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NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

TELEBRIEFING ON WOMEN'S HEALTH INITIATIVE

FEBRUARY 7, 2006

MS. LONG: Good morning. Thank you for participating in this briefing on the dietary modification trial of the Women's Health Initiative. Just as a reminder, this information is embargoed for 4:00 p.m Eastern Time today.

We'll start with a brief statement from Dr. Elizabeth Nabel. She's the director of the National Heart Lung and Blood Institute. And then following Dr. Nabel's remarks, we have several WHI representatives who are here to answer your questions. Dr. Nabel?

DR. NABEL: Thank you. And good morning.

The results of the dietary modifications trial of more than 48,000 women in the Women's Health Initiative show that healthy post menopausal women who followed an eating pattern that is low in total fat did not significantly reduce the risks of

breast cancer, heart disease, or stroke, and did not reduce their risk for colorectal cancer. Although women who reduced their total fat intake had a 9 percent lower risk of breast cancer than women who made no dietary changes, this 9 percent difference was not specifically significant and could be due to chance.

There were some positive findings. For example, a suggestion that a lower fat intake reduced the risk of breast cancer in women who started with a particularly high fat intake, also women who were most successful at reducing their saturated fat and trans fat seemed to lower their risk of heart disease. Women following the study's low fat diet reduced average fate intake by 11 percent in year one and 8 percent going out to year six.

The study was designed to evaluate the low-fat dietary patterns affect on cancer. It focused on a reduction in total fat and did not differentiate between the so-called good fats and the bad fats in an effort to evaluate a widely

believed but untested theory that a reduction of total fat would reduce the risk of breast and colorectal cancers.

Researchers looked at heart disease outcomes as well. It was anticipated that a reduction in total fat would be accompanied by a reduction in saturated fat. The results of this study really do not change any established recommendations for women in terms of disease prevention. Women should continue to get regular screening for breast and colorectal cancers. They should work with their doctors to reduce the risk for heart disease, including following a diet that is low in saturated fat, trans fat, and cholesterol, the so-called bad fats.

With us today are several experts who have contributed to this research, Dr. Ross Prentice--Dr. Prentice a WHI Principal Investigator with the Fred Hutchinson Cancer Research Center, Dr. Rowan Chlebowski, a WHI Principal Investigator from Harbor UCLA Medical Center, Dr. Leslie Ford from the National Cancer Institute, Dr. Barbara Howard, a WHI

Principal Investigator with the MedStar Research Institute here in Washington, D.C., Dr. Eva Obarzanek, a Research Nutritionist with the NHLBI, and Dr. Jacques Rossouw, NHLBI Project Officer for the Women's Health Initiative.

Now, we would be very pleased to take your questions.

MODERATOR: And once again, ladies and gentlemen, if you would like to ask a question, please press the star, then one on your touch tone phone. You'll hear a tone indicating you've been placed in the que. If your question is answered and you wish to remove yourself from the que, please press the pound key.

Once again, if you have a question, please press star, one, and first we'll go to the line of Gina Palada with the New York Times. Please go ahead.

QUESTION: Thank you.

I have several questions. So stop me if I go on too long.

How much did the study cost total, you know, the--

DR. NABEL: Good morning Gina, how are you?

QUESTION: Fine. Thank you.

DR. NABEL: Good. Good.

The total cost of the study from 1992 to 2006 was $725 million. This was a great investment in women's health.

QUESTION: That's includes, though, the part that was the hormone therapy as well?

DR. NABEL: That's correct. We do have the breakdown for the different subsets within that which we're happy to provide for you if you would like.

QUESTION: I'd just like to know how much this particular part that you're just publishing today cost, the part about the three diseases?

DR. NABEL: Yes. The dietary modification trial cost was $415 million.

QUESTION: Okay. Now, if I'm allowed to continue, I have another one.

Why were there unequal numbers of women in the two groups?

DR. NABEL: Dr. Prentice?

DR. PRENTICE: Good morning, Gina.

Forty percent were assigned to the low-fat diet group and 60 percent to the usual diet group. This was to try to reduce total study costs at a given study power we call it. So the women in the lowfat diet group were involved in an intensive intervention that involved 18 group sessions in the first year and four maintenance sessions thereafter. So the costs for an individual woman in the lowfat diet group was considerably higher than for the usual diet group. And this 40/60 split looked as though it would give us the best chance for seeing study differences.

QUESTION: Another question is, would these results apply to men in the cardiovascular and the colon cancer or would you say this is only for women?

DR. NABEL: Well, we know that reducing total fat intake may have had just a small affect on

the risk of breast cancer, had no major affect on the risk of colorectal cancer, heart disease, or stroke in these healthy post menopausal women. And so I think we need to interpret these findings with respect to this group of women.

On the other hand, we know that the diets were safe and very well tolerated. In other words, individuals who reduced their total fat intake in particular reduced their saturated fat, their trans fat, their cholesterol did quite well. They maintained their weight, had a small weight loss. And even though that lowfat diet may have been combined with a high carbohydrate, these individuals did not show any signs of diabetes. Their triglycerides were normal. Their blood glucose was normal. And there was no signs of diabetes.

So in that respect, we believe that the findings of the safety of the lowfat diet certainly can be extrapolated to younger women and to men.

QUESTION: What about the efficacy or the lack of efficacy?

DR. NABEL: Dr. Rossouw?

DR. ROSSOUW: Gina, can I add to that, that we know the effect of dietary fat on blood lipids are basically the same in men and women. So there's no reason for cardiovascular disease to think that the results would be any different. And for colorectal cancer, although we don't have a similar trial in men, the data that led to the need for the study, that's the international comparisons of fat intake versus colorectal cancer across populations are the same in men and women. So, you know, any effect that you see we would expect to be similar, although of course we don't know until we've done the definitive trial, as we have done in this instance.

QUESTION: Okay. Thank you very much. I should let somebody else take a turn.

MODERATOR: Next we go to Lisa Stark with ABC News. Please go ahead.

QUESTION: Actually, I'm sorry. My question was answered. Thank you.

DR. NABEL: Good morning, Lisa. How are you?

QUESTION: Good morning, Dr. Nabel. Thanks.

MODERATOR: Next we go to Michelle Cortez with Bloomberg News. Please go ahead.

QUESTION: Yes. Hi! Thanks for taking the call.

I guess, first of all, I'm wondering if you can give us a little bit of the background of when you actually started the study, was this part of the initiative back in the nineties when we were hearing that not a lot of research was being done on women? And was this kind of a way to check and to look more specifically at women's health issues? Was it part of that whole movement?

And also, tell us, obviously you expect it to have some benefit. So to what extent is it a disappointment or by the time the results had come in had you already moved on with what you were expecting?

DR. NABEL: Well, remember that the Women's Health Initiative was begun back in early 1990. At that time we realized that most, if not all, of our clinical trial results came from data acquired in

men. And we had very little information about health issues as they relate to women.

And so the Women's Health Initiative was conceived and designed with an attempt to look at the most pressing health issues that affect women. And from that regard, I think that the Women's Health Initiative certainly was a dramatic and striking success story in this country.

Over 161,000 women have enthusiastically participated in the study since it's inception going back to 1992. Many of these women are still actively interested in follow up and are volunteering to continue in follow along and ancillary studies.

So we think the results of the Women's Health Initiative in composite has been an extraordinary investment in women's health with huge benefits that really have had a dramatic impact on clinical practice related to women's health.

DR. PRENTICE: Dr. Nabel, if I could add?

DR. NABEL: Yes, Dr. Prentice.

DR. PRENTICE: Michelle, your first part of your question concerned the history of the lowfat trial. And the lowfat intervention that we studied I'd say it began its development in the middle 1980s under the auspices of the National Cancer Institute with a focus primarily on breast cancer. And as Dr. Rossouw mentioned, its motivation was to try to explain the large international variations in breast cancer and colorectal cancer across countries.

So the focus was breast cancer. And when the reports from Dr. Healy came in and initiated the Women's Health Initiative, this earlier work was incorporated in the Women's Health Initiative. I guess that's the history I'd like to mention.

DR. CHLEBOWSKI: Dr. Nabel, this is Rowan Chlebowski. Can I add about the cancer?

DR. NABEL: Yes. Please, please do.

DR. CHLEBOWSKI: Yes. One of the, one of the things that I look at these results when you're about whether we were disappointed or not. I think there's reason for optimism and especially with respect to dietary modification and breast cancer.

Now, I recognize we do not have a specifically significant result. But if you look at the trend, especially every year from year five through nine, it looks like, I mean there are fewer breast cancers in the intervention versus the control group.

And as we've achieved maybe 70 percent of the target intervention, there's--we're really enthusiastic about continuing follow up and so that the breast cancer portion of it may certainly have a good chance of becoming positive in the future.

The other issue, as we end up having other signals in that the women who had the highest dietary fat intake, perhaps the biggest target, that subgroup in the analysis had significant reduction. The women who appeared to be most adherent based on their compliance with visits also had a bigger and statistically, yet, again in the subgroup adherence.

And then the other issue I think that's very exciting is that we're recognizing biology--breast cancer is a heterogenous condition maybe representing four or five separate disease processes. And in one of those conditions, the

progesterone negative receptor cancers, there really was, again, a substantial reduction seen. These are all subgroup analyses hypothesis generating, but there's a lot of reason to think that taken together that we're getting a signal that something is going on in the breast cancer area.

DR. NABEL: Thank you very much, Dr. Chlebowski.

Dr. Howard?

DR. HOWARD: Yes. In addition to the interesting findings that my colleagues pointed out in cancer, I'd like to point out some other important things we learned from this study.

I think we learned, we have learned about the relative safety and the validity of this dietary pattern that's lower in fat and higher in carbohydrate over an eight year period, it tended to maintain weight, with risk factor profile was improved, and it also validated our understanding that in--that it's the type of fat that matters for heart disease so that the women who managed to drop their saturated fat and trans fat more did, in fact,

see measurable improvements in their LDL cholesterol and heart disease.

DR. NABEL: Thank you.

So we think that there is real reason for optimism. You know, in the eight years of [inaudible], we began to see trends towards reduction in cancer, especially in women who started at high levels of fat intake. And we also began to see reduction in heart disease for those women who reduced the specific types of bad fats.

QUESTION: And do you think that there's going to be, you know, any kind of backlash here with, you know, the evidence that maybe the simpler way of just, you know, strive for five, get to that, you know, that certain level, that that's not going to be enough, that people actually do need to do more and really embrace the new food pyramid and exercise and whatnot? Is that, you know, a more daunting public health challenge for you all? And that's the end of my question.

DR. NABEL: We really think these findings are good news. You know, this study was really the

most comprehensive study of its kind, again, 48,000 women. And the findings we think are very consistent with U.S.--current U.S. dietary recommendations about following a diet that's low in saturated fat, trans fat, and cholesterol, keeping fat calories to about 20 to 35 percent of total calories.

Now, remember it's always important when interpreting the findings from any study that a woman consult with her physician. And we encourage women to do that. We encourage women to consult with their physician so that they can understand their risk for breast and colorectal cancer and engage in routine screenings, regular mammograms, regular breast exams, as well as a discussion as to when is the best time to begin screening for colorectal cancer, what types of tests, what are the benefits and risks for those different tests, as well as how often to have those tests.

And, in addition, we know that it is critically important for women to pay attention to the type of fat they consume in their diets. And by

focusing on lower fat intake with an emphasis on the poly and mono unsaturated fats, they should do that within the context of paying attention to their total risk profile. Keeping physically active, controlling blood pressure, treating diabetes, quit smoking, and treating high blood cholesterol.

So we really think that this news is actually, you know, good news. And it's very consistent with current health recommendations.

Dr. Howard?

DR. HOWARD: Yes. You asked about the five a day and our intervention just about achieved that level of vegetable and fruit intake. But as you know, now the current guidelines recommend even more.

One of the values of this data set is the fact that many more analyses can be done. We have seen trends with increasing weight loss and improved cardiovascular disease in the women who actually raised their vegetable and fruit intake more. But we can do a lot more analyses on this data set to

systematically investigate these nutrients and their relationship to our end point.

DR. NABEL: Thank you, Dr. Howard.

MODERATOR: Next question is from Tom Mount with the L.A. Times. Please go ahead.

QUESTION: You talked a little bit about the subgroups that seem to show more improvement. Can you address that a little more, give us some numbers here, put that in context?

DR. NABEL: Yes. In general we know that the women who benefited the most in terms of risks of breast cancer were those women who started with the highest fat intake and had the greatest reduction. And I'll ask Dr. Prentice just to elaborate on those findings further.

DR. PRENTICE: The women that were in the upper half in terms of the fat composition of their diet at enrollment, say above 37 or 38 percent of calories from fat, there we see evidence for 15 to 20 percent lower breast cancer incidents in the lowfat diet group compared to the usual diet group.

DR. NABEL: Yes. And Dr. Howard did mention earlier those women who appeared to benefit most from the lower fat diet. And I'll ask her to elaborate further on those findings.

DR. HOWARD: When we looked at specifically at the changes in saturated fat, the women who were in the group that dropped their saturated fat the most had about an 18 percent reduction in heart disease. And there was about a 19 percent reduction in those who reduced their trans fat the most.

DR. CHLEBOWSKI: Dr. Nabel, this is Rowan Chlebowski again.

In terms of the breast cancer, maybe an opposite look rather than what the patients did, what kinds of tumors were influenced. And, again, in the Women's Health Initiative for women who developed progesterone receptive negative tumors, they ended up having a 24 percent reduction in their risk of developing these cancers. So another potential is there's great interest in further defining risk factors for development of cancers in specific types of cancers. And if we can come up

with a way of identifying women at particular risk of this subgroup of cancers, then, again, you'd have another potential for that kind of dietary intervention.

Some of these principles--some of these issues seen raised in breast cancer in this primary prevention trial we also saw in a separate group of studies in women's intervention studies that was for women who had receptive breast cancer where a very similar dietary intervention resulted in a reduction in recurrence risk for breast cancer patients who were on the diet. And the largest group that benefited in that study were women who had progesterone receptor negative cancer. So we're having a couple signals here that there are some of these subgroups could be of importance.

DR. NABEL: Thank you very much.

Also, just to let all of you know, we are continuing to support follow up studies from the Women's Health Initiative. We have issued what we call a broad agency agreement inviting investigators to submit proposals for additional studies, in which

they can do subset analysis or look at particular groups of women with regard to certain of these diseases in follow up.

So we really do want to take advantage of this very rich data base, really the only data base of its kind in the world, to really try to extract as much information as we can for women's health.

MODERATOR: Our next question is from Roger Sergel with ABC News. Please go ahead.

QUESTION: Yeah. Aren't you all on somewhat questionable ground talking about signals for breast cancer when the confidence intervals include one, when these numbers are not statistically significant and when that is acknowledged that this could be chance as one leading epidemiologist used to say, subgroup analysis kill people?

DR. NABEL: Dr. Prentice?

DR. PRENTICE: Yes. I think a word of caution is a good idea, Roger. So the subset that I think is perhaps our strongest data does relate to the baseline fat content of the diet. And we do see

a significant interaction between the baseline fat content and the magnitude of the potential breast cancer risk. So we would not expect to see a significant interaction there if the lowfat eating pattern that we tested had no relationship to breast cancer at all.

But you're quite right. I think we should not be--we should be cautious in interpreting the magnitude of these reductions. And I think it's better to say at this point that we have evidence of some relationship between breast cancer risk and the baseline fat content of the diet. We have evidence there's some relationship between breast cancer risk and the sub type of breast cancer according to hormone receptor status. And probably should leave it at that at this time.

QUESTION: Should every sound byte and every headline include a subhead or a clause at the end which says, but it also could be chance?

DR. PRENTICE: That would be a good idea also.

DR. CHLEBOWSKI: But Dr. Nabel, I--this is Rowan Chlebowski again. I think the difference, distinction that I would make, I agree with everything that Ross said and certainly the caution is that the distinction is what should women do now is one thing. And that's where the caution comes in. And that's where we don't have a definitive statement.

I think what should the breast cancer scientific research community do, and that's a different issue. And so I think, I think it's a signal to the breast cancer research community it's caution and not a definitive result for women in general.

DR. ROSSOUW: Yeah. Rowan, can I follow onto not so much the scientific issue but the public health issue.

DR. CHLEBOWSKI: Sure.

DR. ROSSOUW: The way we see it, Roger, is that these results are not definitive enough to make a recommendation that most women out there should follow a lowfat diet. We are not recommending that.

But what we are saying is that those women who are following a lowfat diet, these results would encourage them to continue. Because in the longer term, there may well be benefits from all the signals, picking up all the signals that we've touched upon. And finally, I think we have a pretty clear signal that those women who are eating a high amount of fat would be well advised to reduce their fat intake.

So rather than say that these are new findings that change the way we should be thinking about diet and health. These findings are consistent with current recommendations. And on balance, we would say that it does encourage those women that are following a lowfat diet that this is a reasonable option.

DR. NABEL: Thank you, Dr. Rossouw.

Dr. Howard?

DR. HOWARD: Yes. Also, we have a very high proportion of these women, close to 90 percent who are being followed for another five years. And since the diet intervention is not blinded, we

assume that the dietary pattern will be maintained to some extent. And we will be able to then have a longer period of time and thus more power to, perhaps, definitively answer some of these issues that are so close to significance at this point.

DR. : A suggestion at this point.

QUESTION: You wouldn't recommend people start taking these numbers and start projecting the number of breast cancer that are being prevented?

DR. : No. No.

DR. NABEL: No. We're not making that recommendation.

QUESTION: Thank you.

MODERATOR: Next question is from Jess Corbette with Dow Jones. Please go ahead.

QUESTION: Yeah. Hi! Thanks for taking my question. It was kind of answered.

One of the questions I had, it's sort of a two-part question was, you know, if these women had been studied long enough, you know, that eight years might not be long enough to find out if you have any intervention. And then kind of a related question

is if you, you know, since these women were post menopausal when they entered the study, they've already had decades of maybe not such great eating habits and, you know, if you have enough time to reverse the habits and make a big difference?

DR. NABEL: Those are interesting questions. Indeed, as Dr. Rossouw and Dr. Howard have articulated, longer term follow up may be required to show greater benefit. In addition, we know in the cardiovascular literature that it's never too late to reduce your risk factors. In other words, that even if you've had decades of high fat diet or physical inactivity or high blood pressure, it's never too late to lower your risk and engage in healthy behavior.

And, indeed, with adequate lowering of cholesterol, for example, one can achieve stabilization, in some cases, even regression of coronary heart disease.

Dr. Rossouw or Dr. Ford?

DR. FORD: I think it's important to look at these results in the context of overall women's

health and not just post menopausal women as you said. And since obesity is the biggest health risk that we face now as women and men, the idea of lowering fat in the diet and lowering overall weight, excuse me, eating a healthy diet high in fruits and vegetables certainly applies to women starting in their adolescence and through their premenopausal years as well since we know these are chronic diseases they develop late in life but they're based on lifetime exposure.

Also, one thing that was not touched on before in terms of the long term follow up, we did see a reduction on polyps which may in the long term follow up translate into reduction in colorectal cancer.

DR. PRENTICE: Dr. Nabel, if I could add?

DR. NABEL: Yes. Please, Dr. Prentice?

DR. PRENTICE: Just briefly, Jennifer, I think your question is a very good one about the length of follow up. So even though eight years is quite well to ask women to stay on a vigorous dietary intervention program, it is short relative

to the, especially the cancer processes expressed in colorectal cancer. And as you eluded, with a background of say, an unfavorable diet for five or more decades, one doesn't expect the full health benefit to be realized even in eight years. It may take considerably longer. So we think the additional data yet to come will add value to the study.

QUESTION: Does NIH have anything going on in younger women looking at diet?

DR. NABEL: The National Heart Lung and Blood Institute has a number of ongoing studies looking at dietary intervention in younger aged individuals. And perhaps Dr. Obarzanek you could elaborate on this further?

DR. OBARZANEK: We're supporting several studies that includes men and women, not specifically only premenopausal women, but includes women of all ages as well as men looking at healthy diet and also looking at diet composition and weight loss. So those are some of our bigger studies, but they're also relative supporting smaller studies.

DR. NABEL: Okay.

DR. PRENTICE: Dr. Nabel, could I add further?

DR. NABEL: Yes, please.

DR. PRENTICE: This is Ross Prentice again.

There is a companion study in Canada which is nearing completion which focused on women at high risk for breast cancer by virtue of mammographic abnormalities. That study used a rather similar lowfat dietary intervention and included both pre and post menopausal women. And so we expect some additional data relevant to pre menopausal women will emerge within a year or so.

DR. NABEL: Okay. Thank you.

DR. CHLEBOWSKI: Dr. Nabel, there's one more--this is Rowan Chlebowski again--in terms of pre--in terms of women with receptive breast cancer, looking at the diets we've already mention the women's intervention nutrition study, which was mostly post menopausal women. But there's another study that's ongoing, again, with a similar dietary change actually with more emphasis on fruits and

vegetable increase, which is occurring in pre and post menopausal women as well.

DR. NABEL: Dr. Howard?

DR. HOWARD: To follow up on Dr. Ford's pointing out the importance of starting behaviors young. I believe there are a number of studies targeting children and adolescence, both school based and also individual programs that will be testing various aspects of these strategies.

DR. CHLEBOWSKI: Can I add one more thing to--

DR. NABEL: Yes. Please, Dr. Chlebowski.

DR. CHLEBOWSKI: --this long conversation?

We should keep in mind throughout this discussion that this study dealt with really very healthy women who were, for the most part, already following most of the guidelines.

And so when you have a healthy population, your opportunity to decrease their risk for any disease is, of course, less than if you start with a very unhealthy population. And it's possible, therefore, that women who follow a really unhealthy

diet such as we found for the women who were eating quite a lot of fat in the beginning of the study that they may gain more benefit.

DR. NABEL: Thank you.

MODERATOR: Our next question is from Russell Sabin with the San Francisco Chronicle. Please go ahead.

QUESTION: Thank you. Sabin Russell.

I have a question about, a couple questions but one of them as adherence that by the end of eight years it didn't look like anybody was actually following this diet anymore. What impact does that have on the study findings? And also, I was just curious if anybody had some theories about why the kind of expected result from immigrant studies didn't turn up at all in this, in this study?

DR. NABEL: Yes. Dr. Prentice, I'll ask you to address those questions.

DR. PRENTICE: In regard to adherence, as Dr. Nabel mentioned, the two groups differed by about 11 percent that one year in the percent energy from fat. And then out toward the end of the follow

up, that was reduced to about 8 percent. So a reasonable fraction of the dietary change, the dietary difference was maintained.

However, as you implied, the magnitude of this difference between the two groups, which is what drives the precision of the study, was smaller than we projected at the design stage of 70 percent of that projected. And that does affect the precision of the basic comparisons. And that's one reason we don't have definitive results as yet.

In regard to migrant studies or international comparisons, these are sources that motivated this clinical trial. It may be surprising that even the 9 percent lower breast cancer rate that we see in the lowfat diet group is consistent with a rather large potential effect on a population basis of the types that one sees when migrants move from Asia to the United States or when we look across countries. So our actual design assumption started with a lowfat diet of 20 percent versus 40 percent energy from fat translating to a 50 percent reduction in breast cancer risk over the lifetime.

Then when you allow that reduction to come in slowly over a ten year period and acknowledge that our dietary difference was well under 20 percent difference, that actually translates to about a 9 percent lower breast cancer risk in the lowfat diet versus the usual diet group. So our data are consistent both with no effect at all, but also consistent with a rather large fraction of what we see in migrants and international comparisons being potentially attributed to by this lowfat eating pattern with emphasis on total fat.

QUESTION: Does that suggest that if you followed this up long enough, you would see more beneficial and statistically significant results? And if you repeat, someone repeats how long and how many people are going to be follow up?

DR. NABEL: Dr. Prentice, why don't you answer that as well?

DR. PRENTICE: As Dr. Howard mentioned, we are re-enrolling women almost complete in 85 to 90 percent of these women are signing up for an

additional period of time. So the other part of your question?

QUESTION: What additional period of time, I mean, this is a very expensive study. I was just wondering how long is it going to be carried out? I mean, is it five years, ten years?

DR. PRENTICE: An additional five years is what NIH is funding. And that's without continued active intervention. So the study costs are much reduced in this additional phase just following up the clinical outcomes.

DR. NABEL: Dr. Howard?

DR. HOWARD: Yes. I also want to make the point concerning the adherence we achieved that this intervention was designed to be something that could be translatable to a clinical setting with counseling and teaching materials, not feeding women all of their food, etcetera, and therefore, we were actually quite pleased. And I think that the study provides some insight about the magnitude of nutritional change one could expect in very large diverse numbers of people.

DR. NABEL: Thank you.

QUESTION: If I could ask one more question about the--in the group that was the control group, did they gain weight during the study period? And if they did gain weight, and yet had essentially similar, statistically similar results, what does that say about the whole notion that weight gain is bad?

DR. NABEL: Dr. Howard?

DR. HOWARD: Except for the older women, the control group did gain weight over the period just as you expect is happening with all other people in this country.

The important observation was that in the intervention group, their weight was always lower than that in the control group. And in fact, they maintained or loss some weight, a small amount of weight during the trial.

When we did adjust endpoints for that very small difference in weight, there was no impact on our conclusion. I also want to reinforce that this study shows, just as we have always--we have always

assumed and told you that diet composition is not enough. A change in diet composition is not enough to obtain substantial weight loss. And that if one wanted to achieve weight loss, and we did not counsel weight change in this study, one would have to accompany this diet by a concerted effort to reduce calories and increase activity.

QUESTION: Thank you.

MODERATOR: Our next question is from Andy Dworkin with the Oregonian. Please go ahead.

QUESTION: Yes. Thank you.

I had a couple more quick questions about the diet specifically. I know it wasn't a main intention to look at how easy this diet was to follow or how it affected quality of life, but did you collect any information on those variables to look at future diet studies?

DR. NABEL: Dr. Rossouw?

DR. ROSSOUW: Yes, indeed.

We have collected extensive data on quality of life as well as an extensive array of other health outcomes. So when we have a chance to

recover from the roll out of these important publications, there will be many, many more which I think will bring us new information and further illustrate the value, the enormous richness of the data that we've gathered in this program.

QUESTION: And also, I'm focusing on diet because a lot of people care about it. And I'm sure many people will wonder what the strength is of the recommendations for a low sat fat, low trans fat diet that you are still recommending for heart health. Can you address what kinds of studies feed that recommendation or how strong that is?

DR. : Okay. I'll take that in two parts. First, referring to the diabetes. We do have, we have collected data on diabetes, but we haven't analyzed it yet. But I want to remind you that the data on the blood sugar and insulin were favorable with small, not significant, decreases. No tendency towards increases in either blood sugar or insulin levels.

The second part of your question?

QUESTION: The second part was for the diet that is still being recommended overall I think for men and women, you know a low trans fat, a low sat fat, low total fat diet aiming at heart health overall--that wasn't this study, I know--but what is the evidence backing that or how strong is that evidence?

DR. : Well, I think that this study supports a huge body of data up until this point starting with large population studies that have consistently related saturated and trans fat to LDL levels and to heart disease. Many, many short-term diet trials showing that decreasing saturated fat and trans results in a more favorable cholesterol pattern with lower LDL. And also, the older, very long time ago studies in the mid-sixties when people were eating a lot more saturated fat that changed--that reducing the saturated fat in people who already had heart disease did lead to significant reduction.

DR. NABEL: Yes, Dr. Rossouw?

DR. ROSSOUW: Yes. Can I just add a little bit there to frame it a little differently?

Keep in mind that the current recommendations for heart disease prevention do not any longer focus any longer on reducing total fat. As Dr. Nabel said right at the beginning, there's a range of between 20 and 35 percent energy as fat within which it's possible to have a healthy outcome. And for heart disease, it's clearly more important, as Dr. Howard has mentioned, the type of fat. Reducing saturated and trans fat and concentrating on mono and polyunsaturated fats are clearly more important.

The picture may be somewhat different for cancer. As we've discussed before in this call, total fat may still have a role. I think we have suggested evidence here that total fat may be somewhat important for reducing both breast and colorectal cancer. So one has to think about them in a somewhat different framework.

DR. NABEL: And, remember, again, that these were healthy post menopausal women. Certainly

for women with existing heart disease, the recommendations are very straightforward and very clear to engage in a lowfat diet that is focused on intake of poly and mono unsaturated fats, avoiding the saturated fats and trans fats.

Dr. Obarzanek?

DR. OBARZANEK: And just to further amplify, the results from this study also show that the amount that LDL was lowered was exactly what had been predicted based on their observed difference or their reported decreases ins saturated fats. So this study supports what has been studied in feeding studies years ago.

DR. NABEL: Yes, Dr. Rossouw?

DR. ROSSOUW: Can I just add to what you said? Is that for heart disease, high risk, I mean, the focus is still on absolutely reducing the total--the saturated fat and the trans fat. And, you know, within that it can also be a lowfat diet, but it's important to get the order right. The focus is on saturated and trans first, not lowfat diet. Is that correct, Dr. Obarzanek?

DR. OBARZANEK: Yes. For heart disease, absolutely.

DR. ROSSOUW: For heart, absolutely.

DR. NABEL: And also just because I know that messages can be confusing. Thirty or forty years ago, a very large part of the fat that was coming in, in the diet, was saturated fat. So a message to lower fat would result generally in quite a large drop in saturated fat.

Now, because of many reasons, there's much less saturated fat coming into our diet. So even a person with a fairly highly fat intake, tends to not be eating as much saturated fat. And therefore, we need to focus on the specific fat and not assume that just lowering total fat is going to change the composition as we would like.

QUESTION: Thank you.

MODERATOR: Our next question is from Christine Gorman with Time Magazine. Please go ahead.

QUESTION: Yes. I'm sorry if someone else has asked this question before.

But as I was going through the tables, I was confused by one thing. I, I think I'm seeing a decrease in calories in the control group and yet an increase in weight. And I'm, I'm trying to figure out how that's possible. This is specifically in the Howard, et al., on cardiovascular disease, looking at tables two and three.

DR. NABEL: Dr. Prentice?

DR. PRENTICE: That's an interesting question. So the data--the answer is a little bit complicated. The data that we show in the tables you're referring to comes from food frequency data, food frequency questionnaires that we used as a screening tool at the beginning. We screened out about half of the women on the basis that they were already eating a relatively lowfat diet.

The use of the food frequency as a screening tool artificially increases the data enrollment for both baseline energy and fat and percent energy from fat. So the data baseline that we presented are for a technical reason higher than they should be on total energy consumption.

Though, we don't have accurate data at the moment on the energy consumption changes from baseline to one year and subsequently in the control group.

QUESTION: Okay. Just so I'm clear then, for technical reasons, that's why there's a difference, and you also screened about half of the women because they were already eating a healthy diet?

DR. PRENTICE: Right.

DR. NABEL: Yes, Dr. Howard?

DR. HOWARD: Then I'd like to add that the importance--perhaps the more important thing to look at is the difference between the control and intervention group. The intervention group, as you saw, did achieve a small weight loss throughout the course of the study.

Now, we know that human beings don't defy the second law of thermodynamics and, therefore, you will see that the control--the intervention group was reporting slightly fewer calories than the control group, even though our measure is not very

precise. And this supports what nutritionists have been recommending all along that foods like fats are calorie dense. And if one removes fat, one can then wind up eating slightly less calories.

DR. PRENTICE: Dr. Nabel, can I add to my previous answer?

DR. NABEL: Yes, please.

DR. PRENTICE: So, Christine, in addition to the data that we show in the tables that you referred to, we also have data from food records, four-day food records which do not suffer from the bias that I tried to describe. In that case, between baseline and a subset where we've analyzed four-day food records of one year, we do not see any major difference in energy consumption between enrollment in one year in the control group.

QUESTION: Okay. Thank you.

MODERATOR: And ladies and gentlemen, just as a quick reminder, if you do have a question, please press star, one.

And to the presenters on the call, no further questions in que.

DR. NABEL: All right. I want to thank all of you today who have called in. We know that you have a vital role in communicating this important health information to the public. And we do appreciate your work.

For those of you who may have called in a bit late, I just want to remind you that the embargo for all stories on this portion of the WHI is 4:00 o'clock p.m. today Eastern Time.

Just as a reminder, as well, next week there will be two papers published regarding the Vitamin D Calcium supplementation portion of the trial. And we will be sending a notice later this week regarding a call in conference, such as this, that will take place next week in anticipation of those publications.

But thank you again all very much.

MODERATOR: Ladies and gentlemen, that does conclude your conference for today. Thank you for your participation. And you may now disconnect.

[END OF TAPED RECORDING.]

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