

FLORIDA DEPARTMENT OF HEALTH

Moderator: Tisha Crews-Keller
August 17, 2004
11:30 a.m. CT

Operator: Good day everyone, and welcome to this Exercise and Diabetes Conference Call. Today's conference is being recorded.

For opening remarks and introductions, I would like to turn the call over to Tisha Crews-Keller, Education, Health and Communications Coordinator for Florida Diabetes and Prevention and Control Program. Please go ahead, ma'am.

Tisha Crews-Keller: Thank you. Good afternoon. Continuing with our series of audio teleconferences, the Florida Department of Health Bureau of Chronic Disease Prevention and the Diabetes Prevention and Control Program welcome Dr. Jeffrey Horowitz and Dr. Lynn Panton, who together will discuss the topic of exercise and diabetes.

I want to take a moment to mention that many of our participants in south and central Florida were affected by Hurricane Charley and those at our county health departments in some of the devastated areas were not able to join us today. We're keeping them in our thoughts.

Dr. Horowitz joins us from the University of Michigan at Ann Arbor, where he is a professor in the division of kinesiology. He holds a BSE in biomedical engineering and a masters and doctorate degree in exercise physiology from the University of Texas at Austin.

Dr. Horowitz was a research instructor at the Washington University School of Medicine and is a member of many professional organizations, including the American Diabetes Association. He has numerous honors, including the National Research Service Award from the National Institute of Health. His work is currently supported by grants from major institutions such as the ADA and the NIH.

Dr. Lynn Panton joins us from Florida State University's Department of Nutrition, Food and Exercise Sciences, where she is a professor in exercise science. She holds a degree in psychology from Emory University and a masters and Ph.D. in exercise physiology from the University of Florida.

Dr. Panton's research interests are in strength training and the effects on the physiological measurements of strength, blood pressure, cholesterol, body composition and functional outcomes of elderly and chronically diseased populations.

Her work is supported by grants such as the Rockport Walking Institute, the Sigma Kappa Foundation and many private organizations. She recently received a grant to study lifestyle physical activity and success on cardiovascular risk factors.

We are honored and delighted to have Dr. Horowitz and Dr. Panton with us today. I'm now going to give you some important CEU information related to today's call. Continuing education credit has been approved for the following healthcare professionals, nurses and dietitians. Big Bend Area Health Education Center has approved this program for 1.5 contact hours, Nursing Provider Number FBN 2654.

This is not a National Provider, so nurses and health educators in other states – states other than Florida must request approval from the professional boards in their state. All CE credits will be

reported to Florida's new CE Broker Monitoring System. Nurses who want to receive CE credit must complete the appropriate CEU paperwork with the correct license number and a legible name and address.

The commission of dietetic registration has approved this program for nationwide dietetic continuing education credit, CPEU level three, 1.0 major session, topic code CL000. Dietetics practitioners who are not in the PDP process should sign and return the CDR prior approval CTE reporting form. If there were not RDs DTRs in attendance, please return the reporting forms and indicate, "No RDs DTRs attended," at the top.

Dietetics practitioners who are under the professional development portfolio should not sign the CDR prior approval CTE reporting forms. These individuals should sign in on the RD and DTR PDT Education Program sign-in with the Florida Diabetes Prevention and Control Program logo at the top. In addition, these individuals should record this activity on their step four learnings activity log. Please read the flyer attached to the CDR form for more information.

Attendance certificates will automatically be provided for dietitians either directly through CDR or to the dietitian based on the credentialing program. Nurses will receive CEU certificates approximately four weeks from the receipt of complete legible paperwork. Paperwork received after August 24 or paperwork with incorrect or legible names or license numbers will not be eligible for CEU credit.

Nurses should sign in on the participant roster, complete the (ahead) registration form and the impact survey. All participants should complete the impact survey for this program, sign in on the participant roster and complete the post-test.

Each site administrator should send the sign-in sheet and completed forms to Tisha Crews-Keller, Florida Department of Health, 4052 Bald Cypress Way, then A-18, Tallahassee, Florida, 32399 or fax to 850-245-4391 by August 24th.

It is not necessary to fax and mail your forms. CE credit will not be issued to participants who have not signed in, provided their license number and legible address and completed the required forms by that date.

Dr. Horowitz, I'll turn it over to you. Thank you.

Jeffrey Horowitz: Thank you very much. It's a pleasure to be asked to participate in this teleconference. I've not done a teleconference like this before, so it should be fun. I do have a lot of slides and I hope the slides don't become cumbersome or confusing.

I've numbered the slides in the bottom right-hand corner and I'll try to remember to refer to the slide number regularly to make sure that we're on the same page. You currently should be on the title slide, if you want to advance the slide, there should be the title. The title of my talk is "Lipid Mobilization, Oxidation and Obesity: A Link to Insulin Resistance."

So we advance onto slide number two. I have an (edipi-centric) view of the development of insulin resistance. As we're all aware, abdominal obesity is associated with increased risk for insulin resistance, diabetes, cardiovascular disease and so forth. And we believe that alterations in fatty acid mobilization utilization may underline many of these metabolic abnormalities.

If you want to advance to slide four. The main – the primary alteration in fat metabolism that I'll be discussing is an increased (lipolitic) rate and increased fatty acid availability. It may seem counterintuitive, but the fat breakdown or (lipolysis) is actually very high in people with abdominal obesity, and this is the root of many of their metabolic abnormalities.

The data on this slide, again slide four, shows fatty acid availability as it's noted on the Y axis as fatty acid RA or rate of appearance in the circulation. It's data from a study I did a number of years ago now in which we found that as confirming many other studies that obese individuals have a greater rate of fatty acid mobilization in circulation, in this case, the obese had about a 25 percent greater rate of fatty acid mobilization compared to their lean counterparts.

If you want to move to the next slide, this may look like the next slide, but it is very slightly different. The Y axis you can just read instead of RA fatty acid or fatty RA it reads fatty acid RD, which refers to disappearance of fatty acids from the circulation, which is a measure of fatty acid uptake. And again, the obese individuals have a greater rate of fatty acid uptake, and again, I'm suggesting that this is bad. And why is this bad? Advance to the next slide.

Slide six – this slide – this data illustrates that the effect on elevated fatty acids on insulin sensitivity. In this study, insulin sensitivity was measured using a (hyper insulemic aglycemic) clamp. Many of you may be familiar with this clamp technique, but for those of you who are not, during this – during this technique insulin is infused at a set high rate and glucose is infused at a variable rate with the goal being to maintain blood glucose concentration.

So the greater the rate of glucose infusion, the more sensitive to insulin, so the higher rate of glucose infusion the more sensitive the person is. This first slide shows the control condition where fatty acids were naturally low and as you can see a nice progressing increase in glucose infusion rate.

If you go to the next slide, superimposed on this is a separate occasion when the same subjects were infused with lipids under the same conditions and they were infused with lipids and heparin – lipid solution and heparin in order to increase fatty acid concentration.

And you can see the fatty acid concentrations are very high, approaching two (millimolar), and you can see that the glucose infusion rate was dramatically reduced, indicating that there was insulin resistance. So the elevated fatty acid concentration can impair. An elevated fatty acid (availability) can impair in someone's sensitivity, but how does this work?

Move on to the next slide, which is slide eight, first taking a very simple approach to get the general picture of the fate of fatty acids, this scheme is divided into blood compartment and a muscle compartment with fatty acids being in the blood compartment. I'll be running through these slides pretty quickly, so if you're following on slides you may have your – get your trigger finger ready. If you're following on paper, you may want to be shuffling through your papers pretty quickly so hang on. Hopefully this will work.

So going onto the next slide, slide nine, the fatty acids enter the muscle cell through a wide range of complex mechanisms that I'm not going to go into here, so when the fatty acids enter the cell, next slide, they can be shuttled to the mitochondria to be oxidized – next slide – or they could be stored inside the muscle cell as triglycerides – next slide, slide 12 – and/or they can be partially metabolized to form fatty acid intermediates like (diacylglycerol) or (ceramide), which can accumulate within the cell.

Next slide. When the rate of fatty acid uptake is high, as seen in obesity noted here as the bold arrow going into the fatty acids, going into the muscle cell – next slide – and the rate of uptake is high relative to the rate of fat oxidation shown here as the dashed arrow of fatty acids going into the mitochondria denoting a low rate of fatty acids oxidation relative to uptake.

Next slide. The incoming fatty acids can either be (esterified) and increase the store of intramuscular triglycerides – next slide, slide 16 – or they can be partially metabolized and increase the accumulation of these fatty acid intermediates inside the cell. And together these non-

oxidated states, these routes of disposal of the fats that are not going to the mitochondria have been linked to insulin resistance.

Next slide, slide 17. In some pilot work from my lab we've quantified the non-oxidated fatty acid disposal or the non-oxidated – the non-oxidated fatty acid disposal and found that there's a strong relationship between the magnitude of the non-oxidated disposal of fatty acids and glucose intolerance.

These data in this regression show – again, this is preliminary data – but these show that there's a greater – those were the greater non-oxidated disposal of fatty acids have a greater impairment in glucose tolerance as we've noted by the greater concentration of glucose under the curve during a normal glucose tolerance.

Next slide, slide 18. Both of these routes, the non-oxidated fatty acid disposal routes of increasing triglycerides or increasing fatty acid intermediates have been implicated to develop insulin resistance and a look at the mechanisms behind both of these now.

Next slide, slide 19. Many studies have reported inverse relationships between muscle triglycerides stores and insulin sensitivity. In this slide, insulin sensitivity is noted on the Y axis as M or the infusion rate of glucose and intra-muscular triglyceride concentration in this case intra-muscular – (intermyocellular) lipids, IMCL are on the X axis. And you can see that there's a negative relationship with those with the greater amount of intra-muscular lipids have a lower insulin sensitivity.

These data have led many to suggest that intra-muscular triglycerides cause insulin resistance. However, there is more recent evidence to suggest this may not be the case, if you want to advance to the next slide. One of the first examples showing that there's a disconnect between

intra-muscular – the concentration of intra-muscular lipids and insulin sensitivity is something referred to as the athlete's paradox.

And in this case, athletes are known – endurance trained athletes are known to have high insulin sensitivity. If you notice the right side of this figure you see that again the Y axis is M, which is insulin sensitivity so that the trained – if you just look at the two bars on the right side, you see the trained athletes having a very high insulin sensitivity relative to the Type II DM, which is diabetes – diabetes mellitus.

So the trained athletes obviously have a much greater insulin sensitivity than the diabetic subjects. Go to the next slide, but the trained athletes – it's been widely found that the trained athletes have high intra-muscular lipid concentrations.

If you look at this panel on the right, figure 21, the trained athletes have about the same intra-muscular lipid concentration as the – as the diabetes – diabetic subjects. So this evidence, along with others have actually more directly addressed this issue, puts the role of intra-muscular triglycerides with impairing insulin sensitivity into question.

Next slide, however, the accumulation of fatty acid intermediates are much more likely to be a major contributor to the insulin resistance – development of insulin resistance, and how does this work? Go to the next slide, slide 23. Again, I'm going to flip through these next slides pretty quickly, so try to hang on.

And I apologize if this is an oversimplification for most of you, but to understand how fatty acid intermediates may interfere with the insulin media to glucose uptake, it's first important to understand how insulin – how insulin works to increase glucose uptake.

So when insulin binds its receptor on the muscle cell membrane, next slide, this triggers a series of reactions that activate certain cellular factors and one key step is shown here, which is the (phosphorylation) shown as the purple key of the protein IRS one, or insulin receptor substrate one and this (phosphorylation) at a specific site of IRS one activates it and that becomes important here in a second.

Next slide, this activation of IRS one initiates more reactions, and we won't go into detail of those reactions, which ultimately trigger the activation of the glucose transporters, which are (glute) four, shown in green, and the activation of those glucose transporters allows them to migrate to the cell membrane, next slide, slide 26, which allows the glucose to enter the cell. So that's the process of, in very simple terms, the process of how insulin initiates or activates glucose uptake.

Next slide, when fatty acid intermediates accumulate inside the cell, next slide, this activates certain intercellular factors, one in particular being protein (kinase) C, (isophorm fada) or PKC (fada) is shown here. Next slide, the activation of this factor alters the (phosphorylation) state of IRS one. You see the (phosphorylation) of the P is now on a different residue on the IRS one molecule. Next slide, and this ultimately inhibits that stimulatory cascade responsive for glucose – for increasing glucose uptake.

Next slide – so again, while direct evidence for lipid – for increasing lipid storage in muscle on insulin sensitivity is questionable, the accumulation of this intracellular intermediates like (diocoglycerol), (ceramide), (long chain nasal coas) seem to be playing a very important role.

Next slide – to change gears a little bit, I've been explaining the importance of fatty acid uptake and the mechanisms by which they may impair in some resistance, but I want to touch briefly on where these fatty acids are coming from. The two most likely culprits, and we should be on slide 32, the two most likely culprits are intra-abdominal adipose or visceral adipose tissue and subcutaneous adipose tissue.

As you certainly are aware that the negative health effects of body fat are almost always attributed to excessive visceral adipose tissue. However, I'm going to suggest that this may not always be the case, especially in regards to muscle insulin resistance, because if you remember, I'm suggesting that excessive fatty acid uptake from the systemic circulation into muscle seems to be a major player for impairing insulin sensitivity.

Therefore, understanding the contribution of different sources of the fatty acids from different sites at a visceral adipose tissue subcutaneous adipose tissue, the sources of those fatty acids into the systemic circulation will help determine which adipose tissue bed may be most important in determining insulin resistance.

Moving forward to slide 33, in a series of studies from (Michael Jensen's) lab at the Mayo Clinic have clearly demonstrated that the most – that the vast majority of fatty acids delivered to this systemic circulation come from subcutaneous adipose tissue, shown here in blue, the large portion of this bar graph. Eighty percent – more than 80 percent of the fatty acids that are delivered into the systemic circulation are coming from subcutaneous adipose tissue, whereas less than 10 percent are coming from visceral adipose tissue.

Taking this one step further, slide 34, next slide, when breaking down the subcutaneous adipose tissue into different regions of subcutaneous fat, upper body – it's very simply bringing it down to upper body and lower body fat, not surprisingly, most of the subcutaneous adipose tissue delivery is coming from upper body subcutaneous (depos).

So at least when it comes to insulin resistance in muscle, because the fatty acids that are – that the – that the muscle sees are coming from the systemic circulation. It doesn't appear the fatty acids – that many fatty acids interfere with the insulin signal that are coming from visceral adipose tissue. Most seem to be coming from upper body subcutaneous adipose tissue.

Next slide. So being an exercise physiologist, and getting back on track, I feel compelled to talk about the virtues of exercise and the wonders of exercise, and as you certainly are all aware, exercise has an impressive ability to improve insulin sensitivity. What is less respected, I guess, is that even a single session of exercise has profound effects.

Next slide, slide 36. These data demonstrate the effect of a single session of exercise on insulin sensitivity. In this study, subjects perform cycling exercise in one leg while the other leg remained resting and insulin sensitivity was compared in the exercised leg versus the non-exercised leg. This is after the exercised event.

And I appreciate that this slide may be a bit confusing, but I'll try to point out the highlights. The point I want to make is that the exercised leg is less – that with the exercised leg there is less insulin is required to achieve the same rate of glucose uptake noted by the dash lines.

You can see that the arrow pointing to the exercise leg line that to achieve half maximum glucose uptake, the exercise leg needed only 30 micro units per mil of insulin where in the non-exercised leg, the rested leg required 50 micro units per amount to achieve half maximum glucose uptake, which is the definition of insulin sensitivity. And this, again, with one single bout of exercise in one leg. So, again, single session of exercise very important for increasing insulin sensitivity.

Next slide 37. Much of the effects of the post exercise effects of insulin sensitivity are attributed to exercise induced reduction in muscle glycogen. When you exercise muscle glycogen is reduced and this data shows correlation between the amount of glycogen depletion and glucose uptake measured after exercise. The more glycogen that was used during exercise, the greater the rate of glucose uptake after exercise.

Alternatively, a quicker glycogen replenishment after exercise, the quicker the insulin sensitivity returns to base line so you can wipe out the effects of – beneficial effects of exercise by more quickly returning your glycogen stores to base line levels.

So, it's been found that exercise induced increase in insulin action is sensitive to dietary carbohydrate because when you're increasing your dietary carbohydrate content after exercise, you're going to replenish glycogen and thereby reduce insulin sensitivity back to basal levels more rapidly.

Next slide, slide 38. So getting back on track to my overall theme today, which is fat and insulin sensitivity, well, it's been found that increasing dietary carbohydrate after exercise affects the exercise induced increase in insulin sensitivity.

To date it hasn't been shown if the increase in insulin – the increase in lipid availability after exercise attenuates the increase in insulin sensitivity. And we recently completed a study to address this question, to address if you increase lipid availability after exercise, does that affect insulin – the exercise induced increase in insulin sensitivity.

Next slide, slide 39. So to briefly describe this study, we had healthy non-obese subjects perform two separate trials and during each trial they exercised for two hours. The only difference between the trials was the meals – the composition of the meals that they ate after exercise.

On one occasion they ate low-fat meals. On the other occasions they ate high-fat meals. I'll show you the dietary breakdown here in a second. The next morning, on day two, we performed a muscle biopsy to assess muscle lipid content and to measure glucose tolerance using an oral glucose tolerance test.

Next slide, slide 39. This shows the micro – the macronutrient breakdown of the trials. I want to point out that they ate the same amount of carbohydrate. They ate the same amount of protein during the trials. Next slide, same data, just highlighting the fat content, but they ate vastly different contents of fat during the two trials, eating nearly 180 grams of fat in the high-fat trial compared to about 10 grams of low-fat in the low-fat trial.

Next slide, slide 42. Despite these differences in blood – in the amount of fat ingested, blood glucose, blood insulin concentrations were no different the next morning and muscle glycogen (re-synthesis) was no different the next morning.

Next slide. Not surprisingly, and as planned, its excessive amount of fat, dietary fat after exercise, increased intra-muscular triglyceride concentration and it was significantly higher the day after the subjects ate the high-fat diet compared to the low-fat diet. Next slide.

Despite this huge difference in dietary fat and the difference in intra-muscular triglyceride concentration of these intra-muscular lipids that have been thought to be associated with insulin resistance, we found there was no difference in glucose tolerance when measured the next day.

So you can see in the top portion of this oral glucose tolerance test, those lines are basically super imposable as far as the glucose concentration and the bottom panel in the slide shows that the insulin concentration again basically super imposable whether they eat the low-fat or the high-fat diet.

So this suggests that the exercise stimulus may override some of the negative influence of one day of excessive dietary fat on insulin sensitivity. It also provides additional evidence that there is this disconnect between intra-muscular lipid content and in some sensitivity. And this is a situation we've created differences in intra-muscular triglyceride concentrations and much like the athlete's paradox we find similarities in glucose tolerance.

Next slide, we're taking this question a bit further and we're currently wrapping up a companion study to more directly examine the effects of increasing fatty acid availability after exercise on insulin sensitivity. Similar to the design of our other study, the main difference between these two studies is that instead of feeding a high-fat diet or a low-fat diet, in this study we directly infused direct line of fat into the – into the subjects after they've exercised.

They eat the same meals, but in one case they are infused with lipids overnight and in other case they are infused with saline as a control. And we're comparing the overnight lipid infusion to the saline control the next morning when we take a muscle biopsy and measure insulin sensitivity using also a bit more sensitivity measurement of insulin sensitivity using a frequently sampled IV glucose tolerance test. We're using the (minmad) method from (Richard Burtman).

Next slide, slide 46. So quickly this slide just shows the overnight increase in fatty acid concentration with the lipid infusion treatment that the lipid infusion resulted in a large difference, a large increase in fatty acid availability overnight.

Next slide, slide 47, and similar to our earlier study, we found that increasing fatty acid availability after exercise did not affect insulin sensitivity, despite measuring the increase intra-muscular triglyceride concentrations, which I'm not showing here.

Next slide, so again, exercise seems to have some type of perhaps protective effect to excessive fatty acid availability in the hours after exercise. To briefly explain what might be going on here, slide 48 shows – it goes back to the original scheme that I showed you before.

Go to the next slide. It suggests what we think might be going on is that exercise increases fat oxidation, even in the hours after exercise – hours and even go to days afterwards or a day afterwards. So this increase in fat oxidation is noted here in slide 49 as an increase in CO₂.

Next slide, exercise has also been found to reduce intra-muscular lipid concentration as those lipids are used for energy during the exercise.

When exposed to a high-fat diet after exercise or exposed to a high-fatty acid availability, as in that second study – next slide, slide 52 – the increase in – the increase in fatty acids that are taken up, shown by the bold arrow – next slide – are directed to the mitochondria because now we have an increased rate of fat on each patient.

Next slide. Slide 54 shows that the synthesis of fatty acids can also be shuttled to the synthesis of intra-muscular triglyceride as those triglyceride stores increase. Next slide. These increased accelerated routes of disposal leave little of the fat available, we hypothesize, to accumulate as fatty acid intermediates inside the cell, and as a result the fatty acid intermediates impair in some sensitivity. As a result, those fatty acid intermediates are not impairing insulin sensitivity in response to the excessive fat availability after exercise.

Next slide. So to summarize, and to wrap up, I just want to reiterate that the balance between fatty acid uptake and observation seems to be very important in regards to insulin sensitivity. In this slide showing that even in healthy non-obese people, fatty acid uptake is shown in the black bar – this is slide 56 – exceeds the rate of fat oxidation. That gap between the two is noted in the non-oxidated fatty acid disposal, but as long as this difference in this non-oxidated fatty acid disposal is relatively small, things are OK.

Slide 57 shows the situation of obesity. Obesity is characterized by high (glycolytic) rates, high fatty acid availability and high rates of fatty acid uptake. This obviously increases the non-oxidated fatty acid disposal. Next slide.

Additionally, not exercising can reduce fat oxidation. It's showing obese and unfit or unexercised, that the – having the excessive fatty acid uptake and the reduction in fatty acid oxidation further

expands the non-oxidated fatty acid disposal, perhaps creating this worst case scenario, which I think unfortunately is becoming the norm.

Next slide, slide 59, so we're aware the exercise and weight loss are good for us. However, it's less clear what exactly and why exactly it's good for us and I propose that this may explain one important mechanism by which exercise and diet, weight loss is good for us.

By losing body fat, body weight, fatty acid availability and uptake are reduced, shown here with the arrow pointing down in the black bar. And by exercising and increasing fitness, fat oxidation increases. This combination of events shrinks that non-oxidated disposal of fatty acids and thereby reduces insulin resistance as well as risk for diabetes and other metabolic. Thank you very much.

Tisha Crews-Keller: Dr. Panton, please go ahead.

Lynn Panton: Oh, yes. Thank you so much for inviting me to participate in the teleconference this afternoon. Dr. Horowitz explained the mechanisms behind – some of the mechanisms involved with insulin resistance and then some of the mechanisms that exercise may help to attenuate that affect of insulin resistance.

What I'd like to do over the next 20 minutes is talk to you about exercise and how do we get our clientele or the people that we work with, if we know that exercise is beneficial in reducing insulin resistance, how do we get people to exercise and how much is needed to try and get those effects. So my topic today is "Diabetes Exercise For A Lifetime."

Just to start off with, I'd just like to give you a little bit of statistics on the affect of chronic disease on the second slide. Ninety million Americans suffer from some form of chronic disease, and

these are older statistics, but in 1990 the effect of chronic disease on the cost of healthcare expenses of Americans is two-thirds of a trillion dollars.

That's just a huge economic factor. And diabetes falls in as one of the top three diseases that's costing our country half a trillion. So we have coronary artery disease, or heart disease, obesity and diabetes alone costing our country half a trillion dollars each year.

This – the next slide with the little cartoon depicts kind of the thought of our country and as people age we have this gentleman coming up to the Wizard of Oz saying, "Do you have anything that stops the aging process?" and the Wizard goes, "Yes, sure. What kind of disease would you like?"

And I think that's a thought that's very common that as we get older we're going to get some form of chronic disease. Well, I'd like to put it up to you that that is not the case, and if I happened to be the wizard, I would have put this gentleman on an exercise program.

Just to show you a little bit of the studies, one of the large studies and epidemiology study that was carried out in three states in the United States was looking at the physical activity and the research is showing us that physical activity can reduce the risk of disability and disease by either preventing disease, so we can prevent some of these chronic diseases, especially diabetes.

We can reduce the functional impact of the existing disease, so the research is out there showing that individuals that have diabetes, if they start to exercise, we can improve that – the disease process and slow it down and then sometimes even eliminate drug use for diabetes. We also are finding that with exercise and being physically active we can slow down and reverse some of these physiological and functional declines from aging entities.

The next little cartoon, again, very typical. The man – the obese gentleman is standing in front of the elevator and the sign is saying, "Over use of this device may be hazardous to your health," and again, our – the same type of mentality set for our nation is we're finding that things are becoming more and more automated and there is less chance for us to be physically active.

In the next slide, a quote, and if any of you all get a chance to pick up (Walter Boortz's) book, "Dare To Be 100," it's a great book with lots of little stories. But one of the quotes in there is that he says is, "Life is not a spectator sport.

It has to be played and engaged and growing older is a slow process, but can become much faster if we don't participate." And again, this is so very true. We're finding that so many of these chronic diseases are due to our lifestyle choices and being physically inactive.

In 19 – on the next slide – in 1996 the surgeon general published this report and the research is out there that physical inactivity is detrimental to your health, so it's very important to become physically active. So what are some of the benefits of exercise conditioning? This doesn't just apply to the diabetic person, but to all of us.

But the first two, specifically – or the first three – very specific to a diabetic as far as improvement in blood glucose control, and this is what we just saw in the presentation by Dr. Horowitz with the exercise so important in improving insulin sensitivity and improving our glucose control.

Research has shown that if we can get our diabetic patients to become physically active, especially for the Type II diabetics, they can reduce the amount of medication or even wean themselves off medication.

Reduction in fat very important for all of us, but especially important for the diabetic person. Of course, improvement in physical fitness, reduction in coronary artery disease, improvements in blood pressure, reductions in our triglycerides and cholesterol and improving our walking ability

and our functionality for routine activities of daily living. We also find that exercise also helps in reducing our stress and improving self-esteem.

On the next slide what has been over the last 10 years or so, you know, research has come out to show that there are physical activity recommendations that we can have a structured approach and lifestyle approaches and still get improvements in health.

We have some individuals who are very regimented with their exercise. They want to have – be put on an exercise program. They say, "Tell me what I need to do and I'll go out there and do it." But then you have others who don't want to exercise at all. The word exercise is just horrifying to them.

They've had bad experiences in the past with exercise programs and are just not going to exercise, but research has shown us that lifestyle approaches to increasing physical activity can also have some health benefits, and especially for the diabetic, so we don't necessarily have to get them to put on a pair of tennis shoes, per se, or to buy athletic clothing, that we can get them to make adjustments in just their lifestyle activities in just a few minutes throughout the day and they can get health benefits.

So what I'd like to do now is talk a little bit about the structured approach for those individuals who would like to go on an actual program. And then for those that are not really interested in exercising per se, give you some ideas on how you can adjust or make changes just to your lifestyle to try and get benefits from physical activity.

So the structured guidelines, these guidelines are from the American College of Sports Medicine and they have been just a little bit for the – or modified for the diabetic patient. When we give an exercise prescription we usually give it in frequency and duration and intensity and then mode of activity.

For the diabetic patient we recommend that the frequency wise is that they try to exercise daily or at least four times a week, and this is very important. Diabetic individuals need consistency of lifestyle and we try to maintain energy intake with energy expenditure, and so that's one reason why we try to get them to exercise on most days of the week, so daily or at least four times a week.

The duration is recommended from 30 to 40 minutes. Due to usually the lower intensity levels we recommend a little bit of a higher duration. You may have heard with some exercise programs that if you exercise for at least 20 minutes you'll get benefits, and that's true, but for the diabetic person we usually recommend about 30 minutes, a little bit longer.

And then, on the top end, we usually don't recommend more than 40 minutes. Usually this is due to maybe needing extra carbohydrate if you have to – if you exercise more than 40 minutes or heat intolerance. So we usually keep it from 30 to 40 minutes of a continuous type of activity.

The intensity level we recommend from 60 to 75 percent of the maximum heart rate. And to calculate this, you use the 220 minus your age. So for an individual who is 50 years old, you would take 220 minus 50 and that would be 170 and then multiply that by point six and I think that comes out to like 102 beats per minute and if you get it by 75 percent or somewhere in there, 75 percent would give you a heart rate of about 128 beats per minute.

So the individual who is doing the exercise program would like to try and get their heart rate up to about 102 beats per minute at that 60 percent level. So that would be the intensity for the activity. It's nice to be able to quantify the energy expenditure in Kcals for the diabetic person because a lot of times they are watching their food intake as far as their calories, but if not, it's just important for them to get out there and exercise and then activities.

I get a lot of questions about what activities should a person do? What's the best type of aerobic activity? And my answer is always is the activity that someone likes to do and if you don't like to bicycle and you have to bicycle every day, you're not going to stick with it.

So choose an activity that you love, whether it's walking, cycling, dancing, swimming, anything that's going to get the heart rate elevated and get you moving. So these would be guidelines then for a structured regimented program that an individual would go on.

Just some special precautions when getting your clientele exercising, you know, hopefully everybody with diabetes is under a physician supervision. One should not exercise if the plasma glucose is over 250 milligrams per decimeter. Blood glucose needs to be controlled before somebody goes on an exercise program, so they should be working closely with their physician.

Any time you exercise you need to make sure you have adequate fluid replacement, making sure water is available and making sure that you drink it. Just don't use your thirst. Thirst is not a good indicator necessarily of how much fluid you need to continually drinking while you're exercising. It's very important.

Making sure strenuous exercise is avoided until your diabetes is controlled. Making sure you wear proper footwear and have proper foot hygiene very important. You want to make sure that sneakers, running shoes, anything that you wear fits well so you don't get blisters while your taking – clients do not get blisters. You can get a lot of problems with your feet.

Making sure individuals have a slow and gradual progress – you want to slowly get into this. Most times individuals with Type II diabetes haven't exercised in a long time. They may be overweight, so they need to slowly start into this. So gradual progression is really important so no one gets hurt. Proper warm up and cool downs. We usually recommend five or so minutes of an

active warm-up with some type of stretching, and especially stretching after their activity is finished.

We always like to try and recommend exercise with a buddy, especially if an individual has a tendency to become hypoglycemic. This is going to be more important with the Type I diabetic. Again, for the Type I diabetic, it's not recommended that an individual exercises in the evening because it may cause a delay of hypoglycemic response when the person is sleeping.

The next slide talks about special precautions to prevent exercise induced hypoglycemia. And again, this could be more of a problem for the Type I diabetic, but again for both the Type I and Type II diabetic it's so important to maintain consistency of lifestyle as far as the foods that we consume, energy that we intake and then the energy expenditure – very important for the Type I diabetic.

Careful self monitoring of blood glucose – can't stress this enough, very important, especially when you start an exercise program for the Type I diabetic. Especially, you know, testing blood glucose and monitoring it.

We had my cousin's son – he's 13 years old – spent the summer with us, so the first experience I've had with a Type I diabetic and I know he got very frustrated with me because we weren't measuring his blood glucose right away and his blood was all over the place and, you know, I came down on him and said, "That's it. You've got to start measuring it more often."

So his poor finger were so sore from all the sticks that he did, but we were able to maintain his glucose then much better so he would test it himself six to eight times a day throughout the day, maintaining that blood glucose level. So that's important in a good glucose control.

If you are taking insulin, it's always advisable not to inject insulin in the extremity that you are going to be exercising. So if you're going to go out walking or if you're going to go cycling, try to do your injection in your arms or abdominal area and keep from injecting it into your legs.

It's always good, again, especially for the Type I diabetic, to exercise after a light meal or snack. Do not exercise after an insulin injection. Exercise acts like insulin. Insulin pulls in the blood glucose into the system and if you're exercising you're doing the same thing, but if you do that, if you get the insulin before you go out and exercise, you won't have the sugars available or the glucose available for your activity, so you have a greater chance of becoming hypoglycemic.

If you do the exercising for long periods of time, we have a lot of athletes that are diabetics, Type I diabetics, it's recommended that they do have carbohydrate intakes during their exercise, so for every 30 minutes of exercise, if you're going for long bouts, that you should every 30 minutes or so take in about 10 to 15 grams of carbohydrate.

So it's a good idea when you're out exercising, but just in general to have a bracelet and medical I.D. to say that you do have a diabetic condition. Always stop exercising when you become hypoglycemic and if you do feel hypoglycemic then you should make sure you have some kind of carbohydrate snack.

OK. So those are hints, then, for the structure type program if you're working with someone who wants to be very regimented. They want to start an exercise program and those are the guidelines and suggestions. What about the individuals that you work with that just do not want to exercise. They don't want to hear about it, but they do want to get some health benefits?

Well, the surgeon general also has found, and this was published in 1996 or recommended that everybody over the year of two years of age should accumulate at least 30 minutes of endurance type physical activity ultimately at moderate intensity on most or preferably all days of the week.

So this was one of the first reports that came out or was the first report really suggesting that we don't necessarily have to have this real regimented structured exercise program, but we can incorporate activity into our lifestyles and still get in health benefits.

Other research that has been published in the last few years, on the next slide, has also found that exercise doesn't have to be done all at once, that we can accumulate bouts of activities throughout the day and still get the same health benefit.

So if we can exercise 10 minutes in the morning, 10 minutes at lunch and 10 minutes in the evening, we can get that accumulation effect. So for some people that's going to be a very optimal way for them to become more physically active and get those benefits.

So what are some ways that we can get people to be more active? And on the next slide it's just trying to be creative and learn to find opportunities to help us to be more physically active. Well, just like the slide I showed in the beginning of the gentleman standing in front of the elevator, well, instead of using the elevator, use the stairs.

And if you're overweight and very physically inactive, that's going to be a very difficult task for you to do. Well, if you need to get up onto the sixth floor, you don't have to go out immediately and try to get up all six flights of stairs, but at least do something.

If you can climb up one flight of stairs and then take the elevators the rest of the way up, you can do that. But try to find opportunities to increase your activity. So if you could use the stairs instead of the elevator, especially if you're only going up one flight of stairs or if it's difficult to go up the one flight of stairs, then at least take the stairs coming back down.

If you're walking to meetings instead of driving the car, walk during lunch breaks or coffee breaks. Some of our lunch periods are 30 minutes. We get a 30 minute break. If you could take half of that time, 15 minutes, and take a walk around the office, down the halls, get outside the building, walk around the building, that 10 minutes, 15 minutes, it adds up so you can do that throughout the day.

It's better than not doing anything and we're finding that we can get health benefits with even 10 minute increments of activity. You know, increasing the distance to your parked car, you know, in the mall or the grocery stores or we see people fighting for those first few parking spaces that are right at the front.

If you're in a hurry, it's still quicker to park at the far end of the mall parking lot and walk in than it is to wait for somebody who is putting groceries in or putting bags in their car and then deciding to slowly meander out of the parking spot. So even when you're in a hurry sometimes it's better to get out and move. You can get there a lot quicker.

You know, and I talk about people who – talk to people who ride busses. You know, try to get off the bus just a stop earlier and walk the rest of the way. We're starting to see a lot of people with cell phones in our neighborhoods that go out and walk and take their cell phone with them and talk. That's probably a little dangerous. Probably safer than doing it while you're in the car driving, but you know, if you've got to do a lot of business or talk, use the telephone, cell phone and go out and walk and talk.

Watching TV when you're around the house, you know, during the commercial breaks go out, walk, do some exercises while you're – while you're sitting in the chair. And then a lot of times I talk to mothers that are busy with their kids and they just don't have time, but when they – or they're working. They come home and they want to spend quality time with their kids.

They just don't have time to exercise. What better way to spend quality time with your kids than to get out there and play. Kids love you to play with them. That's the best quality time you can spend with your kids is being with them and playing basketball, tag, any activities. Your kids need exercise, too, so it's real important for both of these.

Just some – just some slides with some ideas. I know my two kids love dancing and they love when we put on the music and just goof around the house jumping up and down. Great form of activity and you have a lot of fun with it and a lot of bonding with your children.

You know, doing errands, you know, you've got a picture of somebody cycling with groceries and even in a wheelchair disabled, you can still get out and do – and try to find opportunities to use physical activity to do your – to do your errands. Again, just another slide on doing things with your children, whether it's running errands, walking to the grocery store, walking to school, very important to get them physically active as well.

A lady walking during, you know, during lunch breaks during the office time. A lot of us have a lot of commitments afterwards, whether we're looking after aging parents or children. We don't have much time if we're working full days, but during the day we're more productive when we can get up out of our chairs, you know, spend a few minutes from the computer, walk around.

We can spend even five minutes just walking up and down the hall, walking outside. We're going to get – we're going to be refreshed and then we also get the health benefits of that physical activity. You know, walking along in Florida a lot of us get a chance to get out onto the beach just walking. It helps in stress reduction, just being able to get outside.

So those are some ideas as far as getting people motivated to try and get some activity into their life. Ideally we would like everybody to try and go into that moderate physical activity level, and

that's activity that burns about 150 calories per day or 1,000 per week. And again, it doesn't necessarily have to be regimented exercise.

We can still do lifestyle activities and still burn calories, for example, here like gardening. And gardening can be very – require a lot of energy, especially raking and weeding, but gardening for 30 to 45 minutes, raking, stair walking for 15 minutes.

That's a little bit longer than just going up a few flight of stairs. But walking, again, can get us up into that – for 30 minutes up into that 150 calories, which is optimal. Pushing a stroller for a mother or a father that has a child that may be in a buggy for 30 minutes can help us to get up to that 150 calories per day.

Not many of us have pushed lawn mowers like this little picture, but I know we have – we don't have a lawnmower exactly like this, but we do have a push one and you know it's a great workout when you go out into the garden and exercise by mowing the lawn. This is another picture of one of our staff here at the – at Florida State walking using the stairwell.

Another way, on this last – on the next slide, is trying to get people more physically active and we just completed a study with the agency for healthcare administration with Medicaid women is trying to use pedometers, and there's been a lot of research lately with pedometers and actually we have found that people who have made the 10,000 step per day threshold that's been recommended have – they have found improvements in glucose tolerance and influence sensitivity in these studies.

So pedometers have become a good way to motivate because it keeps good track of the steps. And again, this is more of a lifestyle approach because we can accumulate these steps throughout the day and if you get home and you find you're 2000 steps short, you can go out and

make up that difference by walking. But some of us who have active jobs or do a lot of work on the jobs may get the 10,000 steps without really having to go out and purposely walk.

But pedometers are a great way to motivate individuals. The recommendation right now is 10,000 steps per day as a threshold, but there's not been a lot of research to say, "Yes, It's exactly 10,000 that's going to produce the benefit." We don't really know yet if maybe 8,000 can still give us health benefits or even lower than that.

So more research needs to be done, but if you're going to use pedometers when you're working with individuals, what I would recommend is that you establish a two-week baseline on the baseline steps. So you give the individual a pedometer and ask them not to change what they're doing, anything different from what they have been doing, and just keep a record of the steps that they take over the two week period.

Once that's been established, then what you want to do is try to increase that baseline step by 10 percent and you can increase that by 10 percent every week or every two weeks until a desired level is attained. What we have found with our Medicaid women that was really interesting is that many of them were overweight – well, actually all of them were overweight and obese.

We had women that were at 300 pounds and up and we tried to encourage them to walk their 10,000 steps. A lot of them, you know, that was just impossible for them to do. They were just too big, but what was really interesting in the study, some of our baseline guides were in the 3,000 to 4,000 steps per day and it really didn't matter what their baseline was, if they could increase their steps by 2,000.

So if they went from 3,000 to 5,000 or from 4,000 to 6,000, we found that those women with the year-long study, but even after six months, the women that increased their steps by 2,000 were

getting health benefits, so they decreased their waist circumference and that's that, you know, abdominal obesity there. They decreased their waist circumference.

They had significant reductions in weight and in their BMI. So, you know, for an individual that's, you know, that their activity level is only 3,000 steps per day and you're telling them you've got to get to 10,000 to get health benefits, that can be a very daunting task, but if you can say, you know, "If you can just increase those steps by 2,000 gradually, you will see some health benefits.

And then once you get to that place and get accustomed to it, and then slowly increase from there, we're still, you know, we're still getting some benefit even with that 2,000 increase." So that was a great finding for the study.

The next slide shows a picture of the pedometer here. There are all sorts of pedometers. They come in all styles and complexity. If you're working with individuals that maybe are from a lower socioeconomic group or are illiterate, I would not recommend this pedometer. It's too complicated. For people who can't read, the best pedometer to get is just one that shows stats.

I know when we talked to a lot of our ladies we would ask, you know, "How many steps did you take today?" And they would say, "Oh, point one four." And we were like, "No, that's not the steps." And it was very difficult over the telephone, even though we had trained them to try to get them if they could read to get it back on the modality of steps.

So I'd recommend a much simpler version. And plus, studies have shown that really the pedometers are only accurate for the number of steps that you're taking, not really the calories that you're expending or really the distance because your steps alter during the day.

You know, sometimes you take smaller steps and bigger steps, but there are also speedometers out there, but they are really kind of a misty little gadget and are great for motivation as far as, you know, counting up the steps that you take each day.

So bottom line, on the next slide, I think for all of us, whether we're doing structured exercise programs with our diabetics, our diabetic patients, our emphasis needs to be trying to get people to do a permanent lifestyle change. It's not a – it's not a quick fix. OK? So we get to our goal of weight loss or we reduce our medication, we're there, you know, we can stop.

We've got – that can't be our goal. It has to be a permanent lifestyle change so that exercise is just part of our daily routine, just like getting up in the morning and brushing our teeth and before we go to bed we brush our teeth. Exercise has to be a part of our daily routine and whether it's exercise, per se, or just finding opportunities to be physically active during our day. We've got to try and encourage people to become more physically active.

And I think when we do that, looking on the last two slides, I think we age much slower when we are more physically active. I think we are able to maintain the quality of our life. I know when I get up to retirement I still want to be out there playing tennis and running and enjoying all the leisure time activities that I do now.

And even if I can't be, you know, participating in sports, I think the last slide is so very important, at least we can grow older and healthier with the people that we love and I think that's so important. And that concludes my presentation. Thank you.

Operator: And now we will take our questions. Today's question and answer session will be conducted electronically. If you would like to take – ask a question, you may do so by simply pressing the star key followed by the digit one on your touch-tone telephone. Do remember, if you're using a speakerphone, please make sure your mute function has been turned off to allow your signal to

reach our equipment. Once again, that is star one to ask your question. And we will pause for a moment.

And we do have a question from Audrey Anderson. Please state your company name.

Female: Oh wow. It didn't work.

Operator: Ms. Anderson, your line is open. And they didn't want to ask a question. Once again, that is star one. There does not appear to be any questions at this time. I will turn it back to your host for closing remarks.

Female: Operator, we did have a question here in Tallahassee.

Operator: Go ahead and take your question.

Female: OK. I work at the Department of Health. I've been told that it is best for a person to wait about 30 minutes after exercise to check the blood glucose level because there's some sort of a delayed reduction in the blood glucose and I want to know if that's correct and if 30 minutes is the correct interval.

Operator: Dr. Horowitz?

Jeffrey Horowitz: I will let – I can address that, but I think this may be more in Dr. Pantan's arena.

Operator: Unfortunately Dr. Pantan has disconnected.

Jeffrey Horowitz: Oh, OK. Well, I can – I can address that. Let me preface by saying that most of my research and my knowledge base is in Type II diabetes and insulin resistance, but checking glucose during – it depends on the duration of exercise, I guess.

For a normal healthy 20, 30 minute session of exercise, blood glucose concentration typically stays about the same. It can dip down for a few minutes afterwards. Again, I'm no expert in regulation of glucose concentration, especially in Type I diabetes. Did that – did that come close to addressing your question? I'd be happy, if you want to rephrase the question, I'd be happy to try again.

Operator: We do have a question on the phone line and that question comes from Janet Timkin with the Department of Health and Children.

Janet Timkin: Yes. If the patient is on a long-acting insulin, you know, that's a 24 hours, what's the – what's the concern there with exercise and when the insulin is given or is that not a concern?

Jeffrey Horowitz: Again, am I – can I be heard?

Janet Timkin: Yes.

Jeffrey Horowitz: OK. The – and again I want to remind you that I am not an expert in Type I diabetes and I'm more of the issue of – my expertise is in Type II and insulin resistance, but again, I can address that question that exercise, as Dr. Panton mentioned has a very potent insulin-like effect.

And so you want to be very careful when providing insulin to a patient who is about to exercise because you get the so-called double whammy of the insulin plus the insulin-like effects of muscle contraction during the exercise bout, so caution should be – should be taken when providing the insulin to an individual before exercise.

Janet Timkin: OK. Thank you.

Operator: And there are no further questions in the queue, but I would like to give a final opportunity to participate. It is star one if you have a question. And we'll take a question from Carol Treat.
Please state your company name.

(Therese): (Therese). I'm with Carol Treat in Alaska and my question is for you, and what you said about multiple fatty acids, systemic fatty acids coming from subcutaneous fat versus visceral.

Jeffrey Horowitz: Yes.

(Therese): And so this is kind of a bazaar question, but considering that's the case, why is it that liposuction doesn't work to decrease insulin resistance in preventing diabetes or in people who have diabetes?

Jeffrey Horowitz: That's a great question referring to a very recent study from Dr. (Sam Kline's) lab, who actually I did my training under. The issue is probably – it's probably two-fold. One is that – I'm sorry, more issues than the one I'll discuss here, but one is that the magnitude of even though that there was substantial weight loss and fat removal with the liposuction, there is – there may not be enough to reduce fatty acid availability.

The second point, and in fact, if I remember their data correctly fatty acid availability was still elevated during the post-operative, post-liposuction condition. The other issue is that certainly these issues, these fatty acids are not working alone in their whole host of hormonal and type responses that are certainly playing and probably interacting with fatty acids.

And it's quite possible and probable that subcutaneous adipose tissue, while not contributing to the fatty acid delivery may be contributing somewhat to this hormonal response as we know that adipose tissue has a – is basically we're learning it's more of an endocrine gland now and the whole – secretes a whole host of peptides that have metabolic action, so it's quite possible that visceral adipose tissue may be secreting those peptides that might be interfacing or interacting with the accelerated fatty acid availability.

(Therese): OK. Thank you.

Operator: And we have a question from Karen Digles. Please spell your – please state your company name.

Karen Digles: It's from Florida Medical Quality Assurance down in Tampa and we're doing a project with the underserved African American population and my question is are you finding a difference in the exercise groups based on ethnic background, Hispanic versus African America versus American Indian. And if so, which is progressing quicker?

Jeffrey Horowitz: Which, meaning which sub-population which ethnic group is elevating more quickly or compared to the – the ethnic groups compared to Caucasians?

Karen Digles: Correct. I'm looking at seeing how each of the different ethnic groups are responding to the exercise program. Is there one group that responds better, and if so, is there any reason for that.

Jeffrey Horowitz: All right. It's a great question and to my knowledge – exercise studies especially in the field are very, very difficult to conduct because of adherence issues, and so to my knowledge I'm not aware of well-designed, very well controlled studies that would look at these issues in African Americans. It would exercise in these ethnic groups compared to Caucasians.

They might exist, but to my knowledge I'm not familiar with them. There are certainly differences in fat metabolism and not just propensity to gain weight or the prevalence of obesity, but there are ethnic related differences in fatty acid metabolism that, for example, we found that African American women were the same – for the same degree of body fat mass have reduced ability or reduced rate of mobilization of fat from their adipose tissue stores, which might be actually a protective effect, which was a bit surprising.

But again, back to your question of the exercise question, I'm not familiar with studies that have looked specifically in a well controlled conditions. Again, adherence – if you control for adherence and mandate that they perform certain, you know, maybe a single exercise session or perform a set amount of exercise training.

Karen Digles: Thank you.

Operator: And we will hear from Carol Treat once again.

Carol Treat: Yes. I had question about if a patient with Type II diabetes starts exercising and they come in for some fasting blood draw and their plasma CO₂ goes up, would that be a result of increased exercising or maybe exercising and a high fat diet?

Jeffrey Horowitz: Probably not. I don't think that the sensitivity of measurements to actually measure the CO₂, the blood CO₂ would be sensitive enough to pick up any exercising in a single session of exercise induced increase in CO₂.

Carol Treat: OK.

Operator: And we'll take a question from Markena Conway. Please state your company name. Miss Conway, your line is open.

(Susan Hearst): Hi, I'm – can you hear me?

Jeffrey Horowitz: Yes.

(Susan Hearst): I'm (Susan Hearst) with the City of Fort Worth and Health Outreach and I just had two quick questions. One was I think Dr. Horowitz had talked about exercise that it would decrease the level of lipids systemically. Is that right?

Jeffrey Horowitz: No. I said that weight loss would reduce the available of fatty acids, not triglycerides, but the fatty acids.

(Susan Hearst): OK. So weight loss is what breaks it – what lowers that, right?

Jeffrey Horowitz: Correct. Exercise training, in fact, we found that exercise training – again a bit surprising – the excess training did not affect, without any changes in body composition or body weight, the people just exercised train by itself, we found that fatty acid availability actually is not affected whatsoever.

(Susan Hearst): OK. So the – OK. And the other question I had is just hormones, women's hormones and especially if they're going through menopause, has anybody looked at or studied anything with diabetes and that?

Jeffrey Horowitz: Absolutely. It's certainly a very hotly – I shouldn't say hotly -it's probably under studied compared to the need for information to be – to be learned in that arena. That's a very important sub-population, but I guess I can't address your question without any specifics.

(Susan Hearst): OK. Well, that's – maybe that would be a good research for somebody.

Jeffrey Horowitz: Yes. There is quite a bit of research, but again, it certainly could use to learn more.

(Susan Hearst): OK. Thank you so much.

Operator: And now at this time there are no further questions. I'll turn it back to Miss Keller for closing remarks.

Tisha Crews -Keller: Thank you. Thank you for participating in today's call. We appreciate Dr. Horowitz and Dr. Panton giving us their time and expertise. These insights will be useful for improving diabetes care nationwide.

I want to remind nurses and dieticians who would like CEU credit for this program, you need to mail or fax all completed forms and rosters to me by August 24th. The fax number is 850-245-4391. Thank you to everybody. Have a good day. I'll now turn it over to the operator for call conclusion.

Operator: And that does conclude the program for today. We do thank you for your participation and you may disconnect at this time. Have a wonderful day.

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