Transcript of October 17, 2000 Meeting

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ELECTRICAL STIMULATION FOR THE TREATMENT OF WOUNDS

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

October 17, 2000

Baltimore Convention Center
Baltimore, Maryland

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Panelists
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H. Logan Holtgrewe, MD, FACS

Kenneth P. Brin, MD, PhD
Les J. Zendle, MD
Bruce Sigsbee, MD

Consumer Representative
Phyllis E. Greenberger, MSW

Industry Representative
Marshall S. Stanton, M.D.

Non-Voting Guest
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Director, Coverage and Analysis Group, HCFA
Sean R. Tunis, MD, MSc

Executive Secretary
Constance A. Conrad, RN

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P R O C E E D I N G S

MS. CONRAD: Good morning. Welcome to the panel chairperson, members and guests. I am Constance Conrad, Executive Secretary of the Medical and Surgical Procedures Panel of the Medicare Coverage Advisory Committee. The panel is here today to provide advice and recommendations to the Health Care Financing Administration regarding electrical stimulation regarding electric stimulation for the treatment of wounds.

At the conclusion of today's session, panel members will be asked to vote on a series of questions. The answers to those questions will constitute this panel's recommendation which will be submitted to the Executive Committee when it meets.

When the Executive Committee ratifies the recommendation, it will officially transmit that recommendation to HCFA. HCFA will develop a coverage policy within 60 days of the receipt of that recommendation.

For the purposes of today's panel, Dr. Adrian Oleck, medical director of the durable medical equipment regional carrier for Region B and noted expert in the field of wound healing received an appointment of temporary nonvoting member status.

Dr. Oleck's expertise will enhance this panel's deliberative process.

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

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

Now, a few words from Sean Tunis, the Director of the Coverage and Analysis Group.

DR. TUNIS: Good morning. I guess today we have here the subset of people who could actually find this room, so congratulations for making your way here.

I just wanted to make a couple of comments before Dr. Garber spoke related to the recently issued Medicare coverage decision memorandum on the two technologies for -- the two previous technologies for urinary incontinence, pelvic floor electrical

stimulation and biofeedback. And there has been, just to sort of clarify, you know, in public, sort of what was laid out in the text of the decision memo in terms of the rationale for those coverage decisions.

As many of know, at a meeting of this Medical Surgical Panel where those two technologies were discussed, the conclusion of the panel was that the scientific evidence for the effectiveness for both pelvic floor electrical stimulation and biofeedback was inadequate to make a conclusions based solely on the scientific evidence. The way that those questions were framed to the panel and the way that we discussed them internally, and the way the trials were designed, really addressed the question of these technologies for primary therapy of patients with urinary incontinence, in other words, looking at this as an initial intervention.

There really was no studies, or maybe a single study that had any evidence at all about the

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effectiveness of those therapies for patients who had failed pelvic muscle exercises or conservative therapy, and so the coverage decision essentially was that for initial therapy, or for primary therapy of urinary incontinence, pelvic floor electrical stimulation remained noncovered, and biofeedback remained at carrier discretion, unchanged from previous coverage policy.

However, for patients who had failed conservative therapy with pelvic muscle exercises, or were unable to perform them, the decision was to provide Medicare coverage in those circumstances.

And just to lay out clearly what the rationale was for positive coverage under that set of conditions, the considerations that went into that were four major considerations. One was that there were in fact some positive supportive studies for both technologies. There were also obviously negative studies, studies that showed no benefit. However, there were at least one or two randomized control, placebo control studies that showed some benefit, particularly for pelvic floor electrical stimulation.

We took that then in the context of a second consideration, which is patients that failed

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pelvic muscle exercise have very few other nonsurgical options, and so these technologies represented a possibility at least of a relatively harmless nonsurgical alternative for an important problem, and we took that into account as well.

The third consideration we already mentioned, was essentially there really was no suggestion that either biofeedback or pelvic floor electrical stimulation had a significant risk of harm, and finally, that there was very consistent and very strong expert testimony and consensus from professional organizations that supported both feedback and pelvic floor stimulation.

So those are kind of the four considerations that went into this narrowly defined positive coverage for patients who failed conservative therapy, and I just wanted to sort of lay that out clearly in public.

And then finally, we do say in the decision memo, and we are quite interested in following up on this, that we would in fact like to see the studies done that confirm the effectiveness of either of these technologies in patients who failed pelvic muscle exercise or in fact, better studies that clearly demonstrate the effectiveness of

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either one for primary therapy. So that's just as a wrap-up on those two coverage decisions.

And with that, I think Alan, Dr. Garber has some opening material as well.

DR. GARBER: Thank you, Sean. I think I can be very brief. I thought it would be helpful just to give a little progress report about what is going on with the Executive Committee and I think some of you but perhaps not all of you know that the Executive Committee when they drafted the interim guidelines for how the panels should conduct their business, they also had emphasized that these guidelines could be changed, and in fact, our previous panel meeting was the first opportunity to

really test out the guidelines that the Executive Committee had developed.

And in the wake of that, I know you are all aware of the Executive Committee's decisions to ratify the conclusions of this panel, but there was considerable discussion both at the last panel meeting and at the Executive Committee meeting. A subcommittee was formed from the Executive Committee to take a look at the interim guidelines and see how if at all they should be changed. That subcommittee has not issued its reports yet, and it should be

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ready in time for the Executive Committee meeting in November. And after that meeting, we will have a better idea of where the Executive Committee stands on changing these guidelines.

If it wouldn't be out of order, I'd like to just mention a few of the things that are under consideration. Would that be appropriate?

For the most part -- well, actually the direction in which I think the subcommittee is going is pretty much to preserve the essential features of the existing interim guidelines, in particular the emphasis on the two major questions about adequacy of evidence and also if the evidence is adequate, what is the size of the health effect. There are many criticisms, comments, suggestions that have come to HCFA and to the Executive Committee, about these should be changed, about how the recommendations should be changed, and although the central part of it will not fundamentally be changed as I see it, in the current direction of the subcommittee, there will be much more discussion about types of evidence, and I think it will accommodate many of the concerns that people have expressed, that the types of evidence that would be considered are construed too narrowly, that only a very narrow range of evidence would be

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considered. And so, I think you will see a more explicit statement about additional kinds of evidence that should be considered in the panel deliberations.

There is one substantive change that I will mention, and it's partly because I'm the person

who actually pushed for this, but I think there is a consensus, and that is when the panel concludes that the evidence is not adequate, that there are circumstances in which they should give more information in order to give HCFA guidance.

For example, the evidence may be inadequate because, simply because studies have not been conducted that either have a large number of study subjects, they may have design flaws, there may be numerous reasons why the panel concluded they were not adequate to draw conclusions. Yet, it might be possible to conduct studies and there may be reasons for HCFA to decide to go ahead and cover the technology either within the context of the study, and there's of course precedent for that, that is, they would fund coverage only if the procedure or the intervention is performed in the context of say an NIH approved study, or they might determine to cover it and revisit the issue after adequate time had elapsed for good studies to be conducted that would

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enable panels to draw conclusions.

The Executive Committee I don't think is going to try to tell HCFA what they should do, but if HCFA should decide that they want to make a decision to cover in some form, even though the evidence is inadequate, we might be able to give them more helpful guidance that look, this particular procedure, although the evidence is inadequate, looks very promising. The idea is that this kind of designation might be used on a selective basis where for example, it's a very promising procedure, good or service, or it might be one with very little risk and again, substantial potential benefit, even though the studies are inadequate.

If any of you have further comment about how the Executive Committee interim guidelines should be changed, please send them in. Many of you have commented already; there is still ample time to make changes before this goes to the Executive Committee and certainly in the context of the Executive Committee meeting itself. In the meantime, I believe that the current guidelines of the Executive

Committee stand and the questions that you will hear about that were proposed to the panel today are basically a direct translation of the Executive

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Committee's questions set in the context of electrical stimulation for chronic wounds. Thank you.

MS. CONRAD: I now ask the panel members to introduce themselves, starting, let's start at the far end. Phyllis?

MS. GREENBERGER: Phyllis Greenberger, Executive Director for the Society for Women's Health Research.

DR. STANTON: Dr. Marshall Stanton, Medical Director for Medtronic, industry representative on this panel.

DR. OLECK: Dr. Adrian Oleck, medical director of the Medicare regional carrier, Region B.

DR. ZENDLE: Dr. Les Zendle, Associate Medical Director of Southern California Permanente Medical Group, in Los Angeles.

DR. BRIN: Dr. Kenneth Brin, a practicing cardiologist, Summit Medical Group, Summit, New Jersey.

DR. McBRYDE: Dr. Angus McBryde, orthopedic surgeon at the University of South Carolina, Columbia.

DR. HOLTGREWE: Logan Holtgrewe, urologist on the faculty of Johns Hopkins, here in Baltimore.

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DR. MAVES: Mike Maves, vice chair, and president of the Consumer Healthcare Products Association.

DR. SIGSBEE: Bruce Sigsbee, practicing urologist, member of Salt Marsh Medical Associates in Hyannis, Massachusetts.

DR. GARBER: I guess I have already mentioned this. Alan Garber, chair, Department of Veterans Affairs and Stanford University.

MS. CONRAD: Sean and Connie.

Proceeding with the agenda, Rita Frantz. Dr. Frantz is going to offer an overview of electrostimulation for the treatment of wounds.

DR. FRANTZ: Good morning. It's my pleasure to be here this morning. And my task is simply give, as I was directed by Connie Conrad and others, to simply give you an overview of the role of electrical stimulation in chronic wound healing, and I promise to stay within the time limits of the agenda.

We'll get our technology squared away here. I think it would be safe to say as an opening remark that electrical stimulation is largely an unknown and a poorly understood treatment modality for the treatment of chronic wounds. Appreciation of

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its potential contribution to promotion of chronic wound healing has been limited in the scientific community as well as within the provider community due to a lack of familiarity with the specialized body of knowledge. So today I would like to just review with you briefly some of the points that one can take from a review of this literature.

First of all, I want to just describe a little bit about how electrical stimulation works, and you introducing yourselves this morning, it's obvious you all come from quite a variety of backgrounds and may not be familiar with this particular technology and how it's used in wound healing.

Secondly, I'd like to review for you briefly the treatment modalities, how they're applied to chronic wounds and then look at how effective electrical stimulation can be in promoting various types of chronic wounds and their progression towards healing.

How does electrical stimulation work? Well, there are innumerable laboratory and clinical studies that establish that electrical stimulation has a positive effect, both at the cellular level and in the whole overall repair process. Briefly, these

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studies show us that fibroblast activity is enhanced and actually stimulated by use of electrical current and that wound contraction is facilitated. Studies done at the University of Miami have established that

there's actually an increase in protein and DNA synthesis in a human fibroblast when it's stimulated with electrical current and that in fact, receptor sites on the fibroblast actually are increased for transforming growth factor beta, which is some exciting new work that was recently published.

Now the overall effect that this then has on the repair process is to improve the organization of collagen, that protein network that forms the new wound bed. It also increases the tensile strength or the strength of the scar as -- it also improves blood flow and reduces edema. Now when we look at the tissue level, which is where most of us spend our time, the effect of electrical stimulation is that it is believed to actually restart or accelerate the wound heal process by initiating and imitating the natural electrical current that occurs in the skin.

And researchers in the early 1980s actually established that on the skin surface, there is an endogenous built-in bioelectric system, and you see this illustrated here from the works of Fulton

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and Baker, who showed that on the skin surface, the skin carries more negatively charged, is more negatively charged than are the deeper skin layers, and in fact, the average voltage on the skin is approximately 23 millivolts. This occurs because of the positively charged sodium ions that are present in perspiration actually being pumped through some of the superficially layers of the epidermis, and the deeper cells then are left positive in relation to the chloride ions left on the skin surface which are negative, creating what is often referred to as the skin battery, again, because of the positive and negative poles on a battery.

Now the separation of the positively charged wound tissue from the negatively charged peri-wound skin around the skin, around the wound, creates a low level of bioelectric current. And this current when injury occurs, we have the positively charged ions in the injured dermis exposed, and the combination of the positively charged ions in the wound and the negative charge of the outer layer of

skin creates a skin battery that drives this electrical current as you see here. And this was described in Jaffe and Vanable's work in 1984.

The bioelectric current that we see

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illustrated here, this natural skin battery, is actually facilitated by the presence of a moist wound environment and the use of an electrically conductive solution in a wound bed, such as normal saline, is thought to facilitate this bioelectric process, and actually promote the normal bioelectric system of the body.

Now, in vitro studies show us that cells in culture are actually attracted to the electrical charges of the body and that by applying electrical current, you actually can enhance the migration of cells into the wound bed, this what's called galvanitactic attraction; it simply means they're attracted by the electrical forces, actually exert a natural pulling on these cells in the wound bed. Application of exogenous or outside type electrical current then stimulates this natural attraction of cells towards an electrical charge.

In vitro studies done in various wound centers around the country have shown us that different cells that are involved in the healing process are actually attracted to a positive or a negative charge and that they differ in their preference for a negative or positive charge. For example, the anode, the positive electrode, actually

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attracts neutrophils and macrophages and in so doing, supports autolysis. Similarly, the epithelial cell also likes to or is attracted to the positive anode and this will help to support new epithelialization during the healing process.

The cathode attracts neutrophils and in so doing supports inflammation and fager cytosis. Similarly, fibroblasts are attracted to the cathode, and this helps to support granulation tissue formation.

Now, this has implications when we look at a chronic wound and I promise you, I didn't bring the

worst one of the worst that I had. The case in point here, a wound that is clearly diffusely covered with devitalized tissue and what we would graphically see happening with electrical current being applied to such a wound is on the left of the illustration here, we see that the wound bed filled with a moistened saline gauze dressing and a positive electrode being applied here, and the electrode being placed in that conductive solution of saline is, being a positive electrode, will draw negatively charged neutrophils and macrosages into this area, and help to promote the autolysis of this necrotic tissue.

Similarly, if we look at a wound that is

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beginning to fill with granulation tissue but still needs considerably more granulation matrix to complete the healing process, would be supported by the application of a negative electrode that would promote the attraction of the fibroblast into the wounded area and therefore enhance the laying down of the protein matrix in the wound bed.

Now that's kind of a brief overview of how is it that this electrical current actually promotes the growth of new tissue in a wound bed, what activity it engages in in terms of attracting the very cells that are essential to the normal healing process as we know it.

I would like to turn attention briefly to how is it that we deliver electrical stimulation and I'm aware that all of you got a huge packet of materials, as did I, so this will be brief, because I know you have read many of the papers that describe these different types of stimulation.

Basically there are what I believe are four types that have really been used, at least to some extent with wound healing, and these are them. The low intensity direct current, the high voltage pulse current, actually two forms of alternating current, the low voltage pulse microamperage current,

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and then TENS.

You do see an occasional reference to the use of electromagnetic energy, pulsed electromagnetic

energy. This is actually using electromagnetic fields, it is different than electrical stimulation, which is using current. And so I have sort of set that aside as sort of a different modality than is electrical stimulation.

There is also some reference to using spinal cord stimulation, but most of that work is involved using it for chronic pain control and therefore, I am also setting it aside as a type of modality for chronic wound healing.

Of these four types then that have been most extensively addressed in the literature on wound healing, they differ in the characteristics of the actual current that's delivered, and I will just briefly highlight those for you. It's helpful when I was first learning all of this area of science, it was always helpful to me to be able to look at these diagrams, so I will share them with you.

The low intensity direct current which you see illustrated here is actually a continuous monophasic wave form, as you can see, and it's delivered using anywhere from around 20 to 200

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microamps of current at a very low voltage, only about, less than eight volts of current. This has been used more in the early work on electrical stim and wound healing, and more recently one does not see as much use of the direct current, in part because of problems with heat build up under the electrode when it is used.

Now high voltage pulse current as you see depicted here is short pairs of pulses with a long duration or pause in between, and this is delivered at 75 to 200 volts, and 80 to 100 pulses per second, and provides a total current of about 2.5 microamps when we use a standard electrode. Both the high voltage and the low voltage are capable of being delivered with either the positive or the negative electrode as the active electrode. This is the type of current you see used in some of the more recent research studies that you had the opportunity to review.

Alternating current is basically a

symmetrical biphasic pulse that uses a low voltage milliamperage and as you can see, it's biphasic and so the amount of charge in the two symmetrical phases of the wave form is equal, and consequently, there is no charge left in the tissue, it basically cancels each other out.

And then a similar type of wave form is seen in what is more commonly referred to as TENS, it's technically low voltage pulse milliamperage current. This also is a type of alternating current, as you can tell by the wave form. It delivers anywhere from 15 to 20 milliamps of current at 150 milliseconds pulse width and a standard low frequency of 85 hertz.

Now, the real question is, well, you've got all these different kinds of current, what difference is there between them and does it really make any difference when it comes to wound healing. And the question is not one that is easily answered. In an attempt to try to address this question as well as a few others in this area of electrical stim and wound healing, one of my doctoral students and I, along with the assistance of a statistician at the University of Iowa, recently published a meta-analysis, which I believe you've also had a chance to review, and in that meta-analysis we looked at 15 studies that were judged to be amenable to a meta-analysis.

And in those 15 studies, there were 24 samples that received some form of electrical stimulation and there were 15 that got a control, most often a placebo but not always. What we found when we looked at the different types of current, was that in the case of TENS, and let me go to TENS, that in the case of TENS, the net increase in the rate of healing was just under 11 percent, 10.9 percent, the net increase in the rate of healing over a control.

In the case of the direct current, we had a net increase of 12.6 percent and then in the case of the pulse current, we had a net increase of 15.5 percent. Now, the problem here was that there was a

lot of overlap in the confidence intervals and so consequently, the observed differences, it's difficult to determine whether the observed differences were in fact just a function of sampling error, and the small sample sizes that are in most of these studies contribute to that issue of sampling error.

Furthermore, these devices often were confounded by the fact that some of the devices tended to be used only with one type of wound. For example, the TENS, which you see here, tended to be predominantly used on pressure ulcers. Well, when you look at the control group ulcers, you find that the pressure ulcers were the type of ulcers that

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healed more slowly, and so consequently, the rate of healing that was estimated for TENS may actually have been suppressed somewhat because of the lower rate of healing that was occurring in that type of wound that was most often used to test that type of device. So to say that one of these devices is more effective in healing than the other, that still appears from this data analysis to be an unresolved issue.

Similarly, the question arises about to what extent does the etiology of the chronic wound influence the effect of the electrical stimulation on healing, and the wounds that come to mind when we think of chronic wound healing are of course the pressure ulcer, which you see here, the venous stasis ulcer. Other types of chronic wounds include the arterial ulcer and also the neuropathic ulcer, otherwise sometimes referred to as the diabetic foot ulcer.

Now, what we find when we look at a meta-analysis of these data from these 15 studies is that the predominant type of wound that was looked at when studies addressed only one type of wound in their sample, the type of wound that was most often used was the pressure ulcer; that was in seven studies. Venous ulcers were identified as a single

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type of wound in only two. The remaining six out of the 15 that were looked at in this meta-analysis were

a mix, and this mix consisted of a mix of pressure ulcers, other types of ischemic wounds, as well as some nonhealing surgical type wounds, wounds that had, were healing by secondary intention. There were no studies of diabetic foot ulcers and there are no studies of arterial ulcers, specifically isolating them as the type of wound selected for the sample.

With that in mind, the highest net rate in healing rate between the E-stim and the treated wounds and those that received a control, the biggest net increase was with pressure ulcers and that was 13.3 percent per week. And in this sample, in these samples, there was not any overlap in the confidence interval, which suggests that the sampling error was not a major contributor to the difference between the E-stim group and the control groups in those samples, but the lack of adequate study sample that are specific to a type of chronic wound other than pressure ulcers causes us to have difficulty forming any kind of conclusions about the effectiveness of electrical stim in healing other types of chronic wounds. And this is an unfortunate gap in our research literature at this point in time.

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So then we're left with the question, well, to what extent does the etiology of the chronic wound, the cause of it, actually influence the effect that E-stim would have on healing? And at this point in our understanding of the repair process after injury, what we know is that the normal healing process is mediated by specific cells, and you see those diagrammatically illustrated here, and of course I have referred to them several times this morning. The inflammatory process mediated by lymphocytes and macrophages, the proliferative phase mediated by the fibroblast, and then of course remodeling, and this normal process is very much a function of these cells that come to the wounded area at the time of injury, and these cells play a strategic role in the process of repairing the tissue and regenerating new epithelial cells.

Now, we know that there is an attraction of these cells to a wounded area when electrical

current is put to the wound bed. It would follow that if there is adequate circulation to the wound and there are adequate substrates in that circulation, that the stimulation of the wound such that it provides an attraction of these cells to the wound bed would lead to an improvement in healing,

but those are suppositions I'm making. I do not have, nor does anyone at this point in time have data to tell us whether the stimulation with electrical stim will augment healing in wounds other than pressure ulcers. The data is simply not there.

I would be happy to take questions at this time, or clarify any of the points that I made.

DR. ZENDLE: Question. At the beginning of your talk, you talked about the difference between the positive and negative in attracting the different kinds of cells.

DR. FRANTZ: Yes.

DR. ZENDLE: How does that, and again, this is sort of basic science here, but how does that play into the direct versus alternating current going back and forth between positive and negative?

DR. FRANTZ: Well, you know, that's an interesting question. There's been a lot of, some speculation in the scientific community about how actually does, like an alternating current work. And I actually have done my research mostly with alternating current and although I have seen an effect size from alternating current, when I look at the research on TENS, the small number of studies that there are, the effect size is not as great as it

is when you look at the effect with like the high voltage pulse current. But when we did the analysis using meta-analysis we actually couldn't compute an effect size because the unfortunate way in which many of these studies were reported, they didn't give us a standard deviation or variance, so we couldn't compute a true effect size from a statistical standpoint.

And from a basic science perspective, I am not able to explain and I don't know that anyone else

can, I would certainly welcome anyone in the audience helping us on this, why if you give an alternating current, then you're getting both positive and negative in an alternating fashion, you would get any kind of attraction of cells, because it's the polarity that brings the cells. I am not able to give you an answer to that, I do not know.

DR. ZENDLE: Sort of a follow-up question then is, if the basic science theory is that positive or negative attracts certain kinds of cells, does the opposite repel them?

DR. FRANTZ: I don't know, I have never thought about that. That's a good question. It possibly could. I don't know the answer. Yes?

DR. STANTON: You classified Pulstar F as

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different from the others, and I understand physically why you would, but I think since we're going to consider that with these other therapies. Can you make some comments about potential physiologic mechanisms, how they might differ from the more electrical stimulation and you know, just what your general opinion is.

DR. FRANTZ: The pulsed magnetic fields, the feeling is that those magnetic fields are again, drawing cells into the wounded area. The research on the electromagnetic field has been more limited, particularly in the human wound. Most of the work has been done in the animal model; you may be aware of many of those studies. And they don't provide us with much information then about what this electromagnetic field might do in a chronic wound, which is different than you can get in an animal model where we don't really have a good model of a chronic wound. But the electromagnetic energy is felt to increase blood flow to the area, some of the same kinds of things that happen with electrical stimulation.

DR. OLECK: Question. In terms of the categorization of the different types of devices, you talked about the high voltage pulse current, and I

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was looking at the ECRI report and some of the other

things, and it looked like there was another category, a low voltage pulse current. Am I missing something there, or are they basically dividing things up into pulsed current into two different groups?

DR. FRANTZ: It's interesting how we all have our different sort of categories. They identified direct current, pulse direct current, which is what I called high voltage pulsed current. I'm looking at a table that was included in the memorandum to the Medical and Surgical Procedures Panel, dated September 25th, 2000.

DR. OLECK: I was looking at their main document where they talked about pulse current applications and they distinguished between two subcategories, pulse direct current and high voltage pulse current, and I looked at the table where they had compared the studies of a number of those, and what they put in the pulse direct current had low voltages, like 6 to 12 volts, as opposed to this 75 to 200.

DR. FRANTZ: Well, right. And when you do, with pulsed current, because you have, you're only giving the charge with the pulse and then there

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is that long interlude of space, then the actual voltage is higher, that's delivered with the pulse, but the total accumulation of current in the tissue is not different.

DR. OLECK: So you're saying in your view at least, that all of the pulsed current devices can be lumped together.

DR. FRANTZ: Basically are delivering the same kind or charge to the tissue.

DR. OLECK: Thank you.

DR. SIGSBEE: A quick question. What was the magnitude of the resting potential at cross scan, was that microamps or milliamps?

DR. FRANTZ: I have to look again. It is millivolts.

DR. SIGSBEE: Millivolts?

DR. FRANTZ: Yeah. And it averages -- I mean all those numbers I had on those figures, which

is from Folz and Barker's work, if you take the average of them, it comes to about minus 23 millivolts. Other things?

MS. CONRAD: Dr. Frantz, would you give us for the record a little summary of your credentials?

DR. FRANTZ: Yes, I will be happy to, and I didn't even think about the fact that you wouldn't

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probably know them. I am a professor of nursing at the University of Iowa. I have my Ph.D. And my research is over the last 12 or 15 years, has focused in the area of wound care. I have had two NIH funded studies to address the effects of electrical stim, specifically TENS, on wound healing, and the subject pool that I used for those studies was predominantly elderly patients, many of whom are in nursing homes.

And my involvement in electrical stim really came out of my clinical practice as a nurse in intensive care units some years ago when I came to the realization that chronic wounds, in particular the pressure ulcer, occurred with some frequency and people didn't seem to have any good way to help them get healed. There was all sorts of various ways that people were treating them, but nothing seemed to be very effective. And I went to the literature in search of some better ideas, some better methods, came across some work being done on actually bone healing, that I'm sure many of you are familiar with, that showed some extremely positive benefits in the area of healing of bone with electrical current.

Coincidentally, a colleague of mine was studying pain control using the TENS to control pain and she was doing a study where they were looking at

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pain in donor sites, and some of the patients were getting a placebo TENS, others were getting electrical current with the transcutaneous electrical nerve stimulator, and much to their surprise, totally serendipitously, they were finding that the donor sites at the end of the studies, the donor sites that got the electrical stim had healed so much faster, and these were, you know, these were clean donor sites. These wounds had healed so much faster than

the wounds that were not treated, that got an inactive electrode.

And that sort of spurred my interest in the use of electrical stim, so I sort of came into it via the back door, but I have obviously spent a considerable number of years looking at this modality as an adjunctive treatment, if you will.

MS. CONRAD: Thank you very much.

DR. FRANTZ: You're welcome. Is there any other questions? Thank you very much.

MS. CONRAD: We will now have the presentation of the questions to the panelists, presented by Lorrie Ballantine and Perry Bridger.

MS. BALLANTINE: Good morning, ladies and gentlemen of the panel, and thank you for coming together to review another issue for us. The issue

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we are bringing before you today is electrical stimulation for the treatment of chronic wounds.

Chronic wounds are a significant problem for the Medicare population, with considerable morbidity and mortality. Treatment of wounds costs the Medicare program over $3 billion a year.

For our discussion today, we are looking at three types of chronic wounds, pressure, venous and arterial. Pressure ulcers, the most common type, also known as decubitus ulcers or bed sores, affects 3 to 14 percent of hospitalized patients and 15 to 25 percent of residents in skilled nursing facilities. Venous ulcers are primarily caused by venous hypertension. 1.3 million patients are treated annually for these types of ulcers. The third type of ulcer is arterial, which often occur in patients with peripheral vascular occlusive disease or other clinical condition that has ischemia as an underlying etiology.

Although there is consensus on what constitutes conventional therapy, debridement, cleansing, dressing and nutrition, we do not know the precise role of adjunctive therapies such as the use of electrical stimulation. In keeping with the recommendations from the MCAC Executive Committee, we

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are posing two basic questions to you today. You may want to refer to the questions in your packet that you received today.

The first question for you to answer, is the evidence adequate to draw conclusions about the effectiveness of electrical stimulation as an adjunctive therapy for chronic pressure ulcers? In answering this question the panel should consider the following points: The adequacy of the individual study design; the consistency of results across studies; their applicability to the Medicare population; and the generalizability beyond the research setting.

We ask that you consider the whole spectrum of information presented, which includes expert testimony and public comments, to reach your conclusions on the adequacy of the evidence. Then if you feel the adequacy of the evidence is sufficient, we ask that you determine the size and direction of the effectiveness.

Again keeping with the Executive Committee recommendations, there are seven categories of effectiveness attached to the questions. Is the effectiveness a breakthrough technology, more effective, as effective with advantages, as effective

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with no advantages, less effective with advantages, less effective with no advantages, not effective. We ask that you break down your decisions and answer each question for all indications identified, chronic pressure ulcers, chronic venous ulcers, chronic arterial ulcers.

Also presented in your information and as Dr. Frantz had mentioned, you will find there are several types of electrical stimulation. Direct current, pulse current, alternating current, pulse electromagnetic field, transcutaneous electrical nerve stimulation, pulse electrical energy. In the technology assessment they have varying conclusions based on indications and type of electrical stimulation. Although we did not choose to explicitly ask you 18 separate questions, you may wish to separate your final panel recommendations by

indication and type of stimulation.
Thank you for your time, and we look forward to today's meeting.
MS. CONRAD: Thank you, Lorrie. Okay. Let's do a little summary of coverage history. John Whyte.
DR. WHYTE: Thank you, Connie. Good morning, Dr.Garber and Dr. Maves, as well as other
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members of the panel and public. Over the next ten minutes I am going to provide a general background on the history of Medicare coverage relating to electrical stimulation for the treatment of chronic wounds, as well as discuss why we sent this topic to your panel.
You've all received a background memo in your packet prior to the meeting, a memo dated September 25th, and I'm basically going to go over that document. You might want to take out the rest of your packet, which includes the technology assessment, several letters, the AHCPR clinical practice guidelines for the treatment of pressure ulcers, the literature review prepared by HCFA staff, and a bibliography.
I will first discuss the status of coverage before the technology assessment. You will then hear a presentation on the technology assessment and then finally, I will update you on the activities that have transpired since the assessment.
Now the coverage process dates back essentially to the 1970s, when Medicare contractors reimbursed for some forms of electrical stimulation for wound healing on a case by case basis, but essentially there was no national coverage policy in
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place. Now in 1981, HCFA did issue a national noncoverage policy for low intensity direct current in treatment of pressure ulcers. There is no additional activity until 1994, when the Agency for Health Care Policy and Research, AHCPR, which is now known as AHRQ, convened an independent panel of experts who produced a clinical practice guideline entitled Guideline on the Treatment of Pressure

Ulcers, and you all have that as part of your packet, and you may wish to refer during your deliberations to pages 8, 19 and 55, for some of the comments on electrical stimulation.

Specifically in a section on adjunctive therapy, the guideline advised physicians, "To consider a course of treatment with electrical therapy for stage III and stage IV pressure ulcers that have proven unresponsive to conventional therapy. Electrical stimulation may also be useful for recalcitrant stage II ulcers." The guideline states that the recommendation was based on data from five clinical trials involving a total of 147 patients, and AHCPR assigned this portion of the evidence a strength of evidence of level B. AHCPR defines strength of evidence as level B if there is fair research based evidence to support the

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guideline. Level A is good research based, and Level C is expert opinion. And more information on how AHCPR defines strength of evidence can be found on page 18 of the guideline.

Now in 1995 in an effort to gain greater clarity on this topic, HCFA ordered a technology assessment of electrical stimulation, and ECRI, a technology assessment firm in Plymouth Meeting, Pennsylvania, was awarded the contract. And I think ECRI just arrived with Dr. Lerner and Dr. Turkelson, and at this point of the presentation I am going to defer to Dr. Charles Turkelson of ECRI, who will present the assessment, and you should all have copies of his slides in your materials.

After Dr. Turkelson presents the assessment, you may wish to ask questions then, or you may wish to hold your questions, it's completely up to you, because I will update you as I mentioned earlier, on what transpired at HCFA since the technology assessment. So first, Dr. Lerner.

DR. LERNER: Actually, just before my colleague starts, I'm Jeff Lerner, ECRI. Let me just introduce what Charlie is going to talk to you about. Charles Turkelson is our chief research analyst. ECRI is a nonprofit health services research

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organization, it's often compared to Consumer Reports, it is very independent in its views and it is designated as an evidence based practice center by the Agency for Health Care Research and Quality.

What Charlie is going to present to you is the results of our report, but also how to understand our report. He has a three-part presentation that looks at what basically is an evidence report, what statistics do you need to know to understand this very complex data set that is in the report, and then finally, how this report applies to the questions that you have in front of you. And I can't stress heavily enough that it really is a complex data set. Then at the end, if you'd like, we can talk to you about some next steps that we think would be valuable to take up in terms of research. So, Charles Turkelson.

(Pause while equipment set up.)

DR. TURKELSON: I do apologize for that delay. I want to express my gratitude for having the opportunity to speak before you for several reasons, first, is that it actually gives me a chance to explain the difference between say a technology assessment and hard evidence report, and other kinds of documents. This is a difference that is widely
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unappreciated. If I am saying something that you already know, I apologize for that, but given the commonality of the failure to make a distinction between a technology assessment report and some other kind of document, I would like to begin with that.

And the obvious thing is that it is not a guideline. The primary purpose of this report as in any evidence report, is to synthesize evidence. Evidence is defined as that which comes from clinical trials. An evidence report does not use a consensus process, they do not incorporate opinions, they merely try and state whether available evidence shows whether available evidence shows whether available evidence shows whether a technology works, if you will allow me to put that in quotes.

The ramification of that is the other oft

misunderstood phrase, and that's the phrase no evidence. No evidence means no evidence. It means that an evidence-based conclusion cannot be drawn. It does not mean that a technology is not effective. I will state it another way to emphasize the report, the absence of evidence of effectiveness is not evidence of no effectiveness. In a technology assessment or evidence report, we strive to stay very close to the data and when there are no data, there

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is very little for us to say.

As such, these reports do not make practice recommendations and they do not make coverage decisions. Both of those often involve clinical judgment. Again, these kinds of reports look at data, they do not incorporate opinion. In a practice recommendation or a coverage recommendation, you often times need to consider clinical opinion; this is beyond the purview of such a report.

I want to turn now to the next section of my talk, which is how to understand this report. Where we are headed in all of this is that in general, there is evidence for the efficacy of electrical stimulation, but, and that's a very big but, in general has limited meaning here because this is a complex data set, although it's comprised of only eight or nine studies depending on how you count. It is a very complex data set. And I need to walk you through the logic of this report so that you can see why the data set is so complex. And I am going to take a hypothetical evidence table here which shows the result of five studies, three of which are significant and two of which are not, and the temptation here may be to say that the results of these studies are different, that these studies are

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not consistent in their results.

The temptation may further to be to say that indeed, this vote between the studies is mixed, that well, it's an odd number of studies, either the yeses or nos have to win. We really don't -- had there been a sixth study it may be a tie, and we're not capable of coming to a decision.

We can show another version of this evidence table by now presenting the p-values, the results of the test of statistical significance, and there we see that two trials are again nonsignificant, and Study 5, for instance, finds a miniscule trial, and the temptation in looking at those kinds of results is to say that my goodness, Study 5 found a huge effect where study 1 found almost no effect whatsoever. Unfortunately, that interpretation of the literature is utterly wrong. And to understand why it's wrong requires some understanding of the t-test and the formula for the t-test that I put up here is not as imposing as it locks. There are just a couple of things you need to know about it, first of all, if the value of t increases, the more likely it is you're going to get statistical significance. A big t means a low p value with statistical significance. A t around 1

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means it's nonsignificant.

But the most important point I want to make on this formula is it has two terms, they're each denoted in brackets, one on the left and one on the right. The term on the left is an effect size; you can look at the numerator in the term there, the X sub-e and the X sub-c, and see that that's the difference between the experimental and the control groups. So as your treatment becomes more effective, that difference between the experimental and the control groups will increase, and t will increase. But that is the only part of that formula that actually gives you the size of the effect, the magnitude of the effect. The p-values simply do not. But I do want to say that that concept of effect size, that left-hand term denoted here, I think is arguably the most important concept in research synthesis. It allows you to look at something and say how well it works, and as a matter of fact, that chunk of t-test that we'll be using in the meta-analysis that we present later is our measure of effect size.

If there are any statisticians in the group, that's known as the Hedges G or Hedges D, but

just think of it as a chunk of t-test, that piece
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that tells you how big the effect was.
Again, to restate the point in another way, if we rook at the right-hand term of the equation, it contains only the number of subjects in each group. And you can change the number of subject in each group, increase the value of t, and thereby increase the probability that you will get statistical significance. The t-value in other words, can be strictly related to just the number of subjects in a group, the number of patients in a group. The t-value and the p say nothing about the size of the effect. A p equal to .4 may actually be a bigger effect than a p equal to .0001, because it all depends on the number of subjects in a group.
And if you think back to those first slides, where I had two studies that were nonsignificant and three that were significant, and the subsequent slide where I had p-values, one at the bottom which was very small and one at the top which was relatively large, here's actually how I generated all of those p-values. The means in all of the groups were identical, the means in all of the control groups were identical, the means in the experimental groups were identical, the standard deviations in the control groups were identical, and
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the standard deviations in the control groups were identical, only the number of subjects differed.
I can't reinforce this concept of effect size too much. And lest you think that this is something peculiar to the t-test, it is not. All of statistics boils down to this simple formula. Anytime you test statistical significance, you are multiplying some effect size times some measure of study size. The reason you want to do a meta-analysis is to look at that measure of effect size. You want to ask not just did it work but how well did it work.
Basing decisions on p-values actually leads you to very conservative conclusions. Here's an example of a kind of plot you will be seeing

several times through this talk. You may be familiar with it, but this is a synthetic data set. The first five diamonds there show the effect size now, which is denotable along the X axis and the thinner lines denote the 95 percent confidence intervals. Each of those five trials is statistically nonsignificant, so if I were to look at the five individual results of these studies, I would say five trials, five nonsignificant results, clearly it doesn't work, this technology is ineffective. In point of fact, that's

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wrong. In point of fact, when you combine these results, when you look at the effect sizes, there is indeed effectiveness to this hypothetical trial.

Now, another thing about the problem with significance levels else is that using significance levels prevents one from seeing true patterns in data and also creates false patterns in data. Let's look again at those original five studies. We had a false pattern in the data; we had two that were nonsignificant and three that were significant. Here is a plot of the effect sizes of those studies. As they should, all of the effect sizes are identical, and then the overall result of this hypothetical meta-analysis is shown at the bottom. In other words, those results and those evidence tables were perfectly consistent with each other. They were engineered to be perfectly consistent with each other.

What I want to argue here is that the meaning of statistical tests of individual studies, p-values in particular, is arguably the most overused and misinterpreted concept in research synthesis. They are of limited value. If you have one study at hand, they are valuable; if you have more than one they are probably not valuable. That is one of the

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primary reasons we sought to do a meta-analysis. Another of the reasons we sought to do a meta-analysis was to look for patterns in data.

You can only see those patterns if you look at the effect sizes, and in looking at effect sizes, you are by nature, doing a meta-analysis.

So let me turn now to the report itself. I do have to begin with a couple of caveats, and that is, it's about four and a half years old, the update in the report is about three and a half years old, so it is the case that newer information isn't addressed. And I'm going to try my best to answer the questions that are before you. The upshot of this talk is that I won't be able to do it probably in a complete fashion, but I will explain why.

I do know you have a question before you on arterial ulcers. The report that we have, the ECRI report, is silent on arterial ulcers simply because there is insufficient evidence from which to draw a conclusion about them. That is a case where the absence of evidence should not be taken as evidence of no effectiveness; there's just simply no data, we are not going to comment.

So what I'm going to talk about today is primarily venous and decubitus ulcers. What we have

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done in our meta-analysis first of all, is to take the results of the investigators as published and recompute them wherever possible. The primary reason is because there are some problems ranging from moderate to serious with the outcomes that are reported in many of the clinical trials. One of the outcomes they reported is percentage of patients healed. That is plausible that if you are comparing two groups of patient, one as an experimental group and one as a control group, and the sizes of the ulcers at the beginnings of the studies are different, it's plausible that more patients will have completely healed ulcers if they begin with smaller ulcers.

I know that these trials are randomized, but these trials are small randomized control trials, many less than -- several of them have less than ten patients. It's very difficult to guarantee that the wound sizes are identical, are near identical in the control trials with experimental and control groups of such small trials, and that is yet another reason for not wanting to use the percentage of patients healed.

(Technical problem delay.)
For some reason I have some slides that have died on me here in Power Point. I do want to comment on the quality of the literature. In general, it is the case that the clinical literature as you probably know, is not a perfect literature. The trials we're looking at are essentially nine trials, and if you look at the handout I gave you, they are listed on the slide entitled Primary Studies, and that should be on page 10. And it's those nine trials that comprise the bulk of our conclusions here.

Of these, seven were randomized, and of those seven, four were blinded. All but one trial specified that its controls received a sham device plus additional treatment. In five of the eight trials, this additional treatment was saline soaked gauze. In the electrical stimulation group, those patients received electrical stimulation plus this additional treatment, again, in five of the eight trials, the additional treatment was saline soaked gauze. This doesn't guarantee -- this is not a bad quality literature, I will say that. In looking at this literature, we compared it for instance to the quality of the literature on occlusive and nonocclusive dressings; it is of the same quality.

We also looked at it in a quantitative fashion, because we did something that is fairly radical for a meta-analysis, and that is, we included uncontrolled trials in our analysis. But what we sought to do was determine whether the results of -- not uncontrolled, unblinded trials and nonrandomized trials in our analysis. What we sought to do is determine if the result of the nonrandomized trials and the nonblinded trials were in fact different from those that were randomized and/or blinded. And in fact, those results were not different. The argument here is that we can use those trials because it doesn't make a difference if it doesn't make a difference.

Now there's a tremendous advantage to that

approach. The typical approach is to say if the trial is not randomized and it is not blinded, I am going to discard it. What that typical approach means is that there is nothing of interest to me in any of those trials. Stated another way, those nonrandomized nonblinded trials contain no information whatsoever. Well, I'm not convinced that that's true. As a matter of fact, these trials probably do contain some information, and that is certainly one of the reasons we incorporate these trials in this analysis.

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And again, we verified the fact that we could do so by testing whether including these trials, whether the lack of randomization and whether the lack of blinding would influence our results, and in fact it didn't. So we are allowed now to use the information these trials contain about wound healing, about rates of wound healing, about ulcer size, about the types of device they used, and so on, in considering the results of this analysis.

I know too you were asked a question about whether the results of these studies are consistent. In point of fact, they aren't. Here are the effect sizes for the nine trials. They are very different from each other. This is the basic fact one needs to grapple with when considering this literature, this is the core of the assessment, this is the key to thinking about this literature. This is not so much the result of the ECRI report or the ECRI analysis. This is what these investigators found. This is their effect sizes, we got to them by a simple little algebra. They are different, some of them very different. As a matter of fact, that's not bad.

One of the reasons for doing a meta-analysis is to explain the differences among trials. For those of you who are statisticians,

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philosophers or just obsessive compulsive, to be sure the kinds of result we get out are correlational, we're not getting causation, so we will say that such and such a thing correlates with better or worse wound healing, and not such and such thing causes

better or worse rates of wound healing. In point of fact, what we have here today is real decisions made by real people about real patients, and at least it is our opinion that having correlations is better than having no information at all. You can consider in your deliberations the meaning of correlational data, but you should at least be aware that these correlations exist.

Now immediately when trying to synthesize all nine trials, we ran into a problem. There was no combination of variables we could use to explain the differences among them. As a result, we did have to omit one study. The reason we omitted the study was because its reporting was a little poorer than some of the other studies. We would have liked a complete description of all studies, we didn't get such a complete description, so we had to discard this one. Now it turns out the study we discarded was a study by Salzberg et al. And it also turns out that this study found the largest effect, had the largest

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effect sizes of all trials. You can argue that a consequence of that is that our analysis is conservative, that it is biased, if you will, against finding an effect of electrical stimulation.

So we turned and looked again at the eight studies, again verified that the failure to randomize and the failure to blind had no effect on -- would have no effect on the results of our analysis, and again found an overall statistical significant effect, again found that there is still a lot of disagreement between the results, between the effect sizes of these trials, and found that the only way we could reconcile the differences among those trials was by looking at wound size, the type of ulcer, and how they were treated.

Now it turns out that smaller ulcers appear to heal faster in response to electrical stimulation than do the larger ones. It is possible, maybe even probable, that decubitus ulcers tend to heal better than venous ulcers. There is a caveat that that result may not be generalizable. There is some rather complex statistics we did in the

background that suggests that while this is a strong trend, there are some difficulties in generalizing this.

Then the third thing that we need to explain the differences among these trials is the type of device, and that is, the ulcers that were treated with direct or pulsed current tended to heal less well than other forms of ulcers. Now real caveats are needed when talking about that. For statistical reasons we had to lump those two types of devices together, and we really cannot make conclusions about which individual device is best or which individual device is the worse, if you will.

Now overall, I want to qualify again, to arrive at those conclusions we had to discard the results of one trial. It does hinder our explanation of why these studies are different, why the effect size of these studies are different, and I want to keep coming back to that fact. The effect sizes in these studies are different. This is a thing the investigators found. To understand this data, one needs to understand why they are different. These are little small studies, which is somewhat problematic, even though they are randomized. I alluded to that problem before.

The meta-analysis we conducted partially gets around that fact, perhaps to a large part, although there are some technical criticisms that we

bring out in the report that you could level against that meta-analysis. And I do want to stress that the literature is relatively good but not perfect. That I think is actually a strong positive statement about the quality of this literature. It is in general I think, there is another presentation I give about the quality of medical literature and the figure that I arrive at there is that 85 percent of all randomized control trials have the potential for very serious bias.

Again, I want to stress the fact that this data set is complicated. But I want to stress the fact too that if we just look at the simple

difference between the treated groups, those that received electrical stimulation plus typically saline soaked gauze, versus those that received typically but not always saline soaked gauze, there is a huge difference between the groups.

In terms of standard deviation units, it's 1.1 standard deviation units. That's not a terribly easy figure for most people to grasp. Here's a picture and unfortunately the red doesn't show up, if you look at your slide, you'll see that the electrical stimulation graph is very far to the right. This I think tells a better story, ad if we

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were to express these results as a two-by-two table, the improvement seen in the electrical stimulation is about three, in wound healing rates, is about three times higher than the improvement seen in the control groups. The difficulty is, those effect sizes are on average, and that with a data set like this, averages are very difficult to interpret.

Let's consider the following hypothetical treatment of ten studies. I have five studies on the left, where they show that this hypothetical treatment tends to kill patients; I have five studies on the right that show that this hypothetical treatment tends to cure patients. The average effect here is zero, no effect on average. That doesn't give us a whole lot of information. In fact, there are clearly some patients to whom you want to give this therapy and clearly some patients to whom you do not want to give this therapy. Thinking of that slide in terms of averages simply isn't useful.

We are in an analogous situation with the wound healing data. The information found by the investigators, the effect sizes found by these investigators are quite different from each other. It is partly for that reason that I really cannot address one of the questions that you have before

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you. And that is, to assess the effectiveness, the absolute effectiveness of the healing of venous ulcers versus the healing of decubitus ulcers. All we can do here is state it in relative terms. Again,

we are dealing with essentially eight studies, it's a very small data set for such complexity. But again, I want to stress the notion that the only explanation we could come up with are that the data are consistent with the idea that electrical stimulation is more effective on smaller perhaps decubitus ulcers and ulcers not treated with direct or pulse current. And in fact in those cases, the effects may be large.

The unfortunate situation here is that this is not a simple data set and that there are really no simpler conclusions I can offer you today.

With that having been said, I think I will just close the presentation here and open the floor to questions, if I may.

DR. GARBER: Let me just ask you a quick question for information. When you say you eliminate this Salzberg study because you could not explain the differences, could you elaborate on what you meant by being able to explain?

DR. TURKELSON: These studies find different effect sizes. Study A finds a huge effect,

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study B finds a very small effect. These effect sizes, if you do a statistical test, are significantly different from each other. What that means is that something else is going on in these trials besides electrical stimulation, something in addition to electrical stimulation is affecting these results. We eliminate the Salzberg trial because of its poor reporting, or I should say, less than complete reporting. That probably isn't a bad thing. Because it happened to have the biggest effect size, you can argue again that our analysis is a tad conservative. We didn't --

DR. GARBER: Well, I can understand eliminating the study because of some serious flaw in the study design, including poor reporting, but that's independent of the issue of whether its results were different.

DR. TURKELSON: We can't explain it. We cannot explain -- that is, as we state in the report, that's the difficulty in interpreting this analysis, given that there is no reason we could explain the

differences among all nine trials. Now, that is probably not a weakness of the analysis so much as it is a problem with less than complete reporting. Again, that's a very common thing in the medical literature; I don't want to -- it's very easy for me to stand up and make it look like I'm picking on the electrical stimulation literature. In point of fact, I'm not. I'm picking on, I am trying to indiscriminately offend all the entire body of clinical research.

DR. GARBER: Can you, and this is not something in your presentation, but in the report, a great deal of discussion is devoted to your measure of the healing rate data and how that affected the statistical significance of the results. Can you talk about what effects, can you summarize the basic impact of choosing data as the measure as opposed to some of the end points that were reported in the trials?

DR. TURKELSON: Yeah, and unfortunately those were the slides that went blank on me. Interpretation of the other end points as reported in the trials is a tad difficult. I think the easiest one to handle is some of these subjective rating scales, where the amount of exudate is measured or the amount of granulation is measured. In point of fact, I am not aware of research that addresses whether patients care about that. I would rather imagine they care about whether their wounds are healed. And that, we're really not doing anything novel here, that's just a standard procedure of taking a direct patient outcome over an intermediate patient outcome.

As far as healing rates go, again, those are dependent on the initial wound size, the size of the wounds at the beginning of the study. If the sizes in the experimental, of the wound sizes in the experimental and control groups at the beginning of the study are different, then healing rate or percentage of patients healed is terribly difficult to interpret. Because these are small randomized

trials, it's very easy to compromise the randomization schemes, and that's one reason we could look at it.

Then the wound healing rate is another we didn't look at, because the investigators tend to treat it as linear. It would seem to me that if wound healing rates have something to do with cell division, we have a case of one cell dividing into two, two dividing into four, four dividing into eight, and so on, which is a distinctly nonlinear process, and as a matter of fact, the exponential model that we used, the thetas, is consistent with the notion that cell division is exponential and not

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linear.

DR. GARBER: Well, actually, that wasn't totally clear to me. If you think that -- somewhere in the report it said that the wounds are basically three dimensional, and you're measuring something linear typically for the healing rate, which is, I thought it was wound diameter or something like that.

DR. TURKELSON: Well, it is a three dimensional, and you're also, I'm sure if you read the report, are aware that this is a model we validated in the report as well. Not only is there a publication that addresses this fact, but every time somebody in one of the papers presented raw patient data, we went back and made sure that that followed an exponential model and every time we could attempt to validate the exponential rate, we were able to. There is certainly evidence then to suggest that is the way these wounds heal and there is an absence of data to suggest that they would heal linearly. I am not frankly aware of any general argument, but it is difficult to conceive of any biological process that's linear. Biology just doesn't work that way.

DR. GARBER: No, we dont need to go off on this, the alternatives to linear. There's many other kinds of models.

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DR. TURKELSON: There's many other kinds. This equation seems to fit very well. And again, this isn't our idea, this isn't novel, this was a

notion that was published by Salzberg and again, we take his exponential model, all of the data we are able to get seemed to fit that model. Yes.

DR. OLECK: I have a question that focuses in on the variability of these devices. Again the report and looking through all the studies, it clearly indicated there were several different categories of devices?

DR. TURKELSON: That's correct.

DR. OLECK: And within each particular category, there were different types of devices and a very wide variety of settings within those. Can lumping all those of those things together trying to do this meta-analysis, to try to gain some significance? I guess I would like you to talk again about the appropriateness, the reasonableness of doing those with all those different technologies, and if we come to some conclusion based on putting together all of those technologies, then is that conclusion saying that well, any electrical device would fall into that same category? Why look at things over this broad range of devices rather than

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on at least a particular modality or particular type of device?

DR. TURKELSON: I'm not sure I understand your question, so if I'm not answering it, please interrupt me. I will begin by saying we have a partial answer. We did look individually by devices in the narrative section of the report. The difficulty is that there are probably too few trials of any given device to meta-analyze, so again, a nonmeta-analytic systematic narrative review, if you will, is inherently biased towards being conservative. Hark back to that one slide I showed with five trials that were, each of which had nonsignificant results, and then one trial that had statistically significant results. That's a manifestation of that bias.

So we tried to address the individual wound devices in a narrative review but felt we wanted more statistical power, felt we needed to be a little less biased toward the conservative, and

lumped these devices together. Now unfortunately, the only way you can do it is by lumping these two devices together in sort of a statistical construct category. I think the nice thing about that result is that it satisfies the statisticians and the lunks like me. The bad thing about the result is it's very difficult to interpret.

We could come up with no manipulation of the variables that would explain the differences between these trials other than the ones we used. All I can tell you is that this construct that is comprised of these two devices, tends to get wound healing. This is I suppose one of those points where the stock answer, this is a complex problem in need of future research, is given. I can't offer you the answer I want because I don't have the data.

DR. OLECK: When you say two devices, I guess I was looking through, and in one of those primary studies, it looks like they fall into several different studies.

DR. TURKELSON: The primary studies do. What we did is, we divided the device types into two categories in general. The first category is comprised of those two devices, the AC device and one of the other, and then all of the other devices. It is a very difficult construct to interpret. The difficulty is that, the problem is that, we know that there's clearly something going on here, but we don't know how to explain it.

DR. STANTON: Let me build on something I think Adrian was trying to get at. You and your colleagues I think have probably an exquisite understanding of these studies, and have probably discussed them and debated them and done some very sophisticated analysis on them.

DR. TURKELSON: I will say as of four and a half years ago, I did. Now we'll see.

DR. STANTON: What I would like you to do, which may be abhorrent to statisticians, is to give a qualitative perspective, because I think you have pointed out very nicely the problems with the

meta-analysis on here, and we could spend a day debating the meta-analysis and please, let's not. But if you could, it seems to me there's a reasonable body of literature here about decubitus ulcers and various type of electrical stimulation, if you could give a qualitative assessment of that. And then do the same for venous, which there seems to be almost a reasonable amount of literature on. And then lastly can you do it for arterial/diabetic and incorporate other studies that have come out since the report?

DR. TURKELSON: I cannot incorporate studies that have come out since the report.

DR. STANTON: Okay. You have not looked at anything?

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DR. TURKELSON: I have not looked at that.

DR. STANTON: Okay. Then just the first two, please.

DR. TURKELSON: Obviously, the report was silent on arterial, because at that time there was no data. The first two, the short answer to your question is no, I can't. We can't look at venous ulcers in isolation with this data set. We can't look at decubitus ulcers in isolation with this data set. We have to look at them relative to one another. It's a very complicated explanation, I know. Decubitus ulcers appear to heal faster than venous ulcers. Smaller ulcers appear to heal faster than larger ones. Ulcers treated with a certain type of device or devices appear to heal faster than ulcers treated with another kind of device.

So if I'm looking at say decubitus ulcers, I can't make the blanket statement because it depends, at least from this data set, on the initial size of that ulcer and the type of device used. I can't make a blanket statement about venous ulcers other than to say they appear to heal less fast than the decubitus, because again, the venous ulcers, their healing rates appear to depend on the initial size of the ulcer and the type of device used.

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That having been said, if we look at the positive, the small ulcers, the decubitus ulcers, it

would seem that there is something very large going on. If you recall that two-by-two table, where there is a 75 percent patients healed of patients treated and 25 that are not, that's a massive effect, and that's a massive effect that is an average, so that average can be dragged down by something, as well as pulled up. So somewhere buried in this data set is a big effect. I -- it's all the data will allow me to do. I wanted to harp on the complexity of the data because I can't give you exactly what you want.

DR. STANTON: Right. And I think one of the things that we're going to struggle with is trying to tease that out, and I don't think it's going to be reasonable to say, well, every device is going to have to go out there and do separate randomized control trial on every different type of ulcer subdivided into different sizes of ulcers.

DR. TURKELSON: Right.

DR. STANTON: I think it's just a difficult issue the panel is going to have to struggle with.

DR. TURKELSON: You're now seeing actually why I began the presentation with the difference

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between a technology assessment and say a coverage decision or a guideline. I can tell you what the data is, but I don't want to make those type of clinical judgments that you're going to have to make for this decision. These are the data, and I'm passing the problem on to you.

DR. GARBER: Charles, maybe I can just ask one more detail for your response to Marshall's question there, and it really has to do with distinguishing the venous ulcers from the decubitus ulcers.

DR. TURKELSON: Yes.

DR. GARBER: Now the studies as I understand it for the most part have mixes of these two. So can you elaborate -- we will have to eventually address questions you heard from before about each of these indications separately, and you stated that there is evidence of greater healing rates with the decubitus ulcers.

DR. TURKELSON: With the smaller decubitus ulcers.
DR. GARBER: Okay. I would like you to just explain a little bit how you came up with that conclusion, given the mix of the two types of ulcers in the published studies.

DR. TURKELSON: First of all, none of the studies we used had mixed patients. That was one of our inclusion criteria, so the studies we took all had, either used all decubitus or all venous.
DR. GARBER: You mean within one case?
DR. TURKELSON: Within one trial.
DR. GARBER: Okay.
DR. TURKELSON: None of these nine trials had an add mixture of patients with venous and decubitus ulcers.
The answer to the rest of your question is not so simple. It was essentially a metaregression that we performed. To fully answer it, I'd have to --
DR. GARBER: That's okay. I mean, that's the equivalent of doing something like subgroup analysis on a pool study.
DR. TURKELSON: Yeah, but we were not dealing with heterogenous patient populations within a given trial.
DR. GARBER: Right, okay. So you have separate trials, so you pooled separate -- you could in theory, you used regression analysis, but in theory you could have separately pooled the decubitus, the trials using decubitus ulcers and the

trials using venous ulcers; correct?
DR. TURKELSON: In theory you could have. You'd lose information by doing that.
DR. GARBER: I understand, and that's why you chose the regression analysis.
DR. TURKELSON: Yes.
DR. GARBER: There's another way we can think of this, is that with regression analysis, we are mimicking what you might have done by pooling the two types of trials separately.

DR. TURKELSON: That's an approximation, yes.

DR. GARBER: Yes, understood, okay.

DR. TUNIS: Okay. Well, thanks, Dr. Turkelson, and thanks, Dr. Lerner, as well. Now Dr. Whyte is going to sort of update this for a little bit of filling in the information of what's happened since the report was put together, a little more background, and then we will go to break.

DR. WHYTE: As Dr. Turkelson mentioned, this report was done in 1996 and it is the year 2000, and sometimes we move slow but we don't move that slow, so I'm just going to spend the next few minutes updating on you what we have done since your report was completed.

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When the report was completed in 1996, HCFA referred the topic to the technical advisory committee, and at that time the TAC consisted of government physicians and HCFA contracted medical directors. The TAC reviewed the ECRI report and they noted that wound healing outcomes in many of these studies may have compromised by several confounding factors, and therefore, they voted to issue a noncoverage recommendation.

Dr. Turkelson briefly mentioned how in 1997, ECRI prepared an update of its original report and you also have that as part of your packet. Now based on the update as well as the TAC recommendation, HCFA rescinded carrier discretion -- remember, previous to that it was up to the carriers to decide -- and instead issued a broad national noncoverage policy, in April of '97. However, prior to the implementation of this noncoverage policy, the American Physical Therapy Association, APTA, and five individual plaintiffs, filed suit in Federal District Court in Massachusetts, and the case is called Aitken v. Shalala, to challenge the national noncoverage determination.

What happened since then is the Court issued a preliminary injunction preventing HCFA from

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issuing the national noncoverage policy and instead

remanded the issue back to the Agency to either provide a more detailed explanation of the noncoverage determination or revision of that determination. Since then, the policy has remained a carrier discretion.

Subsequent to the Court's decision, we took several actions, and we actually asked for three responses, and you have three letters in your packet. You may wish to refer to them during the course of your deliberations.

First is a January 23rd, 1998 letter from ECRI to the Agency, and ECRI primarily addressed two issues relating to the Court's decision. The purpose of the letter was to respond to the Court's decision. The first issue, and it's broken down in the letter, focused on wording of minimal versus no therapy, and the second issue centered on the statement that there were no comparative studies of electrical stimulation versus conventional therapy.

The second letter you have is an October 14th, 1998 memorandum from AHCPR center for practice and technology assessment. Basically, this letter was to comment on the ECRI letter, and this memo opined that the overall conclusions of the original

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ECRI report remained valid, and they also commented on the guidelines for the treatment of pressure ulcers and noted that the guidelines simply state that electrical stimulation could be considered as treatment for certain pressure ulcers unresponsive to conventional therapy.

The final letter you had is an April 1, 1999 letter to the Agency from the American Physical Therapy Association, commenting on the ECRI letter about the court decision and then the AHCPR letter on the ECRI letter. There's representatives from the American Physical therapy Association here today that can comment on the letter.

Now since the assessment, we have been meeting with interested parties on this topic, we have conducted a literature search of articles since the ECRI report and its update in 1997. We have provided the extracted literature search as well as

the articles as part of your packet, and that's identified as Appendix A, articles reviewed since the ECRI report.

It's important to note that we set broad search parameters in order to find as much relevant evidence as possible regarding the appropriateness and effectiveness of electrical stimulation. And

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those searches yielded clinical trials, case series, a meta-analysis, literature reviews, and we also included some opinion pieces. We also included several nonpublished articles that the APTA submitted to us that they felt were important to review.

Internally, we felt some questions about the adequacy of the evidence remained, so we decided to refer the issue to the Medicare Coverage Advisory Committee and that's how we got here today. Thank you.

MS. CONRAD: Thank you, Dr. Whyte. At this point, let's take a 15-minute break. Report back here about 10:40 or so.

(Recess taken.)

MS. CONRAD: Let's try to get started with the public presentations. The first speaker is Neil Spielholz from the American Physical Therapy Association, who will be followed by Joseph McCulloch.

DR. SPIELHOLZ: Good morning. My name is Dr. Neil Spielholz. I am a physical therapist and professor of physical therapy at the University of Miami School of Medicine. I am here on behalf of the American Physical Therapy Association and its 65,000 members. I have no current or past financial

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interest in any manufacturer whose products are under discussion today. I am requesting that my testimony today along with my written statement that was already distributed to the panel members, be included in the permanent record of this meeting.

The panel is being asked to address whether the evidence is adequate to draw conclusions about the effectiveness of electrical stimulation for the treatment of chronic ulcers. The APTA responds

unequivocally, yes. There is adequate evidence to support the use of electrical stimulation as an additional treatment to facilitate the healing process of recalcitrant wounds.

As you are aware, an assessment of the literature has been done. At the request of HCFA, ECRI completed a technology assessment of the use of electrical stimulation for the treatment of chronic wounds. In APTA's view, the technology assessment contains some serious flaws and consequently, APTA has concerns with the way this assessment presents the electrical stimulation studies and the results thereof.

APTA believes that with respect to the efficacy of electrical stimulation for chronic wounds compared to sham or placebo stimulation, this

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assessment contains inconsistencies and misrepresentations of those data and study methods. It is important to note that the ECRI report contained a number of positive conclusions concerning the effects of electrical stimulation on the healing of chronic wounds, but the report also questioned the value of a number of the underlying stimulation studies.

One specific is that the assessment mistakenly concluded that patients in the control groups of several studies received no treatment whatsoever for their wounds. Consequently, although ECRI specifically found that, quote, there was a significant difference in the normalized healing rates between some types of electrical stimulation and control groups, unquote, ECRI erroneously concluded that, quote, these studies only demonstrate that patients treated by electrical stimulation may heal faster than those undergoing no therapy at all, unquote.

This significant error resulted from a misinterpretation of the words sham or placebo in many of the underlying studies. In those studies, researchers gave patients in both the study group and the control group conventional therapy, which

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consists of moist dressings, wound cleaning, debridement, et cetera, if it was necessary. The patients in the study group also received electrical stimulation. Patients in the control group received in addition to conventional care, sham or placebo electrical stimulation, i.e., the units were not turned on. Unfortunately, ECRI interpreted the use of the words sham or placebo in these studies to mean that patients in the control group received no therapy at all. This is simply not correct.

As Judge O'Toole expressively concluded, quote, ECRI's statement that there are no studies which compare electrical stimulation to conventional treatment appears simply wrong, unquote. To verify and confirm this misunderstanding, APTA obtained affidavits from the primary investigators of several studies. These affidavits have been submitted to HCFA with our written testimony.

In at least three studies, not only was electrical stimulation plus conventional care compared to just conventional care, but a crossover design was also used. The technology assessment, however, fails to convey, except for one situation, that a number of patients in control groups who had made little or no improvement after a specified

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period of time, were allowed to cross over and have electrical stimulation added to their conventional care. When they did, the wounds healed.

This is evidenced in, if we could have the first overhead please, and unfortunately this is small and you can't see it, but from the study by Kloth and Feedar, as seen in Tables 1 and 2 of this article, nine of nine ulcers in the treatment group healed completely after an average of 7.3 weeks. By contrast, not only did none of the seven ulcers in the control group close after an average of 7.4 weeks, some ulcers actually increased in size. And if I'm given a chance, I would like later to perhaps comment on what Dr. Turkelson said about this is possibly being a flawed outcome, but for now let me just continue with the results.

In fact as a group, talking about the

control group, the average change in ulcer size was an increase of almost 6.5 percent. Kloth and Feedar then described how three of these patients were then crossed over and had electrical stimulation added to their ongoing conventional care. Their average healing rate then increased and all wounds closed within 8 weeks. From this study then, we have actually 12 of 12 treated wounds that closed.

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There is also from the paper by Gentzkow et al., as seen from Figure 1 of this paper, during the first four weeks of the study, wounds in the treatment group had decreased in area an average of 49.8 percent. In the same time frame, ulcers in the sham treatment group increased an average of 23.4 percent. 15 patients out of these 19 in the sham group were then crossed over to receive electrical stimulation. The wounds in these patients had only closed an average of 13.4 percent during the four weeks of sham treatment. In other words, these 15 patients were a subgroup of the original group, which is why they had a somewhat lower heal rate. The wounds in these patients had only closed an average of 13.4 percent during the four weeks of sham treatment, but this then increased to a closure of 47.9 percent less than their size at time of crossover. In other words, there was a four-fold increase in healing during four weeks of stimulation, versus four weeks of sham treatment in the same ulcers.

In fact, at the end of an average of nine weeks, 40 percent of these ulcers were then healed completely. A similar percentage of ulcers, or 41 percent, had healed in the active treatment group

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over an average of 11.8 weeks.

In the paper by Baker et al., and again, don't do overheads on HF printers, it just smears too much, but basically what this is supposed to have shown is that 11 patients had wounds that were treated first under the control protocol and then later under one of two stimulation protocols. The mean healing rate for these patients during the

control protocol was 9.7 percent, and this increased to 43.4 percent per week during active treatment. Seven of these crossed over patients healed during the stimulation period.

It should also be noted that the recognition of what happened to the crossover patients in these and other studies invalidates other criticisms leveled by ECRI that imply that the control patients in all these studies were somehow and for some reason at a healing disadvantage compared to the patients who received treatment. ECRI failed to address the significance of these crossover findings.

On the basis of these and other concerns, APTA would like to caution the panel against formulating a negative recommendation based on the unfounded criticisms of studies found in the ECRI

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technology assessment. It is our belief that these aforementioned studies are profound and render impressive positive results.

And there is additional evidence in the literature that demonstrates the efficacy of this intervention. Next overhead please. For example, Stiller et al. Had closure of 50 percent of wounds, 9 of 18, was achieved over an eight-week period, while none of the control group healed. In Walcott et al., 75 percent, 6 of 8 chronic wounds healed over an average of 7.9 weeks, while none of nine in the control group healed. And in the Wood et al. Article, 58 percent, or 25 of 43 treated wounds closed compared to 3 percent, or 1 out of 33 in the control groups.

Indeed, we want to bring your attention to the fact that despite the criticism that ECRI levels against studies, their report still found the quality of the studies evaluating electrical stimulation to be roughly equivalent to the quality of similar published studies in other wound healing therapies.

And because my time is almost up, let me jump ahead, if I may. Can I have the next overhead please? APTA believes based on our assessment of the literature and all the evidence which is presented in

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detail in our written testimony, that it is clear that the evidence is sufficient to support the use of electrical stimulation for chronic pressure ulcers, chronic venous ulcers and chronic arterial ulcers.

Additionally -- next overhead, and this is the final -- additionally, the panel is being asked to place the therapy in a category of effectiveness. APTA believes the intervention could be placed in category of effectiveness 2, which is more effective, the new intervention improves health outcomes by a significant margin as compared with established services. However, since this intervention is not new and since it has become the standard of care, albeit adjunctive care for ulcers that fail to heal, the intervention could just as accurately be considered breakthrough technology, which is category 1.

There is adequate clinical evidence to conclude that electrical stimulation for chronic wounds is effective. Because its efficacy is supported by valid and reliable evidence and because of a profound benefit it can provide to needy Medicare beneficiaries who suffer from chronic wounds, APTA urges you to recommend to HCFA that the Agency ultimately issue a national coverage policy.

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Thank you.

MS. CONRAD: Thank you, Dr. Spielholz. Joseph McCulloch, followed by Jennifer Dexter.

DR. McCULLOCH: Good morning. My name is Dr. Joseph McCulloch and I'm here today representing the American Academy of Wound Management. The AAWM is a multidisciplinary certification agency that represents over 1600 physicians, nurses, physical therapists, and other health care providers who have achieved board certification as wound care specialists. As wound care specialists, members of the Academy understand well the benefits to be gained from the electrical stimulation in patients with chronic wounds, including both pressure, venous insufficiency and arterial ulcers.

As a matter of formality, I have no

current or prior financial interest in any manufacturer whose products are under discussion here today. I would also like to request that today's testimony, along with my written testimony, be included in the record.

There are have been numerous pieces of literature that examined the effectiveness of E-stim, which have been presented to the panel, including over 60 citations regarding the use of E-stim, and

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they were asked to ask whether the evidence was adequate to draw conclusions about the effectiveness of electrical stimulation as an adjunctive therapy for chronic wounds. Consistently the studies conclude that electrical stimulation is an effective adjunctive therapy in the treatment of chronic wounds. This literature only presents a portion of the studies that exist showing electrical stimulation as a beneficial and effective treatment for the healing of chronic wounds.

Of the over 60 articles provided to the panel, 14 articles were published after 1996. My testimony will focus on this new literature. The literature review is broken down by wound type, as the panel is considering the effectiveness of electrical stimulation on chronic pressure ulcers, venous insufficiency ulcers, and ulcers due to arterial insufficiency.

Beginning first with pressure ulcers. In 1999, Lisa Ovington revisited the AHCPR guidelines concerning surgical dressings and adjunctive therapies for pressure ulcers. On the basis of new literature available since the AHCPR guideline was published, Dr. Ovington concluded that the strength of evidence rating should be raised from a B to an A.

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And A rating, the highest rating possible, is the result of two or more randomized control trials on pressure ulcers in humans. Ovington came to this conclusion after reviewing literature published after 1993. Her work clearly demonstrates that the literature strongly supports the use of electrical stimulation in the treatment of wounds.

In 1996, Baker and all randomly assigned patients to four groups, three receiving treatment with differing wave forms. The fourth group received sham stimulation. It is important to note that all groups continued to receive standard wound care. After 28 days, the percentage of patients in treatment groups who were fully healed was nearly double those in the control group. Control group patients failing to heal were then allowed to cross over into a treatment group. A statistically significant result in healing rates resulted from the crossover.

AAWM recognizes that not all literature is positive. Sheffitt et al. Published a literature review in Ostomy and Wound Management in February of this year. The review is rather limited and in fact some of the literature reviewed were not published studies. The authors did not conduct a critical

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review of the actual literature but merely reviewed the literature abstracts and then drew their conclusions. Moreover, the reviews by the authors are misrepresented and the article suggests research protocols that are clinically unreasonable, unrealistic, and even unethical. This article has come under serious criticisms by Dr. Spielholz, who you just heard from, and Luther Kloth, as being biased and misleading about the articles it includes. This critique was published in a subsequent edition of the Journal.

Looking next at venous insufficiency. In 1996, Kenkre conducted a randomized double blind control clinical trial, which assessed the effects of electromagnetic therapy on chronic venous ulcers in 19 patients. 68 percent experienced improvement in ulcer size, and four individuals, 21 percent, healed completely. The control group was confined to receive conventional care. The results showed that the patients in the treatment group reported increased mobility, decreased pain, and greater healing. This new study provides additional support for the use of E-stim as an effective intervention in the treatment of venous ulcers.

In arterial and diabetic ulcers, in 1998, Gilchrist, a study on electrical stimulation was applied to treat skin perfusion in 132 patients with diabetes. The study analyzed the possible mechanism of wound healing action and the role electrical stimulation potentially played in that mechanism. While not a wound healing study per se, it did support the use of E-stim in older patients, and found that electrical stimulation increased blood flow and decreased edema, two of the primary obstacles in healing of the diabetic foot.

Also in 1998, Peters published the results of his study on the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. In his study, 11 of the 19 subjects were diagnosed with impaired peripheral perfusion. The subjects were studied over a two-day period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements, was measured during the first five minutes of stimulation, P .04. For those patients without vascular disease, there was not a significant increase compared to the baseline, P of .28. What Peters' data suggests is that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion. Such a development can be contributory to the promotion of healing.

In 1997, Jacques published a case report of an 81 year old male with several nonhealing stage IV ulcers on his right foot. The patient was hospitalized for five months with no improvement. He was then placed on high voltage electrical stimulation for 30 minutes five days a week, and obtained 100 percent closure of all ulcers within eight weeks. In their discussions the authors write, quote, the successful use of electrical stimulation in this case was impressive. The usual modalities in treating nonhealing ulcers had proven unsuccessful. There was consensus among medical and surgical consultants that amputation was the only alternative.

End quote.

The electrical stimulation of this patient was certainly breakthrough technology, since nothing else had worked and amputation was being considered, thus supporting the notion that electrical stimulation should be covered when conventional therapy fails.

In 1997, Baker et al. Published a randomized control trial of 80 diabetic patients with 114 wounds, the duration which ranged from six to 640

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days. This study compared four groups, two receiving different types of electrical stimulation, and two very low level or no stimulation. All groups continued to receive standard wound management. Stimulation with A protocol, which was the asymmetric biphasic wave form, enhanced healing by 60 percent. Stimulation with the B protocol, which was symmetric biphasic, did not increase the healing rate when compared to the control groups.

In other and mixed categories, the 1997 article by Frantz in Clinical Geriatric Medicine, reviews a number of adjudavent treatments for recalcitrant wounds, including electrical stimulation. After reviewing eight reports which studied 255 patients in total, the article concludes that although the individual sample sizes were small, quote, these studies suggest that application of electrical stimulation has the potential of enhancing the healing of chronic recalcitrant wounds, end quote. The paper goes on to mention a ninth study that used 185 ulcers, again with good results in the treatment groups. Thus in this review alone, there is an overall sample size of 430 ulcers.

Luther Kloth and I published an article in Advances in Wound Care in 1996, which summarized 13

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clinical studies showing accelerated healing of recalcitrant pressure ulcers, and 14 in vivo studies which investigated how various aspects of the healing process were positively influenced by electrical stimulation. The paper includes a summary of how electrical stimulation parameters can be varied

depending on the therapeutic goals desired.

In summary, because of the efficacy of electrical stimulation as supported by valid and reliable evidence and because of the profound benefit it can provide to needy Medicare beneficiaries who suffer from this condition, the AAWM urges you to reach a positive recommendation on the conclusion of your proceedings today. Thank you.

MS. CONRAD: Thank you, Dr. McCulloch. Jennifer Dexter, followed by Diane Krasner.

MS. BERNISSE: Good morning. My name is Katy Bernisse. I am here on behalf of Jennifer Dexter, and I am assistant vice president for government relations for the Easter Seals national headquarters. Easter Seals appreciates the opportunity to contribute to the advisory committee's evaluation of electrical stimulation in healing chronic wounds. Easter Seals believes that electrical stimulation is a useful and effective

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treatment in promoting the healing of chronic wounds to improve health, function and independence.

Easter Seals supports the findings and recommendations of the American Physical Therapy Association regarding this adjunctive therapy.

Easter Seals is a national nonprofit organization that is dedicated to helping people with disabilities achieve independence. For more than 80 years, Easter Seals has provided home and community based services and advocacy for children and adults with disabilities. Each year Easter Seals serves more than one million people through a national affiliate network operating more than 400 service sites. Easter Seals provides medical rehabilitation and other services to tens of thousands of Medicare beneficiaries, including many with chronic and significant impairments. Easter Seals services are provided at home, comprehensive outpatient rehabilitation facility, rehabilitation agency, skilled nursing, and other settings.

Easter Seals therapists report that electrical stimulation is an effective intervention that contributes to the healing of most types of

wounds including pressure, venous stasis, diabetic, and neuropathetic ulcers, and ulcers due to arterial insufficiency. This treatment is an effective and important option in incidents where wound healing is not progressing.

Easter Seals uses a holistic approach to patient care, where electrical stimulation augments other wound care and patient education and training. Staff inform and assists clients and family members on skin care and healing, often addressing issues relating to incontinence, nutrition, transfer and mobility, prosthetic care, and environmental risks.

Let me share one example cited by an Easter Seals therapist in response to our inquiry concerning the effectiveness of this therapy. He reported that electric stimulation was particularly helpful in healing a chronic wound on the heel of a 75 year old man. This man had preexisting upper and lower limb amputations and despite aggressive dressing changes and other care, the open wound on his heel simply would not heal. He risked bone infection and possible loss of his one remaining foot. Electrical stimulation facilitated healing and contributed to an overall improvement of this man's health, function, mobility and quality of life. We believe that this successful experience is representative of the benefits of this adjunctive treatment.

Easter Seals encourages the committee to consider our positive experience with using electric stimulation for healing chronic wounds. It is a valuable component of comprehensive wound treatment, which fosters improved health outcomes and associated benefits to beneficiaries and society. We believe that research findings support the effectiveness of electric stimulation as an adjunctive therapy for chronic ulcers. Easter Seals hopes the Advisory Committee will conclude likewise in its analysis of the issue.

My colleague, Rini Catalar, assistant vice president for medical health services for Easter

Seals and an experienced physical therapist, and other staff are available to answer questions and provide additional information to assist the committee in its analysis. Contact information is in our testimony. We appreciate the opportunity to share our views today. Thank you very much.

MS. CONRAD: Thank you. Diane Krasner, followed by Joseph Cavorsi.

DR. KRASNER: Good morning. I am Dr. Diane Krasner, and I am I here to read a statement on behalf of the National Pressure Ulcer Advisory Panel. I served on the panel from 1992 to 1994 and am currently an alumni member.

The NPUAP is an independent not-for-profit organization dedicated to the prevention an management of pressure ulcers through education, research and public policy. Formed in 1987, the NPUAP is comprised of leading authorities representing various disciplines, including medicine, nursing, research, physical therapy, nutrition, and education. The NPUAP has a long history of collaborating with HCFA on a number of issues, including the PUSH tool for use on the MDS PAC, assisting with development of categories and usage guidelines for dressing and support surfaces, and assisting with the development of quality indicators for the MQIS pressure ulcer module.

The NPUAP supports the use of electrical stimulation as a generally acceptable method for pressure ulcer healing. Presently, physicians and physical therapists use E-stim as an adjunctive therapy for non-healing pressure ulcers. The U.S. AHCPR guidelines on the treatment of pressure ulcers, 1994, recommends its use for both Stage III and Stage IV pressure ulcers that have proved unresponsive to conventional therapy. Moreover, the AHCPR has noted that E-stim can also be used successfully in recalcitrant Stage III pressure ulcers.

You heard Joe McCulloch previously discuss the update to the AHCPR recommendation that Lisa Ovington published in 1999 that proposes elevating

the strength of the evidence to an A rating, and you also heard previously cited Gardner and Frantz's 1999 meta-analysis, which suggests strong evidence for the effectiveness of E-stim.

The NPUAP recognizes that HCFA has raised some concerns on the efficacy of E-stim based on the ECRI report. However, given the methodological issues raised in the analyses within the report, there were also many positive findings. Most notably, E-stim facilitates the healing of chronic wounds, pulsed current electrical stimulation provides the normalized healing rates of Stage II to Stage IV pressure ulcers, and alternating current E-stim improves the normalized healing rates of pressure ulcers.

The NPUAP agrees that more well designed clinical trials should be conducted. However, present studies do suggest that E-stim is effective in the healing of recalcitrant pressure ulcers as evidenced in the AHCPR pressure ulcer treatment

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guidelines. Until such trials are completed, HCFA can rely on the present studies and considerable expert opinion and experience which clearly suggests a positive difference in the use of E-stim in healing recalcitrant Stage II to Stage IV pressure ulcers.

And with your permission, Dr. Garber, I would like to either now or later, but since I have a few minutes, make a couple of comments on my own as an individual.

As some of you know, I have been involved in chronic wound healing for many years. I co-edit the major text in the area of chronic wound care, and I am the co-director of the interdisciplinary international wound care course at the University of Toronto. And I just, in listening to the comments this morning, wanted to speak to two points.

One is the problems with RCT as a gold standard for this patient population. They leave much to be desired because of the variability in this patient population in particular. It is estimated that only 20 percent of chronic wound patients meet the inclusion criteria in these studies, and so what

about the other 80 percent, the ones with all the co-morbidities and co-factors that drop out of these studies? The diabetics, the people with adherence

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problems. It just is an issue that we come against again and again as we evaluate dressings and new technologies, but it's a very real problem if we only really on RCTs.

And the second is the caution that if we only use time to healing as an outcome measure, I think we are doing a disservice. In fact, probably a more significant variable based on the work, the meta-analyses and the epidemiological work that Dr. Margolis is doing at Penn is how long the wound has been present in the first place. There are other significant outcome measures especially that should be considered for E-stim in future studies, and that includes reduction in pain in chronic wound patients and increasing their quality of life. Thank you.

MS. CONRAD: Thank you, Miss Krasner. Joseph Cavorsi, followed by Pamela Unger.

DR. CAVORSI: Good morning. My name is Dr. Joseph Cavorsi; that's Italian, not Cavorski, or Polish, and certainly not Kevorkian.

(Laughter.)

I am a board certified general and vascular surgeon by trade. I have been in practice since 1984. I am also the medical director of a multidisciplinary hospital based outpatient wound

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care center that treats nearly 1700 patient visits per month. I repeat, 1700 patient visits per month, dealing exclusively with the diagnosis and treatment of all forms of chronic nonhealing wounds.

For the record, I have no financial or other interest in any product which delivers the intervention that is the subject of today's hearing.

It is my understanding that the panel has been asked to determine whether the evidence, both clinical and scientific, is adequate to allow conclusions to be drawn regarding the effectiveness of electric stimulation in the treatment of chronic wounds. I wish to thank the panel for the

opportunity to express my opinion regarding this very important subject. I come to you not as a research scientist, a general quoting one study after another, I have no large database for you to review. I come to you as a physician who has extensive clinical experience dealing with real patients with real wounds on a daily basis.

My initial experience with electric stimulation was strictly incidental. In early 1992 while making early rounds on a patient of mine with a pressure ulcer on her sacrum, I noted another patient in the adjacent bed with a similar sacral wound.

Oddly, however, attached to a small apparatus with wires and an electrode. The young lady attending the machine, who turned out to be a physical therapy assistant, was kind enough to briefly describe the beneficial effects of electric stimulation in wound care when I questioned her. However, when asked for the scientific basis for her contention, she could not respond.

I shrugged the notion off. I watched the same therapist methodically set up her apparatus, with curiosity, on a daily basis. Both patients received excellent care. The pressure ulcers were properly off-loaded, they were free of nonviable necrotic tissue, and provided with protective moisture retentive occlusive dressings. Both patients were receiving nutritional support. However, my curiosity soon turned to amazement when I realized that the other patient's wound was healing better, developing healthier and more granulation tissue, and contracting or closing faster than mine was.

I was in turmoil. Was this just a coincidence? I spoke to the therapist's program director and requested any literature she had available regarding the use of electric stimulation in the treatment of wounds. She immediately provided me with nearly 40 articles, the majority of which were physical therapy based. I read each one, paid particular attention to any prospective randomized

controlled studies. Although there was much variation in how these studies were conducted, one common dominator was repeatedly evident. The study or treated group with electric stimulation fared significantly better than the placebo or control group.

I was still not convinced. I personally researched the literature and encountered excellent preclinical studies showing that externally applied electric stimulation can increase the synthesis of structural proteins, stimulate neoangiogenesis, facilitate the migration of epithelial and fibroblast into a wound site, cells that are essential in the normal healing process, reduce edema, inhibit the growth of infectious pathogens, and even accelerate the recovery of damaged nerve tissue. Certainly all positive effects when related to wound healing.

Soon after, I ordered electric stimulation for the first time in a patient of mine with a recalcitrant diabetic foot ulcer, who was not responding to the usual standard of care. He went on

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to heal uneventfully. I was not convinced.

My early experience with electric stimulation and wound healing was used only in patients who failed to heal with the usual standards of care. For example, patients with ischemic ulcers that were not candidates for arterial reconstructive surgery. Patients with venous ulcers who failed conservative compression therapy. Diabetic patients, or patients with pressure ulcers who did not respond to proper off-loading, debriding and protection. Although all these wounds were caused by different etiologies, they all had one thing in common, their inability to heal, regardless of whether they were receiving appropriate care. They became chronic. No longer could they follow the orderly and predictable path to normal healing. It was my early experience that the addition of electrical stimulation in conjunction with good wound care reestablished that path to normal healing.

As my experience increased with the use of electric stimulation with chronic wounds, I began to

use this modality, not only in patients who failed the usual standards of care, but as an adjunct in all patients with chronic wounds. I soon realized that these patients healed faster than the patients who

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were treated with standard care alone without electric stimulation. This fact turned out to be extremely important, especially to my diabetic patients who are at the greatest risk for infection the longer that wound remains open, thus exposing them to possible limb loss or even death.

Obviously, wounds healing faster is naturally more cost effective. We have entered the 21st century. We will have other wound care issues to deal with in the future. I predict wound care will become a medical specialty in and of itself. We no longer treat chronic wounds passively with just wound dressings, hope and pray that the body will heal itself when it does not have the ability to do so. Today we have the opportunity to treat chronic wounds more proactively.

Electric stimulation has proven effective in that ultimate goal both in the experience of this of this clinician and as evidenced in the volume of literature that now exists. I implore this panel to give this subject their sincerest consideration, as I'm confident you will. To abandon this capability now, especially after so much success over the last eight years, not to provide this truly revolutionary method of assisting wound healing to a segment of our

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population who need it the most, the Medicare patient, would be a travesty. The use of electric stimulation as an adjunct treatment in the care of chronic wounds has become the standard of care in my community. Please, do not send my practice protocols back to the dark ages. Thank you for your attention.

MS. CONRAD: Thank you, Dr. Cavorsi. Pamela Unger, followed by Luther Kloth.

MS. UNGER: Good morning. I am Pam Unger, a physical therapist, and also a certified wound care specialist. I today am representing the Association for the Advancement of Wound Care, of which I am a

current board member. The association is an interdisciplinary organization that has over 950 members. Those members include nurses, physicians, podiatrists, physical and occupational therapists, and industry members. The association and organization gives its members the opportunity to build a collaborative community to facilitate optimal wound care for millions of people who suffer with chronic wounds. Our members have and do currently provide electrical stimulation on patients with chronic wounds. We have seen first hand through clinical intervention the effectiveness electrical stimulation has on chronic wound healing.

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I have personally used electrical stimulation as an adjunctive therapy in my clinics and practices since 1980. In my own clinic, electrical stimulation is now a standard of care. I have no current or past financial interest in any manufacturer whose products are under discussion today. I am requesting that my testimony be submitted, along with the written statement that has already been distributed to the panel member, and included in the permanent record of the meeting.

On behalf of the Association for the Advancement of Wound Care, the evidence does overwhelmingly support the effectiveness of electrical stimulation in the treatment of wounds. The AAWC, which is our abbreviation for the association, would like to present the panel case studies that show clinical evidence. As such, the AAWC would like to focus our testimony on the clinical applications and effectiveness of electrical stimulation in the treatment of chronic wounds.

Before I embark on showing you some slides and case studies, I would also like to ask the panel what a wound really is and when a wound becomes chronic. A wound is an injury to the skin, which I'm sure all of you are well aware of. The skin happens

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to be the largest organ in our body and in fact, I would think that the healing process, regardless of what the underlying etiologies or comorbidities may

be, would be the same, certainly knowing that those variables could in some way, shape or form slow that healing process or alter the rate of healing.

Because there's been such a large amount of literature that has been in front of you related to pressure ulcers, I will not show you a pressure ulcer case study. We will talk about those other types of wounds that have been extremely, benefitted extremely from the use of electrical stimulation. So if we can -- and we need to turn the lights down, I'm certain, so that we can see.

This first patient happens to be the case study that I think you have in front of you noted as DL, happens to be a 47 year male. Now some may say well, gee, that's not our Medicare population. This happens to be a disabled gentleman who has been on Medicare benefits since one year prior to us noting this wound. He was evaluated in March of 1996 in our clinic. He has ulceration on his left B/K amputation site, the amputation had been two years prior. The patient actually has a past medical history that includes ministroke and Beurger's disease, which is

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in fact the most significant thing as to why the ulcer occurred.

His treatment prior to coming to our clinic was silvadene and a dry sterile dressing. We actually looked at this patient looking at an onset of nearly six to eight months prior to him seeing us, that what he may need is some debridement, which would have to be approached in a very cautious fashion, electrical stimulation, and our recommendation for dressing was a saline gauze with an occlusive dressing, to obtain some autolytic debridement. He was also not allowed to wear his prosthesis, so that there would not be any increased pressure on that area.

The goal of course for this patient was to avoid revision of the amputation; that was what was recommended by two previous surgeons who saw the patient. Patient also had two vascular evaluations. Numerous arteriograms were done to find that there was absolutely no possibility of revascularizing this

patient.

Hence, we embarked on a program of electrical stimulation. The patient's goal was to return to work. He certainly wanted to be able to ride his motorcycle, which was at the top of his

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list, probably even rated above returning to work.

As you can see, in two months time there was a significant reduction in the necrotic tissue. There we have what's looking to be a granulating wound bed, certainly some reddened area around the wound periphery.

At approximately six months after treating this patient, we are at a nearly healed position, at which point by certainly nine months, which you may think is a rather long period of time, nothing was working with the patient previously, the wound was completely healed. He has not ever since that point in time had this wound revised, or had the amputation revised; he still in fact is a B/K amputee. His alternative was an A/K amputation or may have actually been a hip disartic, which would have certainly limited his ability to return to the work force. The patient could in fact return to the work force, get off of his Medicare disability, and certainly improve his quality of life.

Our next patient is an arterially insufficient patient. This will be listed as case study WM on your information that was given to you recently. He is a 66 year old white male. We evaluated him the end of March. He was actually

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admitted to the hospital for an amputation or possible revascularization. The patient had actually been treated for eight weeks prior at home. His treatment was to have a Betadine with dry sterile dressing. The patient has a past medical history which includes PVD, insulin dependent diabetes, hypertension, and he has had previous arterial bypass surgery.

When he was hospitalized, an anciobracheal index was obtained on the patient and his ABI was 0.43. The patient rated his pain at 19 over 10,

essentially off the pain scale. He was very very uncomfortable and quite miserable as a patient. The other thing that complicated this is his wife, with whom he resided, indicated that she could not care for him at home and he needed to be admitted to a skilled nursing facility. The patient did not want his leg amputated and begged that in the clinic we would actually treat him with electrical stimulation and attempt to promote healing of this wound. That was a very dramatic type of intervention with this patient because there was so much pain associated with it.

What we did find was, though, not only could we get the wound to respond to the electrical

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stimulation, we could decrease the patient's pain. Certainly he had been medicated as well for pain control. We saw the patient on an outpatient basis three times a week. Of course our goal was to clean that up and maybe even have a potential of placing a skin graft on that if at all possible, to close it quickly.

On treating him with electrical stimulation, we actually noted in two months time, less than eight weeks, it was actually six weeks, the patient had a wound bed that was looking to have necrotic tissue sloughing. The patient did not receive any sharp debridement, of having the risk of having the patient undergo further amputation. It was all done with the use of an occlusive dressing and electrical stimulation. Now here is the patient actually four weeks post that, and we have a healed wound; a rather deformed scar, but a healed wound. Quite frankly, this patient salvaged his limb, salvaged his quality of life, and was allowed to continue to live at home with his family, which is certainly what his objective was.

The next patient case study I would like to present to you is a 65 year old female noted in your notes as DAL. This patient actually had an

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underlying diagnosis of venous insufficiency. She also has diabetes, and what she developed here on the

lateral portion of her leg is a vasculitic type of ulcer. Basically, this patient has had these ulcers for six months, has had severe pain associated with them, and she has gone from silvadene to Bacitracin to Neosporin, all with a dry sterile dressing on top of them. She actually was hospitalized because she was scheduled for bilateral amputations. The patient was not moving, was having multiple problems with her -- she had pneumonia a number of times, she had problems with asthma.

And she was evaluated by our clinic, at which time we recommended that we might be able to do some autolytic debridement to this, and follow this treatment with some electrical stimulation. Basically, we did use some hydrotherapy for about two days, to soften the tissue, but the pain was too great, so we stuck to the electrical stimulation. And because she was venous insufficient and had edema, we also used some light compression.

The patient in about three weeks time doesn't look tremendously better, although we were getting some autolytic debridement. Certainly by the time we're looking at eight weeks, we have a very

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nice looking granulating wound bed, and when we then went on to see the patient, from there we have all but a very small area, a two-centimeter area that was not healed. At this point the patient was fitted with a compression garment.

And then we have our patients always return to us in 60 days to insure that we've used as a maintenance prevention program works. This was the patient coming back to us in December. Very limited scar noted, and certainly a completely healed wound that has stayed healed.

I have one more patient case study which I can present to you, which is a neuropathic diabetic ulcer. This patient is 72 years old, believe it or not, owns a lighting company and works constantly, about ten hours a day. Unfortunately because of that, he did not have appropriate pressure relief. The patient had increased drainage, this wound had been present for approximately six months prior to

him seeing us. He needed debridement, and we utilized electrical stimulation along with a total contact cast. Basically the patient healed very dramatically in an eight-week period of time.

And I need to go on to say to you in conclusion that I certainly believe it is evident

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from the examples displayed that electrical stimulation for the treatment of chronic wounds is an effective and invaluable method of adjunctive therapy. The members of the AAWC treat a tremendous number of patients with chronic wounds. Our focus is to be a patient advocate. Patients will benefit from electrical stim as an adjunctive treatment, and it will assist with limb salvage and significantly improve the patient's quality of life.

Therefore, I respectfully request you as the panel to answer the question, is the clinical evidence supportive of the use of electrical stimulation for the treatment of chronic wounds yes. I would also recommend this adjunctive treatment for the treatment of chronic wounds be considered a breakthrough technology. I certainly implore you to recommend to HCFA for a national coverage policy for the use of electrical stimulation in the treatment of wounds.

MS. CONRAD: Thank you, Miss Unger. Luther Kloth, and next is Jerome Connolly.

MR. KLOTH: Good morning. My name is Luther Kloth. I'm a physical therapist, certified wound specialist, and fellow to the American Academy of Wound Management, also a professor of physical

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therapy at Marquette University, Milwaukee. I also practice at the wound clinic of a large hospital in Milwaukee. For the record, I have no financial interests in any product or device that delivers electrical stimulation to promote wound healing.

I speak to you today representing the National Consortium for Spinal Cord Medicine. This interdisciplinary consortium has recently published an evidence based clinical practice guideline in pressure ulcer prevention and treatment following

spinal cord injury. I hold up the guideline here for your observation.

This practice guideline represents the efforts of 19 professional health care member organizations. As stated in our request to speak today, the consortium has an interest in electrical stimulation to the extent that the guideline recommends the use of this modality in conjunction with standard wound care interventions for the treatment of Stage III and IV pressure ulcers.

Given that many if not most of these individuals who sustain spinal cord injuries are eligible for Social Security disability, and therefore may be Medicare beneficiaries, the consortium wishes to share its views with the panel today. The 32 recommendations contained in the guideline represent, are based on an extensive review and analysis of the available scientific literature related to pressure ulcers.

Between the years 1966 and 1998, approximately 1800 abstracts were reviewed for relevance to the pressure and treatment of pressure ulcers. Nearly 350 articles were deemed relevant to the guideline and were retrieved. Of these, more than 200 clearly met the inclusion and exclusion criteria and were used for data extraction. Panel members were assigned relevant articles with evidence tables for study and consideration. From all of the evidence presented in the guideline, a methodology team used the hierarchy of scientific evidence described by Sackett, that employs five levels of scientific evidence as follows, and you see those five levels of scientific evidence posted on the screen.

A Level I scientific evidence was assigned for large randomized trials with clearcut results, Level II, Level III, Level IV and Level V, Level V being the lowest of the case studies and no controls. In addition, each study was evaluated for internal and external validity. Each recommendation was then classified depending on the level of scientific

evidence supporting this specific recommendation. Categories and the strength of evidence associated with the recommendations are as follows, as shown on this overhead.

An A strength of evidence was assigned if the guideline recommendation was supported by one or more Level I study; B strength of evidence was assigned if the guideline recommendation was supported by one or more Level II studies; and a C recommendation was assigned if the guideline recommendation was supported only by Level, III, Iv and V studies. Scientific evidence supporting electrical stimulation came from Levels I and II, which yielded a grade recommendation of A.

After discussion of each recommended guideline and the supporting evidence, the level of panel agreement with the guideline recommendation was assessed as either low, moderate or strong. In this assessment, each of the 19 panel members was asked to indicate his or her level of agreement on a five-point scale, with one corresponding to neutrality and five representing maximum agreement. The levels of panel agreement with the recommendation are shown on the screen, with low support within the

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range of 1.0 to 2.32; moderate, 2.33 to 3.66; and strong, 3.67 to 5.0. For electrical stimulation, the strength of panel opinion was strong.

The strength of evidence came from three randomized control trials involving a total of 251 spinal cord injured individuals, each with at least one pressure ulcer that had not responded to treatment with standard wound care. Having completed the foregoing very thorough process, the multidisciplinary Consortium for Spinal Cord Medicine recommends the use of electrical stimulation in conjunction with standard wound care interventions for the treatment of Stage III and IV pressure ulcers.

In addition to the clinical practice guideline issued by the consortium, the Agency for Health Care Research and Quality, formerly the Agency for Health Care Policy and Research, published the

clinical practice guideline on the treatment of pressure ulcers. AHCPR was and is the lead government agency charged with supporting research designed to improve the quality of health care, reduce its costs, and broaden access to essential services. The practice guideline established an algorithm for the evaluation and management of

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pressure ulcers. The guideline concluded that electrical stimulation is the only adjunctive therapy with sufficient supporting evidence to warrant recommendation by the panel.

AHCPR recommended that a physician should consider a course of treatment with electrical stimulation for Stage III and IV pressure ulcers, and recalcitrant Stage II ulcers. More specifically, the AHCPR guideline noted, quote, data from five clinical trials involving a total of 147 patients support the effectiveness of electrical therapy in enhancing the healing rate of pressure ulcers that have been unresponsive to conventional therapy, end quote. This finding was consistent across the variety of electrical stimulation protocols.

The AHCPR guideline offers a comprehensive program for treating adults with pressure ulcers and included recommendations for ulcer care based on an expert panel's review of the accumulated scientific evidence as well as the collective clinical expertise of the panel members. Recommendations were assigned a strength of evidence rating of A, B or C, according to the following criteria shown on the screen.

An A rating would result from two or more RCTs on pressure ulcers in humans. B, results of two

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or more control clinical trials on pressure ulcers in humans, or when appropriate, results of two or more control trials on an animal model. And C, results of a single control trial or at least two cases series or descriptive studies on pressure ulcers in humans, or expert opinion. In 1994, the AHCPR guideline reflected the knowledge at the time of publication. At that time the strength of evidence rating was B. As recognized by the panel members, the assignment of

a B rating to electrical stimulation for wounds was a conservative one. Many panel members believed there was sufficient evidence to justify an A rating.

However, since there were multiple modalities included in the electrical stimulation studies reviewed, the study sample sizes were relatively small, and the therapy had not at that time been widely incorporated into practice. As such, the panel took a more conservative position in assigning strength of evidence to its recommendation.

As of May 1998, the AHCRP recommendation was five years old. Dr. Lisa Ovington reevaluated the AHCPR rating based on current evidence and the fact that electrical stimulation is now widely incorporated into clinical practice. Dr. Ovington found that based on all the evidence including

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studies published subsequent to the review for the 1994 guideline, the strength of evidence increased to an A rating. Dr. Ovington's review was published in volume 445 of Ostomy Wound Management in 1999.

As a result of its review of the literature and the development of the clinical practice guideline, the Consortium for Spinal Cord Medicine recommends the, and I quote, use of electrical stimulation to promote closure of Stage III and IV pressure ulcers, combined with standard wound care interventions, end quote. Moreover, based on its literature review, and the literature review conducted by AHCPR, as subsequently updated by Ovington, the Consortium for Spinal Cord Medicine concludes that the evidence is adequate to prove that electrical evidence is an effective treatment for patients with chronic pressure ulcers. The consortium places the intervention in a category of effectiveness of 2, more effective.

The consortium also feels that these results are applicable to the Medicare population, given that many if not most of these individuals are collecting Social Security disability and therefore will become Medicare beneficiaries, and the consortium urges the panel to conclude likewise.

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Thank you very much.

MS. CONRAD: Thank you, Mr. Kloth. Jerome Connolly.

MR. CONNOLLY: Thank you, Connie. Dr. Garber, members of the panel, my name is Jerome Connolly. I am a physical therapist. I am currently serving as the senior vice president for health policy of the American Physical Therapy Association. I have no current or past financial interest in any manufacturer whose products are under discussion today.

I speak to you today on behalf of the National Coalition for Wound Care. The National Coalition for Wound Care, of which APTA is a member, is a broad based coalition of ten member organizations representing over 100,000 providers, suppliers, manufacturers and clinicians with interest in the area of wound care. It is the mission of the NCWC to provide a forum for discussion among these groups and whenever possible, to provide a consensus opinion on issues in which the member groups have an interest. It is the consensus opinion of the NCWC that electrical stimulation has been proven to be an effective treatment for patients with all types of wounds, including venous stasis ulcers, pressure

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ulcers, and ulcers due to arterial insufficieny.

This panel in its deliberations is contributing to a process undertaken by HCFA which is designed to attempt to develop Medicare coverage policy on the basis of evidence, employing evidence based medicine. Given this charge, it may be helpful to reflect for just a moment on the definition of evidence based medicine. According to Sackett, who is known in some circles to be called the father of evidence based medicine, EBM means, and I quote, integrating clinical expertise with the best available external clinical evidence from systematic research. EBM builds on and reinforces, but never replaces clinical skills, clinical judgment and clinical experience. End of quote. The coalition was pleased to note that the instructions to the panel today explicitly include direction to consider

clinical consensus information and clinical expert witness testimony in arriving at your conclusions.

We have heard today references to and discussion of an abundance of scientific and clinical evidence. It includes over 60 pieces of literature published in refereed journals, over 20 pieces of which have been published in the last four years. It includes a compelling presentation on the clinical

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application and the profound clinical effects of this adjunctive therapy. It includes presentations on clinical practice guidelines, including AAHCPR, which is a sister agency of HCFA under HHS, which concluded in 1994 in its guideline that, quote, electrical stimulation is the only adjunctive therapy with sufficient supporting evidence to warrant recommendation by the panel, end of quote. This recommendation, as we've heard, was based on a strength of evidence rating of B, the second highest rating possible, but four years later Ovington reviewed all the evidence including more recent literature, and concluding that strength of evidence should be increased to a strength of evidence of A, the highest possible rating.

Today's discussion also then included a consortium of spinal medicine, spinal cord medicine, and its clinical practice guideline, which represents the efforts of 19 professional health care member organizations. Over 350 articles were reviewed, and the strength of evidence rating again, received the highest possible rating, this time using a widely accepted methodology described by Sackett. The multidisciplinary consortium process resulted in a recommendation for the use of electrical stimulation

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in conjunction with standard wound care interventions for the treatment of Stage III and Stage IV pressure ulcers.

It was also acknowledged today that a technology assessment was conducted in 1996, and it did find fault in some of the studies it reviewed up to that time. Nevertheless, the assessment concluded that all studies reviewed, quote, had at least one

weakness but not all reported results were potentially confounded by these weaknesses, end of quote. In fact, that assessment concluded that electrical stimulation facilitates the healing rate of chronic ulcers, that it facilitates the complete healing of chronic ulcers, that pulsed current improves the normalized healing rate of Stage II through IV decubitus ulcers, that alternating current improves the normalized healing rate of decubitus ulcers, that devices used utilizing pulsed electromagnetic field improve the normalized healing rate of venous ulcers.

The ECRI report finally concluded that the quality of studies evaluating electrical stimulation is roughly equivalent to the quality of similarly published studies of other wound healing therapies. So one can conclude that the quality of the

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literature under discussion today was then about as good as it gets, and that given the abundance of literature published since the technology assessment that the evidence in support of electrical stimulation in the treatment of chronic wounds has only gotten progressively stronger.

Now it's always possible to find fault with the quality of studies, particularly when the research involves human subject design and in this case it involves multiple wound types and several different types of electrical stimulation. But in this case it almost approaches quibbling, given the abundance of the literature, the clinical case studies that you have seen, the expert witness testimony, and the considerable professional community consensus that is represented before you today by numerous multidisciplinary coalitions representing a broad cross-section of providers and practitioners.

One very compelling piece of literature that adds to if not sums up the discussion of this intervention and its effectiveness in the treatment of wounds is the meta-analysis conducted by Gardner and Frantz, that concludes that the rate of healing for stimulated wounds was more than double that of

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wounds just receiving conventional care.
It is clear then that the evidence is adequate, as is demonstrated by the literature, by the clinical case studies, by the consensus opinions of numerous experts, as well as several broad based coalitions of providers and practitioners. In the words of Judge George O'Toole, quote, the Agency must be careful not to transform an understandable preference for one kind of evidence into an impassible barrier, end of quote.
It's the position of the National Coalition for Wound Care that the evidence is adequate to enable conclusions to be drawn about the effectiveness of electrical stim in the treatment of chronic venous stasis ulcers, chronic wounds due to arterial insufficiency, and chronic pressure ulcers. The only remaining question then is, in what category of effectiveness should this intervention be placed? The categories of evidence as defined by HCFA before you, appear designed, at least in some cases, for new technology, which electrical stimulation is not. It is already being widely used based on its proven effectiveness. Thus, you might find that these definitions of categories for this particular instance, may need some refinement.
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The National Coalition for Wound Care believes the intervention could be placed in category 2, more effective, and that reads, the new intervention improves health outcomes by a significant margin as compared with established services. However, since E-stim is not new, and since we have found and heard that it has become and it is the standard of care, albeit adjunctive care, for ulcers that fail to heal, the intervention could just as accurately be considered breakthrough technology, and in some instances in the clinical presentation, we found where it was in fact breakthrough technology, and in accordance with the definition of that category of effectiveness, it is the improvement in health outcomes is so large that the intervention becomes standard of care.

In summary, there is adequate evidence to conclude that electrical stimulation for chronic wounds is effective, and because its efficacy is supported by the valid reliable evidence and because of the profound benefit that it can provide to needy Medicare beneficiaries who suffer from this conditions, the National Coalition for Wound Care urges you to recommend to HCFA that the Agency ultimately issue a national coverage determination.

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Thank you.

MS. CONRAD: Thank you, Mr. Kloth.

This concludes the scheduled presentations. We're going to break for lunch. The panelists have asked that we have a working lunch. They are going to go get their lunch, bring it back, and eat here, and start their deliberations.

If anyone in the room wishes to address the panel again or anew, would you please let me know, and I will break out some time this afternoon for a panel presentation. You may use the aisle mikes, but please let me know. If I don't hear from you, I'm going to assume that you are all happy, and we will just continue.

DR. GARBER: Let me just add that I hope that all of the public speakers will be available. I suspect that the panel members will have questions for you. Thank you very much for the excellent presentations. We do hope that we can ask more of you to aid in our further deliberations.

MS. CONRAD: Okay. Let's meet back here at about 12:30.

(Luncheon recess.)

MS. CONRAD: Let's reconvene here. I have some public speaking requests. Each speaker will be

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allowed five minutes, beginning with Luther Kloth.

MR. KLOTH: Thank you. This morning after Dr. Frantz gave her presentation, which I felt was a very good presentation, I felt that based on some of the questions asked by the panel that perhaps there was clarification needed on the types of current, wave forms and so forth, so I wanted to do that.

First of all, the types of current that are available depends on whether you're talking to a physicist sister or an electrical engineer, or a clinician who uses current to stimulate wounds, there will usually be two types of current, alternating current and direct current. The illustration which you saw this morning in Dr. Frantz's presentation was a unidirectional type of current, okay? The other type of current that is described and used in clinical use that biomedical engineers describe, clinicians describe, is called pulse current.

So we have AC, sinusoidal, DC and PC, okay? Now, in terms of clinical delivery of the currents, there are two methods of delivering current to the body. The clinical method that is used to deliver currents into wounds primarily from the studies, is called the method of capacity coupling. What that means is that you use two electrodes that

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are in contact with the body. One electrode is in contact with the periwound skin, the intact skin surrounding the wound, the other electrode is applied directly to the wound tissue. Usually the current is conducted through some conductive medium such as saline, moist gauze, or some form of conductive material that's placed in the wound cavity with the electrode on top of that. That is called capacitive coupling and of course since you have two electrodes, you can assign a polarity, either positive or negative, to each of those electrodes.

The second method for introducing current, and we're talking about delivering current into the tissue, okay, with capacitive coupling, which is the most widely used method for electrical stimulation in wound healing. The other technique that, I think there were three or four studies, and one of those is the Salzberg study that was described earlier. That method uses a noncontact method called inductive coupling. It uses electromagnetic fields, pulsed electromagnetic fields, PEMF, okay, which is kind of akin to the devices that we use for bone healing.

So in that method you don't have an electrode, or electrodes attached to the tissue. You

have a device that is emitting the electromagnetic
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field that then delivers that electromagnetic field into the tissues and once in the tissues, that electromagnetic field is converted to a current. So you're still delivering a current into the tissue in both cases, so I wanted to clarify that.

With regard to the common types of current that are used or described in the studies for electrical stimulation for wound healing, one type of current that is shown on this illustration is called high voltage pulse current. Why is it called high voltage? It's called high voltage because the duration of the baseline duration of each of those pulses that you see there is extremely short, about 20, somewhere between 20 and 60 microseconds and because of that, the charge quantity, the electrical energy contained under the envelope or under the wave form for each pulse there is very low; its on the order of maybe 1.5 microcoulombs. Because you have such a small quantity of electrical energy in each of those pulses, you need a hire voltage to drive the current across the skin or into the tissues. So that's why it's called high voltage; the high voltage devices allow you to adjust the voltage up to 500 volts, but clinically that's never used; usually the voltage for wound healing is on the order of 75 to
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maybe 200 volts.

In this type of current, there is a charge quantity, okay? And there are five papers, I only have four of them here, but there are five papers that describe how to compute, or actually describe the charge quantity that's delivered into the tissue. That charge quantity amounts to a dosage of charge that's delivered into the tissue. So, the way that charge is derived is simply determining how much charge occurs in each one of those pulses, multiplying it times the frequency, and that allows you to derive the total charge per second or per minute or per hour, and usually it's reported charge quantity per second. In these studies, the charge quantity varies somewhat, there's a window of charge,

okay, and that window of charge falls between 200 and 600 microcoulombs of charge, do that's the dosage that you will see.

The other type of current is monophasic pulse current, okay? These are both pulse current, the one you previously saw as well as this one. The charge quantity can be 200 to 600 microcoulombs of charge, can also be delivered with this type of a more rectangular waive form.

So the main point I want to make is that

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it really comes down to when you review the papers, that it's the dosage of electrical charge that's delivered into the tissue, and it doesn't really matter whether the wave form is triangular, rectangular, or biphasic or monophasic, okay? What really counts is the quantity of electrical charge that ends up being delivered into the wound, and that window of charge is usually between 200 and 600 microcoulombs per second. Thank you.

DR. GARBER: Maybe, this is sort of a technical issue and I don't know if we will have time free to return to it later. I'm wondering if the rest of the panelists would like to ask questions of Dr. Kloth now or wait until general questions. Yes, you have one now?

DR. OLECK: Just to follow up on that because it relates to some of the confusion I had with the ECRI specifications. Some of the things they listed under pulse current, they said were generated by a six-volt battery. Are you saying that has a longer pulse width or something?

MR. KLOTH: Well, the six-volt battery just energizes the device, okay, and then there are other components of the device that are able to increase the voltage appropriately and so the device

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is still, if it's a device used in the study, the device is still delivering that window of microcoulombs per second of 200 to 600 microcoulombs. And you know, that, I don't know if you're familiar with the old bone healing literature, but there was a window of charge in the early bone healing simulators

too, where they inserted a cathode into the fracture space and I believe it was something like, if they delivered 50 microcoulombs of charge, they saw bone healing, if they delivered more than 50 microcoulombs of charge, bone healing actually deteriorated. So there was a narrow window of charge there that was effective in the early bone healing studies.

DR. HOLTGREWE: In looking at the literature, it seems to me there's some variability in how you set the machine.

MR. KLOTH: There is.

DR. HOLTGREWE: My question is, how is it arrive upon where to set it? Is it trial and error?

MR. KLOTH: Well, it really comes down to a couple of things. One, the people who are doing wound healing with electrical stimulation with let's say a high voltage pulsed current device, usually set the voltage at between 75 and 150 volts.

DR. HOLTGREWE: How is that arrived at?

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MR. KLOTH: It's arrived at by adjusting the voltage upward until the patient, a sensate patient, perceives a tingling paresthesia in the perimeter of the wound. If they're insensate, you turn the voltage up until they get a muscle fasciculation, and then you turn it down until that muscle fasciculation disappears. In both cases, you're delivering a comfortable, a moderately strong but comfortable tingling paresthesia in the area of the wound, and they will have a range of as much as 75 to 150 volts and the delivered voltage, you will be delivering 200 to 600 microcoulombs.

DR. HOLTGREWE: Does an increase correlate with better healing?

MR. KLOTH: I can -- well, it's interesting --

DR. HOLTGREWE: Because the bottom line here is to heal the wound.

MR. KLOTH: Exactly. I wanted to go back in Dr. Turkelson's report this morning, because he said they could find no difference in wound healing with direct or pulse current, okay? The reason I feel they couldn't deduct a difference was that it's

the charge quantity, and the charge quantity is the same whether you're using DC, pulse DC, of high

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voltage pulse current or you know, a rectangular wave form, or whatever, the pulse charge is the same. The variables are the voltage and frequency, and you can calculate charge regardless of what the voltage is and what the frequency is; if the frequency is a80 pulses per second or 100 pulses per second, and the voltage is in that range of 75 to 100 volts, you will always come out with a charge quantity in that range of 200 to 600 microcoulombs.

DR. STANTON: Could you clarify something, because I think that I will paraphrase, and I wanted to make sure I understood what you said, because it's very powerful what you said, if it's true, and I'd like to understand where you came from in saying in your presentation, I think you said that it's the total charge that matters, not the wave form.

MR. KLOTH: That's correct.

DR. STANTON: And what's that based on, because in other physiologic responses to electrical stimulation, wave form matters a lot. Why do you say that for wound healing?

MR. KLOTH: Well, in the other physiological responses to electrical stimulation, such as, you are probably referring to neuromuscular electrical stimulation where you elicit a muscle

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contraction, or you're using electrical stimulation for pain suppression, you know, you're also delivering a charge quantity in both of those instances. The charge quantity for eliciting a muscle contraction is much higher than charge quantities of 200 to 600 microcoulombs, and it's also higher for pain suppression, depending on what device you're using and the stimulation mode for doing TENS. So, I don't know if that answers your question or not.

DR. STANTON: No, it doesn't. Let me rephrase then. Is there any experimental evidence that shows that there's no difference in wave form, that it's total charge delivered that makes the

difference?
MR. KLOTH: There is no experimental evidence, but it's the calculation that's easily done by taking one of those two wave forms, for example, that one or that one, and knowing the frequency and the duration. Actually, the formula is right there for this particular wave form. You know the area of one phase, that equals the phase charge. How do you come up with that? Well, because that's a triangular wave form, you take one-half of the phase duration times the amplitude, okay? In this case, the example

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is 20 microseconds, one-half phase duration is 20 microseconds, times .35 amps or 3.25 microcoulombs, so the total charge per second then ends up being 342 microcoulombs per second.
DR. GARBER: I think the question is not how you calculate it, the question is, how do you arrive at the conclusion that it's the total charge per second that matters and that the mode of delivery whether it's pulsatile or flat or whatever is irrelevant? That's your question, right, Marshall?
And so, are there animal studies or something that enable you to determine that whatever device you use, and you described where you go to a point where the patient really feels it, but that doesn't matter what device you use, you will always get equivalent results for wound healing. What is the basis for that statement?
DR. HOLTGREWE: Or to put it another way, is it like stretchy socks, one size fits all, it doesn't really matter where you set the machine?
DR. GARBER: As long as you get the same total charge?
MR. KLOTH: It doesn't matter where you set the machine, as long as the sensate patient is feeling this moderately strong tingling paresthesia.

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The wave form doesn't seem to matter.
DR. STANTON: Another way of looking at that, has anybody looked at the literature and gone and seen whether the separation in studies that seem to have an effect and those that don't, that they

shake out by the charge that's delivered?
MR. KLOTH: No, I don't think anyone has gone to the literature. As I said, these five papers basically describe pretty much that same window of charge, but I see your point, it would be good to go back and look at the other papers that didn't describe the charge quantity to see if wound healing was better or worse.
DR. SIGSBEE: Just to follow up on this area a little bit further, is it that there is no evidence that distinguish between different methods of delivering a charge, or do you think the evidence supports the fact that the method of delivering a charge is irrelevant, the pulse wave form?
MR. KLOTH: I think the wave form is irrelevant.
DR. SIGSBEE: You think, but what's the evidence that supports your thoughts?
MR. KLOTH: There is no hard evidence.
DR. SIGSBEE: All right.

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DR. OLECK: Does the alternating current in those pulse electromagnetic field items, do they deliver a net charge to?
MR. KLOTH: Yes, they do. Alternating current we said is sinusoidal wave form, and in a pulse electromagnetic field device, what is done is they increase the frequency all the way up into the megahertz range, and usually those devices are delivering 27 megahertz, and 27 megahertz is the frequency, and that's an electromagnetic field that is inducing the current in the tissues. We don't have evidence of the charge quantity that is delivered by that method.
DR. OLECK: So you can't really calculate.
MR. KLOTH: Right. The supposition is the three or four studies that have been done with that form of electromagnetic field of energy report favorable outcomes, that the charge quantity is probably favorable, okay, but we don't know what it is.
DR. GARBER: Thank you. Let's move on to the next public speaker.

MS. CONRAD: Thank you, Mr. Kloth. Dr. Cavorsi.

DR. CAVORSI: Thank you. Good afternoon.

While listening to all that expert testimony this morning, I became somewhat concerned over hearing all that testimony concerning the effectiveness of electrostimulation with, in the use of pressure ulcers, that my fear is that this panel may erroneously conclude that electrical stimulation should be used only for electric stimulation.

As clinical director of, again, a large wound care center, I treat a lot more patients than just pressure ulcerations. I use electrical stimulation to treat all nonhealing chronic wounds. And I would advise that electric stimulation is extremely effective in chronic wounds, regardless of etiology. As I previously stated, in my experience, regardless of the etiology, which is usually addressed during the treatments with standard protocols, some of these patients still do not respond. Because of the lack of research data or literature concerning patients with diabetic ulcers or ischemic ulcers, that does not mean that in clinical practice, electrical stimulation does not benefit these patients, it does. How it does it, how does it do it, there's really no literature to indicate how that works.

It was mentioned earlier that electric stimulation changes the polarity and transfers itself to the wound site. That may be one of the reasons why it heals a chronic wound. I wish it were that simple, it's not that simple. I think these patients have wounds that become quiescent and no longer respond. It was interesting, even if you try and correct the underlying cause, it was interesting to see this morning, that it was shown that electric stimulation actually initiated the response in fibroblast to produce transforming growth factor beta and as we well know, growth factors in wound healing, there's a tremendous body of knowledge out there today that indicates it is extremely important.

It may show later, perhaps later, that electric stimulation might either stimulate those receptor cells on the target cells, or might do something similar to that effect. But the point I'm trying to make is, electric stimulation responds or heals and is effective in chronic wounds, not just pressure ulcers. And again, it would be devastating to my practice if I could only use this modality in patients with pressure ulcers.

I would love to put some clinical trials together for you for an arterial ulcer. You saw it clinically this morning, that we can heal a severely

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arterial ischemic ulcer. How do you do that? How do you get a patient with severe popliteal disease, who has a limb threatening lesion, who is nonreconstructable, who has severe pain, and put that patient in a clinical trial? It just can't be done. There are just some things we can't do with clinical trials, and you have to sort of trust the clinicians that are out there doing this thing. And I just wanted to address that point. Thank you.

DR. HOLTGREWE: Let me ask you a question. When you're treating different types of ulcers, do you set the machine at the same setting on all three or do you change it?

DR. CAVORSI: I have no idea because I do not touch those machines. I am not a physical therapist, this is a physical therapy modality.

DR. HOLTGREWE: What does the physical therapist do?

DR. CAVORSI: You would have to ask the physical therapist. Those are technical questions that I cannot answer, and I wouldn't be answering truthfully if I tried.

DR. ZENDLE: You said that you find it valuable no matter what the etiology of the ulcer in recalcitrant nonhealing ulcers?

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DR. CAVORSI: Correct.

DR. ZENDLE: Would you advocate limiting the use of electrical stimulation to only nonhealing recalcitrant ulcers, or would you use it on every

ulcer?
DR. CAVORSI: I tend to use it on every ulcer.
DR. ZENDLE: Why?
DR. CAVORSI: Again, based on that experience that I've had in the past. Remember, I mentioned initially, I only used it in patients who did not respond to standard therapy. After a while, I realized or learned that these patients are actually healing better and faster, and I no longer held that treatment based on that observation. That's a clinical observation on my part, and only on that. I can't give you literature to base that on, but on my clinical observations, these patients who were getting standard of care only and those patients -- and were healing -- and those patients who were getting standard of care with the addition of electric stimulation were doing it better and were doing it faster.
DR. ZENDLE: And what stage, for those patients that you haven't just limited to nonhealing,

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are you using electrical stimulation on all four stages of ulcers?
DR. CAVORSI: On all types of wounds?
DR. ZENDLE: No, the stage of the ulcer. Are you using only Stage III and IV, are you using Stage II, III and IV?
DR. CAVORSI: Well, there is really no significant indication to use electric stimulation in patients with a Stage I pressure ulcer, or even a noncomplicated Stage II pressure ulcer. We would only use it for Stage III and Stage IV, because that's the only type of ulcer that really requires this type of treatment, more aggressive treatment, more proactive treatment, because other ulcers wouldn't even come into play. I wouldn't even consider it.
DR. ZENDLE: That's what I wanted to know, so you would just say Stages III and IV?
DR. CAVORSI: And/or recalcitrant Stage II, one that's just Stage II, a partial thickness pressure ulcer which does not respond to the usual

standard therapy, yes, I would use it.
DR. ZENDLE: And if I understand what you're saying, these Stage II ulcers, they have to be recalcitrant, not responding to the standard

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treatment, before you would use electrical stimulation?
DR. CAVORSI: That is correct, that is my personal bias, that's correct.
DR. SIGSBEE: A couple of questions. You mean to tell me that somebody is using a therapy on your patients and you don't know what it is, that is, the settings of the machine, they type of wave form, the duration of therapy?
DR. CAVORSI: Yes. I know my physical therapist, I know exactly what they're using.
DR. SIGSBEE: That was the question; what are they using?
DR. CAVORSI: That's not what I heard.
DR. SIGSBEE: No, no. That's what we're talking about. You're coming here presenting your personal experience in your wound care center. What are your physical therapists doing for different types of wounds?
DR. CAVORSI: Yeah. We use a high volt pulsed current in our patients, and I can tell you they use 150 volts of power. I mean, that I can tell you, because that's written. I don't understand all the physiology involved, you know, let me say the physics part of it as well as they do, okay? That's

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the truth.
DR. SIGSBEE: I'm just a little bit curious, and I don't have any involvement with wound care. You run a wound care center; is that correct?
DR. CAVORSI: That's correct.
DR. SIGSBEE: Can physical therapists bill independently for what they do compared to your professional services?
DR. CAVORSI: Can physical therapists bill independently?
DR. SIGSBEE: For their wound care services?

DR. CAVORSI: Yes.
DR. SIGSBEE: They can. And do they in your center?
DR. CAVORSI: No.
DR. SIGSBEE: They don't.
DR. HOLTGREWE: Well, my question was, this technology is advocated for three basic types of wounds, and my question was, is the setting on the machine different for the three wounds or is it the same for all three?
DR. CAVORSI: I don't know.
DR. HOLTGREWE: You don't know?
DR. CAVORSI: I can't answer that.

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DR. HOLTGREWE: Who makes the decision, the therapist makes the decision?
DR. CAVORSI: The physical therapist has very specific protocols.
DR. HOLTGREWE: Based on what, what criteria do they use to set the machines?
DR. CAVORSI: I don't know that.
DR. HOLTGREWE: Who would?
DR. CAVORSI: The physical therapist.
DR. ZENDLE: Maybe we should ask a physical therapist.
MS. UNGER: This is a physical therapist, and I would be love to be able to tell you what's going on. Basically in the clinic that I work in, we have a standard protocol that's set up where we treat the patient initially with negative polarity and then switch the patient to positive polarity. You're asking me how many votes I put into the machine?
DR. HOLTGREWE: Stop. Upon what do you base that policy?
MS. UNGER: I base that initial policy on the literature way back in the 1960s and 50s that talked about low intensity direct current and the polarity effects on wound healing with the use of those different type of parameters. And I've used

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that since 1980 to treat patients.
I think the key factor is, again, after looking at these studies and certainly researching

everything about high volt that I could find, about electrical stimulation for wound healing, certainly the numerous times that I myself have gone to HCFA and said let's look at this thing and see how effective it really is on patients, we have looked at total charge, you know, does it matter if it's monophasic or does it matter if it's a biphasic wave form, and people get real confused with that issue. But when you start looking at the research, studies that are out there, and start looking at what wave form was it, what was the pulse duration, what was the pulse width, and calculate out your total charge, almost all of those studies fit into that total charge window that Mr. Kloth talked about.

Where we find that we change with different patients is, I happen to use a particular device that reads peak output on a patient. Certainly if I place electrical stimulation on you, versus placing it on myself or anybody else sitting in the room, your body may respond differently to that electrical stimulation than mine does. It may take an actual increase in voltage to get the right

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amount of current going into the tissues, and I judge it from that perspective.

DR. HOLTGREWE: How do you make that determination?

MS. UNGER: I make that determination by reading as my peak output is where my voltage is reading. The particular device I use, I can dial in voltage and then I can check to see --

DR. HOLTGREWE: No, I understand, but what's the relationship between this and efficacious response in wound healing? How do you know?

MS. UNGER: Well, I want to make sure that the patient is getting that total amount of charge.

DR. HOLTGREWE: So the bottom line is, the more charge you put in, the better the effect?

MS. UNGER: No, I can't answer that.

DR. HOLTGREWE: That's essentially my question.

MS. UNGER: I know that's your question, but I think what you have to remember, and I can only

ask you to please think about this, we're talking about the human body, and the human body responds very very differently depending on those variabilities of diagnoses, comorbidities, the patient's body responds very differently and we know

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this in medical practice. One patient responds very differently to one pain medication versus another.

So when I place electrical stimulation on patient A, I'm able to dial in 100 volts and I may get a peak output that reads 100 volts. Patient B, I may have to dial in 150 volts to get 100, or 500 milliamps of current. And I do that by looking at my patient on an individual basis saying these are the parameters for my protocol, and in the last 20 years I've gotten very tremendous results with electrical stimulation, and that's what I base it on.

DR. HOLTGREWE: Okay. Well, that last statement maybe helps me in that you use your previous experience to determine, where with antibiotics for instance, there's a range of therapy. There's a point at which you don't give enough antibiotic you get no favorable response, you give too much, you get into a toxic profile. But I guess one of my things I don't understand in this is where do you set the machine, because there seems to be a substantial variation in the literature I've read. And I just wondered how you as a therapist decide whether or not the patient is getting enough or too much voltage. Do you give them as much as they can tolerate?

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MS. UNGER: No. You turn your intensity up until you see a slight twitching of the patient.

DR. HOLTGREWE: Yeah, but is that associated with better wound healing? That's my question.

MS. UNGER: Well, if I had a subliminal response from the patient, certainly I might see less. I don't use that. I can't tell you it relates to less healing, because I don't use it in my clinic.

DR. HOLTGREWE: Yeah, I guess that's my problem is that I don't see a correlation between how

much energy you put in and the response. I think that's my question.

MS. UNGER: Well, I guess if we took apart -- you know, these questions have been raised where somebody's talking about the scientific evidence, and I think if I took every one of those studies that's out there, identified the piece of equipment that was used, identified the parameters and then took the total charge that was offered to the patient by those parameters, I might be able to ask the question that was asked here, did those patients that didn't respond have less charge than those patients that did respond? I don't know that now, because that question hasn't been asked before. And

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unfortunately, the frustrating part of being a clinician is, I have a very difficult time when I know a particular treatment is very effective for intervention, and certainly if you look at the baseline outcome in all of these studies, most of it is 2.4 times faster healing. Why would I not use it on a patient? Why wouldn't I move them to a better point in their life? Why wouldn't I make them more independent?

I guess my other thought is that it's very difficult without looking at a wound -- if I put electrical stimulation on a wound and in five days I don't see pink tissue or necrotic tissue loosening and having autolytic properties going on, I don't see a red healthy wound bed, I'm not doing right for my patient. But those are clinical observations, and I would change my parameters at that point in time.

DR. SIGSBEE: Let me, and I don't want to belabor the point, but the decision on how much current to deliver here, and this covers several speakers, has sort of been determined that this is an end point where you either get tingling or muscle twitching, and then back it off a little bit from the muscle twitching, and that's just sort of been the standard, there is no present good evidence that

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that's the right amount of current to deliver, it's just the way it's been done, and it's thought that

that is at least one way of determining at least an effective current; is that right?

MS. UNGER: That's correct; that's all the way back to, I believe it's 1934 that we saw a study that said that, and that's what we based it on.

DR. SIGSBEE: You're commenting on your own personal experience, and I wonder if that's the experience of other physical therapists in the room, is that this is how it is and there isn't good evidence as to what is the most effective mechanism.

DR. TURKELSON: I understand where you're coming from with that, and I think there is some evidence that shows the contrary, that we know from microcurrent studies, when patients are given these very very low level stimulations, they do not respond. On the other extreme, we do not know. And I think one reason we don't go to the other extreme is we don't want the muscle contraction as a compounding variable, plus the fact that the skin is broken, resistance is decreased, and we're putting in possibly way too much current. And we're very concerned in PT not to overstimulate an area to cause an electrical burn, or things of this nature. So we

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do stay off it at a tingling paresthesia, to make sure that we are not giving too much stimulation to the patient that could cause harm. But if you go to the other extreme, too little stimulation will not work.

DR. GARBER: Let me just ask. Dr. Holtgrewe asked the question earlier about the use of different, do you try to set them differently for some other characteristics according to the cause of the wound, that is, whether it's diabetic or venous, or a pressure ulcer. And then you said in your comments before if I heard you correctly, that you take into account the underlying disease, et cetera. So, could you answer his question about that particular question? Do you use a different protocol or do you try to set anything differently according to whether it's a pressure ulcer or one of the other kinds of ulcers?

MS. UNGER: In my clinic it does not

matter what type of ulcer it is; the protocol is the same. The same parameters are there for negative polarity, the same parameters are there for positive polarity. What changes is, when I apply that machine to a patient and I don't read a peak output occurring, which for 100 volts on my particular

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machine, it would be 500 milliamps of current, and if my peak output doesn't reach 500 milliamps of current, I in fact up my voltage until I get 500 milliamps of current.

Now, can I tell you that that is a case that is more medically compromised? I probably could make that assumption now. I have not ever recorded it so I can't tell you it's diabetic versus the arterial versus the pressure, I don't know that. I would make an assumption knowing the physiological processes that it may be that person that's more complicated, but I can't tell you that for sure. The protocols remain the same unless it's not reading the peak output of 500 milliamps.

DR. GARBER: All right. Mike Maves, and then Les is next.

DR. MAVES: Yeah, and I hate to kind of go back because I know we're trying to concentrate on clinical trials in where we're headed, but from the academics in physical therapy, has there been a dose response? I think what Dr. Holtgrewe is trying to find out is, is there a rationale for the amount of current or the voltage that is delivered? We heard from Dr. Frantz this morning that they haven't been able to quantify what the negative potential is on

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the skin, I guess it might be minus 23 millivolts. What's the dose response? Have you had an animal model or something where we've been able -- I hate to kind of go back to basic science, but I think that would help some of the questions up here if there were some references and some data to relate it to.

DR. ZENDLE: Actually, my questions's related so I'd like to ask it and you can answer them both together. And that's in addition to his question about the dose, what about the frequency?

How often or how long? Is it every day, is it three times a week, is it for a half hour, six hours, is it continuous? Can you respond to how those decisions are made?

DR. FRANTZ: Let me make a few general comments as an academic nonphysical therapist nurse, but wound healing academic person and just say that part of the difficulty in responding to the kind of questions you're asking us for chronic wound patients is that we don't have a chronic wound model, and that has hindered us tremendously in terms of laboratory research. In the last decade in particular, we have a much better understanding that acute wounds behave very differently than chronic wounds, and that our assumptions of two decades ago that we could

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extrapolate the acute wound data to chronic wound populations, we know we can't do that anymore, so we don't do that anymore.

We don't take the burn literature and move it to chronic wound care. So until we have that animal model to do the kind of controlled studies that we need to do of all those confounding variables, it makes it very very difficult, and there are people actively working on that model, but nobody has done it.

We also know, and I know some of the people in this room, Dr. Oleck, I think you were at the FDA meeting a couple of years ago, where the FDA struggled to look at study design for wounds, and we spent a day and a half sitting there looking at all the variables, and we couldn't even come up with a consensus of opinion on what the standard controls should be for those studies, because the reality is that if you look at a venous ulcer patient, that's one set of controls, and adjunctive therapies that you need to be evaluating, versus pressure ulcer, versus venous ulcer, versus all the other kind of chronic wounds. So it's tremendously complicated, and so as you pose these questions, part of the reason that my colleagues can't give you any answers

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is because we don't have an arena in which to do the

research yet, and yet, we have to take care of patients every day.

DR. MAVES: Excuse me, but has anything been done on patients where you take a series of patients with pressure ulcers and somebody gets 25 microvolts, somebody gets 50, somebody gets 74 and somebody gets 100, and kind of just look at that then? I understand your concern about not having an animal model, that certainly hinders that, but has anything been done clinically to sort of determine what's the most effective dose?

DR. FRANTZ: I'll let my colleagues in physical therapy answer that, but let me just call to the table significant evidence that's coming out from the most controlled trials of platelet drive growth active beta, the Greenwich trials, that are probably the largest group trials that we've ever had in the history of wound healing, probably the best controlled by the FDA, and we know that the results now for the second phase, where they are looking at the same product in pressure ulcers, is beginning to suggest a different outcome than it was in diabetic neuropathic ulcers, so -- and that's thousands or millions of dollars later.

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MR. KLOTH: I will try to answer your questions about the dosage. There are no studies comparing say 50 microvolts or 50 milliamps or 50 microcoulombs against 500 microcoulombs or 500 microamps, or 500 volts, there are no studies, we need those studies. But, the convincing evidence lies in the fact that we have the clinical trials as I said before, that demonstrate accelerated healing using that window of charge in the range of 200 to 600 microcoulombs, and we arrive at that based on patient perception of tingling paresthesia, and a combination of voltage and frequency.

DR. GARBER: Dr. Kloth, maybe -- I'm hoping we can move on soon, but I just want to ask if I'm correctly summarizing your view of this, and that is, that the levels that are used are the ones that have been tested and proven effective, and we don't have direct studies about whether those levels are

optimal yet, but we do have studies showing that these levels work. Would that be a fair summary?

MR. KLOTH: That is correct. Someone else had a question about how often we do this. Some folks do -- most of the time it's one hour a day. Some people do five days a week, some people do seven days a week. There are no studies indicating that

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seven days a week are better than five days a week.

DR. ZENDLE: How about once a week?

MR. KLOTH: No, there are no studies where it was done once a week. The studies were either five days or seven days, one hour a day.

MS. UNGER: I think what you will see in clinic situations if you just went out and polled all of the therapists, nurses that may be involved in clinics where electrical stimulation is done, on an outpatient basis I think you see a minimum frequency of three times per week, and certainly on the inpatient side of things, acute care, skilled nursing or rehab site, you would see a maximum of seven times per week. So I think your frequency rate is somewhere from three to seven times a week, and I think that has to do with the acuity level of the patient. When you get a patient that's outpatient to come into your clinic three times a week, there may be some more things the patient can do with reference to exercise and off-loading and those kinds of things, where a patient who is acutely ill that's hospitalized, may have far more intervention. I don't think we've done any studies that have actually compared what's the minimum amount to get response. Nobody has compared one time a week to two times a

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week, to three times a week, to seven times a week.

DR. OLECK: One of the things, just to get a little different track here, we've talked and a lot of the discussion today has been focused on the idea that these are being done in a facility setting. So from my perspective from the contractor, I know that we will be getting a number of claims advocating use in the home setting, and I just wonder whether we can get some comments from people about the various types

of devices, whether they are safe. You know, some of these where you are applying electrodes directly to the wound, I guess I have more questions about that, about whether that would be safe in the home setting, and that kind of ties into this other question about how often to treat or how long to treat. Certainly some of the constraints, I'm sure the fact of how often you can reasonably get the patient to come into the outpatient clinic, but at home, I guess they could wear these for long periods of time or use them for long periods of time. Are there any comments about use of these in a home setting?

MS. UNGER: I have some personal comments, so I'll start first and if you want to follow, please do. My personal opinion is that there are some patients, limited, but some patients and patient's

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families that can be taught how to appropriately apply electrical stimulation. I would say high voltage pulse, because that's what I prefer to use for my patients. I also think that that assures me that the patient cannot burn themselves if it would be left on too long. I think the real issue with it is if you have a wound that really requires intervention, I question how often the skilled professional may need to assess that wound, so the patient continues to progress in a timely fashion.

I think the other issue, even though I hate to say that reimbursement drives a lot of what happens clinically, right now a patient would have to pay to either rent or pay out of pocket for that particular device to be used at home, because right now I believe the coverage decision still remains, chronic or intractable pain for a home stimulator. So unless the patient presented with that diagnosis in combination with a wound, the patient would have to pay out of pocket, which many of our Medicare patients will not do. So, I think that limits how much it will be used at home.

DR. OLECK: Well, we're talking about a potential change in coverage here, and if it was covered in the home setting, do you have any problems

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with most people leaving your clinic and just being given one of these devices by the supplier to use at home?

MS. UNGER: I have no problem with that being done as long as the patient is capable of doing that, and I think there are some real questions as to whether the patient would always be capable of doing that. I think the other issue clearly would be what I would call an acuity or severity level of what the patient's, you know, external circumstances may be related to certain comorbidities. There may be some things as a physician. I mean, I know just with the physicians that we work with, they would halt that in a number of situations where they wouldn't feel the patient could appropriately assess the condition. So I think there would be some limitation where that's concerned. Could you teach a patient at home to do it, I certainly think you could. You teach a patient how to do a TENS unit at home, and it's pretty much the same thing.

MR. KLOTH: And if the patient is followed by home health care, nurse or physical therapist on a weekly basis, to make sure that they are following the protocol, or when they come into the clinic, to double check that they are following the protocol,

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there shouldn't be a problem.

DR. SIGSBEE: Okay. Just one follow-up question. We have talked about, obviously our charge is to try to look at the evidence and comment on the evidence, and the coverage issue is really HCFA's decision. One of the things that we have sort of spoken around today but not really talked about is the comparison of electrical stimulation with other some of the newer modalities in management of wound care, specifically some of the gels and the absorbent beads, and some of the other things that are even now being understood in advance. And I wonder if anybody would be willing to --

DR. GARBER: Let me ask that we hold that off for the general discussion later, because we have a lot of issues. Let's move on to the third public speaker.

MS. CONRAD: The final speaker, Dr. Spielholz.

DR. SPIELHOLZ: I just waned to revisit a comment that I had made before about the ECRI comment that looking at the sense of wounds healed over a short period of time may be a flawed outcome measure, and then Dr. Turkelson's concern may rebut what I'm saying.

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But let me just refresh your memory on this. If you have the ECRI report in front of you, on page 84, the section begins, many wound healing studies report the number and/or percentage of patients healed at given time intervals. One might assume that this is a straightforward simple measurement of the therapy to promote healing. Unfortunately, the number or percentage of patients healed is a flawed outcome measure because it depends on study follow-up duration and initial wound size.

What I have copied here just in case you don't have the ECRI report, is that ECRI then goes on to given an example of why looking at wounds healed over a particular period of time may be a flawed outcome measure, and basically, you tell me if I interpret this wrong, basically they're setting up a situation where there are two groups, A and B, and as you see on the slide, they have a particular distribution of wound sizes. In group A -- both have 15 patients in them and if you look at the means and standard deviations of the wound sizes, the means and standard deviations are the same, so they can still have different wound sizes, but the means come out to be the same. The distribution is different in that group A, which is going to be the treated group, has

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some wounds that have an area of 6 square centimeters, whereas group B, which is going to be the control group, has 8 square centimeters as their smallest number. Okay?

Now, ECRI then goes on and says down there, further, the next paragraph says, if the experimental and standard therapies both had linear healing rates of 1 square centimeter per week, then

at the end of six weeks, basically what would happen is that those patients in the group A that had 6 square centimeter ulcers would heal, because they had been healing at a rate of 1 square centimeter per week, at the end of six weeks those would have healed, but nothing or none in group B would have healed, because their smallest ulcers were 8 square centimeters.

So you can see that they could have the same healing rate, that the E-stim was really not making the difference is what ECRI is implying here, yet, it would appear that the E-stim was having a difference because those patients healed sooner. So when we come along and say well, we saw them in seven weeks, all these patients healed in the stim group and they didn't heal in the control group, you're saying that could be a flawed outcome measure.

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The problem with this assumption is that both groups have a linear healing rate of one square centimeter per week, so it would take the larger ulcer longer to heal. So let's assume that they started healing one square centimeter per week after being placed into the treatment groups. I redrew the ECRI healing rates here, and basically what you see if for the two groups, it decreasing in size over the first six weeks, and at the end of the six weeks, one would have healed totally, the other group still would not have healed, but as you can see, there are healing rates that are measurable. Is this reality? That's my question. How much reality is this?

Let us have the next slide please, the next overhead. And let's just look at these examples to see whether this is reality. In the Kloth and Feedar group, which I showed you before, in this situation at the top, all patients, all nine patients at the end of seven weeks healed. In the control group, however, there was not that type of a linear drop. In fact, if you look at the statistics of the control group, the control group if anything, got bigger, by about 6 percent. So there was no concomitant drop that you would have to see if the healing rates were indeed linear the way ECRI

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proposes.

Can we have the next slide please? So, that ECRI model does not mimic reality in this situation. This is from the study of Wood et al., where again, they plotted the healing rate over time and as you can see, one of them is going down very nicely, that's showing the decrease in the percent of the wound that is remaining, whereas the other line is the control group and it is certainly not following a linear drop the way ECRI suggests.

So therefore, I would argue that the ECRI argument that healing over a period of time is a flawed outcome measure is flawed because the basic assumption does not follow what reality is. Thank you.

DR. ZENDLE: Isn't that may be a flawed outcome?

DR. TURKELSON: Yes. We never said that wound healing rates were inappropriate outcome measures. This was an example that illustrated that linear wound healing rates are probably inappropriate. As a matter of fact, the chief outcome measure that we used is an exponential model of wound healing rates. Wound healing rates are out outcome measure. The linear model that I think, one

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can show a hypothetical situation, I think the arguments made here actually prove my point, the linear model clearly doesn't fit the data, and that was our point.

Also, I question whether the argument is even important. The question here really is, you know, we have data that suggests that the exponential model fit all of the data we could get at hand. We could niggle over whether the rates are linear or not. I don't see data that the wound healing rates are linear. I think the argument here is that they are not and I would agree with that wholeheartedly, they clearly are not. Hypothetically, theoretically, linear wound healing rates can't work. That's why we used exponential wound healing rates as the primary outcome measure.

DR. GARBER: Let me suggest that we defer further discussion of the linearity issue until, unless and until it becomes germane to the deliberations of the committee.

I would like to call on John Whyte from HCFA, who has a few comments.

DR. WHYTE: I think Dr. Garber wanted me to go over very briefly Appendix A, which were the articles reviewed since the ECRI report, and I'll

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just give you a very brief synopsis and then if you like, we can go over each article very briefly and then if you have any questions, I can answer them or you can continue that as part of your deliberations.

As I mentioned this morning, since the ECRI report, we have continued to do work on this topic and what we decided to do was search the literature since the update in 1997, and we set very broad search parameters. Essentially we used the terms electrical stimulation and wounds, because we wanted to include as much information as possible. This would not necessarily be our normal operating principles, because normally when we do our literature search we like to look for controlled trials, whether it's an historic control, perspective control, or a retrospective control, but in this situation we wanted to include as much information as possible.

What that yielded was Appendix A, which were a total of 17 articles. Not all of those were studies. There were six case series, there were five randomized clinical trials, there were four literature reviews, there was one meta-analysis, and there was one opinion article. And you should note that three of the 17 articles were not published and

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ones was an abstract, and we would normally not include those as part of a systematic literature review with strict inclusion criteria, but in this situation we did want to be as broad as possible to present all the information to you and allow you to decide how you wanted to weigh that information.

We can go over briefly and just in summary

of the six case series. I know Dr. Turkelson talked earlier this morning about that, to take a certain number of studies and talk which are statistically significant and which aren't. I'm just going to mention it to you in summary and then go over each one and you can decide how you want to look at it.

But of the six case studies, two of those had statistically significant results, four of those did not provide enough statistical information to determine whether or not the data was statistically significant. And of the five randomized clinical trials, three were not statistically significant and two were statistically significant, although you do have to look at the articles to see exactly what they were measuring.

And if you'd like, we can briefly go through the articles. The first two articles are by Baker, which essentially are companion pieces. They

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both appeared -- actually, excuse me -- one appeared in Diabetes Care, and one appeared in Wound Repair and Regeneration. Basically Dr. Baker looked all together at a total of 160 patients with various types of wounds. In the first piece it was primarily diabetic patients with open ulcers and in the second case it was spinal cord injury and pressure ulcers. And basically she had a poor group of patient protocol design where group A received an asymmetric biphasic model, B received a symmetric biphasic, C received minimal current, and a control group which was a sham device. We'll allow you to look at the results as listed in Appendix A, and basically the differences in healing rates overall and for her subgroup analysis were not statistically significant.

The other article, and again, remember, these are just articles that appeared since the update, is an article by Cosmo, and this looked at changes in blood flow by laser doppler imaging. And you will see that several of the articles that are included here may not have necessarily used wound healing rate as a primary outcome measure. And again, this is meant to be as broad as possible and some of these may be more of a basic science

physiology level. Basically they looked at what were
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the changes in blood flow after application of electrical stimulation. They used low frequency TENS applied for 60 minutes and basically they then measured blood flow every five minutes to see how electrical stimulation was changing blood flow. And they talk about how their data was statistically significant at the highest tolerable intensity.

It would also be useful to look at some of the literature reviews and review articles that have appeared since the ECRI report. There is an article from the Journal of Food, which you may want to look at, and Dr. Frantz' article which we spoke about earlier, the Journal of Geriatric Medicine and again, these were literature reviews of some of the same studies (inaudible) as well as some additional studies also.

There's also an unpublished study by Dr. Frantz which looked at originally 50 patients in that inclusion criteria, and then eventually there were 37 patients. Again, this is in pressure ulcer Stages II through IV, and they defined chronic ulcer at least three months duration. And basically she looked at number of days for the ulcer to reduce in volume or surface area by 50 percent from baseline, and she talks about what her results are there, and
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specifically the median time for the volume of the ulcers in the experimental group reduced by 50 percent, and that was statistically significant.

Another article by Dr. Gardner and Dr. Franz, and this was a meta-analysis, and she talked about this earlier this morning. I refer you to her comments this morning. What's important to note is that she actually did include in her meta-analysis included chronic wounds that were not just pressure ulcers but were venous ulcers, arterial ulcers, or neuropathic ulcers. So there are some studies that have included arterial ulcers in there study design.

There is a clinical trial by Gilchrist which one of the speakers earlier this morning talked about. This was the transcutaneous oxygen levels

before, during and after application of electrical stimulation to the foot. Basically it was 132 diabetic patients.

There is an article by Jacques, a case report which was an 81 year old diabetic patient who received application of device, and Mr. Jacques talks about what the results were afterwards.

There's a review article by Dr. Kloth, and I think we all know Dr. Kloth's thoughts on the topic.

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There is an article by Ms. Ovington, and several speakers have talked about Ms. Ovington's article and how she feels that the AHCPR guidelines should be moved up from level B evidence to level A evidence, and what she actually bases that recommendation on is an article by Dr. Wood, which was just referred to in the previous example. Basically the Wood article looked at low intensity pulsed direct current on Stage II through Stage IV pressure ulcers.

And actually at a staff level, we did look at that article to consider what the basis was for the discussion about moving from level B to level A, and we did feel there might be some concerns in the study design about randomization method, about inclusion and exclusion criteria, possibility about the presence of infection, as well as the fact that not all comorbidities may have been controlled for, so the patients may not have truly been similar.

There's a perspective clinical trial which again deals with transcutaneous oxygen measures, by Peter. There's another literature review by Sheffitt, which appeared in Ostomy Wound Management, which you have as part of your packet. There is a case series by Sumano, which appeared in the American

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Journal of Acupuncture, which talked about 44 patients with various skin lesions and second degree burns, and basically of those 44 patients, they talk about 41 patients experiencing an excellent outcome.

Just very briefly going through, there's two articles by Unger which were unpublished studies.

One was a randomized double blinded prospective trial, which randomized 17 patients, nine to an experimental group, eight to a control group, and they either received high voltage pulse current or placebo, and they talk about eight of the nine experimental patients and three of the eight control patients experienced complete healing of the wound. The second trial, which was also by Unger, they had 154 patients, and this is one of those cases where there were 223 wounds, and they actually did look at arterial wounds, venous wounds, diabetic, ulcers, pressure ulcers as well as surgical, and they comment that of the 232 wounds, 200 wounds healed, 23 were nonhealed, and the mean healing time was 10.85 weeks. They didn't provide enough statistical data to determine whether or not that was statistically significant.

And finally, there was an abstract published, or actually it was not published, it was

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an abstract by Zuder, which was a clinical trial looking at microcirculatory changes as measured by capillary density, oxygen, pressure and vascular reserve.

So basically, what I wanted to do in that very quick synopsis is just briefly discuss some of the additional articles, and there were essentially 11 trials, six case series and five randomized clinical trials, that appeared since the ECRI report, and I hope you will take those into consideration s you continue your deliberations. I hope that's helpful.

DR. GARBER: Thank you very much, John. I have a question. Did you or any of the other staff try to pool the results across the better designed studies, however you might define them, to see if there were differences in effectiveness according to the underlying type of ulcer?

DR. WHYTE: Certainly that was a consideration, and I should point out, the reason why we decided to look at arterial ulcers versus venous ulcers, versus pressure ulcers, was a discussion with a wide range of persons that talked about that the

healing of ulcers is not the same across the three groups. And I know there has been controversy over

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that, and discussion, and not everyone would agree with that premise, but we wanted to make sure that all of you had the opportunity to discuss it and to look at that, because we could not come to closure on that. As Dr. Turkelson points out, there is not a lot of data on arterial and venous ulcers, and so it was hard to determine.

I think one point that I would carefully consider in the deliberations is the whole issue of the effect size, and I think you're going to come to later, and that's something that we have struggled with in terms of what is essentially the effect size of this therapy. As many of the speakers have talked about this morning, it is being viewed as an adjunctive therapy and where exactly is that role.

DR. GARBER: Les?

DR. ZENDLE: I am trying to determine what added information we get from these studies as opposed to the studies looked at in the original ECRI report, and so I'm looking at page 4 of your update, September 25th, that has the chart, it has the three types of ulcers across the top and the six types, modes of therapy.

DR. WHYTE: Sure.

DR. ZENDLE: I see that Frantz's article

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uses TENS in decubitus ulcers and appears to have some evidence there that was not considered by ECRI. Do you agree with that, or is this whole methodology of what I'm trying to do not relevant? I'm trying to see where there is more information. It looked like TENS was not addressed in the original set of articles, but that Frantz's article does address it, so we could sort of fill in that box.

DR. WHYTE: Which Frantz article are you talking about?

DR. ZENDLE: The one that's listed here, it says unpublished double blind study, 50 patients.

DR. WHYTE: Okay, I see that.

DR. ZENDLE: Pressure ulcers, medium time

to healing, reduction was 50 percent, reduction in wound surface area.

DR. WHYTE: I think that's something that you have to weigh and take into consideration. What I would say about the study is, as listed there, that the data was not statistically significant between the experimental and the control group at the end of the study for complete healing as well as median time, 50 percent reduction in wound surface area. So I think you have to take that into consideration as you weigh the information.

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DR. ZENDLE: What about where it says median time for volume of ulcer in experimental group to decrease by 50 percent statistically significant?

DR. WHYTE: Right. I think you have to take all that into consideration, how you weigh that versus complete healing, versus median time to 50 percent in wound area. All the outcome measures across studies may not be the same. You have to take that into consideration as you compare studies, and I wouldn't necessarily be able to comment in the ECRI report what their various outcome measures were. The major outcome measure that Dr. Turkelson described was about wound healing rate.

DR. GARBER: Any other questions? Okay. We are at a point now where we have two choices. We can take a quick break and resume with committee deliberation or, that would be early for our break, but we could just go ahead with the open committee deliberation. What is the sense of the panel?

DR. ZENDLE: Go ahead.

DR. GARBER: Go ahead? Anyone who wants to take a break? If you want to take a break before our next break, raise your hand.

Okay. Now is the time for our open committee deliberation. I think it would be helpful

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if everyone grabbed their copy of the questions for the panel and as you see, again, we have the two steps about the evidence, is the evidence adequate, and if we conclude it is adequate, we do need to assign it to a category of effective size.

And now, I would entertain some discussion about how to proceed. That is, first of all, we can consider whether we want to lump together the different types of electrical stimulation or not, and we can also consider whether we want to deal with different indications separately. Does anybody want to start with a suggestion?

DR. ZENDLE: I guess the question is also, how do we discuss the issue of whether this is primary therapy or only for ulcers that fail conventional therapy?

DR. GARBER: Well, the question as posed to us is used as adjunctive therapy, which I always interpret as including primary therapy. And I will have to ask Sean, if the panel feels they would rather distinguish between adjunct and primary therapy, and therapy after other therapies have failed, if it would be helpful to you if we broke it up that way, if that's how the panel feels.

DR. TUNIS: Yeah, I'm happy for the panel

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to proceed along, you know, not to mention the discussion, separating it into primary therapy or to focus on patients who, I guess it would be the chronic nonhealing ulcers as an isolated subset, if that's the feeling from the evidence that's presented, if that's the way you feel that the discussions should break out.

DR. HOLTGREWE: And then there's another factor. We have as I understand it, four energy sources and we have three diseases, so that's 12, times two is 24.

DR. GARBER: Right, and that's one of the questions. Do we want to proceed by -- let's start with the energy sources question, because we've heard a great deal of discussion about the differences and the amount of evidence there is about differences between them. Do we want to treat them as a group as one, basically one set of therapies, or do we want to distinguish them for the point of view of our discussions and our final recommendations?

DR. OLECK: I would express my opinion, again, from the questions that I raised and just I

have looked at those, I guess we heard some information here about what the common features may be of them, and especially with certain subcategories

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of the devices. And there seems to have been a lot of discussion about the high voltage pulse current, and that was the one that got the favorable rating, or there was discussion within the AHCPR guidelines, and a couple of the practitioners here, that's the one they primarily used, and we kind of talked about this delivery of charge per second and the significant things there.

And yet, with some of the other modalities, just the straight direct current, the nonpulsed direct current, and the pulse electromagnetic items, I think we've heard much less information about those, and I'm uncomfortable just from a clinical standpoint without better understanding and without better evidence of those, of just lumping everything together and saying that this works or this doesn't work. That any type of electrical device, if we are looking at these particular devices, and as we get that information or this information is given to HCFA, does this then apply to every conceivable device that someone has that would plug into an electrical outlet or hook up to a battery and you know, could that conceivably used, would this recommendation apply to that or does it only apply to certain categories of devices?

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DR. GARBER: Could I just ask you to turn that into language we could use, or could I take a stab at something?

DR. ZENDLE: I think that's the point, we can't.

DR. GARBER: Well, no. Let me just -- I hate as the chair to propose language, and I'm not proposing this except to find out if this is what the panel would feel comfortable with, and that is that we state that our discussion concerns the forms of electrical stimulation that have been tested in the literature, and we have concluded that there is not enough evidence to determine whether or not the

different forms of electrical stimulation differ in effectiveness. That is not a conclusion about whether or not it should be covered, by the way. This is just about whether we lump them together or not. Is that the sense of the panel or should it be something different? Mike?

DR. MAVES: That's at least where I think I'm at this point, Alan. And in fact, looking at the questions that HCFA posed, I sort of perhaps incorrectly assumed that this would be a group decision from the beginning. But I think you have captured this. I just don't think there is enough

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there for us to say one form is better or worse than the others, so I would go along.

DR. GARBER: And Les?

DR. ZENDLE: I just have a question. And that's, what's to prevent somebody from putting a black box with a plug in it and saying it is one of these six things? Doesn't the FDA have to say it's doing what it says it does? Do we really need to be the ones that say that these different things are all efficacious?

DR. GARBER: Well, I think a body like this cannot get into great detail about differences between devices or any other treatment where there are minor differences. So I mean, if we were to conclude that this broad set performs electrical stimulation, had enough evidence it was effective, it would be HCFA's job to decide if something new fit into this category. It's kind of like getting a, what you call it, clearance. Yes, Bruce.

DR. SIGSBEE: Every device manufacturer has to run it by the FDA to get approval, and they cannot use it on patients until it's been very thoroughly studied, so I don't think that that's really our issue.

DR. GARBER: So, are there any objections

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to proceeding on this basis, that we're lumping together, and I guess they were agnostic about whether or not there are any differences in the effectiveness. Yes, Angus?

DR. McBRYDE: Not just the device, but if you look through all these things, I mean, we're talking once or twice a day, two up to seven times a week, are we talking half an hour duration or ten minutes duration, as well as wave form, charge, the actual hardware itself, so I think all that has got to be lumped, and leave that as a quality control type matter.

Second, a large item that just kind of bothers me is well, let's get rid of this, and then we'll talk about primary versus adjunctive.

DR. GARBER: Yes, Mike.

DR. MAVES: Alan, if I could just suggest one thing, I think that -- and this is sort of separate from any discussion regarding where we're going to go with this, but I think the discussion we had about the dose response, the frequency, type, all are questions, if you will, that would be very good to send back to HCFA and to say, these are the kinds of things I think that ought to be encouraged in future studies. Because I think all of us felt a

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little ambiguous about that, and this is sort of separate from that. I mean, I don't want this to prejudice in any way our discussions, but I had noted down that I thought all of those would be primaries for research, and for HCFA to make that recommendation back to the manufacturer.

DR. GARBER: All right. Incidentally, taking that suggestion, there's nothing to stop us as a panel from putting that into our final conclusions, that is, there are certain areas where we think further research might be helpful, areas of uncertainty that could potentially be addressed with further study.

DR. HOLTGREWE: Well, you know, I am struck in the area of cancer for instance, in chemotherapy and surgery, you have certain parameters. A dose of cisplatin is reasonably established somewhere along the line. And in the area of surgery, certain surgical techniques, the inclusion of the adrenalectomy with radical nephrectomy is included in the literature, and I'm

just struck here that the literature is terribly weak in the area of how long is the machine on, which machine do you use, and it's a total mixed bag. It's just succotash rather than science at this point.

DR. GARBER: Bruce?

DR. SIGSBEE: I just wanted to make a brief comment about technique. There are two fairly large articles that have come out since the ECRI report, both by Baker, and they used a nonstandard technique where they had electrodes that were distal and proximal to the ulcer, and that's quite different from a technique where the ulcer, either the cathode or anode is on wet gauze within the ulcer bed itself. So it may be at least from a technical standpoint, that that seems to be a technique that should not be employed.

DR. ZENDLE: Not? I'm sorry, the last phrase you said there, Bruce?

DR. SIGSBEE: That that's a technique that should not be employed. They seem to be well designed studies with good end points and with large numbers of patients, and they did not reach statistical significance where they used something quite different from the other techniques that have been described here.

DR. GARBER: Okay. Mike?

DR. MAVES: I was just going to make the comment, while I think those are important areas to look at, you're dealing with a biological system, and for instance, as an EENT doctor we fit individuals with hearing aids, and there is a broad parameter over how much amplification you can give someone, but for each individual patient there is a specificity that's determined by their level of hearing loss, their comfortable level. So, while I'd like to see this improved, I think one, you also have to understand you're dealing with a system here where probably inherently, this may be as good as you're going to be able to quantity some of these parameters, at least at this point in time.

DR. GARBER: Were there any other hands up

down there? I can't see that well at that end of the table. Les?

DR. ZENDLE: I'm sort of thinking out loud here, which I know is dangerous, but the idea that studies, some of them are primary, some of them are secondary, some of them had people who failed conventional therapy cross over for the electrical stimulation and then did better, but some of them didn't have that model. Can we sort of say we're not going to address that either, that whether or not this is -- or do we want to go on record as saying that we have an opinion about primary-secondary treatment, or primary but not secondary treatment, or

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something like that? I would be interested in hearing what the rest of the panel has to say about that too.

DR. GARBER: That definitely could be something the panel could come to a decision about, do we split off the group that failed primary therapy and so therefore, deal with two different situations?

DR. ZENDLE: And I mean, the other thing I'm asking is, would HCFA find it totally unuseful if we said we're not going to split out anything because the literature doesn't allow us to do that, we're going to lump everything together and say that there appears to be evidence supporting the efficacy in some patients but the studies don't allow us to distinguish which patients it is.

DR. TUNIS: I just want to try to also tease apart, because I think this notion of primary versus secondary therapy, because I might be two differential notions there. One is, you know, looking at the issue of treating patients with chronic nonhealing ulcers as opposed to, you know, acute ulcers, in other words, by some definition, there is some objective definition that an ulcer is nonhealing. So that's a separate issue from whether you're looking at patients, all of whom are chronic

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nonhealing ulcers, you know, try a therapy and then for those who fail even that, switch them over. It seems like those are two somewhat distinct issues.

DR. ZENDLE: When I say it is nonhealing, it means it has not responded to conventional therapy.

DR. TUNIS: Right. It's just that there are different courses in the process of a wound before it even gets to the point where it's a nonhealing wound, so go ahead.

DR. GARBER: Bruce.

DR. SIGSBEE: The problem is that anybody looking at this may choose to use as their study population the folks who have failed conventional treatment, and you know, obviously I am most familiar with anticonvulsants, and that's where you use the new anticonvulsants, for those who are uncontrolled on standard treatment. And yeah, it's generalized to treatment of all seizures and those medications are assumed to treat. And the question that I think we probably ought to spend some time on is, the bulk of the evidence we have in front of us in on patients who failed conventional treatment. Is there sufficient evidence here to warrant expansion of this to the treatment of decubiti and other chronic

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ulcers, or should we recommend that it be restricted to those who have failed conventional treatment, however that's defined.

DR. GARBER: Logan, and then Angus.

DR. HOLTGREWE: I think Les has summed it up very well. I think the level of evidence, such that we have here, is such that it's very difficult if not in fact impossible to break it out into the three different kinds of ulcers and the four different kinds of clinical energy. I think there is evidence to show that there is some merit to this based on pure clinical grounds. The pathophysiology is obscure, the exact dosages are obscure, and I think to go beyond that, I think is impossible. I personally would be terribly uncomfortable trying to find a certain energy type for a certain treatment for a certain ulcer, I mean, we don't have that. I think all we can say is there seems to be some efficacious advantage to using this therapy, and stop.

DR. GARBER: Angus?
DR. McBRYDE: Well, it seems like we have jumped from the logistics of application to primary and secondary. What bothers me as an orthopedist is, and of course we've got our own problems with the
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bone stimulator, is that there at least are accepted parameters for delayed union, nonunion, and so forth. But even though you say a recalcitrant ulcer or a primary ulcer, there's a huge gray zone in the middle. So that is another piece of the definition that's got to be done in a big way before you can even say what we mean between primary and recalcitrant.
DR. SIGSBEE: That's a job for staff.
(Laughter.)
DR. GARBER: Just to take us on to the next step, I think we're agreed we are not going to separate out the types of machines at all. But now the question we face is do we want to separate out, can we give a good definition of the clinical situation, i.e., failed conventional therapy and we have to define what we mean by fail and what we mean by conventional therapy. But if we have decided, we could just start there and ask if there is adequate evidence in that situation, or we could just say for any lumped together, all different cases, which would include so-called primary therapy, that is chronic but hasn't undergone and failed all conventional therapies. So, which of those two routes would you like to go, or would somebody want to propose another
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one, i.e., only discuss after having failed primary therapy, or just lump it together? Les?
DR. ZENDLE: I think as far as evidence, you can't say that it -- the only evidence presented consistently is for failed therapy, conventional therapy, so I would, I think we should address whether we can accept it for patients who have failed conventional therapy, then talk about whether we want to try to separate the three types of ulcers for people who failed conventional therapy. And I will just tell you that I also don't think we can do that.

But then we can address, what about people who have not failed conventional therapy, and I would say there is no evidence no support its use in that situation.

DR. GARBER: Well, I would just like to take this step-wise, so first let's address that first part. Should we separate failed conventional therapy? Mike?

DR. MAVES: Again, I think perhaps this is just sort of the bias of reviewing these things at home, but my sense was that we were dealing with sort of chronic nonhealing ulcers of a variety of types that I guess by definition were not acute and perhaps, more probably I guess that was maybe my

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assumption, it had some form of prior therapy, but presented real kind of therapeutic dilemmas. And the few cases that we saw here were certainly suggestive of that. So I guess from my standpoint, I assumed we were dealing essentially with a clinical entity called chronic nonhealing ulcers of a variety of etiology, and I did not at least in my mind going through these, consider there to be a difference between an acute and chronic situation.

DR. ZENDLE: Anybody disagree?

DR. GARBER: I'm trying to figure out what that means.

DR. MAVES: I would lump them together.

DR. GARBER: Okay. So you would not distinguish. Well, your --

DR. ZENDLE: He would lump the nonhealing ones together.

DR. MAVES: Yes.

DR. GARBER: Yeah. I think this comes down to precision of definition, what you mean by chronic nonhealing. And I guess this should be driven in part by what you need in terms of language for coverage, what is interpretable in a coverage context.

DR. TUNIS: Yeah. I can also ask some of

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the analysts that worked on this, if it's not out of order, and I would even ask some of the folks who

have come to testify whether there are objective definitions that are usable for chronic nonhealing ulcers, and maybe we can get some thoughts on that.

DR. GARBER: Yeah. Charlie?

DR. TURKELSON: Our report focused on ulcers that have been present greater than 30 days.

DR. GARBER: Regardless of what treatments were given?

DR. TURKELSON: That's right.

MS. UNGER: Just a couple comments. I suggest that you look at the Wound Healing Society definition of a chronic wound and use our conventional wound community distinctions between acute and chronic, and then you know, we're moving in the face of a lack of evidence based to large dialogs about best practices. And so instead of maybe talking about conventional therapies, the issue might be using an adjunctive therapy when best practices have not resulted in healing, and that may then mean something in the wound healing community where there's a body of literature emerging on best practices.

DR. GARBER: You know, I would actually

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like to suggest picking up on a suggestion that somebody else made. If the panel agrees, this is something that we could let HCFA and HCFA staff work out, in consultation with the relevant professional societies, because I think above all, we want whatever recommendations we make to be readily interpretable by you and by the clinical community who will have to deal with it. I'm not sure we can get to that level this afternoon, but I think we would trust you in consultation to define that a little better.

DR. SIGSBEE: I want to be a little bit of a devil's advocate here, and a decubitus is a decubitus, and maybe you have one that's chronic nonhealing, and is the underlying healing process different from that compared to one that perhaps hasn't been given a strong course of conventional therapy? And at least reviewing all these articles, there is some evidence that the rate of healing is

faster using electrical stimulation, and maybe there is an argument to be made, and this may be an analysis that HCFA staff has to go through, the cost effectiveness of dealing with this on an earlier basis rather than ending up with a chronic ulcer that delays going home, all those other kinds of issues.

So I'm not sure that apriori we should restrict our comments purely to just the chronic nonhealing ulcers, even though the evidence before us deals with that issue.

DR. GARBER: Well, let me suggest that we vote on chronic nonhealing ulcers first and after that, we can decide whether we want to extend beyond that. So, I think we have this resolved. Does everybody agree with this proposal, the exact definition of chronic nonhealing can be worked out by HCFA? And so I think we all have a general sense of what that means even if we can't be precise about it.

Then the next question, Les has suggested we lump together pressure ulcers along with the other types. And the alternative is to distinguish pressure, maybe venous, and arterial and neuropathic, or something like that. What is the sense of the panel about lumping versus splitting on the clinical condition?

DR. HOLTGREWE: Lump.

DR. SIGSBEE: Maybe we could phrase it that at present, the quality of evidence before us did not allow us to distinguish.

DR. ZENDLE: That's why we lump.

DR. GARBER: Well, one way to put this, is

do people have concerns that there is -- is there sufficient evidence to be concerned that there really may be differences in effectiveness across these clinical types?

DR. ZENDLE: One of the things, and I think it gets back to your last point, I have less concern about lumping if we restrict it to chronic nonhealing ulcers.

DR. GARBER: Okay. Any disagreement? We haven't had a real vote yet, but we're actually only

discussing procedural issues at this point. So the way things stand now, our first question will be, is there adequate evidence to draw conclusions about effectiveness of electrical stimulation as an adjunctive therapy for chronic nonhealing pressure ulcers? And we are not going to distinguish the ulcer types or the types of --

DR. ZENDLE: Take the word pressure out.

DR. GARBER: Pressure, I'm sorry, yeah. Chronic nonhealing ulcers. Thank you for that correction.

Okay. Now I will entertain a motion.

DR. TUNIS: Before you do that --

MS. CONRAD: Let me read this into the record first. For today's panel meeting, voting

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members present are: Michael Maves, Kenneth Brin, Logan Holtgrewe, Angus McBryde, Bruce Sigsbee, and Les Zendle. A quorum is present, and no one has been recused because of conflicts of interest. Thank you.

DR. GARBER: Go ahead.

MS. UNGER: Just a clarification that the group of wounds that are of interest here are not just ulcers, and the largest groups are probably diabetic, venous, then pressure is the smallest large group; and then the subgroups being arterial -- nonhealing surgical wounds is certainly a large potential group of patients, so perhaps using the word wounds instead of ulcers would be more appropriate.

DR. ZENDLE: I am comfortable with that.

DR. SIGSBEE: But the thing is that we've had absolutely no evidence presented to us that dealt with nonhealing surgical wounds, and at least I don't have any personal knowledge and we haven't had any presented, presentations from the discussions, about whether that pathogen and the treatment has parallels or nonparallels, and I would have a very hard time in any way commenting on whether that's an appropriate step or not. We've really dealt with the ulcers that we have been provided with initially.

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DR. GARBER: So you would reject the

change in language and leave it ulcers?
DR. SIGSBEE: Right.
DR. GARBER: Is that the sense of the panel?
DR. ZENDLE: I have a semantic question. It does refer to, it says specific types of wounds, and then it says decubitus ulcers, venous ulcers, diabetic ulcers, and that indeed is what the literature was that we reviewed. I think if we define it as that, and we can use the word wounds, and then say we are referring to these three types of ulcers.
DR. GARBER: Okay, the panel is in agreement? Marshall?
DR. STANTON: Well, just maybe if Sean could clarify, that might reassure some people in the audience, that just because the panel doesn't address something doesn't mean that HCFA in its coverage language of E-stim is limited to just what the panel has addressed. HCFA is able to still make coverage decisions without the input of the panel on things that we did not address in E-stim.
DR. TUNIS: Right. And obviously to the extent that the panel either briefly or at any length

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wants to discuss, you know, the issue of ulcers outside of these three, or wounds beyond the three that we discussed here or for that matter, wounds other than the chronic nonhealing wounds, any discussion the panel wants to have about that, we would certainly take into account. But you're right, just because the panel decides not to discuss it, doesn't mean that we wouldn't address it in the coverage policy.
DR. HOLTGREWE: Yeah, but our comments here have to be totally restricted to these three types of ulcers, because that is all we have reviewed, we reviewed nothing else, and to go beyond that would be inappropriate.
DR. GARBER: And also Bruce has just pointed out, it also includes arterial ulcers. I mean, there's some question about how much data there is about arterial ulcers.

DR. HOLTGREWE: Well, that's true.
DR. ZENDLE: I thought arterial and diabetic are synonymous, no?
DR. HOLTGREWE: Well, I thought so.
DR. STANTON: The diabetic could be arterial plus minus neuropathic, and you could have some arterial that are pure arterial, but there's not much evidence for anything.
DR. GARBER: Now, I think we are pretty much in agreement on this, so I'll entertain a motion about the first question.
DR. ZENDLE: So moved.
DR. GARBER: The motion is therefore, I assume, to accept, to answer yes to the first question as amended, which now says chronic nonhealing ulcers, that the evidence is adequate. The motion is to answer yes. Is there a second to the motion?
DR. BRIN: Second.
DR. GARBER: Okay. Discussion?
DR. ZENDLE: Is there something specified that we also, when we refer to electrical stimulation, we're not distinguishing between the different types?
DR. GARBER: That's in the transcript.
DR. ZENDLE: Okay.
DR. GARBER: Mike?
DR. MAVES: The only other thing was the little note on the semantics as to how we were going to refer to those, I think that's important to have in the language of the resolution. Someone had that somewhere, and I didn't get a chance to jot that down. It was sort of chronic nonhealing ulcers, but then as sort of a paren, I think we had chronic nonhealing wounds --
DR. SIGSBEE: And then parentheses, the four types of ulcers we've talked about.
DR. MAVES: Is that the language that we want to include?
DR. GARBER: I will make an attempt. Is the evidence adequate to draw conclusions about the

effectiveness of electrical stimulation as an adjunctive therapy for chronic nonhealing wounds (pressure ulcers, venous ulcers, arterial/neuropathic)? That's it. The motion on the floor is to answer that question in the affirmative.

DR. STANTON: Is it possible then for you to vote on that question before having a discussion about what people feel about the level of evidence that's there before deciding that it ought to be lumped together? Does that mean that people have decided for themselves that the level of evidence is either there for all of those or not there for all of those, and that's why they're comfortable lumping them together?

DR. GARBER: That's what we meant by having that discussion about procedures, that people

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felt they would like to proceed to answer the question about the evidence in the aggregate about the different types of machines and the different clinical indications. Now at this point it would be appropriate for you to discuss, if you think you can't answer yes, because you think the evidence is greatly different from one indication to another and you'd say yes to one but not another, we should have actually had that discussion before and not split, if you feel that way. But if you are uncomfortable with it, you should bring it up now before it's really too late.

DR. STANTON: Well, it seemed like we had some discussion on the question of the different pulses and how to deliver them, and people seemed to agree that there wasn't a good way to split it, and so everybody seemed agreeable about lumping. I didn't see that same discussion for the three or four different types of ulcers there are, and I guess my own sense is that I felt there was a difference in the body of literature as best I could split them apart for the different ones, and I just would like to hear some other people's opinions. It seems like we went very quickly to the point of lumping it together and I didn't really hear much opinion, I

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just heard people kind of say yeah, lump it.
DR. GARBER: Les?
DR. ZENDLE: I think there may be a difference in the literature between the different kinds of ulcers, but by limiting it to chronic nonhealing ulcers, which in my mind by definition, they tried other stuff and it hasn't worked, it seems to me appropriate to use electrical stimulation. And that's why if we lump them all together, I can vote yes on electrical stimulation. If you start dividing them up, I don't know how I'm going to vote on each of those things, because I don't think there's enough evidence to allow us to say this is and this isn't, unless we limit it to the broad category.
DR. STANTON: What I wonder about and don't know for sure is whether some people would think the exact opposite, that by lumping it together, it makes the body of evidence less clear and makes some people perhaps less comfortable, where they may have been more comfortable in one area and not others. Now I don't know one way or the other, I would just like to hear a little more discussion on it.
DR. GARBER: Mike, and then Bruce.
DR. MAVES: I concur with that same

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opinion. I think the fact that it is chronic nonhealing, makes me much more comfortable about putting the three together and being able to answer in the affirmative on that. And so, had that not been the case, you know, I think there are at least from what we've seen, perhaps some differences, but it may well be due to simply case accumulation and numbers, more of a problem rather than simply not adequate studies. So I think when it's chronic nonhealing, there has been some therapy tried beforehand, I think that actually makes the distinction between the three of these, which may be a matter of semantics when you're actually on the ground, much easier.
DR. SIGSBEE: You now, I think if you look at it, there is in fact different levels of evidence based on the ulcer type, but I think it's based n

whether they have been studied or not. The pressure ulcers have had a large majority of the studies. There was one study that happened to use alternating current in venous stasis ulcers, but it hadn't really been looked at critically in pressure ulcers, and the others hadn't been studied in the same critical fashion, so I think it's a matter of what patient population we looked at. At least

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pathophysiologically I don't see that there's compelling evidence that there is a basic difference in these chronic nonhealing ulcers and I would be more comfortable dealing with them as an aggregate rather than separating them out without clear evidence that they should be separated out.

DR. GARBER: At the risk of restating the obvious, just to build on what Bruce just said, you don't have to feel that the levels of evidence are equal for all of these areas in order to conclude that the evidence is adequate overall. And inevitably when we're in a situation where you could split things and want things, you're going to have differences in the level of evidence. That's why we have a hard time making a decision. But you certainly could feel that the evidence is much stronger in one area than another, yet conclude that overall the evidence is adequate. And if you felt, though, that there was too large of a discrepancy, then you should clearly not lump them, that is, where you thought there was really no evidence whatsoever for indication three, then we should probably split it off if there's that great a discrepancy. But I had concluded that implicit in the panel's feeling that they should lump these together was that the

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differences in levels of evidence were not so great as to make it necessary to consider each of these indications separately. Dr. Oleck?

DR. OLECK: One of the things that wasn't focused in a lot is in terms of safety, and I think overall the safety of these, you know, seems to be very good. I guess when you raise the issue about arterial ulcers, and there was some discussion about

you know, when you give too much, and could there be some damage. Are people with arterial ulcers more susceptible to giving too much or inappropriate amounts of electrical stimulation, and does that make those people, you know, a little more questionable? I don't know. We really haven't heard very much information about that, but this is just a concern that I have listening to what testimony you have had here.

DR. TUNIS: Can I just make one kind of a comment just on the sort of the preferences expressed on the particular issue that you're talking about, splitting down and having individual voting and discussion. The preference would be that the panel try to do that. You know, going to whether it's feasible to do that given the data that's presented, but it's also possible procedurally to try to do it

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one at a time for the different types of ulcers, and then come back and try to do it as an aggregate or some variation of that. But at least I would just like to pose as, if the panel feels it's feasible, that we try to do it split rather than lumped.

DR. ZENDLE: My concern is that if you break it up, I feel that I am on much shakier ground making any kind of decision. And by lumping it, it allows me to feel semi-okay about reaching a conclusion. By splitting it out, I don't feel I could reach a conclusion.

DR. TUNIS: Okay.

DR. ZENDLE: Except for the decubitus.

DR. TUNIS: I translate that to saying that on each of the sort of four questions about the adequacy of evidence, if you separate it out by type of ulcer, you simply wouldn't be able to answer that, so let's just go ahead and try to answer it as an aggregate; is that right?

DR. ZENDLE: I would probably abstain on everything but decubitus ulcer.

DR. MAVES: And I would concur, Sean. I think it's a situation where I think it may be a problem, and I understand from your standpoint it may be, but you're asking us to look at this evidence and

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come up with our best call. Given the question that HCFA has come up with that makes it a touch uncomfortable for you, I think for us, it makes the decision, at least in my mind, much easier to have these all together at this point, signifying that, though, when you design your payment policy.

DR. GARBER: Sean, if I could just recapitulate parts of the earlier discussion about lumping or splitting, Les and others said that they felt more comfortable because this was restricted to chronic nonhealing, meaning that it had failed some form of good therapy for a long enough time. And as they interpret the evidence, you could draw a conclusion about that, and also perhaps they could draw a conclusion if we split it the way HCFA asks the questions, they could comfortably draw a conclusion about pressure ulcers, and they have more doubts about the other kinds of ulcers, but they didn't feel that was useful. Is that a fair restatement?

So I think you're hearing the panel trying to be responsive to your needs, but they're saying that the scientific evidence stacks up, the totality of evidence stacks up this way and doesn't lend itself easily to the breakdown that you proposed.

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DR. TUNIS: Yeah, and I'm not feeling strongly, like imposing any counterintuitive or counteranswerable framework on the panel, but I just want to make sure that I do understand the point that was just made, I think it was by Les, that sort of restating what you just said, that basically you're saying if you are asked to split this up and vote on the four separate ulcer types, you would have to abstain on everything except pressure ulcers; is that right?

DR. ZENDLE: Well, I think you have to combine it with what Alan just said too, that it also pushes the question for the chronic nonhealing and so I think I misspoke before.

DR. TUNIS: So you would more defer to Alan's formulation of it, the way Alan sort of

expressed the need to try to respond to the question in aggregate as opposed to individually.

DR. ZENDLE: I don't think we have enough information to split out the chronic nonhealing ulcers. We don't have enough information to split out the different kinds, and I'm comfortable voting yes on the lumping because it's chronic nonhealing. Does that make sense?

DR. TUNIS: Yes, that makes sense.

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DR. GARBER: Bruce?

DR. SIGSBEE: Just to elaborate a little bit more, there are pieces of studies that have been done on these different populations. Alternating current was done on venous statis. Some of the stuff in Appendix A looks at blood flow changes in diabetic neuropathic ulcers and shows that there is an increase in blood flow with electrical stimulation. So there are different pieces that have been offered and I think in aggregate, I think it's a pretty compelling group of evidence. If you start dissecting it into subgroups, it becomes less compelling for each of the subgroups, and I think at least for me, it's harder to make a decision about the weight of the evidence and try to advise HCFA on where this is from a clinical medial standpoint.

DR. TUNIS: Well, why don't we proceed? I'm also getting mindful that we are maybe at this point overdue for a break, so maybe you don't want to do that in the middle of a motion.

DR. GARBER: Well, we do have a motion on the table, and we've discussed it. Do people feel ready for a vote? Okay. Do I need to reread the motion? I'll take that as a clear no. All in favor of the motion, raise your hands.

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MS. CONRAD: Unanimous, okay.

DR. GARBER: Now, shall we take a break?

DR. TUNIS: Sure.

DR. GARBER: Okay, 15-minute break please.

(Recess.)

DR. GARBER: Okay, if we could, I would like to beg the indulgence of the panel members. We

had a very helpful discussion and we reached a vote, and I'm left in kind of a quandary because when I report to the Executive Committee and I know this is also something Sean needs, I have to report about the reasons for the decision and so on, and I think I can do that. But I also need to get the sense of the panel about the original three clinical indications, i.e., the pressure ulcers, or four, however you want to describe it.

And I want to make sure, and I would like a vote on this, because I want to be accurate. I stated before that I thought the sense of the panel was that there was strong evidence for pressure ulcers and that the evidence was substantially weaker for the other indications. So first of all, I would like to get a sense of the panel with the vote, is the evidence adequate for pressure ulcers? Again, this is for all of the treatment modalities combined?

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So if you could us just raise your hand, is the evidence adequate for pressure ulcers taken alone?

DR. STANTON: Now, wait a second. Are you voting?

DR. GARBER: This is not -- we are going to proceed along our vote from before. We still have to report something about these indication, or I have to. What we are proceeding, the step two is going to be rating the magnitude of the effect as we had voted before, that is, for chronic nonhealing ulcers, we are not changing any of that. But I am going to have to -- I mean, you could just whisper in my ear, that wouldn't be appropriate, about what you think, but I have to report about the clinical indications.

DR. STANTON: Well really, from a procedure standpoint, I guess I feel a little discomfort with that, because either you vote along what you want to go to the Executive Committee, or you decide for whatever reason there is a better way to vote, and you vote that way, and that's what it seemed like what you were doing. And I don't have a strong -- I don't care either way, but I think that from a process standpoint, you want to have a vote on the message that is sent. I don't think that there

should be an unofficial vote that is going to be the
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message.
DR. GARBER: Well, this is -- go ahead, Les.
DR. ZENDLE: I think most of us could agree that the evidence is best for pressure ulcers. What I'm uncomfortable with, and maybe others are too, is at what point does a yes go to a no, and I'm not sure where that line is. And that's why I'd rather -- I'm not -- that's why I'm not sure that what you're proposing is that helpful to anybody.
DR. GARBER: Actually, Les, let me clarify one thing, though. I'm not saying to vote up and down every indication, but I want to know if I'm accurate in saying that the panel felt, and this was my sense from the discussion, and I could just go and say this without you voting or telling me --
DR. ZENDLE: So you're just asking for one sort of straw poll.
DR. GARBER: Is the evidence much stronger for pressure ulcers than for the other indications?
DR. ZENDLE: Oh, I thought you were going to ask us to vote on the other two.
DR. GARBER: Well, we could do it that way but no, I don't want to give the appearance that we're going to renege on a decision we made, first of
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all. And secondly, when we proceed to question two, that is about the size of the effect, it has to be along the lines that we already voted, that is, divided up and defined the way that we actually did define it. So let me be clear. Marshall, I can appreciate your concerns, but I want to make it clear that we are not talking about revisiting the issue in a different forum.
But certainly when I explain this, and this is what happened at the last Executive Committee meeting, I had to give the panel's reasons and why they went one way and not the other. I am perfectly happy to just give my opinion again, but if there were a vote, it would make it very clear how broad the consensus is about this particular question.

Now you are also welcome if we have a vote, you're welcome to abstain, but I'm not saying up and down on the three different, or four, depending on how you want to define the indications. Yes?

DR. HOLTGREWE: Well, I will explain my vote. I think that when viewed in context with literature that exists in other fields of medicine, that what we have looked at here is quite feeble, even for pressure sores. But of the three disorders,

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clearly the evidence is best for pressure sores. If you look at the other two types of ulcers, it's even more feeble. But since these are poor patients who have a terrible problem and it's really a sad situation, and with little else in the way of options, and given the information that we do have, there does appear to be a benefit which I can't ignore. So that's why I voted yes. But I wouldn't begin to try to splinter it out into three different indications. I mean, I just don't think it was there, so my thought was let's put them all together, and certainly you want to go with the chronic problem, so that anybody that gets a dog bite and somebody gets a sore is not treated with electrical stimulation right of the bat, and some creative people might be inclined to do that. But I think that if you leave it chronic, I don't think we can split out the three indications; there's just no literature there to do it.

DR. GARBER: Bruce?

DR. SIGSBEE: I think if you open that up, then you also open up the issue of what type of stimulation is effective, and some have been looked at. Alternating current was only used in a well controlled study in venous stasis ulcers and was

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shown to be effective. Some of the pulse direct has been primarily used in the pressure ulcers. The pulse electromagnetic stimulation is not probably effective in any of them if you look at it critically, but it delivers a charge to the tissues, and we're not sure it makes any difference. So you

know, I think if we lump it together, we have a much more compelling look at this. I can understand and it is my sense as well, at least we have more studies on pressure ulcers at this point, but is it really any different? So I'm not sure that voting on a sense really reflects accurately the biology of what's going on here.

DR. TUNIS: I think actually this is helpful, and probably gets us to the same place, if the folks on the panel just take a turn explaining their yes vote, because to some degree, it was a unanimous yes vote, but yet I am not sure everybody is voting yes for the same reason, and given what we really need to work with when we go forward in developing the coverage decision is sort of what went into the yes vote. It sounds like with this most recent comment is that what sort of is implicit here is that some of the panel is saying that we're willing to agree that essentially there is no reason

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why chronic ulcers should heal differently, and therefore we're willing to kind of aggregate all these studies together and decide on it en masse. That may be what some of you are thinking.

But you know, if it's sort of to say, it's somewhat more difficult to understand to say well, for each individual indication, each individual type of ulcer, the evidence isn't adequate but when you take it all together, it becomes adequate, that's the conundrum we're trying to have you all sort out for us. So maybe if we could go down and have people speak.

DR. MAVES: Sure, I would be happy to. I think that's pretty much, Sean, where I'm at this point. And I mean, my sense is again, I think the evidence is strongest for pressure, but again, I think when you actually get on the ground treating these patients, the difference between pressure, venous and arterial may really not be very significant as to how you treat them.

The reasons for my yes vote is that I think even reading the ECRI report where they indicated there is a very big effect, I think that

was a direct quote, was certainly persuasive. And a part that hasn't been mentioned, I took a look at the

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notes that I wrote down from your presentation about the urinary incontinence decision with biofeedback, and you gave four reasons. You said there was positive support for the technology, which there is here; the patients had few other options short of surgery, I think that's true here; there's no suggestion that there's any harm done, and I haven't heard or read any suggestion that there is any harm; and there was strong expert testimony. So I think if you will, looking at HCFA's at least policy regarding the decision on urinary incontinence and using biofeedback for that, I think this parallels that argument, and I felt very comfortable with the decision I made.

DR. GARBER: Angus?

DR. McBRYDE: Well, I'm certainly a lumper in this case, and although I wouldn't use the word compelling, I think that the evidence that we have seen, heard and read and reviewed is enough to, for me, for it to be an efficacious thing, so I would vote yes. And to sort it out would take for me more than looking at the physiology a little better about the three different types of ulcerations and I happen to think they are close kin, so I would be a lumper in that regard. And I think it much more important

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to redefine if there is a definition, but to redefine that between the primary and the recalcitrant.

DR. GARBER: Ken?

DR. BRIN: I am just going to mirror what has been said. I think that the data in the aggregate is relatively convincing, although I think the paucity of data is impressive in its own. Given the degree of, or the amount of nonhealing ulcers that we have in the population at large, I am surprised at the lack of the types of literature that we like to see. But we have mostly aggregated data and I think we need to deal with the aggregated data. There hasn't been enough done from subgroups except for the pressure group, and if we exclude the

nonpressure because they are in the aggregate and not in the pressure, I don't think we can conclude anything about those other two groups.

DR. GARBER: Les.

DR. ZENDLE: I have spoken enough.

DR. GARBER: Adrian?

DR. OLECK: I didn't get to vote.

DR. GARBER: Actually, the nonvoting members can just briefly state reasons for agreeing or disagreeing with the vote, not that it's required for the record. You don't have to give your reasons

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since you didn't vote, but you're welcome to comment.

DR. OLECK: I guess I disagree with the way that, the lumping everything together. I would have been more in favor of looking at things individually, not only according to, less in terms of wound types than in terms of the different technologies, and I felt certainly that there was more evidence for the pressure ulcers, less for the venous and arterial ulcers.

DR. GARBER: Marshall?

DR. STANTON: I'm really ambivalent. On the one hand I see the virtues of lumping it together. I think the evidence in toto is more compelling than when you split it, though on the other hand, as I was going through all the literature, I did feel that there was probably enough evidence to make a decision on decubitus ulcers, and I was less confident on the level of evidence that was there to make a decision on venous, and I thought there was not enough evidence on arterial, but I could see it going either way.

DR. GARBER: Thanks. Phyllis?

MS. GREENBERGER: I'm comfortable with the decision. I agree with Dr. Maves in terms of the four categories that you used for the biofeedback.

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And also, I think while if you just looked at the scientific evidence alone, that there might be certainly more evidence in one direction than another, but I think that if you look at all the clinical evidence and the testimony today, then I

don't see that there was that great of difference, so I agree with the vote.

DR. HOLTGREWE: Can I make a comment?

DR. GARBER: Yeah, go ahead.

DR. HOLTGREWE: I would wish that given the millions of patients suffering from this disorder, I would wish that the people involved would figure out where to set the machine. And that surely, I just have a conceptual inability to accept the fact that it doesn't make any difference where you set the machine, one way or another, it doesn't matter. I've got to believe that there might be a difference, and I would hope somebody would do some studies.

DR. GARBER: Thank you for giving your reasons. Now, you know that there is basically a check list of things to consider and I think this is all implicit in your comments, the answer is, so le me just briefly say what I think is the sense of the panel, and raise your hand if you disagree.

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Regarding adequacy of study design, that you felt the studies were adequate to draw conclusions, at least in aggregate, and they showed effectiveness; that they were consistent enough to satisfy you; and there are obviously public benefits where there are a huge fraction of the patients that studies identified were Medicare beneficiaries generalized beyond the research setting. Any disagreement with that? Les?

DR. ZENDLE: One of the things, I feel it may have been consistent with the results but I'm not sure it was with the technologies, and that was a concern, but not enough.

DR. GARBER: Right. Again, we remain uncertain about whether the technologies are different in any.

Okay. Now we are at the next stage, where we have to decide about the magnitude of effectiveness and there are seven categories, breakthrough technology, more effective, as effective with advantages, as effective, less effective with advantages, less effective, not effective.

Let me remind you at this point that we are dealing with this chronic nonhealing ulcer, so it's compared presumably to whatever else would be used in that context.

DR. HOLTGREWE: I move that we consider it more effective.

DR. MAVES: I second that.

DR. GARBER: There is a motion to accept it as more effective. Discussion? Ken?

DR. BRIN: I think a straw vote is again maybe appropriate, as to whether it should be moved up to breakthrough technology. Several of the speakers -- I am not going to promote that, but I'm just going to comment that it might have the potential, if the practitioners can figure out what is the standard of care and figure out the appropriate protocols, can, but at this point it doesn't seem to be.

DR. GARBER: Okay.

DR. HOLTGREWE: Penicillin was breakthrough. This is not a breakthrough.

DR. GARBER: Any other comments or discussion?

DR. SIGSBEE: I had trouble wrestling with this in that there are a number of other therapies for chronic wound healing other than saline gauze, and it wasn't compared to some of them, it was never clearly delineated except for moist saline gauze and dressing changes, so I don't know if we can say that this is more effective than other conventional treatments out there, and we have no data.

DR. GARBER: Les.

DR. ZENDLE: Again, I think the patients with nonchronic wounds were excepted from our definition. Have not responded to conventional therapies, whatever that means, allows me to be comfortable with the more effective. I think the category below that seems to be more patient driven, and I think we've heard enough from the providers that it's not just the patients that are driving this, it's the providers.

In terms of breakthrough, I mean breakthrough implies that it is the standard of care, in other words, to not use it invites malpractice, and I certainly don't think it meets that standard.

DR. OLECK: I'm just thinking whether that, the decision saying it's more effective is consistent with the decision of just saying that it's for chronic ulcers. If it's more effective than other technologies, you know, why would it just be for people that have failed other types of items? It seems like we're saying it's something that can be tried in addition to it or after something else has

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failed, you're not going to use it, and the implication is this isn't a first line therapy to be used. And if you think it's effective, the decision, the vote was that it was effective, but whether it has major additional advantages, I don't know whether that's clear.

DR. GARBER: Yes, Angus.

DR. McBRYDE: Two things, which are very self evident perhaps, make me think that's the right category two, and belongs there. One is that although it's referred to in all our literature, there is a huge body of basic science that shows that electrical stimulation has a heck of a cellular and basic effect. And that coupled with the fact that as we know, the modalities applied in every way, so whether you feel that the modalities are short on the short end on some of the applications of it, or on the long end, as time goes by, whatever we feel is efficacious now will be more so in the future, because the basic science is there. Plus, we don't know the exact center of the spectrum as far as application is, so that makes me feel better about it, if anything, moving up in the scale as time goes by, if that makes sense.

DR. GARBER: Any other comments? I will

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call for the vote. The motion is to place it in the second category, more effective. All in favor?

Unanimous. Okay, thank you.

DR. TUNIS: I just need to verify this, we

probably did this, but the vote before the break, there was a -- it is actually fairly simple to resolve, but was the vote on actually changing the question to lump things, or did you actually vote on that amended question?

DR. GARBER: We voted on the question.

DR. TUNIS: Is that your recollection as well? Okay. So we are good.

DR. GARBER: The floor is yours.

DR. TUNIS: So assuming there is no more comments or reflections on the part of the panel, you have all had your adequate say, any other thoughts? Good.

Well, then the next step is really to thank all our presenters today, as well as the panel for their good work. We now, by our formal process, there will be, this will be summarized and taken forward by Dr. Garber to the next Executive Committee meeting, at which we can discuss this issue for discussion of the ratification of the recommendation of the panel, and then from the time that we receive

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the conclusion about the Executive Committee's recommendation, we would then have 60 days to issue a HCFA coverage decision. So those are the next steps and again, thanks for all of your efforts.

DR. HOLTGREWE: Connie, can we leave our materials here?

MS. CONRAD: The room will be secured, you may leave your materials here. I need a motion to adjourn the meeting.

DR. SIGSBEE: So move.

DR. MAVES: Second.

MS. CONRAD: Thank you.

(The meeting adjourned at 3:25 p.m.)