 grams, so that came to me to 82.5 percent improvement. The electrical stimulation group only had 7.4 grams of

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change in their pad test, but the baseline was a lot higher, a 56 gram loss, so their improvement was 13 percent. I don't know about the statistical methods in this technique, but it seems it's just a little bit biased.

Finally, in the studies on PFMEs, the objective cure rate from the study showed that 11 of 25 patients were cured, which is really excellent, and for electrical stimulation it was 7, which isn't too bad, but of course not as good as the other one. If we look at subjective cure or improved, as stated in the article, that for PFMEs was 92 percent. That for electrical stimulation was 64 percent, and by the way, for vaginal cones it was 63 percent. Considering the Monaco consensus from 1998 that says that if you get 65 to 75 percent receiving exercises and they improve in the short-term, that's not a bad result, so the result for electrical stimulation isn't really that bad, although of course, the muscle exercises is kind of out of sight.

With respect to urge incontinence, we heard about the Brubaker study and others, and it showed efficacy. There's one other; Yamanishi just reported in Urology, March of 2000, reporting on 68

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patients with detrusor instability confirmed by urodynamic testing, in which patients were randomly assigned, so 32 received treatment and 28 received sham. Efficacy was evaluated by frequency volume chart, urodynamic testing. The active group had 81 percent improvement and the sham had 32 percent. It just seems like at least for urge incontinence, there are really no dissenting studies.

In conclusion, we conclude that the evidence regarding clinical efficacy for electrical

stimulation in treating stress, urge and mixed incontinence is present and is adequate to say that yes, it is clinically effective. There must be some allowance for these patients to receive home therapy with home stimulation units. It's convenient, they have no side effects, they can use them in the comfortable environment of home, do not have to travel to the doctor's office, and the therapy in terms of duration, I think somewhere between 12 and 20 weeks. We don't know if there should be maintenance therapy or not; it's a consideration.

I really don't know that it should be first line therapy, if that's any importance, unless of course there are thoughts and suggestions

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on biofeedback go awry, and we can't use that. We are not treating as a statistical condition, but are interacting with a clinical condition that threatens as many as 30 percent of our older Medicare patients. We have to be able to present these elderly patients with viable conservative options other than drugs and surgery, and we need different ones, because everyone is not treated the same way. Some may require electrical stimulation, some require exercise therapy or bladder retaining.

Finally, the panel has a major responsibility in evaluating these therapies which we feel will help our patients progress towards continence. Thank you.

MS. CONRAD: Thank you, Dr. Bent. Dr. Perry? And the final presenter will be Dr. Dmochowski.

DR. PERRY: My name is still John Perry and I represent the Biofeedback Society. I was about to say that my financial disclosure statement from yesterday applies. The fact of the matter is I have no financial interest in any of the companies that sell electrical stimulation devices, but on the other hand, I understand that many of

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them purchase my sensors, so I guess it would be in my personal financial interest if people used more electric stim.

However, I would like to accomplish an

impossible task, and that is to change your conception, your basic category about the nature of electric stim and ask, is electric stim a drug? Now, let me explain. Agency health care policy and research decreed that incontinent individuals could receive therapy from three categories, surgery, pharmaceutical or the catchall category, behavioral interventions, and they put electric stim in the behavioral category. I hope to tell you today, to convince you today that it doesn't belong there, and it needs to be evaluated on entirely different criteria from the behavioral techniques, including the biofeedback that we discussed yesterday.

If you look at the guideline's descriptions, they say very clearly that surgery has certain qualities, the clinician success of any surgical procedure depends on operator expertise. Prospectus comparisons often include different surgeons with different degrees of experience and expertise. Did you ever hear that about drug studies? The personal qualities of the clinician

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are not relevant in a pharmaceutical study. Drugs must be proven to the FDA to be effective, regardless of the clinician's or the patient's belief system. The agency is in the drug, not in the dispenser. But when we turn to clinician characteristics under behavioral therapies, the Agency says all behavioral techniques involve educating the patient and providing positive reinforcement for effort and progress. And they go to on say, require personal and caregiver involvement in continued practice. If motivated, most people show improvement.

Those statements do not apply to electric stim. So, is electric stim a drug? Well, it certainly isn't surgery. It isn't behavior therapy either. It works like a drug, that is, it works regardless of the patient's efforts or beliefs. Therefore, I propose that we should either treat it like a drug or establish a new fourth category. If we treat it like a drug, I suggest that we apply the same rigorous standards of testing randomized control studies that are absolutely essential in the case of a drug.

Let's look at the data that was

presented in the TEC report as far as the
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effectiveness. In comparison with placebo, we have five studies. Sand got 30 percent by diary, 66 by pad weight. Luber got 14 by diary. Laycock got 66 percent by pad weight. Brubaker got no change in his parameters. Yamanishi, 33 percent by diary, 56 percent by pad weight. Comparing E stim with the alternative therapies, Bo got 30 percent by diary and 13 by pad weight. Smith got 53 percent by diary. Olah got 60 percent by diary. Laycock had no data on this aspect. And Hahn had 34 percent by pad weight. Notice the range of numbers we're looking at. Here's an odd ball; Gloman, 100 percent, but that's when combined with PME, and we're only dealing with an N of 7. Smith, '96, got 59 percent. And Moore, '99, got 66 percent, but again, that's when combined with PME. Overall, if you average these two columns, you get 47 percent improvement to 50 percent improvement, and that's improvement in symptom reduction rates.

How effective is 47 to 50 percent? Using Burns category of moderate equals 12 or 13 leaks a week -- I couldn't find a graphic for leaks, so I had to use a graphic for diapers, but I hope you'll understand the editorial liberty here. But a 50 percent reduction in symptoms only means
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going from 12 leaks a week to 6 leaks a week, and that's still virtually one every day, so it's not a lot better. So the TEC conclusion was that for stress urinary incontinence, the literature does not provide strong and consistent evidence that PFES reduces the frequency of incontinent episodes. For urge, no conclusions can be drawn from either of the two trials that they cited. And for post-prostate, research does not demonstrate that the addition of PFES to PME improves the outcome.

The Biofeedback Society therefore, agrees with the major conclusions of the TEC report for PFES. And in addition, we raise serious questions about spending public funds for a technique that is decidedly less effective than other readily available alternatives, namely biofeedback. Thank you.

DR. GARBER: Thank you.
MS. CONRAD: Okay, let's move on to Dr. Dmochowski.
DR. DMOCHOWSKI: Good morning. Roger Dmochowski, of the American Urologic Association. I have no financial interest in any of the companies being evaluated today.

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I'll make a very brief position statement, which is our position statement that you should have in your hands and then I'd like to make further comments, but I should be substantially less than the time allotted.

To quote our position statement, our committee does not feel there is strong consensus on the effectiveness of vaginal, superclevic and/or anal electrical stimulation for urge, stress or mixed incontinence. The committee does urge further randomized trials to be done, looking at all objection and subjective parameters related to incontinence, and that such trials should include a comparison of electrical stimulation to behavioral modification programs within various populations, those populations being specifically men, women, the elderly, children, and neurogenic patients. Therefore, based upon our review of the literature, and somewhat to parrot your TEC report, which again was very well done: Given the above considerations and the strict criteria which you asked us to evaluate and perform this process, we feel that isolated electrical stimulation achieved a rating of level five, which would be less effective but with advantages. However, some data do exist to

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support potentially a level four categorization, which is as effective but with no advantages.

That's our official statement. Now let me make a couple points to amplify some prior speakers' comments. In my own clinical experience and that of many of my colleagues, urology deals specifically with urinary incontinence as a main component of their practice. Electrical stimulation is a difficult therapy to administer for some patients, but it probably has a role for patients with urgency and frequency disorders. You've heard today that patients, older patients

specifically, have trouble with pharmacologic therapies, they have side effects from pharmacologic therapies. This therapy is an intermediate therapy and should be viewed as potentially in integral or an integrated therapy within the global approach to patients with mixed and significantly, urgency frequency symptomologies, because it does give additive benefit, and you can see that in the nonrandomized control trials, which however are objective.

There is good data to suggest that there is not only good urodynamic effect, which is a true objective parameter, but also good subjective

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effect with patients with urgency and frequency disorders. And so, it represents another option and again, that comment has been made several times, for patients who cannot rigidly be categorized as pharmacologic patients or surgical patients. And again, that really applies to a substantive majority of the patients in the Medicare population. Many of these patients are not good surgical candidates and really aren't, surgery would not be beneficial to them because of the urgency and frequency component of their voiding dysfunction. And many patients are not able to tolerate anticholinergic agents because of their side effects.

So I think it's important that you view the potential for this therapy within, again, the point I made yesterday, the larger behavioral modification component. Dr. Perry's comments were very germane and I would like to amplify on something that Dr. Antoci said previously, this parallelism that was made with neuromodulation. And Dr. Lefevre did a very good job of sort of categorizing what is the benefit of this therapy. There is a muscular benefit, but for urgency and frequency patients, potentially the neuromodulatory

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benefit is the more important component. We are neuromodulating these patients. And so, you see results in urgency and frequency patients because of success in neuromodulating those patients.

The parallelism was made with implantable devices that this committee will look

at in a subsequent meeting. In no way is electrical stimulation delivered in an isolated fashion to the pelvic floor as efficacious as that therapy, the implantable therapy, but it is less intrusive obviously, and has less complications associated with it. So it definitely again, it should be viewed much like hypertensive therapy, as an increment in the overall therapeutic delivery for these patients. Any questions from the panel?

DR. EPSTEIN: Can you cite the evidence you think is most compelling for the latter part of the statement that you're making?

DR. DMOCHOWSKI: For the urgency and frequency data?

DR. EPSTEIN: Yeah.

DR. DMOCHOWSKI: Well, that is largely clinical experience. There are some studies, and Dr. Gray actually gave you two references that I believe are in his component. I don't have any

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specific references.

DR. EPSTEIN: Is the new Yamanishi reference one you're referring to?

DR. DMOCHOWSKI: The new Yamanishi reference, and Dr. Gray alluded to the urodynamic references to, which is also very compelling in terms of what this does in terms of neuromodulating overall bladder function in terms of urgency or detrusor instability, which again, is an objective criteria that can be evaluated by urodynamicists.

DR. EPSTEIN: Brubaker and Smith?

DR. DMOCHOWSKI: Brubaker and Smith, thank you. Well, there's another article that Dr. Gray alluded to. The Brubaker article has, as we know, some methodologic problems and again, it's only, if you look at that specifically for urodynamic effect, there is some urodynamic effect. But again, in other trials, we have seen that there is effect of this agent for urgency and infrequency as an isolated symptomatology.

DR. GARBER: Thank you.

MS. CONRAD: Thank you. Next we have John Whyte, medical officer for the coverage and analysis group.

DR. WHYTE: Thank you, Connie. Just a

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reminder to the panel that you do have a copy of my remarks, as well as Dr. Lefevre's slides that are in your supplementary packet.

I do want to thank Dr. Garber and Dr. Maves, as well as the other members of the panel and the members of the public who have taken considerable time over the past day, day and a half, as well as the past few months, to advise us on the topic of urinary incontinence. This is a new coverage process for us, one that is focused on evidence based decision making, and a key component of this evidence based process is the technology assessment.

And for this topic, we ordered a technology assessment by contracting with Blue Cross Blue Shield Technology Evaluation Center, which you heard about yesterday, is an evidence based practice center of the Agency for Health Research and Quality. We looked at three indications, stress incontinence, urge incontinence, and post-prostatectomy incontinence.

And for the purposes of this meeting, we are defining PFES as the use of a nonimplantable electrical device that delivers variable rates of current to the pelvic floor, with the intent of

strengthening pelvic floor musculature. It's important to note the distinction, that we're talking about nonimplantable devices, because there are implantable devices which will not be discussed during this meeting.

Now, there were essentially three questions that formed the focus of the assessment. First, compared to placebo, is treatment with PFES efficacious in reducing incontinence? Two, what is the efficacy of PFES as compared to PFMEs or alternative nonsurgical treatment? And three, does the addition of PFES to PMEs result in improved outcomes above that obtained with PME alone?

For the next couple slides, I will discuss how we selected the articles that we used, as well as the TEC used, to base their assessment. There were several criteria. The first was that they were full-length peer reviewed articles reporting on outcomes of treatment for urinary incontinence, using PFES. They had to include

patients with documented stress, urge, or mixed incontinence, by physician diagnosis and urodynamic testing. They needed to include a concurrent comparison group of patients treated without PFES in one of the following categories: Placebo

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control treatment; was mentioned earlier, treatment with alternative nonsurgical therapy for incontinence. By this we mean PMEs, vaginal cones, bladder training, or pharmacologic agents.

We also wanted to see valid health outcome measures, and by that we mean a percent decrease in incontinence episodes via patient diary, a percent decrease in the volume of urine loss on a standard pad test, the percent of patients with a 50 percent or greater improvement, or the percent of patients dry.

We also wanted to see an adequate description of the patient population, including diagnostic categories of incontinence. And finally, we wanted to see an adequate description of the treatment course, including length of treatment and number of sessions.

At this juncture we will hear the results of the technology assessment. As you all met, Dr. Lefevre yesterday, for other members of the audience that did not hear him yesterday, Dr. Lefevre is an assistant professor of medicine at Northwestern Medical School, and he is a senior consultant with the Blue Cross Blue Shield TEC, where he has been for the past eight years. He's

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been the author of over 25 technology assessments.

Just as a point of reference, after Dr. Lefevre's remarks, I will make some additional comments, so I ask that you hold all of your questions until the end of both of our discussions. So at this point I will yield the mike to Dr. Lefevre.

MS. SMITH: Excuse me, Connie. I didn't get the handout. I'm sharing it with my buddy over here, but I didn't get the handout of all the slides that are being presented.

MS. CONRAD: It's on its way.

DR. LEFEVRE: I want to thank the panel again for the opportunity to present the results of

our work, and again to acknowledge the collaborators on this project with myself, which were primarily Ted Speroff and Naomi Aronson, both PhDs and methodologists.

I'm going to say again a little bit of background that I went through yesterday, and try to go through this quickly, to spend more time focusing on the evidence. I would also like to say that I am encouraged by this debate today which has been focused, the majority of the debate has been focused on the adequacy of the evidence, and I am

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encouraged to hear this kind of debate, because I think there is room for legitimate debate on the evidence, and particularly what threshold should be required for the evidence to meet a standard of efficacy.

So by way of background, just going over what TEC is, TEC was founded in 1985 by Blue Cross Blue Shield Association, which is the umbrella organization for the Blue Cross plans. It provides support services, technology assessments which is one of them, has performed numerous technology assessments, and has evolved from a proprietary organization into now where we perform larger assessments entirely in the public domain in partnership with AHRQ. This is just a diagram of the relationship of TEC with the Blue Cross plans, with Kaiser Permanente, one of our major partners, and with TEC subsribers, who are outside health plans, and also our contract relationship as an EPC with AHRQ.

TEC's major priority is to maintain the scientific integrity of the products. This is what the plans and our subscribers want. They want a review of the best available evidence. There is a critical need for this. And they can use this in

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making the difficult coverage decisions that they have to make. TEC does not make coverage decisions; we provide plans with evidence in order to help them to make coverage decisions. We do not consider costs. We use a formalized set of criteria as an anchor for what constitutes adequate evidence for efficacy, and we have a medical advisory panel which is composed of, the majority

of which are independent of the Blue Cross plans, which has final say over all our assessments, including the current one that we will be presenting today.

Now, the objective of this assessment was to determine whether PFES improves health outcome for patients with urinary incontinence. We'll take an evidence-based approach, similar to what we described yesterday, and look at the adequacy of the evidence, the consistency, and the methodological quality, as well as considering the magnitude of effect.

Systematic review is considered the best available way to synthesize a body of literature to determine treatment effectiveness. And to reemphasize the points I made yesterday, the main strength of systematic review is its a priori

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problem formulation and development of study selection criteria. We set up, what are the patient indications, what is the treatment that we're concerned with, what's the definition of the treatment we're concerned with, what are the outcomes that we consider clinically relevant, I comparisons, and what is the relevant comparisons? Following this, we develop a priori, what are the studies that can answer the question that we're posing in this population? Following this, we systematically search the literature, we abstract the relevant outcome data, and then we synthesize the data either qualitatively or quantitatively.

Going through the problem formulation, just to reiterate John's points, the patient indications are stress, urge and post-prostatectomy incontinence. The intervention is PFES, as described by Dr. Whyte. The outcomes of interest, again, similar to yesterday's outcomes of interest. What we're primarily concerned with is a reduction in the frequency and/or severity of urinary incontinence.

This is most commonly measured by one of two methods, patient recorded incontinence diaries, or a standardized pad test, which is specific for

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stress incontinence. There can be and expected to be a great deal of variability in these

measurements, both in the inherent variability in the incontinence itself, which may be expected to vary with many factors such as activity level, fluid intake, and other such variables, and there also would be expected in patient recorded diaries that, as these being somewhat subjective measures, there may also be an additional level of variability in these measures. And this is important when we get to discuss the outcomes later, regarding the outcomes of the clinical trials.

The reported outcomes that we're concerned with are percent change in incontinence. This is the most commonly reported outcome, percent reduction in frequency of incontinence. Also, the percent of patients improved, which is defined as the percentage of patients with at least a 50 percent improvement in the frequency of incontinence is a valid health outcome. And finally, the percent of patients who are cured, who have no further incontinence, is certainly a valid clinical outcome.

The comparison treatments as stated

previously are placebo. This is an efficacy question, is PFES efficacious? We also would like to compare it to alternative treatments to answer the question of what is the comparison, comparative effectiveness of PFES compared to available alternatives? And finally, it can be used as an adjunct to behavioral treatment, it can be added on to PFMEs, which has been done in several studies, and this is another relevant comparison that we will attempt to make conclusions on. Which gets us to our questions, again. Three indications, stress, urge and post-prostatectomy incontinence, three separate questions which Dr. Whyte has put forth.

And I would like to say just briefly that I believe the questions that HCFA has devised are the relevant clinical questions, both today and yesterday, and I believe that strongly. I don't think it's the proper time to elaborate, but I would be glad to in another forum.

Study selection criteria, as Dr. Whyte has indicated, full-length peer reviewed literature

including a concurrent comparison group, which is the most important aspect of our study selection criteria. We do not feel that uncontrolled trials

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can evaluate the efficacy of this technique adequately.

Now our search results revealed 12 articles that met the study selection criteria, and these 12 articles report on a total of 626 patients. The range of the ends in the studies was 14 to 146. There were six trials comparing PFES to placebo. There were five trials comparing PFES to alternative treatments. And there was one trial which compared the addition of PFES plus PMEs to PMEs alone.

This slide just gives sort of a lay of the land to tell you where the studies fall out and where the N's fall out. And again, across the top column we have the three indications, stress, urge and post-prostatectomy incontinence, and the three separate questions, versus placebo, versus alternatives, and the addition of PFES to PME. As you can see here, the studies sort of cluster in stress incontinence. Similar to biofeedback, most of the literature is on stress incontinence. There is a significant number of studies on the question of PFES versus placebo and versus alternatives. In the other boxes there's only one study in each of the other categories. And I would also note that

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these add up to more than 12 studies, but some of the studies report separately on different indications; that's why you see the -- one study may make it into two different categories of reports on different indications separately.

Now, first let's look at the PFES versus placebo and discuss some of the key methodological features. There were five studies in this category with a total N of 243. Four of the five studies reported that their populations were randomized to PFES versus placebo. Four of the five were double blinded and one was single blinded. Three of the five had at least one potential bias, and I will talk a little bit about that in a second.

One important point to make in this body of literature is there is a great deal of

variability in the treatment delivery. This has been alluded to before; the treatment delivery varies by the type of device used, the frequency of stimulation that's given, where the device is implanted, and the time that it's used. And I would certainly defer to the clinical experts such as Dr. Sand as to the physiological rationale as to why different types of stimulation may produce different results, but I think this remains a

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matter for empiric investigation. There's really no data on telling us which is better and in which situation one may work better than another one.

Unfortunately one of the studies, which was the largest study, the Brubaker study, was severely limited because there was extensive missing diary data, and they were not able to report on the primary outcomes which was the reduction in the frequency of incontinence because there was too much missing data.

Now this slide gives the areas in which we felt there were potential biases in the studies evaluated and three of the five studies, as I indicated, have potential biases. Again, the issue of measurement bias, which I keep in parentheses here, because this is inherent to all the studies because of the way the outcome measures are constructed. It's not necessarily a criticism of the methodology of the study itself, but it's a fact that the outcome measures are not optimal, and it's a recognition that there may be measurement error inherent in these outcome measurements.

Now, I think it's useful to talk a little bit about the Sand study in detail, because this is I think the most influential study in the

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field and it has several strengths in the methodology. And when I put up this box here, it may appear that we're only looking at the weaknesses. It does have strengths. It was a multicenter study, it was double blinded and randomized, and they had a well described and adequate method of randomization. However, I have the box here checked for selection bias. How could that be when they have a good randomization process? Randomization is the best way to minimize

the chance of selection bias, and to minimize the chance that your groups will be noncomparable. However, it doesn't insure that, and particularly with small numbers of patients, it may end up by chance that the groups are not comparable. And when you look at the baseline values in this Sand article, there are differences in age; there's a seven year difference in age. And there are differences in the baseline severity of illness and the severity of incontinence. So, we feel that there may have been not, comparability of the groups may have been not as good as would have been ideal. And this was unfortunate; it was not a problem with the methodology but it happened.

Secondly, regarding attrition bias,

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there was a high dropout rate in the Sand trial. 20 percent of the patients in the PFES group dropped out. Now, when we have high dropouts, we look at whether the analysis took these into account. And Dr. Sand had indicated that there was intent to treat analysis. There was on some of the outcomes. On the outcomes that we're going to look at, the three outcomes that we're looking at, the decrease in the frequency of incontinence, the percent of patients improved, and the percent of patients cured, it was clear that there was intent to treat analysis on two of these three outcomes, the percent of patients improved and for the percent of patients cured. However, I believe that the -- and I still believe after talking with Dr. Sand that the analysis of the reduction in the frequency of incontinence was not done on an intent to treat basis, and I will elaborate on that if people would like to here my thoughts.

Second, regarding the Yamanishi study, the Yamanishi study I have checked here, potential for selection bias. There is no mention in the Yamanishi study of any randomization. There's no mention at all of how the group allocation process was done. Therefore, I feel there is a potential

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for selection bias. Dr. Sand has talked to the researchers, and they have indicated to him that it was randomized. It's not in the study, it's not written anywhere in the article.

Let's look at the results of these five studies for the outcome of reduction in the frequency of incontinence. In the Sand study, and this is where I am indicating I do not believe that the analysis was intent to treat. There were 45 patients analyzed, which was the 52 minus the 7 dropouts. And there was a 42 percent improvement in the leaks per day in the PFES group and in the sham group there was a 26 percent worsening in the frequency of incontinence. The group comparisons between these two groups was statistically significant and it was at the .05 or .04 level. I don't remember which one it was, it was either .04 or .05.

The Luber study, which is of interest, because it treats a population which is somewhat different from the other studies. This study treats patients who have failed or who have not agreed to do PFMEs, and this is a population of interest. Many people have said this is a population that PFS should be applied to. This is

the only study that's looked at that specific population, and there was no difference in the outcomes, as Dr. Luber has indicated previously.

The Laycock study did not report the values pre and post, and were not able to come up with percent improvements, but they did state in the text that there was no group differences in reduction in the frequency of incontinence.

The Brubaker study, this is the largest study, and this was a well designed study. Unfortunately, this was the study with the extensive missing diary data. It did not report on the reduction of the frequency of incontinence. What they did do at the end of the study is they asked the patients to complete a 24-hour diary on the frequency of incontinence, so we have post-measures, we have post-measures for the entire population.

Finally, we have Yamanishi which as I indicated before, did not report randomization. It showed a statistically significant difference between the PFES and the sham group, a 33 percent improvement versus a zero percent improvement in the sham group.

The next outcome of interest, the
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standardized pad test outcomes, here we see similar results, although the magnitude of effect here is somewhat larger. A 66 percent decrease in pad weight in the PFES group versus an 8 percent worsening in the sham group. Luber did not report on this outcome. Laycock reported on it and had a 66 percent improvement in the electrical stimulation group versus a 28 percent improvement in the sham group, a difference that did not reach statistical significance. Brubaker did not report on this. And Yamanishi reported a 56 percent improvement in the PFES group and a 45 percent worsening in the sham electrical stimulation group.

Now in our TEC report we make a point about this worsening of incontinence in the sham group. This is seen both in the Sand study and in the Yamanishi study. And first of all, it's curious to us; why would you expect worsening in a sham group, and you might expect that the first question is a natural history of the disease consistent with a large worsening over a short period of time, and I don't believe that's the case. I don't believe you would expect this type of worsening over an 8 to 12 week period. And secondly, we considered, could there be a negative
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placebo effect? Could the patients have negative expectations if they knew they were getting a sham treatment? That's possible but I can't really say how likely it is; I think it's pretty unlikely. Usually a placebo effect goes in the positive direction. And finally we considered, maybe it's due to instability of these measurements, maybe these measurements are highly variable and they're prone to statistical instability. So I wanted to show just a couple of slides related to that.

This is the Sand data and this is the data on frequency of incontinence, leaks per day. And the aqua bars are the pre values and the red bars are the post values. And the arrow bars represent the standard deviations. Sand reported in his article the standard errors, and we converted these to standard deviations and as you can see, these are quite large, sometimes larger

than the value themselves. And again, the comparison is statistically is statistically significant, but we feel that the comparison is influenced by the worsening seen in the placebo group.

Another way to look at this would be to look at the confidence intervals around these

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values. Again starting with the standard error, we computed the confidence intervals around these values, and as you can see, the confidence intervals are rather large and I would especially point to the placebo group, where there was a worsening from 3 leaks per day to 3.8 leaks per day, and the confidence interval around the post leaks per day which is very large, ranging from 2.3 to 5.3. We also constructed an estimate of the confidence interval for the difference in the post leaks per day, which is an absolute value of 2, but a wide confidence interval. It might be as low as .4, it might be as large as 3.6. So again, I think this indicates that these measures are very highly variable and this needs to be considered when we're considering the robustness of this data in terms of the efficacy.

So in summary for the data on PFES versus placebo, some trials do report a significant benefit with PFES for stress incontinence, but this is not consistent. The majority of the trials do have a potential for bias and the effect size in the trials is of a magnitude that could result in bias. If we look at the effect size, and this is sort of consistent with what Dr. Perry was saying,

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the effect size for frequency of incontinence is in the 30 to 40 percent range, somewhat higher for the pad test, but we do consider the reduction in the frequency of incontinence to be a somewhat more clinically relevant outcome than the pad test. The percent change is modest, the 30 to 40 percent range. And in both studies where statistical significance was reported, that's the Yamanishi study and the Sand study, the P value was in the .04 to .05 range. So it did reach statistical significance, but just very close to the threshold that we use for defining statistical significance.

So again, there is some suggestion that there's efficacy, but I do not feel this is a very robust body of data.

Let's look at the data on PFES versus alternatives. There were five trials with a total N of 260. All five were randomized. Four of the five were unblinded, one was single blinded, and two of the five had potential biases. This is again, a grid of the potential biases identified. In the Laycock study and in the Hahn study, there were potential biases identified.

Now, the results of PFES versus alternatives on the frequency of incontinence are

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shown here. There were three studies that compared directly the results of electrical stimulation versus alternatives, and there was only one study that showed any statistically significant differences on these outcomes, and this was actually in favor of PFMEs as superior to PFES. This was the Bo study, this was 1999, this was the largest study in this group of studies, that had four groups of patients: PFES, PMEs alone with a trained therapist, vaginal cones, which is another variation of PMEs, and a waiting list control. Across all outcome measures, the PME group had superior outcomes consistently across all outcome measures. It reached statistical significance on several of these outcome measures, including the comparison with PFES.

The PFES would roughly give the same amount of improvement compared to the cones and was superior to the control group and it did, the PFES did reach significance over the control group on some of the outcome measures. And again, this is a waiting list control, it is not a placebo control. That's why it's not included in the first body of literature, a waiting list control versus PFES.

The other two studies that reported on

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this outcome, the Smith study with an N of 18, there was a trend towards greater improvement in the PFES which did not reach statistical significance, and in the Olah study there was no difference between groups.

On the standardized pad tests, similar

outcomes, a statistically significant improvement in the PFME group versus the PFES group in the Bo study. And note again, this is a large difference, 78 percent in the PME group versus 13 percent in the PFES group. The Olah study, there was no difference between PFES and vaginal cones, with the trend favoring PFES. While in the Hahn study, there was no difference in the two groups, with the trend favoring the PME group.

A summary of this data is that one study reports that PME may be superior to PFES, but this is not a consistent finding across the body of literature. Therefore, the evidence is not adequate to form conclusions on the comparative benefit of PFES versus alternatives.

Finally, in the last three categories, where there was one trial each, in the pelvic floor plus PME versus sham plus PME, there was one trial with an N of 14. There was significant baseline

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differences in the severity of incontinence, 12.5 leaks per day versus 5 leaks per day in the PFES group. They reported 100 percent improvement in the PFES plus PME, versus a 52 percent improvement in the sham, and this was significant at the P at less than .05 level.

For urge and post-prostatectomy incontinence, there was one trial in each of these categories, neither of which reported any statistically significant group differences.

So in conclusion, our conclusions are the evidence is not adequate to determine the efficacy of PFES for stress incontinence, and this is because of the reasons I enumerated previously. The results of the studies are not consistent, there are potential biases present in the positive studies, and the effect size in the positive studies, which is modest, is of a magnitude that could be explained by bias. The evidence does not suggest that PFES is superior to alternatives for stress incontinence. And evidence for PFES in urge and post-prostatectomy incontinence is sparse.

One final comment I would like to make is regarding the AHCPR guidelines on PFES, the conclusions of which do differ somewhat from our

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conclusions in this current review. In 1996, the AHCPR reviewed the literature on PFES. At this time there were two randomized control trials, this was the Sand trial and this was the Blowman trial, which was the adjunct, the addition of pelvic floor to sham, both of which showed a positive effect. However, they did not feel that that level of randomized control trial evidence met their Level A evidence. They gave it a Level B evidence, which primarily was based on their results of clinical series. They indicated that further controlled trials were necessary to determine the efficacy, and gave it a Level B recommendation. So there was some disagreement. Since then, several studies have come out which has given us more data to interpret this question.

And that ends my presentation. Thank you.

MS. CONRAD: Dr. Whyte.

DR. WHYTE: Thank you. Now along with the technology assessment that you just heard, panel members also received for consideration additional articles and materials. We call them exclusion articles because they were not included in the technology assessment, and they were not

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included in the assessment because they didn't meet the selection criteria that I discussed at the beginning of my presentation. And that was because they were primarily historical controls, or pre-post design, or they were frequently cited articles. But it's important to note that they have been included for consideration as part of your packets. And you've also heard a wealth of information this morning to consider. So having heard all that, I'm going to review the questions that Perry Bridger discussed early on this morning.

The first question is: Is the scientific evidence adequate to draw conclusions about the effectiveness of PFES compared to placebo, PFES compared to PMEs or alternative nonsurgical techniques, and then finally PFES and PMEs compared to PMEs alone.

And you look at those in the Medicare populations for the following three indications, which I'm sure you all know by now: Stress

incontinence, urge incontinence and post-prostatectomy incontinence.

Let me just review, some points that we ask you to consider as you answer these questions are first related to the adequacy of the study

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design, and is there evidence that the studies do not over or underestimate the effect of the intervention. And do the studies permit conclusions about the health outcomes of the technologies? And as you evaluate the studies, we ask you to weigh the different types of study methodologies that exist. There is a recognition that not every type of study has to be a randomized prospective placebo controlled study, and that there are different methodologies to use to answer different types of questions, and we ask you to weigh that in your deliberations.

Other points to consider include the consistency of results, and are the results of the studies consistent or are they contradictory? The applicability to the Medicare populations. Are the results of the studies applicable to our various populations, which include the elderly and the disabled? And the applicability beyond the research setting; are the results likely to apply in routine clinical settings?

We discussed this yesterday, but just to review one more time, if the evidence is inadequate to draw conclusions, which would be first question, your work would be done for the day. If you answer

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yes to those questions, then -- or that question, then we will move on to a series of three additional questions, which are questions 2, 3 and 4. I know you heard this yesterday, but it seems like a long time ago, so just to review one more time, the categories of effectiveness. There are seven categories.

The first is breakthrough technology, that the improvement in the health outcomes is so large that the intervention becomes the standard of care. Second, it's more effective, the new intervention improves health outcomes by a significant, albeit small margin as compared with an established service or medical items. Third,

it's as effective but with advantages; the intervention has the same effect on health outcomes as an established service or medical item, but it has some advantages such as convenience, fewer side effects, or some other advantages that some patients may prefer. It may be as effective and with no advantages, so the intervention has the same effect on health outcomes as an established alternative, but it doesn't have any advantages. It may be less effective but with advantages, so although the intervention is less effective than an

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established alternative, but more effective than doing nothing, it has some advantages. It may be less effective and with no advantages, so the intervention is less effective than established alternative, but again, more effective than doing nothing, and has no significant advantages. And then finally, it may be not effective; the intervention has effect, or it may have deleterious effects on health outcomes when compared to doing nothing.

So those are the categories of effectiveness, the seven categories to keep in mind. If you answer yes to question number 1, we will move on to questions 2, 3 and 4.

So question number 2, and you have all this in front of you: If the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effect of PFES compared to placebo for the treatment of urinary incontinence? And then just to follow through, question number 3 will be, if the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effect of PFES compared to PMEs or alternative nonsurgical techniques for the treatment of urinary incontinence? And then

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finally, your last question, if the evidence is adequate to draw conclusions, what is the size, if any, of the overall health effect of the addition of PFES to PMEs compared to PMEs alone?

So that concludes our presentation, and we look forward to your deliberations.

DR. GARBER: This is important, but it is housekeeping. We are approximately a half hour

behind schedule. A number of panel members have told me that they have flights to catch, actually a little bit early. Let me float a suggestion that we break now or in an hour, a short break to get food, and carry through our deliberations while we eat, so that we can get through the entire agenda. What is the sense of the panel? This is a good breaking point in terms of the agenda, so should we break now to get food? Come back here in 20 minutes.

MS. CONRAD: As soon as possible.

DR. GARBER: As soon as possible, but no later than 20 minutes.

(Recess taken at 11:30 a.m.)

DR. GARBER: I just wanted to mention in terms of comments that you would like transmitted to the Executive Committee, it is certainly my

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intention to communicate faithfully and accurately what all of the panelists said this morning and throughout the rest of the deliberations. But as long as it's not a violation, it would certainly help me if you would send me in written form some of the comments that you would like transmitted to the Executive Committee. Let me add also at this point that the Executive Committee really does want the panel's feedback about how the Executive Committee expressed their recommendations. Some of you expressed reservations about that, and the Executive Committee would certainly welcome hearing from you directly. It would probably be most effective in written form, or if you come to the Executive Committee meeting. But they are seeking input from panel members. So please express yourselves through one of the vehicles that we mentioned.

Now, it is time for the open committee deliberations. Before we start, I didn't get a chance to thank the public speakers from this morning and once again, I think I speak on behalf of the entire panel in expressing our gratitude and also our admiration for the way that your comments were really structured to help us deal with the

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questions at hand. Once again, at least I found it very useful in thinking about these issues.

Again, we have two panel members who are designated reviewers, Lisa Landy and Les Zendle.

DR. LANDY: Can you let Les go first?

DR. GARBER: Okay. Les, are you prepared?

MS. CONRAD: A little housekeeping stuff first. I am required to read the following just for the record. For today's panel meeting, voting members present are: Michael Maves, Linda Bradley, Kenneth Brin, Arnold Epstein, Logan Holtgrewe, Lisa Landy, Angus McBryde, James Rathmell, and Les Zendle. A quorum is present. No one has been recused because of conflicts of interest.

And now, Dr. Garber, you may open the deliberations and then make motions, ask for motions.

DR. GARBER: I think first, let's ask the two designated panel members to comment, and then the panel members generally may comment and ask questions. Dr. Les Zendle.

DR. ZENDLE: I just wanted to make a couple points. I was writing down a few of the things that were said this morning. One speaker

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said that there was no scientific evidence that PFES is not effective, and that's true, but I don't know that it's relevant right now. Another speaker said that the TEC assessment concluded that PFES is not effective, and I don't think that's true. I don't think that's what the TEC assessment said. I think it said there wasn't sufficient evidence to reach conclusions one way or the other, because of not consistent outcomes and some issues of bias in some of the reports, and I agree with that assessment. I think that there isn't enough sufficient evidence to reach conclusions one way or the other. And so therefore, I think that the answer to number 1 is no, there is not enough evidence.

Although there are some bigger numbers today than yesterday, still, when you take into consideration the number of people in just our country alone that are affected by urinary incontinence and the disability that it causes, again, I'm surprised that there isn't more numbers of people in studies to answer these very important

questions. So that's all I want to say.
DR. GARBER: Dr. Landy, are you ready?
DR. LANDY: Yeah. I think to be
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consistent as a panel, we need to apply the same level of rigor we applied yesterday, whether appropriate or not, and not be biased by our feelings about what happened. And I think we shouldn't compensate on what happened yesterday in what we decide today. I think looking at the question is the important thing, and the question put before us, is scientific evidence adequate to draw conclusions? That's the number one question. They are not asking us clinical evidence, clinical experience. I have my own bias about how this panel could have been more of value to HCFA as an advisory panel, and I will save that for my letters to the Executive Committee, but I think our task today has to stay focused in terms of what they asked us to do.
If you look at the data on stress incontinence and the E Stim, I think there are very good trials there. I think the problem goes back to how many randomized control trials are necessary for evidence, what threshold are we using, and if we should use the same threshold we used yesterday? I think as my role as a primary reviewer, and being a urogynecologist, having experience clinically in this area, the problem I
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see with the evidence put before us is one of variability. We have some very good trials here. However, they're not really comparable in certain aspects, and Dr. Sand's trial used different modalities than other trials and that came out earlier, in that of the five trials that were reviewed comparing SUI to placebo, there are different frequencies, different devices used, and that may explain the varying outcomes. That doesn't help us with the issue of consistency of data. And that is one of the criteria to evaluate adequacy of the scientific evidence.
So based on that, looking at my breakdown, there was one trial that used simultaneous therapy with two different frequencies, there was one trial that used single

frequency, another trial at 20 hertz, another trial that -- I'm not sure what the Laycock trial used. Yamanishi, which is most comparable to Sand's in terms of positive outcome towards showing a benefit of stress UI, used 50 hertz, while Sand used simultaneous frequent. I'm not sure we can just sort of lump this all together and say, even address question 2, because of the lack of consistency.

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I also, to go on the topic of comparing it to other alternative therapies, I think we were not given a lot of data there and had small numbers, and really maybe don't have enough data to go by to determine whether there is additive benefit or not.

And then in the third category, I really want to mention the urge incontinence. We have two studies that are very good for us to look at. I don't think the urodynamic data of Brubaker's study should be disregarded. However, we are only talking about two studies and small numbers of patients, and missing data, and I think that limits us, again, with making that decision on question 1 the way it's posed to us as a panel.

I think as a clinician, I would interpret this data very differently and if we were asked to give advice as a clinical panel of experts, I think you would be getting a lot different answers than what you're going to be getting based on the questions as they're posed now.

DR. GARBER: Thank you, Lisa. If I could just beg the panel's indulgence, I just wanted to raise a general question that was

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prompted by Dr. Sand's comments first and now Dr. Landy's comments about the variability in treatments. And I don't have any comments about the treatments we are discussing today, but I think, I wanted to flag this as an issue that will come up to us repeatedly.

In many of the areas of medical literature that I follow more closely, a debate rages when you have multiple trials or studies of similar but not absolutely identical

interventions. Even radiology procedures where they use different CT scan or protocols, or cardiology studies, different ways of giving TPA or streptokinases, there is always this question, should you pool the studies together using different variance on the procedures, or should you keep them separate.

And the first point I would make is that you can't turn to a statistics textbook to answer that question. That's really a judgment call. On the one hand, it is possible that some ways of delivering, in fact it's likely that some ways of delivering these therapies are better than others. Rarely do you have direct trials designed to answer that question. And one of the reasons you don't is

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they would ordinarily have to be huge trials to have statistical significance, to have adequate statistical power.

And the other thing to keep in mind is that if you pool studies using different techniques, remember you're implicitly engaging in something called multiple comparisons. And what I mean that is that when you pool the studies, there is a chance that one method, even if they're all truly identical in terms of efficacy, one method may look superior just by chance, because you have multiple studies and you have a five percent significance level or something. If you do multiple studies, one will show greater effectiveness by chance. And so that statistician's answer in that situation is what you've done, you've looked at the date, you've generated a hypothesis, now you have to do a new study to generate the hypothesis.

Well, that's clearly not something we're going to engage in. We as a panel in all these situations will have to make a judgment call and seek the best possible information about whether it's appropriate to combine these different variants or to say no, these are really treatments

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and the trials of the different treatments should not be lumped together.

Now the consequence of deciding not to lump together ordinarily is that, and I think it's

probably true in this area, then you don't have the statistical power to draw conclusions very often. So that's what people who do meta-analysis constantly fret about, should I lump or should I split? If I split, maybe that's fair in some ways, but then we may lose the chance of answering the question.

So, I'm just saying there's no right answer, and I'm not trying to direct anybody's thinking about this issue, but keep in mind that we will probably come down to a judgment call on this issue every time we encounter it, and I expect that to be frequently.

Other panel comments or questions? Diane, I think you were first.

MS. SMITH: I just wanted to address the panel just a little bit as your, one of your technical experts. And one of the problems with looking at the studies and then answering the questions is that in clinical practice how PFES is being used is as an adjunctive therapy. Now the

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TEC report did address one study that looked at functional electronic stimulation as an adjunctive therapy, but one of the things that you can look at in order to see how clinicians are thinking about using electrical stimulation, how they're currently using them are not in randomized control trials but in descriptive studies or in case series studies, or in some of the studies that, for example, Dr. Mikel Gray talked about in his presentation. And I'm referring to page 5 of his presentation if you want to look at that.

What my point is is that one of the things that clinicians routinely use functional electrical stimulation for is for identification of the pelvic floor muscle. Now none of the studies address whether or not it's efficacious to use that, and yet it's common practice, okay? So they use it for identification, maybe for short-term use for the patients in office to identify their muscles and then comply with PME with biofeedback, for example.

The second way the clinician sometimes use functional electric stimulation is perhaps to augment the behavioral treatment of a patient in

order to assure a certain amount of compliance.

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And this is a clinical judgment in which the therapist or nurse decides that the patient would benefit from the augmentation of their PME routine at home by using functional electric stimulation. That's also not addressed in most of these trials, because you don't really have that factor measured and you don't really know what the clinical judgment is.

So what I'm trying to explain to you is that the studies test, as Dr. Perry said, the effect of a drug, or the effect of just what is FES. Now Magnus Fall, in his many physiological studies, did present a physiological basis for why FES should work, and it is a neuromodulation type of effect on a smooth muscle with lower frequency of hertz, and a higher frequency of hertz for striated muscle, for example, the pelvic floor. And this is well accepted by clinicians and people who routinely use FES in their practice, will use higher frequency when they have stress patients, will use lower frequency when they want to have, let's say modulation of urge responses or frequency, or urge incontinence. And this is really part of what people are currently doing.

If you want to look at some of the

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interesting conclusions that Magnus Fall made about looking at all of the studies, I think that you do have to look at his 1998 article in which he basically talks pro and con FES in general, and he makes some important points for you to consider besides the ones I've already named. One is that there is a physiological basis to FES. And two, that it is in common practice in Europe and the United States, and since it is in common practice in these areas, it would not have been so for the last 15 or 20 years had there not been some clinical efficacy to its use.

If you look at the trials, and I was looking at the randomized control trial of Sand and the ones that are mentioned in the TEC report, I think there is a paucity of evidence that for patients with stress UI as documented by urodynamic evidence, that there is some improvement with FES.

There is perhaps a greater effect for patients that have urge incontinence. And as a geriatric nurse practitioner, since we try to avoid pharmacotherapy in many of our frail elderly patients, there are many people who are treating these patients who look at FES as an alternative or an adjunct to PME in order to avoid pharmacotherapy. And there is

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evidence in some of the trials that you heard today, and there's actually very much more evidence in some of the case reports that urge incontinence is definitely mediated positively by FES.

As far as the radical prostatectomy patient, there isn't a lot in the literature about that. However, if you are going to think about alternative treatments for that population, it is a popular alternative that many clinicians use in order to help the gentlemen understand and identify their pelvic floor, because they've just had a pelvic surgery and this may be a problem for them, and it is a popular alternative that's being considered by clinicians.

So, I just wanted to give you those comments.

DR. GARBER: Thank you. Marshall?

DR. STANTON: Thanks. There's a lot of interesting points that were raised today during the presentations, I also want to echo your comment about the excellent presentations, the quality that was done today. I'll just limit myself to two questions.

The first is, regards something that Dr. Lefevre mentioned but the question may better

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be directed to Dr. Whyte, I'll let them decide who wants to address it. And that was, in Dr. Lefevre's presentation when he was talking about the Bo study, this was the one with four different groups that were randomized, one of them being a control but not a placebo group, he mentioned that this one did not meet the selection criteria for the comparison of PFES to control because it was not placebo control. And I noted in Dr. Whyte's presentation, he listed in the selection criteria placebo control, and I'm wondering why that additional level of rigor was

added, when if you look at the Executive Committee's interim recommendations for evaluating effectiveness, which is a quite stringent criteria for selection of studies for evidence, they do not specify placebo control, they talk about control. And that points out to me at least one study, that I'm glad Dr. Lefevre honestly pointed out, why that was not put in the analysis of the PFES versus control, but it concerns me that, were there others that were excluded from that analysis as well?

I have concern on that specifically as it regards today's discussion, but I also have concern for other panels and for our panel going

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forward. Do we as panel members have to be concerned about the selection process of the studies that are being reviewed? Because I think it's difficult enough for us to actually review the ones that are given to us without having to look at the next level of how were these selected.

DR. WHYTE: I'll let Dr. Lefevre answer the specific question about why the Bo article may not have been included in the discussion of placebo, although an important point is that it is included as part of your materials to review prior to the panel. The part of the question that I would answer is your discussion of whether or not the panel would somehow have to review what the selection criteria were or how essentially articles were determined. I think an important point to keep in mind is that which Dr. Lefevre talked about, in terms of that we used an accepted survey instrument in terms of extracting the materials, and we followed the general principles of a systematic review. So it wasn't as if we arbitrarily decided which articles to accept or what not to accept. We framed the questions and then determined how we would select the best available evidence. Let me turn to Dr. Lefevre to

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answer specifically about the Bo issue.

DR. STANTON: But along those lines, John, my major concern is that you have gone a step beyond what the Executive Committee was recommending in types of articles that are adequate for evidence of efficacy.

DR. GARBER: Maybe I could just step in for a moment about what the Executive Committee recommended. The Executive Committee in the discussions made it absolutely clear they were not prescribing which specific studies would be acceptable every setting. In fact, the major message from the document said a variety of forms of evidence would be suitable, and that the key question would be, is this study design likely to be free of bias. And so the Executive Committee in their discussions made it quite clear they didn't think they could say you always need a double blinded randomized control trial. In fact, they said that wasn't true. Nor did they say that a case control study will always be adequate. They left a great deal to the discretion of the panelists in deciding what constituted adequate evidence, but they asked the panel to adhere to the principle of looking at studies that were likely to

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be free of bias. How you interpret that is really handled on a case-by-case.

DR. LEFEVRE: I think that Dr. Garber's point is very for important and I would echo that, and also say that whenever we're looking at a body of literature or a technology or a treatment, we would first want to say, what is the most appropriate and the most rigorous control that we can have, and that's going to vary by the type of technology we're looking at. For example, with biofeedback, we did not try to look at placebo controls, because it would be very difficult if not impossible to construct a placebo control for biofeedback. Therefore, we agreed that the most appropriate control group would be PME alone.

In this case, for PFES it's nice that it's quite easy, or not maybe easy, but it's appropriate to use a placebo control, where you can use a sham instrument. And this is the most appropriate and the most rigorous type of control that can be used with this technology to show efficacy. So for this technology in the clinical context in which it's used, we feel that the most important comparison is with a placebo control. And we would always prefer a placebo control when

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it's feasible to do that kind of control. When it's not feasible to use that kind of control, we will consider the next level of control that might be most appropriate towards that particular technology.

DR. STANTON: I won't belabor that, but if I may ask a second different question that I will be a little briefer on, a number of speakers made reference to the AHCPR document on urinary incontinence in adults, the clinical practice guidelines. And with it being mentioned a number of times, it seemed like it was a very important document and one that was formed by a panel of experts, all in the field, looking over the literature. I just got a copy of this about an hour ago and I can tell you there's no way I'm going to be able to look at this and have any type of input for this panel discussion based on what these experts have said.

I know that HCFA has to filter the materials that are sent to the panel. Otherwise, it would be an impossible task. However, having sent the TEC assessment, which is in some regards similar to this expert opinion, I'm just wondering why this did not meet the criteria for being sent

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to the panels. And also I'd be interested, am I the only one, or did anybody else on the panel receive this?

DR. WHYTE: If I could address your question, what we mailed to the panel was what the Executive Committee requested to be sent to the panel for consideration as part of a packet of material, which was a technology assessment and evidence tables, and that's what we submitted in this circumstance, also with the articles. Now, as you may recall, in the cover letter that was sent to you with the materials that I just mentioned was a specific statement, there was a catalog of materials, and on that catalog was the AHCPR guidelines. Specifically in that sentence about the catalog, we said we would make it available, any item on that, to any panel member which wished to review it.

And we also had a conference call which I think you were a part of, but I'm not completely

sure. You're nodding your head that you were part of that call. If you remember as part of the call, we spent considerable time on the items that were part of the catalog. Your colleague Diane Smith asked for several items as part of the catalog, as

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well as other members. I made it specifically clear during that meeting that if there was any item that you wanted, you should request it. So in all fairness, there was the opportunity to request that specific item if you so desired.

DR. STANTON: John, that's technically and legally correct. However, I'm a humble cardiologist, so to look at a number of different things in the urologic literature that are listed as things that I could request, I think is somewhat unfair to me.

DR. GARBER: Maybe I could interject, since I bear some responsibility. One of my formal responsibilities as chair is to consult with the HCFA staff about what should be included, and we always make a judgment call. I can tell you when we heard from the first two panels that met, they resented the overwhelming amount of material that they received. We tried to strike a balance. I won't say that we don't make mistakes in this, and that's why we asked for active panel input every step of the way about what materials should be included. So I actually think it might have been a good thing to include this in the materials sent out to everyone. And let me just say that we're

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learning as we're going, and you as panelists, as you see the provisional lists and when we have those conference calls, we kind of need to identify materials that are important. I suspect, if the rest of you are anything like me, that if you got a copy of every single material that was sent in, you would feel overwhelmed, and so we do have to make some judgment call, and I apologize if we didn't press hard to include that in the packet of materials, but that is a responsibility of the chair to consult with HCFA staff and that is not something I pressed for.

DR. RISAGER: Just briefly, I would like to say I loved the way it was organized and we had

the opportunity, but everyone has a different view of what they would like. For me, this was just right.

DR. GARBER: Michael Maves.

DR. MAVES: I've actually made a couple of comments to Connie and to the staff, and I want to join with Michael in saying they did a wonderful job. I might suggest however, and this might be something we should take back to the Executive Committee, is that when there is a relevant AHCPR guideline, which as we all know, tends to be sort

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of the Bible if you will, of guidelines, it's probably appropriate to include it. And I made a suggestion to Connie to perhaps include some selected relevant testimony when it's available ahead of time so that we sort of have not only the pro or the con, but the other side of the argument. So again, I think they have done a wonderful job and have struck a nice balance, but as I've gone through it, it would have been helpful in looking at the information to have an idea or insight of what the opposite argument might potentially be.

DR. GARBER: Les?

DR. ZENDLE: I guess I view the technology assessment as helping us look at the evidence that meets a certain level and put it into evidence tables so that we can understand it. So the question I would have, and Frank, maybe you can answer this, is there any evidence in this that would have met the level that you had decided, the Executive Committee decided to frame the questions, and be relevant to this discussion, that wasn't included in the TEC assessment? I would assume no, because otherwise it would have come up on the MEDLINE search.

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DR. LEFEVRE: No. The two randomized control trials that were discussed in the AHCPR guidelines were included in the TEC assessment. We had additional evidence that has come out since the AHCPR guidelines has been done. The rest of the evidence considered by AHCPR were uncontrolled studies.

DR. ZENDLE: And also, and this is

really trying to answer a different question than at least we so far have been asked to answer.

DR. GARBER: Diane, you had your hand up.

MS. SMITH: I just wanted to make a comment since we're just discussing the materials. It was really nice for the electrical stimulation half to have all the articles, even those that were sort of not considered by the TEC committee. I really appreciated that. It gave me a very easy way to review things. And I had to go search things for the biofeedback, and I think that is really not a good idea. And so, I would encourage you since you're spending so much time reviewing the literature, you know what relevant articles people are interested in, the way they were included for stim was really great, I thought.

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DR. GARBER: Logan.

DR. HOLTGREWE: Well, Les more or less made my point. I would just remind everyone that the AHCPR guidelines on incontinence came out in '96 based on literature that is now at least half a decade old, and the two papers that you discussed were in the materials. The other guidelines were in '92, they're a decade old. And I have been involved in AHCPR guideline production and it takes a year or so to get it done. So you're looking at decade old material in the case of the '92 guidelines, a half a decade old material in the case of the '96 guidelines. I agree with Les that the AHCPR guidelines were aimed at a somewhat different direction than this panel's charge and responsibility.

DR. GARBER: Arnie?

DR. EPSTEIN: I do want to -- I hope I have this right. I want to correct what I think was a misstatement about the AHCPR conclusions. What I heard earlier was that Type B evidence refers to evidence that reflects the strength of clinical trials. Am I speaking incorrectly?

SPEAKER: Clinical series.

DR. EPSTEIN: Let me read to you what it

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does say, so at least there is no confusion amongst the panel. Type A is, the recommendation is

supported by scientific evidence from properly designed and implemented controlled trial providing statistical results that consistently support the guideline stated. B, the recommendation is supported by scientific evidence from properly designed and implemented clinical series that support the guideline statement. And C, the recommendation is supported by expert opinion. And I guess that's consistent with what you were saying, and that innuendo reflects the strength of their opinion and it sounds like in the subsequent years, there have been three additional studies which provide less consistent evidence. Is that fair to say?

DR. LEFEVRE: It's fair to say. There was one study we looked at, Laycock, which was published in '93, which was not in the AHCPR. It was published in a less high profile journal, so that was -- the other two studies were published since the guidelines had come out.

DR. GARBER: Let me ask, this is a little bit early for it, but are the speakers who are scheduled -- oh, we don't have any scheduled

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for this session.

All right. If there's no objection, I thought we would move on to the open public comments period now. Does the panel agree? Arnie?

DR. EPSTEIN: I would just like to request that unlike yesterday, if the open comments could really direct pertinent to the evidence and the task at hand? I think we've gone through a long two days and I don't want to relive the clinical scientific controversy again if we can avoid it.

DR. GARBER: Okay, thank you. We now enter into the period of open public comments.

MS. CONRAD: Okay. Yes.

DR. SAND: Peter Sand, from Northwestern University. I wanted to speak to some of the questions and things that arose after my earlier presentation today. First just briefly, the Yamanishi study that was discussed for stress incontinence, not the one that was just introduced by Dr. Bent from last month in the journal titled

Urology, this was a randomized control trial; it was also double blinded, which would make it hard to understand how it wouldn't be randomized.

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In our trial, and the excellent review that Dr. Lefevre provided us with, there were no dropouts in that study for lack of efficacy. Within the body of paper that's referenced, three of the active group could not comply with the visit schedule, two withdrew because of some vaginal irritation, one dropped because of some urgency with the device in the second week of a 12-week study, and one dropped because her stress incontinence was actually resolved, and she was having problems with her diverticulitis, and needed hospitalization for antibiotic therapy and couldn't comply beyond that with study visits. The one sham patient who withdrew was because of problems with complying with the visit schedule.

In that study also, Frank brought up the point that there may be a selection bias in that we have a difference in patient age. We were concerned about this and in a secondary publication within the International Urogynecologic Journal, 1997, we analyzed those patients over and under the age of 65, and found no differences for outcome. That was not picked up in the survey of articles that were reviewed in the TEC report, nor would I expect it to be.

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In addition, there was some concern about the variability of our measures. I'm not a statistician, I really don't know how to assess that at all. I think it's difficult. These were standard measures, pad tests and voiding diaries, that in a double blinded study we wouldn't expect either the investigators or the participants to be able to manipulate these. To further reflect on that, we did a subanalysis at the end of the study that was not published in this paper because I hoped to write a subsequent paper on the difficulty of randomized control trials, where we asked the patients at the end of the study, did the know what device they were using? 60 percent of the patients guessed incorrectly as to what device they were using. 87 percent of the investigators guessed

wrong as to what device the patients were using. So I don't think we could have really interfered or biased the results based on that sort of analysis of the blind.

In addition, if we bag the stress incontinence information or we put that aside for a moment, I think it's important to recognize that with the introduction of the latest data from Yamanishi in the March study, last month, which

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obviously no one has been able to analyze thoroughly, that we have three randomized control trials which all show by different measures that electrical stimulation is effective, more effective than placebo in treating detrusor instability and its symptoms of urgency, frequency and urge incontinence.

Whatever the measures are, for example in the Brubaker study where you don't have the measures of the voiding diaries or pad tests, you do have urodynamic data. In the other studies, you do have the measures that were reviewed in the text study. So it's hard for me to understand in three rather large studies looking at detrusor instability how we couldn't conclude that there is a significant effect beyond the effect of placebo. Thank you very much.

DR. GARBER: Dr. Sand, could I just ask you a clarifying question? At the beginning of your comments, you went through the dropouts. The intent to treat question was, did you attribute the outcomes among the dropouts, were they included in the group of initial assignment, or you not able to get outcomes for the reasons that you mentioned for those people?

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DR. SAND: The outcomes were obtained at study closure. So when the patients dropped from that trial, they were assessed for their subjective and objective outcomes. The exception was, two patients refused to comply.

DR. GARBER: So everyone except those two patients had their outcomes attributed to one or the other arms of the trial?

DR. SAND: Yes, they did.

DR. SPURLOCK: John Spurlock, from

Bethlehem, Pennsylvania. Yesterday I presented our presentation concerning electrical stimulation combined with biofeedback for urge incontinence and you have copies of those graphs from yesterday. But I didn't have time to state yesterday, or it was inappropriate because it was dealing more with electrical stimulation, was an important component and use of PFES. As a clinician, I'm often, I know that this therapy works, I know my patients are going to get better, but what do I do in the patient that cannot demonstrate any type of pelvic floor contraction, they can't do a Kegel. Therefore, biofeedback, there's nothing to train there. The advantages of electrical stimulation or several weeks of electrical stimulation is that it

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will produce adequate contractility and identify, allow the patient to identify and begin contracting the pelvic floor muscles.

And I think that's a very important point about electrical stimulation, it allows me as a clinician to get these patients over the hump so to speak, to the point where they can begin to, whatever therapy you decide is adequate after that point, to begin contracting those muscles. Thank you.

DR. GARBER: Thank you. Dr. Angus McBryde, I think had his hand up before.

DR. McBRYDE: Yeah. While Dr. Sand was at it, I just had a question. As an orthopedist, we use a lot of muscle stimulators and muscle stimulation, for instance for chronic back and for rehabilitation after total joints, and there is indeed a great variability in the duration and all the other parameters of the hardware. And I just want to hear you say again, I know you mentioned it in your talk, but what, in the context of the positive and negative articles as we heard Dr. Lefevre broach them, how big a factor do you think the variability of the different products that were used was? Again, can you tell me that?

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DR. SAND: Even greater than the pronunciation of Frank Lefevre's name.

DR. McBRYDE: I did pretty well.

DR. STANTON: Just for the record, I

think it's really a shame that this wonderful young investigator has done all this work for us and we're still not all sure how to pronounce his name. I think if the panel concludes anything, we should conclude that.

DR. SAND: There is really significant variability when we look at over 200 studies in the literature, because of the numerous commercial devices that are out there. With the Yamanishi device, the pulse duration of this device was 1 millisecond. The pulse duration of the device reported in our trial was .3 milliseconds. The pulse duration is uniquely different in the devices used in the Luber and Brubaker trial, these were the same; they both used the same device and that was 2 milliseconds.

In basic science research in cats that Magnus Fall did in his original treatise on electrical stimulation some 30 years ago, they favored 2 milliseconds, along with a frequency of 10 hertz, for the stimulation and treatment of

detrusor instability that was invoked in cats. Now they concluded that this was their recommendation, and they also had some practical concerns regarding amperage, voltage, expending batteries and having a practical device electronically. But this became the norm for treatment in detrusor instability. And then when companies that tried to formulate new devices, they had to be electronically unique in order to patent them. And so, we have come up with numerous devices that stimulate in different ways.

If I can just segue, the panel has brought up the point and it's great, yesterday and today, why don't we have better studies when there's so many patients with this problem? This is probably not perfectly appropriate for this panel, but I mean, one thing to realize is to do these trials, it took me four years to convince the U.S. Corporation to fund our trial. The Brubaker trial was supported by the American Urogynecologic Society tangentially, and they were given free stimulators. Part of their problem with being able to collect the data completely was no funding and not enough manpower and resources. We are never going to get the data if we don't have some

reimbursement. I know that is not the issued of
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the panel, but it is an explanation of a question that keeps coming up. It's very difficult, very expensive.

MS. CONRAD: I think Dr. Whitmore was next.

DR. WHITMORE: Yes, just very briefly, I wanted to review what it means to use a sham device for PFES. Normally, patient is brought in, evaluated, and a practitioner works with the patient on how to use the device, and the intensity is turned up until the patient feels a contraction and usually the practitioner will see an anal wink or a contraction. Now, when you get into an RCT with a sham device, and the way it was done in the Sand trial, and I didn't understand this until it became part of the trial, the patients are not given any instruction. The inactive or sham device and the active device are given to the patient, and the patient is told to turn the device up to a certain number. Therefore, in the active group, we cannot be assured that they are reaching maximal intensity, which is required to sometimes get a pelvic floor contraction for stress incontinence, or to inhibit a bladder contraction for urge incontinence. Therefore, we may be underestimating
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our results.

DR. GARBER: Thank you. Please identify yourself.

MS. GARDNER: My name is Pat Gardner. I'm director of reimbursement for a very small medical products company called Tim Medical Technologies out of Minnesota, and I don't have a question and I don't have any clinical data to support or provide, but I do have a statement I would like to make. My understanding of the procedures that are being followed in the legislation, and from the notice establishing the Medicare Coverage Advisory Committee, that there are several options available to HCFA once the panel and the Executive Committee have completed their work. They can either issue a national coverage policy for the therapy, issue a national noncoverage policy as they did with PFES in the

early '90s, issue a coverage policy with limitations as they did with Contagium, make no decision and therefore leave the decision of coverage in the hands of the carriers.

Dr. Hill stated earlier today that industry wants us, HCFA, to make evidence based coverage decisions. He also mentioned industry's

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desire for more transparency to the coverage process. Dr. Hill and other HCFA representatives, and also Dr. Garber, stressed to the panel and the audience today that all evidence would be taken into consideration in rendering a coverage decision.

Taking all that into account, I am still left with the opinion that transparency of the coverage decision process has not been met. While I now have access to these panel meetings as required under law, and as opposed to the previous process under the technology advisory committee meetings, and I do find this process incredibly educational, the actual process HCFA will use for weighing all the evidence is still unknown. Again, therefore, the test of transparency has not been met as I see it. Thus, I'm left to conclude that HCFA's coverage decisions will, in fact must focus solely on the issue of whether the scientific evidence is adequate to draw conclusions about the therapy's effectiveness.

And to discount all other evidence since there is no mechanism, at least none stated to assign a weight to the other evidence provided to it, as such, I agree with Dr. Stanton's comments

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made at the start of today's meeting, that new technology, and none of the technologies we've talked about in the last two days are new, will be stifled under this process, because the scientific evidence will likely never be adequate to draw conclusions, because the cost and time required to collect such evidence is cost prohibitive, especially for small start-up companies.

I would recommend that the panel urge the Executive Committee to address the issue of weighting nonscientific evidence, or if that is not the purview of the MCAC Executive Committee or

these panels, to urge HCFA coverage and analysis group to state its methodology for weighing all types of evidence and testimony. Thank you.

DR. GARBER: I believe that comment was primarily about procedural issues, most of which are outside the purview of this panel, but I wonder if Dr. Hill would care to make a comment.

DR. HILL: Just to thank you and to urge your participation in and support for our efforts to publish a regulation which defines what we think Congress meant when it told us to pay for that which is reasonable and necessary.

MS. JENSEN: I'm Deborah Jensen from

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EMPI. I guess my comments at this point in time are really addressed to what the question the panel should be answering is, and I want to make one point of clarification with respect to the current Medicare coverage policy for PFS. I'm not sure if all of the panel is aware; right now, this technology does have a national noncoverage policy that was instituted in 1994. What this means from a patient point of view is that under no circumstances can any patient under the Medicare program receive reimbursement for this technology, regardless of the clinical situation and the judgment of their clinician. There is no opportunity for appeal. And earlier this morning, I talked about the fact that what does that mean from a scientific point of view? This decision seems to imply that the scientific literature has demonstrated that this therapy is either not safe or not effective for any beneficiary, and I think a careful review of the literature does not allow this particular conclusion to be drawn. Thank you.

DR. GARBER: Thank you. Yes?

MS. WEST: My name is Linda West. I'm a nurse and I have done biofeedback since the mid-1970s and have been involved with pelvic floor

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work for the past 15 years. I'm currently a consultant with SRS Medical Systems, which is a biofeedback instrumentation company. I teach for them. I wanted to maybe offer an answer as to why there are no more studies. When you go through medical school and as a nurse, when we went through

nursing school, we were not taught behavioral techniques. We were taught about medications and surgery, and it's only been recently in the last few years that it has become more aware that behavioral techniques can be an adjunct to medical practice. So when you're trained as a surgeon or to use medications, you really don't think about using the behavioral techniques. And the physicians that we have had going through workshops and that I have done on-site in-services with become more acutely aware that there's more to this than just squeeze and relax as they have been telling patients. So I think if we, you know, hopefully in my lifetime, medical schools will begin to teach behavioral techniques and the appropriateness of using them as an adjunct to medical practice. Thank you.

DR. GARBER: Thank you. Yes.

DR. WHITMAN: Hi. My name's Lisa

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Whitman. I am the director of clinical research and regulatory affairs for EMPI. First of all, I'd like to compliment Dr. Lefevre and his colleagues for a fine job on the technology assessment, considering it's one of the best jobs I have seen, at least in reviewing the basis of incontinence, and I would also like to sympathize with him for the mispronunciations, because with a name like Rugermanhyniak (phonetic), I can feel his pain.

One point of clarification with regard to the review that I discussed with him is in reviewing the Karri Bo study --

DR. GARBER: Please speak up into the microphone.

DR. ZENDLE: Hearing aids aren't covered by Medicare.

DR. WHITMAN: With regard to the Karri Bo study, within the groups, I would contend that there is a performance bias issue because the PME group actually had visits into the clinic on a weekly basis, whereas the other groups only went in on a monthly basis, so it was 24 visits versus 6 visits for the other groups, and I just wanted to make that clarification. Thank you.

DR. GARBER: Thank you. Yes?

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MS. SEMPLE: I'm Carolyn Semple. I'm a registered nurse and I work for seven urologists. I just wanted to go on record as saying that I had a man ten years post-prostatectomy, and he had never been dry. He came in and I asked him to do a bladder chart and he just laughed at me. I leak all day. But with electrical stim he is now voiding. And so I think that's important to know, that we can treat these people with electrical stim. Thank you.

DR. GARBER: Thank you. Frank.

DR. LEFEVRE: It is pronounced Lefevre. And I think Dr. Whitman is correct; she pointed out that there is a difference in the intensity of treatment in the Bo study, and I wanted to just clarify that. That was an error in the TEC report. It wouldn't change the conclusions, because even though Bo did show an improvement as compared to the pelvic floor, we don't think the body of evidence is sufficient to make that conclusion, and we said that. So that was an error, but I don't think it would change at all the overall conclusions.

But the real point I wanted to make was regarding the issue of future studies being done.

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I disagree with the statement that if a noncoverage policy is issued and if the panel decides that the evidence is inadequate, that that will suppress future studies. I believe the opposite is true. I believe if a coverage decision is issued, and that this is covered, there will be no further incentive to do the studies. This is the case with many technologies, old technologies in the past, where they've been disseminated without good studies, they become the standard of care, and we never get the good studies. I believe that if the panel recommends that the evidence is inadequate, and a noncoverage policy is issued, this should stimulate further studies to be done. I understand the difficulty with the funding issues and the difficulty in doing studies. I would hope that someone would pick up the ball on this and take charge and recognize the need to fund these studies, whether that be HCFA, NIH, Blue Cross Blue Shield, or somebody with the appropriate resources

to do so. And I believe that is true.

DR. STANTON: I'd like to comment. Dr. Lefevre, I think you're dead wrong on that. One example is implantable cardiac defibrillators. They were approved and are covered by HCFA, by

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Medicare, and the definitive study showing that implantable defibrillators prolong life compared to antiarrhythmic drugs in people who suffer sudden death was just published in 1998, the Avid trial. HCFA initiated coverage of ICDs in 1985. That's one example; I could give you many others.

I'd also like to say that as someone who oversees all the arrhythmia management clinicals in a very large medical device company, that you're also wrong about noncoverage not inhibiting future trials. I guarantee you, it will inhibit future trials, because you get noncoverage from Medicare, you also get insurance companies that follow suit and all of a sudden there is noncoverage for that technology for everyone in the United States.

DR. GARBER: All right. We've actually begun to stray rather far from the questions in front of us. These are extremely interesting questions and we could have a spirited debate, and they are relevant to HCFA's coverage decision making process, but I'm afraid this panel is not the right place, and this is the sort of comment that I believe is appropriate to submit to HCFA in the Executive Committee, but I would like to stay focused on incontinence please. Yes.

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MS. PALUMBO: Mary Val Palumbo. I'm representing the Continence Coalition, a group of nurses providing incontinence therapy across the country. I do believe HCFA wants to from a clinician. I don't think they would have put a consumer representative on the panel unless they did.

I want to make the point that, I'd like to describe the different ways a clinician may use the research that was presented. I would like to emphasize that the studies do no provide evidence that E Stim is not effective, and here are several examples of how electrical stimulation may be used in clinical practice in combination with other

therapies.
Dr. Spurlock talked about the woman who could not identify a pelvic muscle contraction, so electrical stimulation would be used right then and there to show her how to contract the muscles. And older woman with urge incontinence might be seen for six visits in a row where a combination of behavioral therapy, voiding diaries, biofeedback, and electrical stimulation at the 10 hertz level would be used in office visits. If the woman Dr. Spurlock talked about, an older woman who did not

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want to have surgery, was unable to meet her goals after a six-month period with PMEs on her own, she could be offered a home electrical stimulation unit.
So there is really different ways to use electrical stimulation for an incontinent patient and it's an adjunct to behavioral therapy. Thank you.
DR. GARBER: Yes.
DR. NORTHROP: I'm Steve Northrop. I'm the executive director of the Medical Device Manufacturers Association. In the interest of full disclosure, I should note that EMPI is a member of our association.
I just want to make one point, to reiterate what Dr. Stanton said and to correct the panel's impression if they have one from what Dr. Lefevre said. If there is a national noncoverage, there is no one who will pick up the ball. The ball will not picked up. HCFA won't pick it up, NIH won't pick it up. I think it's important for the panel to recognize that, that there is no one that picks up the ball.
DR. GARBER: I congratulate you. You do have the last word on that subject. I am going to

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call anyone out of order on this question, and I'm sorry. We really need to stick to the questions before us about the adequacy of evidence and the effectiveness of the technology. Les?
DR. ZENDLE: I don't know if you want to do six motions, or three motions.
DR. GARBER: We're still in public session. Any other public comments? I didn't mean

to turn off discussion, just on that subject.
MR. CONNELLY: My name is Jerry Connelly. I'm senior vice president for health policy of the American Physical Therapy Association. I appreciate the dilemma that the panel is being placed in and I would not trade places with any of you at this point in time. I think that the issue that was raised today as well as raised yesterday relative to the question of adequacy is the main dilemma that you have. Dr. Lefevre did say that there is some evidence, some suggestion of efficacy, but he said that the data in their opinion was just not that robust. Where is the cutting point here? What is adequate? What is the judgment call that was called for yesterday? Where is the adequacy? Maybe this is efficacious and maybe this is as good

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as clinical trials get when human subjects are the study case. So you're in a very difficult position to decide what is adequate, and what is not.
There is demonstration of efficacy, there is evidence from the clinic that this intervention is necessary and effective, and that it ought to be an option for patients. But where is that judgment call and how do you come down on the side of adequacy when there is evidence of efficacy, but there may not be the robustness, there may not the numbers of studies, there may not be the convincing evidence. But is it adequate or not? You're in a very difficult position.
MS. GREENBERGER: I really think that this definition is really key and although we're not supposed to talk about it, it goes back to the previous comments, because what I'm concerned about is that new technologies come more quickly, that we're always going to be faced with this, that we're never going to have enough randomized clinical trials to base this kind of decision upon, and we're going to lose the opportunity to have a lot of new therapies and devices that we might otherwise have. And I think it's going to chill research in those area, because how long can small

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companies wait to find out whether they are going to have coverage, and why would other companies do

investigations of those same areas when they're struggling like this? So I think this question is very important, because we may never have enough scientific evidence on a lot of these devices and therapeutics that are coming so quickly, and how can we base a judgment on this?

DR. GARBER: Thank you. Let me just ask, the period for public comment is drawing to a close. Are there any other people who wish to be heard before we turn to open panel deliberations.

Okay. We now move to the phase of open panel deliberations. Les?

DR. ZENDLE: I want to try the opposite approach of what I suggested yesterday, split rather than lump. And since there are three sort of comparisons and three parameters or diagnoses, stress incontinence, urge incontinence, and post-prostatectomy incontinence, I would suggest that we discuss and then vote when we're discussing on those nine parameters one at a time, and starting with PFES compared with placebo first, with stress incontinence, then urge incontinence, and then post-prostatectomy incontinence. And I

would word it a positive so that:

I would move that there is enough evidence, scientific evidence adequate to draw conclusions. So that a yes vote means you think there is enough evidence and a no vote means you don't think there's enough evidence.

DR. GARBER: All right. I'm just trying to --

DR. ZENDLE: So the first motion then would be, if somebody seconds it: Move that there is enough scientific evidence adequate to draw conclusions about PFES compared to placebo in stress incontinence.

DR. GARBER: So the first comparison would be the first vote. Is there a second to that motion? This is a procedural motion.

DR. EPSTEIN: I hesitate to do it, having gone down this track yesterday. I feel like we are a fated combo, to withdraw it as soon as we do it, but I am going to tentatively second it.

DR. GARBER: Okay. Is there a discussion on the motion to divide the question

that way for voting purposes? If not, all in favor?

DR. LANDY: Of the motion?

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DR. ZENDLE: Of the procedure.

DR. GARBER: Yeah. The motion is on the procedure to evaluate the procedures.

(Unanimous vote from the panel.)

DR. GARBER: Okay. I think it's a procedural matter, so I don't think we have to explain ourselves here. Okay.

DR. MAVES: Mr. Chairman, point of order. I wonder if Connie has to do her thing.

MS. CONRAD: It was unanimous, so we're okay. I already listed the voting members for this panel.

DR. GARBER: So now we are dealing with, if I understand this correctly, with the first question, and it's PFES compared to placebo in stress incontinence. So then, if we go this route, we're going to do nine votes on questions. Arnie.

DR. EPSTEIN: Is it open for discussion at this point?

DR. GARBER: Yes.

DR. EPSTEIN: Am I allowed to request one of the public members provide some information?

DR. GARBER: Yes.

DR. EPSTEIN: I have Dr. Lefevre's

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written report in front of me which makes a fairly clear case about why the evidence is not adequate. I would wonder whether I could ask Dr. Sand to speak again and repeat, for stress incontinence, which has five studies, three consistent studies, or three studies showing some effect, why he thinks that evidence is adequate? And I guess I would ask him to speak to not only adequacy in general but for external generalizability to the Medicare population. And this is a token that, if you can do this in a compelling way, it will help.

DR. SAND: Well, far be it for me to sway anyone's vote at the last moment. But my point was that I specifically looked at four, there are four sham controlled randomized studies: Yamanishi, Sand, Brubaker and Luber. I felt that

these were all well designed studies and we have two of those showing no benefit for stress incontinence, and two of those showing benefit for stress incontinence. And like Dr. Lefevre's point about instability of the data, and the negative effects in the control groups in the Yamanishi study and my study, I don't know how to fully factor that in based on the clinical blind that I discussed earlier in recent comments.

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But what we have are well designed studies that seem to show divergent results or conflicting results. When I look at those data and I look at what was done, there were two things that stood out to me immediately. One, Brubaker and Luber were done with one device, and that device has been shown in my practice as well as in Dr. Brubaker's study to be very efficacious in treating detrusor instability, urgency and frequency. The device we use, I still use to treat genuine stress incontinence, it seems to work very very well. So rather than saying I have four studies, two versus two, I felt that I had one device that wasn't very good for stress incontinence and another device, or if we consider Yamanishi's, two other devices that are very good for genuine stress incontinence. If we pick up on that in the uncontrolled literature, I think that point is well reverberated.

The other thing to consider that hasn't come up in the discussions either, to be fair, is another wrench in the program. In our trial, we excluded people who had prior PFS and prior PFMEs with biofeedback. Karl deliberately excluded people who were unsuccessful. So we were trying to find a very pure cell of people who hadn't been

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exposed to this, where we could show them maximal effect. Perhaps Karl had biased this group because he took out the people who were going to perform with some sort of pelvic floor muscle strength thing, because of neuromuscular changes. And so that can explain the differences perhaps also in those two studies.

DR. EPSTEIN: Thank you very much.

DR. SAND: Thank you.

DR. HILL: I'm sorry. The little

tete-a-tete up here was because I thought the question was whether or not a question could be asked of one of the members of the committee and not from the floor, and I misunderstood. I'm afraid as a procedural issue, we have to keep it to the committee discussion at this point in the program.

DR. EPSTEIN: It's done.

DR. HILL: Yeah, strike that.

(Laughter.)

DR. ZENDLE: Call the question.

DR. GARBER: There's not a motion on the floor, is there? Oh, the one of nine. Connie, could you give us the motion?

MS. CONRAD: The motion is: The

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scientific evidence is adequate to draw conclusions about the effectiveness of PFES compared to placebo in stress incontinence.

DR. McBRYDE: Point of order?

DR. GARBER: Yes?

DR. McBRYDE: Can I again, as yesterday, say positive conclusion as opposed to negative, because we're going to draw a conclusion, and conclusions are not what we're looking for. We're looking for a positive or a negative.

DR. GARBER: An affirmative vote on this means that we believe the scientific evidence is adequate to draw conclusions; a negative vote means that you believe the scientific evidence is not adequate.

DR. ZENDLE: And if it passes, then we'll decide what kind of conclusions it draw.

DR. GARBER: Okay. Is everybody clear about that? Jim?

DR. RATHMELL: Do you need a second?

DR. GARBER: All right. I wasn't sure that I heard either of them. Could you make the motion for this part?

DR. ZENDLE: If you want.

DR. RATHMELL: I second the motion to

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call the question.

DR. GARBER: Okay. We're ready to take the vote now. All those in favor, meaning that the evidence is adequate to draw conclusions about PFES

compared with placebo in stress incontinence, raise your hand.

(Dr. Landy voted in the affirmative.)

DR. GARBER: One vote. All those opposed are answering no.

(All panelists with the exception of Drs. Landy and Epstein voted in the negative.)

DR. EPSTEIN: Can we abstain?

MS. CONRAD: Yes.

DR. EPSTEIN: So be it.

DR. GARBER: All right. All abstaining?

(Dr. Epstein abstained.)

DR. GARBER: Now, in the order, do you want to do these en block or one at a time? Okay, anybody care to explain their yes vote?

DR. LANDY: I guess that means me.

DR. GARBER: Not to name names.

DR. LANDY: I think it goes back to the issue of what is adequate, and knowing the field of incontinence, this may be as good as the data that we get in this area of study, and maybe my

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requirements are not as robust as the TEC assessment, but I think based on the data we have now, I could make a decision regarding the second question.

DR. GARBER: Okay. Would anyone care to explain their no vote?

DR. RATHMELL: I'll say quite simply that the technology assessment is clear and even though it was stricken from the record, the most recent discussion pointed out just what the problems with the data are, and there's an inconsistency in the devices used and there's an inconsistency in the outcome shown, and I think we don't have any basis for making a scientific decision. And this doesn't say yea or nay, this is an effective therapy, or it has a niche. It has nothing to do with that; it says the scientific evidence is inadequate.

DR. GARBER: Anyone else care to add any further explanation for a not vote?

Not to name any names, but any explanations for an abstention?

DR. EPSTEIN: You know, after two days, there's nothing I have to say that's profound.

When I look at the weight of the evidence, I think
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that, it boggles me, and it came out about abstentions. The studies are inconsistent; there's reasons to think why the negative studies would have been negative in their design, and so I weight that lack of evidence less. And I can't really quite figure out where my P value is from .05 to .5, but I look on balance and I think for this condition, for this disease, the scientific studies are stronger than they were yesterday. That doesn't say that the coverage decision will come down differently, because in fact this sort of face validity of the measure is not as powerful to me as the face validity of biofeedback, which has a lot of face validity. This seems more like black magic, but that's it.

DR. GARBER: Okay. We will move on to the next question, which is, if I have the order right, are we doing urge incontinence, or are we doing compared to PME?

DR. ZENDLE: Urge.

DR. GARBER: Okay. So PFES compared to placebo for the second indication, which is urge incontinence. Do I have a motion?

DR. BRIN: So move.

DR. MAVES: Second.

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DR. GARBER: Okay. It's moved and seconded. Any discussion? Should I read that again? PFES compared to placebo for urge incontinence, is the scientific evidence adequate to draw conclusions? If there's no discussion, all those answering yes, it is adequate? All those answering no?

(Unanimous in the negative.)

DR. GARBER: Unanimous, and no abstentions.

All right. Any reasons for your vote on this one?

DR. ZENDLE: It's all been said.

DR. GARBER: Can we repeat your reasons from the prior?

DR. GARBER: Then the third one is --

DR. ZENDLE: Alan, also, I mean, our comments earlier, comments not just from the last

question but from the entire discussion.
DR. LANDY: I have a different reason, because I have a different answer. My answer is no because I really don't think I can base a decision about efficacy about one trial that we were exposed to, the Brubaker study, though possibly showing efficacy, has some limitations due to the

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statistical analysis or study. And the other trial, Yamanishi of 2000, we weren't even given that or analyzed that study, so it's really hard to make a decision based on a single trial.
DR. GARBER: Thank you. The third question is, again, PFES compared with placebo, this time for the indication of post-prostatectomy incontinence. Is there a motion?
DR. MAVES: So move.
DR. McBRYDE: Second.
DR. GARBER: Any discussion? Logan?
DR. HOLTGREWE: Yeah. If our information is inadequate on stress and urge incontinence, it's even weaker in this area. There is really practically nothing, so you really cannot make a decision whether the treatment for this type of incontinence helps in any way. Of course we heard some anecdotal situations but anecdotes don't make for science, so I think we really have no information of significance.
DR. GARBER: Any further discussion? So the motion on the table is that the scientific evidence is adequate to draw conclusions about the effectiveness of PFES compared to placebo for post-prostatectomy incontinence. A yes means that

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you do find the scientific evidence adequate. All those voting yes? All those voting no?
(Unanimous in the negative.)
DR. GARBER: It's unanimous, with no abstentions. Next is the --
DR. HILL: While no one has to speak, we do want to be sure to give them the opportunity just in case they want to explain their vote.
DR. GARBER: Yeah. Logan gave a reason for his vote. Did anybody want to add to that? Okay. Now, it is PFES compared to PMEs or alternative nonsurgical techniques, for stress

incontinence.
DR. MAVES: So move.
DR. BRIN: Second.
DR. GARBER: Any discussion?
DR. LANDY: Could you repeat that again?
DR. GARBER: We're now saying, is the scientific evidence adequate to draw conclusions about the effectiveness of PFES compared to PMEs or alternative nonsurgical techniques for the indication of stress incontinence? Any discussion? A yes, again, means the scientific evidence is adequate.
All those voting yes? No?

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(Unanimous in the negative.)
DR. GARBER: It's unanimous. Okay.
Any explanation of the no votes? This is all the same as before, okay.
Now, PFES compared to PMEs or alternative nonsurgical techniques for urge incontinence.
DR. MAVES: So move.
DR. RATHMELL: Second.
DR. GARBER: Any discussion? All those voting yes, the evidence is adequate? All those voting no?
(Unanimous in the negative.)
DR. GARBER: Unanimous, with no abstentions.
DR. LANDY: Can I explain my no vote? On this topic, I think there may be efficacy in its use but we don't have that data, we only have one trial to support it.
DR. GARBER: Lisa, was your comment specific to the indication of urge incontinence?
DR. LANDY: Yes.
DR. GARBER: Thank you. Okay.
Now, we are at the third indication for the second comparison. Is the scientific evidence

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adequate to draw conclusions about the effectiveness of PFES compared to PME, et cetera, for the third indication, i.e., post-prostatectomy incontinence?
DR. MAVES: So move.
DR. BRIN: Second.

DR. HOLTGREWE: I have the same comment as before.
DR. GARBER: Any other discussion? All those voting yes, saying the evidence is adequate? All those voting no?
(Unanimous in the negative.)
DR. GARBER: Unanimous. Any further explanation? I will report that Logan noted the same reason as his prior. Okay.
Now, the third comparison is PFES and PME compared to PME alone, for the indication of stress incontinence.
DR. MAVES: So moved.
DR. RATHMELL: Second.
DR. GARBER: Any discuss?
All those voting yes, the scientific evidence is adequate? All those voting no?
(Unanimous in the negative.)
DR. GARBER: Unanimous. No
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abstentions. Any further explanations? Okay.
Now, same comparison, PFES and PME compared to PME alone, this time for the indication of urge incontinence.
DR. ZENDLE: So move.
DR. BRIN: Second.
DR. GARBER: Any discussion? Okay. Now we vote on the question, is the scientific evidence adequate to draw conclusions for the indication of urge incontinence. All those voting yes? All those voting no?
(Unanimous in the negative.)
DR. GARBER: Unanimous. Any further explanation of your votes?
And now the third comparison for the third indication, our ninth vote on the adequacy question: Is the scientific evidence adequate to draw conclusions about the effectiveness of PFS and PME compared to PME alone, for post-prostatectomy incontinence?
DR. MAVES: So move.
DR. ZENDLE: Second.
DR. GARBER: Discussion? Logan?
DR. HOLTGREWE: Same comments as before.
DR. GARBER: Thank you. All those
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voting yes? All those voting no?
(Unanimous in the negative.)
DR. GARBER: Unanimous. Any further explanation?
DR. HILL: If I may, by way of closing, in addition to thanking all of you, both voting and nonvoting members, and thanking all the commenters for participating in this process, and for your willingness to participate under the guidelines that we laid down about how we wanted this structured and what kind of comments we were hoping for. I want to say it's especially appropriate to have you communicate to us your concerns about the questions, because I hope you all understand, and those of you that have looked at the Executive Committee's interim recommendations for evaluating effectiveness will recognize that the question about adequacy of evidence was drawn right from that document. And so if you have recommendations to how that should be changed or what alterations should be made, we hope that you will. Also, internally and procedurally, when and how we can involve you, your panel chairman in the formulation of the questions, and how to balance that against our needs to have the questions track the referral

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to the TEC assessment when we do that, how closely those two things have to be related. All of those sorts of things that we've heard discussion about, we will need to think about and we will need to take seriously whatever you want to send to use by way of both argument and points you want to make.
DR. HOLTGREWE: Question. What should we do with our materials? Are they to be left here or are you going to deal with that?
MS. CONRAD: We will deal with that.
DR. GARBER: Before we formally adjourn, I would like to add a note of thanks on my own to the panelists for the obvious effort you put into these deliberations. I found them very difficult and as I said yesterday, I feel very fortunate that I did not have to vote on these questions.
I want to thank the public speakers who came here very well prepared and very much on the topic, and I want to also emphasize that if the voting did not go the way that you had hoped it

would, it does not mean that your comments were ignored. It's quite clear that you made some very good points that the panel did take into account.

Finally, I want to thank the HCFA staff who put in a tremendous amount of effort, along

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with the TEC center and Frank Lefevre, who actually helped to structure this process and deliver a great deal of information. Whether you agree with the conclusions or not of the report that Frank and his colleagues prepared, I think it was an extraordinary amount of effort and it really shows, so thanks very much to all of you.

MS. CONRAD: To conclude today's panel meeting, let me announce that the future meetings for this panel are tentatively scheduled June 14th and 15th, and October 17th and 18th. These dates are subject to change.

I'm going to ask the panel members to linger just a few more minutes to accept a second evaluation form from Perry Bridger. And finally, leave all your materials. We are very concerned about any personal notes that may be made in any of the margins, so we will collect your materials and have them shredded.

At this point, could I have a motion that the meeting be adjourned?

DR. McBRYDE: So move.

MS. CONRAD: Second.

DR. HOLTGREWE: Second.

(The meeting adjourned at 1:30 p.m.)