

Transcript for April 12, 2000 Meeting

Please Note: This transcript has not been edited and CMS makes no representation regarding its accuracy.

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BIOFEEDBACK THERAPY FOR THE TREATMENT OF  
URINARY INCONTINENCE

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HEALTH CARE FINANCING ADMINISTRATION

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Medicare Coverage Advisory Committee

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Medical and Surgical Procedures Panel

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April 12, 2000

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Baltimore Convention Center

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Baltimore, Maryland

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Panelists

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Chairperson

Alan M. Garber, MD, PhD

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Vice-Chairperson

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Michael D. Maves, MD, MBA

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Voting Members

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Angus M. McBryde, MD, FACS

6

H. Logan Holtgrewe, MD, FACS

7

Kenneth P. Brin, MD, PhD

7

Les J. Zendle, MD

Bruce Sigsbee, MD (Not present)

8

Linda D. Bradley, MD

James P. Rathmell, MD

9           Arnold M. Epstein, MD  
10           Temporary Voting Member  
              Lisa Landy, MD  
11  
              Consumer Representative  
12           Phyllis E. Greenberger, MSW  
13           Industry Representative  
              Marshall S. Stanton, M.D.  
14  
              Non-Voting Guests  
15           Michael Risager, MD  
              Diane Smith, RN  
16  
              Acting Director, Coverage and Analysis Group, HCFA  
17           Hugh F. Hill, MD, JD  
18           Executive Secretary  
              Constance A. Conrad, RN

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00003

1	TABLE OF CONTENTS	
	Page	
2	Welcome and Conflict of Interest Statement Constance A. Conrad, RN	5
3	Summary of MCAC Executive Committee Recommendations	
4	Alan M. Garber, MD, PhD, Chairman	8
5	Overview of Evidence Based Methodology Hugh F. Hill, III, MD, JD	22
6	Office of Clinical Standards and Quality	
7	Deborah A. Zarin, MD	24
8	Presentation of Questions Perry Bridger, HCFA	44
9	Open Public Comments & Scheduled Commentaries	
10	Joey Spauls Smith, RNC, BCIAC, MA Diane Newman, RN, MSN, CRNP, FAAN	58 61
11	John Spurlock, MD Michel Boileau, MD	69 82
12	Cheryl LeCroy, RN	89

	Roger Dmochowski, MD	91
13	Lindsey Kerr, MD	101
	Cyndy Feldt, PT	108
14	Catherine Dubeau, MD	117
	Barbara Woolner, RN, CRNA	123
15	Geoff Cundiff, MD	129
	Alfred Bent, MD	136
16	John Perry, PhD	144
17	LUNCH	150
18	HCFA Presentation	
	Kenneth Simon, MD, MBA	150, 183
19	Technology Evaluation Center Assessment - Blue	
20	Cross/Blue Shield	
	Frank V. Lefevre, MD	154
21	Open Committee Deliberation	186
22	Open Public Comments	219
23	Open Committee Deliberation	241
24	Final Panel Recommendations	251

25

00004

1                   TABLE OF CONTENTS  
                           (Continued)

2

Next Steps

3     Hugh F. Hill, III, MD, JD           270

4     Closing Remarks

      Constance A. Conrad, RN       274

5

Adjournment                           274

6

7

8

9

10

11

12

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19  
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1           P R O C E E D I N G S

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

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

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

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

10           The following announcement addresses  
11 conflict of interest issues associated with this

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

23 With respect to all other participants,  
24 we ask in the interest of fairness, that all  
25 persons making statements or presentations disclose  
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1 any current or previous financial involvement with  
2 any firm whose products or services they may wish  
3 to comment upon.

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

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

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

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

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

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

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

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

6 Otolaryngology.

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

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

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

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

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

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

24 MS. SMITH: I'm Diane Smith, nurse  
25 practitioner. I am a continence specialist at the  
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1 WOCN, which is the Wound Ostomy and Continence  
2 Nurses, in Philadelphia.

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

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

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

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

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

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

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

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

20 expecting some feedback about how well these  
21 recommendations work.

22 And in fact, as you will see, this panel  
23 will follow all the operational recommendations of  
24 the Executive Committee, but if we've got some  
25 question about whether it would be feasible with  
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1 more advance notice and so on, or whether some  
2 performance recommendations need to be acted upon  
3 and which may not be feasible under the  
4 circumstances, that's information that the  
5 Executive Committee really needs to have.

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

18 One other aspect about why these are  
19 interim is that we are not in the business of  
20 trying to tell HCFA what they should do. And as I  
21 said, we are not making coverage decisions; we are  
22 answering the questions posed to us. The nature of  
23 the questions and how we answer them might change  
24 after HCFA releases its rules regarding the  
25 procedures for coverage determinations, and are one  
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1 of the processes we use as advisory bodies to  
2 provide HCFA insight of the regulations and laws  
3 that they may issue. So, these are provisional in  
4 that sense as well.

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



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

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

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

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

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

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

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

24           And this criteria, and I will read from  
25 the document, concerns the size of the health  
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1 effect. Evidence from well designed studies,  
2 meeting the adequacy criteria, must establish how  
3 the effectiveness of the new intervention compares  
4 to the effectiveness of established service and  
5 medical items. We're asked to make a statement  
6 about the comparative effectiveness of the  
7 intervention under study, to assign it to one of  
8 seven categories. Now, in fact, we could have come  
9 up with 14 or 21 categories without too much  
10 difficulty, we could have narrowed it down to three  
11 or four. The Executive Committee felt that the  
12 seven categories that are in the document best  
13 capture the full range of possible outcomes of the  
14 medical evidence in terms of effectiveness, without  
15 being unduly complex.

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

24           So, that's the broad principles of how  
25 we will operate and as you think about how we  
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1 approach this task, you should recognize what this

2 is not, this is not a discussion, should we cover  
3 or should we not. We are asked to evaluate  
4 evidence, and to say what the evidence says. This  
5 is not a discussion of cost effectiveness or cost.  
6 Cost is not part of our charge as a panel or the  
7 Medicare Coverage Advisory Committee as a whole.  
8 This is not a discussion of how  
9 important the disease entity that we're considering  
10 is, about the toll of the illness, or about whether  
11 there should be coverage for some treatment of the  
12 illness because the illness is so important. I  
13 hope that HCFA always brings us questions where the  
14 health condition is important. I think all of us  
15 who've had any personal experience as providers or  
16 family members, know that incontinence in  
17 particular, can be a devastating problem and I  
18 think we can start with that as an assumption that  
19 we're all working from, that this is a very  
20 important problem, and our task is not to determine  
21 how important the problem is, but to determine  
22 whether there is enough evidence to conclude  
23 whether these treatments we are considering work,  
24 and if we do determine there is enough evidence,  
25 what does that evidence say.

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

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

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

24 In fact, many people would argue that if  
25 you are sure that one treatment is considerably  
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1 more effective than the alternative, it would be  
2 unethical to perform a randomized control trial.  
3 So we are not saying, what do you think works  
4 better, or how much better do you think it works,  
5 what's your best guess. We're saying, is the  
6 evidence strong enough for you to be sure of the  
7 conclusion that you draw. That's our task.

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

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

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

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

20         There is one constraint that this  
21 process works under that doesn't apply to every  
22 professional society or group that evaluates  
23 evidence, and that is timeliness. And I think  
24 everybody pays lip service to timeliness, but we  
25 are particularly aware in our deliberations that  
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1 HCFA needs our advice in making coverage  
2 determinations themselves, that the public is  
3 waiting for answers about these questions, and a  
4 lot hangs in the balance. So it's incumbent upon  
5 us to make this process work as quickly as  
6 possible, and our goal is to have the highest  
7 quality product in a very short duration of time.  
8 And of course, the time that we take is undoubtedly  
9 going to be too long as far as some people are  
10 concerned, but we're trying to strike a balance  
11 between very high quality and timeliness of the  
12 report.

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

24         Any questions from the panel? Les?

25         DR. ZENDLE: Yeah. Alan, I wondered if  
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1 comments are made either by panel members or the  
2 public about coverage issues, will they be ruled  
3 out of order, or how will you handle those?

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

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

9         MS. CONRAD: Exactly.

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

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

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

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

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

9 Dr. Zarin comes to us from a sibling  
10 agency; she's the director of the technology  
11 assessment program at AHRQ, the Agency for Health  
12 Research and Quality, in the federal Department of  
13 Health and Human Services. Dr. Zarin oversees a  
14 comprehensive national program which performs  
15 assessments of diagnostic and therapeutic  
16 interventions in order to glide -- guide clinical  
17 and policy decision makers. It's infrequently a  
18 glide, certainly a guide. Prior to this, Dr. Zarin  
19 was medical director and the director of the Office  
20 of Quality Improvement and Psychiatric Services for  
21 the APA, the American Psychiatric Association, and  
22 in this capacity she directed the APA's practice  
23 guidelines project, and was co-director of the  
24 APA's practice research network. Dr. Zarin is a  
25 nationally recognized expert in evidence based  
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1 medicine, clinical decision making, practice based  
2 research and practice guidelines, and she has  
3 published more than 50 peer reviewed journal

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

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

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

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

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

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

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

24 synthesis.

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

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

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

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

17 Why do you need the compared to what?



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

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

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

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1 whether that patient has better outcomes at the  
2 end.

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

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

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

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

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

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

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

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

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

22 Patient decisions. I'll give you a  
23 couple of examples in a second where, especially if  
24 it's an observational study where it's things that  
25 the patients are in control over, either requesting  
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1 a treatment or something that they do on their own  
2 like taking certain vitamin, the patients might  
3 make decisions that you might be able to guess  
4 about which way the bias goes, and you might not be  
5 able to.

6 Let me just run through, to give you  
7 pause, two recent newsworthy issues where  
8 nonrandomized studies, in fact including big ones,  
9 have led to results that are discrepant with new  
10 large randomized control trials. The first is  
11 hormone replacement therapy in heart disease, in  
12 fact in secondary prevention of heart disease. I  
13 prepared this slide yesterday, but coming in this  
14 morning on NPR I heard yet a new report about  
15 this. And basically the story is that there were  
16 several large well done observational studies of  
17 secondary prevention of coronary heart disease,  
18 showing a large benefit of hormone replacement  
19 therapy. A meta-analysis of 30 of these showed a  
20 35 percent reduction in risk, with up to 89 percent  
21 for those with a severe coronary heart disease.

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

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

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

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

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1 studies.

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

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

19         Another issue is time frame, and this is

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

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

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

18 Validity of the measures. In part, what  
19 I mean by that, if they're intermediate measures,  
20 are they in fact related to the real measures of  
21 importance which might be more -- you know, some  
22 measure of morbidity or mortality, but also, are  
23 they relevant? If it's sort of a quality of life  
24 measure, are these the measures that the patients  
25 and their clinicians care about?

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1 And then statistical analysis. Again,  
2 I'll leave it at saying details matter a lot, that  
3 you know, very well done studies can be analyzed in  
4 ways that would make the inferences invalid. I  
5 will just mention the issue of power, especially  
6 for negative studies. Was the study, did it have  
7 enough patients, were the measures such that it  
8 would have been able to detect a meaningful  
9 difference.

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

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

24 That was did it work in the study that  
25 we're reporting; now, this is the external  
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1 validity, will it work in the relevant group?  
2 Again, let me remind you, compared to what? This  
3 is another, there's an external validity issue of  
4 the comparison treatment. Was the comparison that  
5 was chosen in the studies you read in fact the real  
6 comparison in the real world? You have seen drug  
7 studies where a new drug is compared to  
8 quote-unquote a standard drug, but in fact you  
9 might realize that in your day-to-day clinical  
10 life, that quote-unquote standard drug is no longer  
11 what anyone uses, and something else is what they  
12 use. So in fact, the real life decision isn't the  
13 experimental drug compared to that standard, it's  
14 something else. And then you're left not really  
15 knowing how it compares to what the real  
16 alternative is.

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

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1 et cetera?

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

8           So all of these are very critical in  
9 determining, will it work in the relevant group.  
10 And there is no, none of these issues have  
11 answers. I mean, this is really clinical judgment,  
12 carefully thinking about what the issues are.  
13           Let me just mention briefly, that was  
14 sort of up to now was really how do you evaluate  
15 individual studies. Okay. Now, what do you have  
16 when now you have 10 in front of you and you have  
17 to synthesize a group of studies? Just to give you  
18 a sort of menu here, in general, research syntheses  
19 can be qualitative, which is basically a narrative,  
20 preferably a critical narrative saying there were  
21 five studies and here's comments on each one of  
22 them. They can be quantitatively synthesized, for  
23 example, at a meta-analysis. In essence a  
24 meta-analysis is saying, okay, we have for example,  
25 five randomized control trials of this study, each  
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1 with 100 patients; let's act as if those were 500  
2 patients in one study, and look at the results that  
3 way. And there is obviously, details are important  
4 in all of these in terms of the validity of the  
5 analysis.

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

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

22           The issue in answering the question, was  
23 this an appropriate synthesis, is was the  
24 appropriate technique chosen, meaning, did the  
25 technique match the question you're trying to  
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1 actually answer. And was it done appropriately,

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

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

10 MS. CONRAD: Thank you, Dr. Zarin.

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

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

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

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



22 were just described.

23 DR. GARBER: Thank you. Let me just  
24 make one brief comment. I think these are very  
25 important points and this is exactly what the panel  
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1 will need to grapple with, but let me just say  
2 though, that our questions do not concern the  
3 therapies or interventions that are not before us.  
4 And we can tell HCFA, not as panelists but as  
5 individuals, you might tell HCFA you should cover  
6 because other existing therapies don't meet these  
7 standards. But our question is really not about  
8 the currently covered therapies or things that may  
9 have disseminated to widespread use before. Our  
10 question is, is there adequate evidence that  
11 enables us to make comparative effectiveness  
12 statements.

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

23 And I think we will, we may have  
24 differing views among the panelists about whether  
25 nonrandomized studies are adequate in this  
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1 context. One of the reasons the Executive  
2 Committee did not make blanket statements about  
3 that is that everything tends to be situation  
4 specific. That is, we have to look at the specific  
5 studies and decide whether the randomization was  
6 adequate, the study design was adequate, and so on,  
7 presumably on a case-by-case basis.

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

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

23 MS. CONRAD: Okay. Let's proceed with  
24 today's agenda topic, biofeedback for the treatment  
25 of urinary incontinence. And we will start off  
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1 with Mr. Perry Bridger, who's an analyst in the  
2 coverage and analysis group.

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

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

20 In the following two slides, I have  
21 outlined for you several of the treatments which  
22 exist for the management of urinary incontinence.  
23 These include behavioral treatments, PFES,  
24 pharmacologic therapy, bulking agents, sacral nerve  
25 stimulation, and surgery. In general, which  
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1 treatment option to pursue for the different types  
2 of urinary incontinence is dependent upon specific  
3 patient indications, comorbid states, cognitive  
4 function, and the willingness and ability to  
5 participate in treatment.

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

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

18 For the purposes of this meeting,  
19 biofeedback therapy is defined as a therapy that  
20 uses an electrical or mechanical device to provide  
21 the patient a visual and/or auditory evidence of  
22 pelvic floor muscle tone in order to increase the  
23 patient's awareness of the musculature and to  
24 assist the patient in the performance of PFMEs.

25 The panel has had the opportunity to read the  
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1 technology assessment, evidence and other materials  
2 related to biofeedback.

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

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

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

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1 the Medicare population, and their applicability  
2 beyond research settings.

3 If the evidence is adequate to draw

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

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

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

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

4 MS. CONRAD: Thank you, Perry.

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

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

9 DR. GARBER: Yes.

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

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

24 that you need more evidence to be able to quantify  
25 the effectiveness, but in order -- you have got to  
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1 be comfortable in saying there is enough evidence  
2 to assign this at least in broad terms to one of  
3 the categories in question 2, although I would  
4 suspect that none of us believe you have to be  
5 precise about that assignment in answering  
6 number 1.

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

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

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1 control trial to determine effectiveness.

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

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

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

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

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

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

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

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

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

00052

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

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

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

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

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

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

00053

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

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

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

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

00054

1 all the technology addresses.

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

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

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

16 DR. GARBER: That's correct.

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

25 DR. GARBER: Well, I have to apologize.  
00055

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

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

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



00056

1 incontinence as compared to PFMEs alone.

2 DR. GARBER: Well, it sounds as though  
3 we're all in agreement, and there was one version  
4 at least that did have the incorrect language. But  
5 let me just make sure that we have agreement from  
6 Hugh and the panelists that we are comparing the  
7 combination to PME alone.

8 DR. HILL: Perhaps it seems to be  
9 incorrect because we may have made a nonarticulated  
10 assumption. We regard that as first tier therapy,  
11 and this is as an addition. The question is about  
12 the addition to the first tier therapy, so does  
13 that --

14 DR. GARBER: Yeah. As well as we're all  
15 operating on the same assumption. I think there  
16 were definitely some versions of the question that  
17 left out that that was the explicit comparison. I  
18 understand what the confusion about. The way Dr.  
19 Rathmell stated it before, the way it was just  
20 stated, is the question we're dealing with.

21 DR. RATHMELL: Just to be very clear,  
22 and it's important, because when we get to part  
23 two, if we get to that second question, we have to  
24 put it in a category, is it as effective but with  
25 advantages, or as effective with no advantages.

00057

1 Now we are going to be asked to make a judgment  
2 versus other treatments that are out there, okay?  
3 We may not be able to do that, but that's okay.  
4 That's why it's so important to understand what  
5 we're doing.

6 DR. GARBER: Oh, absolutely. And let me  
7 also add that one of the difficulties that we will  
8 face in dealing with question number 2 generically,  
9 not just with regard to this technology, is we'll  
10 have to have a discussion about what those other  
11 things are. So we will deal with that as  
12 appropriate.

13 MS. CONRAD: Okay. Let's proceed with  
14 the individual presenters. Let me caution you  
15 first of all, please stick to the topic, please  
16 stick to the time limit. And as we said before, no  
17 pleas for Medicare coverage or codes.

18 And the first speaker is Joey Spauls  
19 Smith.

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

00058

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

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

23 The results were that of the 41 patients  
24 with stress, urge and mixed urinary incontinence,  
25 34, or 83 percent were successful, meaning success

00059

1 defined as greater than 90 percent in reduction of  
2 leakage. The number improved were 6 of the 41, or  
3 15 percent, improvement being defined as less than  
4 90 percent reduction in leakage. And there was one  
5 unsuccessful patient, or 2 percent. Of the  
6 post-prostatectomy urinary incontinence patients  
7 numbering 13, 9 of those were successful, or  
8 69 percent, again, having 90 percent or greater  
9 reduction in leakage. Four, or 31 percent, were  
10 improved, and everyone was successful. So of the  
11 54 patients, 43 were successful, or 80 percent; 10  
12 were improved, or 18 percent, for a total of 53  
13 patients having success or improvement, or a total

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

16 The conclusions are that in this group  
17 of patients, PME alone without biofeedback did not  
18 work for them, yet with biofeedback all but one had  
19 symptom improvement. Biofeedback is effective and  
20 in this case, the work was done in a routine  
21 clinical setting as opposed to a strict research  
22 study. Biofeedback is the accepted way to do PME,  
23 as Dr. Kegel did it in the late 1940s, and I  
24 believe that the Blue Cross/Blue Shield TEC report  
25 is flawed, and I believe others will be discussing  
00060

1 that. Thank you.

2 DR. GARBER: Thank you.

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

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

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

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

20 MS. CONRAD: Go ahead, Dr. Zendle.

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

22 DR. HOLTGREWE: I have a question of the  
23 last speaker. When you treated post-prostatectomy  
24 incontinence, what was the interval of the onset of  
25 your therapy following the procedure?  
00061

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

3 DR. HOLTGREWE: Thank you.

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

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

8 DR. BRADLEY: And male, female?

9 MS. SPAULS SMITH: I do not have that  
10 breakdown. It could be retrieved. By far, mostly  
11 women.

12 DR. BRIN: What was the low percentage  
13 that would still put someone in the improved  
14 category? Was that 10 percent or 15 percent?

15 MS. SPAULS SMITH: Usually at least 25  
16 percent reduction in leakage.

17 MS. CONRAD: Is that it? Thank you.  
18 Miss Newman?

19 MS. NEWMAN: I'm sorry. I only have one  
20 copy of my full presentation. I am going to give a  
21 summary because of the time frame, and I gave it to  
22 Connie so that she will have to copy it for you.

23 My name is Diane Newman and I am an  
24 adult practitioner in private practice in  
25 Philadelphia, Pennsylvania. I'm also a visiting

00062

1 professor at Rutgers, the State University of New  
2 Jersey, College of Nursing. I have an appointment  
3 to the Food and Drug Administration's GI neurologic  
4 panel.

5 I would like to acknowledge the  
6 assistance of Dr. Andrew Fantel on this  
7 presentation. Dr. Fantel is a urogynecologist who  
8 is in private practice in Long Island, New York.  
9 Dr. Fantel has been funded by NIH, NIA, and  
10 conducted clinical trial RCTs, of which the most  
11 famous is bladder retraining, and biofeedback  
12 assisted pelvic floor rehabilitation treatments in  
13 persons with urinary incontinence. Dr. Fantel and  
14 I both provide behavioral treatments in our  
15 practice.

16 Dr. Fantel and myself were the co-chairs  
17 of the 1996 Agency for Health Care Policy and  
18 Research urinary incontinence in adults panel. We  
19 were also a member of the 1992 panel, so we were  
20 with that panel looking at that work for I guess a  
21 total of seven years. Neither Dr. Fantel nor  
22 myself have any financial involvement with  
23 manufacturers of any products being discussed  
24 here. However, I do provide and have provided  
25 consultations to individuals, insurers, facilities,

00063

1 institutions, who want to start nonsurgical

2 behavioral treatment for urinary incontinence.

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

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

21 These guidelines were developed by a  
22 panel of UI experts, selected through a thorough  
23 exhaustive review of health disciplines, clinical  
24 expertise, and consultation with professional  
25 organizations. And the following slide shows  
00064

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

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

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

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

22 consistently support the guideline statement. A  
23 rating of B was a recommendation supported by  
24 scientific evidence from properly designed and  
25 implemented clinical series that support the  
00065

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

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

13         The panel attempted to try to clarify  
14 behavioral treatments. The 1996 guideline outlines  
15 the application of pelvic muscle rehabilitation,  
16 which includes behavioral modification, bladder  
17 retraining specifically for those patients with  
18 urge incontinence and overactive bladder, PME's and  
19 the use of methods to enhance the rehabilitation of  
20 the internal pelvic floor and bladder muscle.

21         Based on the database evidence, the  
22 panel made the following recommendations: Pelvic  
23 muscle rehabilitation and bladder inhibition which  
24 are the interventions, using biofeedback therapy  
25 which is the method, are recommended for patients  
00066

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

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

14         A second study by Wyman and Fantel  
15 compared bladder retraining to PME's to combination

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

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

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

23 MS. NEWMAN: Okay. The third RCT was  
24 published in JAGS last year and this was done at  
25 home by the individual, and again, they had a  
00067

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

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

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

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

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

24 MS. NEWMAN: Which one?

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

00068

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

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

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

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

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

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

24 MS. NEWMAN: Yes. I mean, the issue is  
25 that one of the statements of the TEC report is  
00069

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

4 DR. GARBER: Thank you.

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

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

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

00070

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



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

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

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

25         Now we do treat pelvic prolapse and also

00071

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

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

23         The problems with this therapy is that

24 it's very difficult to ever have a pure controlled  
25 group. As soon as -- and some of the other  
00072

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

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

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

23 And I do apologize. We tend to combine  
24 biofeedback and pelvic electrical stimulation,  
25 because we do see such a rapid increase in  
00073

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

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

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

18 frequency, nocturia. And after they had completed,  
19 this was about, the average was about seven  
20 sessions of treatment, they were asked to rate in  
21 their own words, were they satisfied. And again,  
22 78 percent felt that their problem was improved, 82  
23 percent felt that they were satisfied. Could we  
24 have the next overhead, and this will correspond to  
25 the second page.

00074

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

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

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

00075

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

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

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

20         What we found is that on our patients,  
21 and this was five years ago, that only about 10 to  
22 20 percent of patients with urgency had motor  
23 urge. Most of the patients -- in other words,  
24 detrusor instability, they could actually  
25 demonstrate a contraction on urodynamics. And the  
00076

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

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

15         If they have a severe prolapse, or a  
16 severe stress incontinence where they're wearing  
17 three or four or five pads a day, this type of  
18 therapy does not improve that that much. For those  
19 patients who are probably going to go on for  
20 surgical management, we will do a preoperative  
21 urodynamics to try to elucidate the type of  
22 incontinence that they have. But for some therapy  
23 like this, a benign therapy that doesn't involve  
24 medication, doesn't involve surgery, we've always  
25 felt that urodynamics was an expensive procedure  
00077

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

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

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

18 DR. SPURLOCK: I will attempt to answer  
19 it from my own personal experience. For 10 years I  
20 practiced general obstetrics and gynecology, and I  
21 was as guilty as the next person of, when a patient  
22 would come in and mention incontinence, I'd put my  
23 hands over my ears, and then when they would drag  
24 my hands off my ears they would say, well, what can  
25 I do about it? And I'd say, well, just go home and  
00078

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

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

25 DR. ZENDLE: But some of the studies

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1 that we're comparing are called exercises alone  
2 without biofeedback. It says eight weekly sessions  
3 with a trained therapist. Now, to me, that's not  
4 just giving verbal instructions. They must be  
5 doing something during that time, but it's  
6 distinguished from say an EMG biofeedback.

7 DR. SPURLOCK: Yeah. I think the  
8 instruction would just be explaining, not doing --

9 DR. ZENDLE: Forget about just  
10 instruction. Let's talk about these sessions.

11 DR. SPURLOCK: Okay. The next level I  
12 would say would be actually placing a probe or some  
13 type of device into the vagina, or the rectum in  
14 post-prostatectomy men, it's placing a device that  
15 can sense pressure into the vagina or the rectum.  
16 In our case, it's hooked up to a computer screen  
17 and the patient can see and hear how well they are  
18 squeezing that probe. And then over time, over  
19 weekly sessions, they can see their progress in  
20 terms of being able to squeeze that muscle stronger  
21 and longer.

22 DR. ZENDLE: Couldn't that be done  
23 without the machine?

24 DR. SPURLOCK: I guess the only other  
25 way to do it would be for the person with them to

00080

1 put a finger in the vagina or the rectum. Most of  
2 our patients are not intimidated by being able to  
3 sit in a comfortable chair like a Lazy Boy chair  
4 and be covered, and insert the probe themselves and  
5 watch the screen. I think that many of, or some of  
6 our 70 or 80 or 90-year-old patients are a little  
7 bit intimidated by having a finger in the vagina,  
8 of the examining person, trying to teach them how  
9 to squeeze the right muscles. So I think -- does  
10 that answer your question?

11 DR. ZENDLE: Well, I guess, then, you  
12 would say that they probably wouldn't do as well?

13 DR. SPURLOCK: Yes.

14 DR. ZENDLE: And I guess, where is the  
15 evidence for that?

16 DR. SPURLOCK: Again, it's just my  
17 personal experience as a clinician out there in the  
18 field doing it, and you know, I have to see these  
19 elderly ladies every week, and I know they are

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

00081

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

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

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

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

14 interest?

15 DR. BOILEAU: Definitely. Good  
16 morning. My name is Michel Boileau. I'm a  
17 urologist in private practice in Bend, Oregon, a  
18 clinical professor of urology at Oregon Health  
19 Sciences University, a chairman and cofounder of  
20 Deschutes Medical Products. You probably assume  
21 that I am a proponent of PME with biofeedback  
22 because I'm a principal of a medical production  
23 company. Actually, the opposite is true.

24 I became a founder of Deschutes Medical  
25 Products because I was a proponent of this

00083

1 treatment. When I entered private practice 13  
2 years ago I was a urologic oncologist. It quickly  
3 became apparent that urinary incontinence with its  
4 consequences would become a significant part of my  
5 work. 13 years ago, about all we offered was  
6 pro-Bhantine or surgery. But even today, most  
7 people who start medical therapy quit because of  
8 poor results or side effects, and less than 20  
9 percent stay on therapy for six months or longer.  
10 Most patients do not want surgery, considering  
11 conservative treatment such as PME their first  
12 choice.

13 I was only vaguely aware of PME with  
14 biofeedback, but my interest led me to a course  
15 taught by Dr. John Perry. With new knowledge, I  
16 attempted to incorporate this treatment into our  
17 practice, but my colleagues were resistant because  
18 of expense related to space, staffing, equipment,  
19 time constraints, poor reimbursement, and economic  
20 conflict. Why would a surgeon promote nonsurgical  
21 treatment? But I was convinced that this treatment  
22 should be an integral part of multimodal therapy  
23 for urinary incontinence.

24 All of us would agree that correcting,  
25 that exercising muscles makes them stronger, but

00084

1 biofeedback does much more. It facilitates  
2 contraction, relaxation, the ability to convert  
3 between those two states, strength, and endurance.  
4 Still, someone argued that biofeedback is  
5 unnecessary and you know, it's hard to prove common  
6 sense.

7 If I am to believe the technology



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

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

00085

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

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

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

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

00086

1 maintenance, and reduce the need for surgery or

2 medication.

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

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

00087

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

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

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

22 directed home based care, we can simplify and  
23 broaden access to treatment, preserve privacy and  
24 alleviate embarrassment, provide durable results,  
25 reduce the need for surgery and medication, and we  
00088

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

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

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

13 DR. GARBER: Thank you.

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

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

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

24 MS. CONRAD: Okay. Our missing  
25 individual speaker has been found, Mary Cate  
00089

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

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

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

12 MS. LECROY: Not at all.

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

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

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

00090

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

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

17 Average number of times patients  
18 responded on the survey to having urinated per day  
19 initially was 9.3, which had been reduced now to  
20 5.9. Number of daytime incontinence episodes was  
21 initially 2.9, reduced now to 1.2, five years out.  
22 Number of times urinating per night was initially  
23 2.8, now 2.3. Our number of nighttime incontinent  
24 episodes, initially 0.9 is now 0.7. Average number  
25 of pads worn per day before biofeedback was 2.4,

00091

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

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

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

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

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

15 DR. ZENDLE: Thank you.

16 DR. GARBER: Thank you.

17 MS. CONRAD: Dr. Dmochowski.

18 DR. DMOCHOWSKI: Good morning. I am  
19 Roger Dmochowski. I am a urologist at the North  
20 Texas Center for Urinary Control, I also have a  
21 clinical appointment at the Uniformed Services  
22 Medical School at Bethesda. I was the data manager  
23 and facilitator for the American Urologic  
24 Association's guidelines on stress incontinence  
25 that were published in mid-1997, which specifically  
00092

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

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

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

16 So, I will give you our verbatim  
17 position on biofeedback and then I'll amplify a few  
18 points. With respect to biofeedback, there is much  
19 confusion regarding use of this term when in  
20 effect, most investigators are really referring to  
21 biofeedback assisted behavioral modification. This  
22 makes it extremely difficult to evaluate the  
23 effectiveness or relative noneffectiveness of  
24 biofeedback as it is classically defined as an  
25 isolated entity. Although there does not appear to  
00093

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

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

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

17 Further, on the basis of expert opinion  
18 and based somewhat on results that are expressed in  
19 the literature, our committee would like to go on  
20 record as recommending a tabled biofeedback within  
21 such a program of behavioral modification.

22 Treatment sessions are recommended no more than  
23 once weekly not to exceed a total of 10 sessions in  
24 one year. The selection of the frequency and total  
25 number of treatments is obviously arbitrary and is

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1 based upon expert opinion of our subcommittee.

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

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

24 four intervention.

25 I would like to amplify our comments

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

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

25 We would like to ask the Committee

00096

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

18 without PME is effective therapy.

19 Yes, sir?

20 DR. GARBER: I just wanted to ask a  
21 brief clarifying question. It sounds like the AUA  
22 did a very very thoughtful job, and I commend you  
23 on that. And what I wanted to be sure of was how  
24 you would, or to what extent the AUA  
25 recommendations or conclusions apply specifically  
00097

1 to the question of PME plus biofeedback, versus PME  
2 alone. You went through it all quickly and I think  
3 you may have said it, but I didn't quite catch it,  
4 so could you just elaborate on that point?

5 DR. DMOCHOWSKI: Yeah. I mean again, if  
6 you look at our summary recommendation number one,  
7 where we have in bold type, I think you see that we  
8 specifically feel that biofeedback alone represents  
9 between a level three and level four intervention.  
10 However, we feel that it may approximate higher  
11 degrees, at least a level three, solely a level  
12 three, if it's included in a global continence care  
13 delivery system, because I think it's very  
14 important that the coaching, the volume intake  
15 modifications, the other behavioral therapies that  
16 are instigated as part of a global continence care  
17 program, really devolve and give substance and draw  
18 sustenance, if you will, from the isolated  
19 biofeedback.

20 Again, many of the panel members have  
21 asked specifically, what about biofeedback versus  
22 biofeedback with PME, and there is data on both  
23 sides of the fence. And specifically, if you'll  
24 look at references, Berghmans' reference, which is  
25 reference number two in our literature survey,  
00098

1 versus Weatherall's reference, which is reference  
2 number eight, they use the same data to come to  
3 different conclusions, and the different  
4 conclusions are based on methodologic differences.  
5 Berghmans used a stratifying type analysis, whereas  
6 Weatherall used much more of a meta-analysis, using  
7 numbers of patients and explicit outcomes.

8 So, we view it in the context of a  
9 global approach. As an isolated therapy, we would  
10 have to rate it between a level three and level  
11 four intervention, which I think is what you wanted



12 us to do.

13 DR. GARBER: Thank you. Any other  
14 questions from the panel members?

15 DR. STANTON: Do you see biofeedback as  
16 being something that is, that you recommend being  
17 used right at the onset along with PME, or is it  
18 something that's added for difficult cases, and if  
19 so, why?

20 DR. DMOCHOWSKI: Well, I will speak for  
21 myself and also for our review of the literature,  
22 and also for what we do in our continence care  
23 system in patients who elect conservative therapy.  
24 And I think it's important to keep in mind that we  
25 are dealing with a symptomatic disease and we have  
00099

1 to present our patients with options. And we as  
2 urologists have been very self critical of  
3 ourselves over the last two decades because a woman  
4 with incontinence who presented to a urologic  
5 clinic in the 1980s was either offered pro-Banthine  
6 or surgery.

7 And let's face it, we realized with our  
8 experience with PTH that patients want a few more  
9 options. And especially when you're dealing with a  
10 non-life threatening, but significantly quality of  
11 life threatening disease, which urinary  
12 incontinence is, patients want options to therapy.  
13 So we integrate in my practice and in the practice  
14 of many people who contributed to this, biofeedback  
15 assisted PME intensely very early in therapy in  
16 those patients who elect a behavioral component to  
17 the overall therapeutic approach.

18 Behavioral therapy is not of interest to  
19 some patients and that's an individual patient's  
20 choice, but I think it should remain a patient's  
21 choice. It should not be mandated that a patient  
22 can't have that as a component to their therapy  
23 based on reimbursement or whatnot.

24 So, I think your question to wit is, do  
25 we use PME alone or with biofeedback, we use an  
00100

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

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

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

21         I do not think that PME in and of  
22 itself, a coach sitting there with fingers in the  
23 vagina, is as good as instrumental therapy,  
24 utilizing patient assisted observation of their  
25 pelvic floor contractions. That is my personal  
00101

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

6         DR. GARBER: Thank you.

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

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

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

00102

1 done in 1996 on incontinence.

2 Now we've been asked to provide  
3 testimony today on the efficacy of biofeedback  
4 therapy for urinary incontinence using evidence  
5 based methodology, and although many technologies  
6 and pharmaceutical interventions can easily be  
7 evaluated using this technique, biofeedback for  
8 incontinence is not one of those that can be easily  
9 looked at in this way. And I'm sure having now  
10 reviewed the literature, probably many of you would  
11 agree with that statement.

12 I'd like to take a few moments to put  
13 the problem and my organization in perspective for  
14 you, because we are a consumer advocacy group. I'm  
15 not doing studies to present here today, and I  
16 certainly am not representing a physician  
17 organization, before I get to address the  
18 literature directly.

19 NAFC is a national 501.C(3) not for  
20 profit organization that was chartered in 1982 as  
21 help for incontinent people. We are dedicated to  
22 improving the quality of life for individuals  
23 impaired or troubled by incontinence. The success  
24 of our 17 year old organization is reflected in the  
25 size of its membership, numbering approximately

00103

1 128,000 across North America and beyond. The  
2 readership of our publications, the quarterly  
3 quality care newsletter, its now annual resource  
4 guide, and the quarterly COS affiliates bulletin,  
5 and our subject specific educational pamphlets, is  
6 estimated to reach about 250,000 people because of  
7 its known shelf life.

8 Urinary incontinence was conservatively  
9 estimated by the AHCPR in 1996 to affect  
10 approximately 15 to 30 percent of community  
11 dwelling adults, and at least half of the  
12 individuals confined to nursing homes. That  
13 translates to 13 million Americans, 85 percent of  
14 whom are women. In studies done by Kimberly Clark  
15 and Neal Resnick, of the Brigham and Women's  
16 Hospital, find that the figure may actually be  
17 closer to 25 million, when we take into  
18 consideration those with temporary or periodic  
19 incontinence.

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

00104

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

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

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

00105

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

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

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

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

24       The average age of the respondents was  
25 67 years. Women to men in our readership, the  
00106

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

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

23       Our overall results do demonstrate how  
24 positively people feel about their outcomes with  
25 conservative measures. 52 percent of all men and  
00107

1 40 percent of all women rated these treatment  
2 modalities at the top of their list. PME was  
3 considered the most helpful treatment, and clearly  
4 our readership believes in the utility of these  
5 treatments.

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

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

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

00108

1 biofeedback.

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

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

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

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

00109

1 physical therapy. I have no current or prior

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

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

19       The AHCPR guidelines state that PME  
20 intervention using biofeedback is recommended for  
21 patients with stress, urge and mixed urinary  
22 incontinence. The AHCPR gave an A rating, the  
23 highest rating possible to the strength of evidence  
24 supporting this recommendation, and you heard about  
25 this earlier today by Miss Newman. The AHCPR  
00110

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

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

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

22 experts, the Blue Cross Blue Shield TEC assessment  
23 was authored by one individual. While the AHCPR  
24 assessment was performed under the auspices of a  
25 neutral government agency, the Blue Cross Blue  
00111

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

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

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

00112  
1 group.

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

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



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

25       Burgio in '98 found PME plus biofeedback  
00113

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

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

00114

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

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

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

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

22 MS. FELDT: Sorry.

23 DR. RATHMELL: But the question I want  
24 to ask you is, does it have to be an electronic  
25 device that provides the biofeedback? Can we go  
00115

1 back to Kegel's original pneumatic device?

2 MS. FELDT: You mean the pressure versus  
3 electronic?

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

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

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

00116

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

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

11 MS. CONRAD: Thank you.

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

17 MS. FELDT: Yes, sir.

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

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

25 MS. SMITH: There's two Berghmans. The  
00117

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

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

14 MS. FELDT: Any other questions? Thank  
15 you.

16 DR. GARBER: Thank you.

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

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

24 10 years and has been a long-term care medical  
25 director for six years. I have no financial

00118

1 conflict of interest to talk to you about this  
2 morning.

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

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

22 I would like to take a moment to explain  
23 why incontinence in the long-term care population  
24 is different than in community based populations.  
25 The long-term care population has the highest

00119

1 prevalence of incontinence of any population known,  
2 with at least 50 percent of persons in long-term  
3 care affected. However, this high rate often leads  
4 to denialism by residents and staff that  
5 incontinence is normal in this setting. The target  
6 population in long-term care is one that is often  
7 immobile and cognitively impaired. 76 to 83  
8 percent of incontinent persons in long-term care  
9 have dementia and they are also more likely than  
10 their continent peers to have impaired mobility,  
11 depression, stroke, diabetes, and Parkinson's  
12 disease, with at least one-third having multiple  
13 such conditions. Thus, both the assessment and  
14 treatment of incontinence in long-term care are  
15 more difficult, and translation of any behavioral  
16 therapy or biofeedback outcomes from community  
17 dwelling older persons is unreliable.

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

00120

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

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

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

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

00121

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

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

14         What they found was the control subjects  
15 had a median 6 percent decrease in their  
16 incontinence, while the intervention subjects had a  
17 75 percent reduction. They found that better  
18 outcomes were associated with stress as compared  
19 with urge incontinence, and in terms of outcome  
20 predictors, failure was more associated with male  
21 gender and the need to ambulate with an assistive  
22 device.

23         This is however, despite being a very  
24 well designed and executed study, does not address  
25 the question of whether the addition of biofeedback  
00122

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

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

21         DR. GARBER: Thank you.

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

25         MS. WOOLNER: Dr. Garber, Ms. Conrad,  
00123

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

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

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

18 Biofeedback for pelvic muscle  
19 rehabilitation is a standard of care in the  
20 community. Literature supporting its use has grown  
21 10-fold in the past 10 years. Many excellent  
22 clinical studies are never published, and  
23 randomized control clinical trials of biofeedback  
24 of this type of design are severely limited due to  
25 lack of funding. Aside from that, the design of  
00124

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

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

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

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

00125

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

8 In my own personal practice, we found an  
9 even higher number of our patients unable to  
10 identify the pelvic floor correctly. 51 percent of  
11 216 women we evaluated for incontinence were unable  
12 to identify or recruit their pelvic muscles.  
13 Further, 65 percent had either abandoned the  
14 exercises or were performing them incorrectly with  
15 no benefit at all.

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

00126

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

12 In the 216 people that we evaluated, we  
13 had statistically analyzed by Vital Research in  
14 Santa Monica, California. These patients were all  
15 seen in a private urogynecology practice. Of the  
16 216 patients, their mean age was 59.9 years of age;  
17 they ranged from 27 years of age to 90. They were  
18 seen in a range of two to five biofeedback visits,  
19 a mean of 3.242 biofeedback visits. The inclusion



20 criteria was mixed, stress, urge incontinence as  
21 determined by urodynamic testing. The patients had  
22 been seen for two or more biofeedback visits and  
23 they all attended a three-month follow-up. The  
24 exclusions were quite a few, and I'm not going to  
25 go through that extensively now. However, we did  
00127

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

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

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

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

00128

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

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

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

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

25         MS. CONRAD: Thank you, Miss Woolner.  
00129

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

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

17         The American Urogynecologic Society is a  
18 21 year old nonprofit organization whose nearly  
19 1,000 members have a special interest and expertise  
20 in the field of urogynecology and reconstructive  
21 pelvic surgery. Our membership includes  
22 gynecologists, urologists and allied health  
23 professionals, many with fellowship training who  
24 practice in academic and clinical practices. The  
25 mission of the society is to promote research and

00130

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

8           One area not addressed in the assessment  
9 that our society feels would be helpful for the  
10 panel to know, and has been alluded to some before,  
11 and that is the history of PMEs, commonly known as  
12 Kegel exercises. Dr. Arnold Kegel is famous for  
13 his work developing resistance exercises to restore  
14 the pelvic floor muscles. In 1948 the literature  
15 barely addressed exercises for regeneration of  
16 muscle function and therefore, Kegel decided to  
17 experiment with various means of exercising pelvic  
18 floor muscles. After 15 years of study and  
19 research, Kegel concluded, and I quote: "Only  
20 exceptional women would continue to exercise long  
21 enough to produce results on a mere instruction to  
22 do so. Many women, in addition have no awareness  
23 of function, and unless provided with some way of  
24 knowing whether or not they are successful, soon  
25 become discouraged or are unwilling to make even an  
00131

1 initial attempt at exercise."

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

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

21           Dr. Zarin already referred to randomized  
22 clinical trials as the gold standard, and we've  
23 spoken about some of the limitations. Certainly,  
24 they can also suffer from design flaws, including  
25 the lack of external validity, inadequate power,  
00132

1 and an outcome measure that is not valid or does

2 not completely capture the benefits of an  
3 intervention.

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

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

22 Shepherd also used a randomized trial in  
23 allocating 22 women with stress incontinence to  
24 either PMEs or PMEs with the perineometer. 91  
25 percent of those with biofeedback were cured or  
00133

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

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

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

22 patients how to contract the pelvic floor muscles.  
23 Some patients will do fine with verbal instructions  
24 but others will not. Many patients have difficulty  
25 identifying the pelvic floor muscle groups when  
00134

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

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

23       Glavind and co-workers revealed an  
24 indirect benefit of biofeedback in patients  
25 continuing exercises, versus the dropout rate that  
00135

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

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

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

18 In summary, the American  
19 Urogynecological Society believes the use of  
20 biofeedback offers the possibility to control and  
21 correct contractions of the pelvic floor muscles  
22 and to visualize the strength and duration of any  
23 contractions. Biofeedback treatment of urinary  
24 incontinence is an efficacious management method  
25 that yields significant therapeutic benefits and  
00136

1 low risk for selected patients. Thank you.

2 MS. CONRAD: Thank you. No questions?

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

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

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

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

24 I received a summary of the technology  
25 assessment provided by Dr. Frank Lefevre, director  
00137

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

9 Both the Agency for Health Care Policy

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

24 Interestingly, the AHCPR in 1996 also  
25 stated that the intensity of the exercise performed  
00138

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

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

18 It's interesting that the protocol or  
19 the decision or the statement presented to HCFA  
20 considered the studies that showed improvement to  
21 be flawed. One of the coauthors of the 1998  
22 Berghmans study is Dr., or Professor Kerri Bo, who  
23 is very well published in the area of pelvic floor  
24 muscle exercises for stress incontinence, and who  
25 herself usually does not look at biofeedback as a  
00139

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

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

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

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

25 Recently, Hirsch in 1999 studied 33

00140

1 patients treated with electromyography controlled  
2 biofeedback home training for six months, and  
3 showed improvement in 85 percent of these patients,  
4 although urodynamic parameters did not change. And  
5 that's the usual, the urodynamic parameters very  
6 seldom change with this therapy. The number of  
7 patients asked to enroll was 67. He only acquired  
8 33 patients.

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

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



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

00141

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

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

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

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

00142

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

4 MS. CONRAD: Thank you, Dr. Bent.

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

13 DR. ZENDLE: Outcomes, not incomes.

14 DR. RATHMELL: I'm sorry.

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

18 obviously trying to --

19 DR. RATHMELL: But his conclusion says  
20 there's not enough evidence. Would you comment on  
21 that? Do you feel there is enough evidence? Do  
22 you conclude something different than this?

23 DR. BENT: I feel that there is  
24 evidence; there is probably not enough evidence to  
25 conclude without any question one or the other. I  
00143

1 feel that in practice we are able to teach our  
2 patients in the clinical setting that's hard to  
3 reproduce in the study setting. That's the issue  
4 we're dealing with here. It's very difficult to  
5 apply the clinical to the study setting. There may  
6 be the need for further study to look at specific  
7 how to do this in a very large number of patients.  
8 The studies out there, if you look at the studies  
9 you want to look at, conclude ineffectiveness. In  
10 clinical practice, we see this effectiveness. Most  
11 of the time, however, we do use biofeedback to help  
12 do this.

13 I think it would be an error to conclude  
14 that it therefore should be dropped because it may  
15 not work.

16 DR. RATHMELL: But remember, the  
17 position we're in is to assess the adequacy of the  
18 evidence. That's what we're here to do, so that's  
19 why I posed the question.

20 DR. BENT: Well, I just want to make  
21 sure you look at all the evidence, both positive  
22 and negative.

23 MS. CONRAD: Thank you, Dr. Bent. John  
24 Perry.

25 DR. PERRY: Thank you. I've asked my  
00144

1 colleague and friend Linda West to help me with the  
2 mechanics of the presentation here. As  
3 unaccustomed to public speaking as I am, I get a  
4 little nervous. I'm a psychologist. I am the  
5 inventor of the EMG vaginal sensor in 1975, this  
6 device that is responsible for most of this  
7 evolution, and I have a quarter century of personal  
8 involvement in its promotion. Also, since 1994,  
9 100 percent of my income has come from royalties on  
10 the EMG sensor. I hold the highest credentials in  
11 the field of biofeedback, certification as a senior

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

16 In summary, the review is based on a  
17 very selective literature review. The cited papers  
18 actually contradict the conclusion, and the  
19 academic objective is of debatable value in the  
20 real world. The panel's objective, as you know, is  
21 seeing whether biofeedback adds to improvement  
22 compared to PMEs alone, but that's not as simple as  
23 it seems. It's very narrow, and it's particularly  
24 interesting to compare that with the objective used  
25 for tomorrow's presentation, which is to determine  
00145

1 whether pelvic floor stimulation improves health  
2 outcomes.

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

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

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

25 And Burns, the other one, the PME alone  
00146

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

5 If you want to look at what PMEs alone

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

10 Now looking at the stress incontinence  
11 studies that Blue Cross did examine, the first  
12 studies had no significant differences between  
13 them, but from the point of view of a person  
14 skilled in biofeedback quality review, there are  
15 several problems. One is that the quality of the  
16 biofeedback work that was done in these groups was  
17 extremely poor. Burns used an untrained therapist  
18 to bring his improvements down to 61, and she used  
19 EMGs, which brings her PME alone up to 54.  
20 Berghmans, he used a stim electrode and you just  
21 can't do that and get good results; that's what  
22 brings his PME group up is that vaginal palpation  
23 an verbal feedback. That wasn't PME alone, so  
24 that's no comparison either. And finally, the  
25 quality issues from a biofeedback perspective with  
00147

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

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

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

00148

1           So look at the levels of what the  
2 literature shows. Verbal instruction, 27 percent  
3 symptom improvement. Add palpation and verbal  
4 feedback, 51 to 60 percent. Add EMG testing, 54 to  
5 77 percent. Add formal biofeedback training, 80 to  
6 94 percent.

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

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

24           MS. CONRAD: Thank you. Panelists?  
25 Okay.

00149

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

7           MS. CONRAD: Thank you also.

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

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

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

20 pelvic muscle exercises in routine clinical use in  
21 the Medicare populations for the following three  
22 indications: Stress incontinence, urge  
23 incontinence, and post-prostatectomy incontinence?  
24 And you will consider the following points when  
25 answering these questions, and Dr. Simon will  
00150

1 elaborate again on these points.

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

7         MS. CONRAD: Thank you. Well, it's  
8 12:04. Let's try to make it at 1:15, please.

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

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

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

15         DR. SIMON: Greetings, Mr. Chairman,  
16 panel members and guests. Continuing our dialog  
17 today on the topic of urinary incontinence with the  
18 focus on biofeedback in particular, I would like to  
19 begin with the definition that we use for the  
20 purposes of our discussions today: Biofeedback, by  
21 definition, is a therapy that uses either  
22 electronic or mechanical device that relays visual  
23 and/or auditory evidence of pelvic floor muscle  
24 tone. This is done in an effort to improve the  
25 awareness of the pelvic floor musculature and to  
00151

1 assist patients in the performance of PMEs.

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

13         Kegel's exercises have been the mainstay

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

23         With this as the backdrop the question  
24 that we raise is: Does the addition of biofeedback  
25 as an adjunctive therapy to pelvic floor muscle  
00152

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

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

23         There should be a concurrent comparison  
24 group of patients treated with pelvic floor muscle  
25 exercises without the aid of biofeedback. And it  
00153

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

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

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

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

25 Dr. Lefevre is an assistant professor of  
00154

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

5 MS. CONRAD: Thank you, Dr. Simon.

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

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

00155

1 had very substantial input into this project. And



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

6 I was asked to give a little history of  
7 TEC, because many people may not be aware of what  
8 TEC is, and I wanted to first bring you up to speed  
9 on what TEC is and what we do at TEC. TEC was  
10 founded in 1985 by the Blue Cross Blue Shield  
11 Association, and the association is the umbrella  
12 organization for the Blue Cross Blue Shield plans.  
13 It provides support services for the plans in areas  
14 such as credentialing, certain types of quality  
15 assurance activities, as well as technology  
16 assessment. And TEC has been in existence since  
17 1985, as I said, and since that time has produced  
18 over 400 full-length technology assessments, making  
19 it one of the oldest and most active bodies in the  
20 area of technology assessment.

21 There has been a significant evolution  
22 of TEC since it was founded. During the period  
23 from 1985 to 1993, it was purely a proprietary  
24 organization, where the products of TEC were  
25 disseminated only to the Blue Cross plans. In  
00156

1 1993, TEC partnered with Kaiser, and in essence  
2 went public in 1993, partnered with Kaiser and at  
3 the same time offered their product to outside  
4 subscribers, such as health plans and HMOs, whereas  
5 they can subscribe to the TEC program and receive  
6 the TEC products. And most recently, the latest  
7 enhancement to the TEC program was in 1997 when TEC  
8 was named one of the 12 AHRQ evidence based  
9 practice centers. This has given us the  
10 opportunity to participate in larger evidence based  
11 projects that are entirely in the public domain.

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

22 down to purchasers of individual assessments, who  
23 can just simply buy one assessment if they're  
24 interested in that particular assessment. And  
25 finally, our relationship with AHRQ, which has been  
00157

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

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

23 Next, the TEC program has what we call  
24 TEC criteria. These TEC criteria are sort of a set  
25 of rules for which we can judge evidence against,  
00158

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

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

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

24 So again, that brings us to the  
25 objective of the current assessment, and this has  
00159

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

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

25 Now when we're talking about PMEs, PMEs  
00160

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

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

24 I would also point you to the AHCPR  
25 guidelines, which have been cited many times today,  
00161

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

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

24 Now, when AHCPR in 1996 stated that  
25 biofeedback assisted PFMEs are effective, they were  
00162

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

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

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

00163

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

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

24 type of effectiveness review. And this was edited  
25 by Cindy Moreau, from the University of Texas at  
00164

1 San Antonio, and Deborah Cook, who is from  
2 Scotland.

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

22 Thirdly, we defined, where are the  
23 outcomes that you look at. Where are the most  
24 clinically relevant outcomes in this field that  
25 we're going to abstract and that we're going to  
00165

1 consider important and relevant to our decisions on  
2 effectiveness? And finally, the fourth aspect of  
3 the problem formulation is, what is the comparison  
4 group? There always needs to be a comparison group  
5 that we're comparing the technology with.

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

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

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

00166

1 quantitatively.

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

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

00167

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

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

12 the most common outcome that's reported is a  
13 percent change in incontinence, and this is a  
14 comparison of the pretreatment level of  
15 incontinence versus the post-treatment level of  
16 incontinence, and looking at the percent reduction  
17 in the frequency of incontinence. Also, you can  
18 look at the percent of patients improved, which the  
19 International Incontinence Society has defined  
20 improvement as a greater than 50 percent reduction  
21 in incontinence. So the percent of patients  
22 improved refers to the percent of patients who have  
23 achieved at least a 50 percent reduction in  
24 incontinence. And finally, the percent of patients  
25 who are cured, who no longer have any incontinence,  
00168

1 is also a relevant outcome.

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

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

23 The study selection criteria, as Ken had  
24 outlined, I think the most important point here is  
25 that we required a concurrent control group, and  
00169

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



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

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

21 Of the six controlled trials, there were  
22 a total of 321 patients, with a range in the  
23 studies of 22 to 135. This is a relatively small  
24 body of literature, especially if you look at it in  
25 relation to the many, many patients who have  
00170

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

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

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

00171

1 bias.

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

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

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

00172

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

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

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

00173

1 the potential is there.

2 Let's look at the outcomes for these  
3 studies, and we'll go look at two outcomes, and  
4 this is a simplification of the table in the full  
5 assessment of Table II. And this is the outcome of  
6 percent change in incontinence, which is leaks per  
7 day. And of the six studies, there were four of  
8 them that reported on the outcome measure of leaks  
9 per day, and of these four studies that presented  
10 data on leaks per day, one of them showed a  
11 statistically significant difference between  
12 groups, and that was the Burgio study with a 76  
13 percent improvement in the combined group, versus a  
14 51 percent improvement in the PME alone group. The  
15 Shepherd study, which showed a rather large  
16 difference between the two groups, 83 percent  
17 versus 25 percent, did not perform any tests of  
18 statistical significance. And the other two  
19 studies, the Burns study and the Berghmans study,  
20 showed no differences in the rate of change in  
21 incontinence.

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

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

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

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

16 So what can we say in summary from this  
17 body of data on -- okay. Before I go on to the  
18 next slide, the summary of body of data on stress  
19 incontinence, what can we say in summary? Okay.  
20 There are six studies and three of them report a  
21 statistically significant difference in favor of  
22 biofeedback. Three of them report no difference  
23 between the groups. Another way of assessing the  
24 results is to do what may be called a sensitivity  
25 analysis, by grouping the studies by certain  
00175

1 measures of quality or by certain factors of  
2 methodological interest.

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

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

22 Okay. Going on to the other categories  
23 of incontinence, urge and post-prostatectomy  
24 incontinence, again, there was very sparse  
25 literature in this category. There was one study  
00176

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

7 So, our overall conclusions are listed

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

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

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

00177

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

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

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

25 I would like to make a couple more

00178

1 points about prior systematic reviews that were

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

7 First of all, Berghmans in 1998 did a  
8 systematic review of controlled trials similar to  
9 what we did, for stress incontinence. Came up with  
10 a total of six studies, four of which were  
11 identical studies to what we have. They came up  
12 with two studies which we did not include, and we  
13 came up with two studies that they did not include,  
14 because of slight differences in our selection  
15 criteria. What did they find? First of all, they  
16 did an assessment of methodological quality that  
17 was much different from what they did; they did an  
18 overall assessment of methodological quality, and  
19 they made a cut point of what they considered  
20 sufficient methodological quality or not. And of  
21 the six trials, only two of them met what they  
22 called sufficient methodological quality. So  
23 overall, their assessment was that this was not a  
24 high quality body of literature. And of the two  
25 studies which met their criteria for sufficient  
00179

1 methodological quality, both reported no group  
2 differences.

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

22 close to one; Burns and Berghmans had an odds ratio  
23 of 1.5 and 1.8, with confidence intervals of 0.5 to  
24 4.3, and 0.4 to 8.0. The Glavind study had an odds  
25 ratio of 4.8 for cure, with a very wide confidence  
00180

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

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

15 So I think that our conclusions as we  
16 put them forth here, we firmly stand by the  
17 conclusions that the evidence is not adequate to  
18 determine whether the addition of biofeedback to  
19 PFMEs has a benefit. I think there is certainly  
20 room for legitimate scientific debate as to how we  
21 performed the systematic review, and when people  
22 are critiquing our study and looking at the ways  
23 that we did our study, it should be looked at in  
24 that light. Were the methods that we took to  
25 perform this systematic review valid methods and if  
00181

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

7 DR. GARBER: Thank you, Frank. Les?

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

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

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

00182

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

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

00183

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

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



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

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

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

00184

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

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

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

00185

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

4 preferable to patients. As effective with no  
5 advantages refers to those interventions that are  
6 as effective as existing therapies, however they  
7 offer no advantages, but are clearly better than  
8 doing nothing. Less effective but with advantages  
9 refers to those interventions that are less  
10 effective than existing therapies, but they do have  
11 advantages such as, again, there may be fewer side  
12 effects or more tolerable for patients. Less  
13 effective and with no advantages refers to those  
14 interventions that are less effective than existing  
15 therapies that offer no advantages but are better  
16 than doing nothing. And lastly, not effective  
17 refers to interventions that are either not  
18 effective at all, or clearly may be harmful to  
19 patients and are much worse than doing nothing at  
20 all.

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

00186

1 conclusions about the health outcome of the  
2 technology?

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

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

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

24 me if I don't see at first when you raise your  
25 hand. Some of your faces I can't see at all, so if  
00187

1 I see your hands, I may not know whose it is.  
2 We'll try to work it out. If it looks like things  
3 are getting a little too chaotic, maybe we'll ask  
4 you to stand when you have a point to make or a  
5 question to ask.

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

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

24 The first one is, the task set before us  
25 is a very specific one, and it's to answer a series  
00188

1 of efficacy and additional benefit. The MCAC  
2 committee has helped us and set forth guidelines  
3 for us as panel members specifically to follow, and  
4 these guidelines were set up to assess new  
5 technologies and compare them to established  
6 practices. And we're to use evidence based  
7 medicine as the foundation for our decisions.

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

17 The 1998 NIH consensus statement

18 recognized the efficacy of behavioral intervention  
19 and specifically biofeedback. There are guidelines  
20 of practice that we all use when we practice in  
21 this field based from the AHCPR guidelines which  
22 recommend the use of behavioral interventions,  
23 including biofeedback, as first line therapy. We  
24 also heard presentations of a technology assessment  
25 which confirmed biofeedback efficacy, and then  
00189

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

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

18 From 1948 on, when PME was introduced,  
19 Kegel himself recognized the need of using a device  
20 to assist and be adjuvant to the PME alone. And  
21 from the very beginning of therapy in this area, a  
22 device or perineometer, or some kind of  
23 intervention was utilized. So it has always been a  
24 part of established care and standard to use some  
25 form of biofeedback method. It really isn't a new  
00190

1 technology.

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

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

12 they came up with these guidelines based on strong  
13 scientific evidence, rated their evidence, and this  
14 is akin to our task set before us today. Their job  
15 as panel of experts back in 1996 was very similar  
16 to what we are being charged with today. And they  
17 felt that based on their review and the strength of  
18 evidence, they've made recommendations regarding  
19 pelvic muscle rehabilitation and bladder inhibition  
20 using biofeedback therapy as recommendations for  
21 treatment of these patient groups. They  
22 specifically did not sort out biofeedback and  
23 remove it from the formula. And I think there is  
24 something flawed with that whole question of taking  
25 away a therapy that's always been part of the  
00191

1 treatment from the very beginning.

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

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

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

00192

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

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

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

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

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

00193

1 DR. GARBER: Thank you, Lisa. Arnie?

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

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

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

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

22 DR. HILL: We have it in our handout.

23 MS. SMITH: We have it in our handout.

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

00194

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

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

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

00195

1 results.

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

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

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

00196

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

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

00197

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

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



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

00198

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

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

00199

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

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

8 differences less than that, I can't really say.

9 DR. GARBER: Arnie?

10 DR. EPSTEIN: Yeah. There are a couple  
11 of numbers I keep in my head. If you're looking at  
12 differences in means, it obviously depends on how  
13 variable your population is. If you're looking at  
14 a proportion, like the proportion of people who  
15 improved or stopped, whatever, if you think of the  
16 baseline proportion being 50 percent, sample size  
17 of about 380 gets you plus or minus 4 percent. So  
18 keep that in your -- when you're talking about a  
19 sample size of 22, it's plus or minus a very large  
20 number.

21 DR. GARBER: Marshall?

22 DR. STANTON: I had a question for Dr.  
23 Lefevre also. I'm struggling with one of the  
24 questions we have to answer, which is the adequacy  
25 of the evidence, before even moving on to any

00200

1 others. And one aspect that's weighing heavy on  
2 that is the variability of the published results.  
3 One of the things -- you listed three  
4 possibilities. There's another possibility that I  
5 would like you to comment on and that is, it could  
6 be that the control limb, the PME, may have varied  
7 between the different studies that were assessed.  
8 When you went over the studies that met the  
9 criteria, did you look to see how much difference  
10 there was in how the PME was done and particularly,  
11 could that have been contaminated by some types of  
12 biofeedback that may have lessened the difference  
13 in some of the studies, and had zero types of  
14 biofeedback that would have had an effect?

15 DR. LEFEVRE: There was a lot of  
16 variability in the PME, in the delivery of PME.  
17 This is one of the problems with this body of  
18 literature. And this varied from -- some studies  
19 such as the Burns study, which I just alluded to,  
20 the three arms, where they gave the patients a  
21 videotape and written instructions, okay? So they  
22 gave them a videotape, written instructions, and  
23 then had follow-up visits; that doesn't appear to  
24 be biofeedback. This is the study that had a 60  
25 percent improvement in that group.

00201

1 Then there's other studies that had the

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

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

20 DR. STANTON: Well, it is a problem  
21 within a study, because it can narrow the  
22 difference. If the PME incorporates some very  
23 effective, quote, biofeedback, that's not the  
24 mechanical biofeedback that we're talking about  
25 here, that's raising the gold standard of the  
00202

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

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

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

22 PME because there was EMG testing of the PME group,  
23 and during that EMG testing it basically, not only  
24 measurement of muscle occurred, but patient  
25 reeducation could have occurred. So she was  
00203

1 actually testing a modified form of biofeedback.

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

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

24 DR. LEFEVRE: Again, it's possible. I  
25 don't think I can say from the evidence in the  
00204

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

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

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

19         And I appreciate the comment that there  
20 are features of the study that do not appear in the  
21 print version. That is undoubtedly true of every  
22 single study that we will publish, that we will  
23 review. But our deliberations should largely stick  
24 to what's in the published literature and what has  
25 been described in print, because we just don't know  
00205

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

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

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

20         If you look at Dr. Perry's slide that we  
21 talked about, if you take a look at PME alone, his  
22 conclusion is that it's about 27 percent effective,  
23 and if you add biofeedback, he says that should be  
24 80 to 90 percent effective. It seems to me as an  
25 ear, nose and throat specialist far removed from  
00206

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

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

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

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

24         DR. LEFEVRE: Again, we didn't do a  
25 systematic review of the data on PME effectiveness  
00207

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

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

20         But I think, again, in a peer study  
21 comparing PME by whatever definition you give, and  
22 where PME is equal between two groups, and then  
23 biofeedback is added on, that kind of study has the  
24 potential to isolate the effect of biofeedback  
25 apart from what the baseline PME is. So I think, I  
00208

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

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

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

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

00209

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

7 The problem we have with that  
8 clinically, and that was actually shown by Glavind,  
9 1996, there was a high dropout rate in the people  
10 in the PME alone group. There was lack of, less  
11 compliance, and we lost some motivational factor  
12 there. And I think if you start to apply that  
13 concept clinically, a lot of patients are going to  
14 go untreated.

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

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

24 kind of my way of looking at it. Although  
25 certainly, that excellent report that Dr. Lefevre  
00210

1 worked on, it doesn't make a definitive, something  
2 in my mind, as to biofeedback as a successful  
3 adjunct. But I don't know how we are going to get  
4 around the fact that the definitions are different  
5 in studies and across studies.

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

18 So in other words, if you were  
19 interested in intensive blood pressure management,  
20 you couldn't ethically conduct a trial denying the  
21 usual character of blood pressure treatment. And  
22 the trials are designed in those circumstances to  
23 pick up a difference, if you want to find out  
24 whether more intensive use of the intervention  
25 works. And what that means is to ask a very pure  
00211

1 question, and we just heard how difficult it is to  
2 ask a pure question in this context, to ask a pure  
3 question, what would it be like to use no  
4 biofeedback whatsoever, might not be possible, but  
5 you may have some hints.

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

17 But this is a problem that we will



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

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

00212

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

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

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

00213

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

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

12 stress, urge and post-prostatectomy.

13 DR. HOLTGREWE: Is a motion  
14 appropriate?

15 DR. GARBER: Well, we're going to vote  
16 at the end of the day, but the question is, should  
17 we have further discussion of the  
18 post-prostatectomy.

19 DR. HOLTGREWE: Well, I feel very  
20 strongly that we have inadequate information to  
21 make any kind of decision. I'm not saying that  
22 biofeedback in conjunction with PMEs wouldn't work  
23 in post-prostatectomy incontinence; I'm simply  
24 saying we have no evidence that it's good, bad or  
25 indifferent. We just don't know.

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1 DR. GARBER: I think I jumped the gun  
2 there. We will have to wait until the end of the  
3 day even to take up that question. We can still  
4 have discussion though, about all of those points.

5 DR. ZENDLE: What do you want to  
6 discuss?

7 DR. HILL: This isn't a great discussion  
8 issue, but I just wanted to ask the point. Maybe  
9 the biofeedback isn't so much in the eye of the  
10 beholder as in the cerebellum of the receptor. The  
11 reason people dropped out, maybe I'm making a wrong  
12 assumption, but I just didn't know why they dropped  
13 out. We don't know if they dropped out of the  
14 studies because they got better or they weren't  
15 getting better or for some other reason, and I  
16 don't see how the dropout rate always goes in one  
17 direction, and maybe I can get a response on that.  
18 I thought I was hearing sort of the underlying  
19 assumption that the dropout rate suggested a  
20 unidirectional bias.

21 DR. LANDY: Both of the treatment groups  
22 initially got the same treatment in the Glavind  
23 study. He gave two to three sessions of  
24 instruction and PME, then added four weeks of  
25 biofeedback training, and the dropouts were in the

00215

1 period of time in that initial -- actually, I'm not  
2 sure at what point in time they occurred, but it  
3 happened at a greater rate in the PME alone group.

4 DR. GARBER: I think Hugh's point,  
5 though, is that a priori, you can't say with

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

10 DR. LANDY: Yeah.

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

24 And there is pretty universal agreement,  
25 you should use intention to treat, count the  
00216

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

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

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

00217

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

13           DR. GARBER: Any comments?

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

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

00218

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

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

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

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

20 eight weeks?

21 DR. STANTON: The effect didn't  
22 disappear; the other group caught up.

23 DR. ZENDLE: Okay. The difference  
24 disappeared. And so if the physiologic -- if the  
25 long-term outlook were going to be better, you  
00219

1 would expect it to go the other way?

2 DR. STANTON: Except I was thinking  
3 long-term like a year, something like that.

4 DR. GARBER: I saw somebody else?  
5 Okay.

6 Connie just informed me of a very  
7 important fact. The refreshment stand closes at  
8 three. Our original schedule had us beginning our  
9 break at three, so I would like to propose that we  
10 break now, and resume with the open public  
11 commentary at three o'clock. Thank you.

12 (Break taken at 2:50 p.m.)

13 DR. GARBER: We are about to resume.

14 MS. CONRAD: Okay. We are going to take  
15 the next few minutes, maybe as many as 30 minutes,  
16 to allow anyone in the audience to approach any of  
17 the microphones, there's two aisle microphones, one  
18 podium microphone. This is the opportunity for  
19 those who forgot to ask for speaking time, or who  
20 were too late, or who just all of a sudden  
21 remembered something that they would like to  
22 mention to the panel members. So at this time, if  
23 you wish to, first come, first serve, approach the  
24 mike, state your name, your affiliation, and  
25 address the panel. Yes, ma'am.

00220

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

13 I am very pleased to write in support of

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

00221

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

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

11 MS. FELDT: I appreciate being able to  
12 address the panel again, due to the time constraint  
13 on my verbal testimony earlier this morning and a  
14 notice in the Federal Register that stated a March  
15 22nd deadline, the American Physical Therapy  
16 Association submitted written comments to HCFA so  
17 that comments could be available to the panel prior  
18 to this meeting. I have, however, received  
19 information that the members of the panel did not  
20 receive our written statement, but did receive the  
21 TEC report. What I would like to is to insure that  
22 you have access to this information, so we are  
23 going to hand out our position papers so you may  
24 use them in your deliberations later. Thank you.

25 DR. HILL: Sorry. I have to speak up

00222

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

8 submitted by the deadline.

9 MS. FELDT: Sir, it was submitted by the  
10 deadline. It was submitted by March 22nd, and I am  
11 under the impression --

12 DR. HILL: Well, if we received it by  
13 March 22nd, it was included.

14 MS. SMITH: No. It is part of the  
15 catalog of items that was available to the panel.  
16 But what Cindy Feldt is talking about is that the  
17 panel members received in hand the TEC report, and  
18 had to request other things that were part of the  
19 catalog items, so that's what she's talking about.

20 DR. HILL: Yeah, I'm sorry; that's  
21 correct. That's like some of the excluded  
22 articles, and some of the other things. If the  
23 panel members has asked for them, they would have  
24 been distributed to them.

25 MS. FELDT: So if I would have submitted  
00223

1 this morning along with my written testimony, it  
2 would be accepted?

3 DR. HILL: No, because what we asked for  
4 with your written testimony was a transcript, which  
5 you did give us, and it was appreciated.

6 MS. FELDT: Thank you.

7 MS. CONRAD: Yes, sir?

8 DR. SAND: Hi. I'm Peter Sand, from  
9 Northwestern University Medical School, and I'm the  
10 secretary treasurer of the International  
11 Urogynecological Association. And one thing that  
12 came to mind in listening to the deliberations and  
13 the discussion that's always impressed me about  
14 biofeedback is that in some of the literature that  
15 you're looking at, which has an international base,  
16 the discussion came up earlier this morning about  
17 applicability of studies. And while prospective  
18 randomized or prospective controlled trials are  
19 very useful, I think we also, to make the waters  
20 even more muddy, we had to consider that in  
21 different countries we see different outcomes and  
22 different results.

23 Those of us who are familiar with Karri  
24 Bo's work, which was discussed earlier for example,  
25 recognize that Karri has been able to maintain

00224

1 populations of women in pelvic floor therapy with

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

14         The other thing, and the other issue  
15 that I don't think we have good data on  
16 unfortunately, but it seems to be very clinically  
17 relevant to myself and my peers, is compliance. We  
18 talk about compliance in control trials, we try to  
19 track this and report this, but in clinical  
20 practice it is very clear that compliance improves  
21 with the intervention and the strength of the  
22 intervention, and obviously if there's biofeedback,  
23 and there are visits associated, and there's what  
24 we like to call in our office the coach effect, in  
25 which you have to report to the coach on a regular  
00225

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

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

16         MS. CONRAD: Thank you.

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



22 and I think this can be shown most clearly in the  
23 fact that the American centered Association for  
24 Applied Psychophysiology and Biofeedback just  
25 celebrated its 32nd annual meeting last week in  
00226

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

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

23 MS. CONRAD: Thank you. Diane?

24 MS. NEWMAN: I didn't get enough time  
25 this morning. You know, Dr. Landy brought up a few  
00227

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

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

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

25 But what's important about what we did,  
00228

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

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

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

25 And the second point: If the studies  
00229

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

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

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

24 DR. LANDY: What we're saying is that is  
25 the clinical situation that is the most common  
00230

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

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

12 DR. RISAGER: Excuse me. You referred  
13 to a clinical practice of just handing out paper.  
14 I think one of the reasons why there may not be  
15 that much in the way of studies is because what  
16 people do out there, certainly speaking about our  
17 area here in Maryland, is urology and neurology  
18 groups, when women come in complaining of stress  
19 incontinence, or whatever, generally they're well  
20 organized groups; they have a nurse who is  
21 particularly skilled, and she takes the patient in  
22 hand and will teach them pelvic floor exercises.  
23 She does hand out sheets of paper, but actually  
24 teaches, changes -- there is the other bladder  
25 training pieces as well. And this is certainly the  
00231

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

3 So what I'm seeing here, there are

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

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

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

24 DR. ZENDLE: Could you distinguish the  
25 different kinds of biofeedback, from the bells and  
00232

1 whistles to the more simple?

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

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

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

24 FES. And one of the things that was fascinating to  
25 me about his work and that article in 1998 was that  
00233

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

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

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

00234

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

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

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

24 DR. GARBER: Let me just ask if there  
25 are any more public comments. We sort of glided  
00235

1 into -- yes?

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

24 MS. GREENBERGER: I would like to say  
25 something. As the consumer rep, I think I'd like  
00236

1 to speak to the consumer. First of all, I'm  
2 puzzled as to why we would have all these public  
3 comments and patients, and the letters, which I did  
4 receive and read, and then sort of ignore it  
5 because it's not scientific evidence in the  
6 research that we're getting. So I think that, I  
7 mean I'm concerned that all these people have  
8 weighed in, they are professional organizations,  
9 the advocacy organizations and the patients, and it  
10 seems that up until the last couple comments they  
11 were sort of being disregarded.

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

20           So I think that -- and I also think that  
21 we've had a fair amount of discussion about the  
22 confusion of the definition of what pelvic exercise  
23 really is and whether that does, ipso facto,  
24 include biofeedback. So I, this first question is  
25 sort of a nonstarter. I mean, we're not going to  
00237

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

7           DR. GARBER: Thank you.

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

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

23          MS. GREENBERGER: I know it's available  
24 and I've read it. That's not my point. The point  
25 is that using the word scientific negates the  
00238

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

5           But under these circumstances, at least

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

22 DR. GARBER: Maybe I could just quickly  
23 address that, Phyllis, because I think you raise  
24 very important points. The testimonial  
25 information, the consumer letters, the opinions of  
00239

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

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



00240

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

6 I think we have one other public  
7 speaker.

8 MS. CONRAD: This is absolutely the last  
9 one.

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

00241

1 MS. CONRAD: Thank you.

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

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

20 thereof.

21 Now, having said that, I certainly don't  
22 want anyone to think that there isn't in my mind  
23 any place for this. I just don't know, and I don't  
24 think there's a compelling body of evidence that  
25 has been presented that available in the literature  
00242

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

9 DR. GARBER: Is there a second?

10 DR. EPSTEIN: Second.

11 MS. SMITH: I would like to bring  
12 something out. I gave Connie Conrad a copy of an  
13 article in a recent journal of the Lancet, in  
14 January, 2000, there was an article with a fairly  
15 good end that showed that men prior to  
16 prostatectomy, radical prostatectomy, were given  
17 biofeedback, and then those men were given  
18 biofeedback again post their procedure. And there  
19 was a control group where the men who were just  
20 receiving the procedure of radical prostatectomy,  
21 and it showed that there was an efficacious benefit  
22 in using biofeedback to train those men. In other  
23 words, the men who received biofeedback pre and  
24 post had incontinence for less of a period of time  
25 than the men who basically just had the procedure  
00243

1 alone.

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

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

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

24 MS. CONRAD: Excuse me. Before we go  
25 any further with this, I have a piece that I have  
00244

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

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

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

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

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

00245

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

8 upon at this point.

9       So I say again, I think that this is  
10 different from stress incontinence and urge  
11 incontinence in men and women who haven't had a  
12 prostatectomy. Of course women don't need to worry  
13 about having a prostatectomy. But I really do  
14 believe that we have inadequate information to make  
15 a decision. You just can't scientifically say we  
16 know that biofeedback is of any value in this  
17 situation. Maybe it is. We need to find out, and  
18 we hope there are studies, and they will hopefully  
19 be soon on the horizon and available to us. In the  
20 meantime, I don't see that we can decide.

21       DR. GARBER: Les?

22       DR. ZENDLE: For the purpose of  
23 efficiency, could we vote on a motion that sort of  
24 added the words, any of the following three  
25 indications? Because if that get voted down, it's

00246

1 silly to then separate it out, if a majority feel  
2 that none of these meet the criteria. Now if they  
3 feel any of them should, they should vote yes, and  
4 then we'll have to divide it up and see which ones,  
5 but it seems to me that that's unlikely.

6       DR. GARBER: Well, it seems to me that  
7 we have a motion that's been seconded. And either,  
8 I guess the motion could be withdrawn or it could  
9 be amended, but we have a motion. Let me ask. I  
10 thought I heard somebody second it.

11       DR. EPSTEIN: I was going to second it,  
12 but I decline to second that motion in that Les has  
13 as an alternative. I think it will be more  
14 efficient and drive us more quickly to where we  
15 need to go.

16       DR. GARBER: This really gets well  
17 beyond my meager knowledge of Robert's Rules. So  
18 as I understand it, we have a motion that was  
19 seconded and the second was withdrawn, and  
20 therefore, the motion does not stand.

21       Now Les has a motion.

22       DR. ZENDLE: I move that we vote on  
23 question one with the understanding that we're  
24 adding the words, the Medicare populations for any  
25 of the following indications. If there is a yes

00247

1 vote, then we'll have to separate them out, but

2 we'll see what happens.

3 DR. LANDY: I thought we were supposed  
4 to address each of those individually.

5 DR. EPSTEIN: I think he's saying if  
6 none of them are going to win, then why do we have  
7 to drag ourselves three times over the same coals?

8 DR. LANDY: Because they are different  
9 issues.

10 DR. GARBER: That's part of the  
11 discussion on his motion, but I haven't heard a  
12 second.

13 DR. EPSTEIN: I second.

14 DR. GARBER: Okay, there's a second.  
15 Now we can discuss it. Dr. Landy?

16 DR. LANDY: I am very confused about the  
17 motion. Can you clarify it, because I'm under the  
18 understanding we were going to address each of  
19 these independently.

20 DR. ZENDLE: We will, if my motion  
21 passes, that we say that there is scientific  
22 evidence on any of these, then we will address them  
23 individually. If we don't, then there is no reason  
24 to address them individually.

25 DR. LANDY: So, if you can clarify what  
00248

1 an affirmative vote is versus a negative vote?

2 DR. GARBER: Do you want to restate your  
3 motion?

4 DR. ZENDLE: If you believe that there  
5 is scientific evidence to draw conclusions about  
6 the effectiveness of biofeedback as an adjunct to  
7 PMEs, blah, blah, blah, in any of these conditions,  
8 you should vote yes. If you feel there is no  
9 scientific evidence in any of these, you should  
10 vote no.

11 DR. LANDY: Thank you.

12 DR. HILL: HCFA is interested in why you  
13 vote, so under either rubric, whether you divide  
14 them out issue by issue or take on overall vote  
15 like this, we would still very much like to hear  
16 what's the thinking behind the vote on a per  
17 indication basis.

18 MS. CONRAD: May we have a show of hands  
19 please, those for, in favor of the motion? Is this  
20 unanimous?

21 DR. LANDY: No.

22 DR. GARBER: Actually, I think I may  
23 share some of the uncertainty about what the motion  
24 is. As I first understood you to propose it, Les,  
25 you're asking for the panel to decide en block if  
00249

1 maybe none of these conditions meets the adequacy  
2 questions.

3 DR. ZENDLE: Or any of them.

4 DR. GARBER: Okay. So anyway, there's  
5 first going to be a determination about whether any  
6 at all meets the evidence, the adequacy criterion.  
7 You're proposing we do that en block, ask that  
8 question and if the answer is yes, then we proceed  
9 individually among each one.

10 So the motion is not to make a  
11 determination about adequacy of evidence but about  
12 the procedure that we will use; is that correct?

13 DR. ZENDLE: No. If the majority of the  
14 panel doesn't vote yes on my question, we're done.

15 DR. GARBER: Okay. So you want to go  
16 directly to the evidence determination?

17 DR. ZENDLE: Of any of them. But  
18 granted, if the majority feels that there is  
19 evidence for any of them, we have to go on to see  
20 which ones they think there's evidence for and  
21 which ones they don't. Maybe it's not efficient.

22 MR. WHITE: I'm John White, and I work  
23 in the coverage group with Dr. Hill.

24 DR. HILL: Temporarily he is serving as  
25 parliamentarian.

00250

1 MR. WHITE: Just in terms of  
2 parliamentary procedure, if Dr. Zendle has made a  
3 motion which was seconded to modify the question,  
4 you should vote on whether or not to accept that  
5 modified question. That really should be the first  
6 order of business. And then depending on what  
7 happens there, then you should decide to vote yes  
8 or no. But you do have that motion to modify the  
9 question which has been seconded. You've had  
10 deliberations about that motion, but you still have  
11 to vote as a whole group whether or not to accept  
12 that modified question.

13 DR. GARBER: Thank you. That explains  
14 my confusion, I think, because it's really a  
15 two-part thing that you're talking about, and

16 you're leaping to a changed question and asking for  
17 a vote on that.

18 DR. ZENDLE: I didn't realize there was  
19 a motion on the floor that I was asking an  
20 amendment for. I thought it was a primary motion.

21 DR. EPSTEIN: Les, I'd be willing to  
22 withdraw my second if you withdraw your motion. I  
23 think we might move more quickly going right in the  
24 order as suggested.

25 DR. ZENDLE: Yeah, it's proven not to be  
00251

1 very efficient, so I withdraw it.

2 DR. EPSTEIN: I can always tell when I  
3 back a losing cause.

4 DR. GARBER: Okay. It sounds like we  
5 are going to do things in order since we rejected  
6 Logan's motion by lack of a second to start with  
7 the post-prostatectomy.

8 So let us first deal with stress  
9 incontinence, unless there is an alternative  
10 proposal on the table.

11 Is the scientific evidence adequate to  
12 draw conclusions about the effectiveness of  
13 biofeedback as adjunct to pelvic muscle exercises  
14 in routine clinical use in the Medicare population  
15 for stress incontinence?

16 Discussion?

17 DR. ZENDLE: Call the question.

18 DR. GARBER: Okay. An affirmative here  
19 means that the evidence is adequate for the  
20 indication.

21 DR. RATHMELL: For the parliamentarian,  
22 I'll second the motion that we call the question.

23 DR. GARBER: Okay. Affirmative means  
24 the evidence is adequate and a negative means that  
25 the evidence is not adequate. All in favor, or all

00252

1 answering yes?

2 I count two.

3 Okay. All who answer no?

4 (Drs. Bradley and Landy voted in the  
5 affirmative; all other panelists voted no; there  
6 were no abstentions.)

7 DR. GARBER: Okay. I do have a  
8 procedural question that I seek the panel's  
9 guidance on. You are asked to explain your votes.

10 Would you rather do that at the end after we have  
11 done all these? Okay. Anybody disagree with  
12 that?

13 Is there a motion to address question 2,  
14 the same question, except for urge incontinence  
15 rather than stress incontinence?

16 DR. ZENDLE: So move.

17 DR. BRIN: Second.

18 DR. GARBER: Okay. All who answer yes,  
19 meaning that the evidence is adequate, please raise  
20 their hands. All those answering no.

21 I believe that's unanimous.

22 (All panelists voted no.)

23 DR. GARBER: Number 3, the same question  
24 except with regard to post-prostatectomy  
25 incontinence.

00253

1 DR. MAVES: So move.

2 DR. ZENDLE: Second.

3 DR. GARBER: All answering yes? All  
4 answering no? I believe that's unanimous.

5 (All panelists voted no.)

6 DR. GARBER: Now, what -- Logan, do you  
7 have a comment?

8 DR. HOLTGREWE: Personally, I voted no  
9 because I feel the available current peer review  
10 literature does not adequately confirm that  
11 biofeedback in conjunction with PME provides any  
12 advantage over existing other therapies, and  
13 particularly muscle exercises by themselves. In  
14 other words, simply stated, there's inadequate peer  
15 review literature to support the position.

16 DR. GARBER: Before we proceed, let me  
17 just explain one thing. We take very seriously the  
18 obligation to explain the votes, we don't want to  
19 put anybody on the spot, so let me suggest that if  
20 you have a reason for voting yes or no and if the  
21 reason has not been given, that you do take  
22 responsibility to give your reasons here openly, so  
23 that we at least can collect all of the reasons  
24 people gave on both sides of each of these  
25 questions, and so that this will be entirely

00254

1 transparent, why people voted as they did.

2 So, not everybody has to explain how

3 they voted, but I hope that all the reasons you



4 used in reaching your determinations are expressed  
5 by at least one person.

6 DR. HILL: If I may, if you perceive a  
7 difference in the three indications, would you  
8 please also explain that to us?

9 DR. GARBER: Okay. Les?

10 DR. ZENDLE: I wanted to say what my no  
11 vote is not, and it is not that I do not feel that  
12 this should be covered or that it should be  
13 provided to patients. My no vote was that I don't  
14 feel the scientific standards of evidence have been  
15 reached by the common definition of statistical  
16 significance. But that does not mean that I don't  
17 think that there is some use to this technology or  
18 that it should be provided. I do feel that there  
19 are appropriate indications that don't require a  
20 scientific evidence standard, but that is not what  
21 this group has been asked to do.

22 DR. GARBER: Jim?

23 DR. RATHMELL: I feel very strongly that  
24 the peer review literature, there is a paucity  
25 there, and the technology assessment was very well

00255

1 done, and it really does pretty much agree with  
2 systematic analyses that appeared earlier as well  
3 as the recent meta-analysis. And the question, the  
4 big problem that I have here is the question that  
5 we have answered is not the efficacy of one  
6 intervention versus the other, it's -- or two  
7 interventions that are standardly used, biofeedback  
8 versus the PME. It's this arbitrary distinction  
9 between what constitutes the two, and trying to  
10 draw a very discrete line through this of  
11 biofeedback versus PMEs alone. And I would agree  
12 with what the AHCPR had done, lumping all the  
13 behavioral treatments together and saying that they  
14 are very effective, and that would be the outcome  
15 that I would favor. But the question we have been  
16 asked is about the adequacy of the scientific  
17 evidence to divide these two very discrete things,  
18 and it just isn't there.

19 DR. GARBER: Arnie?

20 DR. EPSTEIN: Yeah. I'll go off the  
21 reservation a bit, and use this as an opportunity  
22 to make a comment for the record, which will at  
23 least be read if not used by those who come after

24 and make the more important decisions about  
25 coverage. I think there is a difference -- from  
00256

1 the beginning this morning when I asked you the  
2 question about adequacy, this has hung on the word  
3 adequacy, and adequacy depends often on who and for  
4 what purpose. If you're a scientist, you define  
5 adequacy conventionally as there's only a 5 percent  
6 chance that you will say something is true and it's  
7 not, or sometimes a 1 percent chance. If you  
8 happen to be a policy maker, which is different  
9 than a scientist, adequacy is often .5. I think  
10 I'm better off going this way than that way, since  
11 I clearly have to go in one direction versus the  
12 other.

13 When I reviewed the information that I  
14 have available from the scientific literature, and  
15 we've all commented on its adequacy or its  
16 inadequacy, it seemed to me that Dr. Perry may have  
17 had some version of it right. Probably written  
18 training does something, a little bit. Probably if  
19 you do more than training and get a nurse to  
20 reinforce it with or without digital reinforcement,  
21 you get more, and maybe even get more with some  
22 biofeedback, although I don't know.

23 I would say that if I was forced to bet  
24 on this like a policy maker is on the 50-50 level,  
25 I would probably bet you'd get something, but not  
00257

1 at the 95 percent where scientific adequacy is. So  
2 for me, it is easy to, one, vote no on the  
3 question, which I did, and then at the same time  
4 comment here, urge HCFA to consider the fact that  
5 this may very well be an efficacious therapy, and  
6 they should consider that in their decision making,  
7 lest they be penny wise and pound foolish.

8 DR. HILL: Dr. Epstein, can you tolerate  
9 a question?

10 DR. EPSTEIN: Yeah, as long as I get a  
11 chance to respond.

12 DR. HILL: I heard you say .5 percent,  
13 and we've used that figure when we talk about P  
14 values. Then you talk about 95 percent, and I want  
15 to know if that's the mirror or how you got that.

16 DR. EPSTEIN: I think two different  
17 ways. If you're a scientist and you're trying to

18 say this exists, the classical scientific proof is  
19 at P .05 or P .01, which means that there is only a  
20 5 percent chance or a 1 percent chance that you're  
21 going in a certain direction and in fact it's  
22 wrong. That's the sort of classic Type A error.  
23 If you are like a policy maker, like HCFA is in  
24 this condition, where you either have to encourage  
25 its use or discourage its use, then for some policy  
00258

1 questions, not every one because it's more of a  
2 subtlety, you really make a decision, do I think  
3 I'm more likely to win this way or win that way,  
4 and then your P value is .50. And all I was  
5 drawing with the analogy here is if you wanted me  
6 to take my best guess. If someone said you're  
7 going to make 20 bucks or lose 20 bucks, do you  
8 really think you're better off with biofeedback,  
9 I'd would probably put it on yeah, you probably,  
10 are. But if someone is going to say are you sure,  
11 adequacy, then I'm back to a 95 percent. Does that  
12 clarify it?

13 DR. ZENDLE: You went from percentage to  
14 a point. The point is, it's 5 versus 50 percent?

15 DR. EPSTEIN: Thank you.

16 DR. GARBER: I don't have a very clear  
17 view at the end of the table. I thought I saw Dr.  
18 Bradley's hand up.

19 DR. BRADLEY: I think you also wanted  
20 the yes answers also. I voted yes on the issue  
21 because probably like an orthopedic or ENT, the  
22 question is whether someone is pregnant or not,  
23 pregnant and virgin or not virgin. And looking at  
24 it in black and white, the data that was shared at  
25 the end of the morning by Dr. Perry, looking at  
00259

1 what we would now consider a very archaic method of  
2 instruction, as you mentioned in terms of just  
3 handing out something, talking with the patient,  
4 obviously in real life this millennium is no longer  
5 being practiced that way, and then looking at the  
6 other studies that we have available to us, the  
7 definition of just basic instruction often is  
8 muddy. But I think if we just look at the very  
9 pure definition of PME with written instruction or  
10 handouts given, and then add on all the other  
11 things that biofeedback does when it come to

12 enhancing the patient's perception of body parts,  
13 the kinesthetic or the subtleties that the patient  
14 is able to determine by having the biofeedback,  
15 that it does add in my mind a positive benefit or  
16 is an adjunct to PME. And that testimony from  
17 patients, and just the actual procedure itself, I  
18 think it does make a difference in terms of patient  
19 outcome, and I am very comfortable with my decision  
20 and vote, again, using the very basic definition of  
21 written instruction and handout, and I think the  
22 other method does add to patient care.

23 DR. GARBER: Thank you. Maybe I could  
24 take this opportunity to make somewhat of a general  
25 comment. I didn't have the opportunity to vote and  
00260

1 therefore, I don't have the obligation to explain  
2 my vote, but I did want to address a point that  
3 Dr. Perry raised, which I think is a very important  
4 one. And he pointed out that companies  
5 manufacturing equipment don't have the money to  
6 support clinical trials, and I think that's likely  
7 to be true in a number of contexts, and it's a very  
8 unfortunate circumstance. There are some areas for  
9 a variety of reasons why trials either can't be  
10 performed or won't be performed because there is no  
11 interested party with the money to pay for it.

12 And I think what the panel has done here  
13 is just addressed the adequacy of evidence, and Dr.  
14 Perry's statement is not really about whether the  
15 evidence is adequate, but whether it's really  
16 feasible to put together adequate evidence, and  
17 that's an important message, and I have to say that  
18 just speaking as an individual, I hope that HCFA  
19 takes that into consideration. Our panel is  
20 structured to give a clean answer to a clean, or we  
21 thought clean question. But it would really muddy  
22 the waters to say that evidence is adequate when it  
23 isn't, solely because it's difficult to conduct  
24 well designed trials. That does not mean that HCFA  
25 should ignore that fact.

00261

1 There are situations when the trials  
2 can't be done and I think that HCFA should exercise  
3 some discretion in deciding to cover in some  
4 circumstances, when we as a panel say that the  
5 evidence is simply not adequate. So I don't think

6 that those considerations should be ignored. It is  
7 a sad truth that it is not always feasible to  
8 conduct well designed studies, and HCFA has the  
9 responsibility to decide whether to cover or not in  
10 those circumstances.

11 But we've spoken about what the evidence  
12 said, we have not expressed an opinion about  
13 whether it's feasible to get better evidence.  
14 That's not really part of our role, although we are  
15 certainly welcome to comment on that, if you think  
16 for example it just wasn't feasible in this area to  
17 conduct studies. Les?

18 DR. ZENDLE: Well, I guess this is sort  
19 of related to that. If I were asked to vote  
20 whether handing out a written instruction sheet or  
21 giving verbal instructions on the PME's was useful,  
22 I would say there is pretty good evidence that it's  
23 not, and that there needs to be more than that to  
24 be considered. My understanding is that we were  
25 including, we were not limiting the PME group to  
00262

1 only those people that got sheets of paper or  
2 verbal instructions, but it was a broader group,  
3 and if there is a way of separating that group out,  
4 I think if we were able to look at that evidence,  
5 we would see that there is a difference.

6 DR. BRADLEY: Most of the studies, I  
7 think unfortunately in terms of inclusion criteria,  
8 as Diane has mentioned, it's just not very clear in  
9 terms of what's actually happening. So much of  
10 what we actually do, we just incorporate it into  
11 clinical practice. We are incorporating a lot of  
12 -- it becomes the standard in terms of the issue  
13 of some of the subtleties of biofeedback, however  
14 you want to define it, whether it's hands in the  
15 vagina, whether it's a visual analog, whether it's  
16 bells and whistles, somehow that's being  
17 incorporated, and very few of the studies just look  
18 purely at just written.

19 I mean, if we had six studies or eight  
20 studies that purely said we handed out a handout  
21 and just said read it and do it, and then add on  
22 whatever instrument or instrumentation is used, we  
23 would end up with the kind of data that Dr. Perry  
24 has talked about. But the studies at least as far  
25 as I've looked, as I have read them and listened to

00263

1 discussions, so much else is -- there's a lot of  
2 little fine things that are happening sort of off  
3 record.

4 DR. ZENDLE: Which is why AHCPR did not  
5 separate out the different kind of biofeedback, and  
6 I agree with that.

7 DR. MAVES: Alan, in my no vote, I think  
8 it helps just to corroborate that. I think I feel  
9 a little bit the way both of you did, and I'll try  
10 to explain that. I was presented with the  
11 difficulty of making an incremental decision when  
12 essentially you have a continuum of evidence. And  
13 the interventions, if I can sort of take a look at  
14 pure PME, and I was looking at the categories of  
15 effectiveness, I suppose it would fall somewhere in  
16 the five or six category. If we looked at  
17 biofeedback, I think I would agree with our  
18 colleagues from the AUA, it's somewhere in the  
19 three to four. The problem I had is that when you  
20 went back to the literature, when you looked at  
21 what documentation did you have to make that  
22 decision, it just simply wasn't there.

23 DR. LANDY: I didn't get to explain my  
24 yes vote, and part of it is my interpretation of  
25 the question is different. I read this question,

00264

1 is the scientific evidence adequate to draw  
2 conclusions about effectiveness of biofeedback as  
3 an adjunct to PMEs? Biofeedback is always used as  
4 an adjunct to PME; it's never been used any other  
5 way. So to me the question was really  
6 effectiveness of biofeedback and there is a wealth  
7 of information on the effectiveness of biofeedback  
8 as a therapy.

9 DR. HILL: May I ask a hopefully  
10 clarifying question? If you assume arguendo HCFA's  
11 definition for the purpose of the question when we  
12 asked the mechanical and electrical device as  
13 biofeedback, as distinct from other kinds of  
14 biofeedback.

15 DR. LANDY: Yes, I still answer that.

16 DR. HILL: Is that first line therapy,  
17 is that's what's always done, and would that change  
18 your vote?

19 DR. LANDY: Yes. And no, that would not

20 change my vote. I think if you worded the  
21 question, and that's very similar to the original  
22 question we got, but if you worded the question  
23 biofeedback, does it confer additional benefit,  
24 then I would have more trouble based on the data  
25 answering the question. But the wording of it is  
00265

1 biofeedback as an adjunct to PME. That's how it's  
2 always used, that's how it's studied in the  
3 literature, and all these case controlled studies,  
4 and randomized control trials are looking at  
5 biofeedback as an adjunct to PME.

6 DR. HILL: She's right. That's a word  
7 game in there.

8 DR. McBRYDE: McBryde. I'm probably  
9 saying the same thing just in my own words, and  
10 that is that I believe that biofeedback as  
11 described by all of you is efficacious and I think  
12 it's being used and being used in practice settings  
13 all over the country, and for the most part it's  
14 mainstream, which makes a little bit of this vote  
15 almost after the fact, because it's kind of a done  
16 deal. I voted no though, because given the rigid,  
17 the shotgun standard for PME, and kind of the rigid  
18 definition of biofeedback, and looking at the  
19 literature and correlating those things, you have  
20 to say no, and that's why my vote was no. Perhaps  
21 the future will tell a different story, if indeed  
22 there will be more.

23 MS. GREENBERGER: I obviously can't  
24 vote, and I think I made my position, but I just  
25 want to say, this is really uncomfortable. I mean,  
00266

1 there's so much confusion about the question,  
2 whether biofeedback has been used, as Lisa said.

3 And I know we're not supposed to be  
4 talking about coverage, but let's face it, this is  
5 about coverage ultimately, and this is a big issue  
6 that's been going on at HCFA, and I am involved in  
7 other diagnostics, and other issues, where again,  
8 there aren't large enough clinical trials to make  
9 determinations on the scientific evidence and yet  
10 in my case, since this is the group that I  
11 represent, women don't have access to these  
12 diagnostics because they don't have large clinical  
13 trials, and it's because they're not drugs and

14 they're not manufactured by the drug companies,  
15 they're just are unable to support them.

16       So I just, I want to go on record also  
17 saying that since my group is the Society for  
18 Women's Health Research, I understand research, I  
19 understand the importance of peer review scientific  
20 research, and I am not for a moment discrediting  
21 that or overlooking the importance of that. But I  
22 just think in this case and in other cases I am  
23 familiar with, we don't have the scientific  
24 research for other reasons and because we don't  
25 have it, we may ignore an efficacious treatment for  
00267

1 people, and I think that's a real problem. I don't  
2 know how to get around it. I know you've got to  
3 have the research, but I would hate to see a  
4 treatment that works and that people are  
5 supporting, both patients and providers, ultimately  
6 not be available.

7       DR. ZENDLE: But sometimes when research  
8 isn't done, treatments are made available that  
9 actually cause harm.

10       MS. GREENBERGER: I know, but this is  
11 not one of them. And what may happen is that  
12 people will be put on drugs or have surgery, and  
13 they will have more invasive and more problems,  
14 when they could have had a less invasive and an  
15 easier treatment. I'm aware of that, and generally  
16 speaking you're right, but in this case, I think  
17 there is a lot of confusion about separating this  
18 from the traditional therapy and that makes me, I  
19 would hate to see people not being able to use this  
20 because of this decision.

21       DR. ZENDLE: And I wanted to make clear  
22 that I was not voting on a coverage issue. If I  
23 had been, my vote would be different.

24       DR. LANDY: I think there is a big  
25 problem with the question, and what was put forth  
00268

1 to the panel to answer, is what I'm getting from  
2 this discussion, and that people may have addressed  
3 this topic differently.

4       DR. ZENDLE: How would you word the  
5 question differently?

6       DR. LANDY: Well, I think the first set  
7 of questions we got a month ago, the first question



8 was effectiveness of biofeedback in routine  
9 clinical use, just determining effectiveness of  
10 biofeedback as a standalone therapy. And then the  
11 second part of the question was, comparing the  
12 effect of adding biofeedback to PME alone. And  
13 answering that in a two phased question I think  
14 would discern and weed out part of the feelings of  
15 what we're discussing here. And I think it would  
16 give maybe HCFA a little more information to make  
17 their decision with.

18 DR. RATHMELL: Just a comment. I think  
19 that if we were to adopt one question that we could  
20 answer today, it would be exactly what's in the  
21 technology assessment. And it's very clear and  
22 it's better worded. For urinary incontinence  
23 patients, does adding biofeedback to PMEs result in  
24 greater improvement in health outcomes than the use  
25 of PMEs alone? That's very clear. We may not be  
00269

1 able to make that decision, but that's what the  
2 technology assessment does, that's what all of the  
3 discussion today did. The written question is more  
4 nebulous.

5 DR. GARBER: I think the written  
6 question was supposed to be interpreted as  
7 corresponding to what you just read from the  
8 assessment.

9 DR. RATHMELL: I think they were  
10 supposed to be the same thing.

11 DR. GARBER: Yeah. I think the panel's  
12 deliberations, and I hope if any of you who  
13 disagree will correct me now, have worked on that  
14 assumption, that it's a comparison of PME plus  
15 biofeedback to PME alone, not a comparison of PME  
16 plus biofeedback to placebo or something like  
17 that.

18 DR. ZENDLE: Or inadequate PME.

19 DR. GARBER: Right.

20 DR. ZENDLE: Could we clarify the motion  
21 then?

22 DR. LANDY: Can we answer question 2?

23 DR. GARBER: No. The procedure is that  
24 if it's no on 1, we cannot go to 2.

25 Well, if nothing else, I think this

00270

1 illustrates the importance of framing the question

2 very carefully, and this is something that we will  
3 always face, but it's what is the comparison that  
4 we're making? Is it between two treatments, is it  
5 between a treatment and a placebo? What's the  
6 standard of care, what's a relevant question, and  
7 in fact, the questions come from HCFA, they do not  
8 originate with any member of the panel. I'm sure  
9 that HCFA would appreciate our input to make them  
10 reasonable, but since they ultimately will be  
11 making coverage decisions, I assume that the  
12 phrasing of the questions is in part dependent upon  
13 reimbursement issues. So something that we may not  
14 feel is clinically the most important thing might  
15 turn out to have a great deal of relevance to their  
16 reimbursement decisions, so we have to depend upon  
17 -- well, they have to exercise their judgment in  
18 formulating the question and we have to do the best  
19 we can to answer them.

20 DR. HILL: I had a couple closing  
21 remarks since we are at the end here, if I may. I  
22 just wanted to say real briefly what's going to  
23 happen next. As Allen said this morning, this is  
24 not a coverage decision. HCFA has the  
25 responsibility of deciding whether or not this

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1 treatment modality is reasonable and necessary  
2 within the meaning of the statute that Congress has  
3 given us. We hope that this panel will follow the  
4 Executive Committee's recommendations in this  
5 regard and explain its conclusions in writing. In  
6 addition to the opportunity to explain the vote,  
7 statements that any of you care to submit can be  
8 sent in and they will be considered by us in our  
9 decision making about coverage.

10 And so, Miss Smith, if you want to send  
11 that article in at that point, that gets to be  
12 included in our subsequent deliberations, even  
13 though we couldn't allow it to be handed out here.

14 And then there will be a summary of this  
15 that we will try to compose and get Alan to look  
16 at, and that will be part of the record as well,  
17 and that will go the Executive Committee on June  
18 6th, where they will look at it and hopefully  
19 ratify it and pass it on to HCFA, and that will be  
20 the basis of our making a coverage decision on  
21 this.

22           Despite the questions about the  
23 question, despite the disagreements about the  
24 procedure, this has been very helpful to up us and  
25 it will go a long way towards giving us what we  
00272

1    want, which is an evidence based decision about  
2 coverage. Thank you.

3           DR. McBRYDE: Mr. Chairman?

4           DR. GARBER: Yes.

5           DR. McBRYDE: I just want to say, this  
6 question number 2, if the evidence is adequate to  
7 draw conclusions -- it was, wasn't it -- what is  
8 the size -- it doesn't say positive or negative --  
9 if any, to the overall health effect of addition of  
10 biofeedback and so forth. That might be next time  
11 rephrased differently too, because that implies you  
12 should go ahead to number 2 whether it's positive  
13 or negative, as long as you draw a conclusion,  
14 whether it's no or yes.

15          DR. GARBER: That's correct. If you  
16 conclude that the evidence is adequate, you go to  
17 number 2 even if the evidence shows that the  
18 intervention under study is worse than whatever  
19 it's compared to. Number 2, you proceed to  
20 number 2 after you've made a determination of  
21 adequacy.

22          DR. McBRYDE: Did we proceed to  
23 number 2?

24          DR. GARBER: No. We concluded that the  
25 evidence was not adequate to make any conclusion  
00273

1    for or against.

2           DR. McBRYDE: I know I'm confused. I  
3 thought we did conclude that it was --.

4           DR. GARBER: Not adequate.

5           DR. McBRYDE: Well, that's a conclusion.

6           DR. ZENDLE: We did not conclude that  
7 there was evidence that it's not efficacious.

8           DR. McBRYDE: That's not what the  
9 question says. It doesn't say do not go to  
10 number 2 if you vote. Am I crazy? I don't think  
11 so. But at any rate, I think that can be phrased a  
12 little better.

13          MR. COYNE: As I recall, the  
14 presentation by Dr. Simon had a decision tree on it  
15 which may have helped clarify the very

16 understandable question by Dr. McBryde. But I  
17 believe the intent as clarified by the description  
18 was that it, that there not be necessarily a  
19 progression to number 2 if indeed a finding of an  
20 inadequacy was first arrived at in number 1.

21 DR. McBRYDE: So that should be  
22 reflected here too.

23 MR. COYNE: I agree editorially, that's  
24 a very valid point. Thank you.

25 MS. CONRAD: Okay. To conclude today's  
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1 panel meeting, I would like to announce the  
2 proposed schedule for future meetings. The  
3 tentative dates, and I mean tentative, for June,  
4 are 14th and 15th, and secondly, October 17th and  
5 18th, and I emphasize, these dates are subject to  
6 change.

7 For continuing information, you may  
8 visit our web site at <https://www.cms.hhs.gov/mcac/default.asp>.  
9 I would like to ask the panel members to please  
10 linger for a few moments. Perry Bridger and Sue  
11 Gleeson wish to distribute some evaluation forms,  
12 and if you would just take a moment to complete  
13 them, that will make them happy.

14 DR. GARBER: At this point I would  
15 entertain a motion that this meeting be adjourned.

16 DR. EPSTEIN: So moved.

17 DR. MAVES: Second.

18 DR. GARBER: All in favor?

19 MS. CONRAD: Thank you very much.  
20 (The meeting adjourned at 4:30 p.m.)

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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

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HEALTH CARE FINANCING ADMINISTRATION

Medicare Coverage Advisory Committee

Medical and Surgical Procedures Panel

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April 13, 2000

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Baltimore Convention Center

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Baltimore, Maryland

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Panelists

2

Chairperson

Alan M. Garber, MD, PhD

3

Vice-Chairperson

4

Michael D. Maves, MD, MBA

5

Voting Members

Angus M. McBryde, MD, FACS

6

H. Logan Holtgrewe, MD, FACS

Kenneth P. Brin, MD, PhD

7

Les J. Zendle, MD

Bruce Sigsbee, MD (Not present)

8

Linda D. Bradley, MD

9 James P. Rathmell, MD  
 Arnold M. Epstein, MD  
 10 Temporary Voting Member  
 Lisa Landy, MD  
 11  
 Consumer Representative  
 12 Phyllis E. Greenberger, MSW  
 13 Industry Representative  
 Marshall S. Stanton, M.D.  
 14  
 Non-Voting Guests  
 15 Michael Risager, MD  
 Diane Smith, RN  
 16  
 Acting Director, Coverage and Analysis Group, HCFA  
 17 Hugh F. Hill, MD, JD  
 18 Executive Secretary  
 Constance A. Conrad, RN

19  
 20  
 21  
 22  
 23  
 24  
 25  
 00003

1		TABLE OF CONTENTS	
		Page	
2	Welcome and Conflict of Interest Statement		
	Constance A. Conrad, RN		4
3	Presentation of Questions		
4	Perry Bridger, HCFA		6
5	Open Panel Discussion		11
6	Open Public Comments & Scheduled Commentaries		
	Margaret Degler, MSN, CRNP, CUNP		40
7	Peter Sand, MD	45	
	Kristine Whitmore, MD	55	
8	Karl Luber, MD	58	
	Joseph Antoci, MD	64	
9	Deborah Jensen	67	
	Francie Bernier, RNC, BSN	74	
10	Nicolette Horbach, MD	83	
	Julie Pauls, PT, PhD	90	
11	Mikel Gray, PhD, CUNP, FAAN		96
	Alfred Bent, MD	104	

12	John Perry, PhD	110
	Roger Dmochowski, MD	144
13	HCFA Presentation	
14	John Whyte, MD. MPH	119, 143
15	Technology Evaluation Center Assessment - Blue Cross/Blue Shield	
16	Frank V. Lefevre, MD	123
17	Open Committee Deliberation	150
18	Open Public Comments	174
19	Open Committee Deliberation	196
20	Final Panel Recommendations	201
21	Next Steps	
	Hugh F. Hill, III, MD, JD	212
22	Closing Remarks	
23	Constance A. Conrad, RN	214
24	Adjournment	274

25  
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1           P R O C E E D I N G S.  
2           MS. CONRAD: We have a quorum, we are  
3 going to begin. Good morning, panel chairperson,  
4 members, temporary voting members. I am Connie  
5 Conrad, executive secretary of the Medical and  
6 Surgical Procedures Panel of the Medicare Coverage  
7 Advisory Committee. The panel is here today to  
8 provide advice and recommendations to the Agency  
9 regarding pelvic floor electrical stimulation for  
10 the treatment of nonneurogenic urinary incontinence  
11 in adults. At the conclusion of today's session,  
12 panel members will be asked to vote on a series of  
13 questions. The answers to those questions will  
14 constitute this panel's recommendation, which will  
15 be submitted to the Executive Committee when it  
16 meets on June 6th. When the Executive Committee  
17 ratifies the recommendation, it will officially  
18 transmit that recommendation to HCFA. HCFA will  
19 develop a coverage policy within 60 days of receipt  
20 of that recommendation.  
21           For the purposes of today's panel,  
22 Dr. Lisa Landy, standing member of the Durable  
23 Medical Equipment Panel and noted expert in the  
24 field of urinary incontinence received an  
25 appointment to temporary voting status.

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1 Dr. Landy's expertise will enhance this panel's  
2 deliberative process.

3 In addition, we welcome Dr. Michael  
4 Risager, carrier medical director for Trailblazers  
5 Health Enterprises in the state of Maryland, and we  
6 welcome Diane Smith, a urotechnology consultant and  
7 continence specialist, as nonvoting guests.

8 The following announcement addresses  
9 conflict of interest issues associated with this  
10 meeting, and is made part of the record to preclude  
11 even the appearance of impropriety. To determine  
12 if any conflict existed, the Agency reviewed the  
13 submitted agenda and all financial interests  
14 reported by the panel participants. The conflict  
15 of interest statutes prohibit special government  
16 employees from participating in matters that could  
17 affect their or their employers' financial  
18 interests. The Agency has determined that all  
19 members and consultants may participate in the  
20 matters before the panel today.

21 With respect to all other participants,  
22 we ask in the interest of fairness that all persons  
23 making statements or presentations disclose any  
24 current or previous financial involvement with any  
25 firm whose products or services they may wish to  
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1 comment on.

2 Okay. Let's start with presentation of  
3 questions by Perry Bridger, analyst with the  
4 coverage and analysis group.

5 MR. BRIDGER: Good morning. Thank you,  
6 and I apologize to those of you who were here  
7 yesterday and heard similar remarks. As many of  
8 you are well aware, urinary incontinence is a  
9 significant health problem for the Medicare  
10 populations. For example, the prevalence of  
11 urinary incontinence in the above age 65 Medicare  
12 population is estimated to be near 35 percent for  
13 females and 20 percent for males, with rates even  
14 higher in hospitalized older adults and those in  
15 long-term care institutions. Urinary incontinence  
16 affects individuals' quality of life and often  
17 leads to other comorbidities, isolation and  
18 depression. Frequently, patients do not report  
19 this problem to their families, caregivers and  
20 health professionals, and urinary incontinence has



21 remained an under reported and under studied  
22 condition.

23 In the following two slides I have  
24 outlined for you several of the treatments which  
25 exist for the management of urinary incontinence.

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1 These include behavioral interventions, pelvic  
2 floor electrical stimulation, pharmacologic  
3 therapy, bulking agents, sacral nerve stimulation,  
4 and surgery. In general, which treatment options  
5 to pursue for the different types of urinary  
6 incontinence is dependent on specific patient  
7 indications, comorbid states, cognitive function,  
8 and the willingness and ability to participate in  
9 treatment.

10 During this two-day panel meeting the  
11 Medical and Surgery Procedures Panel of the  
12 Medicare Coverage Advisory Committee will review  
13 the evidence and make recommendations to HCFA about  
14 two of these treatment modalities, biofeedback and  
15 pelvic floor electrical stimulation. Yesterday the  
16 panel heard testimony and reviewed the scientific  
17 evidence about biofeedback and today the panel will  
18 hear testimony and review the scientific evidence  
19 regarding the use of pelvic floor electrical  
20 stimulation. Currently, pelvic floor electrical  
21 stimulation therapy is not paid for by the Medicare  
22 program.

23 For the purposes of this meeting, pelvic  
24 floor electrical stimulation is defined as the use  
25 of a nonimplantable electrical device that delivers

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1 variable rates of current through the pelvic floor  
2 with the intent of strengthening pelvic floor  
3 musculature.

4 The panel has had the opportunity to  
5 read the technology assessments, evidence tables  
6 and other materials related to pelvic floor  
7 electrical stimulation. After hearing the public's  
8 comments and scheduled commentary presented here  
9 today, the panel will be asked to vote on a  
10 sequence of questions regarding this therapy. All  
11 of these questions are directly related to the  
12 scientific evidence regarding pelvic floor  
13 electrical stimulation therapy, and comments made  
14 today should be directly relevant to this topic.

15 Dr. John Whyte, during the HCFA  
16 presentation, will more fully address these  
17 questions, the points to consider, and the  
18 categories of effectiveness. We will now briefly  
19 outline these for you. In response to yesterday's  
20 comments regarding these questions, we have  
21 clarified question 1 to make it more precise.  
22 Connie has a copy of these questions, which she  
23 will distribute to the panel, and we will provide  
24 to the public at the end of my comments copies as  
25 well.

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1 The first question we are asking the  
2 panel to discuss for pelvic floor electrical  
3 stimulation therapy is the following: Is the  
4 scientific evidence adequate to draw conclusions  
5 about the effectiveness of pelvic floor electrical  
6 stimulation compared to placebo, pelvic floor  
7 electrical stimulation compared to PME's or  
8 alternative nonsurgical techniques, PME's and pelvic  
9 floor electrical stimulation compared to PME alone,  
10 in the Medicare populations for the following three  
11 indications: Stress incontinence, urge  
12 incontinence, and post-prostatectomy incontinence.

13 In answering this question, the panel  
14 should consider the following points: The adequacy  
15 of the individual study design, the consistency of  
16 results across studies, their applicability to the  
17 Medicare population, and their applicability beyond  
18 the research setting.

19 If the evidence is adequate to draw  
20 conclusions about pelvic floor electrical  
21 stimulation in these cases and the panel votes  
22 affirmatively on question 1, the panel will move on  
23 to questions 2, 3 and 4, which address the size and  
24 direction of effectiveness. Therefore, question 2  
25 asks: If the evidence is adequate to draw

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1 conclusions, what is the size, if any, of the  
2 overall health effects of pelvic floor electrical  
3 stimulation compared to placebo for the treatment  
4 of urinary incontinence?

5 When answering this question, as well as  
6 questions 3 and 4, the panel will be asked to place  
7 the size and direction of effectiveness into one of  
8 the following seven categories: Breakthrough

9 technology, more effective, as effective but with  
10 advantages, as effective with no advantages, less  
11 effective but with advantages, less effective with  
12 no advantage, and not effective.

13 Keeping in mind these categories,  
14 question 3 asks: If the evidence is adequate to  
15 draw conclusions, what is the size, if any, of the  
16 overall health effects of pelvic floor electrical  
17 stimulation compared to PME's or alternative  
18 nonsurgical techniques for the treatment of urinary  
19 incontinence?

20 And finally, question 4: If the  
21 evidence is adequate to draw conclusions, what is  
22 the size, if any, of the overall health effects of  
23 the addition of pelvic floor electrical stimulation  
24 to PME's, compared to PME's alone. Please remember  
25 that Dr. Whyte will elaborate on those points more

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1 fully during the HCFA presentation, and you will  
2 have the opportunity as well to discuss them during  
3 your deliberations.

4 We thank the panel members and all of  
5 you who have made efforts to participate in this  
6 panel meeting regarding biofeedback and pelvic  
7 floor electrical stimulation. We look forward to  
8 your deliberations.

9 MS. CONRAD: Thank you, Perry.

10 DR. STANTON: Alan?

11 DR. GARBER: Yes, Marshall?

12 DR. STANTON: Yes. Before we head into  
13 the discussions for today, I think there's a couple  
14 points that are very relevant that need to be  
15 discussed. When I was reflecting on yesterday's  
16 deliberations, I think there were a lot of  
17 excellent points that were made regarding the  
18 burden of proof for conclusive scientific evidence  
19 and comparing that with the evidence that's  
20 necessary for pointing towards possible improved  
21 outcomes for beneficiaries. I think Dr. Epstein's  
22 points, vis a vis, P equals .05 versus P equals .5  
23 were particularly poignant on that regard. In  
24 clinical practice, our treatment decisions for  
25 patients are made by physicians based on his or her

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1 assessment of the literature and not on a  
2 meta-analysis that requires achieving a P value of

3 less than .05. If the latter were the case, then I  
4 think that few treatment decisions would be  
5 instituted in clinical practice today.

6         At the conclusion of yesterday's  
7 session, Hugh Hill made some points thanking the  
8 panel for assisting in an evidence based process  
9 for coverage decision making. These are not his  
10 exact words but it certainly was the tone and the  
11 point that I took away from his comments. All of  
12 this for me raises a lot of concern regarding the  
13 weight that this panel's vote is going to play in  
14 the coverage decision making process and I think  
15 again, as I said yesterday, we should not be so  
16 naive as to think that this vote will not play a  
17 major role in that decision process.

18         The process as it is presently designed  
19 ignores expert testimony, it ignores public  
20 comment, and it ignores the views of the panel's  
21 consumer representative. And I asked myself why  
22 they should even bother presenting their views.  
23 HCFA has convened this panel of experts here who  
24 have invested much of their own time and yet the  
25 questions that are posed leaves the panel too

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1 constrained to be of any practical use. As a  
2 nonvoting member, I sensed the obvious discomfort  
3 of panel members yesterday in being forced to vote  
4 one way on a specific question while stating their  
5 opposite true beliefs about the therapy that was  
6 discussed.

7         If this new high standard of multiple  
8 randomized control trials all having to have the  
9 same positive outcome is to be the bar against  
10 which all new therapies must clear to obtain  
11 coverage, then I fear there are going to be dire  
12 consequences. A national noncoverage decision  
13 means that no Medicare patient can get the  
14 therapy. There is no room for patient appeal.  
15 Future clinical trials of that therapy are going to  
16 be very unlikely in that scenario. This will  
17 stifle the development of new technologies, and I  
18 think it's worthwhile for the panel to note that  
19 new technologies that come to the market won't be  
20 ready for this type of assessment for many years  
21 after they achieve regulatory approval.

22         I see ourselves going down the same road

23 today and that we went down yesterday, and I have a  
24 lot of concerns about that.

25 DR. GARBER: Okay. Thank you. It's a  
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1 little bit off the agenda, but I don't think we  
2 have a better place to put it, so with the  
3 indulgence of the panel I would like to set aside a  
4 little time if other panelists would like to  
5 comment. Yes, Linda.

6 DR. BRADLEY: I am very happy that  
7 Dr. Stanton had these comments over dinner, and  
8 just thinking about this whole process yesterday, I  
9 left extremely frustrated. I understand that the  
10 Executive Committee needs to set standards, but I  
11 think either the bar is so high or if you're doing  
12 the limbo, it's so low that you just cannot get  
13 under in order to make a decision to move forward.

14 And I think I have the same feelings.  
15 I'm not sure why we have all these people convening  
16 here if their testimony both from patients,  
17 patients' letters, practicing physicians in the  
18 specialty, people who have spent collectively  
19 centuries of personal time studying this, and we  
20 really are not able to include their personal  
21 expertise because of the lack of potential  
22 scientific rigor, I think the hurdle is extremely  
23 high, and I just am so glad that these comments, I  
24 couldn't have said it anymore eloquently. But I  
25 also hope that we don't leave today with the same  
00015

1 spirit that we left with yesterday. And I would  
2 love comments from others that we haven't talked  
3 with directly. This is a very frustrating problem.

4 DR. GARBER: Les?

5 DR. ZENDLE: If our job had been  
6 different, if we had been asked to make  
7 recommendations on a coverage decision, I think we  
8 would have done it differently, and I think the  
9 comments from the public and the professional  
10 organizations and the clinical experts would have  
11 been quite relevant. I guess because I have been  
12 involved in looking at evidence purely from the  
13 scientific point of view in reaching a conclusion,  
14 and then taking that to decide how you're going to  
15 implement that in the real world, that I can  
16 separate the two.

17 I think that it's not unreasonable to  
18 decide to cover something even if there isn't  
19 scientific evidence, or evidence to a scientific  
20 level that it is more effective than other things.  
21 But in that case, you have to give some other  
22 reason to cover it. And what I don't want to see  
23 happen is to have things covered because somebody  
24 says there is scientific level of evidence and not  
25 say the real reason why it might be covered,

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1 whether it's a more efficient way of doing it, or  
2 it's the standard of practice, those are all valid  
3 reasons to cover something. But personally, I like  
4 separating what is a purely scientific rationale  
5 from other reasons to cover something.

6 If HCFA, and I guess HCFA is acting  
7 under what it perceives were the congressional  
8 instructions were, if they decide they want to  
9 change what we do to make recommendations on  
10 coverage, then I can do that and I would be happy  
11 to do it, and I would have reached a different  
12 conclusion yesterday. So, I think we do have to  
13 get some -- maybe HCFA and Congress and whatever,  
14 have to take another look at this to decide what  
15 the best way to do this is. But I didn't have any  
16 problem with yesterday just looking at the  
17 scientific question and reaching a conclusion. I  
18 agree though, that if I thought that was going to  
19 be, without any kind of other input, the coverage  
20 decision, I would be uncomfortable too.

21 DR. GARBER: Hugh?

22 DR. HILL: Thanks. A couple of  
23 responses. While I appreciate the comments and do  
24 acknowledge that they are about coverage and not  
25 necessarily about specific evidence on a specific

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1 case, I do appreciate hearing them. Let me assert  
2 to you that we have not ignored expert opinion,  
3 public opinion, consumer opinion, that those were  
4 all taken into account in the design of the  
5 process, that industry and other stakeholders  
6 wanted us to go to an evidentiary basis, an open  
7 transparent process for scientific evidence as the  
8 basis for making coverage decisions, and this is a  
9 part of that. And I hope that the panel did not  
10 ignore the presentations of experts, the public and

11 consumers yesterday.

12       If by not acceding to or agreeing with  
13 them we are regarded as having ignored them, that  
14 seems a bit extreme. I hope we took them into  
15 account. And I didn't hear us asking about whether  
16 or not the technology had met the bar of a national  
17 randomized trial, and we certainly don't intend to  
18 stifle new technologies. But on a hierarchy of  
19 evidence we hope that there's some agreement, and  
20 there has been in the design of the process, that  
21 some sorts of studies are more reliable and the  
22 results of those studies are more predictably  
23 reproducible than other studies. And hopefully, we  
24 can use that hierarchy of evidence and the  
25 suggestions of the Executive Committee to try to

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1 make rational decisions about what we should cover  
2 and we shouldn't. And that's why we focus on  
3 evidence and your comments about the evidence.

4       We haven't set the hurdle extremely  
5 high. I disagree with that specifically and  
6 emphatically. We wanted to hear about it and we  
7 did hear about comments about other evidence, and  
8 all sorts of things that might be regarded as  
9 evidence by some people and not by others were  
10 available to you. If you think that the apocryphal  
11 story or the odd case report, or the letters to the  
12 editors in the journals are evidence and you want  
13 to decide on that basis, we want to hear about  
14 that. And as you noticed yesterday, we wanted to  
15 know what's behind your vote, the thinking behind  
16 your vote.

17       I'm sorry you're frustrated with  
18 voting. We think we need that for clarity, but we  
19 always want to know the thinking behind it, and we  
20 hope you felt like you had adequate opportunity to  
21 express your reasoning.

22       DR. GARBER: Maybe I could just add a  
23 brief comment on two points. The first is, the  
24 comments of the public speakers, and as I said  
25 yesterday, I was personally very grateful to the

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1 public speakers, because I think that the  
2 presentations of the public speakers by in large  
3 really did address the questions the panel was  
4 posed, and although I didn't ask the panelists if

5 they were influenced by the public speakers, I got  
6 the very clear sense that the panelists took those  
7 comments very critically, and the fact that the  
8 panelists did not vote the way that some of the  
9 public speakers might have wanted them to vote  
10 should not be construed as meaning that the panel  
11 ignored their comments. I personally found the  
12 comments very helpful and it doesn't, the fact that  
13 one votes the other way doesn't make that testimony  
14 worthless or in any sense less valuable. I think  
15 that was a very important part of yesterday's  
16 process, whatever the outcome of the voting was.  
17 And I hope that we continue to have public  
18 commentary of this high quality and I would suspect  
19 that in many cases it will turn out to be  
20 decisive. So I was not, did not have the sense  
21 that that was just an exercise that we went  
22 through; I thought it was extremely valuable to our  
23 deliberations.

24         The other point that Marshall raised,  
25 which I would like to say a word about on behalf of  
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1 the Executive Committee, is about the standard of  
2 evidence and in clinical practice what the standard  
3 of practice is. We are not making coverage  
4 decisions but as you correctly pointed out, we as a  
5 panel are making recommendations that will be an  
6 important part of coverage considerations. And by  
7 widespread practice, the level of evidence that is  
8 used to make coverage decisions is entirely  
9 different from what is used in the clinical  
10 setting, in the doctor to patient relationship,  
11 because in the doctor-patient one-on-one setting,  
12 all kinds of individual factors come into play,  
13 things the physician, the patient know that aren't  
14 fully reflected in the literature, and we make our  
15 best guess every day about what's the best  
16 treatment, and here making the best guess is  
17 absolutely appropriate.

18         Now I'm not going to comment on how HCFA  
19 should make coverage decisions. I don't really  
20 know the answer to that, but what I do know is that  
21 when it comes to coverage, you use a different  
22 standard of evidence. That is what is done around  
23 the world, it's what is done by different  
24 organizations in the US. A coverage decision is



25 not the same thing as a one-on-one patient-doctor  
00021

1 treatment decision. They are clearly related since  
2 coverage is a way to enable the doctor to apply a  
3 treatment and have it covered by insurance, but the  
4 standard of evidence by standard of practice is  
5 different. And that is something that the  
6 Executive Committee unanimously agreed to as a  
7 concept.

8 Now, it is entirely possible that the  
9 panel set the bar too high for the evidence  
10 standards yesterday. HCFA and the Executive  
11 Committee did not say specifically what kinds of  
12 studies would be needed because they expected the  
13 panels to come to a conclusion in each context and  
14 you did reach a conclusion yesterday rightly or  
15 wrongly, and there was a strong majority on these  
16 questions.

17 Now, that doesn't mean that you have to  
18 use the same standard in every case. As I said  
19 yesterday, we're feeling our way through this  
20 process. But I don't think that it would be  
21 appropriate, at least from the Executive  
22 Committee's point of view, to say the best guess  
23 should be the standard of evidence, that is, what  
24 we happen to think is best regardless of the  
25 quality of the evidence. That's why such a big  
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1 point was made about evaluating adequacy of  
2 evidence. Jim?

3 DR. RATHMELL: I guess this would be a  
4 segue into today's topic. My discomfort is very  
5 very specific. Yesterday we considered a  
6 technology called biofeedback and we were posed a  
7 very narrow question comparing one type of control  
8 versus the technology itself. And today we are  
9 considering a different technology, the electrical  
10 stimulation and yet, we're looking at the efficacy  
11 versus many different controls. I feel as though  
12 we were steered into a very narrow decision, where  
13 there was much more information about that  
14 technology available, and if we were really  
15 supposed to look at the scientific evidence about  
16 that technology, we should have looked at  
17 everything that was available. Very similar to  
18 what we're doing today, versus placebo, versus

19 other types of controls.

20           There's much more information about  
21 biofeedback that we ignored, to the point where  
22 when we were asked a question, the question was so  
23 narrow that the majority of the testimony that we  
24 heard, and the allusions or the references to a  
25 body of literature that wasn't in the technology  
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1 assessment, we had to ignore. But I was left to  
2 vote opposite my feeling about the technology  
3 without really knowing the scientific evidence, and  
4 this is a scientific panel, and I really would have  
5 liked to have access to all of the scientific  
6 evidence about that technology.

7           DR. GARBER: Hugh.

8           DR. HILL: Thank you, Dr. Rathmell. We,  
9 as you pointed out, we're learning in this process,  
10 and this is the third meeting of a Medicare  
11 coverage advisory panel, and the first one of this  
12 panel. And one of the discussions that we had  
13 internally was how specific to be. We acknowledged  
14 and intended yesterday's question to be very  
15 specific. And we've learned in the first couple of  
16 panels that if we are not very specific about  
17 questions, if it's vague or if we're just sort of  
18 going to have a discussion about a technology, the  
19 information we get back may not be as useful to us  
20 in a scientific sense. So, would you extend your  
21 remarks and comment a little further about how you  
22 would strike that balance?

23           DR. RATHMELL: Well, let's just be very  
24 specific. Can you address why today we have three  
25 questions posed about a technology versus other  
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1 control groups, and yesterday we were posed only  
2 the third question, which is the additional benefit  
3 of adding that to PMEs? This is very specific  
4 about this. Why do today's questions differ so  
5 much from yesterday's questions, and why were the  
6 first two components of the question posed today  
7 left out of yesterday's question and technology  
8 assessment?

9           DR. HILL: In some cases the answer to  
10 that will be historical, because of the way the  
11 requests have come in or the questions have  
12 developed. Sometimes the questions will grow

13 nationally out of our own review of the evidence  
14 and what we think can be usefully asked. But in  
15 this case, perhaps we can, if you don't mind me  
16 asking the analysts who were involved in this, to  
17 comment on why there is a difference. John, is  
18 that appropriate.

19 DR. WHYTE: It's a very reasonable  
20 question. On the issue of biofeedback, we made the  
21 decision to view biofeedback purely as an  
22 adjunctive therapy, so in that context we would  
23 have to look at PME and biofeedback compared to PME  
24 alone. That was not the same assessment that you  
25 will hear about today.

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1 One question did deal with pelvic floor  
2 electrical stimulation as adjunctive therapy, but  
3 based on many of the requests that we received as  
4 well as data we had looked at, there was also an  
5 understanding that pelvic floor electrical  
6 stimulation could be used as a primary therapy and  
7 not as adjunctive. So given that, we then had to  
8 look compared to placebo, and compared to other  
9 therapies, nonsurgical therapies. But that was not  
10 the case in terms of how we interpreted the use of  
11 biofeedback. I hope that answers your question.

12 DR. RATHMELL: It does, except that we  
13 heard extensive testimony yesterday about how  
14 biofeedback was inextricable from the way that PMEs  
15 are practiced in this day and age, and so I was  
16 left with the feeling that an artificial  
17 distinction had been drawn that couldn't be drawn.  
18 It's impossible. There's a continuum between PMEs  
19 where a pamphlet or videotape is given to the  
20 patient and no further instruction or interaction  
21 with the patient, and an electronic device at the  
22 other even of the spectrum, that is hooked up to  
23 the musculature, and there is extensive interaction  
24 with the patient. So there is a continuum and yet,  
25 we tried to make some distinction that's impossible

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1 to make from the daily practice in this day and  
2 age. And from the literature alone, it was  
3 impossible to make either way, but yet we made it  
4 yesterday, and were forced on a decision that had  
5 an artificial boundary.

6 DR. GARBER: Michael Risager?

7 DR. RISAGER: I need to differ from the  
8 previous speaker. I believe we had ample  
9 literature and ample resources. One thing that  
10 struck me after yesterday was the, here's something  
11 that appears to have a place. It's amazing how  
12 with 13 million people with stress incontinence who  
13 have been treated for years with some form of  
14 biofeedback, whatever you use to monitor, to assess  
15 the, to develop the musculature, why there have not  
16 been better studies. It amazes me. So I think we,  
17 I feel we did the right thing to have a clear and  
18 precise objective. I would with respect, suggest  
19 that we go on, and rather than compare and agonize  
20 about the today's, yesterday's proceedings compared  
21 to today, let's go on and do today what we have to  
22 do, and then learn from that. In short, I think we  
23 did the best we could yesterday.

24 DR. GARBER: Ken?

25 DR. BRIN: I share a lot of the

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1 discomfort that has already been raised, but I also  
2 recognize that this is a new process and that we're  
3 blazing new grounds. I think a lot of my level of  
4 discomfort will be assuaged when I see what the end  
5 result ends up being. We were asked a very very  
6 specific focused question. I believe we answered  
7 appropriately, given the question we were asked.  
8 The question then arises, how that will be used by  
9 HCFA to determine coverage? If it's used with all  
10 of the comments that have been made, such as the  
11 fact that the baseline comparison is giving  
12 biofeedback as part of the standard of care, and  
13 that's factored in there, I think we will be very  
14 comfortable that our advice was used  
15 appropriately. If in fact the outcome is  
16 different, there will be some concerns. And I  
17 think we should just move on and then watch what  
18 the end result of the process is, because it's a  
19 new process.

20 In my own area of cardiovascular  
21 disease, stenting is an adjunct to coronary  
22 angioplasty. For certain lesions, there's never  
23 been and there never will be a good double blind,  
24 or certainly not double blind, but randomized study  
25 of stenting and nonstenting, because it's standard

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1 of care. And if a panel were convened to take a  
2 look at stinting as an adjunct, it probably would  
3 have to make a very similar decision, because the  
4 studies haven't been done and won't be done. And  
5 if the outcome of that were, well, stinting won't  
6 be covered, that would be a different issue. I  
7 think we need to see what the end result of our  
8 deliberations and advice is, as passed on by the  
9 Executive Committee, and as coverage decisions are  
10 made by HCFA.

11 DR. GARBER: Thank you. Arnie?

12 DR. EPSTEIN: I think I can articulate  
13 with some difficulty, but I think I can do it  
14 profitably, what makes the discomfort level of some  
15 of the individuals so high, and set that in relief  
16 for people from HCFA to consider. I'm going to  
17 flip for a moment into the coverage decision. I  
18 could imagine many, but at least two ways that  
19 people might think about coverage decisions. One  
20 is, we're only going to cover procedures where  
21 there is clear scientific evidence indicating the  
22 procedure's effective or efficacious, you'd like  
23 both.

24 The second runs orthogonal to that. It  
25 says, in the face of broad consensus from medical  
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1 experts that a procedure is effective, we will  
2 cover it absent evidence that it's not effective,  
3 so long as the clinical downsides are minimal.

4 We have -- I can think of both of those  
5 approaches being a reasonable approach for  
6 coverage. What makes everybody uncomfortable is  
7 that the scientific question that we've been asked  
8 is designed to lead to the former approach as  
9 opposed to the latter approach. We could have been  
10 asked two questions: Is the scientific evidence  
11 adequate to show that the procedure works? Answer,  
12 no. Is the scientific evidence adequate to show  
13 the procedure doesn't work? Answer, no. We didn't  
14 get asked the latter question, which makes  
15 everybody worry that when we get to the coverage  
16 decision, we're going to take method A and as  
17 opposed to method B, and I think that's what the  
18 discomfort level is all about.

19 MS. GREENBERGER: I think -- I would be  
20 astounded if the coverage decision went the other

21 way. It would be historical precedent frankly, if  
22 we came out with the results that we did yesterday  
23 and that HCFA decided to cover this. So I think  
24 what you're saying is correct, but we're left with  
25 the decision that we made yesterday.

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1 I also think that perhaps we should ask  
2 why there aren't, why there haven't been clinical  
3 trials. And I heard a lot of good reasons  
4 yesterday that people told me that haven't come  
5 out, that perhaps they would like to share, if  
6 they're able to. And I think this is going to be  
7 the case. Dr. Stanton said there are a lot of new  
8 tests, diagnostics and therapies unfortunately,  
9 that cannot be, that nobody can afford to do mass  
10 clinical trials. And I understand that we need to  
11 have the scientific evidence; we can't do a  
12 procedure or have a diagnostic that we don't know  
13 for sure that it works.

14 But this particular one we're  
15 discussing, and certainly the one yesterday, I  
16 mean, this is not something that's going to be  
17 dangerous. And clearly, I think the clinical  
18 evidence has shown, and still we have confusion  
19 over other whether we're even asking the right  
20 question. If this is standard practice, then it's  
21 being used anyway. So I think the question -- I  
22 mean, I don't know what the procedure is now at  
23 this point, but I just think that the way we  
24 answered this question is going to ultimately  
25 result in a noncoverage decision, and I think that

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1 for all these people out there that have been  
2 covered by this or have been treated in this  
3 manner, not to be covered now I think is  
4 outrageous.

5 I also think that we're changing the  
6 question. My understanding, and correct me if I'm  
7 wrong, that the question today was changed again.  
8 I was told by some people in the audience that it  
9 was changed again. The testimony from the public  
10 is given to us now so that we don't have time to  
11 read it. And I'm just very uncomfortable with the  
12 whole process. I think this committee took  
13 indicate years from congressional mandate to  
14 actuality, and you would think that we could do a

15 better job than taking so many years to put this  
16 together.

17 DR. HILL: Your comments are reinforcing  
18 our perception of the importance of the questions,  
19 the critical nature, the central nature of the  
20 questions that we ask you, and I hope that you will  
21 give us your thoughts after this, and we will pass  
22 them on to the Executive Committee and they will  
23 form a part of our discussions about how we modify  
24 this process as we go along.

25 MS. GREENBERGER: We would like to write  
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1 a letter, some of us, to the Executive Committee,  
2 if we may.

3 DR. GARBER: Diane?

4 MS. SMITH: I just would like to say, I  
5 think the problem really was the question, and I  
6 think that was because of the misunderstanding of  
7 those posing the question, and I think that that is  
8 a central issue to why almost every person who  
9 voted no then said, but if I had to made a coverage  
10 decision, I'd say yes. And that's because, if the  
11 question had been, if biofeedback has efficacious  
12 applicability in doing pelvic muscle reeducation,  
13 does it? You would have several studies that were  
14 thrown out that would have shown that compared to a  
15 waiting list or a placebo effect, overwhelming it  
16 has efficacious evidence, significant efficacious  
17 evidence, better than some other continence  
18 therapies that are routinely reimbursed.

19 So I think that is really a very valid  
20 point and should really be considered by HCFA when  
21 they are making their coverage decision, that the  
22 question was narrow enough to achieve a no, because  
23 the evidence simply was not there because the  
24 people doing that research never even assumed that  
25 you would ask that kind of a question, because the  
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1 common practice is to think of using biofeedback to  
2 teach pelvic muscle reeducation. That is in all of  
3 the professional literature, urology, nursing,  
4 gynecology, physical therapy, and this is very  
5 important.

6 Even Dr. Garber said, I don't have a  
7 vote, but I want to make a statement about  
8 coverage. He said, I think that there is evidence

9 for coverage. And I think that's very important,  
10 and should be part of what people are considering  
11 when they are making this decision. And I think  
12 that it's unfortunate that biofeedback was the  
13 first therapy to be looked at in this manner,  
14 because it actually isn't new technology which  
15 would -- there are examples in urology which is new  
16 technology, which there is some clear scientific  
17 evidence perhaps, that could have given the panel a  
18 level of comfort, you know, to play around with  
19 appropriate questions. Biofeedback, because it's  
20 been around for so long and because it has become a  
21 standard of care, it's just inherently difficult to  
22 make that type of a question stick.

23 So I was uncomfortable also, but I  
24 really wasn't depressed. Of course, if you know  
25 me, you know that I never get depressed. And the  
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1 reason was because every no was punctuated with a  
2 yes, in my mind. Every no was punctuated with a  
3 yes for coverage, because they said clearly as a  
4 physician today, I am voting no because of the  
5 question. If I had to tell you if I wanted my  
6 patient to have this, I would say yes. And that's  
7 what I heard.

8 DR. GARBER: Before I recognize Les,  
9 Diane, I do want to correct a statement you made,  
10 or else a statement I made and didn't mean. I  
11 don't believe I ever expressed an opinion about  
12 coverage. But what I did express an opinion about  
13 was that I hoped very much that HCFA would include  
14 other information such as the public testimony in  
15 making their coverage decision. And if you ever  
16 hear me making a recommendation about coverage from  
17 the chair, consider me to have a ministroke, and  
18 strike it from the record.

19 MS. SMITH: Really, to me of course, it  
20 seemed like a very positive statement.

21 DR. EPSTEIN: Give some balance to the  
22 record.

23 DR. GARBER: Thank you. Les.

24 DR. ZENDLE: I think if we had been  
25 asked to make some decisions about coverage, then  
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1 there would have been some other questions that we  
2 might have wanted to go into, like for example, how



3 much biofeedback is needed. Because don't forget,  
4 when HCFA is going to decide whether it's going to  
5 cover something, it means that they're going to pay  
6 somebody to do something. Now, if something that  
7 costs \$50 is as efficacious as something that costs  
8 \$10,000 dollars, I hope that HCFA won't use our tax  
9 dollars to pay for the \$10,000 thing. That's a  
10 different question, which would require lots of  
11 different kinds of information. So I guess that's  
12 why I was comfortable yesterday with not having to  
13 address the coverage issue.

14 I would hope that when HCFA does address  
15 the coverage issue, they are going to have to look  
16 at some of those other things and take that into  
17 consideration. I don't personally know how they  
18 will do it, but I guess I'm okay with the fact that  
19 they didn't ask us to do that.

20 MS. GREENBERGER: Let me ask a  
21 question. What are we doing here? If this is, the  
22 decision that we came to yesterday, are they going  
23 to look at it and say, well, they didn't think  
24 there was enough scientific evidence to prove that  
25 it was efficacious, but we're going to cover it

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1 anyway?

2 DR. ZENDLE: Yeah. They do it all the  
3 time, and other insurers do it too.

4 MS. GREENBERGER: I find that hard to  
5 believe.

6 DR. GARBER: Let me just make a comment  
7 about this. There were extensive discussions about  
8 the role of this panel. We don't know all the  
9 details about how Medicare is going to make  
10 coverage decisions and as I mentioned yesterday,  
11 they are formulating their set of rules. So I  
12 assume this is a work in progress from their point  
13 of view as well, and I hope you will comment on  
14 that. But they are asking for very specific kind  
15 of information from us, and the fact that they said  
16 that this panel will not make coverage decisions  
17 indicate they want a particular kind of evaluation  
18 from us. And since we are not making coverage  
19 decisions, it would seem it's incumbent on them to  
20 include other kinds of information in their  
21 decisions.

22 And again, if they happen to make a

23 coverage decision when we say as a panel that the  
24 evidence was inadequate, that doesn't mean that we  
25 were ignored. It's just that the information we

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1 provide is one component of their decision making  
2 about coverage, it may or may not be decisive. We  
3 don't have experience with this process to be able  
4 to say anything about how it will be used, it will  
5 be a guess at this point. But the fact that the  
6 coverage decisions might not go the way one would  
7 predict on the basis of the panel deliberations,  
8 does not mean that the panel's deliberations were  
9 pointless.

10 MS. GREENBERGER: But if you flip it --  
11 I mean, let's say it was an invasive procedure that  
12 could have some danger attached to it, and the  
13 committee decided based on the research that this  
14 was not efficacious and could have possible  
15 negative results, you wouldn't expect HCFA to cover  
16 it then, would you? I mean, how do you make the  
17 distinction between a decision based on everything  
18 that we have said here today and how they're going  
19 to get that information, and a decision based on  
20 something that we really think is not a good idea  
21 to cover? So I don't understand how it's going to  
22 be translated.

23 DR. GARBER: Well, let me just give you  
24 an example based on other organizations that do  
25 similar kinds of analyses. It may be that the

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1 literature is not clear on just routine reading;  
2 until a study is done, we can't be sure whether the  
3 evidence is adequate. And a massive amount of time  
4 went into this evidence report that we were given.  
5 And they may conclude on the basis of an exhaustive  
6 review that the evidence is inadequate. For  
7 example, a disease may be very rare, so it's  
8 absolutely infeasible to do well designed studies,  
9 you simply cannot recruit enough patients to have  
10 adequate statistical power. It would be very  
11 reasonable for any coverage body to decide the  
12 evidence is inadequate, but it will never be  
13 feasible to study this adequately, and the  
14 preponderance of evidence supports making this  
15 available, and therefore, they make a coverage  
16 decision. And that can happen sometimes.

17 Now obviously, if our panel concludes  
18 there is clear evidence that a treatment is  
19 harmful, then it would be shocking if HCFA made a  
20 decision to cover, but I suspect that the disparity  
21 between what the panel concludes and what the  
22 coverage decision will be will revolve around this  
23 issue of adequacy of evidence. They might decide  
24 it would just not be feasible to get adequate  
25 evidence in a particular area.

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1 DR. HILL: We had hoped that this kind  
2 of discussion would occur in the context of the  
3 Executive Committee's meetings. I appreciate  
4 hearing all this. I hope that we will be able to  
5 move on to the agenda today and get an answer to  
6 the questions that we've asked, and invite you all  
7 to send in these good comments, appear before the  
8 Executive Committee at it's June 6th meeting. I'm  
9 sure they would be pleased to hear and take into  
10 account your comments about how these panels should  
11 be functioning. In the design of the process, that  
12 was the intention, that the Executive Committee  
13 would have some oversight.

14 I understand that some of this is  
15 necessary, but I'm hoping that it might be possible  
16 before the day runs too far and too long into our  
17 agenda, to go ahead and address the specifics.

18 DR. GARBER: Thank you. Logan, and then  
19 Marshall.

20 DR. HOLTGREWE: I think we have a  
21 substantial body of work to do today, and I wonder  
22 if we shouldn't press on and do it rather than to  
23 constantly revisit what we did yesterday by a  
24 substantial overwhelming majority. So I would  
25 certainly think we ought to press on with our

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1 duties.

2 DR. GARBER: Thank you.

3 DR. ZENDLE: Can you just confirm that  
4 the Executive Committee will have the transcripts  
5 of our meetings, of our comments? We don't have to  
6 repeat our comments, do we?

7 DR. HILL: No. That will form a part of  
8 the record that they have. But they will be  
9 focused on the outcomes in deciding whether or not  
10 to pass that on, ratify and pass that on to HCFA.

11 So, if there's some point that you particularly  
12 want to emphasize, or some argument that you want  
13 to elaborate how this process should be undertaken,  
14 I encourage you to go ahead and send that in. Not  
15 only do we want to look at it, but the Executive  
16 Committee will too.

17 MS. CONRAD: Thank you. Appreciate your  
18 tolerance. Let's proceed with the open public  
19 comments, the scheduled speakers. And the first  
20 scheduled speaker is Margaret Degler, who will be  
21 followed by Dr. Peter Sand.

22 MS. DEGLER: Good morning, panel members  
23 of the Medical and Surgical Procedures Panel. My  
24 name is Margaret A. Degler. I am a nurse  
25 practitioner, duly certified in geriatrics and  
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1 urology nurse practitioner. I have absolutely no  
2 financial gain from being here today from any of  
3 the parties that are here today. I am in practice  
4 at Geneto Urinary Associates, Limited, a urology  
5 practice in Reading, Pennsylvania, as the  
6 continence director of a nonsurgical program for  
7 urinary incontinence.

8 The information that I'm going to share  
9 with you today is from my typical routine clinical  
10 setting. What I have done is extrapolated data  
11 from the age population 65 and over from the dates  
12 of January 2nd, 1998, through December 31st, 1999.  
13 The total number of patients that I have seen for  
14 electrical stimulation in that time frame was 106.  
15 The question that we are all here to answer today  
16 is, is the scientific evidence adequate to draw  
17 conclusions that functional electrical stimulation  
18 is efficacious in this patient population? As an  
19 expert clinician in this area, I can absolutely say  
20 yes, the clinical basis is there. Is the  
21 scientific data there? We are going to hear from  
22 some of the principal investigators from the  
23 studies that were reviewed in the TEC report later  
24 today.

25 I share with you now the findings of the  
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1 106 patients whom I saw over those two-year time  
2 period for electrical stimulation. Of the 106  
3 patients, 15 were male; of those 15 male, 13 were  
4 post-prostatectomy, two were Parkinson's disease.

5 Of the female, the majority was combined stress  
6 urge incontinence, and there were a few simple  
7 stress or detrusor instability patients. That data  
8 was extrapolated from urodynamic studies that  
9 clearly indicated whether there was detrusor  
10 instability, sensory urgency, or combined stress  
11 detrusor instability components.

12 In terms of percentage of improvement,  
13 of those 103 patients, in the 95 to 100 percent  
14 category, there were 19. In the 76 to 94 percent  
15 category, there were 20. In the 50 to 75 percent  
16 category, there were 32. And in less than 50  
17 percent, there were 35. If you look at those  
18 statistics, over 70 percent of those patients aged  
19 65 and older were significantly improved by the use  
20 of electrical nerve stimulation.

21 And to that, I call your attention to an  
22 article which you have by Magnus Fall, Advantages  
23 and Pitfalls of Functional Electrical Stimulation.  
24 And in the Advantages and Pitfalls, he bullets some  
25 particular areas of interest. He refers to this as  
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1 FES, functional electrical stimulation. On page 4,  
2 with the pitfalls of functional electrical  
3 stimulation, it is interesting that the first  
4 pitfall he notices is treatment tradition as one  
5 obstacle. The clinician using FES for incontinence  
6 is trained to use drug therapy or surgery, FES is  
7 an alien principle, and the physiologic rationale  
8 may be difficult to accept, not having had the  
9 opportunity to learn the mechanisms of action in  
10 more detail.

11 In terms of the positive advantages, he  
12 notes, for FES, this method has a firm physiologic  
13 basis. A variety of lower urinary tract  
14 dysfunctions are accessible to FES. Many research  
15 groups at many centers have consistent, similar and  
16 favorable results as reported above. It is very  
17 difficult to believe that the great number of  
18 patients treated in different clinical environments  
19 in a number of different countries would respond so  
20 favorably had the treatment not had good efficacy.

21 Next he states, FES is a cheap  
22 nondestructive method with very few side effects.  
23 In standard external electrical stimulation, no  
24 irreversible surgery is involved. As with drugs,

25 there is no general influence on the receptor  
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1 systems because of specific peripheral activation  
2 of complex reflexes. The cost of one year of  
3 treatment equals that of one year of conventional  
4 drug therapy, and FES has a potential curative  
5 effect; drugs do not provides that unique effect.

6 In closing, I would like to read  
7 excerpts of a patient letter, one of my patients  
8 that was sent to the panel. This is a  
9 post-prostatectomy individual and he has given me  
10 permission to read this today. I Glen Hostetter,  
11 was diagnosed as having prostate cancer April,  
12 1997. I had a radical prostatectomy done on July  
13 23rd, 1997, followed by 33 treatments of radiation  
14 therapy training, in January of 1998. A few months  
15 after the therapy I began to have urinary  
16 incontinence. My doctor prescribed numerous  
17 medications which were not helpful.

18 MS. CONRAD: Time.

19 MS. DEGLER: He then referred me for  
20 electrical nerve stimulation, and with that I had a  
21 welcome success. I strongly urge that the  
22 treatment for incontinence be continued.

23 And to answer the question on a clinical  
24 basis, yes, functional electrical nerve stimulation  
25 does have efficacy in this patient population.

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1 Thank you.

2 MS. CONRAD: Thank you. Dr. Sand. And  
3 the following speaker will be Dr. Whitmore.

4 DR. SAND: Thank you. Good morning.  
5 Thank you very much, Miss Conrad, for the  
6 opportunity to present before the panel. I am  
7 Peter Sand. I am an associate professor of  
8 obstetrics and gynecology at Northwestern  
9 University Medical School, and the director of the  
10 Evanston Incontinence Center. My travel and  
11 expenses here today were supported by EMPI  
12 Corporation. I've participated in numerous  
13 clinical trials using US stimulators and  
14 international stimulators over the last 15 years.

15 I want to talk to you and establish that  
16 there is consistent objective data to support that  
17 PFES is effective in the treatment of genuine  
18 stress incontinence, and there is a study that has

19 shown that PFES is also successful in resolving  
20 detrusor instability in the Medicare aged  
21 population, as well as having a long-term efficacy  
22 and durability.

23         The uncontrolled trials, while not as  
24 scientifically rigorous, are certainly useful to  
25 evaluate the subgroups that aren't of value by  
00046

1 randomized control trials. And they are certainly  
2 available to us; there are more than 200 such  
3 studies in literature, and may be valuable as  
4 evidence if we have established the placebo effect  
5 in the controlled trials. And certainly, these are  
6 very valuable to evaluate the long-term effects  
7 that can't be effectively evaluated in randomized  
8 control trials because of practicality and  
9 expense.

10         Long-term efficacy and durability, I've  
11 selected four papers that were rejected from the  
12 TEC analysis because they're uncontrolled trials,  
13 but they are available to you and are in the  
14 bibliography. And in the notes of my presentation,  
15 those references are also listed. These trials  
16 clearly show at one to six years, significant  
17 durability and long-term efficacy with continued  
18 use of the device. And if there is time later on  
19 in the discussion, I would like to address some of  
20 the long-term efficacy and even cure of patients  
21 with the use of PFES. In a report that I report  
22 that I've highlighted by both Krajl and Lukanovic,  
23 in more than 300 patients, women specifically over  
24 65, we also see that this is quite effective,  
25 specifically applicable in the Medicare  
00047

1 population.

2         Now, I wanted to pose a challenge to the  
3 panel or a question to the panel, to look carefully  
4 at this picture, to look carefully at the TEC  
5 report. This is an excellent, excellent review  
6 that Frank has put before you. But I would contend  
7 that when we look carefully at this, we have to  
8 really examine the question that, did the TEC  
9 report show that four sham control trials that  
10 we're going to discuss today were conflicting, like  
11 the two faces on this picture? Or, is there one  
12 unified opinion that stimulation is significantly

13 better than placebo in the treatment of genuine  
14 stress incontinence and detrusor instability?

15       It's very very difficult to do  
16 controlled, good controlled trials. We have to  
17 realize though, when it comes to electrical  
18 stimulation, that different stimulators are  
19 available to us that have different parameters, and  
20 I wouldn't think to necessarily use the same  
21 stimulator or the same device to treat different  
22 conditions. It's just like surgery; I wouldn't use  
23 one surgery to treat all the conditions that I face  
24 as a practicing urogynecologist. We use different  
25 operations in specific different indications.

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1       When we look at the four sham controlled  
2 trials that were reviewed in the TEC study, our  
3 study, the first in 1995, was a multicenter, sham  
4 controlled, random and double blinded trial, 52  
5 women, 35 active, 17 sham. These data were  
6 evaluated on an intent to treat basis, which isn't  
7 quite what's stated in the TEC report. And while  
8 there may be some unbalance in the enrollment of  
9 subjects to the two groups despite the blinded  
10 randomized process, this on balance would tend to  
11 favor the sham group, in that the patients in the  
12 sham group had more incontinence episodes and thus,  
13 they had more opportunity to improve.

14       Nonetheless, pad test data and voiding  
15 diary data which were highlighted in the TEC report  
16 showed significant improvement or cure with the  
17 active device compared with the sham group. In  
18 addition, all symptomatic subjective scales were  
19 significantly improved with the active device  
20 compared to the sham device, leading us to conclude  
21 that clearly, PFES with this particular device was  
22 effective in treating genuine stress incontinence.

23       With a similar device with similar  
24 stimulation parameters, which is key, Yamanishi, in  
25 the Japanese study, looked at just a four-week

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1 trial. Again, this was randomized and this was not  
2 recognized in the TEC report. This is a  
3 randomized, one-to-one block randomization, sham  
4 controlled double blinded trial of 33 patients;  
5 again, 20 active, 13 sham -- excuse me,  
6 two-to-one. 45 of the active patients were cured



7 while only 13 percent were, excuse me, were in the  
8 sham group. He showed significant changes in pad  
9 tests and voiding diaries.

10 In Luber's study, using a US device, he  
11 showed no significant benefit in treating patients  
12 with genuine stress incontinence.

13 MS. CONRAD: Time, Doctor Sand.

14 DR. SAND: In a similar study, Dr.  
15 Brubaker showed, in 60 patients with stress  
16 incontinence, no significant difference. Yet in  
17 the 61 women she treated with detrusor instability,  
18 there was 50 percent resolution of detrusor  
19 instability.

20 I'm sorry. I'll quickly go to  
21 conclusions. The Sand and Yamanishi papers support  
22 genuine stress incontinence as more effective than  
23 the placebo sham. The Brubaker and Luber study,  
24 which used the same device, do not support this  
25 conclusion. It was a different device. A device  
00050

1 that we used that is very effective for the  
2 treatment of detrusor instability, but not useful  
3 in the treatment of genuine stress incontinence. I  
4 believe that there is adequate evidence to support  
5 the efficacy of PFES for the treatment of women  
6 with genuine stress incontinence based on the  
7 objective placebo controlled sham studies that are  
8 listed in the TEC report. These are also effective  
9 for Medicare patients, and it's been shown in our  
10 control trials to be a durable long lasting  
11 therapy.

12 MS. CONRAD: Thank you, Dr. Sand.

13 DR. LANDY: You said different device,  
14 bud why is a device at issue when the  
15 frequencies --

16 DR. SAND: With electrical stimulation  
17 devices, thank you, Lisa, there are different  
18 devices that have different pulse parameters,  
19 different frequencies and different duty cycles.  
20 Then there's also the protocol that's used. We've  
21 shown in animal studies, in dog studies, that I can  
22 make dogs incontinent, using most available  
23 commercial stimulators, if we don't allow  
24 appropriate rest cycles. This is well known in the  
25 physical therapy literature.

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1           So we can't just look at this  
2 literature. I don't mean to divide the literature,  
3 but we can't look at it without that clinical  
4 insight. And Frank and I had some discussions  
5 yesterday. I mean, that's not possible, for an  
6 internist and a statistician; he did an excellent  
7 review. But we have to look inside of those data,  
8 and understand.

9           So Karl and Linda, in their studies,  
10 used one device, that we don't use for genuine  
11 stress incontinence, and they showed it doesn't  
12 work for genuine stress incontinence. I think it's  
13 an excellent stimulator for detrusor instability,  
14 which is tough to cure on urodynamic testing, and  
15 hopefully we can talk more about that. That device  
16 does that. The other device that we used in our  
17 studies, very similar to what Yamanishi used, those  
18 devices work for stress incontinence. Things  
19 aren't as they seem. So I think we have very  
20 strong objective evidence, and we'll hear more  
21 about some of the information from uncontrolled  
22 trials later by the other speakers.

23           DR. GARBER: Arnie?

24           DR. EPSTEIN: Yeah. I'm an internist  
25 who knows a bit of statistics, so I'm really going  
00052

1 to need your help.

2           DR. SAND: Well, please. I don't mean  
3 to insult the people who graduated in the top 10  
4 percent of my medical school class.

5           (Laughter.)

6           DR. EPSTEIN: Can you just clarify to me  
7 the types of devices that you think are effective,  
8 the types that are ineffective, and any evidence  
9 you have that the distinctions that you make are  
10 broadly made in the community?

11           DR. SAND: I think these differences are  
12 well recognized in the treatment community.

13           DR. EPSTEIN: Do you have any evidence  
14 for that assertion?

15           DR. SAND: What community use is, I  
16 think I would find that evidence in the over 200  
17 uncontrolled trials. Probably the best evidence,  
18 and a lot of us I think draw upon the cat studies  
19 done by Magnus Fall some 30 years ago. Fall -- let  
20 me not start to list the coauthors, because I'll

21 forget them, but basically Magnus Fall showed that  
22 frequencies of 5 to 10 hertz were most effective in  
23 treating detrusor instability, whereas frequencies  
24 of 50 hertz were most effective in treating genuine  
25 stress incontinence. Unfortunately, when that  
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1 information was given to biomedical engineers who  
2 wanted to create one stimulator to treat all, many  
3 of these stimulators showed up with frequencies of  
4 20 or 25 hertz, which significantly diluted our  
5 literature unfortunately, because you couldn't just  
6 average those frequencies. So that's a problem in  
7 our uncontrolled literature and clinical teaching.

8 In addition, the concept of having a  
9 duty cycle that allows for a rest period that's  
10 twice as long as the active stimulation period is  
11 crucial. Then there is a lot of debate as to the  
12 actual pulse duration, which range from anywhere,  
13 in devices built in the United States, from .1  
14 milliseconds to 2 milliseconds, what's ideal? And  
15 I'm not a good enough electrical engineer to really  
16 understand those principles.

17 But those three things, as well as the  
18 amperage, the duration of treatment, can have  
19 profound differences in how effective a device is.  
20 I don't know if that makes it any easier.

21 DR. EPSTEIN: Well, I understand that  
22 there are different dimensions by which, that lead  
23 to efficacy. I think one issue here is whether  
24 these different dimensions have been codified into  
25 distinct groups of instruments, and whether the  
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1 broad, when HCFA reimburses this, or we judge the  
2 evidence, is there any way to tease these out?

3 DR. SAND: You know, I think the  
4 greatest problem with trying to tease that out is  
5 that you make a decision based at one point in time  
6 with current devices, which have been sort of  
7 frozen by the economic freeze of nonreimbursement  
8 for these treatments. Clearly, the best parameters  
9 with a stimulator are also individual to a patient,  
10 and I don't think we have the best device yet.  
11 Certainly, looking at some of the international  
12 devices we've tested that aren't available here, I  
13 think they are better than what we use and have  
14 available of FDA approved devices in the States.

15 So, that's a real loaded question.

16 DR. GARBER: All right. I'm just going  
17 to have to remind you, in asking questions of the  
18 public speakers, try to distinguish those that need  
19 to be answered immediately, directly, relevant to  
20 their current presentation, and you can ask  
21 questions of them again in the open committee  
22 deliberations period. I just bring this up now  
23 because as you know, we're not quite on schedule.  
24 Marshall?

25 DR. STANTON: I can save mine for the

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1 open period.

2 DR. SAND: Thank you very much.

3 MS. CONRAD: Kristine Whitmore, and the  
4 following speaker will be Karl Luber.

5 DR. WHITMORE: Good morning. Thank you  
6 for allowing me a brief time to speak with you. I  
7 am Kristine Whitmore, clinical associate professor  
8 of urology at Hahnemann MCP University in  
9 Philadelphia. My expenses to this function were  
10 supported by EMPI Corporation.

11 The question is, is there scientific  
12 evidence adequate to draw conclusions about the  
13 effectiveness of PFES or PFS in routine clinical  
14 use in the Medicare population? Unfortunately,  
15 urinary incontinence affects many people; public  
16 awareness is recent. Many patients don't tell and  
17 doctors don't ask. Few funds have been allotted to  
18 do studies that show adequate evidence. However,  
19 many guidelines have been established to help a  
20 large segment of society with conservative  
21 therapy. The objectives of this talk will be to  
22 provide an overview of the published guidelines for  
23 the treatment of urinary incontinence, discuss  
24 pelvic floor stimulation parameters and treatment  
25 protocols, and review appropriate patient selection

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1 criteria for PFS, for which you have been afforded  
2 an outline.

3 The American Urological Association had  
4 an ad hoc committee to suggest broad guidelines for  
5 the management of urinary incontinence. Behavioral  
6 therapy was recommended as first line of treatment,  
7 and PFS was included in the guidelines for both  
8 stress and urge incontinence. Subsequently, when

9 asked to assess PFS on a scientific evidence based  
10 only evaluation, the answer was that there was not  
11 evidence to draw conclusions about efficacy.

12 Now I'm sure you have all been provided  
13 with the AHCPR guidelines to review prior to this  
14 meeting, which convened in 1992. The  
15 recommendations were for behavioral therapies as  
16 the first line of treatment. It was updated in  
17 1996 and levels of evidence were established to  
18 assess the quality and amount of evidence,  
19 consistency of the findings among studies, clinical  
20 applicability of the evidence, and evidence of  
21 harms and costs. Subsequently, the AHRQ then asked  
22 TEC to do an unrelated scientific evaluation, which  
23 showed the question could not be answered with  
24 statistical certainty.

25 The first international consultation on  
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1 incontinence sponsored by WHO, showed that  
2 behavioral therapies are recommended as a first  
3 line of treatment, and PFS is included in the  
4 guidelines for the management of the frail disabled  
5 older people, a population which is not unlike  
6 these of Medicare.

7 There was an AUA update series published  
8 in 1999 by Dev Lightner, which recommends  
9 conservative treatment of urinary incontinence as  
10 first line, behavioral therapies are recommended as  
11 first line, and PFS is included in the guidelines  
12 as a behavioral therapy for both stress and urge  
13 incontinence.

14 The NIDDK launched a promotional public  
15 awareness campaign, Let's Talk About Bladder  
16 Control. Many organizations included here, or  
17 more, showed PFS is included as a behavioral  
18 treatment option.

19 In conclusion, the guidelines  
20 recommendations concur, begin with the best and  
21 least invasive treatment option. Not all  
22 behavioral therapies are created equal. Behavioral  
23 therapy is safe and effective. The primary goal of  
24 therapy should be patient satisfaction and patient  
25 motivation is required.

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1 Question number 1 leaves us with a  
2 dilemma, clinical versus rigorous scientific

3 evidence. Can I agree that there is statistical  
4 certainty? No. I'm a clinician and follow the  
5 AHCPR clinical guidelines. Yes, there is clinical  
6 evidence. Thank you.

7 MS. CONRAD: Thank you, Dr. Whitmore.  
8 Karl Luber. Following Dr. Luber will be  
9 Dr. Antoci.

10 DR. LUBER: Good morning. My name is  
11 Karl Luber, and I would like to thank the panel for  
12 the opportunity to share some information with you  
13 on our experience with electrical stimulation. I  
14 present to you with no conflicts of interest with  
15 any device developer, corporation or professional  
16 organization. My position currently is as the  
17 director of the division of urogynecology and  
18 reconstructive pelvic surgery for the Southern  
19 California Permanente Medical Group in San Diego.  
20 There I am responsible for delivery of care  
21 decisions for a very large group of women with  
22 urinary incontinence. I also co-direct a  
23 fellowship in urogynecology and reconstructive  
24 pelvic surgery at the University of California at  
25 San Diego.

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1 What I would like to do this morning is  
2 just very briefly talk to you about -- I'm not  
3 getting this to come up, will you help me out?  
4 Thank you very much -- about what we have learned  
5 about the efficacy of electrical stimulation in the  
6 treatment of women with genuine stress urinary  
7 incontinence. And my comments and all patients  
8 that I'm going to present on today are patients  
9 with genuine stress incontinence, that is, genuine  
10 stress incontinence consistent with the  
11 International Continence Society definitions.

12 Very quickly, the background information  
13 on functional electrical stimulation, in the early  
14 1960s there were some anecdotal trials. Connie,  
15 I'm getting asked to stop here. I don't know if  
16 that's --

17 MS. CONRAD: I've got you timed.

18 DR. LUBER: Thank you very much. And  
19 then in the 1970s, these clinical trials, anecdotal  
20 trials went on to look at animal studies, where we  
21 learned the theoretical mechanisms of electrical  
22 stimulation and how they work. In the 1980s we saw

23 a number of open ended clinical trials. And then  
24 all of this information drove folks in the early  
25 '90s to look at doing RCTs. The reason it drove  
00060

1 us to doing RCTs and the reason I very strongly  
2 feel that nonrandomized, noncontrolled trials are  
3 not of particular value in making these decisions,  
4 is that there is a huge confounding effect of  
5 electrical stimulation, not a simple placebo  
6 effect. In other words, if I'm asked to carry an  
7 anal plug around in my rectum for a half an hour a  
8 day, or perhaps more as happened in many of these  
9 trials, there's a darned good chance it's going to  
10 affect my ability to contract my pelvic floor,  
11 consistent with what I think a lot of us felt, if  
12 not voted on yesterday, with the effects of  
13 feedback on the pelvic floor musculature. So I  
14 think that uncontrolled trials in electrical  
15 stimulation are not of a particularly large amount  
16 of value to us in making decisions.

17 We set out to try to understand whether  
18 electrical stimulation as recommended by the  
19 manufacturers was an effective treatment for  
20 genuine stress incontinence. The study design was  
21 a prospective randomized double blind control trial  
22 done within our facility, a single center, and  
23 supported by a Kaiser Foundation grant. The  
24 inclusion criteria and exclusion criteria I won't  
25 dwell on, as we have to move along quickly. I will  
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1 share with you that the treatment parameters we  
2 used were identical to those used in the studies  
3 that Dr. Sand described. We used a two-to-one rest  
4 to work cycle, we used 50 hertz for our  
5 stimulation, so there's really not a huge  
6 difference there. As far as the amplitude, I  
7 believe it was two million amps; I frankly would  
8 have to review my own paper to look back at that,  
9 which was the manufacturer's recommendation at that  
10 time.

11 We randomized people, and I show this to  
12 demonstrate to you that the randomization was  
13 consistent with what you'd expect. I know you  
14 don't need to do this; if it's randomized, you're  
15 going to assume that everybody comes out equal.  
16 But as you can see, there was no statistically

17 significant difference in the number of patients  
18 enrolled, dropped out, age, previous surgeries, or  
19 other potentially confounding variables. Results  
20 from our trial demonstrated that the subjective  
21 improvement and cure, as well as objectively cured  
22 groups showed no statistically significant  
23 difference.

24 Now when I first presented this, I was  
25 castigated by my colleagues and told, you just want  
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1 to do surgery, you don't want to show that this  
2 works. The truth of the matter was, we embarked  
3 upon this trial with the bias that this was going  
4 to work. We wanted to demonstrate the efficacy of  
5 this, because we wanted to extend this therapy  
6 throughout our organization. And it in a sense  
7 blew up in our face and I wasn't very happy with  
8 that. But you know, once again, I had to go with  
9 the information that came to me from the trial, I  
10 had to be honest about the outcomes that I was  
11 looking at.

12 Based upon this trial and frankly based  
13 upon my interpretation of the other trials, we made  
14 the conclusion that functional electrical  
15 stimulation was no more effective in approving or  
16 eliminating the symptoms of stress or genuine  
17 stress incontinence than was the daily retention of  
18 the control probe. Functional electrical  
19 stimulation may be of value in conjunction with a  
20 physiotherapist who uses it to help patients as we  
21 say, jump start their muscles, that is, to teach  
22 them an awareness of where that musculature is, and  
23 then go on to help them to learn to contract those  
24 muscles. But as a standalone therapy to take home,  
25 we could not support its use.

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1 MS. CONRAD: Time please.

2 DR. LUBER: It's all yours. There are  
3 hundreds of thousands of operations done for  
4 genuine stress urinary incontinence in the United  
5 States each year. We need to seek alternatives  
6 that are nonsurgical to help these women. There's  
7 no question about that. But in our zeal to embrace  
8 and learn about these techniques, we should be  
9 careful not to initiate a process which would  
10 establish a standard of care for which there are



11 not adequate scientific underpinnings. And I  
12 frankly believe that that's where we are. We may  
13 find with adjustments and changes, and redesign,  
14 that electrical stimulation is of value. At the  
15 current point, we do not have the data to support  
16 that. Thank you very much.

17 MS. CONRAD: Thank you, Dr. Luber.

18 DR. STANTON: A quick question. I may  
19 have missed this if you said it at the beginning.  
20 Were these results published?

21 DR. LUBER: Yes, sir. These results  
22 were published in the Journal of Neurourology and  
23 Urodynamics, and that's in the TEC report, sir.

24 DR. BRADLEY: What was the treatment  
25 time? I may have also missed that. How many weeks  
00064

1 of therapy?

2 DR. LUBER: 12 weeks of therapy.

3 DR. BRADLEY: How did you assess  
4 compliance in that study?

5 DR. LUBER: The device itself has a  
6 compliance meter in it. In other words, the  
7 patient would have to be sneaking to turn it on and  
8 leave it without using it, but we can download the  
9 daily use of the device to demonstrate efficacy.

10 DR. BRADLEY: And what was the  
11 compliance?

12 DR. LUBER: 87 percent. It was  
13 surprisingly good. Thank you very much.

14 DR. GARBER: Thank you.

15 MS. CONRAD: Dr. Joseph Antoci.

16 DR. ANTOCI: Good morning. I'm Dr. Joe  
17 Antoci. I'm a community practice urologist in  
18 Connecticut, and I have no financial conflicts in  
19 being here today. I would like to submit to the  
20 panel written documentation of what I'm going to  
21 say.

22 It was first shown in animal studies  
23 dating back to 1895 that bladder contractions could  
24 be inhibited by cutaneous and rectile stimuli. In  
25 modern times, human studies have continued to

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1 support the observation that PFS inhibits bladder  
2 contractions. Janus showed in 1979 that true  
3 physiologic responses could be recorded on  
4 urodynamic evaluations in patients undergoing

5 pelvic floor neuromodulation. Tanago and Schmidt's  
6 work, published in 1988, demonstrated that  
7 electrical enhancement of the tone of the external  
8 sphincter suppressed the detrusor and improved  
9 bladder storage. In his 1991 paper, which is  
10 referenced in HCFA's TEC assessment, Dr. Magnus  
11 Fall elucidated the principles of PFS. He worked  
12 out the optimal energy levels and pulse  
13 configurations that would inhibit detrusor  
14 contractions.

15 In 1997, de Grote described the  
16 neurophysiologic pathway that accounts for these  
17 consistent observations. Basically, PFS prevents  
18 the pudendal nerve from telling the brain that the  
19 bladder is filling, and therefore the brain does  
20 not send the message to the bladder to contract.  
21 It's also been noted by Fall in his '91 paper that  
22 PFS is a useful tool in facilitating PME training.

23 HCFA's own TEC assessment indicates that  
24 PFS is better than placebo and equal to alternative  
25 therapies in the majority of studies evaluated.

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1 This TEC assessment also focused on studies  
2 published since 1980 but ignored previous work,  
3 including 24 other PFS studies performed from 1967  
4 to 1979, which encompassed data on 793 patients. I  
5 was able to retrieve data on 38 studies published  
6 from '68 to '98. A total of 1,375 patients were  
7 treated with PFS and 863, or 62 percent of those,  
8 were improved.

9 In this day and age, cost is always a  
10 factor. The cost of PFS compares very favorably to  
11 alternative treatments. When HCFA Connecticut  
12 covered PFS, the rate was \$84 for a six-week  
13 treatment period. Modern day anticholinergics such  
14 as Ditropan, Excel or Detrol, cost anywhere from 90  
15 to \$180 per month.

16 Although the panel is not considering  
17 implantable neuromodulation technology, it is  
18 noteworthy to note that the total patient cost, for  
19 instance, for a Metronics Inter-Stim device is  
20 \$25,000. The Inter-Stim literature also notes that  
21 there is a one-third reoperation rate on these  
22 patients. Compare then the 67 percent patient  
23 improvement rate at \$25,000 per patient to the 62  
24 percent patient improvement with PFS at a fraction

25 of the cost.

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1 In summary, we know that PFS works, we  
2 know how it works, we know that it's a useful  
3 teaching tool for PME, we know that it's better  
4 than placebo, and we know it is equal to  
5 alternative therapies. And ladies and gentlemen of  
6 the panel, this is a critical point: As all  
7 clinicians who treat incontinence know, there is no  
8 single therapy for all incontinent patients.  
9 Patients need options and choices.

10 Finally, please consider the following  
11 in your deliberations: When a body such as  
12 Medicare does not cover a given treatment, that  
13 effectively dissuades health care providers from  
14 offering that treatment to their patients. That is  
15 tantamount to denying patient care. Thank you very  
16 much.

17 MS. CONRAD: Thank you, Dr. Antoci. We  
18 are going to move along with the industry  
19 presentation. Deborah Jensen, representing EMPI,  
20 followed by Francie Bernier.

21 To try to pick up a little time, we are  
22 going to try to not schedule a morning break. Just  
23 leave the room as you need to.

24 MS. JENSEN: Good morning. My name is  
25 Deborah Jensen and I'm the vice president of

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1 regulatory affairs, clinical research and quality  
2 assurance for EMPI. EMPI is a medical device  
3 manufacturing firm based in St. Paul, Minnesota,  
4 that specializes in devices to assist patients with  
5 functional disabilities, including the Inova PFES  
6 device for the treatment of incontinence. EMPI has  
7 been involved in the manufacture and distribution  
8 PFS devices since 1991, and we are grateful for the  
9 opportunity to discuss the place of PFS therapy in  
10 the treatment of incontinence patients of Medicare  
11 age before today's panel meeting. We trust that  
12 the panel members will listen carefully to the  
13 evidence presented today.

14 Clearly, the task of the panel to  
15 qualify whether conclusions can be drawn regarding  
16 the scientific evidence supporting this technology,  
17 and then quantify the size of the health effects  
18 for this technology, is not an easy task. But it

19 certainly is an important one for the beneficiaries  
20 who could benefit from this treatment option but  
21 are currently not able to access this therapy as a  
22 result of the national noncoverage policy.

23         It is clear from the scientific  
24 literature that there is not support, or sufficient  
25 evidence to say that this therapy has no benefit  
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1 for any beneficiary. Rather, it is our opinion and  
2 the opinion of several clinicians presented today,  
3 that there is scientific evidence to draw  
4 conclusions about the effectiveness of PFES in  
5 routine clinical use for the Medicare population.

6         I would urge the panel members to  
7 consider the following point: PFS is a technology  
8 that has been around for a long time. EMPI's Inova  
9 PFES device received FDA clearance in 1991. In  
10 these past nine years, EMPI has made the  
11 development of scientific and clinical evidence to  
12 support the safety and efficacy of this therapy a  
13 constant goal through the support and sponsorship  
14 of four separate clinical trials.

15         The first, a randomized placebo control  
16 trial of stress incontinence subjects, published in  
17 1995 by Dr. Peter Sand, demonstrated the  
18 statistically significant improvement when compared  
19 to placebo. EMPI subsequently completed two  
20 treatment optimization studies that evaluated the  
21 effect of treatment frequency on patient outcome  
22 when PFS was used to treat stress, and then urge  
23 and mixed incontinence. These were subsequently  
24 published by Dr. Richardson in 1996, and Dr. Siegel  
25 in 1997. Both of these trials documented with  
00070

1 statistical significance that improvements were  
2 seen in incontinence symptoms in patients from  
3 their baseline values.

4         Most recently, the encouraging results  
5 for a PFS study in post-prostatectomy incontinence  
6 patients pointed out that this therapy also holds  
7 promise for this group of patients. Publication of  
8 the results of this trial is pending.

9         Concurrent to the development of  
10 scientific evidence to support this technology,  
11 EMPI has developed relationships with health care  
12 providers in the private health care peer community

13 in an effort to determine the place of PFS in the  
14 care of patients suffering from incontinence. As  
15 evidenced by the reviews of this technology  
16 undertaken by such prestigious independent expert  
17 groups as AHCPR and the World Health Organization,  
18 PFS does have a place in the continuum of care.

19 This place has been further  
20 substantiated by the over 300 private health plans  
21 in the United States that are providing  
22 reimbursement for this technology. Collectively,  
23 three of the largest plans, Aetna U.S. Health Care,  
24 Blue Cross Blue Shield, and United Health Care  
25 provide coverage for over 40 million Americans.

00071

1 This information provides strong support that the  
2 clinical community and a significant number of  
3 private health plans have determined that the  
4 support for PFS is sufficient for it to be a  
5 standard of care, and that it has a place in the  
6 treatment of incontinence patients. Thus, they  
7 have answered the question put before the panel  
8 regarding the effectiveness of PFS affirmatively.

9 At this point in time, I would like to  
10 yield the remainder of my time to Dr. Kristine  
11 Whitmore, so that she may further discuss the  
12 adequacy of the scientific literature. Thank you.

13 DR. WHITMORE: Thank you. We are going  
14 to go on to the treatment parameters and  
15 protocols. The evidence is adequate. The study  
16 design underestimates the effect. Randomization in  
17 the RCTs limit the dose response, ala, we cannot  
18 get to maximum intensity, so for stress  
19 incontinence we cannot produce a muscle  
20 contraction, and for urge incontinence it's hard to  
21 obtain maximal stimulation to cause an inhibitory  
22 effect on the bladder.

23 For stress incontinence, we'll talk  
24 about treatment parameters. The scientific  
25 literature supports a production of an involuntary

00072

1 muscle contraction. Magnus Fall, of course, has  
2 many papers that have established that a frequency  
3 of 50 hertz is achieved at maximum urethral closure  
4 pressure. There is variable intensity, zero to 100  
5 milliamps, to maximum muscle recruitment. This is  
6 done to produce a contraction, often seen as an

7 anal wink. There is a duty cycle or work-to-rest  
8 ratio of one to one or one to two, five on, five  
9 off, five seconds on, ten seconds off. Usually 15  
10 minutes treatment two to three times daily will  
11 produce up to 120 contractions per day. Initial  
12 treatments are usually six to eight weeks.

13 There is also support for urge  
14 incontinence, during which we want to achieve a  
15 reflexive bladder inhibition. The most common  
16 frequency is 10 hertz. Maximal intensity has to be  
17 achieved, usually to the point of discomfort, and  
18 then backing off to a sensation tolerable to the  
19 patient. The duty cycle is usually one to one.  
20 There are 15-minute treatments, two to three times  
21 a day, and initial treatments are as short as four  
22 weeks.

23 There was a question asked about  
24 utilizing the same parameters among various  
25 studies. For the randomized control trial by  
00073

1 Yamanishi in 1997 for the treatment of genuine  
2 stress incontinence, did use a frequency of 50  
3 hertz, did achieve maximal intensity level by  
4 urodynamics of maximal urethral closure pressure.  
5 Had a number of contractions, 15 minutes, 120 a  
6 day. 15 minutes two to three times a day of  
7 treatment. The treatment period was four weeks,  
8 and the objective cure rate was 45 percent.

9 Additionally, Richardson, 1996, stress  
10 incontinence treatment. Utilized a frequency of  
11 50, visualized pelvic floor muscle contractions as  
12 maximal intensity. Compared daily versus every  
13 other day treatment protocols. Used 15 minutes of  
14 treatment twice a day for 120 contractions, or 60  
15 contractions per day. The duty cycle was one to  
16 two. Treatment was 20 weeks. And the objective  
17 cure rates, daily, 22 percent and every other day,  
18 53 percent.

19 Let's switch to urge incontinence.  
20 Brubaker, 1997, utilized 20 hertz frequency, lower  
21 frequency. Digitalized pelvic floor muscle  
22 contractions at maximal intensity. Had 20 minutes  
23 twice a day of treatment. The duty cycle was one  
24 to two. Treatment was eight weeks. And if you  
25 pull out the urge incontinence portion of her

00074

1 population, the estimated cure rate is 50 percent.

2 Another optimal treatment protocol for  
3 urge incontinence, Siegel et al, 1997. Again, low  
4 frequency, 12.5 hertz. Pelvic floor muscle  
5 contractions were visualized at maximal intensity.  
6 There were 15-minute sessions twice a day. The  
7 duty cycle was one to two. 20 treatment weeks, and  
8 objective cure rate, 28 percent.

9 In conclusion, the final question then  
10 to number one, clinical versus rigorous scientific  
11 evidence, can I agree that there is statistical  
12 certainty, no. Since I am a clinician, however,  
13 there certainly is clinical evidence. Thank you.

14 MS. CONRAD: Thank you, Dr. Whitmore.  
15 Francie Bernier. And the next group of public  
16 presenters, the professional organizations, I have  
17 been asked to rearrange a little bit, so the first  
18 speaker for the professional organizations  
19 following Ms. Bernier will be Nicolette Horbach.  
20 Thank you.

21 MS. BERNIER: Good morning. My name is  
22 Francie Bernier, I am a nurse from Colorado. Over  
23 the last nine years I have offered continence care  
24 to my patient, mostly women, and I am now a  
25 clinical consultant. My trip has been sponsored by  
00075

1 Hollister so that I may speak to you about the use  
2 of electrical stimulation.

3 The question you've been charged today  
4 is, is there adequate clinical evidence to support  
5 the use of electrical stimulation in the treatment  
6 of urinary incontinence? The answer is yes. For  
7 the over 20 million Americans who suffer from  
8 urinary incontinence, there are few treatments that  
9 offer little risk or side effects except a  
10 conservative management program. Pelvic floor  
11 therapy includes a variety of interventions, to  
12 include behavioral modifications, biofeedback  
13 directed PME's, and intercavity or surface  
14 electrical stimulation. The integration of these  
15 options into a continence program has created a  
16 multimodality approach for the treatment.

17 Up until recently, medications and  
18 surgery have dominated the continence care.  
19 Surgical risks include morbidity and mortality.  
20 Additionally, these procedures may not cure

21 incontinence and have been known to worsen symptoms  
22 in some cases. The surgery failure rate has been  
23 reported at about 30 percent.

24         The AHCPR guidelines have encouraged the  
25 use of the least invasive or the intervention with  
00076

1 the least risk, such as behavioral modification, as  
2 the first treatment option for those that suffer  
3 from incontinence. The significant side effects  
4 from medication, such as dry mucous membranes of  
5 the mouth and eyes, constipation, headache, and  
6 visual disturbances, and general malaise, have  
7 compromised their use, especially in the elderly.

8         Electrical stimulation is a successful  
9 treatment modality for the treatment of  
10 incontinence. This option has been effectively used  
11 to retrain the pelvic floor musculature in those  
12 with weakened or atrophic muscles. Additionally,  
13 the effect of electrical stimulation on the bladder  
14 and voiding symptoms has been shown to decrease or  
15 eliminate the symptoms associated with urgency and  
16 frequency.

17         The use of electrical stimulation is not  
18 new to the medical community. In Europe,  
19 stimulation has been used to treat incontinence for  
20 many years and historically it's been reported and  
21 traced back to 1895. Over the years, the increased  
22 use of electrical stim has been applied to  
23 technology which now uses internal sensors or  
24 surface electrodes to directly provide stimulation  
25 to the muscles and nerves. Electrical stimulation  
00077

1 has increased use in the medical and rehabilitative  
2 communities over the years. The application of  
3 specific frequencies of electricity to muscle  
4 causes a chemical response which has been  
5 demonstrated to relax a spasming muscle, or recruit  
6 muscle tissue in order to reeducate a muscle  
7 dysfunction.

8         It is the standard of care for specific  
9 cardiac conditions in which the heart muscle is  
10 experiencing an arrhythmia, such as in ventricular  
11 type of cardio, or in a cardiac arrest. The  
12 electrical charge of a cardiac muscle can calm the  
13 tachycardia and set the heart muscle into a normal  
14 sinus rhythm. Additionally, when applied to the



15 cardiac muscle during an arrest, the application of  
16 an electrical stimulation will recruit and  
17 reeducate the electrical conduction system of the  
18 cardiac musculature to contract and function  
19 efficiently.

20         Used in rehabilitative medicine,  
21 electrical stim again provides a calming sensation  
22 to the muscle in spasm, or can reeducate a flaccid  
23 muscle. In a recent interview with Dana Reeve, the  
24 wife of Christopher Reeve, she reports the daily  
25 application of electrical stimulation had kept her

00078

1 husband's large skeletal muscles in a completely  
2 functional state. His muscles are reported to be  
3 in the same condition they were in previous to his  
4 spinal cord injury.

5         Fall's study, which has been referred to  
6 this morning, conducted research using low  
7 frequency of 5 hertz to obliterate bladder spasms  
8 in cats. When the same frequency is applied to  
9 those who suffer from urge incontinence, the  
10 results have been duplicated. A vaginal  
11 electrosensor or surface electrodes can deliver the  
12 application. This stimulation is applied to the  
13 pudendal nerve, which then induces a pelvic floor  
14 muscle contraction. The induced passive  
15 contraction causes initiation of the inhibition  
16 reflex and directly stimulates the sacral afferent  
17 nerve fiber.

18         Additionally, when applied to the pelvic  
19 floor at higher frequency, electrical stimulation  
20 causes activation of the somatic nerve to the  
21 striating muscles of the pelvic floor. Efferent  
22 stimulation of the periurethral striating muscles  
23 and leading to the ani, cause an increase in  
24 urethral closure pressure. By encouraging the  
25 patient to contract the pelvic floor muscles when

00079

1 the stimulus is active, helps the incontinent  
2 patient identify, recruit and coordinate pelvic  
3 floor muscle movement. This reeducates the patient  
4 and the pelvic floor, and decreases urine loss  
5 associated with stress and urge incontinence.

6         This increased benefit can move a  
7 patient closer to becoming successful in their  
8 biofeedback training. A significant reduction in

9 incontinent episodes, from 41 to 72 percent, has  
10 been reported in electrical stimulation for stress  
11 and urge incontinence. The long-term efficacy of  
12 treatment has been reported in up to two years  
13 following.

14 Various settings have been proven  
15 successful to treat the different types of  
16 incontinence. These settings have been accepted as  
17 the standard of care and range from 5 to 12.5 hertz  
18 for urge incontinence, 20 hertz for mixed  
19 incontinence, and 50 and 100 hertz for stress  
20 incontinence. Most recently, a study evaluated  
21 stimulation of 200 hertz; it has received FDA  
22 approval to induce a pelvic floor muscle  
23 contraction, and has improved voiding in those who  
24 suffer from nonobstructive urinary retention.

25 The use of this therapy should only be

00080

1 applied when indicated. After careful assessment  
2 as to the muscle function, the decision to apply  
3 electrical stimulation should be when the pelvic  
4 floor musculature is determined to be weakened as  
5 documented by digital exam and a pressure monometry  
6 of less than 10 centimeters of water with no  
7 endurance to the contraction.

8 Additionally, when the symptoms of urge  
9 incontinence is impacting quality of life, the  
10 application of electrical stimulation has been  
11 included so to reduce the symptoms. Although a  
12 lack of a perfect randomized controlled study has  
13 yet to be done, this evidence is clear. The  
14 results specifically demonstrate that electrical  
15 stimulation can normalize urodynamic parameters in  
16 those who suffer from urge incontinence.

17 In those with stress incontinence,  
18 electrical stimulation has not demonstrated the  
19 same in some cases. This may be due to the  
20 anatomic defect which exists within the lower  
21 urogenital system. However, during proper  
22 continence reeducation sessions, the patient is  
23 instructed how to reuse the pelvic floor muscles  
24 during exertional activity which precipitates the  
25 incontinent episodes. These would then normalize

00081

1 the parameters that are evaluated for stress  
2 incontinence.

3 Exclusion to the therapy should include  
4 those who have a pacemaker implant, a copper IUD,  
5 those who suffer from mental confusion, during  
6 pregnancy, and in the presence of a pelvic  
7 malignancy. Additionally, this treatment should be  
8 withheld during episodes of acute urinary tract  
9 infection, any episode of vaginal bleeding or  
10 vaginal infection in women, and in the presence of  
11 fecal impaction. The use of electrical stimulation  
12 should only be considered after careful assessment  
13 has been made to evaluate for the presence of these  
14 contraindications.

15 The number of visits may not exceed 12  
16 visits for most patients. In most cases,  
17 improvement in symptoms can be seen within the  
18 first few weeks. However, most patients require  
19 reinforcement of the new behavior and as with any  
20 rehabilitative program, the chance of symptoms  
21 returning, if the patient does not comply with the  
22 program.

23 Also, the elderly often require more  
24 frequent visits than the younger population, as the  
25 rehab process seems to take more time in that  
00082

1 group.

2 The patient's response to electrical  
3 stimulation is very positive. Those who were  
4 previously frustrated by the inability to contract  
5 the pelvic floor muscles report great satisfaction  
6 in their awareness and spontaneous performance of  
7 pelvic floor exercises. This is often experienced  
8 immediately after the first session. Once the  
9 patient is able to contract the pelvic floor  
10 musculature and reuse the pelvic floor, there is a  
11 decrease or elimination of urinary incontinence  
12 symptoms.

13 As we face the decisions about  
14 electrical stimulation, please consider the  
15 patient. Incontinence is a symptom of another  
16 medical problem. The studies you have evaluated  
17 have judged the outcomes but have not measured  
18 value in all of the factors which affect results.  
19 Recognizing how each patient differs in their  
20 presentation, I am asking you to be aware of the  
21 variability within the patient population. These  
22 studies come to their conclusions from the

23 technical report and the consistency of the results  
24 are dependent upon too many variables which have  
25 not been considered.

00083

1 The value of muscle reeducation process  
2 as well as the calming effect this treatment option  
3 has on the bladder should be available as a  
4 treatment for those who suffer from incontinence.  
5 Electrical stimulation offers no risks. It is cost  
6 effective by decreasing the number of office visits  
7 required to achieve a continent status and improved  
8 quality of life. Thank you.

9 DR. GARBER: Thank you.

10 MS. CONRAD: Okay. Nicolette Horbach.  
11 And the following speaker will be Julie Pauls, Dr.  
12 Julie Pauls.

13 DR. HORBACH: Good morning. I am  
14 Dr. Nicolette Horbach, associate clinical professor  
15 of obstetrics and gynecology at George Washington  
16 Medical Center, a practicing physician in northern  
17 Virginia, and the current president of the American  
18 Urogynecologic Society. I have no financial  
19 disclosure to report. On behalf of the AUGS I am  
20 pleased to provide expert testimony on the need to  
21 provide insurance coverage for PFES for the  
22 treatment of urinary incontinence.

23 Urinary incontinence has been estimated  
24 to affect over 20 million Americans, the majority  
25 of whom are women. As surgery is not always

00084

1 appropriate or effective treatment options for all  
2 types of urinary incontinence, the availability of  
3 noninvasive treatment alternatives is a major  
4 concern for urogynecologists and their patients.

5 The American Urogynecologic Society is a  
6 21 year old nonprofit organization whose nearly  
7 1,000 members have a special interest and/or  
8 expertise in the field of urogynecology and pelvic  
9 reconstructive surgery. Our membership includes  
10 gynecologists, urologists, and allied health  
11 professional in academic and clinical practice.  
12 The mission of our society is to promote research  
13 and education in the specialty, and to improve the  
14 quality and delivery of health care to women with  
15 pelvic floor disorders. Many of our members are  
16 fellowship trained and national and international

17 leaders in the field of urogynecology.

18         Our members were instrumental in the  
19 development of the first AHCPR clinical guideline  
20 on urinary incontinence, chairing the panel of  
21 experts for the 1996 revision of the urinary  
22 incontinence guideline. The NIDDK, the NICHD, the  
23 NIA, the NINR, and AHRQ continually fund research  
24 conducted by our members. Because of our society's  
25 efforts, NICHD now has a urogynecologist on staff

00085

1 to coordinate the expanded research in this field.

2         PFES is a therapeutic modality indicated  
3 for the treatment of urgency and urge, stress, and  
4 mixed urinary incontinence. The therapeutic effect  
5 of pelvic stimulation rely on electrical activation  
6 of nerves. Detrusor inhibition is mediated through  
7 low frequency stimulation of the sacral afferent  
8 and potentiated by pudendal nerve stimulation.  
9 Electrical stimulation of the urethral musculature  
10 is via higher frequency activation of the somatic  
11 nerves to the striated muscles. Thus, the  
12 treatment of urinary incontinence with PFS involves  
13 the, physiologic coordination of both bladder and  
14 urethral function.

15         There are two reasons that providers use  
16 pelvic floor stimulation as a treatment modality.  
17 One reason to use PFS is to neurally inhibit  
18 inappropriate bladder contractions. Another reason  
19 is to hypertrophy the skeletal muscle for the  
20 treatment of stress incontinence. PFS involves an  
21 electrical probe that provides the contact surface  
22 for transmitting current to stimulate specific  
23 nerves.

24         The effectiveness of the pelvic floor  
25 electrode will depend on its size, shape and

00086

1 material, as well as the critical parameters of  
2 pulse amplitude and duration, wave form, frequency  
3 and duty cycle. The study parameters that the  
4 technology assessment relied upon in evaluating the  
5 effectiveness of PFS were not adequate and  
6 therefore, did not yield consistent results.

7         The first question that the technology  
8 assessment posed to the Medical and Surgical  
9 Procedures Panel relates to the efficacy of pelvic  
10 stim in reducing incontinence. Although the

11 technology assessment provided to the panel  
12 concluded that electrical stimulation does not meet  
13 the appropriate criteria for establishing its  
14 effectiveness in the treatment of urinary  
15 continence, a report by Aetna in 1996 determined  
16 that PFS is effective in treating urinary  
17 incontinence. Two randomized placebo control  
18 trials provide evidence of the efficacy of PFS in  
19 the treatment of urinary stress incontinence.

20 Yamanishi conducted a four-week double  
21 blinded trial comparing electrical stimulation to  
22 placebo treatment in 44 patients with stress  
23 urinary incontinence. Efficacy of pelvic floor  
24 stimulation therapy was judged using several  
25 outcome measures, including the number of

00087

1 micturitions and leakage episodes, the number of  
2 pad changes, degrees of disturbance in daily  
3 activity, and patient impressions. There was a  
4 significant decrease in the daily frequency of pad  
5 change and disturbances in daily activities in the  
6 active device group compared to the sham device  
7 group. Also, there were significantly more cured  
8 or improved patients for frequency of leakage and  
9 pad tests.

10 In previous assessments, Blue Cross and  
11 Blue Shield Association discounted the findings  
12 reported in the Yamanishi study because their  
13 results were, quote, inconsistent and conflicting,  
14 unquote, with other studies. However, Blue Cross  
15 Blue Shield report failed to identify any flaws in  
16 the methodology of this study, nor were complaints  
17 issued about the reliability and validity of these  
18 results.

19 Although the technology assessment  
20 discounts the Sand report for, quote, sufficient  
21 methodologic quality, unquote, an independent  
22 review by MedTap International summarized the study  
23 as a multicenter prospective randomized, double  
24 blinded trial comparing 35 women receiving PFS to  
25 17 women receiving a sham device. To determine

00088

1 treatment efficacy, Sand and the other  
2 investigators conducted urodynamic testing  
3 accompanied by a pad test, and subtractive  
4 phystometry (phonetic) before and after device

5 use. After 12 weeks of treatment, the patients  
6 using the active device had significantly greater  
7 improvement in weekly and daily leakage episodes,  
8 pad testing, and vaginal muscle strength, when  
9 compared with the patients treated with the sham  
10 device. The pad test also showed that stress  
11 incontinence was improved by at least 50 percent in  
12 62 percent of the patients using PFS, compared with  
13 only 19 percent of patients using the sham device.

14 In the largest randomized trial,  
15 Brubaker compared PFS to sham device in 146 women  
16 with stress incontinence, detrusor instability and  
17 mixed incontinence. This study utilized  
18 multichannel testing, testing, urinary diary, and  
19 assessment of quality of life, to determine the  
20 efficacy of pelvic floor treatment. After eight  
21 weeks, 49 percent of the women with detrusor  
22 instability who used the active electrical device  
23 were cured.

24 Despite the concerns regarding study  
25 design, the 1996 AHCPR clinical guidelines on  
00089

1 urinary incontinence concluded, research indicates  
2 that PFES can significantly reduce urinary  
3 incontinence in women with stress incontinence, and  
4 may be effective in men and women with mixed, urge  
5 and stress incontinence. Treatment using  
6 stimulation requires monitoring by a health care  
7 professional to determine effectiveness.

8 The technology assessment also asked the  
9 panel to compare the efficacy of PFS as compared to  
10 PME or alternative treatments. If a patient can  
11 spontaneously perform PMEs, she does not need PFS.  
12 However, as with all areas of weakened or poorly  
13 enervated skeletal muscles, PFS augments  
14 strengthening of muscles. This approach has been  
15 used in other parts of medicine for many years,  
16 including orthopedics and physical therapy.

17 The third inquiry of reference in the  
18 technology assessment questions the addition of PFS  
19 to PMEs to improve outcome above those obtained  
20 from PMEs alone. As professionals treating urinary  
21 incontinence with the above treatments, AUGS feels  
22 that this question was the result of lack of  
23 knowledge or understanding regarding application of  
24 the two modalities. PFS for stress incontinence

25 contracts the same muscles as a correctly performed  
00090

1 Kegel exercise.

2 The advantages of PFS are twofold. The  
3 correct muscles are always contracted, and  
4 voluntary compliance to exercise is not required.  
5 Electrical stim and PME's are used for different  
6 people. Women with muscles that simply have mild  
7 disuse and atrophy can exercise without any device,  
8 and women with more moderate disuse and atrophy  
9 need additional treatment. Thank you.

10 DR. GARBER: Thank you.

11 MS. CONRAD: Julie Pauls, and the  
12 following presenter will be Mikel Gray.

13 DR. PAULS: Thank you. Good morning.  
14 My name is Dr. Julie Pauls. I'm a physical  
15 therapist and an assistant professor at Texas  
16 Women's University at the Texas Medical Center in  
17 Houston, Texas. I am here on behalf of the  
18 American Physical Therapy Association, representing  
19 its almost 69,000 members. And I have no current  
20 or past financial interest in any manufacturers  
21 whose products may be under discussion today.

22 And Connie, I have asked that you  
23 distribute my testimony, and ask that it be put in  
24 the permanent record of this proceeding.

25 To the question of the day, is the  
00091

1 evidence adequate, the APTA responds that yes,  
2 there is adequate clinical evidence to support the  
3 use of PFES in the care of urinary incontinence.  
4 And we believe that, because the Agency for Health  
5 Care Quality, formerly the AHCPR, is the lead  
6 governmental agency charged with supporting  
7 research design to improve the quality of health  
8 care, reduce its costs, and broaden access to  
9 essential services. The clinical practice  
10 guidelines that we've discussed and were updated in  
11 '96 established an algorithm for the evaluation  
12 and management for urinary incontinence. These  
13 guidelines state that PFES has been shown to  
14 decrease incontinence in women with incontinence,  
15 and that it may be useful for urge and mixed  
16 incontinence as well.

17 These guidelines were given a B rating  
18 as mentioned earlier, which is the second highest



19 rating available. And they based this on the  
20 scientific evidence from properly designed and  
21 implemented clinical studies that support the  
22 guideline statement. Because these guidelines were  
23 formulated by a neutral government agency comprised  
24 of health care research experts, the APTA strongly  
25 urges this panel to weigh the findings of this  
00092

1 report heavily in the deliberations regarding  
2 Medicare utilization of PFES for incontinence.  
3 As you are aware, another assessment has  
4 been done. At the request of HCFA, Blue Cross and  
5 Blue Shield association completed this technology  
6 assessment we've been discussing. Some remarkable  
7 contrasts exist that should be noted. For example,  
8 while the AHCPR practice guidelines were based on a  
9 review of literature by a panel of 16 leading  
10 health care experts who are experts in urinary  
11 incontinence, the Blue Cross TEC assessment was  
12 authored by one individual with input from other  
13 reviewers. While the AHCPR guideline was performed  
14 under the auspices of a neutral government agency,  
15 the technology assessment was done by a health care  
16 insurance organization, many of whose members are  
17 for profit organizations. Thus, the APTA has some  
18 concerns with the way this assessment presents the  
19 PFES studies and the results thereof.

20 We believe that with respect to the  
21 efficacy of PFES compared to sham PFES or placebo,  
22 this assessment contains inconsistencies and  
23 misrepresentations of those data. It is on the  
24 basis of these and other concerns that we would  
25 caution the panel against formulating any  
00093

1 recommendations solely based on this assessment.

2 In reviewing the study by Sand, PFES  
3 compared to placebo, the assessment offers a good  
4 deal of conjecture without any justification for  
5 statements it makes. For example, the assessment  
6 suggests an increase in leakage in the placebo  
7 group would have been statistically significant if  
8 the sample size was larger, but then suggests that  
9 if this increase had been found to be significant,  
10 it was not biologically plausible. In other words,  
11 the assessment first hypothesizes that a situation  
12 might exist, and then declares that it is not

13 biologically plausible.

14         The assessment goes on to explain that  
15 this biological implausibility occurrence might  
16 instead have been due to an artifact, due to  
17 instability of the measurements of incontinence, in  
18 this case the use of patient diaries, a point the  
19 assessment fails to make in criticizing other  
20 studies that use the exact same methodology.

21         None of these statements in the  
22 assessment are supported by quantifiable methods  
23 and more importantly, none disprove the profound  
24 clinical results of the Sand study, namely that  
25 PFES is superior to sham PFES.

00094

1         In the Joe Laycock and Jerwood study,  
2 the assessment places emphasis on the findings that  
3 the percent of patients cured was not statistically  
4 significant. It also emphasizes that the percent  
5 of patients showing greater than 50 percent  
6 improvement was not reported. The assessment  
7 chooses to downplay, if not ignore, the profound  
8 finding that the PFES group showed significantly,  
9 up to two times more greater decrease in the grams  
10 of urine leakage compared to the placebo group.  
11 Anyone who's suffered from urinary incontinence  
12 will tell you that decreased leakage is absolutely  
13 significant. And this study demonstrated how much  
14 difference PFES can make.

15         In its summary the assessment concludes  
16 that the body of literature does not support strong  
17 and consistent evidence that PFES reduces the  
18 frequency and severity of incontinent episodes. It  
19 bases its conclusion on the observation that the  
20 studies investigated different parameters of PFES,  
21 and that the administration of the interventions  
22 varied. While it's true that the studies did  
23 investigate various parameters such as frequency,  
24 duration, intensity and location, as we've  
25 discussed earlier today, the literature clearly

00095

1 shows PFES to be superior to placebo.

2         However, studies by Kerri Bo in Norway,  
3 and Olah, while confirming these findings, also  
4 suggest that the positive effects of PFES may be  
5 similar to that obtained from a structured PME  
6 program. But there is considerable difference

7 between no effect versus no better than. The  
8 important issue here, which we feel is missing from  
9 the assessment, is whether it is appropriate, worth  
10 the extra time, equipment and effort to employ  
11 PFES, while other less expensive ways can  
12 frequently but not always accomplish the same  
13 thing. That conclusion is missing. We read  
14 instead that PFES is ineffective. Clearly the  
15 assessment draws a conclusion that it's not  
16 supportable by an objective analysis of the  
17 literature.

18 PFES has been shown to be effective, and  
19 is particularly useful, and this is the critical  
20 key, please underline it in your papers, it's  
21 particularly useful intervention for those patients  
22 who are not capable of a voluntary muscle  
23 contraction. For these reasons, PFES is a valuable  
24 adjunctive intervention and should be covered under  
25 the Medicare program. With the increased frequency  
00096

1 of urinary incontinence in the aging American  
2 public, the APTA believes that it's imperative that  
3 Medicare rely heavily on the medical and research  
4 experts at the AHRQ, the neutral governmental  
5 agency.

6 In closing, the APTA urges this panel to  
7 adopt a recommendation for utilization of PFES for  
8 the treatment of incontinence at a level three  
9 category of effectiveness. We do so because number  
10 one, clinically, there is adequate evidence to  
11 conclude that it's effective. Secondly, because  
12 its efficacy is supported with valid and reliable  
13 scientific literature recognized by a panel of  
14 experts. And thirdly, probably most importantly,  
15 because of the profound benefit it can provide to  
16 your beneficiaries who suffer from this condition.  
17 Thank you for your attention.

18 DR. GARBER: Thank you.

19 MS. CONRAD: Thank you. Next is Mikel  
20 Gray, with Alfred Bent on deck.

21 DR. GRAY: My name is Mikel Gray. I am  
22 representing the Continence Coalition today. My  
23 travel to this meeting was not financed by any of  
24 the manufacturers or any manufacturer at all. I  
25 have no existing, nor do I have any previous

00097

1 conflicts of interest or financial relationship  
2 with any of the manufacturers involved today. My  
3 titles are assistant professor of urology and nurse  
4 practitioner with the department of urology at the  
5 University of Virginia. I'm also associate  
6 professor of nursing at the University of  
7 Virginia.

8 I want to first limit my comments, and I  
9 also want to take Miss Conrad's advice, and be a  
10 little supplemental to some of the comments that  
11 are already made. Therefore, I'm not going to  
12 spend significant time talking about PFES as model  
13 therapy in the management of stress urinary  
14 incontinence; that has been discussed previously.  
15 I am going to focus on the use of PFES in the  
16 management of urge urinary incontinence,  
17 particularly detrusor instability, or motor urge  
18 incontinence.

19 So, I think the first thing that I must  
20 say to you is, and to remind you that when you talk  
21 about PFES for urinary incontinence that is indeed  
22 a broad topic. Its application for urge urinary  
23 incontinence and the physiologic response to urge  
24 urinary incontinence, its application to stress  
25 urinary incontinence are two completely different  
00098

1 things.

2 There are several possible therapeutic  
3 benefits to electrical stimulation as you know, and  
4 there has been evidence presented today, and I will  
5 not again repeat that evidence, that electrical  
6 stimulation in the low hertz frequency range, using  
7 duty cycles of one to one or generally one to two,  
8 is effective in the inhibition of bladder  
9 contractions. There have been two particular  
10 randomized studies that have reported the  
11 usefulness of transvaginal electrical stimulation  
12 for the treatment of motor urge urinary  
13 incontinence.

14 Smith, in the Journal of Urology,  
15 randomized a group of 38 women with urge UI and  
16 urodynamically documented detrusor instability to  
17 treatment with either an anticholinergic medication  
18 or maximal electrical stimulation using an  
19 intravaginal probe. Outcome measures for this  
20 particular study are point on relevant to the

21 questions we've been asked to address. That is, he  
22 looked at the number of pads used within a 24-hour  
23 period, he looked at the frequency of urination  
24 reported on bladder log or voiding diary, and he  
25 also looked at the number of UI episodes within a  
00099

1 24-hour period.

2 In this particular study, cure was  
3 defined as complete obliteration of urinary  
4 incontinence, and discontinuation of pad usage,  
5 both a scientifically relevant and a clinically  
6 relevant outcome. Improvement was defined as at  
7 least 50 percent reduction in pad usage and UI  
8 episodes, as well as a drop to 10 or less voiding  
9 episodes over a 24-hour period.

10 Based on these particular outcomes 22  
11 percent of the 38 subjects were assessed as cured,  
12 and 50 percent were improved by stimulation,  
13 yielding an overall improvement rate of 72  
14 percent. Now these results were reported in the  
15 report as comparable to that achieved by pharmacological  
16 therapy.

17 However, in the author's discussion,  
18 there is an important point that must be made, and  
19 that is to say that individuals who were treated by  
20 PFES were able to avoid the bothersome side effects  
21 of anticholinergic therapy. There is good  
22 documentation in the literature that up to 82  
23 percent of patients who were started on an  
24 anticholinergic therapy, specifically Ditropan and  
25 media release, will discontinue therapy within one  
00100

1 year of starting because of intolerable side  
2 effects. And when we look at scientific evidence  
3 and balance that against clinical relevance, I  
4 would point out that there are no side effects  
5 associated with anticholinergic therapy that are  
6 specific and relevant to PFES.

7 Therefore, Dr. Antoci's point is well  
8 taken, that there must be alternative treatments  
9 for urinary incontinence, particularly for urge  
10 urinary incontinence.

11 What can we take away from this study?  
12 We can take away that the efficacy is comparable to  
13 that achieved by pro-Panthylene, a specific  
14 anticholinergic. We can also take away the lesson

15 that these patients were able to achieve these  
16 comparable results without any cholinergic side  
17 effects.

18 A second study is that of Brubaker in  
19 '97, who reported on a randomized trial, a  
20 transvaginal stimulation versus an intravaginal  
21 sham probe. This particular group included 121  
22 women who completed the study. 61 of those  
23 particular studies had urodynamically proven  
24 detrusor instability, motor urge urinary  
25 incontinence. The outcome measures in this

00101

1 particular study included subjective perceptions of  
2 improvement, objective comparisons, and pre and  
3 post-treatment urodynamic testing.

4 The most interesting and the most  
5 provocative finding in this is that among those  
6 with urodynamically proven detrusor stability,  
7 motor urge urinary incontinence, 49 percent  
8 reverted to stable detrusor function, were cured  
9 following the treatment course, as compared to 6  
10 percent who used the sham device.

11 It is unfortunate, and I certainly would  
12 acknowledge that there is a limitation in this  
13 study, because there was insufficient bladder log  
14 entries in order to measure that as an outcome.  
15 However, if you look at what she reports, which is  
16 adequate subjective improvement, you will find that  
17 there was a 35 percent adequate subjective  
18 improvement, while only 17 percent of those on the  
19 sham device achieved similar results.

20 In this particular study, chi square  
21 analysis was used to analyze that. The statistical  
22 significance, the P value unfortunately failed to  
23 reach statistical significance, although if we  
24 apply the .05 rule talked about earlier, it would  
25 have achieved statistical significance, but she

00102

1 used a .01.

2 There are uncontrolled trials that I  
3 believe are relevant. Again, I would urge the  
4 panel and I submit to you that when you look at the  
5 preponderance of data, the uncontrolled trials are  
6 helpful as supplemental to the controlled trials,  
7 although I agree with the comment that the  
8 controlled trials must form the basis of your

9 judgment. However, again, I submit to you that the  
10 uncontrolled trials can prove valuable as providing  
11 adjunctive information.

12 Primus and Kramer in 1996 used  
13 transvaginal and transrectal electrical stimulation  
14 in a group of 75 patients. They were diagnosed  
15 with urgency and/or urge urinary incontinence  
16 again, urodynamically documented. This particular  
17 study I'm pointing out, and I believe it's notable  
18 because it includes 51 women and 24 men. In many  
19 instances there are significantly greater data on  
20 men; in this case, there's significantly greater  
21 data on women, and what data we do have on men  
22 should be pointed out as well.

23 30 of these particular subjects had  
24 neuropathic basis for their hyperactive detrusor  
25 contractions; that is, they had detrusor

00103

1 hyperreflexia owing to multiple sclerosis. 45 had  
2 idiopathic detrusor instability. Following  
3 three-week of treatment with maximal electrical  
4 stimulation of at least 15 sessions, 59 percent  
5 experienced both urodynamic, objective, and  
6 subjective improvement. Follow-up was done, and it  
7 showed that the improvement persisted for  
8 approximately two years within the majority of the  
9 idiopathic group, but the neuropathic group  
10 unfortunately had a relapse of symptoms  
11 approximately two months after.

12 Jonnasen in 1990 also provided a trial  
13 that was uncontrolled. Again, subjective  
14 evaluation showed a 65 percent improvement, 67  
15 percent subjective improvement. Ericson in 1989  
16 again showed similar things. And finally, one of  
17 the first trials was done by McGuire, who showed a  
18 75 percent achievement rate of complete continence,  
19 and 15 percent were reported as improved, using  
20 strictly urodynamic criteria.

21 Can we say that there is adequate  
22 evidence that PFES is effective in the management  
23 of motor urge urinary incontinence, particularly  
24 detrusor instability proved motor urge urinary  
25 incontinence, using the strict ICS definition? I

00104

1 submit the preponderance of data shows that there  
2 is.

3           There is also an advantage that has not  
4 been adequately discussed in my opinion over  
5 pharmacal therapy, for patients who are intolerant,  
6 and I am not arguing that all patients are  
7 intolerant. That is fortunately a smaller  
8 proportion than it has been because of recent  
9 advances in pharmacal therapy. Nevertheless, of  
10 the many patients who prove intolerant of the side  
11 effects of anticholinergic therapy, transvaginal,  
12 transrectal electrical stimulation using specific  
13 parameters is effective. Thank you very much.

14           DR. GARBER: Thank you.

15           MS. CONRAD: Dr. Bent. Dr. Perry on  
16 deck.

17           DR. BENT: Good morning again. I am  
18 Alfred Bent, a practicing obstetrician and  
19 gynecologist up the street at the Greater Baltimore  
20 Medical Center. I've been program director for  
21 ACOG for a considerable length of time, so I  
22 represent ACOG today, the organization of 39,000  
23 physicians dedicated to women's health. I  
24 appreciate the opportunity to address the panel. I  
25 have no financial interest in the products being  
00105

1 discussed and have traveled at my own expense the  
2 12 miles downtown.

3           I did participate in two studies using  
4 the Hollister device which was provided to us. We  
5 were not funded. In fact, I think we spent more  
6 money to try to do the studies than we received.  
7 However, we are of the opinion that there is  
8 adequate evidence to conclude clinical efficacy of  
9 electrical stimulation. We heard about the AHCPR  
10 guidelines from 1996 that determined electrical  
11 stimulation may be helpful in mixed urge and stress  
12 incontinence, and that it was most likely helpful  
13 for stress incontinence. For stress incontinence,  
14 the studies have been presented and I don't need to  
15 repeat them. I have summarized them in my previous  
16 submission to you.

17           Brubaker's study did not show efficacy.  
18 There's a question regarding the parameters. Sand  
19 and Yamanishi showed efficacy. Luber did not,  
20 although in Luber's study, most patients had either  
21 refused or failed PME as a form of therapy.

22           I would like to spend a little bit of



23 time discussing the study that was presented in  
24 some detail in the report to HCFA, and that's the  
25 Karri Bo study, which composed patients who were  
00106

1 treated by PMEs, electrical stimulation, vaginal  
2 cones, and a control group. Once again, I probably  
3 am showing my bias, but Professor Bo is known for  
4 her rejection of electrical stimulation therapy and  
5 formal biofeedback techniques, and it does show  
6 that result in her study, in my particular bias.  
7 She does discuss the use of PFMEs, however, by a  
8 trained physical therapist through a structured  
9 program, although that's not considered formal  
10 biofeedback, and we discussed that yesterday.

11 Although the average age of the patients  
12 in the Bo study was 49.6 years, the report to HCFA  
13 stated that this study was generalizable for the  
14 Medicare population. The mean age in the Yamanishi  
15 study from '97 is 63 years; it seems to me that's a  
16 little bit more Medicare age than 49 years.

17 The biases in the Bo study do need some  
18 clarification in my opinion. The PFME group  
19 performed their exercises daily, had training in  
20 groups once a week with a physical therapist, had  
21 an audiotape with verbal guidance for 12  
22 contractions to use at home, and kept a training  
23 diary. The electrical stimulation patients were  
24 seen monthly and were observed by the physical  
25 therapist receiving their stimulation therapy,

00107

1 probably through one-way glass. Oh, sorry.

2 They used their devices for 30 minutes  
3 daily. The compliance was 93 percent in the  
4 exercise group compared to 73 percent in the  
5 electrical stimulation group, which is not  
6 surprising considering the extra stimulation in  
7 terms of contact that the PFME group received. The  
8 baseline stress pad test for the exercise group was  
9 36.6 grams and that for the electric stimulation  
10 group was 56 grams. So, I suppose you could say  
11 there's a bias in starting there in terms of what  
12 they're starting with in their pad test results.

13 A statement was made in the report that  
14 there was a 78 percent improvement on the pad test  
15 for those patients receiving exercise therapy  
16 compared to only 13 percent in the electrical

17 stimulation group. This figure wasn't really found  
18 in the Bo study, or at least I just didn't see it  
19 or read it, and it look like it was derived by  
20 comparing baseline pad test measurement and the  
21 change that occurred after therapy. Well, for the  
22 exercise group, the change that occurred was 30.2  
23 grams less and their baseline was 36 grams, so that  
24 came to me to 82.5 percent improvement. The  
25 electrical stimulation group only had 7.4 grams of  
00108

1 change in their pad test, but the baseline was a  
2 lot higher, a 56 gram loss, so their improvement  
3 was 13 percent. I don't know about the statistical  
4 methods in this technique, but it seems it's just a  
5 little bit biased.

6 Finally, in the studies on PFMEs, the  
7 objective cure rate from the study showed that 11  
8 of 25 patients were cured, which is really  
9 excellent, and for electrical stimulation it was 7,  
10 which isn't too bad, but of course not as good as  
11 the other one. If we look at subjective cure or  
12 improved, as stated in the article, that for PFMEs  
13 was 92 percent. That for electrical stimulation  
14 was 64 percent, and by the way, for vaginal cones  
15 it was 63 percent. Considering the Monaco  
16 consensus from 1998 that says that if you get 65 to  
17 75 percent receiving exercises and they improve in  
18 the short-term, that's not a bad result, so the  
19 result for electrical stimulation isn't really that  
20 bad, although of course, the muscle exercises is  
21 kind of out of sight.

22 With respect to urge incontinence, we  
23 heard about the Brubaker study and others, and it  
24 showed efficacy. There's one other; Yamanishi just  
25 reported in Urology, March of 2000, reporting on 68  
00109

1 patients with detrusor instability confirmed by  
2 urodynamic testing, in which patients were randomly  
3 assigned, so 32 received treatment and 28 received  
4 sham. Efficacy was evaluated by frequency volume  
5 chart, urodynamic testing. The active group had 81  
6 percent improvement and the sham had 32 percent.  
7 It just seems like at least for urge incontinence,  
8 there are really no dissenting studies.

9 In conclusion, we conclude that the  
10 evidence regarding clinical efficacy for electrical

11 stimulation in treating stress, urge and mixed  
12 incontinence is present and is adequate to say that  
13 yes, it is clinically effective. There must be  
14 some allowance for these patients to receive home  
15 therapy with home stimulation units. It's  
16 convenient, they have no side effects, they can use  
17 them in the comfortable environment of home, do not  
18 have to travel to the doctor's office, and the  
19 therapy in terms of duration, I think somewhere  
20 between 12 and 20 weeks. We don't know if there  
21 should be maintenance therapy or not; it's a  
22 consideration.

23 I really don't know that it should be  
24 first line therapy, if that's any importance,  
25 unless of course there are thoughts and suggestions

00110

1 on biofeedback go awry, and we can't use that. We  
2 are not treating as a statistical condition, but  
3 are interacting with a clinical condition that  
4 threatens as many as 30 percent of our older  
5 Medicare patients. We have to be able to present  
6 these elderly patients with viable conservative  
7 options other than drugs and surgery, and we need  
8 different ones, because everyone is not treated the  
9 same way. Some may require electrical stimulation,  
10 some require exercise therapy or bladder  
11 retaining.

12 Finally, the panel has a major  
13 responsibility in evaluating these therapies which  
14 we feel will help our patients progress towards  
15 continence. Thank you.

16 MS. CONRAD: Thank you, Dr. Bent.  
17 Dr. Perry? And the final presenter will be  
18 Dr. Dmochowski.

19 DR. PERRY: My name is still John Perry  
20 and I represent the Biofeedback Society. I was  
21 about to say that my financial disclosure statement  
22 from yesterday applies. The fact of the matter is  
23 I have no financial interest in any of the  
24 companies that sell electrical stimulation devices,  
25 but on the other hand, I understand that many of

00111

1 them purchase my sensors, so I guess it would be in  
2 my personal financial interest if people used more  
3 electric stim.

4 However, I would like to accomplish an

5 impossible task, and that is to change your  
6 conception, your basic category about the nature of  
7 electric stim and ask, is electric stim a drug?  
8 Now, let me explain. Agency health care policy and  
9 research decreed that incontinent individuals could  
10 receive therapy from three categories, surgery,  
11 pharmaceutical or the catchall category, behavioral  
12 interventions, and they put electric stim in the  
13 behavioral category. I hope to tell you today, to  
14 convince you today that it doesn't belong there,  
15 and it needs to be evaluated on entirely different  
16 criteria from the behavioral techniques, including  
17 the biofeedback that we discussed yesterday.

18         If you look at the guideline's  
19 descriptions, they say very clearly that surgery  
20 has certain qualities, the clinician success of any  
21 surgical procedure depends on operator expertise.  
22 Prospectus comparisons often include different  
23 surgeons with different degrees of experience and  
24 expertise. Did you ever hear that about drug  
25 studies? The personal qualities of the clinician

00112

1 are not relevant in a pharmaceutical study. Drugs  
2 must be proven to the FDA to be effective,  
3 regardless of the clinician's or the patient's  
4 belief system. The agency is in the drug, not in  
5 the dispenser. But when we turn to clinician  
6 characteristics under behavioral therapies, the  
7 Agency says all behavioral techniques involve  
8 educating the patient and providing positive  
9 reinforcement for effort and progress. And they go  
10 to on say, require personal and caregiver  
11 involvement in continued practice. If motivated,  
12 most people show improvement.

13         Those statements do not apply to  
14 electric stim. So, is electric stim a drug? Well,  
15 it certainly isn't surgery. It isn't behavior  
16 therapy either. It works like a drug, that is, it  
17 works regardless of the patient's efforts or  
18 beliefs. Therefore, I propose that we should  
19 either treat it like a drug or establish a new  
20 fourth category. If we treat it like a drug, I  
21 suggest that we apply the same rigorous standards  
22 of testing randomized control studies that are  
23 absolutely essential in the case of a drug.

24         Let's look at the data that was

25 presented in the TEC report as far as the  
00113

1 effectiveness. In comparison with placebo, we have  
2 five studies. Sand got 30 percent by diary, 66 by  
3 pad weight. Luber got 14 by diary. Laycock got 66  
4 percent by pad weight. Brubaker got no change in  
5 his parameters. Yamanishi, 33 percent by diary, 56  
6 percent by pad weight. Comparing E stim with the  
7 alternative therapies, Bo got 30 percent by diary  
8 and 13 by pad weight. Smith got 53 percent by  
9 diary. Olah got 60 percent by diary. Laycock had  
10 no data on this aspect. And Hahn had 34 percent by  
11 pad weight. Notice the range of numbers we're  
12 looking at. Here's an odd ball; Gloman, 100  
13 percent, but that's when combined with PME, and  
14 we're only dealing with an N of 7. Smith, '96, got  
15 59 percent. And Moore, '99, got 66 percent, but  
16 again, that's when combined with PME. Overall, if  
17 you average these two columns, you get 47 percent  
18 improvement to 50 percent improvement, and that's  
19 improvement in symptom reduction rates.

20 How effective is 47 to 50 percent?

21 Using Burns category of moderate equals 12 or 13  
22 leaks a week -- I couldn't find a graphic for  
23 leaks, so I had to use a graphic for diapers, but I  
24 hope you'll understand the editorial liberty here.  
25 But a 50 percent reduction in symptoms only means

00114

1 going from 12 leaks a week to 6 leaks a week, and  
2 that's still virtually one every day, so it's not a  
3 lot better. So the TEC conclusion was that for  
4 stress urinary incontinence, the literature does  
5 not provide strong and consistent evidence that  
6 PFES reduces the frequency of incontinent  
7 episodes. For urge, no conclusions can be drawn  
8 from either of the two trials that they cited. And  
9 for post-prostate, research does not demonstrate  
10 that the addition of PFES to PME improves the  
11 outcome.

12 The Biofeedback Society therefore,  
13 agrees with the major conclusions of the TEC report  
14 for PFES. And in addition, we raise serious  
15 questions about spending public funds for a  
16 technique that is decidedly less effective than  
17 other readily available alternatives, namely  
18 biofeedback. Thank you.

19 DR. GARBER: Thank you.

20 MS. CONRAD: Okay, let's move on to Dr.

21 Dmochowski.

22 DR. DMOCHOWSKI: Good morning. Roger

23 Dmochowski, of the American Urologic Association.

24 I have no financial interest in any of the

25 companies being evaluated today.

00115

1 I'll make a very brief position  
2 statement, which is our position statement that you  
3 should have in your hands and then I'd like to make  
4 further comments, but I should be substantially  
5 less than the time allotted.

6 To quote our position statement, our  
7 committee does not feel there is strong consensus  
8 on the effectiveness of vaginal, superclevic and/or  
9 anal electrical stimulation for urge, stress or  
10 mixed incontinence. The committee does urge  
11 further randomized trials to be done, looking at  
12 all objection and subjective parameters related to  
13 incontinence, and that such trials should include a  
14 comparison of electrical stimulation to behavioral  
15 modification programs within various populations,  
16 those populations being specifically men, women,  
17 the elderly, children, and neurogenic patients.  
18 Therefore, based upon our review of the literature,  
19 and somewhat to parrot your TEC report, which again  
20 was very well done: Given the above considerations  
21 and the strict criteria which you asked us to  
22 evaluate and perform this process, we feel that  
23 isolated electrical stimulation achieved a rating  
24 of level five, which would be less effective but  
25 with advantages. However, some data do exist to

00116

1 support potentially a level four categorization,  
2 which is as effective but with no advantages.

3 That's our official statement. Now let  
4 me make a couple points to amplify some prior  
5 speakers' comments. In my own clinical experience  
6 and that of many of my colleagues, urology deals  
7 specifically with urinary incontinence as a main  
8 component of their practice. Electrical  
9 stimulation is a difficult therapy to administer  
10 for some patients, but it probably has a role for  
11 patients with urgency and frequency disorders.  
12 You've heard today that patients, older patients

13 specifically, have trouble with pharmacologic  
14 therapies, they have side effects from  
15 pharmacologic therapies. This therapy is an  
16 intermediate therapy and should be viewed as  
17 potentially in integral or an integrated therapy  
18 within the global approach to patients with mixed  
19 and significantly, urgency frequency  
20 symptomologies, because it does give additive  
21 benefit, and you can see that in the nonrandomized  
22 control trials, which however are objective.

23         There is good data to suggest that there  
24 is not only good urodynamic effect, which is a true  
25 objective parameter, but also good subjective  
00117

1 effect with patients with urgency and frequency  
2 disorders. And so, it represents another option  
3 and again, that comment has been made several  
4 times, for patients who cannot rigidly be  
5 categorized as pharmacologic patients or surgical  
6 patients. And again, that really applies to a  
7 substantive majority of the patients in the  
8 Medicare population. Many of these patients are  
9 not good surgical candidates and really aren't,  
10 surgery would not be beneficial to them because of  
11 the urgency and frequency component of their  
12 voiding dysfunction. And many patients are not  
13 able to tolerate anticholinergic agents because of  
14 their side effects.

15         So I think it's important that you view  
16 the potential for this therapy within, again, the  
17 point I made yesterday, the larger behavioral  
18 modification component. Dr. Perry's comments were  
19 very germane and I would like to amplify on  
20 something that Dr. Antoci said previously, this  
21 parallelism that was made with neuromodulation.  
22 And Dr. Lefevre did a very good job of sort of  
23 categorizing what is the benefit of this therapy.  
24 There is a muscular benefit, but for urgency and  
25 frequency patients, potentially the neuromodulatory  
00118

1 benefit is the more important component. We are  
2 neuromodulating these patients. And so, you see  
3 results in urgency and frequency patients because  
4 of success in neuromodulating those patients.

5         The parallelism was made with  
6 implantable devices that this committee will look

7 at in a subsequent meeting. In no way is  
8 electrical stimulation delivered in an isolated  
9 fashion to the pelvic floor as efficacious as that  
10 therapy, the implantable therapy, but it is less  
11 intrusive obviously, and has less complications  
12 associated with it. So it definitely again, it  
13 should be viewed much like hypertensive therapy, as  
14 an increment in the overall therapeutic delivery  
15 for these patients. Any questions from the panel?

16 DR. EPSTEIN: Can you cite the evidence  
17 you think is most compelling for the latter part of  
18 the statement that you're making?

19 DR. DMOCHOWSKI: For the urgency and  
20 frequency data?

21 DR. EPSTEIN: Yeah.

22 DR. DMOCHOWSKI: Well, that is largely  
23 clinical experience. There are some studies, and  
24 Dr. Gray actually gave you two references that I  
25 believe are in his component. I don't have any

00119

1 specific references.

2 DR. EPSTEIN: Is the new Yamanishi  
3 reference one you're referring to?

4 DR. DMOCHOWSKI: The new Yamanishi  
5 reference, and Dr. Gray alluded to the urodynamic  
6 references to, which is also very compelling in  
7 terms of what this does in terms of neuromodulating  
8 overall bladder function in terms of urgency or  
9 detrusor instability, which again, is an objective  
10 criteria that can be evaluated by urodynamicists.

11 DR. EPSTEIN: Brubaker and Smith?

12 DR. DMOCHOWSKI: Brubaker and Smith,  
13 thank you. Well, there's another article that Dr.  
14 Gray alluded to. The Brubaker article has, as we  
15 know, some methodologic problems and again, it's  
16 only, if you look at that specifically for  
17 urodynamic effect, there is some urodynamic  
18 effect. But again, in other trials, we have seen  
19 that there is effect of this agent for urgency and  
20 infrequency as an isolated symptomatology.

21 DR. GARBER: Thank you.

22 MS. CONRAD: Thank you. Next we have  
23 John Whyte, medical officer for the coverage and  
24 analysis group.

25 DR. WHYTE: Thank you, Connie. Just a

00120



1 reminder to the panel that you do have a copy of my  
2 remarks, as well as Dr. Lefevre's slides that are  
3 in your supplementary packet.

4 I do want to thank Dr. Garber and Dr.  
5 Maves, as well as the other members of the panel  
6 and the members of the public who have taken  
7 considerable time over the past day, day and a  
8 half, as well as the past few months, to advise us  
9 on the topic of urinary incontinence. This is a  
10 new coverage process for us, one that is focused on  
11 evidence based decision making, and a key component  
12 of this evidence based process is the technology  
13 assessment.

14 And for this topic, we ordered a  
15 technology assessment by contracting with Blue  
16 Cross Blue Shield Technology Evaluation Center,  
17 which you heard about yesterday, is an evidence  
18 based practice center of the Agency for Health  
19 Research and Quality. We looked at three  
20 indications, stress incontinence, urge  
21 incontinence, and post-prostatectomy incontinence.

22 And for the purposes of this meeting, we  
23 are defining PFES as the use of a nonimplantable  
24 electrical device that delivers variable rates of  
25 current to the pelvic floor, with the intent of

00121

1 strengthening pelvic floor musculature. It's  
2 important to note the distinction, that we're  
3 talking about nonimplantable devices, because there  
4 are implantable devices which will not be discussed  
5 during this meeting.

6 Now, there were essentially three  
7 questions that formed the focus of the assessment.  
8 First, compared to placebo, is treatment with PFES  
9 efficacious in reducing incontinence? Two, what is  
10 the efficacy of PFES as compared to PFMEs or  
11 alternative nonsurgical treatment? And three, does  
12 the addition of PFES to PME result in improved  
13 outcomes above that obtained with PME alone?

14 For the next couple slides, I will  
15 discuss how we selected the articles that we used,  
16 as well as the TEC used, to base their assessment.  
17 There were several criteria. The first was that  
18 they were full-length peer reviewed articles  
19 reporting on outcomes of treatment for urinary  
20 incontinence, using PFES. They had to include

21 patients with documented stress, urge, or mixed  
22 incontinence, by physician diagnosis and urodynamic  
23 testing. They needed to include a concurrent  
24 comparison group of patients treated without PFES  
25 in one of the following categories: Placebo

00122

1 control treatment; was mentioned earlier, treatment  
2 with alternative nonsurgical therapy for  
3 incontinence. By this we mean PMEs, vaginal cones,  
4 bladder training, or pharmacologic agents.

5 We also wanted to see valid health  
6 outcome measures, and by that we mean a percent  
7 decrease in incontinence episodes via patient  
8 diary, a percent decrease in the volume of urine  
9 loss on a standard pad test, the percent of  
10 patients with a 50 percent or greater improvement,  
11 or the percent of patients dry.

12 We also wanted to see an adequate  
13 description of the patient population, including  
14 diagnostic categories of incontinence. And  
15 finally, we wanted to see an adequate description  
16 of the treatment course, including length of  
17 treatment and number of sessions.

18 At this juncture we will hear the  
19 results of the technology assessment. As you all  
20 met, Dr. Lefevre yesterday, for other members of  
21 the audience that did not hear him yesterday,  
22 Dr. Lefevre is an assistant professor of medicine  
23 at Northwestern Medical School, and he is a senior  
24 consultant with the Blue Cross Blue Shield TEC,  
25 where he has been for the past eight years. He's

00123

1 been the author of over 25 technology assessments.

2 Just as a point of reference, after  
3 Dr. Lefevre's remarks, I will make some additional  
4 comments, so I ask that you hold all of your  
5 questions until the end of both of our  
6 discussions. So at this point I will yield the  
7 mike to Dr. Lefevre.

8 MS. SMITH: Excuse me, Connie. I didn't  
9 get the handout. I'm sharing it with my buddy over  
10 here, but I didn't get the handout of all the  
11 slides that are being presented.

12 MS. CONRAD: It's on its way.

13 DR. LEFEVRE: I want to thank the panel  
14 again for the opportunity to present the results of

15 our work, and again to acknowledge the  
16 collaborators on this project with myself, which  
17 were primarily Ted Speroff and Naomi Aronson, both  
18 PhDs and methodologists.

19 I'm going to say again a little bit of  
20 background that I went through yesterday, and try  
21 to go through this quickly, to spend more time  
22 focusing on the evidence. I would also like to say  
23 that I am encouraged by this debate today which has  
24 been focused, the majority of the debate has been  
25 focused on the adequacy of the evidence, and I am

00124

1 encouraged to hear this kind of debate, because I  
2 think there is room for legitimate debate on the  
3 evidence, and particularly what threshold should be  
4 required for the evidence to meet a standard of  
5 efficacy.

6 So by way of background, just going over  
7 what TEC is, TEC was founded in 1985 by Blue Cross  
8 Blue Shield Association, which is the umbrella  
9 organization for the Blue Cross plans. It provides  
10 support services, technology assessments which is  
11 one of them, has performed numerous technology  
12 assessments, and has evolved from a proprietary  
13 organization into now where we perform larger  
14 assessments entirely in the public domain in  
15 partnership with AHRQ. This is just a diagram of  
16 the relationship of TEC with the Blue Cross plans,  
17 with Kaiser Permanente, one of our major partners,  
18 and with TEC subscribers, who are outside health  
19 plans, and also our contract relationship as an EPC  
20 with AHRQ.

21 TEC's major priority is to maintain the  
22 scientific integrity of the products. This is what  
23 the plans and our subscribers want. They want a  
24 review of the best available evidence. There is a  
25 critical need for this. And they can use this in

00125

1 making the difficult coverage decisions that they  
2 have to make. TEC does not make coverage  
3 decisions; we provide plans with evidence in order  
4 to help them to make coverage decisions. We do not  
5 consider costs. We use a formalized set of  
6 criteria as an anchor for what constitutes adequate  
7 evidence for efficacy, and we have a medical  
8 advisory panel which is composed of, the majority

9 of which are independent of the Blue Cross plans,  
10 which has final say over all our assessments,  
11 including the current one that we will be  
12 presenting today.

13 Now, the objective of this assessment  
14 was to determine whether PFES improves health  
15 outcome for patients with urinary incontinence.  
16 We'll take an evidence-based approach, similar to  
17 what we described yesterday, and look at the  
18 adequacy of the evidence, the consistency, and the  
19 methodological quality, as well as considering the  
20 magnitude of effect.

21 Systematic review is considered the best  
22 available way to synthesize a body of literature to  
23 determine treatment effectiveness. And to  
24 reemphasize the points I made yesterday, the main  
25 strength of systematic review is its a priori

00126

1 problem formulation and development of study  
2 selection criteria. We set up, what are the  
3 patient indications, what is the treatment that  
4 we're concerned with, what's the definition of the  
5 treatment we're concerned with, what are the  
6 outcomes that we consider clinically relevant, I  
7 comparisons, and what is the relevant comparisons?  
8 Following this, we develop a priori, what are the  
9 studies that can answer the question that we're  
10 posing in this population? Following this, we  
11 systematically search the literature, we abstract  
12 the relevant outcome data, and then we synthesize  
13 the data either qualitatively or quantitatively.

14 Going through the problem formulation,  
15 just to reiterate John's points, the patient  
16 indications are stress, urge and post-prostatectomy  
17 incontinence. The intervention is PFES, as  
18 described by Dr. Whyte. The outcomes of interest,  
19 again, similar to yesterday's outcomes of  
20 interest. What we're primarily concerned with is a  
21 reduction in the frequency and/or severity of  
22 urinary incontinence.

23 This is most commonly measured by one of  
24 two methods, patient recorded incontinence diaries,  
25 or a standardized pad test, which is specific for

00127

1 stress incontinence. There can be and expected to  
2 be a great deal of variability in these

3 measurements, both in the inherent variability in  
4 the incontinence itself, which may be expected to  
5 vary with many factors such as activity level,  
6 fluid intake, and other such variables, and there  
7 also would be expected in patient recorded diaries  
8 that, as these being somewhat subjective measures,  
9 there may also be an additional level of  
10 variability in these measures. And this is  
11 important when we get to discuss the outcomes  
12 later, regarding the outcomes of the clinical  
13 trials.

14         The reported outcomes that we're  
15 concerned with are percent change in incontinence.  
16 This is the most commonly reported outcome, percent  
17 reduction in frequency of incontinence. Also, the  
18 percent of patients improved, which is defined as  
19 the percentage of patients with at least a 50  
20 percent improvement in the frequency of  
21 incontinence is a valid health outcome. And  
22 finally, the percent of patients who are cured, who  
23 have no further incontinence, is certainly a valid  
24 clinical outcome.

25         The comparison treatments as stated

00128

1 previously are placebo. This is an efficacy  
2 question, is PFES efficacious? We also would like  
3 to compare it to alternative treatments to answer  
4 the question of what is the comparison, comparative  
5 effectiveness of PFES compared to available  
6 alternatives? And finally, it can be used as an  
7 adjunct to behavioral treatment, it can be added on  
8 to PFMEs, which has been done in several studies,  
9 and this is another relevant comparison that we  
10 will attempt to make conclusions on. Which gets us  
11 to our questions, again. Three indications,  
12 stress, urge and post-prostatectomy incontinence,  
13 three separate questions which Dr. Whyte has put  
14 forth.

15         And I would like to say just briefly  
16 that I believe the questions that HCFA has devised  
17 are the relevant clinical questions, both today and  
18 yesterday, and I believe that strongly. I don't  
19 think it's the proper time to elaborate, but I  
20 would be glad to in another forum.

21         Study selection criteria, as Dr. Whyte  
22 has indicated, full-length peer reviewed literature

23 including a concurrent comparison group, which is  
24 the most important aspect of our study selection  
25 criteria. We do not feel that uncontrolled trials

00129

1 can evaluate the efficacy of this technique  
2 adequately.

3 Now our search results revealed 12  
4 articles that met the study selection criteria, and  
5 these 12 articles report on a total of 626  
6 patients. The range of the ends in the studies was  
7 14 to 146. There were six trials comparing PFES to  
8 placebo. There were five trials comparing PFES to  
9 alternative treatments. And there was one trial  
10 which compared the addition of PFES plus PME to  
11 PMEs alone.

12 This slide just gives sort of a lay of  
13 the land to tell you where the studies fall out and  
14 where the N's fall out. And again, across the top  
15 column we have the three indications, stress, urge  
16 and post-prostatectomy incontinence, and the three  
17 separate questions, versus placebo, versus  
18 alternatives, and the addition of PFES to PME. As  
19 you can see here, the studies sort of cluster in  
20 stress incontinence. Similar to biofeedback, most  
21 of the literature is on stress incontinence. There  
22 is a significant number of studies on the question  
23 of PFES versus placebo and versus alternatives. In  
24 the other boxes there's only one study in each of  
25 the other categories. And I would also note that

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1 these add up to more than 12 studies, but some of  
2 the studies report separately on different  
3 indications; that's why you see the -- one study  
4 may make it into two different categories of  
5 reports on different indications separately.

6 Now, first let's look at the PFES versus  
7 placebo and discuss some of the key methodological  
8 features. There were five studies in this category  
9 with a total N of 243. Four of the five studies  
10 reported that their populations were randomized to  
11 PFES versus placebo. Four of the five were double  
12 blinded and one was single blinded. Three of the  
13 five had at least one potential bias, and I will  
14 talk a little bit about that in a second.

15 One important point to make in this body  
16 of literature is there is a great deal of

17 variability in the treatment delivery. This has  
18 been alluded to before; the treatment delivery  
19 varies by the type of device used, the frequency of  
20 stimulation that's given, where the device is  
21 implanted, and the time that it's used. And I  
22 would certainly defer to the clinical experts such  
23 as Dr. Sand as to the physiological rationale as to  
24 why different types of stimulation may produce  
25 different results, but I think this remains a

00131

1 matter for empiric investigation. There's really  
2 no data on telling us which is better and in which  
3 situation one may work better than another one.

4         Unfortunately one of the studies, which  
5 was the largest study, the Brubaker study, was  
6 severely limited because there was extensive  
7 missing diary data, and they were not able to  
8 report on the primary outcomes which was the  
9 reduction in the frequency of incontinence because  
10 there was too much missing data.

11         Now this slide gives the areas in which  
12 we felt there were potential biases in the studies  
13 evaluated and three of the five studies, as I  
14 indicated, have potential biases. Again, the issue  
15 of measurement bias, which I keep in parentheses  
16 here, because this is inherent to all the studies  
17 because of the way the outcome measures are  
18 constructed. It's not necessarily a criticism of  
19 the methodology of the study itself, but it's a  
20 fact that the outcome measures are not optimal, and  
21 it's a recognition that there may be measurement  
22 error inherent in these outcome measurements.

23         Now, I think it's useful to talk a  
24 little bit about the Sand study in detail, because  
25 this is I think the most influential study in the

00132

1 field and it has several strengths in the  
2 methodology. And when I put up this box here, it  
3 may appear that we're only looking at the  
4 weaknesses. It does have strengths. It was a  
5 multicenter study, it was double blinded and  
6 randomized, and they had a well described and  
7 adequate method of randomization. However, I have  
8 the box here checked for selection bias. How could  
9 that be when they have a good randomization  
10 process? Randomization is the best way to minimize

11 the chance of selection bias, and to minimize the  
12 chance that your groups will be noncomparable.  
13 However, it doesn't insure that, and particularly  
14 with small numbers of patients, it may end up by  
15 chance that the groups are not comparable. And  
16 when you look at the baseline values in this Sand  
17 article, there are differences in age; there's a  
18 seven year difference in age. And there are  
19 differences in the baseline severity of illness and  
20 the severity of incontinence. So, we feel that  
21 there may have been not, comparability of the  
22 groups may have been not as good as would have been  
23 ideal. And this was unfortunate; it was not a  
24 problem with the methodology but it happened.

25 Secondly, regarding attrition bias,

00133

1 there was a high dropout rate in the Sand trial.  
2 20 percent of the patients in the PFES group  
3 dropped out. Now, when we have high dropouts, we  
4 look at whether the analysis took these into  
5 account. And Dr. Sand had indicated that there was  
6 intent to treat analysis. There was on some of the  
7 outcomes. On the outcomes that we're going to look  
8 at, the three outcomes that we're looking at, the  
9 decrease in the frequency of incontinence, the  
10 percent of patients improved, and the percent of  
11 patients cured, it was clear that there was intent  
12 to treat analysis on two of these three outcomes,  
13 the percent of patients improved and for the  
14 percent of patients cured. However, I believe that  
15 the -- and I still believe after talking with  
16 Dr. Sand that the analysis of the reduction in the  
17 frequency of incontinence was not done on an intent  
18 to treat basis, and I will elaborate on that if  
19 people would like to here my thoughts.

20 Second, regarding the Yamanishi study,  
21 the Yamanishi study I have checked here, potential  
22 for selection bias. There is no mention in the  
23 Yamanishi study of any randomization. There's no  
24 mention at all of how the group allocation process  
25 was done. Therefore, I feel there is a potential

00134

1 for selection bias. Dr. Sand has talked to the  
2 researchers, and they have indicated to him that it  
3 was randomized. It's not in the study, it's not  
4 written anywhere in the article.



5           Let's look at the results of these five  
6 studies for the outcome of reduction in the  
7 frequency of incontinence. In the Sand study, and  
8 this is where I am indicating I do not believe that  
9 the analysis was intent to treat. There were 45  
10 patients analyzed, which was the 52 minus the 7  
11 dropouts. And there was a 42 percent improvement  
12 in the leaks per day in the PFES group and in the  
13 sham group there was a 26 percent worsening in the  
14 frequency of incontinence. The group comparisons  
15 between these two groups was statistically  
16 significant and it was at the .05 or .04 level. I  
17 don't remember which one it was, it was either .04  
18 or .05.

19           The Luber study, which is of interest,  
20 because it treats a population which is somewhat  
21 different from the other studies. This study  
22 treats patients who have failed or who have not  
23 agreed to do PFMEs, and this is a population of  
24 interest. Many people have said this is a  
25 population that PFS should be applied to. This is  
00135

1 the only study that's looked at that specific  
2 population, and there was no difference in the  
3 outcomes, as Dr. Luber has indicated previously.

4           The Laycock study did not report the  
5 values pre and post, and were not able to come up  
6 with percent improvements, but they did state in  
7 the text that there was no group differences in  
8 reduction in the frequency of incontinence.

9           The Brubaker study, this is the largest  
10 study, and this was a well designed study.  
11 Unfortunately, this was the study with the  
12 extensive missing diary data. It did not report on  
13 the reduction of the frequency of incontinence.  
14 What they did do at the end of the study is they  
15 asked the patients to complete a 24-hour diary on  
16 the frequency of incontinence, so we have  
17 post-measures, we have post-measures for the entire  
18 population.

19           Finally, we have Yamanishi which as I  
20 indicated before, did not report randomization. It  
21 showed a statistically significant difference  
22 between the PFES and the sham group, a 33 percent  
23 improvement versus a zero percent improvement in  
24 the sham group.

25           The next outcome of interest, the  
00136

1   standardized pad test outcomes, here we see similar  
2   results, although the magnitude of effect here is  
3   somewhat larger. A 66 percent decrease in pad  
4   weight in the PFES group versus an 8 percent  
5   worsening in the sham group. Luber did not report  
6   on this outcome. Laycock reported on it and had a  
7   66 percent improvement in the electrical  
8   stimulation group versus a 28 percent improvement  
9   in the sham group, a difference that did not reach  
10  statistical significance. Brubaker did not report  
11  on this. And Yamanishi reported a 56 percent  
12  improvement in the PFES group and a 45 percent  
13  worsening in the sham electrical stimulation group.

14           Now in our TEC report we make a point  
15  about this worsening of incontinence in the sham  
16  group. This is seen both in the Sand study and in  
17  the Yamanishi study. And first of all, it's  
18  curious to us; why would you expect worsening in a  
19  sham group, and you might expect that the first  
20  question is a natural history of the disease  
21  consistent with a large worsening over a short  
22  period of time, and I don't believe that's the  
23  case. I don't believe you would expect this type  
24  of worsening over an 8 to 12 week period. And  
25  secondly, we considered, could there be a negative  
00137

1   placebo effect? Could the patients have negative  
2   expectations if they knew they were getting a sham  
3   treatment? That's possible but I can't really say  
4   how likely it is; I think it's pretty unlikely.  
5   Usually a placebo effect goes in the positive  
6   direction. And finally we considered, maybe it's  
7   due to instability of these measurements, maybe  
8   these measurements are highly variable and they're  
9   prone to statistical instability. So I wanted to  
10  show just a couple of slides related to that.

11           This is the Sand data and this is the  
12  data on frequency of incontinence, leaks per day.  
13  And the aqua bars are the pre values and the red  
14  bars are the post values. And the arrow bars  
15  represent the standard deviations. Sand reported  
16  in his article the standard errors, and we  
17  converted these to standard deviations and as you  
18  can see, these are quite large, sometimes larger

19 than the value themselves. And again, the  
20 comparison is statistically is statistically  
21 significant, but we feel that the comparison is  
22 influenced by the worsening seen in the placebo  
23 group.

24 Another way to look at this would be to  
25 look at the confidence intervals around these  
00138

1 values. Again starting with the standard error, we  
2 computed the confidence intervals around these  
3 values, and as you can see, the confidence  
4 intervals are rather large and I would especially  
5 point to the placebo group, where there was a  
6 worsening from 3 leaks per day to 3.8 leaks per  
7 day, and the confidence interval around the post  
8 leaks per day which is very large, ranging from 2.3  
9 to 5.3. We also constructed an estimate of the  
10 confidence interval for the difference in the post  
11 leaks per day, which is an absolute value of 2, but  
12 a wide confidence interval. It might be as low  
13 as .4, it might be as large as 3.6. So again, I  
14 think this indicates that these measures are very  
15 highly variable and this needs to be considered  
16 when we're considering the robustness of this data  
17 in terms of the efficacy.

18 So in summary for the data on PFES  
19 versus placebo, some trials do report a significant  
20 benefit with PFES for stress incontinence, but this  
21 is not consistent. The majority of the trials do  
22 have a potential for bias and the effect size in  
23 the trials is of a magnitude that could result in  
24 bias. If we look at the effect size, and this is  
25 sort of consistent with what Dr. Perry was saying,  
00139

1 the effect size for frequency of incontinence is in  
2 the 30 to 40 percent range, somewhat higher for the  
3 pad test, but we do consider the reduction in the  
4 frequency of incontinence to be a somewhat more  
5 clinically relevant outcome than the pad test. The  
6 percent change is modest, the 30 to 40 percent  
7 range. And in both studies where statistical  
8 significance was reported, that's the Yamanishi  
9 study and the Sand study, the P value was in  
10 the .04 to .05 range. So it did reach statistical  
11 significance, but just very close to the threshold  
12 that we use for defining statistical significance.

13 So again, there is some suggestion that there's  
14 efficacy, but I do not feel this is a very robust  
15 body of data.

16 Let's look at the data on PFES versus  
17 alternatives. There were five trials with a total  
18 N of 260. All five were randomized. Four of the  
19 five were unblinded, one was single blinded, and  
20 two of the five had potential biases. This is  
21 again, a grid of the potential biases identified.  
22 In the Laycock study and in the Hahn study, there  
23 were potential biases identified.

24 Now, the results of PFES versus  
25 alternatives on the frequency of incontinence are  
00140

1 shown here. There were three studies that compared  
2 directly the results of electrical stimulation  
3 versus alternatives, and there was only one study  
4 that showed any statistically significant  
5 differences on these outcomes, and this was  
6 actually in favor of PFMEs as superior to PFES.  
7 This was the Bo study, this was 1999, this was the  
8 largest study in this group of studies, that had  
9 four groups of patients: PFES, PMEs alone with a  
10 trained therapist, vaginal cones, which is another  
11 variation of PMEs, and a waiting list control.  
12 Across all outcome measures, the PME group had  
13 superior outcomes consistently across all outcome  
14 measures. It reached statistical significance on  
15 several of these outcome measures, including the  
16 comparison with PFES.

17 The PFES would roughly give the same  
18 amount of improvement compared to the cones and was  
19 superior to the control group and it did, the PFES  
20 did reach significance over the control group on  
21 some of the outcome measures. And again, this is a  
22 waiting list control, it is not a placebo control.  
23 That's why it's not included in the first body of  
24 literature, a waiting list control versus PFES.

25 The other two studies that reported on  
00141

1 this outcome, the Smith study with an N of 18,  
2 there was a trend towards greater improvement in  
3 the PFES which did not reach statistical  
4 significance, and in the Olah study there was no  
5 difference between groups.

6 On the standardized pad tests, similar

7 outcomes, a statistically significant improvement  
8 in the PFME group versus the PFES group in the Bo  
9 study. And note again, this is a large difference,  
10 78 percent in the PME group versus 13 percent in  
11 the PFES group. The Olah study, there was no  
12 difference between PFES and vaginal cones, with the  
13 trend favoring PFES. While in the Hahn study,  
14 there was no difference in the two groups, with the  
15 trend favoring the PME group.

16 A summary of this data is that one study  
17 reports that PME may be superior to PFES, but this  
18 is not a consistent finding across the body of  
19 literature. Therefore, the evidence is not  
20 adequate to form conclusions on the comparative  
21 benefit of PFES versus alternatives.

22 Finally, in the last three categories,  
23 where there was one trial each, in the pelvic floor  
24 plus PME versus sham plus PME, there was one trial  
25 with an N of 14. There was significant baseline  
00142

1 differences in the severity of incontinence, 12.5  
2 leaks per day versus 5 leaks per day in the PFES  
3 group. They reported 100 percent improvement in  
4 the PFES plus PME, versus a 52 percent improvement  
5 in the sham, and this was significant at the P at  
6 less than .05 level.

7 For urge and post-prostatectomy  
8 incontinence, there was one trial in each of these  
9 categories, neither of which reported any  
10 statistically significant group differences.

11 So in conclusion, our conclusions are  
12 the evidence is not adequate to determine the  
13 efficacy of PFES for stress incontinence, and this  
14 is because of the reasons I enumerated previously.  
15 The results of the studies are not consistent,  
16 there are potential biases present in the positive  
17 studies, and the effect size in the positive  
18 studies, which is modest, is of a magnitude that  
19 could be explained by bias. The evidence does not  
20 suggest that PFES is superior to alternatives for  
21 stress incontinence. And evidence for PFES in urge  
22 and post-prostatectomy incontinence is sparse.

23 One final comment I would like to make  
24 is regarding the AHCPR guidelines on PFES, the  
25 conclusions of which do differ somewhat from our  
00143

1 conclusions in this current review. In 1996, the  
2 AHCPR reviewed the literature on PFES. At this  
3 time there were two randomized control trials, this  
4 was the Sand trial and this was the Blowman trial,  
5 which was the adjunct, the addition of pelvic floor  
6 to sham, both of which showed a positive effect.  
7 However, they did not feel that that level of  
8 randomized control trial evidence met their Level A  
9 evidence. They gave it a Level B evidence, which  
10 primarily was based on their results of clinical  
11 series. They indicated that further controlled  
12 trials were necessary to determine the efficacy,  
13 and gave it a Level B recommendation. So there was  
14 some disagreement. Since then, several studies  
15 have come out which has given us more data to  
16 interpret this question.

17 And that ends my presentation. Thank  
18 you.

19 MS. CONRAD: Dr. Whyte.

20 DR. WHYTE: Thank you. Now along with  
21 the technology assessment that you just heard,  
22 panel members also received for consideration  
23 additional articles and materials. We call them  
24 exclusion articles because they were not included  
25 in the technology assessment, and they were not  
00144

1 included in the assessment because they didn't meet  
2 the selection criteria that I discussed at the  
3 beginning of my presentation. And that was because  
4 they were primarily historical controls, or  
5 pre-post design, or they were frequently cited  
6 articles. But it's important to note that they  
7 have been included for consideration as part of  
8 your packets. And you've also heard a wealth of  
9 information this morning to consider. So having  
10 heard all that, I'm going to review the questions  
11 that Perry Bridger discussed early on this morning.

12 The first question is: Is the  
13 scientific evidence adequate to draw conclusions  
14 about the effectiveness of PFES compared to  
15 placebo, PFES compared to PME's or alternative  
16 nonsurgical techniques, and then finally PFES and  
17 PME's compared to PME's alone.

18 And you look at those in the Medicare  
19 populations for the following three indications,  
20 which I'm sure you all know by now: Stress

21 incontinence, urge incontinence and  
22 post-prostatectomy incontinence.

23 Let me just review, some points that we  
24 ask you to consider as you answer these questions  
25 are first related to the adequacy of the study

00145

1 design, and is there evidence that the studies do  
2 not over or underestimate the effect of the  
3 intervention. And do the studies permit  
4 conclusions about the health outcomes of the  
5 technologies? And as you evaluate the studies, we  
6 ask you to weigh the different types of study  
7 methodologies that exist. There is a recognition  
8 that not every type of study has to be a randomized  
9 prospective placebo controlled study, and that  
10 there are different methodologies to use to answer  
11 different types of questions, and we ask you to  
12 weigh that in your deliberations.

13 Other points to consider include the  
14 consistency of results, and are the results of the  
15 studies consistent or are they contradictory? The  
16 applicability to the Medicare populations. Are the  
17 results of the studies applicable to our various  
18 populations, which include the elderly and the  
19 disabled? And the applicability beyond the  
20 research setting; are the results likely to apply  
21 in routine clinical settings?

22 We discussed this yesterday, but just to  
23 review one more time, if the evidence is inadequate  
24 to draw conclusions, which would be first question,  
25 your work would be done for the day. If you answer

00146

1 yes to those questions, then -- or that question,  
2 then we will move on to a series of three  
3 additional questions, which are questions 2, 3 and  
4 4. I know you heard this yesterday, but it seems  
5 like a long time ago, so just to review one more  
6 time, the categories of effectiveness. There are  
7 seven categories.

8 The first is breakthrough technology,  
9 that the improvement in the health outcomes is so  
10 large that the intervention becomes the standard of  
11 care. Second, it's more effective, the new  
12 intervention improves health outcomes by a  
13 significant, albeit small margin as compared with  
14 an established service or medical items. Third,

15 it's as effective but with advantages; the  
16 intervention has the same effect on health outcomes  
17 as an established service or medical item, but it  
18 has some advantages such as convenience, fewer side  
19 effects, or some other advantages that some  
20 patients may prefer. It may be as effective and  
21 with no advantages, so the intervention has the  
22 same effect on health outcomes as an established  
23 alternative, but it doesn't have any advantages.  
24 It may be less effective but with advantages, so  
25 although the intervention is less effective than an  
00147

1 established alternative, but more effective than  
2 doing nothing, it has some advantages. It may be  
3 less effective and with no advantages, so the  
4 intervention is less effective than established  
5 alternative, but again, more effective than doing  
6 nothing, and has no significant advantages. And  
7 then finally, it may be not effective; the  
8 intervention has effect, or it may have deleterious  
9 effects on health outcomes when compared to doing  
10 nothing.

11         So those are the categories of  
12 effectiveness, the seven categories to keep in  
13 mind. If you answer yes to question number 1, we  
14 will move on to questions 2, 3 and 4.

15         So question number 2, and you have all  
16 this in front of you: If the evidence is adequate  
17 to draw conclusions, what is the size, if any, of  
18 the overall health effect of PFES compared to  
19 placebo for the treatment of urinary incontinence?  
20 And then just to follow through, question number 3  
21 will be, if the evidence is adequate to draw  
22 conclusions, what is the size, if any, of the  
23 overall health effect of PFES compared to PME or  
24 alternative nonsurgical techniques for the  
25 treatment of urinary incontinence? And then  
00148

1 finally, your last question, if the evidence is  
2 adequate to draw conclusions, what is the size, if  
3 any, of the overall health effect of the addition  
4 of PFES to PME compared to PME alone?

5         So that concludes our presentation, and  
6 we look forward to your deliberations.

7         DR. GARBER: This is important, but it  
8 is housekeeping. We are approximately a half hour



9 behind schedule. A number of panel members have  
10 told me that they have flights to catch, actually a  
11 little bit early. Let me float a suggestion that  
12 we break now or in an hour, a short break to get  
13 food, and carry through our deliberations while we  
14 eat, so that we can get through the entire agenda.  
15 What is the sense of the panel? This is a good  
16 breaking point in terms of the agenda, so should we  
17 break now to get food? Come back here in 20  
18 minutes.

19 MS. CONRAD: As soon as possible.

20 DR. GARBER: As soon as possible, but no  
21 later than 20 minutes.

22 (Recess taken at 11:30 a.m.)

23 DR. GARBER: I just wanted to mention in  
24 terms of comments that you would like transmitted  
25 to the Executive Committee, it is certainly my

00149

1 intention to communicate faithfully and accurately  
2 what all of the panelists said this morning and  
3 throughout the rest of the deliberations. But as  
4 long as it's not a violation, it would certainly  
5 help me if you would send me in written form some  
6 of the comments that you would like transmitted to  
7 the Executive Committee. Let me add also at this  
8 point that the Executive Committee really does want  
9 the panel's feedback about how the Executive  
10 Committee expressed their recommendations. Some of  
11 you expressed reservations about that, and the  
12 Executive Committee would certainly welcome hearing  
13 from you directly. It would probably be most  
14 effective in written form, or if you come to the  
15 Executive Committee meeting. But they are seeking  
16 input from panel members. So please express  
17 yourselves through one of the vehicles that we  
18 mentioned.

19 Now, it is time for the open committee  
20 deliberations. Before we start, I didn't get a  
21 chance to thank the public speakers from this  
22 morning and once again, I think I speak on behalf  
23 of the entire panel in expressing our gratitude and  
24 also our admiration for the way that your comments  
25 were really structured to help us deal with the

00150

1 questions at hand. Once again, at least I found it  
2 very useful in thinking about these issues.

3           Again, we have two panel members who are  
4 designated reviewers, Lisa Landy and Les Zendle.

5           DR. LANDY: Can you let Les go first?

6           DR. GARBER: Okay. Les, are you  
7 prepared?

8           MS. CONRAD: A little housekeeping stuff  
9 first. I am required to read the following just  
10 for the record. For today's panel meeting, voting  
11 members present are: Michael Maves, Linda Bradley,  
12 Kenneth Brin, Arnold Epstein, Logan Holtgrewe, Lisa  
13 Landy, Angus McBryde, James Rathmell, and Les  
14 Zendle. A quorum is present. No one has been  
15 recused because of conflicts of interest.

16           And now, Dr. Garber, you may open the  
17 deliberations and then make motions, ask for  
18 motions.

19           DR. GARBER: I think first, let's ask  
20 the two designated panel members to comment, and  
21 then the panel members generally may comment and  
22 ask questions. Dr. Les Zendle.

23           DR. ZENDLE: I just wanted to make a  
24 couple points. I was writing down a few of the  
25 things that were said this morning. One speaker

00151

1    said that there was no scientific evidence that  
2 PFES is not effective, and that's true, but I don't  
3 know that it's relevant right now. Another speaker  
4 said that the TEC assessment concluded that PFES is  
5 not effective, and I don't think that's true. I  
6 don't think that's what the TEC assessment said. I  
7 think it said there wasn't sufficient evidence to  
8 reach conclusions one way or the other, because of  
9 not consistent outcomes and some issues of bias in  
10 some of the reports, and I agree with that  
11 assessment. I think that there isn't enough  
12 sufficient evidence to reach conclusions one way or  
13 the other. And so therefore, I think that the  
14 answer to number 1 is no, there is not enough  
15 evidence.

16           Although there are some bigger numbers  
17 today than yesterday, still, when you take into  
18 consideration the number of people in just our  
19 country alone that are affected by urinary  
20 incontinence and the disability that it causes,  
21 again, I'm surprised that there isn't more numbers  
22 of people in studies to answer these very important

23 questions. So that's all I want to say.

24 DR. GARBER: Dr. Landy, are you ready?

25 DR. LANDY: Yeah. I think to be

00152

1 consistent as a panel, we need to apply the same  
2 level of rigor we applied yesterday, whether  
3 appropriate or not, and not be biased by our  
4 feelings about what happened. And I think we  
5 shouldn't compensate on what happened yesterday in  
6 what we decide today. I think looking at the  
7 question is the important thing, and the question  
8 put before us, is scientific evidence adequate to  
9 draw conclusions? That's the number one question.  
10 They are not asking us clinical evidence, clinical  
11 experience. I have my own bias about how this  
12 panel could have been more of value to HCFA as an  
13 advisory panel, and I will save that for my letters  
14 to the Executive Committee, but I think our task  
15 today has to stay focused in terms of what they  
16 asked us to do.

17 If you look at the data on stress  
18 incontinence and the E Stim, I think there are very  
19 good trials there. I think the problem goes back  
20 to how many randomized control trials are necessary  
21 for evidence, what threshold are we using, and if  
22 we should use the same threshold we used  
23 yesterday? I think as my role as a primary  
24 reviewer, and being a urogynecologist, having  
25 experience clinically in this area, the problem I

00153

1 see with the evidence put before us is one of  
2 variability. We have some very good trials here.  
3 However, they're not really comparable in certain  
4 aspects, and Dr. Sand's trial used different  
5 modalities than other trials and that came out  
6 earlier, in that of the five trials that were  
7 reviewed comparing SUI to placebo, there are  
8 different frequencies, different devices used, and  
9 that may explain the varying outcomes. That  
10 doesn't help us with the issue of consistency of  
11 data. And that is one of the criteria to evaluate  
12 adequacy of the scientific evidence.

13 So based on that, looking at my  
14 breakdown, there was one trial that used  
15 simultaneous therapy with two different  
16 frequencies, there was one trial that used single

17 frequency, another trial at 20 hertz, another trial  
18 that -- I'm not sure what the Laycock trial used.  
19 Yamanishi, which is most comparable to Sand's in  
20 terms of positive outcome towards showing a benefit  
21 of stress UI, used 50 hertz, while Sand used  
22 simultaneous frequent. I'm not sure we can just  
23 sort of lump this all together and say, even  
24 address question 2, because of the lack of  
25 consistency.

00154

1 I also, to go on the topic of comparing  
2 it to other alternative therapies, I think we were  
3 not given a lot of data there and had small  
4 numbers, and really maybe don't have enough data to  
5 go by to determine whether there is additive  
6 benefit or not.

7 And then in the third category, I really  
8 want to mention the urge incontinence. We have two  
9 studies that are very good for us to look at. I  
10 don't think the urodynamic data of Brubaker's study  
11 should be disregarded. However, we are only  
12 talking about two studies and small numbers of  
13 patients, and missing data, and I think that limits  
14 us, again, with making that decision on question 1  
15 the way it's posed to us as a panel.

16 I think as a clinician, I would  
17 interpret this data very differently and if we were  
18 asked to give advice as a clinical panel of  
19 experts, I think you would be getting a lot  
20 different answers than what you're going to be  
21 getting based on the questions as they're posed  
22 now.

23 DR. GARBER: Thank you, Lisa. If I  
24 could just beg the panel's indulgence, I just  
25 wanted to raise a general question that was

00155

1 prompted by Dr. Sand's comments first and now  
2 Dr. Landy's comments about the variability in  
3 treatments. And I don't have any comments about  
4 the treatments we are discussing today, but I  
5 think, I wanted to flag this as an issue that will  
6 come up to us repeatedly.

7 In many of the areas of medical  
8 literature that I follow more closely, a debate  
9 rages when you have multiple trials or studies of  
10 similar but not absolutely identical

11 interventions. Even radiology procedures where  
12 they use different CT scan or protocols, or  
13 cardiology studies, different ways of giving TPA or  
14 streptokinases, there is always this question,  
15 should you pool the studies together using  
16 different variance on the procedures, or should you  
17 keep them separate.

18         And the first point I would make is that  
19 you can't turn to a statistics textbook to answer  
20 that question. That's really a judgment call. On  
21 the one hand, it is possible that some ways of  
22 delivering, in fact it's likely that some ways of  
23 delivering these therapies are better than others.  
24 Rarely do you have direct trials designed to answer  
25 that question. And one of the reasons you don't is

00156

1 they would ordinarily have to be huge trials to  
2 have statistical significance, to have adequate  
3 statistical power.

4         And the other thing to keep in mind is  
5 that if you pool studies using different  
6 techniques, remember you're implicitly engaging in  
7 something called multiple comparisons. And what I  
8 mean that is that when you pool the studies, there  
9 is a chance that one method, even if they're all  
10 truly identical in terms of efficacy, one method  
11 may look superior just by chance, because you have  
12 multiple studies and you have a five percent  
13 significance level or something. If you do  
14 multiple studies, one will show greater  
15 effectiveness by chance. And so that  
16 statistician's answer in that situation is what  
17 you've done, you've looked at the data, you've  
18 generated a hypothesis, now you have to do a new  
19 study to generate the hypothesis.

20         Well, that's clearly not something we're  
21 going to engage in. We as a panel in all these  
22 situations will have to make a judgment call and  
23 seek the best possible information about whether  
24 it's appropriate to combine these different  
25 variants or to say no, these are really treatments

00157

1 and the trials of the different treatments should  
2 not be lumped together.

3         Now the consequence of deciding not to  
4 lump together ordinarily is that, and I think it's

5 probably true in this area, then you don't have the  
6 statistical power to draw conclusions very often.  
7 So that's what people who do meta-analysis  
8 constantly fret about, should I lump or should I  
9 split? If I split, maybe that's fair in some ways,  
10 but then we may lose the chance of answering the  
11 question.

12 So, I'm just saying there's no right  
13 answer, and I'm not trying to direct anybody's  
14 thinking about this issue, but keep in mind that we  
15 will probably come down to a judgment call on this  
16 issue every time we encounter it, and I expect that  
17 to be frequently.

18 Other panel comments or questions?

19 Diane, I think you were first.

20 MS. SMITH: I just wanted to address the  
21 panel just a little bit as your, one of your  
22 technical experts. And one of the problems with  
23 looking at the studies and then answering the  
24 questions is that in clinical practice how PFES is  
25 being used is as an adjunctive therapy. Now the  
00158

1 TEC report did address one study that looked at  
2 functional electronic stimulation as an adjunctive  
3 therapy, but one of the things that you can look at  
4 in order to see how clinicians are thinking about  
5 using electrical stimulation, how they're currently  
6 using them are not in randomized control trials but  
7 in descriptive studies or in case series studies,  
8 or in some of the studies that, for example,  
9 Dr. Mikel Gray talked about in his presentation.  
10 And I'm referring to page 5 of his presentation if  
11 you want to look at that.

12 What my point is is that one of the  
13 things that clinicians routinely use functional  
14 electrical stimulation for is for identification of  
15 the pelvic floor muscle. Now none of the studies  
16 address whether or not it's efficacious to use  
17 that, and yet it's common practice, okay? So they  
18 use it for identification, maybe for short-term use  
19 for the patients in office to identify their  
20 muscles and then comply with PME with biofeedback,  
21 for example.

22 The second way the clinician sometimes  
23 use functional electric stimulation is perhaps to  
24 augment the behavioral treatment of a patient in

25 order to assure a certain amount of compliance.

00159

1 And this is a clinical judgment in which the  
2 therapist or nurse decides that the patient would  
3 benefit from the augmentation of their PME routine  
4 at home by using functional electric stimulation.  
5 That's also not addressed in most of these trials,  
6 because you don't really have that factor measured  
7 and you don't really know what the clinical  
8 judgment is.

9         So what I'm trying to explain to you is  
10 that the studies test, as Dr. Perry said, the  
11 effect of a drug, or the effect of just what is  
12 FES. Now Magnus Fall, in his many physiological  
13 studies, did present a physiological basis for why  
14 FES should work, and it is a neuromodulation type  
15 of effect on a smooth muscle with lower frequency  
16 of hertz, and a higher frequency of hertz for  
17 striated muscle, for example, the pelvic floor.  
18 And this is well accepted by clinicians and people  
19 who routinely use FES in their practice, will use  
20 higher frequency when they have stress patients,  
21 will use lower frequency when they want to have,  
22 let's say modulation of urge responses or  
23 frequency, or urge incontinence. And this is  
24 really part of what people are currently doing.

25         If you want to look at some of the

00160

1 interesting conclusions that Magnus Fall made about  
2 looking at all of the studies, I think that you do  
3 have to look at his 1998 article in which he  
4 basically talks pro and con FES in general, and he  
5 makes some important points for you to consider  
6 besides the ones I've already named. One is that  
7 there is a physiological basis to FES. And two,  
8 that it is in common practice in Europe and the  
9 United States, and since it is in common practice  
10 in these areas, it would not have been so for the  
11 last 15 or 20 years had there not been some  
12 clinical efficacy to its use.

13         If you look at the trials, and I was  
14 looking at the randomized control trial of Sand and  
15 the ones that are mentioned in the TEC report, I  
16 think there is a paucity of evidence that for  
17 patients with stress UI as documented by urodynamic  
18 evidence, that there is some improvement with FES.

19 There is perhaps a greater effect for patients that  
20 have urge incontinence. And as a geriatric nurse  
21 practitioner, since we try to avoid pharmacotherapy  
22 in many of our frail elderly patients, there are  
23 many people who are treating these patients who  
24 look at FES as an alternative or an adjunct to PME  
25 in order to avoid pharmacotherapy. And there is  
00161

1 evidence in some of the trials that you heard  
2 today, and there's actually very much more evidence  
3 in some of the case reports that urge incontinence  
4 is definitely mediated positively by FES.

5 As far as the radical prostatectomy  
6 patient, there isn't a lot in the literature about  
7 that. However, if you are going to think about  
8 alternative treatments for that population, it is a  
9 popular alternative that many clinicians use in  
10 order to help the gentlemen understand and identify  
11 their pelvic floor, because they've just had a  
12 pelvic surgery and this may be a problem for them,  
13 and it is a popular alternative that's being  
14 considered by clinicians.

15 So, I just wanted to give you those  
16 comments.

17 DR. GARBER: Thank you. Marshall?

18 DR. STANTON: Thanks. There's a lot of  
19 interesting points that were raised today during  
20 the presentations, I also want to echo your comment  
21 about the excellent presentations, the quality that  
22 was done today. I'll just limit myself to two  
23 questions.

24 The first is, regards something that  
25 Dr. Lefevre mentioned but the question may better  
00162

1 be directed to Dr. Whyte, I'll let them decide who  
2 wants to address it. And that was, in  
3 Dr. Lefevre's presentation when he was talking  
4 about the Bo study, this was the one with four  
5 different groups that were randomized, one of them  
6 being a control but not a placebo group, he  
7 mentioned that this one did not meet the selection  
8 criteria for the comparison of PFES to control  
9 because it was not placebo control. And I noted in  
10 Dr. Whyte's presentation, he listed in the  
11 selection criteria placebo control, and I'm  
12 wondering why that additional level of rigor was



13 added, when if you look at the Executive  
14 Committee's interim recommendations for evaluating  
15 effectiveness, which is a quite stringent criteria  
16 for selection of studies for evidence, they do not  
17 specify placebo control, they talk about control.  
18 And that points out to me at least one study, that  
19 I'm glad Dr. Lefevre honestly pointed out, why that  
20 was not put in the analysis of the PFES versus  
21 control, but it concerns me that, were there others  
22 that were excluded from that analysis as well?

23 I have concern on that specifically as  
24 it regards today's discussion, but I also have  
25 concern for other panels and for our panel going  
00163

1 forward. Do we as panel members have to be  
2 concerned about the selection process of the  
3 studies that are being reviewed? Because I think  
4 it's difficult enough for us to actually review the  
5 ones that are given to us without having to look at  
6 the next level of how were these selected.

7 DR. WHYTE: I'll let Dr. Lefevre answer  
8 the specific question about why the Bo article may  
9 not have been included in the discussion of  
10 placebo, although an important point is that it is  
11 included as part of your materials to review prior  
12 to the panel. The part of the question that I  
13 would answer is your discussion of whether or not  
14 the panel would somehow have to review what the  
15 selection criteria were or how essentially articles  
16 were determined. I think an important point to  
17 keep in mind is that which Dr. Lefevre talked  
18 about, in terms of that we used an accepted survey  
19 instrument in terms of extracting the materials,  
20 and we followed the general principles of a  
21 systematic review. So it wasn't as if we  
22 arbitrarily decided which articles to accept or  
23 what not to accept. We framed the questions and  
24 then determined how we would select the best  
25 available evidence. Let me turn to Dr. Lefevre to  
00164

1 answer specifically about the Bo issue.

2 DR. STANTON: But along those lines,  
3 John, my major concern is that you have gone a step  
4 beyond what the Executive Committee was  
5 recommending in types of articles that are adequate  
6 for evidence of efficacy.

7 DR. GARBER: Maybe I could just step in  
8 for a moment about what the Executive Committee  
9 recommended. The Executive Committee in the  
10 discussions made it absolutely clear they were not  
11 prescribing which specific studies would be  
12 acceptable every setting. In fact, the major  
13 message from the document said a variety of forms  
14 of evidence would be suitable, and that the key  
15 question would be, is this study design likely to  
16 be free of bias. And so the Executive Committee in  
17 their discussions made it quite clear they didn't  
18 think they could say you always need a double  
19 blinded randomized control trial. In fact, they  
20 said that wasn't true. Nor did they say that a  
21 case control study will always be adequate. They  
22 left a great deal to the discretion of the  
23 panelists in deciding what constituted adequate  
24 evidence, but they asked the panel to adhere to the  
25 principle of looking at studies that were likely to  
00165

1 be free of bias. How you interpret that is really  
2 handled on a case-by-case.

3 DR. LEFEVRE: I think that Dr. Garber's  
4 point is very important and I would echo that,  
5 and also say that whenever we're looking at a body  
6 of literature or a technology or a treatment, we  
7 would first want to say, what is the most  
8 appropriate and the most rigorous control that we  
9 can have, and that's going to vary by the type of  
10 technology we're looking at. For example, with  
11 biofeedback, we did not try to look at placebo  
12 controls, because it would be very difficult if not  
13 impossible to construct a placebo control for  
14 biofeedback. Therefore, we agreed that the most  
15 appropriate control group would be PME alone.

16 In this case, for PFES it's nice that  
17 it's quite easy, or not maybe easy, but it's  
18 appropriate to use a placebo control, where you can  
19 use a sham instrument. And this is the most  
20 appropriate and the most rigorous type of control  
21 that can be used with this technology to show  
22 efficacy. So for this technology in the clinical  
23 context in which it's used, we feel that the most  
24 important comparison is with a placebo control.  
25 And we would always prefer a placebo control when  
00166

1 it's feasible to do that kind of control. When  
2 it's not feasible to use that kind of control, we  
3 will consider the next level of control that might  
4 be most appropriate towards that particular  
5 technology.

6 DR. STANTON: I won't belabor that, but  
7 if I may ask a second different question that I  
8 will be a little briefer on, a number of speakers  
9 made reference to the AHCPR document on urinary  
10 incontinence in adults, the clinical practice  
11 guidelines. And with it being mentioned a number  
12 of times, it seemed like it was a very important  
13 document and one that was formed by a panel of  
14 experts, all in the field, looking over the  
15 literature. I just got a copy of this about an  
16 hour ago and I can tell you there's no way I'm  
17 going to be able to look at this and have any type  
18 of input for this panel discussion based on what  
19 these experts have said.

20 I know that HCFA has to filter the  
21 materials that are sent to the panel. Otherwise,  
22 it would be an impossible task. However, having  
23 sent the TEC assessment, which is in some regards  
24 similar to this expert opinion, I'm just wondering  
25 why this did not meet the criteria for being sent  
00167

1 to the panels. And also I'd be interested, am I  
2 the only one, or did anybody else on the panel  
3 receive this?

4 DR. WHYTE: If I could address your  
5 question, what we mailed to the panel was what the  
6 Executive Committee requested to be sent to the  
7 panel for consideration as part of a packet of  
8 material, which was a technology assessment and  
9 evidence tables, and that's what we submitted in  
10 this circumstance, also with the articles. Now, as  
11 you may recall, in the cover letter that was sent  
12 to you with the materials that I just mentioned was  
13 a specific statement, there was a catalog of  
14 materials, and on that catalog was the AHCPR  
15 guidelines. Specifically in that sentence about  
16 the catalog, we said we would make it available,  
17 any item on that, to any panel member which wished  
18 to review it.

19 And we also had a conference call which  
20 I think you were a part of, but I'm not completely

21 sure. You're nodding your head that you were part  
22 of that call. If you remember as part of the call,  
23 we spent considerable time on the items that were  
24 part of the catalog. Your colleague Diane Smith  
25 asked for several items as part of the catalog, as  
00168

1 well as other members. I made it specifically  
2 clear during that meeting that if there was any  
3 item that you wanted, you should request it. So in  
4 all fairness, there was the opportunity to request  
5 that specific item if you so desired.

6 DR. STANTON: John, that's technically  
7 and legally correct. However, I'm a humble  
8 cardiologist, so to look at a number of different  
9 things in the urologic literature that are listed  
10 as things that I could request, I think is somewhat  
11 unfair to me.

12 DR. GARBER: Maybe I could interject,  
13 since I bear some responsibility. One of my formal  
14 responsibilities as chair is to consult with the  
15 HCFA staff about what should be included, and we  
16 always make a judgment call. I can tell you when  
17 we heard from the first two panels that met, they  
18 resented the overwhelming amount of material that  
19 they received. We tried to strike a balance. I  
20 won't say that we don't make mistakes in this, and  
21 that's why we asked for active panel input every  
22 step of the way about what materials should be  
23 included. So I actually think it might have been a  
24 good thing to include this in the materials sent  
25 out to everyone. And let me just say that we're  
00169

1 learning as we're going, and you as panelists, as  
2 you see the provisional lists and when we have  
3 those conference calls, we kind of need to identify  
4 materials that are important. I suspect, if the  
5 rest of you are anything like me, that if you got a  
6 copy of every single material that was sent in, you  
7 would feel overwhelmed, and so we do have to make  
8 some judgment call, and I apologize if we didn't  
9 press hard to include that in the packet of  
10 materials, but that is a responsibility of the  
11 chair to consult with HCFA staff and that is not  
12 something I pressed for.

13 DR. RISAGER: Just briefly, I would like  
14 to say I loved the way it was organized and we had

15 the opportunity, but everyone has a different view  
16 of what they would like. For me, this was just  
17 right.

18 DR. GARBER: Michael Maves.

19 DR. MAVES: I've actually made a couple  
20 of comments to Connie and to the staff, and I want  
21 to join with Michael in saying they did a wonderful  
22 job. I might suggest however, and this might be  
23 something we should take back to the Executive  
24 Committee, is that when there is a relevant AHCPR  
25 guideline, which as we all know, tends to be sort

00170

1 of the Bible if you will, of guidelines, it's  
2 probably appropriate to include it. And I made a  
3 suggestion to Connie to perhaps include some  
4 selected relevant testimony when it's available  
5 ahead of time so that we sort of have not only the  
6 pro or the con, but the other side of the  
7 argument. So again, I think they have done a  
8 wonderful job and have struck a nice balance, but  
9 as I've gone through it, it would have been helpful  
10 in looking at the information to have an idea or  
11 insight of what the opposite argument might  
12 potentially be.

13 DR. GARBER: Les?

14 DR. ZENDLE: I guess I view the  
15 technology assessment as helping us look at the  
16 evidence that meets a certain level and put it into  
17 evidence tables so that we can understand it. So  
18 the question I would have, and Frank, maybe you can  
19 answer this, is there any evidence in this that  
20 would have met the level that you had decided, the  
21 Executive Committee decided to frame the questions,  
22 and be relevant to this discussion, that wasn't  
23 included in the TEC assessment? I would assume no,  
24 because otherwise it would have come up on the  
25 MEDLINE search.

00171

1 DR. LEFEVRE: No. The two randomized  
2 control trials that were discussed in the AHCPR  
3 guidelines were included in the TEC assessment. We  
4 had additional evidence that has come out since the  
5 AHCPR guidelines has been done. The rest of the  
6 evidence considered by AHCPR were uncontrolled  
7 studies.

8 DR. ZENDLE: And also, and this is

9 really trying to answer a different question than  
10 at least we so far have been asked to answer.

11 DR. GARBER: Diane, you had your hand  
12 up.

13 MS. SMITH: I just wanted to make a  
14 comment since we're just discussing the materials.  
15 It was really nice for the electrical stimulation  
16 half to have all the articles, even those that were  
17 sort of not considered by the TEC committee. I  
18 really appreciated that. It gave me a very easy  
19 way to review things. And I had to go search  
20 things for the biofeedback, and I think that is  
21 really not a good idea. And so, I would encourage  
22 you since you're spending so much time reviewing  
23 the literature, you know what relevant articles  
24 people are interested in, the way they were  
25 included for stim was really great, I thought.

00172

1 DR. GARBER: Logan.

2 DR. HOLTGREWE: Well, Les more or less  
3 made my point. I would just remind everyone that  
4 the AHCPR guidelines on incontinence came out in  
5 '96 based on literature that is now at least half  
6 a decade old, and the two papers that you discussed  
7 were in the materials. The other guidelines were  
8 in '92, they're a decade old. And I have been  
9 involved in AHCPR guideline production and it takes  
10 a year or so to get it done. So you're looking at  
11 decade old material in the case of the '92  
12 guidelines, a half a decade old material in the  
13 case of the '96 guidelines. I agree with Les that  
14 the AHCPR guidelines were aimed at a somewhat  
15 different direction than this panel's charge and  
16 responsibility.

17 DR. GARBER: Arnie?

18 DR. EPSTEIN: I do want to -- I hope I  
19 have this right. I want to correct what I think  
20 was a misstatement about the AHCPR conclusions.  
21 What I heard earlier was that Type B evidence  
22 refers to evidence that reflects the strength of  
23 clinical trials. Am I speaking incorrectly?

24 SPEAKER: Clinical series.

25 DR. EPSTEIN: Let me read to you what it

00173

1 does say, so at least there is no confusion amongst  
2 the panel. Type A is, the recommendation is

3 supported by scientific evidence from properly  
4 designed and implemented controlled trial providing  
5 statistical results that consistently support the  
6 guideline stated. B, the recommendation is  
7 supported by scientific evidence from properly  
8 designed and implemented clinical series that  
9 support the guideline statement. And C, the  
10 recommendation is supported by expert opinion. And  
11 I guess that's consistent with what you were  
12 saying, and that innuendo reflects the strength of  
13 their opinion and it sounds like in the subsequent  
14 years, there have been three additional studies  
15 which provide less consistent evidence. Is that  
16 fair to say?

17 DR. LEFEVRE: It's fair to say. There  
18 was one study we looked at, Laycock, which was  
19 published in '93, which was not in the AHCPR. It  
20 was published in a less high profile journal, so  
21 that was -- the other two studies were published  
22 since the guidelines had come out.

23 DR. GARBER: Let me ask, this is a  
24 little bit early for it, but are the speakers who  
25 are scheduled -- oh, we don't have any scheduled  
00174

1 for this session.

2 All right. If there's no objection, I  
3 thought we would move on to the open public  
4 comments period now. Does the panel agree?  
5 Arnie?

6 DR. EPSTEIN: I would just like to  
7 request that unlike yesterday, if the open comments  
8 could really direct pertinent to the evidence and  
9 the task at hand? I think we've gone through a  
10 long two days and I don't want to relive the  
11 clinical scientific controversy again if we can  
12 avoid it.

13 DR. GARBER: Okay, thank you. We now  
14 enter into the period of open public comments.

15 MS. CONRAD: Okay. Yes.

16 DR. SAND: Peter Sand, from Northwestern  
17 University. I wanted to speak to some of the  
18 questions and things that arose after my earlier  
19 presentation today. First just briefly, the  
20 Yamanishi study that was discussed for stress  
21 incontinence, not the one that was just introduced  
22 by Dr. Bent from last month in the journal titled

23 Urology, this was a randomized control trial; it  
24 was also double blinded, which would make it hard  
25 to understand how it wouldn't be randomized.

00175

1 In our trial, and the excellent review  
2 that Dr. Lefevre provided us with, there were no  
3 dropouts in that study for lack of efficacy.  
4 Within the body of paper that's referenced, three  
5 of the active group could not comply with the visit  
6 schedule, two withdrew because of some vaginal  
7 irritation, one dropped because of some urgency  
8 with the device in the second week of a 12-week  
9 study, and one dropped because her stress  
10 incontinence was actually resolved, and she was  
11 having problems with her diverticulitis, and needed  
12 hospitalization for antibiotic therapy and couldn't  
13 comply beyond that with study visits. The one sham  
14 patient who withdrew was because of problems with  
15 complying with the visit schedule.

16 In that study also, Frank brought up the  
17 point that there may be a selection bias in that we  
18 have a difference in patient age. We were  
19 concerned about this and in a secondary publication  
20 within the International Urogynecologic Journal,  
21 1997, we analyzed those patients over and under the  
22 age of 65, and found no differences for outcome.  
23 That was not picked up in the survey of articles  
24 that were reviewed in the TEC report, nor would I  
25 expect it to be.

00176

1 In addition, there was some concern  
2 about the variability of our measures. I'm not a  
3 statistician, I really don't know how to assess  
4 that at all. I think it's difficult. These were  
5 standard measures, pad tests and voiding diaries,  
6 that in a double blinded study we wouldn't expect  
7 either the investigators or the participants to be  
8 able to manipulate these. To further reflect on  
9 that, we did a subanalysis at the end of the study  
10 that was not published in this paper because I  
11 hoped to write a subsequent paper on the difficulty  
12 of randomized control trials, where we asked the  
13 patients at the end of the study, did they know what  
14 device they were using? 60 percent of the patients  
15 guessed incorrectly as to what device they were  
16 using. 87 percent of the investigators guessed



17 wrong as to what device the patients were using.  
18 So I don't think we could have really interfered or  
19 biased the results based on that sort of analysis  
20 of the blind.

21 In addition, if we bag the stress  
22 incontinence information or we put that aside for a  
23 moment, I think it's important to recognize that  
24 with the introduction of the latest data from  
25 Yamanishi in the March study, last month, which  
00177

1 obviously no one has been able to analyze  
2 thoroughly, that we have three randomized control  
3 trials which all show by different measures that  
4 electrical stimulation is effective, more effective  
5 than placebo in treating detrusor instability and  
6 its symptoms of urgency, frequency and urge  
7 incontinence.

8 Whatever the measures are, for example  
9 in the Brubaker study where you don't have the  
10 measures of the voiding diaries or pad tests, you  
11 do have urodynamic data. In the other studies, you  
12 do have the measures that were reviewed in the text  
13 study. So it's hard for me to understand in three  
14 rather large studies looking at detrusor  
15 instability how we couldn't conclude that there is  
16 a significant effect beyond the effect of placebo.  
17 Thank you very much.

18 DR. GARBER: Dr. Sand, could I just ask  
19 you a clarifying question? At the beginning of  
20 your comments, you went through the dropouts. The  
21 intent to treat question was, did you attribute the  
22 outcomes among the dropouts, were they included in  
23 the group of initial assignment, or you not able to  
24 get outcomes for the reasons that you mentioned for  
25 those people?

00178

1 DR. SAND: The outcomes were obtained at  
2 study closure. So when the patients dropped from  
3 that trial, they were assessed for their subjective  
4 and objective outcomes. The exception was, two  
5 patients refused to comply.

6 DR. GARBER: So everyone except those  
7 two patients had their outcomes attributed to one  
8 or the other arms of the trial?

9 DR. SAND: Yes, they did.

10 DR. SPURLOCK: John Spurlock, from

11 Bethlehem, Pennsylvania. Yesterday I presented our  
12 presentation concerning electrical stimulation  
13 combined with biofeedback for urge incontinence and  
14 you have copies of those graphs from yesterday.  
15 But I didn't have time to state yesterday, or it  
16 was inappropriate because it was dealing more with  
17 electrical stimulation, was an important component  
18 and use of PFES. As a clinician, I'm often, I know  
19 that this therapy works, I know my patients are  
20 going to get better, but what do I do in the  
21 patient that cannot demonstrate any type of pelvic  
22 floor contraction, they can't do a Kegel.  
23 Therefore, biofeedback, there's nothing to train  
24 there. The advantages of electrical stimulation or  
25 several weeks of electrical stimulation is that it  
00179

1 will produce adequate contractility and identify,  
2 allow the patient to identify and begin contracting  
3 the pelvic floor muscles.

4 And I think that's a very important  
5 point about electrical stimulation, it allows me as  
6 a clinician to get these patients over the hump so  
7 to speak, to the point where they can begin to,  
8 whatever therapy you decide is adequate after that  
9 point, to begin contracting those muscles. Thank  
10 you.

11 DR. GARBER: Thank you. Dr. Angus  
12 McBryde, I think had his hand up before.

13 DR. McBRYDE: Yeah. While Dr. Sand was  
14 at it, I just had a question. As an orthopedist,  
15 we use a lot of muscle stimulators and muscle  
16 stimulation, for instance for chronic back and for  
17 rehabilitation after total joints, and there is  
18 indeed a great variability in the duration and all  
19 the other parameters of the hardware. And I just  
20 want to hear you say again, I know you mentioned it  
21 in your talk, but what, in the context of the  
22 positive and negative articles as we heard  
23 Dr. Lefevre broach them, how big a factor do you  
24 think the variability of the different products  
25 that were used was? Again, can you tell me that?

00180

1 DR. SAND: Even greater than the  
2 pronunciation of Frank Lefevre's name.

3 DR. McBRYDE: I did pretty well.

4 DR. STANTON: Just for the record, I

5 think it's really a shame that this wonderful young  
6 investigator has done all this work for us and  
7 we're still not all sure how to pronounce his  
8 name. I think if the panel concludes anything, we  
9 should conclude that.

10 DR. SAND: There is really significant  
11 variability when we look at over 200 studies in the  
12 literature, because of the numerous commercial  
13 devices that are out there. With the Yamanishi  
14 device, the pulse duration of this device was 1  
15 millisecond. The pulse duration of the device  
16 reported in our trial was .3 milliseconds. The  
17 pulse duration is uniquely different in the devices  
18 used in the Luber and Brubaker trial, these were  
19 the same; they both used the same device and that  
20 was 2 milliseconds.

21 In basic science research in cats that  
22 Magnus Fall did in his original treatise on  
23 electrical stimulation some 30 years ago, they  
24 favored 2 milliseconds, along with a frequency of  
25 10 hertz, for the stimulation and treatment of  
00181

1 detrusor instability that was invoked in cats. Now  
2 they concluded that this was their recommendation,  
3 and they also had some practical concerns regarding  
4 amperage, voltage, expending batteries and having a  
5 practical device electronically. But this became  
6 the norm for treatment in detrusor instability.  
7 And then when companies that tried to formulate new  
8 devices, they had to be electronically unique in  
9 order to patent them. And so, we have come up with  
10 numerous devices that stimulate in different ways.

11 If I can just segue, the panel has  
12 brought up the point and it's great, yesterday and  
13 today, why don't we have better studies when  
14 there's so many patients with this problem? This  
15 is probably not perfectly appropriate for this  
16 panel, but I mean, one thing to realize is to do  
17 these trials, it took me four years to convince the  
18 U.S. Corporation to fund our trial. The Brubaker  
19 trial was supported by the American Urogynecologic  
20 Society tangentially, and they were given free  
21 stimulators. Part of their problem with being able  
22 to collect the data completely was no funding and  
23 not enough manpower and resources. We are never  
24 going to get the data if we don't have some

25 reimbursement. I know that is not the issued of  
00182

1 the panel, but it is an explanation of a question  
2 that keeps coming up. It's very difficult, very  
3 expensive.

4 MS. CONRAD: I think Dr. Whitmore was  
5 next.

6 DR. WHITMORE: Yes, just very briefly, I  
7 wanted to review what it means to use a sham device  
8 for PFES. Normally, patient is brought in,  
9 evaluated, and a practitioner works with the  
10 patient on how to use the device, and the intensity  
11 is turned up until the patient feels a contraction  
12 and usually the practitioner will see an anal wink  
13 or a contraction. Now, when you get into an RCT  
14 with a sham device, and the way it was done in the  
15 Sand trial, and I didn't understand this until it  
16 became part of the trial, the patients are not  
17 given any instruction. The inactive or sham device  
18 and the active device are given to the patient, and  
19 the patient is told to turn the device up to a  
20 certain number. Therefore, in the active group, we  
21 cannot be assured that they are reaching maximal  
22 intensity, which is required to sometimes get a  
23 pelvic floor contraction for stress incontinence,  
24 or to inhibit a bladder contraction for urge  
25 incontinence. Therefore, we may be underestimating  
00183

1 our results.

2 DR. GARBER: Thank you. Please identify  
3 yourself.

4 MS. GARDNER: My name is Pat Gardner.  
5 I'm director of reimbursement for a very small  
6 medical products company called Tim Medical  
7 Technologies out of Minnesota, and I don't have a  
8 question and I don't have any clinical data to  
9 support or provide, but I do have a statement I  
10 would like to make. My understanding of the  
11 procedures that are being followed in the  
12 legislation, and from the notice establishing the  
13 Medicare Coverage Advisory Committee, that there  
14 are several options available to HCFA once the  
15 panel and the Executive Committee have completed  
16 their work. They can either issue a national  
17 coverage policy for the therapy, issue a national  
18 noncoverage policy as they did with PFES in the

19 early '90s, issue a coverage policy with  
20 limitations as they did with Contagium, make no  
21 decision and therefore leave the decision of  
22 coverage in the hands of the carriers.

23 Dr. Hill stated earlier today that  
24 industry wants us, HCFA, to make evidence based  
25 coverage decisions. He also mentioned industry's  
00184

1 desire for more transparency to the coverage  
2 process. Dr. Hill and other HCFA representatives,  
3 and also Dr. Garber, stressed to the panel and the  
4 audience today that all evidence would be taken  
5 into consideration in rendering a coverage  
6 decision.

7 Taking all that into account, I am still  
8 left with the opinion that transparency of the  
9 coverage decision process has not been met. While  
10 I now have access to these panel meetings as  
11 required under law, and as opposed to the previous  
12 process under the technology advisory committee  
13 meetings, and I do find this process incredibly  
14 educational, the actual process HCFA will use for  
15 weighing all the evidence is still unknown. Again,  
16 therefore, the test of transparency has not been  
17 met as I see it. Thus, I'm left to conclude that  
18 HCFA's coverage decisions will, in fact must focus  
19 solely on the issue of whether the scientific  
20 evidence is adequate to draw conclusions about the  
21 therapy's effectiveness.

22 And to discount all other evidence since  
23 there is no mechanism, at least none stated to  
24 assign a weight to the other evidence provided to  
25 it, as such, I agree with Dr. Stanton's comments  
00185

1 made at the start of today's meeting, that new  
2 technology, and none of the technologies we've  
3 talked about in the last two days are new, will be  
4 stifled under this process, because the scientific  
5 evidence will likely never be adequate to draw  
6 conclusions, because the cost and time required to  
7 collect such evidence is cost prohibitive,  
8 especially for small start-up companies.

9 I would recommend that the panel urge  
10 the Executive Committee to address the issue of  
11 weighting nonscientific evidence, or if that is not  
12 the purview of the MCAC Executive Committee or

13 these panels, to urge HCFA coverage and analysis  
14 group to state its methodology for weighing all  
15 types of evidence and testimony. Thank you.

16 DR. GARBER: I believe that comment was  
17 primarily about procedural issues, most of which  
18 are outside the purview of this panel, but I wonder  
19 if Dr. Hill would care to make a comment.

20 DR. HILL: Just to thank you and to urge  
21 your participation in and support for our efforts  
22 to publish a regulation which defines what we think  
23 Congress meant when it told us to pay for that  
24 which is reasonable and necessary.

25 MS. JENSEN: I'm Deborah Jensen from  
00186

1 EMPI. I guess my comments at this point in time  
2 are really addressed to what the question the panel  
3 should be answering is, and I want to make one  
4 point of clarification with respect to the current  
5 Medicare coverage policy for PFS. I'm not sure if  
6 all of the panel is aware; right now, this  
7 technology does have a national noncoverage policy  
8 that was instituted in 1994. What this means from  
9 a patient point of view is that under no  
10 circumstances can any patient under the Medicare  
11 program receive reimbursement for this technology,  
12 regardless of the clinical situation and the  
13 judgment of their clinician. There is no  
14 opportunity for appeal. And earlier this morning,  
15 I talked about the fact that what does that mean  
16 from a scientific point of view? This decision  
17 seems to imply that the scientific literature has  
18 demonstrated that this therapy is either not safe  
19 or not effective for any beneficiary, and I think a  
20 careful review of the literature does not allow  
21 this particular conclusion to be drawn. Thank you.

22 DR. GARBER: Thank you. Yes?

23 MS. WEST: My name is Linda West. I'm a  
24 nurse and I have done biofeedback since the  
25 mid-1970s and have been involved with pelvic floor  
00187

1 work for the past 15 years. I'm currently a  
2 consultant with SRS Medical Systems, which is a  
3 biofeedback instrumentation company. I teach for  
4 them. I wanted to maybe offer an answer as to why  
5 there are no more studies. When you go through  
6 medical school and as a nurse, when we went through

7 nursing school, we were not taught behavioral  
8 techniques. We were taught about medications and  
9 surgery, and it's only been recently in the last  
10 few years that it has become more aware that  
11 behavioral techniques can be an adjunct to medical  
12 practice. So when you're trained as a surgeon or  
13 to use medications, you really don't think about  
14 using the behavioral techniques. And the  
15 physicians that we have had going through workshops  
16 and that I have done on-site in-services with  
17 become more acutely aware that there's more to this  
18 than just squeeze and relax as they have been  
19 telling patients. So I think if we, you know,  
20 hopefully in my lifetime, medical schools will  
21 begin to teach behavioral techniques and the  
22 appropriateness of using them as an adjunct to  
23 medical practice. Thank you.

24 DR. GARBER: Thank you. Yes.

25 DR. WHITMAN: Hi. My name's Lisa

00188

1 Whitman. I am the director of clinical research  
2 and regulatory affairs for EMPI. First of all, I'd  
3 like to compliment Dr. Lefevre and his colleagues  
4 for a fine job on the technology assessment,  
5 considering it's one of the best jobs I have seen,  
6 at least in reviewing the basis of incontinence,  
7 and I would also like to sympathize with him for  
8 the mispronunciations, because with a name like  
9 Rugermanhyniak (phonetic), I can feel his pain.

10 One point of clarification with regard  
11 to the review that I discussed with him is in  
12 reviewing the Karri Bo study --

13 DR. GARBER: Please speak up into the  
14 microphone.

15 DR. ZENDLE: Hearing aids aren't covered  
16 by Medicare.

17 DR. WHITMAN: With regard to the Karri  
18 Bo study, within the groups, I would contend that  
19 there is a performance bias issue because the PME  
20 group actually had visits into the clinic on a  
21 weekly basis, whereas the other groups only went in  
22 on a monthly basis, so it was 24 visits versus 6  
23 visits for the other groups, and I just wanted to  
24 make that clarification. Thank you.

25 DR. GARBER: Thank you. Yes?

00189

1 MS. SEMPLE: I'm Carolyn Semple. I'm a  
2 registered nurse and I work for seven urologists.  
3 I just wanted to go on record as saying that I had  
4 a man ten years post-prostatectomy, and he had  
5 never been dry. He came in and I asked him to do a  
6 bladder chart and he just laughed at me. I leak  
7 all day. But with electrical stim he is now  
8 voiding. And so I think that's important to know,  
9 that we can treat these people with electrical  
10 stim. Thank you.

11 DR. GARBER: Thank you. Frank.

12 DR. LEFEVRE: It is pronounced Lefevre.  
13 And I think Dr. Whitman is correct; she pointed out  
14 that there is a difference in the intensity of  
15 treatment in the Bo study, and I wanted to just  
16 clarify that. That was an error in the TEC  
17 report. It wouldn't change the conclusions,  
18 because even though Bo did show an improvement as  
19 compared to the pelvic floor, we don't think the  
20 body of evidence is sufficient to make that  
21 conclusion, and we said that. So that was an  
22 error, but I don't think it would change at all the  
23 overall conclusions.

24 But the real point I wanted to make was  
25 regarding the issue of future studies being done.

00190

1 I disagree with the statement that if a noncoverage  
2 policy is issued and if the panel decides that the  
3 evidence is inadequate, that that will suppress  
4 future studies. I believe the opposite is true. I  
5 believe if a coverage decision is issued, and that  
6 this is covered, there will be no further incentive  
7 to do the studies. This is the case with many  
8 technologies, old technologies in the past, where  
9 they've been disseminated without good studies,  
10 they become the standard of care, and we never get  
11 the good studies. I believe that if the panel  
12 recommends that the evidence is inadequate, and a  
13 noncoverage policy is issued, this should stimulate  
14 further studies to be done. I understand the  
15 difficulty with the funding issues and the  
16 difficulty in doing studies. I would hope that  
17 someone would pick up the ball on this and take  
18 charge and recognize the need to fund these  
19 studies, whether that be HCFA, NIH, Blue Cross Blue  
20 Shield, or somebody with the appropriate resources



21 to do so. And I believe that is true.

22 DR. STANTON: I'd like to comment. Dr.  
23 Lefevre, I think you're dead wrong on that. One  
24 example is implantable cardiac defibrillators.  
25 They were approved and are covered by HCFA, by  
00191

1 Medicare, and the definitive study showing that  
2 implantable defibrillators prolong life compared to  
3 antiarrhythmic drugs in people who suffer sudden  
4 death was just published in 1998, the Avid trial.  
5 HCFA initiated coverage of ICDs in 1985. That's  
6 one example; I could give you many others.

7 I'd also like to say that as someone who  
8 oversees all the arrhythmia management clinicals in  
9 a very large medical device company, that you're  
10 also wrong about noncoverage not inhibiting future  
11 trials. I guarantee you, it will inhibit future  
12 trials, because you get noncoverage from Medicare,  
13 you also get insurance companies that follow suit  
14 and all of a sudden there is noncoverage for that  
15 technology for everyone in the United States.

16 DR. GARBER: All right. We've actually  
17 begun to stray rather far from the questions in  
18 front of us. These are extremely interesting  
19 questions and we could have a spirited debate, and  
20 they are relevant to HCFA's coverage decision  
21 making process, but I'm afraid this panel is not  
22 the right place, and this is the sort of comment  
23 that I believe is appropriate to submit to HCFA in  
24 the Executive Committee, but I would like to stay  
25 focused on incontinence please. Yes.

00192

1 MS. PALUMBO: Mary Val Palumbo. I'm  
2 representing the Continence Coalition, a group of  
3 nurses providing incontinence therapy across the  
4 country. I do believe HCFA wants to from a  
5 clinician. I don't think they would have put a  
6 consumer representative on the panel unless they  
7 did.

8 I want to make the point that, I'd like  
9 to describe the different ways a clinician may use  
10 the research that was presented. I would like to  
11 emphasize that the studies do not provide evidence  
12 that E Stim is not effective, and here are several  
13 examples of how electrical stimulation may be used  
14 in clinical practice in combination with other

15 therapies.

16 Dr. Spurlock talked about the woman who  
17 could not identify a pelvic muscle contraction, so  
18 electrical stimulation would be used right then and  
19 there to show her how to contract the muscles. And  
20 older woman with urge incontinence might be seen  
21 for six visits in a row where a combination of  
22 behavioral therapy, voiding diaries, biofeedback,  
23 and electrical stimulation at the 10 hertz level  
24 would be used in office visits. If the woman Dr.  
25 Spurlock talked about, an older woman who did not

00193

1 want to have surgery, was unable to meet her goals  
2 after a six-month period with PME's on her own, she  
3 could be offered a home electrical stimulation  
4 unit.

5 So there is really different ways to use  
6 electrical stimulation for an incontinent patient  
7 and it's an adjunct to behavioral therapy. Thank  
8 you.

9 DR. GARBER: Yes.

10 DR. NORTHROP: I'm Steve Northrop. I'm  
11 the executive director of the Medical Device  
12 Manufacturers Association. In the interest of full  
13 disclosure, I should note that EMPI is a member of  
14 our association.

15 I just want to make one point, to  
16 reiterate what Dr. Stanton said and to correct the  
17 panel's impression if they have one from what Dr.  
18 Lefevre said. If there is a national noncoverage,  
19 there is no one who will pick up the ball. The  
20 ball will not be picked up. HCFA won't pick it up,  
21 NIH won't pick it up. I think it's important for  
22 the panel to recognize that, that there is no one  
23 that picks up the ball.

24 DR. GARBER: I congratulate you. You do  
25 have the last word on that subject. I am going to

00194

1 call anyone out of order on this question, and I'm  
2 sorry. We really need to stick to the questions  
3 before us about the adequacy of evidence and the  
4 effectiveness of the technology. Les?

5 DR. ZENDLE: I don't know if you want to  
6 do six motions, or three motions.

7 DR. GARBER: We're still in public  
8 session. Any other public comments? I didn't mean

9 to turn off discussion, just on that subject.

10 MR. CONNELLY: My name is Jerry  
11 Connelly. I'm senior vice president for health  
12 policy of the American Physical Therapy  
13 Association. I appreciate the dilemma that the  
14 panel is being placed in and I would not trade  
15 places with any of you at this point in time. I  
16 think that the issue that was raised today as well  
17 as raised yesterday relative to the question of  
18 adequacy is the main dilemma that you have.  
19 Dr. Lefevre did say that there is some evidence,  
20 some suggestion of efficacy, but he said that the  
21 data in their opinion was just not that robust.  
22 Where is the cutting point here? What is  
23 adequate? What is the judgment call that was  
24 called for yesterday? Where is the adequacy?  
25 Maybe this is efficacious and maybe this is as good

00195

1 as clinical trials get when human subjects are the  
2 study case. So you're in a very difficult position  
3 to decide what is adequate, and what is not.

4 There is demonstration of efficacy,  
5 there is evidence from the clinic that this  
6 intervention is necessary and effective, and that  
7 it ought to be an option for patients. But where  
8 is that judgment call and how do you come down on  
9 the side of adequacy when there is evidence of  
10 efficacy, but there may not be the robustness,  
11 there may not the numbers of studies, there may not  
12 be the convincing evidence. But is it adequate or  
13 not? You're in a very difficult position.

14 MS. GREENBERGER: I really think that  
15 this definition is really key and although we're  
16 not supposed to talk about it, it goes back to the  
17 previous comments, because what I'm concerned about  
18 is that new technologies come more quickly, that  
19 we're always going to be faced with this, that  
20 we're never going to have enough randomized  
21 clinical trials to base this kind of decision upon,  
22 and we're going to lose the opportunity to have a  
23 lot of new therapies and devices that we might  
24 otherwise have. And I think it's going to chill  
25 research in those area, because how long can small

00196

1 companies wait to find out whether they are going  
2 to have coverage, and why would other companies do

3 investigations of those same areas when they're  
4 struggling like this? So I think this question is  
5 very important, because we may never have enough  
6 scientific evidence on a lot of these devices and  
7 therapeutics that are coming so quickly, and how  
8 can we base a judgment on this?

9 DR. GARBER: Thank you. Let me just  
10 ask, the period for public comment is drawing to a  
11 close. Are there any other people who wish to be  
12 heard before we turn to open panel deliberations.

13 Okay. We now move to the phase of open  
14 panel deliberations. Les?

15 DR. ZENDLE: I want to try the opposite  
16 approach of what I suggested yesterday, split  
17 rather than lump. And since there are three sort  
18 of comparisons and three parameters or diagnoses,  
19 stress incontinence, urge incontinence, and  
20 post-prostatectomy incontinence, I would suggest  
21 that we discuss and then vote when we're discussing  
22 on those nine parameters one at a time, and  
23 starting with PFES compared with placebo first,  
24 with stress incontinence, then urge incontinence,  
25 and then post-prostatectomy incontinence. And I  
00197

1 would word it a positive so that:

2 I would move that there is enough  
3 evidence, scientific evidence adequate to draw  
4 conclusions. So that a yes vote means you think  
5 there is enough evidence and a no vote means you  
6 don't think there's enough evidence.

7 DR. GARBER: All right. I'm just trying  
8 to --

9 DR. ZENDLE: So the first motion then  
10 would be, if somebody seconds it: Move that there  
11 is enough scientific evidence adequate to draw  
12 conclusions about PFES compared to placebo in  
13 stress incontinence.

14 DR. GARBER: So the first comparison  
15 would be the first vote. Is there a second to that  
16 motion? This is a procedural motion.

17 DR. EPSTEIN: I hesitate to do it,  
18 having gone down this track yesterday. I feel like  
19 we are a fated combo, to withdraw it as soon as we  
20 do it, but I am going to tentatively second it.

21 DR. GARBER: Okay. Is there a  
22 discussion on the motion to divide the question

23 that way for voting purposes? If not, all in  
24 favor?

25 DR. LANDY: Of the motion?

00198

1 DR. ZENDLE: Of the procedure.

2 DR. GARBER: Yeah. The motion is on the  
3 procedure to evaluate the procedures.

4 (Unanimous vote from the panel.)

5 DR. GARBER: Okay. I think it's a  
6 procedural matter, so I don't think we have to  
7 explain ourselves here. Okay.

8 DR. MAVES: Mr. Chairman, point of  
9 order. I wonder if Connie has to do her thing.

10 MS. CONRAD: It was unanimous, so we're  
11 okay. I already listed the voting members for this  
12 panel.

13 DR. GARBER: So now we are dealing with,  
14 if I understand this correctly, with the first  
15 question, and it's PFES compared to placebo in  
16 stress incontinence. So then, if we go this route,  
17 we're going to do nine votes on questions. Arnie.

18 DR. EPSTEIN: Is it open for discussion  
19 at this point?

20 DR. GARBER: Yes.

21 DR. EPSTEIN: Am I allowed to request  
22 one of the public members provide some  
23 information?

24 DR. GARBER: Yes.

25 DR. EPSTEIN: I have Dr. Lefevre's

00199

1 written report in front of me which makes a fairly  
2 clear case about why the evidence is not adequate.  
3 I would wonder whether I could ask Dr. Sand to  
4 speak again and repeat, for stress incontinence,  
5 which has five studies, three consistent studies,  
6 or three studies showing some effect, why he thinks  
7 that evidence is adequate? And I guess I would ask  
8 him to speak to not only adequacy in general but  
9 for external generalizability to the Medicare  
10 population. And this is a token that, if you can  
11 do this in a compelling way, it will help.

12 DR. SAND: Well, far be it for me to  
13 sway anyone's vote at the last moment. But my  
14 point was that I specifically looked at four, there  
15 are four sham controlled randomized studies:  
16 Yamanishi, Sand, Brubaker and Luber. I felt that

17 these were all well designed studies and we have  
18 two of those showing no benefit for stress  
19 incontinence, and two of those showing benefit for  
20 stress incontinence. And like Dr. Lefevre's point  
21 about instability of the data, and the negative  
22 effects in the control groups in the Yamanishi  
23 study and my study, I don't know how to fully  
24 factor that in based on the clinical blind that I  
25 discussed earlier in recent comments.

00200

1 But what we have are well designed  
2 studies that seem to show divergent results or  
3 conflicting results. When I look at those data and  
4 I look at what was done, there were two things that  
5 stood out to me immediately. One, Brubaker and  
6 Luber were done with one device, and that device  
7 has been shown in my practice as well as in Dr.  
8 Brubaker's study to be very efficacious in treating  
9 detrusor instability, urgency and frequency. The  
10 device we use, I still use to treat genuine stress  
11 incontinence, it seems to work very very well. So  
12 rather than saying I have four studies, two versus  
13 two, I felt that I had one device that wasn't very  
14 good for stress incontinence and another device, or  
15 if we consider Yamanishi's, two other devices that  
16 are very good for genuine stress incontinence. If  
17 we pick up on that in the uncontrolled literature,  
18 I think that point is well reverberated.

19 The other thing to consider that hasn't  
20 come up in the discussions either, to be fair, is  
21 another wrench in the program. In our trial, we  
22 excluded people who had prior PFS and prior PFMEs  
23 with biofeedback. Karl deliberately excluded  
24 people who were unsuccessful. So we were trying to  
25 find a very pure cell of people who hadn't been

00201

1 exposed to this, where we could show them maximal  
2 effect. Perhaps Karl had biased this group because  
3 he took out the people who were going to perform  
4 with some sort of pelvic floor muscle strength  
5 thing, because of neuromuscular changes. And so  
6 that can explain the differences perhaps also in  
7 those two studies.

8 DR. EPSTEIN: Thank you very much.

9 DR. SAND: Thank you.

10 DR. HILL: I'm sorry. The little

11 tete-a-tete up here was because I thought the  
12 question was whether or not a question could be  
13 asked of one of the members of the committee and  
14 not from the floor, and I misunderstood. I'm  
15 afraid as a procedural issue, we have to keep it to  
16 the committee discussion at this point in the  
17 program.

18 DR. EPSTEIN: It's done.

19 DR. HILL: Yeah, strike that.

20 (Laughter.)

21 DR. ZENDLE: Call the question.

22 DR. GARBER: There's not a motion on the  
23 floor, is there? Oh, the one of nine. Connie,  
24 could you give us the motion?

25 MS. CONRAD: The motion is: The

00202

1 scientific evidence is adequate to draw conclusions  
2 about the effectiveness of PFES compared to placebo  
3 in stress incontinence.

4 DR. McBRYDE: Point of order?

5 DR. GARBER: Yes?

6 DR. McBRYDE: Can I again, as yesterday,  
7 say positive conclusion as opposed to negative,  
8 because we're going to draw a conclusion, and  
9 conclusions are not what we're looking for. We're  
10 looking for a positive or a negative.

11 DR. GARBER: An affirmative vote on this  
12 means that we believe the scientific evidence is  
13 adequate to draw conclusions; a negative vote means  
14 that you believe the scientific evidence is not  
15 adequate.

16 DR. ZENDLE: And if it passes, then we'll  
17 decide what kind of conclusions it draw.

18 DR. GARBER: Okay. Is everybody clear  
19 about that? Jim?

20 DR. RATHMELL: Do you need a second?

21 DR. GARBER: All right. I wasn't sure  
22 that I heard either of them. Could you make the  
23 motion for this part?

24 DR. ZENDLE: If you want.

25 DR. RATHMELL: I second the motion to

00203

1 call the question.

2 DR. GARBER: Okay. We're ready to take  
3 the vote now. All those in favor, meaning that the  
4 evidence is adequate to draw conclusions about PFES

5 compared with placebo in stress incontinence, raise  
6 your hand.

7 (Dr. Landy voted in the affirmative.)

8 DR. GARBER: One vote. All those  
9 opposed are answering no.

10 (All panelists with the exception of  
11 Drs. Landy and Epstein voted in the negative.)

12 DR. EPSTEIN: Can we abstain?

13 MS. CONRAD: Yes.

14 DR. EPSTEIN: So be it.

15 DR. GARBER: All right. All abstaining?

16 (Dr. Epstein abstained.)

17 DR. GARBER: Now, in the order, do you  
18 want to do these en block or one at a time? Okay,  
19 anybody care to explain their yes vote?

20 DR. LANDY: I guess that means me.

21 DR. GARBER: Not to name names.

22 DR. LANDY: I think it goes back to the  
23 issue of what is adequate, and knowing the field of  
24 incontinence, this may be as good as the data that  
25 we get in this area of study, and maybe my

00204

1 requirements are not as robust as the TEC  
2 assessment, but I think based on the data we have  
3 now, I could make a decision regarding the second  
4 question.

5 DR. GARBER: Okay. Would anyone care to  
6 explain their no vote?

7 DR. RATHMELL: I'll say quite simply  
8 that the technology assessment is clear and even  
9 though it was stricken from the record, the most  
10 recent discussion pointed out just what the  
11 problems with the data are, and there's an  
12 inconsistency in the devices used and there's an  
13 inconsistency in the outcome shown, and I think we  
14 don't have any basis for making a scientific  
15 decision. And this doesn't say yea or nay, this is  
16 an effective therapy, or it has a niche. It has  
17 nothing to do with that; it says the scientific  
18 evidence is inadequate.

19 DR. GARBER: Anyone else care to add any  
20 further explanation for a not vote?

21 Not to name any names, but any  
22 explanations for an abstention?

23 DR. EPSTEIN: You know, after two days,  
24 there's nothing I have to say that's profound.



25 When I look at the weight of the evidence, I think  
00205

1 that, it boggles me, and it came out about  
2 abstentions. The studies are inconsistent; there's  
3 reasons to think why the negative studies would  
4 have been negative in their design, and so I weight  
5 that lack of evidence less. And I can't really  
6 quite figure out where my P value is from .05  
7 to .5, but I look on balance and I think for this  
8 condition, for this disease, the scientific studies  
9 are stronger than they were yesterday. That  
10 doesn't say that the coverage decision will come  
11 down differently, because in fact this sort of face  
12 validity of the measure is not as powerful to me as  
13 the face validity of biofeedback, which has a lot  
14 of face validity. This seems more like black  
15 magic, but that's it.

16 DR. GARBER: Okay. We will move on to  
17 the next question, which is, if I have the order  
18 right, are we doing urge incontinence, or are we  
19 doing compared to PME?

20 DR. ZENDLE: Urge.

21 DR. GARBER: Okay. So PFES compared to  
22 placebo for the second indication, which is urge  
23 incontinence. Do I have a motion?

24 DR. BRIN: So move.

25 DR. MAVES: Second.

00206

1 DR. GARBER: Okay. It's moved and  
2 seconded. Any discussion? Should I read that  
3 again? PFES compared to placebo for urge  
4 incontinence, is the scientific evidence adequate  
5 to draw conclusions? If there's no discussion, all  
6 those answering yes, it is adequate? All those  
7 answering no?

8 (Unanimous in the negative.)

9 DR. GARBER: Unanimous, and no  
10 abstentions.

11 All right. Any reasons for your vote on  
12 this one?

13 DR. ZENDLE: It's all been said.

14 DR. GARBER: Can we repeat your reasons  
15 from the prior?

16 DR. GARBER: Then the third one is --

17 DR. ZENDLE: Alan, also, I mean, our  
18 comments earlier, comments not just from the last

19 question but from the entire discussion.

20 DR. LANDY: I have a different reason,  
21 because I have a different answer. My answer is no  
22 because I really don't think I can base a decision  
23 about efficacy about one trial that we were exposed  
24 to, the Brubaker study, though possibly showing  
25 efficacy, has some limitations due to the

00207

1 statistical analysis or study. And the other  
2 trial, Yamanishi of 2000, we weren't even given  
3 that or analyzed that study, so it's really hard to  
4 make a decision based on a single trial.

5 DR. GARBER: Thank you. The third  
6 question is, again, PFES compared with placebo,  
7 this time for the indication of post-prostatectomy  
8 incontinence. Is there a motion?

9 DR. MAVES: So move.

10 DR. McBRYDE: Second.

11 DR. GARBER: Any discussion? Logan?

12 DR. HOLTGREWE: Yeah. If our  
13 information is inadequate on stress and urge  
14 incontinence, it's even weaker in this area. There  
15 is really practically nothing, so you really cannot  
16 make a decision whether the treatment for this type  
17 of incontinence helps in any way. Of course we  
18 heard some anecdotal situations but anecdotes don't  
19 make for science, so I think we really have no  
20 information of significance.

21 DR. GARBER: Any further discussion? So  
22 the motion on the table is that the scientific  
23 evidence is adequate to draw conclusions about the  
24 effectiveness of PFES compared to placebo for  
25 post-prostatectomy incontinence. A yes means that

00208

1 you do find the scientific evidence adequate. All  
2 those voting yes? All those voting no?

3 (Unanimous in the negative.)

4 DR. GARBER: It's unanimous, with no  
5 abstentions. Next is the --

6 DR. HILL: While no one has to speak, we  
7 do want to be sure to give them the opportunity  
8 just in case they want to explain their vote.

9 DR. GARBER: Yeah. Logan gave a reason  
10 for his vote. Did anybody want to add to that?  
11 Okay. Now, it is PFES compared to PMEs or  
12 alternative nonsurgical techniques, for stress

13 incontinence.  
14 DR. MAVES: So move.  
15 DR. BRIN: Second.  
16 DR. GARBER: Any discussion?  
17 DR. LANDY: Could you repeat that again?  
18 DR. GARBER: We're now saying, is the  
19 scientific evidence adequate to draw conclusions  
20 about the effectiveness of PFES compared to PMEs or  
21 alternative nonsurgical techniques for the  
22 indication of stress incontinence? Any  
23 discussion? A yes, again, means the scientific  
24 evidence is adequate.  
25 All those voting yes? No?

00209

1 (Unanimous in the negative.)  
2 DR. GARBER: It's unanimous. Okay.  
3 Any explanation of the no votes? This  
4 is all the same as before, okay.  
5 Now, PFES compared to PMEs or  
6 alternative nonsurgical techniques for urge  
7 incontinence.  
8 DR. MAVES: So move.  
9 DR. RATHMELL: Second.  
10 DR. GARBER: Any discussion? All those  
11 voting yes, the evidence is adequate? All those  
12 voting no?  
13 (Unanimous in the negative.)  
14 DR. GARBER: Unanimous, with no  
15 abstentions.  
16 DR. LANDY: Can I explain my no vote?  
17 On this topic, I think there may be efficacy in its  
18 use but we don't have that data, we only have one  
19 trial to support it.  
20 DR. GARBER: Lisa, was your comment  
21 specific to the indication of urge incontinence?  
22 DR. LANDY: Yes.  
23 DR. GARBER: Thank you. Okay.  
24 Now, we are at the third indication for  
25 the second comparison. Is the scientific evidence

00210

1 adequate to draw conclusions about the  
2 effectiveness of PFES compared to PME, et cetera,  
3 for the third indication, i.e., post-prostatectomy  
4 incontinence?  
5 DR. MAVES: So move.  
6 DR. BRIN: Second.

7 DR. HOLTGREWE: I have the same comment  
8 as before.

9 DR. GARBER: Any other discussion?

10 All those voting yes, saying the  
11 evidence is adequate? All those voting no?  
12 (Unanimous in the negative.)

13 DR. GARBER: Unanimous. Any further  
14 explanation? I will report that Logan noted the  
15 same reason as his prior. Okay.

16 Now, the third comparison is PFES and  
17 PME compared to PME alone, for the indication of  
18 stress incontinence.

19 DR. MAVES: So moved.

20 DR. RATHMELL: Second.

21 DR. GARBER: Any discuss?

22 All those voting yes, the scientific  
23 evidence is adequate? All those voting no?  
24 (Unanimous in the negative.)

25 DR. GARBER: Unanimous. No

00211

1 abstentions. Any further explanations? Okay.

2 Now, same comparison, PFES and PME  
3 compared to PME alone, this time for the indication  
4 of urge incontinence.

5 DR. ZENDLE: So move.

6 DR. BRIN: Second.

7 DR. GARBER: Any discussion? Okay. Now  
8 we vote on the question, is the scientific evidence  
9 adequate to draw conclusions for the indication of  
10 urge incontinence. All those voting yes? All  
11 those voting no?

12 (Unanimous in the negative.)

13 DR. GARBER: Unanimous. Any further  
14 explanation of your votes?

15 And now the third comparison for the  
16 third indication, our ninth vote on the adequacy  
17 question: Is the scientific evidence adequate to  
18 draw conclusions about the effectiveness of PFS and  
19 PME compared to PME alone, for post-prostatectomy  
20 incontinence?

21 DR. MAVES: So move.

22 DR. ZENDLE: Second.

23 DR. GARBER: Discussion? Logan?

24 DR. HOLTGREWE: Same comments as before.

25 DR. GARBER: Thank you. All those

00212

1 voting yes? All those voting no?

2 (Unanimous in the negative.)

3 DR. GARBER: Unanimous. Any further  
4 explanation?

5 DR. HILL: If I may, by way of closing,  
6 in addition to thanking all of you, both voting and  
7 nonvoting members, and thanking all the commenters  
8 for participating in this process, and for your  
9 willingness to participate under the guidelines  
10 that we laid down about how we wanted this  
11 structured and what kind of comments we were hoping  
12 for. I want to say it's especially appropriate to  
13 have you communicate to us your concerns about the  
14 questions, because I hope you all understand, and  
15 those of you that have looked at the Executive  
16 Committee's interim recommendations for evaluating  
17 effectiveness will recognize that the question  
18 about adequacy of evidence was drawn right from  
19 that document. And so if you have recommendations  
20 to how that should be changed or what alterations  
21 should be made, we hope that you will. Also,  
22 internally and procedurally, when and how we can  
23 involve you, your panel chairman in the formulation  
24 of the questions, and how to balance that against  
25 our needs to have the questions track the referral  
00213

1 to the TEC assessment when we do that, how closely  
2 those two things have to be related. All of those  
3 sorts of things that we've heard discussion about,  
4 we will need to think about and we will need to  
5 take seriously whatever you want to send to use by  
6 way of both argument and points you want to make.

7 DR. HOLTGREWE: Question. What should  
8 we do with our materials? Are they to be left here  
9 or are you going to deal with that?

10 MS. CONRAD: We will deal with that.

11 DR. GARBER: Before we formally adjourn,  
12 I would like to add a note of thanks on my own to  
13 the panelists for the obvious effort you put into  
14 these deliberations. I found them very difficult  
15 and as I said yesterday, I feel very fortunate that  
16 I did not have to vote on these questions.

17 I want to thank the public speakers who  
18 came here very well prepared and very much on the  
19 topic, and I want to also emphasize that if the  
20 voting did not go the way that you had hoped it

21 would, it does not mean that your comments were  
22 ignored. It's quite clear that you made some very  
23 good points that the panel did take into account.

24 Finally, I want to thank the HCFA staff  
25 who put in a tremendous amount of effort, along  
00214

1 with the TEC center and Frank Lefevre, who actually  
2 helped to structure this process and deliver a  
3 great deal of information. Whether you agree with  
4 the conclusions or not of the report that Frank and  
5 his colleagues prepared, I think it was an  
6 extraordinary amount of effort and it really shows,  
7 so thanks very much to all of you.

8 MS. CONRAD: To conclude today's panel  
9 meeting, let me announce that the future meetings  
10 for this panel are tentatively scheduled June 14th  
11 and 15th, and October 17th and 18th. These dates  
12 are subject to change.

13 I'm going to ask the panel members to  
14 linger just a few more minutes to accept a second  
15 evaluation form from Perry Bridger. And finally,  
16 leave all your materials. We are very concerned  
17 about any personal notes that may be made in any of  
18 the margins, so we will collect your materials and  
19 have them shredded.

20 At this point, could I have a motion  
21 that the meeting be adjourned?

22 DR. McBRYDE: So move.

23 MS. CONRAD: Second.

24 DR. HOLTGREWE: Second.

25 (The meeting adjourned at 1:30 p.m.)