UNITED STATES OF AMERICA

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DEPARTMENT OF AGRICULTURE
AND
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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DIETARY GUIDELINES ADVISORY COMMITTEE

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FIFTH MEETING

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TUESDAY, APRIL 13, 2010

The meeting came to order at 9:00 a.m. via webcast, Dr. Linda Van Horn, Chair, presiding.

MEMBERS PRESENT:

LINDA VAN HORN, PhD, RD, LD, CHAIR
NAOMI K. FUKAGAWA, MD, PhD, VICE CHAIR
CHERYL ACHTERBERG, PhD
LAWRENCE J. APPEL, MD, MPH
ROGER A. CLEMENS, DrPH
MIRIAM E. NELSON, PhD
SHARON M. NICKOLS-RICHARDSON, PhD, RD
THOMAS A. PEARSON, MD, PhD, MPH
RAFAEL PEREZ-ESCAMILLA, PhD
XAVIER PI-SUNYER, MD, MPH
ERIC B. RIMM, ScD
JOANNE L. SLAVIN, PhD, RD
CHRISTINE L. WILLIAMS, MD, MPH

ALSO PRESENT:

SHANTHY BOWMAN, PhD, ARS, USDA
CAROLE DAVIS, MS, RD, CNPP, USDA
KATHRYN McMURRY, MS, ODPHP, HHS
HOLLY McPEAK, MS, ODPHP, HHS
RADM PENELOPE SLADE-SAWYER, PT, MSW, ODPHP, HHS
ROBERT POST, PhD, CNPP, USDA
WENDY BRAUND, MD, MPH, MSEd, ODPHP, HHS

C-O-N-T-E-N-T-S

P-R-O-C-E-E-D-I-N-G-S

9:00 a.m.

DR. POST: Ladies and gentlemen, good morning from Alexandria, Virginia. Thank you for standing by. Raj Anand, the executive director of the Center for Nutrition Policy Promotion of the United States Department of Agriculture is on the agenda. Unfortunately, he is unable to be here.

My name is Robert Post, and I'm the deputy director for the Center. I will be representing USDA and officiating on his behalf.

Welcome to this webinar of the 5th meeting of the 2010 Dietary Guideline Advisory Committee. I'd like to begin by thanking the Committee members for their continuing support and invaluable contributions in developing the 2010 Dietary Guidelines for Americans.

As we move closer to the end of this process, I can't express my gratitude enough to the members for their dedicated

service in evaluating the science for the development of the ever-so-important Dietary Guidelines recommendations. Their work has never been more critical as USDA and its collaborator, the Department of Health and Human Services, work toward reducing the public health problems of obesity in preventing diet-related diseases.

I'd also like to recognize the continued cooperation between CNPP and the Agricultural Research Service at USDA, as well as our wonderful partners and collaborators, the Department of Health and Human Services, in seeing the 2010 Dietary Guidelines process further. Today, all of the Committee members are participating in two-way webinar from their home site. At our onsite locations in Virginia are Ms. Carole Davis, the director of the Nutrition Guidance and Analysis Division of CNPP. Carole is the designated federal officer and co-executive secretary for the DGAC.

Rear Admiral Penelope Slade-Sawyer, director of the Office of Disease Prevention and Health Promotion at HHS.

Dr. Wendy Braund, acting deputy director, Office of Disease Prevention and Health Promotion, and Ms. Kathryn McMurry, senior nutrition adviser at the Office of Disease Prevention and Health Promotion of HHS, and a co-executive secretary for the DGAC.

The Dietary Guidelines Advisory Committee has a very important charge which includes informing the Secretaries of both departments of changes to the Dietary Guidelines that are warranted based on a preponderance of the most current scientific and medical knowledge. Placing their primary focus on the review of scientific evidence published since the last DGAC deliberation placing their primary emphasis on the development of food-based recommendations. And preparing and submitting an advisory

report of technical recommendations with rationales to the Secretaries of USDA and HHS.

The charters also state that DGAC responsibilities did not include translating recommendations into policy or communications documents.

I'd like to explain the purview under which the Committee operates. This Committee is governed by the Federal Advisory Committee Act, or FACA. FACA was established to assure that advisory committees provide advice that is relevant, objective and open to the public, act promptly to complete their work, and comply with reasonable cost controls and recordkeeping requirements.

Therefore each public meeting has been and will continue to be announced in the Federal Register through a public notice. As part of the open transparent process the meetings of the full Committee are open for observation by the public, and any deliberations that occur between meetings such

as those in topic-specific subcommittees, are brought back to the full Committee at a public meeting - as you will hear today and tomorrow.

During the meeting all public participants will be in a listen-only mode. The public has opportunities to participate in the process by providing written comments to the Committee through our online public comment database, www.dietaryguidelines.gov.

In addition to the rules of FACA, I'd like to also remind the Committee of some rules of engagement. The Dietary Guidelines Advisory Committee members should continue to refer any individuals to the dietary guidelines management team to contact them personally so that they get information about their work to the Committee. To support the requirement that the Committee's work be transparent to the public, Committee members are not able to speak or give presentations to any individual or outside group regarding the work of the Committee as this would be

inconsistent with the advisory committee operations.

Let me now turn the microphone over to Penny Slade-Sawyer from HHS who would like to say a few words.

REAR ADMIRAL SLADE-SAWYER: Good morning. I am Penny Slade-Sawyer, deputy assistant secretary for disease prevention and health promotion from the Department of Health and Human Services. And on behalf of HHS I'd like to join Dr. Post in welcoming members of the Dietary Guidelines Advisory Committee, as well as the listening members of the public. As the Committee enters the home stretch I'd like to convey the deep appreciation of the Department of Health and Human Services for your many hours of service to ensure that the Dietary Guidelines for Americans continue to reflect the preponderance of current scientific and medical evidence relating nutrition and health.

Your expertise is invaluable, and

your commitment to public service is noble. The Department of Health and Human Service leaders are looking forward to receiving your completed report in the coming months, in order to begin development of the official federal policy along with the Department of Agriculture staff. Perhaps the excitement at the Department is overshadowed only by the excitement of the staff members in this room who have provided technical and organizational support to your Committee throughout this process. We are grateful for all that has gone on and continues to move forward as this report is developed.

Best wishes for a productive and enjoyable meeting. Thank you.

DR. POST: Well, thank you, Penny. And speaking about transparency earlier, we are very excited to be broadcasting this meeting live via the worldwide web, again, like we did at the last two meetings. And having the Committee

participate from their home locations is exciting as well. Using this technology enables us to reach a more varied and larger audience of interested parties, and have the added benefit of providing for a recording of the meeting that can be used for future reference. These recordings are easily accessed at an archive at www.dietaryguidelines.gov.

These individuals who have registered for this meeting from across the nation as well as internationally are participating today and tomorrow. We were quite impressed at the last meeting that we had registered attendees from around the world. At this meeting, now that we have about 500 registrants for each day, from the national side, but we have also doubled the global reach with attendees viewing the participation from Mexico, Brazil, China, Canada, Uruguay, Lebanon and Peru just to name a few.

I'd like to review a few technical points for public participants who are viewing today. On your screen you see some relevant information. If you experience technical difficulties you may contact WebEx technical support, toll free, at 1-866-239-3239. This information was also emailed to you at the time you registered for the meeting. A separate technical assistance number for our international participants was also provided, and also can be seen on your screen.

The staff here in the room with us will be monitoring an email line, so to speak, where the public participants can send notes of any technical difficulties while the meeting proceeds.

As you see on the screen, the email address is tech_issue@yahoo.com. Please note that the staff will not respond to emails. It is simply one of the several ways that we are monitoring the streaming efficiency of the meeting for the public. We

value your feedback on these webinar meetings, and after the meeting you will receive a survey from WebEx in order to measure your satisfaction with attending this online meeting.

As in the past a transcript and a written summary of this event will be posted to our website as they become available. The transcript and the minutes from the fourth meeting held in November, 2009, are available at www.dietaryguidelines.gov.

Because this meeting is being streamed live to the public, I'd like to ask that Committee members clearly state their names before speaking. This is particularly important in facilitating clear deliberations for the public for following this proceeding. And with that I'd like to turn the meeting over to the chair of the Dietary Guidelines Advisory Committee, Dr. Linda Van Horn.

Linda.

DR. VAN HORN: Thank you, and

good morning to Committee members and DGAC support staff, and welcome to our public participants who are watching via the web today. Although the Committee members are not all in the same room today we are expecting to have a very productive and successful meeting.

As the Committee has been reviewing the state of nutritional science we are all continually reminded of the relevance of our work to public health in the United States, especially as it relates to the obesity epidemic we are facing. As we all know the work undertaken by this Advisory Committee is immense, but also provides us with the opportunity to develop a strong, concise advisory report of food-based recommendations to inform the federal government as they develop the 2010 Dietary Guidelines for Americans policy.

Since the fourth meeting of the DGAC in early November the Committee and our support staff have been working very hard to

complete proposed conclusion statements and supporting summaries of the evidence of our remaining research questions and have been preparing drafts of the chapters of the report. The focus of this meeting will be to come to consensus on the science for these questions and consider the integration of our conclusions and food-based recommendations.

We will hold our sixth and final public meeting next month where we will present and come to consensus on our Advisory Report as well as discuss any remaining issues. As a reminder for the public, the Committee has seven subcommittees, each with its own topic listed on the agenda. In addition to the seven subcommittees we also have the science review subcommittee that provides oversight and guidance related to the technical review of the evidence.

We have also initiated formulating a new chapter for the Report which will address the total diet concept. Key numbers

are the energy balance and weight management carbohydrate, protein, nutrient adequacy and sodium, potassium and water subcommittee will be working together to prepare this chapter.

Other Committee members will be actively involved in the writing of the translational integration chapter of the report. These will be further discussed at the end of tomorrow's session.

Today and tomorrow we hope to propose conclusions supported by the evidence and have discussions on the research questions that are presented.

Since time is limited and we have a lot to accomplish over the next few days our Committee members have agreed to keep their presentations succinct. In addition to our evidence reviews that will be summarized in our report. The details of the evidence reviewed will also be available in the electronic database accessible by the public called the USDA Nutrition Evidence Library, or

NEL. As you may have heard it referred to in past meetings, we will refer to it as NEL.

Having a Nutrition Evidence Library ensures that the details of our science review are well documented, transparent and reproducible. Our systematic process also reduces reviewer bias and better standardizes the approaches used by the various subcommittees. For questions using a NEL systematic review, there are some general criteria and information that apply broadly to our work that I'd like to briefly review.

The first step of the evidence review process was to generate research questions that led to the search and sort plan to search the scientific literature. In general, literature in our review met the following inclusion and exclusion criteria. Inclusion criteria generally entail studies with human subjects, English language, as well as international. Sample sizes of the minimum of 10 subjects per study arm, and a preference

for larger sizes if available, dropout rates less than 20 percent, with a preference for smaller dropout rates, and populations of healthy individuals and those with elevated chronic disease risk.

Most questions only considered healthy or risk populations, but other populations were included when it was pertinent to the question.

Exclusion criteria generally entailed studies of medical treatment or therapy, disease subjects such as people already diagnosed with a disease related to the study's purpose, hospitalized patients, malnourished or Third World populations, or disease incidences that are not relevant to the U.S. population such as malaria, animal studies, in vitro studies, and articles that are not peer reviewed.

One main exception to this list resulted after much discussion among the DGAC members regarding the use of cross-sectional

studies. The agreement was made to not use cross-sectional studies except in cases where only limited data were available. The Committee favored the use of randomized controlled trials and prospective cohorts. Other exceptions to the list of inclusions and exclusions as well as additional criteria considered will be noted by each subcommittee during their presentations. In some cases the systematic review of the literature went back to cover literature on infants whose potential manifestation of disease in infancy can continue on across the lifespan.

The Dietary Guidelines themselves however provide recommendations for ages two and above. Now the Committee is grading the body of evidence supporting our conclusions using an approach that the group had agreed to. You can see the criteria here which takes into account the quality of the studies, the consistency of finding, number of studies supporting the evidence, magnitude of the

effect or outcome, and generalizability.

Based on these criteria the conclusions statement will be given a grade of I, strong, II, moderate, III, limited, IV, expert opinion, or V, grade not assignable. The grading chart you see on this slide further describes each grade and can be found on the Dietary Guidelines website under meeting five. Most of our questions were answered using the NEL systematic review process. For some questions it was decided that a formal NEL review was not needed. In some cases, such as when only a brief update was needed, other sources of evidence were used when appropriate, such as the 2005 Dietary Guidelines Advisory Committee report, IOM reports, and the Physical Activity Advisory Committee report.

For other questions, food pattern modeling was used to understand the implications of specific recommendations on the total diet. And for others data analyses

were used to answer the question.

It is important to note that only conclusion statements for which there was a formal DGAC NEL review are graded. I'd also like to mention that over 900 public comments were received throughout the process thus far. Each subcommittee has, and will continue, to take these into consideration as they continue their work.

Now that we have reviewed the overall systematic approach being used, we are ready to begin hearing some specific results. Each subcommittee will present their research questions, propose conclusion statements, and then briefly describe the evidence supporting those conclusions. The proposed conclusions will be presented first, but I would like to remind the public that the subcommittees began with open-ended questions and conducted extensive surveys of the scientific literature and graded the evidence before drafting these conclusions.

When appropriate the recommendations from other national organizations will also be summarized. When there are inadequate data the DGAC has drafted research recommendations. I would also like to remind everyone that everything being presented today and tomorrow is in draft form. As a Committee we need to come to agreement on all conclusions if possible.

Lastly each Committee member should please remember to announce themselves when speaking to help the public follow along.

With that I would like to begin with our first subcommittee which will be from the Carbohydrates and Protein Subcommittee chaired by Joanne Slavin.

Joanne.

SUBCOMMITTEE TOPIC AREA DISCUSSIONS:

CARBOHYDRATES AND PROTEIN

DR. SLAVIN: Nice to be here today, and I think that I won't have control of my slides, so I will just have to say next

slide as we move on.

So I'd like to first thank my Committee members that are listed on the first slide, and also the staff that helped us with the large number of questions.

So we are going to start with the protein questions, and then we will go on to the carbohydrate questions.

Two protein questions of the relationship between the intake of animal protein products and selected health outcomes, and then the relationship between vegetable protein and/or soy protein and selected health outcomes.

And we have a long list of carbohydrate questions that we will then go through. The first: health benefits of dietary fiber, whole grains and selected health outcomes. In adults, the associations between intake of sugar-sweetened beverages and energy intake and body weight.

Number four, non-caloric

sweeteners related to body weight.

Number five, the impact of liquid versus solid foods on energy intake and body weight.

Number six, the role of carbohydrates, fiber, protein, fat and food form on satiety.

And number seven, the role of prebiotics and probiotics and health.

I do want to mention number three, some of these overlaps with our Committee and other Committee, the childhood sugar-sweetened beverages was actually in the energy balance Committee, and other of these questions for our subcommittee have been presented before. So these are the remaining questions that have not been publicly presented before.

Next slide. Animal and vegetable protein, the search strategy for these questions was the same, so we are going to talk first about the search strategy. These were questions - protein was a new area for

the Dietary Guidelines. It really wasn't a separate question before, and because of the importance of protein many public comments about the importance of protein, we wanted to include protein as a focus of this 2010 DGAC review.

So we were starting from no data for proteins, so the way we went after this was a NEL evidence-based review. We made the decision to go back to January of 2000 to present to search, and for the cancer outcomes we only looked at prospective cohort studies, and I know Linda has mentioned that before that as we went into this process we tried very hard to go with the strongest studies we could find. So we tended to stay away from cross-sectional studies if we could find other studies.

The cross-sectional studies did come up at the beginning but they were later excluded because we had other stronger study designs. Original articles included in

systematic reviews or meta-analyses were excluded, and I really appreciate the staff for helping us out on this, because we didn't want to essentially double count studies that had already been reviewed in other reviews. And we excluded participants with chronic disease, which had already been diagnosed. Next slide.

So our first question: what is the relationship between intake of animal protein products and colorectal, prostate, and breast cancer; type 2 diabetes; cardiovascular disease; hypertension; and body weight. I want to note the note on the bottom there that milk and milk products were analyzed separately and seafood was also analyzed separately, so there are different questions for that that have already been done. So in this we were not looking at those animal protein products. Next slide.

So our overall draft conclusion, and I think you will see as we go through here

that draft is in big letters, and we want to make that clear, that these are draft and they should not be thought to be final conclusions at all.

So most studies find no association with intake of animal protein products and risk of disease including cardiovascular disease, Grade II, blood pressure and hypertension, Grade II, type 2 diabetes, Grade III, and body weight, Grade III. Animal protein intake seems to be related to some cancers including colorectal cancers, Grade II, and pre-menopausal breast cancer, Grade III, but this relationship varies by cancer type and possibly differences in preparation of cooking methods, processed well done meat, and this is a Grade III. So next slide.

The animal protein products and colorectal cancer. Draft conclusion: inconsistent positive associations have been reported between colorectal cancer and the

intake of certain animal protein products, namely red and processed meat, Grade II.

Review of the evidence, 13 studies, and these were prospective cohorts from the U.S., Europe, Australia, Finland, Japan, China and Sweden. Next slide.

This I really appreciate the help of our staff, Eve, in putting these together. And as you can see the studies are listed to the left, so all the different studies that are included in this review. And one problem we have with this is that not everyone looks at it the same. So as you can see a lot of times they'll look at total meat, red meat, processed meat, poultry, and there is not a consistent way of doing this. You are going to see some of these categories will have nothing in them because they didn't look at that.

The way this table is designed too, if - on the bottom there you can see if there's a positive association, you will see a

plus, an inverse association, a negative, or no association will get a circle with a line through it.

As you go down you can see that for total meat it's fairly - there doesn't seem to be much going on there; you see a little bit with different types. Going down red meat the same thing. There is no - you can see a few studies where you get a positive with colorectal cancer, sometimes with just one type rectal cancer, not colorectal. So there are inconsistencies. In some of these studies too they'll sometimes actually look at the type of meat. So is it beef, is it hamburger, ask those types of questions.

Go down processed meat, you can see the other kind of confusing issue, and sometimes you will see a relationship with different places of the cancer, whether it's distal cancer. You will see some relationship. Sometimes you will see it in men as opposed to women, and if you go over to

the right looking at poultry, also fairly inconsistent findings. Some studies look at eggs, some look at chickens, some look at overall poultry. So a little bit of - some. No inverse relationships at all. No relationships at all, but not much going on there in that category. Next slide.

Draft conclusion for prostate cancer: there is little evidence from prospective cohort studies that animal protein products are associated with prostate cancer incidence, this is a Grade III. Six articles, and all were prospective cohort studies from the U.S. Next slide.

Same type of table that you looked at before except it is for prostate cancer. The studies are listed. These are all U.S.-based studies, and same thing with different types of meat, total meat, red meat, processed meat, poultry. In general you don't see - very few positives here. Most of the circles have lines through them. A couple of things

are different. If you look at the different categories, sometimes with different cancers. So advanced metastatic cancer, you see a positive. Different - black men only, lunch meats. There are differences. But overall very little going on here. Next slide.

Breast cancer, animal protein products. The draft conclusion: cohort studies show little association between intake of animal protein products and overall breast cancer risk, although animal protein intake may alter risk for different types of breast cancer, this is a Grade III. We've found six articles, and they were prospective cohort studies from the U.S. and United Kingdom. Next slide.

Same type of table here, looking down there is this health study, PLCO, NIH AARP, Nurse’s Health again, the UK prospective study. Going across looking at this data you see some differences with different types of estrogen receptors. Sometimes you will see a

relationship with one but not the other. Going down with total meat, you see in general there are a lot of circles with lines through them but in some cases differences between premenopausal and post-menopausal breast cancer.

In general though, not any consistent findings at all. So fairly mixed data, a little bit there on different types of food, hot dogs, but under the processed category, but not a lot going on. Next slide.

The type 2 diabetes, our draft conclusion for animal protein products for type 2 diabetes, prospective cohort studies suggest that intake of animal protein products, mainly processed meats, may have a link to type 2 diabetes although results are not consistent. And this is a Grade III. Seven articles were reviewed, and these are prospective cohorts from the U.S. Next slide.

Looking at the same type of study,

total meats, red meats, processed meats, poultry. You see some positives here down in total meat in the two studies there, otherwise, let's see; Halton, Nurse's Health, no relationship. Going down to red meat, you can see a couple of positives there for Nurses' Health, one for hamburgers. The Health Professionals differences between different types of meat, so no real consistency, going to processed meat. A little more with different processed meats, not completely consistent, but there are more positives there, and then if you look on the right on the poultry side, you can see how these questions are asked differently, but in general, no real relationship for poultry, a little bit in the Physician's Health Study for eggs. Next slide.

Animal protein products and cardiovascular disease. Our draft conclusion: prospective cohort studies show little relationship between intake of animal protein

products and cardiovascular disease, this was in Grade II.

We had seven articles that were included, and these were prospective cohorts from the U.S. and Japan. Next slide, same type of table here. You can see a lot of the studies didn't - if there is nothing there we were not able to get that from the study. A little bit - if you look at some of the studies they are done differently. So looking at that - going down three, substituting red processed meat for carbohydrate-dense food, they saw some positive relations there with CAC mortality, and same thing, they did a similar thing substituting poultry. If you go over to the right you don't see anything there. Eggs, no real relationship here. And then, in the top study of only white meat there was CVD mortality only in men. There didn't seem to be a lot going on there. Next slide.

Hypertension/blood pressure: our

draft conclusion, no clear association was found between intake of animal protein products and blood pressure in prospective cohort studies, a Grade II. Six articles, these were prospective cohorts in the U.S., United Kingdom and Spain. Next slide.

Again as we go through these you will see a lot of these are the same cohorts. These were endpoints that were measured in studies, so there is lots of repetition in the studies here. Looking at total meat, the only one that shows a little bit of a difference there is the Steffen study, you get a positive; otherwise nothing else. Under total meat, a little bit. Under red meat, certain types, but not consistent. And then poultry, a little bit of that in the Western Electric, but otherwise no real consistent relationship. Next slide.

Body weight: animal protein products and body weight, our draft conclusion, existing research finds little

link between meat intake and body weight, this is a Grade III. We only found three articles that got at this question. And there was a different type - these were not prospective studies. There was one, but then there was one randomized control trial and then one cross-sectional study, and as Linda mentioned we tried not to use cross-sectional studies except when we had very little information, so in this case we did include the cross-sectional study. The Mahon study they looked at weight loss with different types of animal protein compared to vegetarian and found no differences in weight loss. These studies are always difficult, because often the calories are controlled. You probably wouldn't expect to see a lot of changes in prospectives. There were inconsistent findings across gender and the types of meat. In some analyses there was a link with red meat and some processed meat, but that was not consistent. And then in the cross-sectional study, there was an

association there. Next slide.

So implications: proteins found in animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide the nine indispensable amino acids and are referred to as "complete proteins." When protein needs are high - so in case of pregnancy, lactation, and childhood - complete proteins in foods are important components of the diet. And if you do not consume animal products you do need to consider complementary protein sources. Obviously, it is very possible to get your protein from plant products, but you do need to know enough to combine those amino acids so, especially at times where protein needs are higher that we are not limiting protein intake. Next slide.

So the kind of converse here is the vegetable protein. So in this case -- I don't know if there are any questions, or we can take questions at the end of this protein section. What is the relationship between

intake of vegetable protein, including soy protein, and chronic disease? And as we go through this I want to mention that in this data there were a lot of studies on soy protein and that's why we included that. But we did -- a lot of those studies were done differently. They were feeding studies. So we tried to separate those questions out. So the first question is intake of vegetable protein including soy protein and chronic disease. The second was the relationship between the intake of vegetable protein and blood pressure. And then the relationship between intake of soy protein and blood pressure, body weight and blood lipids. Next slide.

Our overall conclusion, fairly long. Little evidence exists that supports unique health benefits of vegetable protein including soy protein on measurable health outcomes. Few studies are available, and the limited data collectively suggest that

vegetable protein does not offer special protection against type 2 diabetes, coronary heart disease and selected cancers, Grade III. Intake of vegetable protein is generally linked to lower blood pressure in both cohorts and cross-sectional studies, Grade II. And some data suggest that soy protein may lower blood pressure in adults with normal blood pressure, Grade III. Soy protein had no advantage over other proteins when consumed in an isocaloric study on body weight. Soy protein may have small effects on total and LDL cholesterol in adults with normal or elevated blood lipids, although results from systematic reviews are inconsistent. Grade II.

So our first draft conclusion: few studies are available, and the limited data collectively suggests that vegetable protein does not offer special protection against type 2 diabetes, coronary heart disease and selected cancers, Grade III.

In this review we had seven articles, six prospective cohort studies and one ecological study. Next slide.

Selected chronic diseases: this is a - when we get into this dataset there isn't a lot of data in here, so this is - you see some mixing here of diseases. But same design here, down the left all the different studies that we examined. The type of study, and then vegetable protein, did they look at that, and soy protein. So with vegetable protein typically this would be from a food frequency, estimating based on food intake, and then soy protein. Typically those were studies in areas where soy protein is actually consumed in higher amounts than in the U.S.

You can see for the Halton, no relationship with CHD and vegetable protein. This other study, the Iowa Women's Health Study, where they did the substitution, you see a little bit of an effect. But overall not. Most of those circles have a line

through them, type 2 diabetes, no relationship.

And then over to the soy protein, some differences with pre- and post-menopausal breast cancer, in the Lee study. And if you look at the Japanese study a little bit of difference in stomach cancer, and colorectal cancer, but no differences with heart disease and breast, prostate or lung mortality. Next slide.

So, overall, for that, not a real consistent relationship. So if we move on to vegetable protein and blood pressure, our draft conclusion: intake of vegetable protein is generally linked to lower blood pressure in both cohort and cross-sectional studies, Grade II. The evidence reviews six articles, four prospective observational and two cross-sectional studies.

So in these types of studies trying to measure vegetable protein with food frequencies, and then looking at either

hypertension, diastolic, systolic blood pressure, so you can see those are summarized on the slide. If we go down to the Wang, the premier study, there were differences at six months but by 18 months there were not differences, for both systolic and diastolic at six months, and for hypertension, there were protective effects of vegetable protein. As you go through that you can see plant food for the Steffen study that was examined. Otherwise - I just lost - okay I'm back, good. So there's enough studies here that suggest that there is a potential relationship between vegetable protein and blood pressure. Next slide.

Soy protein and blood pressure. Some data suggest that soy protein may lower blood pressure in adults with normal blood pressure, Grade III. There were five articles, three randomized controlled trials, one prospective cohort and one cross-sectional study. Next slide.

Summarized on this slide you can see that in the He study up on top they found differences. The other Australian study, people that had normal blood pressure, they saw differences in blood pressure. Some of the other studies, the China study, no differences, and then the prospective cohort you see differences, and inconsistent in the other cross-sectional study.

So a little bit of data there, but not completely consistent. And remember these are different types of studies where people actually are interviewing and given soy and soy protein. Next slide.

So body weight, draft conclusion: soy protein had no advantage over other proteins when consumed in an isocaloric study on body weight, Grade II. Four articles, one systematic review, one randomized control, one randomized crossover, and one cross-sectional study. Next slide.

So the systematic review, you can

see, no differences, when they reviewed all the articles. And then the other controlled trials, no differences. And these studies, you will hear more about similar studies in the energy balance area, that if you do control calories, obviously, you wouldn't expect to see differences. Soy protein is no different than other protein sources in affecting body weight. Next slide.

Blood lipids: draft conclusion: soy protein may have a small effect on total and LDL cholesterol in adults with normal or elevated blood lipids, although results from systematic reviews are inconsistent, Grade II. So in this there were six articles, four systematic reviews, one randomized controlled trial and one cross-sectional study that was included in the evidence review. Next slide.

So the meta-analysis, one of the issues, always, with the meta-analysis when we use these is trying to go back and figure out - we don't want to double count studies, so

depending on which studies are used in these different meta-analyses, it's difficult to sort this out and not double count. But if you look overall, in general the amounts of soy protein that are needed to lower blood lipids are fairly high, too. So typically the usual - the 25 grams per day of soy protein is accepted for lowering blood lipids. So in general, it takes high doses like that to have an effect. There is some concern about - are the isoflavones important, are they the key and in the two - Zhan and - the two second meta-analyses they attempted to sort out the isoflavone question to see how important that was, and that was pretty inconsistent, of, are the isoflavones important, are they the primary part, pretty unclear on that.

If you look at the randomized controlled trial with weight loss, we did see some changes but no changes in HDL or triglycerides, and then the cross-sectional, no changes in triglycerides or HDL. Next

slide.

So, implications of vegetable protein. To achieve optimal nutrition intake, recommended levels of dietary protein sources must be consumed with protein derived from both animal and plant sources. Our review indicated that intake of vegetable protein is generally linked to lower blood pressure in both cohorts and cross-sectional studies, but obviously this could be due to other components in plant food such as fiber or other nutrients besides protein. Individual sources of vegetable protein have no apparent unique health benefits, so choice of protein sources can come from a wide range of plant-based foods depending on preferred eating pattern.

Recommendations to lower calorie intake to combat obesity by increasing plant-based food intake must be linked to cautionary messages to maintain protein intakes at recommended levels. Next slide.

So I think we can take a break here and talk, if anybody has questions about protein before we move on to carbohydrates.

DR. RIMM: This is Eric. I have a few questions if I can start. Is that okay?

DR. SLAVIN: Absolutely.

DR. RIMM: So, what an incredible amount of work! Congratulations on putting that all together, not only in finding all the studies but in presenting it so nicely. I think it was very clear to me, and actually the way you lined things up, it almost made me think some of your conclusions should be stronger.

And, for me, some of it was the contrast. You showed the studies for processed meat in diabetes and processed meat in colon cancer, and it looked like almost all of those who had measured it had found a positive association, and a lot of those same studies that looked at blood pressure found absolutely nothing, which makes me think that

the associations for diabetes and colon cancer are that much stronger, and maybe we should have something - I don't know, the diabetes one I think was Grade III evidence, and made me think like it should be Grade II. But I wonder if we should have something in the implications that does point to the fact that it's probably better for animal protein sources to come from sources that are not processed. I mean, I don't know if we can do that. And also I know, sitting in the back of my head is, I just heard a meta-analysis at the AHA epidemiology meeting on processed meat and coronary heart disease, again sort of pointing out the fact that the fat content was much less important than the fact that the meat was processed or not. And this is I know a meta-analysis that was just accepted that also points to the same thing, that there is not just the fact that it has protein and it has fat, but there is something about the processing of the meat.

I don't know, did you get a sense for that? It was just the diabetes one that was so striking to me, that in the processed meat column almost everything was positive.

DR. SLAVIN: I think that as we went through this data it would be nice if studies used the same ways of looking at it. Because what goes into processed meat, and what's different between processed meats versus unprocessed meats. And as you mentioned, it probably has nothing to do with fat. Is it sodium? Is it other things that - and overall we didn't see that processed meats came out across the board as potentially - you know, we talk about lighting up the screen. But we may need to go back and think that through, because there may be certain diseases where there is more of a relationship.

DR. RIMM: I think it is a challenge, especially when you look at cohorts across the world, the way people measure things, and what does it mean to have

processed meat in China versus Europe versus the U.S? The constituents are probably different. I don't know. There is clearly never going to be a trial. It's not going to be a four-year trial of processed meat versus non-processed meat. So maybe the best evidence we get is from observational studies. And it's only because of the contrast that I felt - we see it for a few diseases and you don't see it for a few others. So if it really was just confounding by processed meat eaters, then we may be seeing, as you say, lighting up across all diseases. But that doesn't seem to be the case. Which just made me think that diabetes and colon cancer, maybe we should be a little stronger about our implications and our grade.

DR. SLAVIN: I appreciate that, and in thinking of what comes out in both fat, fatty acid subcommittee too - I don't know with diabetes what kind of things you found, in bringing this stuff together. Because I

think when we focus in on macro-nutrients, sometimes we miss things.

DR. RIMM: Yes. Well, we will get to that when we talk about it. It's not as focused on diabetes. There were some differential results from diets among diabetics, but not necessarily as much looking at instance of diabetes.

DR. SLAVIN: Okay.

DR. VAN HORN: I might also add - this is Linda - that that is in fact one of the reasons why the total diet chapter that we alluded to earlier will become so relevant, I think, because we don't pick and choose our diet around, well, I would like to avoid diabetes today, but tomorrow I think I will risk this. We have to put this all into context, and recognize that, I was thinking, even as you were talking about the absence of evidence in regard to vegetable protein, that doesn't in any way negate the value of vegetable protein in a diet that is attempting

to maximize things like dietary fiber for example. So I think Eric's point is well taken, and as the rest of these subcommittees present their data, it's probably important for all of us to think about what implications some of these conclusion statements have in terms of translating this to a total diet concept.

DR. FUKAGAWA: This is Naomi. A point of clarification. What - how are we defining process? Both in what Eric just said and with respect to this report?

DR. SLAVIN: Well, I think in these studies, Naomi, that was up to the investigator. So it's typically people are counting luncheon meat, they're counting hot dogs, meats that are processed. And I'm sure as the meat industry has changed, there is more turkey, poultry, than there was 20 years ago, so I don't think it's a static thing. And I don't know - Eric, can you help me out on this? Because having been involved in

those types of studies, I assume salami, bacon, those would fit in that category?

DR. RIMM: Yes, I mean a lot of it just depends on how the questionnaire is designed, and when you have a question that just says, red meat or pork, that is not processed. But then you have questions on hot dogs and other - I mean, our question that we use in our cohorts specifically says I think hot dogs and other processed meats. And then, it's also, deli meats are also considered processed meats because most of them are not just turkey cooked and cut, most of them are truly processed with salt and nitrates and things like that. So those are the two or three things that we put together. And I think a lot of other questionnaires are designed the same way, you try to separate out the - beef, pork, and lamb that is served as a main dish separately from those that are processed.

DR. SLAVIN: Processed or

preserved in some way, then.

DR. RIMM: Correct.

DR. CLEMENS: I appreciate that comment, Naomi. I think as we go forward that this very important question is certainly on the minds of many consumers. As the USDA attempted to define minimally processed it didn't do that adequately. So the FDA has not defined processed foods. So it may be beneficial for our consumers that we put a little bit of effort into trying to define or at least clarify what processed might be. And I appreciate your remark, there, Eric, that in fact the processed word is actually being modified as we go down the line here, and that's beginning to change. Unfortunately those changes do not necessarily reflect what we are able to see in the clinical studies.

DR. ACHTERBERG: And this is Cheryl. What I wanted to circle back to and address Eric's initial questions is, actually very few of these studies included any

separation of processed meat from other fresh meat, and in another category that we haven't talked about or mentioned yet is barbecued meat, smoked meat, so people measured differently, they measured different things, and there aren't many data, and that's why we have a lower grade.

DR. SLAVIN: I appreciate that, Cheryl, and also this idea of grilled meats and all that relationship to carcinogens.

DR. RIMM: This is Eric again, I'm not clear on what Cheryl was pointing out. I think most of the studies that look at processed meat do separate it out, but you are right, if someone says they eat red meat, you don't know whether it's cooked on the grill or not. The assumption is that when they bought it it was not processed. So there are some aspects of cooking methods which we don't know about even though people ask about it. That's really - could be measured. But I think most of the cohorts here do separate out the

purchase of processed meat versus purchasing meat that is not processed.

DR. SLAVIN: But I think Cheryl's point is that when we looked at all the studies there was no real consistent way of getting at that, but then when you look at those tables you see a lot of blanks, because it wasn't asked in every study.

DR. RIMM: Okay, that I understand.

DR. SLAVIN: That's how you could get a higher grade.

DR. APPEL: This is Larry. I have a few questions, comments. First of all this is a tremendous body of work, very impressive. But first is right up front, animal protein products, it seems like you focused on meat, yet in the implications then you mentioned milk, yogurt and other things. And I'm wondering whether you should just really replace the term animal protein products with meat. And I assume that the

health issues related to milk and dairy are going to be covered elsewhere.

DR. SLAVIN: Right, milk and dairy are in a separate section. Fish is in a separate section. But animal protein really included everything else. So poultry, eggs, anything else in that category.

DR. APPEL: But shouldn't you use meat, then, rather than animal protein products, which is really more generic?

DR. SLAVIN: Well, that is the way we did the search, though. So go back in our search term, we tried to completely open it up, both the vegetable protein side and the animal protein, because all these studies are done differently. How do you capture that? So anything - eggs, those would be all in our search. So that's just the way the question was done. We could go back and see that probably what the percentage of meat; it's probably pretty high. Obviously poultry is going to be a fairly high amount of what we

found.

DR. APPEL: Yes, there just seems to be a disconnect.

A second issue is - has to do with sort of the issues related to blood pressure and protein. I notice for example with soy that you still are mostly cohort studies. But there are actually a fair number of trials in this area, and also there are a fair number of trials with mixed protein, meat and vegetable protein. I know one that I've led Omni Heart. So I'm just - were those just excluded? Because I think there are actually quite a few clinical trials of soy protein.

DR. SLAVIN: I think the ones - anything that was in a meta-analysis that they would have been excluded only for that reason, if they had already been reviewed and included in any of the systematic reviews or meta-analyses. Otherwise, if we go back and look at our search terms, if there was blood pressure and animal protein, by any of the

ways we got there, it should have come up.

DR. APPEL: Okay.

DR. SLAVIN: You could go see why it was and include it.

DR. APPEL: And then what about total protein? Because as I said, perhaps the biggest study of protein and blood pressure was done Omni Heart. And that was - I think most of the protein actually came from vegetable protein, and there was an effect of total protein on blood pressure.

DR. SLAVIN: Yes, you know I think the way we did this search, and since it had never been done before we probably - the next time we might be able to do a better job. But we specifically looked at animal proteins and we looked at vegetable proteins. I think though if a study only looked at total protein and blood pressure it should have come up, but maybe Eve or someone can help me out here if we would have missed that. And you are right that there are probably some studies - you

know a lot of those studies too, those high protein studies with weight loss, typically you would - you would expect to see a difference in blood pressure. But we may not have caught those if it was just a protein study, sometimes a carbohydrate or some kind of design like that.

DR. VAN HORN: I do think Larry raises a very important point though in regard to meta-analyses which we actually discussed in some of the other subcommittees, and that is that studies that have a certain amount of weight in terms of their quality and their design, et cetera, et cetera, could potentially get sort of lost in the shuffle if only being viewed within a meta-analysis. So it could very well be that we should, especially with – Omni Heart, but there may be other landmark studies kind of that nature that we might want to zero in on and make sure we haven't sort of obliterated the strongest messages from those major studies just by

virtue of the approach that meta-analyses take.

DR. APPEL: Yes, and there is also a related issue when you're dealing mostly with cohort studies, and that is it sort of treads on the approach to analysis, which is that at least when we do clinical trials it's a substitution, and I know there are some cohort studies that present their data through substitution, like substituting carbohydrate for protein, but I think especially in the context of trying to avoid messages that increase confusion it really is - I think it's more of a substitution question. You are eating more protein instead of something else as an energy source. And I know that in the controlled feeding studies that is exactly what we do. In Omni Heart it was substitution of carbohydrate with protein.

DR. SLAVIN: I think I would agree that any studies we have missed should

definitely be part of our hand search and included. We could not find studies where the question was a randomized controlled trial where people compared protein balance, animal versus vegetable. There's lot of descriptive studies, there are lots of review articles with health benefits. But there really aren't studies that have looked at that. I think especially with lower calories one of the concerns is because protein quality is not as high as we want people to eat fewer and fewer calories, protein quality is an issue too. So to have a study where you actually compare animal protein to vegetable protein in a randomized controlled trial, we didn't really find anything like that. There were a few with the soy, but there really isn't anywhere where the question is vegetable protein.

Most of our data really is the cohort study.

DR. PEREZ-ESCAMILLA: Can you hear me?

DR. SLAVIN: Yes, now we can, Rafael, go ahead.

DR. PEREZ-ESCAMILLA: Joan, thank you for a wonderful presentation. My question is about how do these conclusions regarding animal and vegetable protein and cancer compare with the conclusions reached by the World Cancer Research Forum Report that was widely disseminated a couple of years ago?

DR. SLAVIN: We compared our results to their results, and they, if you look at a lot of theirs are certain types of foods; there were some inconsistencies also. They found similar results. They also included cross-sectional studies so there are some differences in their summary table if you look at the picture where they look at all different cancers and different foods and eating patterns, I don't think they found big differences from ours. I guess I don't see a big inconsistency, and I know as our Committee has discussed that we would use that, make

sure in our section that we can refer to that just to make sure we are not giving out inconsistent results.

They did processed meats, fruits and vegetables. There is a lot of overlap with what we looked at, but I think that overall - different cancer studies do find inconsistencies.

DR. APPEL: This is Larry again. I'm wondering, I don't know if it's the grading or the conclusion, but I'm seeing some differences in how the conclusions are phrased that leads to different impressions, and even where Grade II comes across as less strong than some Grade III recommendations. Like the colon cancer one starts off with an inconsistent positive association, that's Grade II, and later on for like the animal products in breast cancer cohort - maybe that isn't the best one, the diabetes one - prospective cohort studies suggest that intake may have a link which is a Grade III.

And we're probably not supposed to wordsmith, but I do see some sort of disconnect between grade level and sort of the phrasing.

DR. SLAVIN: I think Larry, we've had discussions in committees chime in here and help me out, that we've struggled with that, and a lot of times the Grade III is just that there is less data, and it's still fairly inconsistent but there were just fewer studies to base it on, so some of those differences between II and III are based more on the amount of data than the consistency of finding. But Cheryl maybe you can help me out, Linda, I'd be happy to take any comments or reconsider any of the grades. I think that these are draft conclusions, so we're absolutely open to input on that.

DR. VAN HORN: And I think this goes along with what I was trying to get across earlier which is as we march through each of the subcommittees, I have a feeling

that this concept will come up again, and therefore we should be conscious of it and try not only within Committee reports but across them try to apply equal judgment in interpreting some of these results which is not easy. But I think we will hear it frequently throughout the day, and perhaps we can try to fine tune our precision in qualifying one against the other.

DR. ACHTERBERG: This is Cheryl Achterberg. I might offer too that I think this subcommittee was pretty conservative with its grades, because there were very few randomized controlled trials, and we tended to stay with a Grade II without studies of that design. So there may be some variation for us to work out today in the way that different subcommittees generally graded certain kinds of designs.

DR. WILLIAMS: This is Christine. Joanne, thank you for that excellent presentation. I just had a few questions

about the soy protein and blood pressure and body weight and blood lipids. It looks like all the data related to adults; is that true, were there no pediatric studies?

DR. SLAVIN: That is a good question. We probably focused on adults, and I don't know if we excluded – Eve or somebody help me, I'm not sure if we wouldn't have picked up - I doubt that there are many feeding studies on kids at all would be my guess, but whether we would not have picked those up, I think we would have. So yes, you are right, what is out there are mostly adult studies.

DR. EVE ESSERY: Joanne, this is Eve.

DR. WILLIAMS: It should be clear in the conclusion statements that it only relates to adults.

DR. SLAVIN: Did you hand me a note? Whether kids would have been excluded?

DR. ESSERY: Sorry, Joanne, can

you hear me now?

DR. SLAVIN: I can.

DR. ESSERY: This is Eve. Children were not excluded in this search, so they would have been included, and there just were very few studies in that group that were included.

DR. SLAVIN: Thank you. So the search wasn't specific just to adults. That conclusion statement can be worded to address adults since that was where your data was, not necessarily specific to adults.

DR. SLAVIN: And Christine, are you thinking of like recommendations for kids?

DR. WILLIAMS: Well, I agree, I think there are very few studies, but I just wondered if you had identified any data if there were cross-sectional.

DR. ACHTERBERG: I don't recall any in the search. I read through all the articles as well, and I don't recall any about children, though they were not excluded.

DR. SLAVIN: And I do think that is probably an important research recommendation that we want overall with fiber and some of the other recommendations, be increasing plant food and potentially plant protein to make sure there are no other - are there some positives, are there some negatives, and there probably needs to be more studies or cohorts where people are followed to make sure protein quality and growth are not impacted.

DR. WILLIAMS: It might be included in research recommendations?

DR. SLAVIN: Right.

DR. VAN HORN: All right, well, we should probably move forward unless there are other comments.

DR. SLAVIN: I do want to note that in our protein chapter, the introduction, there is a lot more background on protein, so today we are just discussing our NEL questions. So the chapter on protein will

have a lot more discussion on protein and kind of this discussion as calories go down, protein - we have an RDA for protein and it's based on our body weight. The percentage of protein in the diet will potentially go up as people - and I know we had a lot of public comment on the importance of higher protein diets, and increasing protein and in our review we looked for any potential on high protein diets, so I think that will also be in our chapter.

Any other protein questions before we go to carbohydrates?

(No response.)

DR. SLAVIN: All right, carbohydrates. I don't know why we took on proteins, because we had too much to do on carbohydrates, but we did. We have a lot of carbohydrate topics, and some of the other carbohydrate topics are already presented at the other public meetings, but what is left to present today, health benefits of fiber,

relationship between whole grain intake and selected health outcomes, in adults, association between intake of sugar-sweetened beverages and energy intake and body weight and energy intake, we'll talk about children in that same question. How are non-caloric sweeteners related to body weight? What is the impact of liquids versus solid foods on energy intake and body weight? What is the role of carbohydrates, fiber, protein, fat and food form on satiety, and the role of prebiotics and probiotics?

And I want to mention that, as we go through these we'll talk about the ones that were done with the NEL review and some that were not. And part of the reasons those decisions were made was, workflows really for our Committee, and kind of net gain in doing a NEL review. So we were limited in how many NEL reviews we could do, so some of these questions were looked at with the literature review, and therefore they will not be graded.

So as we go through these topics, you will see some of them do not have a grade. When we get to those, and that is because they were not done with the NEL topic.

Next slide. So what are the health benefits of dietary fiber? We actually addressed this using a non-NEL review of the literature and the reason that decision was made is that the American Dietetic Association had conducted a NEL review of dietary fiber and health that was published in 2008, so we are essentially going to update the data from that since that had already been published in 2008, we didn't want to go back and redo all that.

So draft conclusion - this is not a NEL conclusion - dietary fiber from whole foods, including whole grains, protects against cardiovascular disease and obesity, and it's essential for digestive health. Not all isolated fiber or functional fiber have proven physiological effect and need to be

evaluated in randomized controlled trials. Next slide.

The way we set this up too, in the chapter there is a discussion of carbohydrates and we kind of entered into first dietary fiber, and then we moved into whole grains, and the whole grains was done with a NEL review, and the questions that were asked with the NEL review is: what is the relationship between intake of whole grains and first, incidence of cardiovascular disease; second, incidence of type 2 diabetes; and third, incidence of - or body weight or measures of adiposity.

Next slide. So this question was addressed by a 2005 DGAC. So the answer - the NEL question, we went back to articles published in 2004, and all study designs were originally included in the searches, and this was basically to get as many studies as possible. Later the cross-sectional studies were excluded when we had sufficient evidence

from stronger studies. So we started out with a very open search to get as much as possible, but later - we went with the strongest designs we could find.

Original articles included meta-reviews or meta-analyses were then excluded, and also we excluded studies that only considered participants diagnosed with chronic disease, hyperlipidemia, hypertension, other diseases. Next slide.

Our overall draft conclusion: whole grain intake which includes cereal fiber, protects against cardiovascular disease. Whole grain intake is also associated with lower blood pressure, Grade II. Evidence suggests that consumption of whole grains is associated with reduced incidence of type 2 diabetes, the lack of randomized controlled trials limits a stronger conclusion. Grade III. And intake of whole grains and grain fiber is associated with lower body weight, Grade III. We'll go

through each one of these questions separately.

The first is, whole grains and cardiovascular disease. Our draft conclusion: whole grain intake which includes cereal fiber, protects against cardiovascular disease. Whole grain intake is associated with lower blood pressure in prospective cohort trials. Limited RCTs find little differences in surrogate CVD endpoints when whole grains are consumed. Grade II evidence.

For review of the evidence, we had seven articles, two systematic reviews, one meta analysis, three prospective cohorts and a randomized controlled trial.

As we go through this, these studies are very different, so I'm going to talk probably in a little more detail than I have in other studies just to give you an idea of kind of the differences here. So the DeMoura study up on top was a systematic

review. And what they did is they went in and used only the FDA definition that is accepted for whole grains, which is 50 percent of weight of the product has to come from whole grains, and they reanalyzed the data based on that, and then they actually did an expanded definition where they included a broader amount of whole grain and evaluated the data based on that.

And as we go through this, one of the concerns there've been with whole grains is that there aren't accepted definitions, and there aren't good ways of measuring whole grains, so the data on whole grains if you go back to when they were first measured in epidemiological studies, typically there is a -- 25 percent is considered what is a whole grain. Other people have newer studies, and I know Eric, some of the newer studies you guys have done actually have grams of whole grain, so as this field has moved on there have been a lot of different ways of approaching whole

grains. So therefore these studies tend not to be easily compared because of how they look at whole grain.

But you can see in that first study there when they used the FDA definition of whole grains they found much less; they found much less of a protective effect. So it does point out that deciding on a definition of whole grains, and the measurement of whole grains is really importance.

The systematic review, the Kelly, they looked at some results on cholesterol and saw some differences with whole grain intake. The other Mellen analysis looking at CVD, addressing CVD, finding a protective effect. The prospective cohort, differences, protective effect, of Flint, and this is on hypertension; Eric can help us out on this one. The protective effect for hypertension. The Nettleton, incidence heart failure. So if you look at the epidemiological studies, if

you use the definition, and I know, the Flint study they actually used grams of whole grain so that was different, and I think that was probably a better measure, but using the accepted way of sorting whole grains, you see pretty consistent effects, if you go up and use the 50 percent of FDA definition then you don't see a protective effect.

And then there is a recent randomized controlled trial where they actually gave whole grain, so that is - there are very few randomized controlled trials of whole grains, but this WHOLEheart study. In this study they put people on three servings of whole grains at the beginning, and then they actually upped the whole grain serving. So these were people that were considered high risk for cardiovascular disease. This was done in the UK, and they were randomized to whole grains to see if there were any differences in different lipid profiles. And in this study there were no differences in

lipid profiles, in the two different amounts of whole grains we were given. So first 60 and then they went up to 120 grams per day for eight more weeks and in this study no effect on blood lipids.

So that's the cardiovascular, and that is where there is the most data for whole grains. And I don't know if people want to ask questions. We can ask questions when we get done with all of whole grains, since we want to take a break then. Next slide.

So for diabetes, the draft conclusion: evidence from prospective cohort suggests that consumption of whole grains is associated with reduced incidence of type 2 diabetes. The lack of randomized controlled trials limits a stronger conclusion. Four articles, one systematic review with a meta-analysis, and then another systematic review alone, one prospective cohort, and one randomized controlled trial. Next slide.

This, the one up on top was kind

of a systematic review and a meta-analysis that was put together. There is a protective effect you can see in the red column there. The other systematic review, where they had one randomized control, and this is a little hard to look at just because there is some overlap here, so we attempted to sort that out as best as possible. There was a protective section on diabetes, the prospective cohort, looking at whole grain ready-to-eat cereal, there was a protective effect on diabetes. But again, like the WHOLEheart study, it is the only randomized controlled trial, and in these high-risk subjects, giving them whole grains in two doses over a fairly long time period had no effect on fasting glucose or insulin. Next slide. Body weight or adiposity. Draft includes, a intake of whole grains and grain fiber is associated with lower body weight, although few RCTs or prospective cohort studies are published in this area, Grade III.

Eight studies, one systematic review, with meta-analysis, one systematic review, a nonrandomized crossover trial, two randomized trials, and three cross-sectional studies. And I want to note here that the cross-sectional studies were included just because we didn't have a lot of data, but we tried with our Committee to give them less weight in our overall grades and conclusions. Next slide.

So looking at this, the systematic reviews, you can see there are positive effects of whole grains; the Behall study was a nonrandomized crossover trial, and in some of the studies, fairly small datasets, but body weight was actually decreased with the whole grain treatment, and some of these studies too, like these are oat studies or wheat studies, that are whole grain, that were given. The Katcher is a study where they actually gave - there are no differences in body weight between whole and refined, but

there were differences in abdominal fat and in this study, similar to other studies, both groups lost weight. So they randomized people to both a whole grain or a refined grain. So, overall, everybody lost weight, but there were differences in abdominal fat between the two groups.

Same thing for the Brownlee study you've already seen, the third time through. But in this study they followed these people and nothing changed as far as BMI, they measured BMI, percent body fat and waist circumference, and there were no differences. And then the cross-sectional study. So in these cross-sectional studies you'd see differences with body mass index, with whole grains compared to not whole grains.

So next slide. Whole grains, something on implications. Typically in these studies there is a lot of overlap with these studies looking at grain fiber or whole grain depending on how they ask the question, and a

lot of these cohort studies there are data that has been presented both for grain intake, whole grain intake and grain fiber intake, and typically grain fiber is a stronger predictor than whole grain in these epidemiological studies, although there is a lot of overlap, just because of how those things are measured.

This may be due to the inability to define whole grains and measure whole grain content of food. So there isn't a consistent approach to this. There has been change as interest in whole grains has gone on, so looking at how people evaluate whole grain intake in studies has - would have been nice right from the beginning to accept some ways of doing that and move forward with that, but that is not the data that is out there. So some of it may have to do with this inability to define whole grains at that recent reanalysis based on 50 percent; then, if you use a different standard for whole grains you cannot see an association.

The strongest data is grain fiber, less cardiovascular disease, type 2 diabetes and obesity. The unique benefits of whole grain versus grain fiber is really lacking, and so the idea with whole grains is just the whole thing beyond the fiber, but if you look at the epidemiological data, hopefully Eric is going to help me out here at the end, and give me some ways of thinking about this.

So based on our review, grain fiber is pretty consistent protected in these large cohort studies, and whole grains typically don't have anything beyond that. The randomized controlled studies that have been published - and there are very few that are out there - but they don't show measurable health outcomes of whole grain interventions compared to refined grain intervention. Next slide.

I don't know, does anybody want to ask a whole grain before we - I know we have time at the end, to talk about other

carbohydrates, but I'd really like to take a break now if anybody has a fiber or whole grain question that we could address now.

DR. RIMM: Joanne, is there anything unique about that trial that was just published? It seems like that one was throwing a lot of cold water. And sorry, this is Eric Rimm. Was it very highly processed whole grain? I think that is an issue that's come up is that it's kind of hard to judge differences in whole grains just because sometimes they are highly processed, and the sugar is more exposed to absorption. I don't remember seeing that trial; I haven't read it. So was there something unique about that trial?

DR. SLAVIN: I believe when it was set up, it was free living people and it was whole grains that were - they had a whole list of things and they were given them, so I think they had some choice. But whole grain cereal, whole grain snack foods, whole grain

breads compared to refined grains. So it was set up that way that they would take that - and actually the amounts they were given are fairly significant, so it wasn't like they didn't get any. But people would come in, they were counseled to take in these whole grains, but they were commercially available whole grains; that is my impression of how that study was conducted.

So one of the concerns, I was at a meeting where it was presented, and they said, you know, just adding whole grains to the diet you wouldn't expect people to lose weight, because they are eating more whole grains, you know, rather than substituting for other things.

DR. RIMM: Oh, so the trial wasn't set up for it to be a substitution?

DR. SLAVIN: I think that was the goal that they were supposed to do that, but that when they looked at food intake, people a lot of times weren't eating fewer calories.

DR. RIMM: I think that is a point that Linda has talked about many times during these meetings is that, it's nice to talk about things that are healthy but if we just keep on adding calories then of course there is not going to be great benefit from it.

DR. SLAVIN: Right.

DR. RIMM: I mean, one of the benefits of whole grains is it's supposed to be satiating. If that didn't work in these studies, it means either they are not satiating, or there was something about these over-processed whole grains that ultimately led to people absorbing more sugar quickly.

DR. SLAVIN: Yes, and I think from that - although they did, in their defense, they measured a lot of endpoints; it was very involved - the study was funded by the UK standards - so it was a very large study, and they measured a lot of endpoints. I think it was pretty well run. But you know

it's actually pretty hard to lower blood cholesterol even with oat bran or things, we don't lower cholesterol without a fairly large intake.

DR. RIMM: No, I think I agree, and the effects you see from oat bran generally are relatively small. They can be important at a population level but they are relatively small, so I think you are right. I wasn't questioning the integrity of the study. It sounds like it was a well-run study. The issue is if you run a trial where you give people free food, it doesn't mean it's going to magically make things change.

DR. SLAVIN: No, and then the Katcher study too, that study was published in AJCN, and in that study they measured refined versus whole, and everybody, when people were on the intervention, everybody improved, so they all lost weight, so in those types of designs too typically - because carbohydrates, and this comes out kind of in the beginning of

our chapter, that a lot of the data on carbohydrates is across the board pretty good. Carbohydrates, no matter how you measure them, tend to be linked to lower body weight. So even if you give people refined grains in these studies, you see similar changes in endpoint and body weight.

DR. RIMM: So does your Committee think - I mean, I'm just sort of thinking down the line, and maybe - I hope this is not out of line - but the current dietary guidelines say, try to eat half your carbohydrates or half your grains as whole grains. Do you think there is enough evidence now or enough new evidence that we should make a stronger case about eating as much as possible of whole grains?

DR. SLAVIN: We have two - the modeling exercise, and you will hear it from Shelley when we talk, that because refined grains are fortified with folic acid, I don't think we would recommend more than half, and I

also think based on some of this newer data that the idea, if we are giving out, telling people to eat more whole grains and there is no more fiber in those whole grains, or there is not a significant amount of whole grain in those products, we are probably misleading people. So if we are going to have recommendations for whole grains we are really going to have to tighten up what is a whole grain. That is kind of my read on this area is that, now that we have whole grain snack foods, then telling people to eat more, green light, is not a good recommendation. Overall, people need to eat fewer calories, whether they are whole grains or not. We don't want to give people the impression that because it's whole grains, eat more, and in some way needing better data and better regulation on what a whole grain is.

And your point about, you know, how do we set the standard for that, right now it's kind of unregulated. And I guess I

shouldn't - I don't want to get myself in trouble. My impression of regulation is that you can put on grams of whole grain on your product and that's fine. So I think with your Flint study where people are actually measuring grams of whole grain, that is probably where we need to go, and a few grams is really not going to have much positive help with that.

I know our Committee struggled, because I think grain fiber is a very consistent strong message, so I think that dietary fiber in food, there is very strong data that we want higher fiber in food, and whole grains are part of that message.

DR. CLEMENS: Joanne, Roger.

DR. SLAVIN: Yes.

DR. CLEMENS: Do you recall any of the studies that included children of teenage years?

DR. SLAVIN: For whole grain?

DR. CLEMENS: Yes.

DR. SLAVIN: No, there is very little. There are hardly any intervention studies at all. Prospective studies, whole grain, I can't even think of - maybe - I don't think we found anything. I think there is definitely a need for research recommendations. A lot of interest in fiber for kids, whole grain for kids, but very little research has been done in that area that I'm aware of.

DR. CLEMENS: I agree, I'm not able to find much either, so thank you for that affirmation.

DR. NICKOLS-RICHARDSON: Joanne, this is Shelly. I have a question. In relation to the grain fiber, because I know that the Committee is also looking at other sources of fiber, it's - is there a way that you can connect the grain fiber with other food sources of fiber, and maybe comment on total dietary fiber at this point and how those pieces will fit together? Because I

want to make sure that the consistency among carbohydrate as well as other sources of dietary fiber is consistent from this part to when we look at nutrient inadequacies, so is there a way to connect these pieces yet?

DR. SLAVIN: Well, hopefully Eric can help me on this. My sense is that the average person eats mostly grain fiber in the U.S. Intake of fruit fiber and vegetable fiber is very low, and in cohort studies the grain fiber tends to be most protective. But there is this question about it's most of the fiber too. So the strongest data that our Committee finds is grain fiber from cohort epidemiological study. Cheryl, I guess everybody can - but I also think that if you look at the overall dietary fiber and protective cardiovascular disease, that's also strong. It's in the DRI, so there is no question that overall dietary fiber, fiber that is intact, intrinsic, in food, is a positive message, and we want to promote that

message. And that's going to also be in fruits, vegetables, legumes. But our strongest other data for the prospective cohort studies is really for grain fiber.

DR. NICKOLS-RICHARDSON: Okay, thank you.

DR. ACHTERBERG: This is Cheryl, just to add a little bit more information, I don't recall in the literature any statement that suggests what percent of dietary intake for dietary fiber comes from vegetables and fruits, but I do recall that it's only about 3 percent of calories. So when you just consider what form we eat our vegetables and fruit in and then try to figure what fiber contributions might come from that intake, it's really very very low. So I think we need to conclude we don't know what impact vegetable and fruit fibers have yet, because we haven't seen any studies at least in this review where people are consuming enough, Americans are consuming enough, to come up

with a good conclusion.

DR. SLAVIN: I think there is some cancer data in other countries where you get higher intakes of fiber. In those data sets, cereal fiber tends to be the most protective.

DR. RIMM: This is Eric. I wasn't quite clear on the line of questions. We do get a fair bit of fruit fiber and vegetable fiber in our diets. It's not that cereal fiber is the only source of fiber. I think that most of the cereal fiber is coming from wheat in this country. But I think cereal fiber only represents 30 - 50 percent of all the fiber we get, maybe even less. But there is credible consistent evidence across at least the cardiovascular field that people who have looked at it find most of the benefits coming from cereal fiber, and we hypothesize, well, is it really that different, or is it the fact that most of the cereal fiber is coming from whole grains, and

there is something else about the whole grains? I don't think we know, but it's not that cereal fiber predominates the total fiber intake in this country.

DR. SLAVIN: Yes, definitely in cardiovascular disease, cereal fiber is consistently more protective. I know Cheryl is going to talk later on fruits and vegetables and on this discussion. Probably should have brought you in here. Because a lot of fruits and vegetables are really low in fiber, so maybe one to two grams per serving, while a lot of cereal products are actually pretty high in fiber. So there is a dose issue there.

DR. WILLIAMS: Joanne, this is Christine. A few years ago I looked at dietary sources of fiber in U.S. children versus children in other countries. And it was interesting that in the U.S. these sources of fiber were about two-thirds from grains, whereas for example like France it was just

the opposite, about two-thirds were from fruits and vegetables. Interesting.

DR. SLAVIN: I am sure that is true. In countries where they don't consume whole grains. If you look across countries, you see a lot of whole grains up in the Nordic countries, but France, Spain, you just don't see a lot of that intake. So I would not be surprised at that at all.

I do think that overall the dietary fiber recommendation is a really important one, and it's one that is scientifically sound, and a good recommendation, and it will include whole grains, fruits, vegetable, legumes, so you can get your fiber from different sources, but getting it from whole foods is I think a really important method.

DR. VAN HORN: All right, are we ready to move on? Any other fiber, whole grain?

All right, now we are going to go

into more digestible carbohydrates, and some of the questions we asked for that. Added sugar: so our original question, and remember the kids' comparable question is in energy balance, and you will hear more about that, but in adults, what is the association between the intake of added sugars including sugar-sweetened beverages and energy intake and body weight.

So from 2005 DGAC, their question was, what is the significance of added sugar intake to human health? And the conclusion was, compared with individuals who consume small amounts of foods and beverages that are high in added sugar, those who consume large amounts, tend to consume more calories but smaller amounts of micro-nutrients. Although more research is needed, available prospective studies suggest a positive association between the consumption of sugar-sweetened beverages and weight gain. The reduced intake of added sugar, especially sugar-sweetened beverages,

may be helpful in achieving recommended intakes of nutrients and in weight control.

So that was their conclusion. For our review, since that wasn't an evidence-based review in the same sense we are doing it now, so it wasn't a NEL review, we decided to go back to 1990 to present. And we included ages 19 and older, childhood overweight section is going to address the sugar-sweetened beverages. The original article included in systematic reviews or meta-analyses were excluded, and cross-sectional studies were excluded. And we tried to give more support to the systematic reviews that excluded cross-sectional studies but it was difficult, because most of them included them. Next slide.

In adults what is the association between intake of sugar-sweetened beverages and energy intake. Draft conclusion: little evidence that intake of added sugar including sugar-sweetened beverages is linked to higher

energy intake. Grade II. And in adults what is the association between intake of sugar-sweetened beverages and body weight? Limited evidence from epidemiological studies and RCTs that added sugars, including sugar-sweetened beverages, are more likely to cause obesity than any other source of energy and Grade II.

And I wanted to mention as we go on here is that at the beginning of our carbohydrate section, we reviewed overall carbohydrates and energy balance, adiposity, and similar to 2005. And in their review typically carbohydrates are not linked to higher body weight. So you start from this, overall carbohydrate intake if anything is protective against obesity. And then you ask the question, are there differences with different carbohydrates.

So energy intake was based on a review of one meta-analysis and three trials. So the meta-analysis the way this was set up, it was soft drink consumption and nutrition

and health outcome. Eight-eight original studies, and some of that data was unpublished. So the data had been gotten from investigators. So in that study it also included cross-sectional studies. So that was the difficulty in trying to put that in a balance with what else was out there that we could find.

So the other three studies were different types of studies, and I'll just talk a little bit about them. Very difficult to do these studies, so you can see that there is not a perfect design. But the first one, the Reid study, a parallel arm with four soft drinks added to the daily diet, and then the comparison was regular soft drink versus diet soft drink over four weeks, and they found differences.

Now obviously in these types of studies if you get more calories you would expect obviously to get higher energy intake, so not too surprising.

The randomized cross-over trial, the Flood study, with ad lib beverage at lunch. So the differences were regular sweetened cola versus diet cola. And this is a one-day test meal. So they suggested that there was a relationship between sugar-sweetened beverages and energy intake.

And then the last study was a crossover trial with a preload followed by test meal. So in these they actually compared different types of beverages. So a sucrose beverage with just regular sucrose, and then a high fructose corn sweetener beverage where they balanced for calories, and then they also compared milk and a diet drink and they saw no differences with those different types of drinks that were calorie balanced.

It's very difficult to do these types of studies, depending on what your question was, you can see they are really different the way they were designed. So next slide.

Added sugar and body weight in energy-balance setting. We tried - you can see we went back a long time to get some of these studies that they tried to compare different diets. So the Raben study, crossover case-control with three diets, sucrose-, starch-, fat-rich, in normal weight adults. Sucrose diet, 23 percent of the energy came from sucrose. And then they compared it against these other diets. These are energy controlled diets, so not too surprisingly you don't see differences in body weight. And obviously you only have 14 days, so it would be difficult to find that also.

The 2009, this was an interesting study where they compared glucose to fructose at a pretty high energy level over 10 weeks. So on this the parallel arm study so you either got glucose or fructose sweetened beverages. And over 10 weeks was there a relationship between body weight and the energy balance? No, they saw no differences

for body weight, and same amount in both groups and then the last study they compared high and low sucrose weight loss programs. And they went really high. So 43 percent of the energy in sucrose compared with 4 percent in the low sucrose diet, and found no relationship between these different diets and body weight. But remember, these are energy balanced settings. So obviously if you believe calories count, and I think everybody on this Committee does, and you balance calories, you are not going to see any differences whether those calories come from sucrose or starch or however you - fructose versus glucose, that if you balance your calories you will not have any difference in body weight.

Next slide. All right, so those are the - you know there are very few studies looking at added sugar per se and body weight, and not much is there. Typically as we started the literature review it is pretty

hard to assess carbohydrates. There hasn't been a lot of effort to assess carbohydrates. I don't think the data is really good. And overall when you look at carbohydrate intake and body weight, carbohydrates across the board are pretty protective.

So that data is - if you just ask the question, if people eat more sugar do they weigh more, that data isn't there that they do. But if you go in and ask some of the conclusions - something that you can count fairly well probably in epidemiological studies, which would be, sugar-sweetened beverages, are there relationships to body weight. So if you ask that question, are sugar-sweetened beverages related to body weight, we had three systematic reviews, a meta-analysis, four perspective observational studies, and two trials.

So if you look at the systematic reviews, they are really messy. So we put them all up there just so you could compare

them, and you see on the note on the bottom studies that are in blue are actually cross-sectional studies. We were trying to not include cross-sectional studies, but all the systematic reviews that were out there actually in some way included them. So you can also see the people who asked for, who sponsored it, that's over in the right column there, and then in the middle are the authors' conclusions.

So the Gibson article, sugar-sweetened beverages are a source of energy, and there is a typo there, but there is little evidence that they are more causing of weight gain than any other source of energy. And that is pretty much what you got from the first set of studies that if you balance energy, whether it comes from sugar or any other calorie source you are going to expect the same amount of body weight.

But Malik, this one is a little hard to see because of the way it's set up.

It's different - a very different design. So there is some data, some original data in there, plus some inclusion of four prospective cohorts and three intervention studies. A positive epidemiological and experimental evidence indicates greater consumption of sugar-sweetened beverages is associated with weight gain and obesity.

The Ruxton study that was recently - came out, in this one they actually had a fairly detailed description of what was included. So they included fewer studies, and their conclusion is the possibility that considerable intake of sugar-sweetened beverages can contribute to obesity risk cannot be discounted. So they looked at really high intake, there would potentially be a link.

And the other study that we have already looked at is this meta-analysis, and they conclude that clear associations between soft drink intake with increase energy intake

and body weight were observed.

So overall these were all meta-analysis, systematic reviews, in general the people are saying that if calories are controlled, obviously sugar-sweetened beverages are no different than any other calories. So we need to consider them as calories, and obviously if you have no room for calories then they need to go. They could be extra calories and they could contribute to obesity if they are part of the extra calorie problem. Next slide.

Okay, some of the studies that have been done, and I mentioned, some of these you have already seen, but this is the question that is going to affect body weight. So this is the relationship between sugar-sweetened beverages and body weight. So going through some of the studies on the top, prospective studies, the Palmer study, more than one soft drink a day versus less than soft drink a day, it does support a

relationship according to the authors on that one.

The Framingham Heart looking at different, less than one versus more drinks over four years, there is an association.

The Chen study, the Premier Study, compared sugar-sweetened beverages to other beverages, supports a relationship, yes.

And then the Stookey, comparing water to sweetened caloric beverages and at different time points, yes, it does support a relationship.

If you look at trials, the 2009 this parallel arm over 10 weeks, in the outpatient, and this is a little complicated study, because there are different groups that are looked at, and this has been published in a couple of different places. But looking at - giving beverages with glucose and fructose, there was a relationship with weight gain, and then the Reid study regular versus soft drink, and I can't, under my tab here, so I guess I

have my notes.

So overall there is a fairly consistent relationship with soft drinks, sugar-sweetened soft drinks, although the Reid study did find - and this is over four weeks - they saw no differences in a parallel arm trial with soft drinks compared to diet soft drinks.

If you think of what is the right design, what is the perfect way to get at this, overall I think if you control calories obviously you are not going to see any differences. If you just add calories you would expect, if you have a study that is long enough, you would potentially see weight gain. Next slide.

So implications: measurement of added sugars in studies in inconsistent making study comparisons difficult. It's probably easier to count sugar-sweetened beverages. So if you look at some of the inconsistencies of these studies, carbohydrates assessment tools

are fairly limited. Added sugars is a calculation; there is no way to measure added sugar, so it's a hard thing to really get out of epidemiological studies as opposed to sugar-sweetened beverage people ought to be pretty good at counting how many they can consume, so that data is a little stronger.

Different types of carbohydrates, whether it's sucrose, high fructose corn sweeteners, there are no differences in satiety or energy intake if you control calories. So there is no - fructose, sucrose, any of those carbohydrates on a calorie controlled basis aren't going to show differences.

And I think overall added sugar is not any different than any other extra calorie for energy intake and body weight. So there is nothing uniquely different that sugar is going to - it's four calories per gram just like starch, so if you control calorie intake there is nothing different about added sugar

than any other calorie. And if you go back to 2005, the discretionary calorie, it would fit in that category of calories that could go out of the diet and people need to cut calories. Next slide.

Any questions? Does anybody want to ask a question about that before we go down the non-caloric sweetener path here?

DR. NICKOLS-RICHARDSON: Yes, this is Shelly, I'm going to ask a couple of questions.

DR. SLAVIN: Okay.

DR. NICKOLS-RICHARDSON: Can you give us a sense of the total energy intake in the studies that were not energy-balanced? So what were the total energy intakes in those participants who were consuming the extra - or the sugar-sweetened beverages in relationship to what energy needs might have been?

What I'm getting at here, I think when we look at, and when we get to this tomorrow, when we look at total energy in the

diet of Americans, and we look at sources of added sugars and how much - a third of calories come from added sugars and solid fats, we know that about 37 percent of the sugar that is added is from sodas in particular. So what I'm getting at is that while these lab-based studies are interesting and that is how we want to conduct our scientific reviews here, but America is not an energy balance. So in this sort of large, broad, population based ecological study that we are undergoing, how relevant are these for energy balanced studies? So what is the energy intake in these non-energy balanced studies in relation to energy needs and how do these sugar-sweetened beverages fit in? Because I'm a little concerned about - and maybe it's the wording of the questions and the conclusions - but I'm a little concerned to just leave it at sugar-sweetened beverages don't come at a cost to the American population.

DR. SLAVIN: Maybe Eric can help me too on these. I think you can count sugar-sweetened beverages pretty well, but I don't know in a cohort study how you are going to get at added sugars as a number. And you have to remember that in these studies that overall carbohydrates across the board are pretty protective.

DR. NICKOLS-RICHARDSON: Sure.

DR. RIMM: This is Eric. I think Shelly's point is an excellent one. The question is, if you hold calories constant, then it can come from soda or come from other things. In the free living population, is it true that people who consume sugar-sweetened beverages end up consuming more calories.

DR. SLAVIN: I don't know --

DR. RIMM: That's why I think in this case some of the prospective studies may shine some light on it, because we do measure soda consumption pretty well because it is such a unique distinctive food in portion

size. It may be more challenge to measure protein because it is in so many different foods in small amounts. But when people report their sugar-sweetened beverages or diet beverages it's pretty accurately reported.

DR. SLAVIN: And you know we may need to have this discussion after the next section, because the data on non-caloric is not totally going to help us out if we say, okay, if we get rid of sugar-sweetened beverages and go to non-caloric there is going to be a net gain. We don't have great data on that. Unfortunately. And as I mentioned, I don't think our carbohydrate assessments tools are that good. So you know I completely agree with you, Shelly, I personally think that sugar-sweetened beverages, obviously there aren't lots of other nutrient densities that go along with them, so it's something that could be excluded, but we wouldn't want someone to turn around and then take in fruit juice or energy drinks to think that somehow

that would be better or starch, you know like cookies or something. So by focusing on added sugar we need to really focus on calories, so we don't want to get away from the calorie message.

DR. APPEL: Hi, this is Larry. The one study that I'm more familiar with than the others is PREMIER, because I was a co-author on that, and it does address Shelly's question, actually provides calories, both for liquid calories and sugar-sweetened beverages. There is also one point, because it's not just a cohort study, it's really - it's a study of changes in intake in a clinical trial so it's probably the closest thing to a long term trial. The thing that wasn't mentioned that I think is very important is that there was a direct dose-response relationship between weight change and change in sugar sweetened beverage, so the more people reduce their sugar-sweetened beverage intake the more weight they lost. The way the table is

phrased it's sort of a comparison of sugar-sweetened beverage versus other beverages, but that is not the primary analysis. It really was the one I just mentioned; it was a clear direct dose-response relationship, and that was presents at six months and at 18 months. So both for weight loss and weight maintenance.

DR. VAN HORN: Great. Good points. Other people? Any other comments? How are you holding up, Joanne?

DR. SLAVIN: Good. I think that once we go through maybe the next section we can have some other questions, and try to bring those together. All right, next slide, added sugars. Next slide. Non-caloric sweeteners. How are non-caloric sweeteners, related to energy intake and body weight? This one is a little different in that the ADA did an evidence - their Evidence Analysis Library completed a review of non-nutritive sweeteners for children and adults in 2006.

And the NEL search really provided an update for this review. Next slide.

Our draft conclusion: this is obviously the same calorie issue. If non-caloric sweeteners are substituted for higher calorie foods or beverages, they are associated with weight loss. Observational studies find that individuals who use non-caloric sweeteners are more likely to gain weight or be heavier. This does not support that non-caloric sweeteners cause weight gain; only that they are more likely to be used in overweight and obese individuals. This is a Grade II. Next slide.

Some of the ADA EAL conclusions. First in adults, using non-nutritive sweeteners in either a calorie-restricted or ad lib diet will affect the overall energy balance only if non-nutritive sweeteners are substituted for higher calorie food and beverages, Grade II.

And then children and adolescents,

studies do not support the use of non-nutritive sweeteners that they cause weight gain. If non-caloric beverages, including non-nutritive sweeteners, are substituted for sugar-sweetened beverages there is a potential for energy savings in adolescents, Grade III.

The NEL update identifies three additional articles that we looked at. The meta-analysis, 2006, body weight as an outcome. Significant reduction in weight with intake of aspartame. Energy intake over 24 hours as an outcome. Significant reduction in energy intake when aspartame was compared with all types of controls except non-sucrose controls such as water.

The one randomized trial participants consumed significantly more energy at a meal when cola was provided versus diet cola or water.

And then the prospective study, significant positive dose-response relationship between artificially sweetened

beverage consumption and incidence of over weight and obesity. The point - it's pointed out that this association does not establish causality.

Non-caloric sweeteners, implications. Obviously if you take sugar out with calories and you are replacing it with sugar free, you should theoretically reduce body weight. There are many questions that remain because epidemiological studies typically will find a positive link with use of non-nutritive sweeteners and BMI. While animal studies which we have not used in our reviews suggest that the inclusion of non-nutritive sweeteners in the diet promotes energy intake and contributes to obesity. So there is a concern in some people, in animal studies, that non-nutritive sweeteners, if you allow animals in some of these studies they will actually consume more calories, and that is something - a concern that people make up those calories in other ways.

Typically non-nutritive sweeteners are not used randomly across the population. They tend to be more female, women who are dieting, people that are already overweight. So epidemiological studies are somewhat limited because of that, so that if you try to do a fair question here it would be difficult to do. I think long term randomized control will be required to resolve whether non-nutritive sweeteners can actually aid weight loss or prevent weight gain. We really don't have - some of the studies we saw early on and there is an overlap with the added sugar chapter, some of the studies we found where you compare a diet soft drink to a soft drink in these types of short term weight loss studies, there are really not many of those studies that show, theoretically, yes, if you cut calories you should have an effect on body weight. But you don't have large scale randomized trials that show that, the type of data we would really like to have. We just

don't have that.

So any questions about artificially sweetened beverages or added sugar before we go on?

DR. APPEL: Yes, this is Larry. I have a little bit of concern when you mentioned a randomized trial needed, because I actually think these -- I mean I try to do these studies, and this might be one area where you can't actually do a randomized controlled trial. I'd have to really think through - there have been a lot of issues dealing with sugar-sweetened beverages I don't think lend themselves easily to trials, and I don't want to leave the impression in the Report that we are waiting for something to be done or that might be done but is unlikely to be done if it's done, might not be done well.

DR. SLAVIN: Well, I agree with you that it would be a hard study, people would say, okay, it's easy if you put - move all the sugar-sweetened beverages to diet

without even telling people, and how much weight, according to this calculation, you should lose this much weight, I think those would be very difficult studies to do.

DR. APPEL: Or you do a two-armed study and one person gets the sugar - I mean the non-nutritive sweetener, and the other person gets a sugar-sweetened beverage and you don't know whether it's the reduction in sugar-sweetened beverage or the non-core sweetener that was substituted. I actually think you should retract that piece from that implication, or just modify it because it implies – we should be doing trials.

DR. SLAVIN: I think if you go into the non-caloric sweetener literature there is a ton of data on safety; there are really a lot of animal studies out there. But I think the public is kind of wanting, if I switch to an artificial sweetener I'm going to lose weight, well, yes, you probably are right it would probably not be possible to even have

that kind of data, and we don't have that data that says, yes, if you switch, if you are going to switch over to non-caloric you are going to loose weight. Theoretically you should. If all other calories are the same and you cut out 100 calories a day theoretically you should lose weight, and maybe that's the way to leave it, that the likelihood of having a controlled trial to prove - and there really is - because of the animal data there is a lot of concern that people actually eat more, like they somehow, because they are not gaining digestible carbohydrates they pick up more calories throughout the day in other ways, and that is only animal data that I have seen on that, not human data.

DR. RIMM: Larry, this is Eric, but don't you think you could do a trial where you had three arms where it was water, non-nutritive sweetener, and sugar-sweetened beverage just to see if there was - some

people say it's a training of the palette that you have Nutrasweet or non-nutritive sweetener that you are training the palette to still like very sweet foods, so it is driving you to eat more energy during the day. But if you replace it with water you could have a meaningful comparison.

DR. APPEL: Yes, I think it also gets to some of the complexities related to the total amount of calories from these beverages. Because you'd have to start off with a baseline of very high consumption, or at least make that one of the arms be that, so that the sugar sweetened beverages would be four drinks or five drinks a day or something like this for the contrast. I tried to think about these studies and I'm sure others have, I just - you are going to have a tough time doing this.

DR. RIMM: You don't think you could do a two-year trial like the POUNDS LOST study where it was just three arms? You could

see a weight difference over two years? I mean you are right, it's a really difficult study, but I think by comparing - I don't think we should throw it away completely, because there is this issue where there is the data from animal studies suggesting that if you give them non-nutritive sweeteners that they tend to want sweeter food even though there is no calories in that food per se. So I don't know if -

(Simultaneous voices)

DR. RIMM: -- the hypothesis, so if you had three arms you could test that.

DR. APPEL: I guess what I would - that we are not - I wouldn't end the conclusion with the long term problem. So unless we really thought that these could be easily done. I still think there are big logistic issues in doing this, and - but I just don't want to see an implication that ends with a trial where we are not really the best employed, best designed, best of proposed

trial.

DR. FUKAGAWA: This is Naomi. I support sort of you, Larry, in terms of not having that recommendation or implication also, because in many ways what we are trying to get at is the whole issue of whole diets and whole foods, and in a sense going down the path of non-caloric sweeteners takes us away from what we really are trying to do, namely, alter or have an impact on choices that people make, not as substitutes for reducing calories. Does that make sense?

DR. NELSON: This is Mim. I just joined, sorry for having to teach this morning. But I also don't think in the implication that we have been really putting sort of research directions in the implications. I think I agree; I think it could be elsewhere but it doesn't need to be here.

DR. SLAVIN: That is not a problem. I think that probably was in the

research section and got added. So it definitely doesn't fit under that.

DR. FUKAGAWA: Because maybe one of our broader questions is, do we really need non-caloric sweeteners in the food supply. Just a question.

DR. NELSON: I would say no.

DR. SLAVIN: But I do think giving people tools, as we know they are going to need to eat fewer calories, are those tools successful to help people, and theoretically they should help people.

DR. FUKAGAWA: I guess if you phrase it in that manner, as tools to get from one end to the other, but not the answer to how we might be able to maintain energy balance.

DR. NELSON: Yes, the place where this gets real sticky I think is when you consider children, and the fact is the data show that consumption of sugar-sweetened beverages in children does not influence their

reduced intake of calories later, which we kind of had thought was a possibility in fact we haven't seen that. Therefore, the temptation to provide non-caloric sweetened beverages for children so that they can drink something besides water and not add unnecessary calories becomes a real target of question. So I think while data and research on the subject of whether non-caloric sweeteners actually contribute to weight gain certainly would have a major impact on that sub-group within our population, perhaps, again we just don't have the data right now to give us any guidance on that. So the training of the palette issue I think does become an important one especially when it comes to children, because long term adaptations to a non-caloric sugar - not sugar-sweetened beverage could have major implications for them in terms of their cravings for higher sugar flavored food. I don't think we can resolve it here.

DR. SLAVIN: Well, we will definitely take it out of implications, and come up with some research recommendations. But I would love to get to solids versus liquids, because there is a lot of overlap in all these categories, and I have a little note here that I am a little behind.

So liquids versus solids, what is the impact of liquids versus solid foods on energy intake and body weight, a question from the 2005 DGAC. What is the evidence to support caloric compensation for liquids versus solid foods? An unresolved issue: the evidence is conflicting that liquid and solid foods differ in their effect on calorie compensation.

For our review we went back to 2000 to present, and only included articles that compare a liquid to a solid or semi-solid form. We only included articles that considered energy intake and/or body weight not appetite or hunger. This was a very

difficult review.

And here is our draft conclusion. When calorie consumption of preloads is balanced, in these studies, a lot of these studies are done with preloads, there are few differences in energy intake between liquid versus solid treatments. So if you actually control calories at your preload and figure out how much somebody would eat at lunch, is kind of a typical design, calories are controlled at the beginning, you don't see differences. Reduction in liquid calorie intake had a stronger effect on weight loss than did a reduction in solid calorie intake in the PREMIER study, but the different was statistically significant at six months, not 18 months. I appreciate Larry's comments on this and how they fit in here. On an energy-restricted diet soup consumption is associate with 50 percent or greater weight loss. You can see our conclusions are really all over the place, and part of this is because the

designs are really different in this area. So here are the studies. I'm not going to spend a lot of time on this, but if you will look the PREMIER study they separated liquid calories and dissolved calories and saw differences. If you go down, you have already heard about some of the - like the jelly bean study where they compared - they compared pop versus jelly beans. They saw some differences with liquids versus solids. But if you go down some of the - like the Mattes study that was recently published looking at different food forms, no differences with food form and daily energy intake. Same thing with the Flood, looking at that one. There were differences between apples and apple juice, but if you put - added fiber into the apple juice that didn't really affect food intake. It wasn't just the fiber. The 2004 crossover trial with preload followed by the ad lib lunch, no differences depending on food forms.

So in general food form in these

studies, inconsistent results. And you see the different colors on the bottom: these are the soup studies. The soup studies are done differently. There is a concept that perhaps the temperature of something affects food intake; having the forms - there are typically a lot of foods have solids within a liquid, a lot of times people having soup before a meal they eat less later. So these are very different study designs. And overall you see some effect of soup consumption actually as a liquid decreasing calorie intake. So that kind of confounds this whole concept of people thinking that liquid calories don't work as well as solid calories or number of calories that people take in.

Our next slide: so some of the implications. Macronutrients of a liquid diet and a solid diet are the same. There is little data - there are little data that food form affects energy intake in those types of studies. Food structure does seem to play

some role in food intake. So whole foods may affect satiety; there is a little bit of data on that. And people may eat less at a subsequent meal when they eat a whole food. And also soup liquid calories as far as soup seems to be an aid for weight loss. So the soup data doesn't quite fit in with some of the other data for unknown reasons. Okay, next slide. Any questions on food form? Really hard topic. Really appreciate all the help in trying to find the data. That is another thing that typically cohort studies don't pick up food form, but that is something people ask about, or even how many beverages do people drink, how much water do people drink in a given day.

All right, satiety. This was a non-NEL review. And because it's huge, and we were kind of - ran out of time basically. And so it wasn't NEL, but the draft conclusion: many factors affect satiety, and most studies are conducted in laboratory

settings to control for variables. Therefore these results may not be generalized for more complicated eating environment in the outside world.

In general foods high in fiber are generally more satiating than low fiber foods, although you just heard about this study when fibers are added to drinks, that a lot of times that doesn't affect satiety. In general small changes in macronutrients are probably not going to have large differences in satiety. If you get into all the macronutrient proteins, fats - carbohydrates in the reviews that have been done, you get mixed messages. Probably protein comes up the most likely, but it's not consistent. Next slide. And then our last - or this question was the role of prebiotics and probiotics in health. And this was really based on a lot of the public questions we go. We wanted to make sure we addressed this. We also used a non-NEL review of this literature.

And our conclusion, and I guess I'm speaking for our Committee here, but we believe that the gutmicrobiota does play a role in health although the research in this area is still developing. No recommendations for intake of prebiotics or probiotics for the American public can be made, although foods high in prebiotics - wheat, onions and garlic - should be consumed as well as food concentrated in probiotic, such as yogurt. Next slide.

Cheryl, any questions for me? I'm going to give the last time that we have here to Cheryl, because in the November public meeting we still had fruit and vegetable data that didn't get presented. So any questions on added sugar or liquids, anything, before I turn this over to Cheryl.

DR. PEREZ-ESCAMILLA: Joan, this is Rafael Perez-Escamilla.

DR. SLAVIN: Yes.

DR. PEREZ-ESCAMILLA:: It seems to me that your conclusions on satiety and

fiber are fairly consistent with the energy density weight loss conclusions that we reached in the energy balance of the Committee. So I was wondering if you agree with that, because I think it is important for the integration chapters to integrate these two questions.

DR. SLAVIN: No, I think as we go - you can see a lot of the topics that we have in this subcommittee overlap big time with energy balance, so as we get to that discussion any time there are any inconsistencies we definitely want to have that pointed out. But I don't think I see one for the satiety.

DR. PEREZ-ESCAMILLA: I agree; thank you.

DR. APPEL: It's Larry again. I wanted to go to your conclusion and the implications for added sugar. And I'm wondering whether you need to pull out the sugar-sweetened beverage and weight. I'm

looking at the slides that you show on the three systematic reviews and the meta-analysis, and also the studies of - since then, the next slide. And it seems to me that the evidence is stronger than a Grade II and worthy of pulling it out from the added sugar.

DR. SLAVIN: All right, I'm on - let's see - well, when we - we did split it up because we thought okay the data on sugar-sweetened beverages is - it seems like there is more data, a little more consistent, so we did split it out.

DR. APPEL: The conclusion, though, on this slide, the question is related to sugar-sweetened beverages and body weight, and the draft conclusion starts out with added sugar, which I agree with you are more difficult to measure. But your data that you present in the subsequent slide on sugar-sweetened beverages looks to me to be pretty - pretty consistent with one exception being the

largest systematic review but it also included all the cross-sectional studies.

DR. NICKOLS-RICHARDSON: This is Shelly, and I agree with that, and I think maybe it's limited evidence, but it's pretty strong and consistent, so I think that is the discrepancy that I see is the little evidence that doesn't quite - there is just something a little bit missing there for me.

DR. APPEL: I think I'd be interested in hear what Xav said, because he was tortured a few years ago on this question. But part of the problem was that people were stuck with sort of crappy evidence, these cross-sectional studies. And there is better evidence now, and it's been reviewed and been done in a systematic way, especially for some of the prospective studies and now some trial or secondary analysis at trial. It's a stronger body of evidence, and it doesn't come across right now in the conclusion.

DR. SLAVIN: I guess, too, Larry,

what I didn't present here was the whole overall - the carbohydrates and body weight. I think in the research section we are really going to have to come up with better measurement tools. And carbohydrates are linked to more body weight, so that is where we start with this data. So the nice thing about sugar-sweetened beverages is, typically, you can count those. So you usually get a little more information but if you look at the systematic reviews, they are pretty inconsistent depending on how people go after it. And I think the question is, does it really matter who sponsored them or whether you take in the cross-sectional. And if you take out the cross-sectional then you really don't have - it's much weaker. Xav is here, so I would love for - we are more than - our Committee would be happy to reconsider the grade. I don't think it's a Grade I, though.

DR. APPEL: No, I agree it's not a Grade I. But I think the phrasing of it,

limited evidence, I think part of the problem is that the evidence previously was not particularly robust evidence, so if you look at more of the prospective studies, it's stronger. But --

DR. VAN HORN: Growing evidence, or limited? But increasing evidence?

DR. SLAVIN: Yeah.

DR. NICKOLS-RICHARDSON: This is Shelly, I agree, too, I'm not saying that the grade should necessarily be changed, but I think there should - there is something missing between either how the question is phrased and the conclusion is phrased and then the evidence, the modifier that precedes the evidence statement, so there is just - I don't have a problem with the grade, because the data are what they are, but it's the phrasing of that limited and little --

DR. APPEL: You might have - and I don't think we are here to wordsmith, you might just say, although previous evidence

which is predominantly cross-sectional studies, was inconclusive, more robust evidence from prospective studies supports the relationship between sugar-sweetened beverage intake and weight.

DR. SLAVIN: And I was wondering if in the energy intake section, is Christine on, are we going to be - because I know that we have summarized a lot of this data from a kid and an adult site. We probably need to bring that together and make sure we are consistent on that.

DR. NICKOLS-RICHARDSON: This is Shelly, and I'm not disputing the whole overall carbohydrate conclusion. But because this has been separated out from overall total carbohydrate, I don't think it should be lost within total carbohydrate. It needs to stand alone as sugar-sweetened beverages, and not even added sugars per se, but sugar-sweetened beverages.

DR. SLAVIN: I'm wondering, Eric,

if you are here, is there anything - can you think of a cohort sitting there, are there any studies that need to be pulled out as strong new evidence that doesn't kind of get washed out in these systematic reviews?

DR. RIMM: I think there have been. Again I know more about the ones that we have done here than the totality of evidence. The Malik study which you talked about where she looked at our data here and then did a sort of meta-analysis at the end, I thought there was something - maybe it was sugar-sweetened beverage and diabetes also where there was analysis that really changed in sugar-sweetened beverage, showing that people who increased their intake prospectively had an increased risk of diabetes, so it wasn't just cross-sectional, and it wasn't just one point in time prospectively; it was actually two points in time. So I - it is a really hard thing to measure, and you can really dilute messages by

looking at things that were not done with the best methods available. It's not that they were incorrect; it's sort of all the data that they had. So it is tough to weight, but I think trying to - looking at those studies, I look at change over time may be the best way to do it. I have to go back and look at the Malik study, but I thought that's what she did.

DR. APPEL: This is Larry again. I think that you are right on target, Eric, sort of like the one way - or just sort of the cross-sectional cut or the prediction without looking at change, that is not done in most of the cohort studies.

DR. SLAVIN: I really think that what happens in these meta-analyses is that we lose our signal, it washes out. So if we had some good prospective studies or other ways of looking at this to make sure that that doesn't get lost, we should definitely include that and bring that kind of to the front of the

line. Because I think everybody here kind of has an agenda. So trying to sort the prospective - these meta-analyses out is very difficult.

DR. VAN HORN: Exactly. And this is Linda again, as we have said before, and this I know will come up again in reading the chapters, this is a constantly recurring problem in how you phrase something that is based on a grade that incorporates certain types of studies that may be more robust than others, even though there is a grade attached. And interpreting that really does become problematic. But I think we need to move ahead. Are there any other statements for Joanne?

DR. SLAVIN: Right, and Cheryl has her part.

DR. VAN HORN: Oh, Cheryl, that's right.

DR. SLAVIN: So I will defer to Cheryl. I'm sorry to take all your time.

DR. ACHTERBERG: I will go quickly.

I first want to commend Joanne for yeoman's task, not only presenting today but for all the work she's done, a huge amount of questions and papers and data to sort through for this chapter.

My mission today is to wrap up a small piece that was not presented in November relative to the effect of vegetables and fruit on health outcome, and more specifically on type 2 diabetes. The question was: what is the relationship between the intake of vegetables and fruits, not including juice, on type 2 diabetes. For the review strategy the topic was addressed in 2005, by the Dietary Guideline Committee, so their conclusions informed this Committee. But in addition we did a literature review using the NEL process from 2004 to 2009, focusing solely on adults.

There were a total of five

studies. Our draft conclusion is that the evidence is inconsistent, but suggests an inverse association between the development of type 2 diabetes and total vegetable and fruit consumption with a Grade III. All five studies were prospective and long term, a couple of them actually lasted over an 18 or 20-year period. Two of the five focused on only specific foods, the Halton on potatoes and more specifically French fries, and the Wang study was solely in this paper on tomato-based products.

Altogether with the other three studies, not focused on potatoes or tomatoes, the number of fruit and vegetable services range from 2-1/2 to more than 10 servings per day. So if you look at the outcomes for these, it's basically a null outcome in the Bazzano study, the Nurses' Health Study as well as the Women's Health Study. A null outcome for the tomato-based products. A positive outcome and association between

intake of potatoes and French fries with the results being stronger for French fries than potatoes in general with type 2 diabetes, and that effect was stronger in obese women than in non-obese women.

And then finally if you look at Villegas, this study was conducted in China and did break down vegetables into different categories. It was the only one that did so here. So you can see the inverse relationship for vegetables but not for fruit when you look at these various subgroups.

So no information on children and overall we think this supports that draft conclusion that follows, that the evidence thus far is inconsistent. But the Committee believes there is an inverse association probably present between consumption of vegetables and fruits and type 2 diabetes.

So that opens us up into the larger fuller discussion if we want to dedicate any more time.

DR. PEREZ-ESCAMILLA: Cheryl, this is Rafael Perez-Escamilla. The intake of vegetables in the U.S. is so low, and the variety also so limited, that this is an area perhaps studies from countries outside the U.S. where there is a much higher intake of vegetables, much more variety, and a wider range, maybe better suited to determining the relationships between the vegetable intake and type 2 diabetes.

DR. ACHTERBERG: In my drafting of the chapter here focusing on vegetables and fruits, there is considerable discussion given to the difficulty in these studies and in the comparison across studies given the fact that as you are looking at different countries, the kinds of vegetables and fruits as well as the amount of vegetables and fruit consumed vary quite a bit. And since there are very few hypotheses or mechanisms suggesting for how it impacts my work whether it's about diabetes or cardiovascular disease or other health

outcomes it gets very tricky when any given vegetable for example might contain 400, 500, 600 different compounds. So one cannot presume that these results would be constant across nations here, given the different dietary patterns, not only with fruit and vegetables themselves but also in the context of the whole diet. So I would suggest that we need a lot of further research in this area, and a much more rigorous research conducted in terms of data collection on vegetable and fruit intake.

DR. RIMM: This is Eric. I mean I wonder it starts and points you to sort of the differences between the fruits and vegetables, just in their impact on diabetes. You could say that the potatoes were positive and some of the other fruits and vegetables are negative. And I know that potatoes in the past have systematically been put into the vegetable category. But clearly the amount of starch and free starch, free glucose, that

comes from potatoes and French fries is much greater than what you'd see from other fruits and vegetables.

DR. ACHTERBERG: Correct.

DR. RIMM: I don't know, I guess there aren't enough studies out there yet that have looked specifically at potatoes for other outcomes or for diabetes, but it does point to the glycemic quality of the fruit or vegetable.

DR. ACHTERBERG: In our NEL search there was only the one study on potatoes. And as you know probably tomorrow we will talk about the modeling that was done so in part we wanted to model what would happen if we looked at these starchy vegetables from a different perspective. So I think you are right, we need to look at vegetables, starchy vegetables and others as well in a more nuanced way than we have in the past, not just lumping them all together.

DR. CLEMENS: This is Roger.

Thank you for that excellent insight. It would interesting to raise the issue on starch vegetables that we be careful how we define what a starchy vegetable might be, at what point do we want to look at insulin response or digestibility or actual composition of those types of products.

DR. ACHTERBERG: I grant you, and I think especially because of our time pressure here, I defer to the discussion that will arise tomorrow when more of this modeling has been done, and we can present those recommendations.

DR. CLEMENS: Thanks, Cheryl.

DR. VAN HORN: Other comments from anyone on the panel? Or Joanne or Cheryl, do you have more to add?

All right, then, well, it's been an incredible and very comprehensive start today. But I think now our group will take a 15-minute break, and please return by 11:45 Eastern time, and we will proceed with the

fatty acid report.

Thank you.

(Whereupon at 11:35 a.m. the proceeding in the above-entitled matter went off the record to return on the record at 11:49 a.m.)

DR. VAN HORN: All right, well welcome back everyone. We are about to proceed with the fatty acid cholesterol subcommittee. And the chair of that Committee is Dr. Tom Pearson how is going to lead us through the next set of slides.

FATTY ACIDS AND CHOLESTEROL SUBCOMMITTEE

DR. THOMAS PEARSON: Well, thank you, Linda, and it's a pleasure to begin this report on behalf of our Fatty Acids and Cholesterol Subcommittee. And I want to thank the members. We are going to be hearing from Eric and Roger as well as I will mention in a moment, I think we want to thank and really a great note of appreciation to our staff who have been really so terrific, Shirley Blakely,

Thomas Fungwe, Patricia Guenther and Molly McGrane. So this is the end of a lot of discussions on these important topics. Next slide.

What we are going to do is finish up some of the topics that we hadn't fully done in previous sessions. The first question is: What is the influence of dietary fat on cardiovascular disease and other health outcomes? I am going to be covering the first two topics, that is, monounsaturated fatty acids and n-6 Polyunsaturated Fatty Acids.

That will be followed by Eric Rimm who is going to look at n-3 Polyunsaturated Fat, particularly in seafood and seafood-derived n-3s versus plant-derived n-3s.

And then Roger Clemens is going to talk about maternal intake of seafood and breast milk composition and health, a new topic for the advisory guidelines fatty acid group.

Then I'll be back talking about

the association between the consumption of fat of particular foods that are high in fats and their relationship to health outcomes. And the two I'm going to talk about is nuts and chocolate.

And then we have the final question of what dietary components of the trans-fatty acids, natural versus synthetic, affect plasma LDL, HDL, and non-HDL cholesterol? And then finally report on three food pattern modeling exercises. In terms of cholesterol-raising fat is, what is the impact on food choices and overall nutrient adequacy of limiting cholesterol raising fatty acids to less than 7 percent of total calories and less than 5 percent of total calories.

And the second one that I will be presenting is: what is the impact on food choices and overall nutrient adequacy of limiting dietary cholesterol to less than 200 milligrams per day?

And then Eric will be back looking

at the modeling question of what is the impact on nutrient adequacy of increasing seafood in the USDA food patterns. So this will be what we will be covering in the next hour and a half or so.

So in terms of the monounsaturated fatty acids, we've expanded this into two questions, particularly individuals with type 2 diabetes. So the first question: what is the effect of dietary intake of MUFA when substituted for saturated fat on increase risk of cardiovascular diseased in type 2 diabetes mellitus, including intermediate health outcomes such as lipid/lipoprotein levels, markers of inflammation and a blood pressure in the general population.

And then the second particularly focused on what is the effect of replacing a high carbohydrate diet with a high MUFA diet in type 2 diabetics? We felt that this was an important subset of the population, not just because diabetes is now affecting about 7

percent of the U.S. population; another 25 percent or so have metabolic syndrome which of course is the extremely high levels for developing diabetes.

The data looking at these qualities of fat has to do with the isocaloric dietary substitutions. And most of the literature that we have been looking at has been isocaloric in nature, so that you're substituting calorie for calories, and you can see this reviewed by Frank Hu in 2001 the various substitutions, saturated fat for carbohydrates, monos for carbohydrates, polys for carbohydrates, saturated for monos, et cetera, et cetera, and in terms of the change of CHD risk from this epidemiologic study you can see that there are various substitutions that have a wide range of impacts on change, particularly down below where the three saturated fats traded for monos and polys and the *trans* fatty acids for mono and poly unsaturates, obviously, have sizeable

reductions in cardiovascular risks. So the search of the literature was particularly focusing on updating this literature since the 2005 guidelines.

So for the first question, the inclusion criteria obviously for the monounsaturated literature looked at literature since 2004. You can see the inclusion criteria here. The healthy population and those with chronic disease risk. Now the study design really excluded cross-sectional studies because of the many biases you have in eating patterns, so we are particularly looking at randomized control trials or controlled clinical studies, prospective studies, meta-analyses and systematic reviews. We really did require a feeding period of more than four weeks, and at least 10 patients, 10 persons per study group.

So with the review of this literature since 2004, the top 11 studies have to do with the isocaloric substitution models

for saturated fats; the five studies below are in individuals with isocaloric substitutions of monos for carbohydrates. And you can see from the next slide there are two outcomes. This was an expansion over the 2005 guidelines which focused on cardiovascular disease, cardiovascular disease risk, and given the diabetes epidemic as well as the literature in this area, type 2 diabetes was added as a second study outcome.

And you can see here that of the randomized control trials, five were positive and three were neutral. Some of these studies had endpoints with intermediary markers for cardiovascular. Those are particularly the proteins, but some inflammatory markers as well, and also the two positive - two studies for intermediate markers, type 2 diabetes, those would be a variety of measures of insulin resistance, et cetera. Also the four studies, meta-analyses, were also supportive of improved risk for cardiovascular diseases.

So our draft conclusion statement, and this was particularly assisted by some of the large epidemiologic studies and meta-analyses, we were looking at the energy replacement, our draft statement: Dietary monounsaturated fatty acids are associated with improved health outcomes related to both cardiovascular disease and type 2 diabetes when monounsaturated fatty acid is a replacement for dietary saturated fatty acids. The evidence shows that 5 percent energy replacement of saturated fats with monounsaturated fats decreases intermediate markers and risk of cardiovascular disease and type 2 diabetes in healthy adults. It also improves insulin response, in insulin resistant and type 2 diabetic subjects.

This is particularly relevant to some of the modeling studies we will be talking about later with about 11 percent of energy in the American diet as saturated fats, which has been quite stable over the last 15

or even 20 years, and replacement of 5 percent would obviously be in the 7 percent or less saturated fat range. So we feel that this Grade I evidence.

The second part of this question really looked at replacing a high carbohydrate diet with a high MUFA diet in type 2 diabetics. This had five randomized trials, two were positive quality, and three were neutral. All five supported the conclusion that MUFA replacement would be beneficial, that included intermediate markers of fasting glucose, hemoglobin A1C and the triglyceride-rich glycoproteins. And the - also the high MUFA diet was well tolerated.

So our conclusion statement here would be: Increased MUFA intake, rather than high carbohydrate intake, may be beneficial for type 2 diabetics. High MUFA intake, when replacing a high carbohydrate intake, results in improved biomarkers of glucose tolerance and diabetic control. And we felt that was

Grade II evidence.

So the implications of this is that there are - there really are isocaloric in the study design, and so it may assume these isocaloric changes. We are all very aware of the nutrient - the caloric density of fats, and this obviously needs to be taken into account, so we are attempting to factor this in to maintain an ideal body weight.

The high MUFA diets were well tolerated in these studies, and the favorable changes in glucose tolerance, inflammatory markers, such as the lipoprotein, were all common in diabetics, and they have health implications around the diabetes and cardiovascular disease.

The issues for future research, and this is going to come up on the flip side of looking at n-6 PUFAs versus MUFAs. And really the question is sorting out which of those two is more effective in decreased cardiovascular and diabetes risk. And we do

need additional studies with MUFA replacing carbohydrate and relating to cardiovascular disease in type 2 diabetes clinical endpoints rather than the intermediary metabolic endpoints.

So let's move on to the n-6 polyunsaturated fatty acids. And the question here is what is the effect of dietary intake of n-6 polyunsaturated fatty acids on risks of cardiovascular disease and type 2 diabetes, and again looking also particularly in the randomized control trial literature for intermediate health benefits of lipid levels, lipoprotein levels, markers of inflammation and blood pressure.

Of the inclusion criteria they were virtually the same as the MUFAs, so I'm not going to go over them again, excluding cross-sectional studies. There were 10 studies in the literature, five randomized control trials, four prospective cohort studies, and one meta-analysis, since the 2004

period. And you can see that six of the 10 studies were positive while four were neutral. And generally the PUFA replacement of saturated fat as a percent of energy improved the intermediate markers, and the endpoint health outcomes.

So the actual studies are seen here. We do have randomized control trials. Again this is mostly intermediate markers. But again, but very I think very well established, particularly the lipoprotein markers, as being part of the causal pathway between dietary fat and cardiovascular disease event.

You could also see the one of the clinical trials also had a type 2 diabetes outcome with intermediary and glucose insulin resistance markers.

The core studies looked at risks of these chronic diseases, and you can see that all four of those studies reported the conclusion of improving risk with trading

PUFAs and MUFAs for MUFAs for both cardiovascular disease and diabetes after meta-analysis.

So our draft conclusion statement then is that the n-6 polyunsaturated fatty acids are associated with improved health outcomes related to cardiovascular disease when replacing dietary saturated fatty acids or trans-fatty acids. The evidence that as you replace saturated fats with PUFA it decreases total cholesterol, LDL cholesterol and triglycerides, numerous markers of inflammation. They also in epidemiologic studies significantly decreases cardiovascular disease risk, and at least one study, risk of type 2 diabetes. So this is a Grade I conclusion.

The implications again very parallel to the ones for monounsaturated fats, is that these also assume an isocaloric replacement of polyunsaturated fats. The risks of both cardiovascular disease and type

2 diabetes my be reduced with PUFA replacement for saturated fats and *trans* fatty acids, or carbohydrates, and the mechanisms for cardiovascular risk protection which includes serum lipid levels, markers of inflammation, maybe have additional health benefits being picked up or examined in these cohort studies or randomized trials.

So again the flip side of the others is really to try to sort out, and it may be a very difficult task in comparing them, hence PUFAs with MUFAs, in terms of the effects on cardiovascular and type 2 diabetes risk. But given the distributions of these and their sources in whole foods, it will be I think an important area for future research.

Okay, now I think we can move on. Is there any discussion at this point?

DR. APPEL: Yes, Tom, this is Larry. One sort of detailed question and one sort of general picture. Aren't there some - and maybe Eric can comment - some already fair

amount of cohort studies dealing with the MUFA versus the PUFA issue at this point? Because your research recommendations basically that we need to do research in this area, but I think it's mostly we need to do some trials in this area, but there is evidence from cohort studies.

DR. THOMAS PEARSON: I think I was particularly talking about the need for head-to-head randomized trials. But Eric, any comments?

DR. RIMM: Yes, Larry, I mean I think that is a good point. One issue when people think of MUFAs in this country, or as scientists when we think of MUFAs; we think olive oil and canola oil, but that is not where most of our MUFAs come in this country, although a lot of it comes from red meat or other places. So I think what we really want to do as we said here, I think it really would be a head-to-head comparison more than trying to dissect the existing diets of the U.S.

population.

DR. THOMAS PEARSON: I think the observational studies are very difficult to do without - and some of the studies as we'll talk about later, the Lyon study, et cetera, were steps in the right direction, but I think really fell short for a variety of reasons from what we wanted to look at in this particular question format.

DR. APPEL: And then a more detailed issue is, the - when I looked at the MUFA or the question - the MUFA question talks about intermediate outcomes such as inflammation. I hope that it's not the inflammation results that are driving the conclusion, because I guess I may be more of a purist on this one, but we probably should be focusing on accepted modifiable risk factors. Because at least the summary tables don't mention, it just says it improves intermediate outcomes without stating blood pressure, lipids.

DR. THOMAS PEARSON: Yes, obviously the full tables with the outcomes, obviously, get down to that level of granularity. I think the important point is that they are all essentially heading in the right direction. And as you know I've been involved with some of the inflammatory biomarker guidelines, so I will agree with your point that the full understanding of the meaning of what changes an inflammatory marker is still a raging debate. On the other hand they certainly on a correlational population basis the - they are a modestly useful indicator of cardiovascular risk heading one way or the other.

The single largest data here are the lipids and lipoproteins, and that really is I think beyond reproach in terms of really being a significant intermediary indicator of the chain of causation going in a positive - that is a beneficial direction, if you are able to change LDL cholesterol.

DR. APPEL: Okay.

DR. PI-SUNYER: Tom this is Xavier. With regard to the MUFA conclusions relating to type 2 diabetes, I know that you said that this was isocaloric substitution, but I think somehow that might be in the conclusion statement more strongly because you know the fear is that these people are all obese to start with, and if they had MUFA they add more calories, and a lot of the MUFA foods are high in calories and energy dense. So I think somehow it would be important to caution the need for isocaloric substitutions.

DR. THOMAS PEARSON: Yes, Xavier, we obviously put it in the implications. But I think putting it right into the conclusion is correct, as we have struggled with as you know with the total fat consumption, and so we have been particularly focusing on the quality of fats, and therefore replacing them on a calorie for calorie basis, one fat with another, in terms of our recommendations.

Okay, can we go to the n-3 fatty acids within plant sources, and Eric Rimm will lead this discussion.

Eric.

DR. RIMM: Thank you, Chairman Pearson, I will move on. Okay, n-3 fatty acids, we are going to - next slide please - address several different research questions. One is what is the relationship between consumption of seafood and seafood-derived n-3 fatty acids, so we will be focusing on foods only here. And the risk of CVD events in individuals without cardiovascular disease and those with cardiovascular disease.

And a second question we will address is what is the relationship between the consumption of a plant derived n-3 fatty acid diet and the risk of CVD in subjects with and without cardiovascular diseases. Next slide.

I will go over this quickly, but for the most part our inclusion criteria was

based on updating a previous ADA systematic review of the evidence, and then adding on the NEL review from 2007 forward, and like other studies, other searches, we've excluded for the most part cross-sectional studies, and looked at cardiovascular endpoints for this set of questions because of the WCRF summary two years ago on cancer where overall looking at all the seafoods the strongest evidence they had is that there is limited and insufficient evidence to suggest that fish consumption lowers risk of colon cancer, so we focus on cardiovascular disease only.

So the first question is, what is the relationship between seafood in subjects without cardiovascular disease. Next, please.

Our draft conclusion statement here is that consumption of two servings of seafood per week, which is approximately three to five ounces per serving, which provides on average 250 milligrams per day of n-3 fatty acids is associated with reduced cardiac

mortality from coronary heart disease or sudden death in persons without previous cardiovascular disease, and we've given this a Grade II.

The review of the evidence here, I don't have them all listed, Joanne did that, we didn't do that here, there are a lot of studies, there were 27 in total, four randomized control trials, 15 prospective cohort studies, a number of meta-analyses. In fact this is one of the favorite for people to do meta-analyses on, so we have six systematic reviews or meta-analyses.

For the most part again we are focusing on seafood and seafood-derived n-3, so for the randomized control trials there were several of them looking at primary prevention, essentially looking at improved biomarkers for cardiovascular disease, improved blood pressure, and reduced risk in cardiovascular disease. We name several cohort studies. Sort of a mixed bag here,

those that found an association found a decrease incidence risk, and that is where the primary number of studies were. A few found no association when we're looking at a fib, and one found no association with stroke mortality.

Systematic reviews for the most part found that fatty fish consumption in the range that we are talking about of approximately two servings per week on average, or about 250 milligrams per day, decrease cardiovascular disease and cardiovascular events. Next slide.

So the implications for this, as we started drafting future research here, is that the consumption of seafoods high in n-3 fatty acids and low in methyl-mercury and other pollutants is desirable and feasible. Another implication of this obviously will be that we need efficient and eco-friendly strategies to continue to be developed to allow for greater consumption of seafood and

seafood-derived n-3 fatty acids across the population and then further research is needed, especially from randomized control trials that are looking specifically at increased consumption of seafood as opposed to giving individuals n-3 supplements.

Next slide. And then second question, part of this, is what is the relationship between consumption of seafood and seafood-derived fatty acids and risk of CVD and individuals with cardiovascular disease. And this is secondary prevention. Next slide.

The draft conclusion here is that the consumption of two servings of seafood per week which provides an average of 250 milligrams per day is associated with reduced cardiac mortality from CVD or sudden death. And I think we are actually wavering back and forth in Grade I or Grade II here. And as I was reading it and thinking about it, I forget why we didn't do this, call it a Grade I, and

maybe we can have some discussion on that, because I think this is where there is the strongest evidence. Next slide.

The review of the evidence here where there are four studies, three prospective cohort studies, one meta-analysis, and again we are building on the ADA evidence analysis, and also in fact on the 2005 dietary guidelines submitted. Next slide.

Here there were three cohort studies that found a protective effect of fish-derived n-3 fatty acids on risk for CVD, and found reduction in all cause mortality, although some of the associations were not as strong here, and in this particular case overall did not find associations with combined fatal and non-fatal cardiovascular events.

If you look at the systematic review overall associated, we do stress for nonfatal myocardial infarction. I guess that was the key issue here, is that if we are just

talking about fish and fish-derived fatty acids, there are fewer studies than just those that gave an n-3 fatty acid supplements. Next slide.

Our implications here the same as the implications, and certainly wrapped together with the implications in the first part of this question, is that we do need a fish and eco-friendly strategy to continue to develop ways to increase the consumption of seafood and seafood-derived n-3 fatty acids, and again I think it would be helpful here to have randomized control trials to determine the long term health effect of the recommendation to increase consumption of seafood in individuals with previous cardiovascular disease.

DR. NELSON: Eric, this is Miriam.

DR. RIMM: Yes.

DR. NELSON: Can I ask you a quick question here? Is there any - you had

put in the conclusion slide it was a certain amount. Is there a dose response here at all? I mean more is better, or is it actually sort of a threshold.

DR. RIMM: This is one of the areas where there is apparently it looks like an apparent threshold. It's difficult to know biologically but when we put all the studies together you can see there is a huge drop in the risk of cardiovascular mortality up to that range of 250 - 300 milligrams per day, and then as -- there are studies that go way out, if you look at the Japanese study people eat a gram or two grams per day, they don't see as much benefit; and sometimes they see no benefit.

DR. NELSON: Okay, great, thanks.

DR. RIMM: So that's how we picked that. That was based on a few other meta-analyses that were done sort of at an inflection point.

DR. NELSON: Got it, thank you.

DR. RIMM: Okay. So our next thought is to look at what is the relationship between the consumption of plant-derived n-3 fatty acids and the risk of CVD events in subjects without CVD. And here there was less evidence. WE felt that the plant - the main plant-derived n-3 fatty acids is alpha-linolenic acid, and intake here is alpha-linolenic acid intake between point six and one point two percent of total calories meets the prior recommendations in the IOM Seafood Report for essentially fatty acids, and may lower CVD, but there is not sufficient new evidence to warrant greater intake beyond this level. That is a Grade II conclusion. Next slide.

For this we reviewed the evidence from eight studies, four were prospective cohort studies, one was a systematic review, and three were case controlled studies. Next slide. And this is again, I've listed the slide there, this is a mix of studies. Some of

it is based on diet, some of it is looking at fatty acids in adipose and other areas. But in most part, for instance, the Rastogi study was an interesting one because it was ALA oil for cooking, lower risk of ischemic heart disease, but it wasn't in this country, so it was a different type of ALA and a very different background type of diet. The other studies have found a membrane ALA associated with changes in sudden cardiac disease. Looking at the cohort studies, again, these are prospective studies from several different areas around the country, several of them finding lower risk of cardiovascular disease from higher ALA, others did not find an association for serum ALA, dietary ALA or ALA, and then the meta-analysis in 2006, overall did not include that increased intake of ALA does not reduce the rate of all-cause mortality in cardiac or sudden death, sudden cardiac death.

So I think there is a mixed bag

here. There was some suggestion, but overall not a strong enough statement for us to make as Grade II evidence. Next slide. The implications for this is currently there is insufficient evidence to increase n-3 intake from plant sources. We all have discussed in the past that there is low conversion from plant n-3 to marine n-3, so we do I think need further evidence from randomized controlled trials and prospective observational studies among participants with a broad range of entry intake, especially with and without adequate intake of n-3 fatty acids from marine sources. On this point, and something that we have discussed before, clearly there are many populations in the world that in the U.S. where people don't eat fish, and they are not walking around with n-3 deficiency type diseases. So people do convert enough of the plant sources to the longer chain entry fatty acids. The question is are they getting maximum benefit, and I think we don't know

that, so I think it is interesting to be able to make suggestions for research in the future to be able to look at ALA among populations who have no n-3 from fish, have moderate amounts from fish, and have larger amounts from fish, to see if there really are differences in subsequent risk for disease as well as differences in conversion.

Next slide: so lastly we wanted to look at what is the relationship between consumption of plant-derived n-3 fatty acids, and risk of cardiovascular diseases in events subject with CVD. Next slide.

And for the most part here this is the Lyon heart study. So our conclusion is, there is limited evidence that higher intake of n-3 from plant sources may reduce mortality among individuals with existing cardiovascular disease. We gave this a Grade III. Next slide. And again this is the Lyon heart study. And overall while this did find a protective effect, this was not a trial solely

on ALA. This is one of the things we use in the interventions, but there were other factors in the intervention, so we can't call this strictly an ALA trial. Next slide. Plasma ALA tended to be inversely associated with recurrence of MI because ALA was put into a margarine, into a spread, in the Lyon study. Next slide.

So our research recommendations here are again while we can look at observational studies, I think it is important in the secondary prevention study. I think randomized trials are needed to examine the impact of higher intakes of n-3 from plant sources in reducing mortality from CVD.

And locations from this is relatively little ALA converts to EPA or DHA, suggesting that plant-derived n-3 fatty acids and on a gram-per-gram basis alone may not provide the cardiovascular protective effect that we've seen through DHA or EPA. So this insufficient evidence to make a formal

guideline to increase n-3 intake from plant sources, without additional randomized clinical trials and/or prospective studies, among participations across a broad range of n-3 fatty acid intake. Next slide. Is that the end for me? Yes, that is the end for me.

DR. THOMAS PEARSON: Why don't we open it up for some questions at this point. I did want to make one comment, and that is that this issue of efficient and eco-friendly strategies for assuring the source of n-3 marine fatty acids, it was quite an interest of a speaker at the recent cardiovascular epidemiology meetings, the health effects of various health policies in the UK. And he had not made a recommendation on fish and was asked that question in the discussion period. And it really dealt with this issue, that the feeling was that they recommended to the British Isles population to increase the intake of fish that they would deplete the entire region of fish sources. So I think the

fish while an efficient and eco-friendly strategy for the supply of fish is a very important one when we start talking about these recommendations.

DR. NICKOLS-RICHARDSON: This is Shelly. I have a question, and I do understand the emphasis here on food based sources of DHA/EPA. But did the Committee look at some of the supplements, trials, anything? Does the fish recommendation with the 250 milligrams per day equate to what the supplement studies were showing?

DR. RIMM: That is a good question, Shelly. The supplement studies are little more challenging, because they don't have - they are not like supplement studies that have a beautiful dose response across the range. Most of them give quite a fair bit, and most of them are giving a gram or more. So it's more challenging to look at a threshold effect below that.

But I think in the back of our

mind when we are writing the conclusion statements, we are knowledgeable about the relatively strong evidence for the supplements for the trials at higher levels. But I think if all those had found no association we would definitely not be as comfortable giving the conclusion about n-3 from seafood. The point is that I think we want to recognize that fish is not just a source of n-3. It's also a good protein package, as well as - contributes to other components of the diet, so that is why we wanted to focus on fish. But I do appreciate the fact that the supplement trials exist.

DR. NICKOLS-RICHARDSON: Okay, and we will address that with nutrient adequacy, but I just wanted to get your sense of looking at those trials, what - how did the levels sort of stack up there?

DR. RIMM: Yes, they don't make supplements across the whole range.

DR. NICKOLS-RICHARDSON: Yes.

DR. APPEL: This is Larry to follow up on that question. I did read the conclusion and then compare that to the question, and it - the question deals with marine n-3 fatty acids, and the conclusion is seafood, but I'm just wondering if you should change it to seafood, because I think that as you pointed out Eric, you do have like the GC Prevention that shows a benefit from the supplements. And I think your conclusion is really more based on the food.

DR. RIMM: So what are you saying we should change?

DR. APPEL: Well, it says - the seafood-derived fatty acids. You don't really - you could have two types of conclusions, one for seafood and one for the fatty acids. Your conclusion is really the seafood and not the fatty acid.

DR. RIMM: Yes, I guess so we should say n-3 - seafood containing n-3 fatty acids, throughout --

DR. APPEL: Yes, and potentially drop the --

DR. RIMM: Seafood derived?

DR. APPEL: -- seafood derived fatty acids from your caution, because that is not what you are testing here, or at least that is not your statement in your conclusion.

DR. RIMM: Yes, that's a good idea. Shirley, can you make note of that. I think you are right. We went back and forth on this, and then really consciously said, look, we're talking about this as a dietary guidelines; we're talking about food. And I don't know how the seafood-derived snuck in there unless - but you are right, I mean most of the supplements are seafood-derived supplements, so we should not - we should take that out I guess.

DR. APPEL: And you would reach an Evidence I conclusion I think at least in those with CVD for that one.

DR. RIMM: Yes, I mean the

problem is, there are not a lot of trials on fish; that's why I think we backed down to Grade II. Because there is a lot of observational data. Some trials are shorter term on a few. But to do a long term trial on randomizing people to fish per se, there are some on fish advice, but that usually invites and includes other things. And that's why we shied away from it. But I'd be happy to call it a Grade I if everybody felt the evidence was strong enough. I mean I think that's what the 2005 dietary guidelines struggled through.

DR. APPEL: Yes, no I think your Grade II is fine, but I - the way I would deal with it would be to just drop seafood-derived fatty acids from your question.

DR. RIMM: Thanks.

DR. APPEL: You're not saying omega 3 or omega - you're talking about fish.

DR. RIMM: Great.

DR. THOMAS PEARSON: There clearly is an assumption that this is the

intermediary mechanism, and obviously there are many other things - taurine, and a variety of other - selenium components, et cetera - that it is in the fatty acid section rather than the protection section because of that just to point out -

DR. POST: This is Bob Post. I've got a clarification request for Tom, and this goes back to the slide on n-6 PUFA implications.

DR. THOMAS PEARSON: Okay.

DR. POST: Specifically the first bullet. It's a rewording. It might be stated backwards. So we are suggesting, all recommendations assume an isocaloric replacement of saturated fatty acids or trans-fatty acids with PUFA. That's the more correct way of stating the first bullet.

DR. THOMAS PEARSON: Okay, we will make a note of that. I see what you mean.

DR. POST: Great, thanks.

DR. THOMAS PEARSON: Okay, let's move on. And our next topic is a new one, we go on to, and that is to look at fatty acids from seafood on breast milk composition, and infant health outcomes. This is a new question, but one which I think as you will see from Roger Clemens when he presents this is, we've got a lot of evidence in support of it. Roger.

DR. CLEMENS: Thank you so much, Tom, and thank you so much, Eric, and the entire fatty acid team.

This is very important topic. It's received a great deal of attention from the public. It's obviously received a great deal of attention and questions from the medical community. So we thought it was important that we started providing direction and guidance on this particular issue. And certainly maternal diet.

And you will find that as we look at the kinds of data that we think we

actually see consistency across the board relative to recommendations in terms of accuracy, I think fatty acids as well as the food safety issue, and that food safety issue will be addressed tomorrow by our colleagues Rafael.

Obviously maternal diets containing n-3 fatty from seafood that was investigated across the last 10 years. We are looking at the healthy population of pregnant and lactating women, and certainly went to examine the mother-infant pairs. We examined several RCTs and controlled studies, meta-analyses, very systematic reviews. Hopefully feeding periods of more than four weeks. The four weeks was chosen because that's when you begin to see some differences metabolically. Obviously sample size of greater than 10 are consistent with our original criteria.

And the exclusion criteria not to confuse and in an attempt to separate the use of food versus that of dietary supplement that

contains the various n-3 fatty acids, and of course across the board we've excluded various cross-sectional studies that might be published. Next slide.

So in review of the evidence we examined nine studies, seven of which were prospective cohort studies. We have a balance there of one RCT and one meta-analysis.

And the balance here there were a couple of positives and most of them were neutral including the RCT, yet in the meta-analysis we see a positive association which we indicate in the next graphic. This graphic indicates the distribution and the type of outcomes that have achieved great attention. Most of the attention has been directed to visual acuity and neurological development, as well as a variety of biomarkers such as methyl mercury and the risk benefits associated with consuming fish and relative to the exposure of methyl mercury and the n-3 fatty acid analysis. And throughout the RCTs and the

meta-analysis again we are looking at cognition, visual acuity, as well as when we come to women who are nursing their children, we want to look again at the impact on the composition of breast milk and how that composition can be changed by fish consumption, and obviously through fish consumption the end that changes the composition relative to DHA and relative to n-3 fatty acids.

Next. Based on those studies we see that in fact we have increased maternal dietary intake of long chain fatty acids, particularly n-3, and particularly DHA from two servings of seafood a week. That goes out to the three to five ounces twice a week to which Eric referred. During pregnancy and lactation is in fact associated with improved infant health outcomes, such as we measure visual acuity and neurological and cognitive development. And we also we might expect, and we do see it, an increased DHA levels in

breast milk.

Based on the evidence we have right now we believe this is a Grade II. These kinds of today's the word is Grade II. Next.

And that's it.

DR. THOMAS PEARSON: Let me just point out, Roger is going to be back with our seafood modeling question later talking about what diets with this two servings a week might look like, and so there will be some further comment on this. Is that fair, Roger?

DR. CLEMENS: That's' fair to say. Thank you.

DR. THOMAS PEARSON: Questions?

DR. PI-SUNYER: Roger, I just have a comment on your wording here. Shouldn't you put it improves infant health outcomes, shouldn't you put during pregnancy and lactation showing that the increased DHA levels in breast milk and then go on to say that that risk is associated with improved

health outcomes? Isn't it backwards? I mean the mother eats the food and it gets into the breast milk and then it gets into the baby and then it causes improvement.

DR. CLEMENS: That is a good observation. Thank you so much, and I will certainly make that adjustment.

DR. APPEL: This is Larry, and this is really interesting to me, but I am also trying to process this in comparison to the other databases where there is a lot more evidence. This comes across as a pretty strong conclusion, I know it's Grade II. I mean are these - we haven't drilled down on the individual studies - they are not clinical trials, but are these cohort studies well designed with potential confounders dealt with? I think this potentially could get a lot of attention the way this is worded?

DR. CLEMENS: I really believe we are, Larry, and I appreciate the remark. These kinds of studies, we went back 10 years

as you saw, I had worked in this particular area for 20 or 30 years, as you have in your particular area of expertise. And this is consistent with all the data if we were to go back even 20 or 30 years, and most of the attention has received a great deal of research effort in the last 20 years, so we examined this the last 10 years. So this is consistent with the data presented in the IOM report, and all the other reports that we reviewed for this particular question.

DR. THOMAS PEARSON: I just wanted to emphasize just recently the WHO and some European bodies have weighed in on this, again on the basis of recent strength of the evidence, in further statements really just in the last six months or so.

DR. CLEMENS: Indeed, the pharma group, the EFSA group out of Parma, Italy, certainly weighed in on this. And this statement is actually supported by the European group on this particular issue.

DR. NICKOLS-RICHARDSON: This is Shelly again, just the same sort of question about the supplement trials. I think my understanding of the supplementation trials is that the level is a little bit higher, 300 to 500 milligrams of DHA per day. So again did you guys look at some of that supplement data, and I understand again dropping that because you want to look primarily at the food first, and I am very supportive of that. But just in terms of evidence, and how that fits with the supplementation and making the case for food versus supplementation during pregnancy and lactation.

DR. CLEMENS: I certainly appreciate that, Shelly. And frankly we've really focused on the food outcomes. We really try to tease away the implications that it might have on the dietary supplement side. Clearly as Tom and Eric have indicated, there are many many studies that have been conducted with supplements, and many of those

supplements it is nicely stated that they were in fact conducted with doses much higher than this.

DR. NICKOLS-RICHARDSON: Okay.

DR. NELSON: Shelly, it seems like in our conversation yesterday in our subcommittee that this is in agreement with the supplement studies as well. As he said, it's higher in some of the supplement studies, correct?

DR. NICKOLS-RICHARDSON: Yes, and again I think it will be consistent and these two pieces will hang together. And again I do want to advocate the total diet, the diet approach first, but also recognizing that, if the benefit is really from a little bit higher level, then what is the balance in the fish consumption related to some of the health risks related to heavy metal.

So I just want to make sure that the food recommendation fits with the key outcomes from the supplement trial so that we

are recommending a level in food which is equivalent and would provide some benefit.

DR. THOMAS PEARSON: I think the food safety group on which Roger also sits, and I think Rafael is going to comment on this later, but also with the seafood modeling exercise, I think it all does fit together, and as the two days come together, I think it is going to be very clear that we have all talked together and think the benefit-to-risk ratio is in favor of fish consumption. And some of the food modeling provides us insights as to what that diet would look like.

DR. RIMM: This is Eric. Larry, I think you have a really important question, because we don't want to make a strong statement without being able to back it up. And I think it's actually in the accounting for the heavy metals and other covariants that the signal really comes through stronger, like in the Project VIVA study that Emily Oken has been working on for some time, the beneficial

effect of the n-3 fatty acid on fine motor skills and other outcomes is somewhat muted, and then you account for mercury, and you can see the n-3 benefits are a bit stronger because there was a slight positive effect from mercury. So I think overall you're right, not every study does a great job of dealing with covariants, but I think there are a large number of them that carefully control for potential confounders.

DR. WILLIAMS: I think the vast majority of pregnant women now get their n-3 fatty acids from supplemental drugs.

DR. CLEMENS: Christine, Rog. Yes, indeed. That has been my experience as well, Christine. It seems that the medical community has said, if it contains any methyl mercury in the fish, they advise the patients and moms wannabes to not consume any fish whatsoever, and at the same time, then the physicians and the patients and consumers started examining the dietary supplement

world, and do they come, do they screen even for methyl mercury. And the answer is no, typically. And Rafael will actually address some of these very important issues on the risk-benefit and the issues associated or surrounding the methyl mercury issue.

DR. WILLIAMS: Would it be preferable for women to get their n-3 fatty acids from places rather than the supplements? Is that what you are suggesting?

DR. CLEMENS: No, it's not what we are suggesting. We really recommend that we get them from food. To Eric and Tom's earlier remarks, certainly fish are more than just n-3 fatty acids. There's a hope - this is important for natural development. For instance, for better nutrition for mom.

DR. APPEL: This is Larry. I think there are going to be a ton of issues that this conclusion statement raises. This is one of those where we probably should have an implication slide or statement. Are you

guys planning that, or were you planning on sort of bundling that up after the food and safety discussion?

DR. THOMAS PEARSON: The implications, I think we could add that.

DR. APPEL: Because I think the food versus supplement source is going to be an important one and at least a cross-reference to the mercury issue.

DR. NELSON: This is Mim. I think that it will be important if we do that, and I agree that we need to have an implication statement, that we need to - because this is, the supplement is dealt with in the nutrient adequacy subcommittee, and the food is dealt with here, in this chapter, I think if we do have an implication statement that we need to make sure that it's coordinated in one, as opposed to two different ones.

DR. CLEMENS: We certainly agree with that, Mim, and we've done that, we

examined the data across fields. And as a matter of fact in this particular case the fatty acid team has been working with the food safety team to address this issue on methyl mercury, and the other teams have done similarly on related questions.

DR. NELSON: Yes, so, Shelly, somebody just needs to make sure we keep track of that.

DR. NICKOLS-RICHARDSON: Yes, this is Shelly again, and I know this will bring up some more discussions tomorrow, because I think that this pregnancy/lactation is one of those times during the lifespan when we are going to at least from nutrition adequacy suggest that supplementation may be important. Just so you are prepared for tomorrow and maybe think about it overnight. So reflect a little on that, because we certainly want to propose this consumption for DHA as well as other nutrients.

DR. CLEMENS: And to your point,

this is the first time we've gone beyond - or younger than two years of age, and we are addressing a very important topic of course, that is, the health of moms and mom wannabes. And the impact of their health on infants, and Christine can chime in and sort of reinforce that issue.

DR. THOMAS PEARSON: I'm coming to the time. I think what we should do is go on to the next one, and I think there will be some opportunities with the seafood modeling later if there is further discussion.

The group felt we had considered a number of foods, whole foods, high in fats, and a number of these have been elsewhere. And so we were going to cover two of them here, nuts and chocolate.

So the first question here is, what are the health effects related to consumption of nuts? The search criteria you can see here has gone back to 2004, the NEL and then the 2003. Children and adults, down

to age two, healthy populations, again, limiting it not to include cross-sectional studies, so it's randomized controlled trials and prospective studies and meta-analyses, eating period of more than four weeks and sample size of greater than ten, as we had before. And the health outcomes included both cardiovascular disease endpoints as well as blood lipids and lipoproteins, measures of glucose intolerance and insulin sensitivity in type 2 diabetes incidence.

The interesting part of this evidence is that nuts is obviously a whole family of foods, so there are some studies which just talk about nuts in general, and a variety of nut types, and then there are others particularly focused on specific nuts, in which case, in this slide, almonds. So for nuts including peanuts there is one systematic review, five cohort studies and one randomized trial. For almonds there are three randomized trials and one meta-analysis.

And just to say, there have been 17 studies all in general including many on some of the other types of nuts. So here is the walnuts, systematic review of three randomized trials; macadamia, one trial; pistachio, two randomized trials. And then some of the other nuts may be represented in their analyses.

So it's a bit of a diverse evidence, particularly with the possibility of nut-to-nut variation that one may expect on the basis of their fatty acid composition et cetera. Next slide.

Here are some of the health effects related to nut consumption, and this includes peanuts, which of course would be frequently consumed not only as peanut butter but also peanut oils, et cetera. Generally what you can see is many of these prospective cohorts compared to low consumers with the times consumption per week, so the quantification of nut consumption obviously is

not only frequency but also quantity in general, which you can see in the increased consumption of nuts is related to reduced clinical outcomes, cardiovascular disease in particular, but also metabolic syndrome, et cetera. And also an inverse relationship to LDL cholesterol and total cholesterol.

And just to note the one systematic review from earlier had 23 studies, so there is a reasonable literature particularly on all nut consumption.

Similarly with almonds, what you have is with intermediary metabolites decreasing total LDL cholesterol, one study had also I think decreasing cholesterol, you can see with particularly the intermediary metabolites there, the favorable effects of almond consumption. Next slide.

Similarly to walnuts, particularly with lipid endpoints, some discussions of weight also in the last randomized trial. The one study on macadamia nuts, obviously you had

some lipid benefits in pistachios as well. Next slide.

So our draft conclusion statement is the consumption of unsalted peanuts and tree nuts, specifically walnuts, almonds and pistachios, within an energy-balanced diet, has a favorable impact on cardiovascular disease risk factors, particularly serum lipids. We gave that a Grade II. One of the adjectives here is the unsalted with, as we will talk about the implications, is this is frequently a food which is served at least in snack forms with added salt, and there wasn't any discussion of those in most of these trials, so the assumption is that the evidence base had to do with unsalted peanuts and tree nuts.

So if one were to look at the range of consumption the nut consumption is in the form of peanuts, and this is an important source of plant protein and other nutrients in addition to its oil, so it, I think, is an

important issue to look at and perhaps make recommendations about, and as we had said before, many nuts are sold with added salts, and obviously the limiting to unsalted nuts would be a way to limit sodium intake.

Many of these trials were over short periods of time, with intermediary endpoints rather than clinical endpoints. So it would be helpful to have longer studies with health outcomes. And trying to make distinctions between the types of nuts. Many of these trials were funded by industry, and so it would be well to have a broader and more general comparison of the various nut meats to look at health benefits.

Discussion on nuts?

(No response.)

Okay, why don't we go ahead, I want to go on to chocolate, watching our time here. And a similar question is, what are the health effects related to consumption of chocolate. Next slide.

The inclusion criteria went back to the year 2000, and both healthy and at-risk individuals, again excluding cross-sectional studies, same criteria as we have used in the past. Thirteen studies over this 10-year period were identified; three reviews with meta-analyses, eight randomized controlled trials, one cohort study and one population-based case control study. Next slide.

Here you can see the evidence of both the intermediate markers - may of those were lipids - as well as cardiovascular disease outcomes, and among the reviews, particularly the Ding et al, was a - included a larger number of previous studies, and a lot of the section on particularly the flavonoids in chocolate having a benefit on CHD and MI mortality, particularly with some use of high flavonoid versus lower flavonoid forms of chocolate, but also there was evidence that there are intermediate markers particularly the lipids and lipo-proteins.

The one study by Hooper looked at flow -- diameters of vascular flow measures as an intermediate measure, and there was the Desch study looking at cocoa chocolate improving blood pressure.

In terms of the randomized controlled trials, you can see again the serum lipids, blood pressure, blood flow information, and generally a number of positive studies showing improvement with chocolate or cocoa, and there are two observational studies with one neutral and one positive quality with a relationship of cocoa and chocolate consumption improving - associated with reduced CHD/MI mortality.

So the draft conclusion statement is that there are health benefits associated with moderate consumption of some types of dark chocolate or cocoa, that would be Grade II evidence. Next slide.

The number of implications here, many of these beneficial effects of chocolate

have been attributed to the polyphenolic compounds in the discussions of these papers, et cetera. There is also obviously an interesting fatty acid distribution in chocolate with high amounts of stearic acid. So really many plant foods contain polyphenols, and chocolate is really a minor source of it when you look at the whole diet. This is a full fat food, and so potential benefits obviously need to be balanced with caloric intake. It's very clear that particularly from a research standpoint making sense of the data, formulations in chocolate are known to have polyphenolic profiles, and that is the mechanism. And different forms of chocolate may confer different benefits. And you should always keep in mind that this is - the number of calories involved, the chocolate is currently a small component of the total diet, and any benefits from the food is likely to be minimal.

DR. NELSON: Tom?

DR. THOMAS PEARSON: Yes.

DR. NELSON: This is Mim. Can I ask a question?

DR. THOMAS PEARSON: Sure.

DR. NELSON: Or if you want me to wait, I'm happy to.

DR. THOMAS PEARSON: That's fine.

DR. NELSON: The conclusion, I think it was the slide before, about moderate amounts of - that there are health benefits. I think that as we have done with the other kinds of conclusions that within calorie limits, or something like that, I mean I'm worried about a conclusion statement like this then you know, if it's not weighted a bit with being careful about calorie intake, because a lot of the chocolate has a lot of calories and sugar as well.

DR. THOMAS PEARSON: A lot of the studies were isocaloric. And certainly in our implications slide we felt the need to make this point as well.

DR. NELSON: Where is it in the next slide? I mean it was more that it's a small amount. I think maybe it's in the implications that it needs to be balanced - okay, there, got it.

DR. THOMAS PEARSON: It's an important point. Very high density of calories.

DR. NELSON: Yes.

DR. PEREZ-ESCAMILLA: This is Rafael. What is known about the impact of saturated fat in chocolate vis-à-vis saturated fat in animal products in relationship to cardiovascular disease rate?

DR. THOMAS PEARSON: We - this actually harkens back to something we have presented previously relative to stearic acid and the concept of cholesterol-raising fats. Again, there are a variety - there is a range of fatty acid distributions, but particularly if you are talking about dark chocolate with relatively little milk fat in it, you are

talking about cocoa butter having upwards of 40 - 50 percent of its fat as stearic acid. Stearic acid again, and this goes way back to Ansel Keys and the early studies, really as we had mentioned before does not have the metabolic protective rate on the LDL cholesterol that the other fats that are solid at room temperature have, and so though it is - if you were to use the old definition of saturated fat, it would be a high saturated fat compound food, but in effect, if you look at the cholesterol-raising fats of chocolate, again, upwards of half of it is stearic acid which in fact is not a cholesterol-raising fat; does that help?

DR. PEREZ-ESCAMILLA: Thank you very much.

DR. APPEL: Tom, this is Larry. I just wanted to follow up on Mim's comment. I look at the implications in the draft conclusion, and I'm a bit worried, because if you go to the last line of the implications,

you state: chocolate is currently a small component of the total diet and benefits will likely be minimal. I think - I don't want to wordsmith, but it sounds as though it's a small component, and because it's small, benefits will likely be minimal. And I go to the conclusion statement that moderate consumption - and it seems like I need to increase, because the benefits are small - or minimal because it's a small amount of the diet now. You might even want to just drop the word, moderate, because I think people are going to view that as increase.

DR. THOMAS PEARSON: I think one is the evidence, and one is the particularly randomized trial evidence, again, derived in the evidence based conclusions, versus the other one which has to do with more of population based information.

DR. NELSON: It gets tricky. This is Mim. I just think it's a bit tricky here. I think also, what is - I mean what is

moderate consumption? It is sounding like we are trying - the implication is - I know it sounds a little - it sounds like we are trying to get people to eat more chocolate.

DR. APPEL: I agree; that's what it sounds like.

DR. THOMAS PEARSON: A lot of the randomized trials used, in a variety of forms, more chocolate than would be ordinarily consumed.

DR. NELSON: Right, and that may be just a little bit unreasonable.

DR. THOMAS PEARSON: Yes.

DR. APPEL: Then you could put that in the discussion. But I really worry about this moderate term in the conclusion. You could just leave it as consumption, then talk about the range of distribution when you talk about the articles.

DR. THOMAS PEARSON: Yes, I think we could just talk about consumption, how many times a week, rather than the grams or

whatever.

DR. APPEL: Or not even get into dose in the conclusion. I just think there is a risk with this one more so than others.

DR. NELSON: I agree.

DR. CLEMENS: This is Rog. I think Tom did a nice job of summarizing the data. I think it's important that we also understand when the term "dark chocolate" was used, that not all dark chocolates are created equal, and certainly to Tom's comments on the polyphenolic content, that is clearly dependent on how it's harvested, how it's fermented, and how it's processed.

DR. THOMAS PEARSON: Right. Okay, I think we have to watch our time here. And let's move on, and Roger is going to help us with the next topic, and that is the ruminant versus industrial *trans* fatty acids. Roger.

DR. CLEMENS: Thanks very much, Tom.

This basic question about *trans* fatty acids was addressed in the 2005, the 2005 document did not differentiate the ruminant versus industrial *trans* fatty acids. With this becoming more of a question from consumers and amongst the medical/scientific community we thought it was incumbent upon us to look at what data are in fact available, hence the question, what effect do the consumption of ruminant versus synthetic or industrially produced *trans* fatty acids have on various biomarkers relative to lipid metabolism and cardiovascular disease.

In fact we find that many people don't even know that there is a difference, in fact that there are these things called naturally occurring fatty acids, *trans* fatty acids in foods. As we look at the next chart, you will see here based on some data that we were able to pull out thanks to our wonderful team that these are the typical *trans* fatty acids in a variety of products. These

products - in fact the *trans* fatty acids in these products are typically we could call it an industrial or synthetic fatty acids that are based on hydrogenation process.

Next. So as you look at the kinds of studies that we examined in the last 10 years, because it was not addressed in the last dietary guidelines, we went back to 2000, we looked in those studies, as criteria from two years of age to adults, and we looked at various outcomes for includes criteria, cardiovascular disease, metabolic syndrome, and so forth, and the kinds of studies are consistent with our original inclusion criteria.

Again, the exclusion criteria were the same as we did for all of our particular charges. The health outcomes that we chose were consistent with, we examined the entire fatty acid scheme, that is, the biomarkers associated with lack of protein levels. Next slide.

As we look at the evidence from the last 10 years, interestingly enough, there are only three studies, two of the studies were RCTs, those two studies were positive, and one systematic review was somewhat negative.

And what's really important here as we look at the overt, at face value, you would say, well, looking at coronary heart disease endpoints we show no difference between the ruminant and industrial *trans* fatty acid. However we have to examine this a little bit more closely. And as we examine this more closely we realize in fact the levels of the ruminant *trans* fatty acids are seven to 10 times what you and I would consume in a normal diet. So let's look at the next slide, please. And these are the three studies that we examined. And in each case it was the levels that we were looking at -- times the amount of *trans* fatty acids. These are very carefully designed, carefully

designed products, because these things do not occur normally at this concentration. That effect, we had to look at these outcomes. And in each case we saw that while we had LDLs increased in the Chardigny study, and the small studies there, and we looked at the other RCT study, Motard-Belanger. Again, the LDLs tended to be higher. We also took a look at the HDLs; HDLs tend to be lower. And yet we look at the non-systematic reviews and look at the variety of studies, and they seem to corroborate that the effect on lipids and *trans* fatty acids relative to the sources were not differentiated, as in fact the most significant difference.

So on the outside we would say that there aren't any differences. Well, let's take a look at what we might say next. As we look at this conclusion, there is little evidence for substantial biological difference, of detrimental effects between the two sources of fatty acids. However, the

evidence does not suggest an appreciable effect on health in ruminant *trans* fatty acids on the average current intake by the population of approximately .5 percent. That is really critical. Those studies had doses from about seven to 10 percent - excuse me - about 5 percent of the energy level, which obviously is 10 times what we would normally consume. Based on those three kinds of studies, including the meta-analysis, would give us a Grade II.

Comments. Implications, here we go. Clearly this is consistent with what we - what it was last time we said in the dietary guidelines that truly industrial *trans* fatty acids should be eliminated. And clearly we have seen that across the country and throughout the food industry and baking industry. Again because ruminant *trans* fatty acid includes such a small amount of calories that are unlikely to provide any effect in terms of the clinical outcomes that were

assessed, that is on serum lipids and lipoproteins. And ruminant *trans* fatty acids, normal constituents of dairy products and in meat products, and therefore obviously a complete removal of ruminant *trans* fatty acids would obviously restrict the nutrient contributions of these kinds of foods to the total diet.

Recommendations: we certainly see that - we would agree that more research in this area is required to look at the impacts of ruminant *trans* fatty acids relative to industrial fatty acids relative to cardiovascular disease or any other type of chronic disease risk.

Comments?

DR. THOMAS PEARSON: Discussion? No one here is surprised that they are differentiated, Tom.

DR. FUKAGAWA: Can you hear me? Can you hear me?

DR. THOMAS PEARSON: Yes, go

ahead.

DR. FUKAGAWA: This is Naomi. I'm having problems with sound. But since we are saying that industrial *trans* should be eliminated from the American diet, why would we want to study it further?

DR. CLEMENS: We want to study it further relative to the ruminant to see if in fact even at the levels we recommend, Naomi, would they have any impact. Right now the data suggest that they would not have an impact.

DR. FUKAGAWA: Industrial or ruminant?

DR. CLEMENS: Ruminant.

DR. FUKAGAWA: Ruminant, oh you mean testing ruminants at the level that we are now consuming?

DR. CLEMENS: Yes. As you know a lot of the data came out of Wisconsin, and you may recall the data by Mike, and we need to examine that. We certainly see that being

used, Naomi, in a lot of livestock applications, in terms of animal feed. What happens in terms of when, those kind of products we see, if they have any impact in terms of our biomarkers in terms of cardiovascular disease or any other types of risk.

DR. FUKAGAWA: Okay.

DR. THOMAS PEARSON: Roger, if the average --

DR. CLEMENS: And it is complicated because there are so many isomers of these naturally occurring *trans* fatty acids.

DR. FUKAGAWA: Exactly, so is that perhaps what one would want to investigate?

DR. CLEMENS: I think at the end of the day the answer would be yes.

DR. PI-SUNYER: Roger, even though .5 percent is taken by the population as a whole, are there a significant number of

people who are very big meat eaters who would get significantly more than this? And for whom it might be a risk?

DR. CLEMENS: That is a really good question, Xav. There was actually one study that we looked at, it was at .7 percent of the energy, and the conclusion of that study indicated that there wasn't any apparent risk at that level. Clearly to your point as well, there may well be some outliers in the general population. Yet for the general population the .5 percent seems to be the normal intake and consumption level, and without any apparent risk.

DR. THOMAS PEARSON: Roger, I think we need to move on. We have a few modeling pieces, so let's move on to the food pattern modeling. And we had three questions, each of them very helpful, particularly in discussing the implications of some of our questions previously.

The first one talking about

saturated fatty acid modeling, looking at the impact of food choices and overall nutrient adequacy, when you limit cholesterol-raising fatty acids to less than 7 percent of total calories and less than 5 percent of total calories, cholesterol-raising fatty acids here, operationalized as total saturated fatty acids minus stearic acid. So stearic acids are about 2 percent of calories in the diet.

And the food patterns that would meet all of the nutritional goals within the caloric limits obviously has to do with using lean ground beef, low fat or fat-free cheeses, and baked chicken without the skin.

The next slide shows the various models, across a variety of calories and fatty acid patterns that you see here that were used in these models. Next. And the summary from our modeling team is that the USDA food patterns include foods only in nutrient-dense forms without excess solid fats. So the small amounts divided equally between calories from

solid fats and calories from added sugars is included. A small amount of discretionary calories is available, therefore, with these models, and the current patterns have 8 to 9 percent of calories from saturated fats and 6 - 7 percent of calories from cholesterol-raising fats.

And basically the - if you are going to then reduce cholesterol-raising fatty acids further, you would have to replace all solid fats isocalorically with oils, and you could then lower cholesterol-raising fatty acids further to 5 - 5.5 percent of calories and total saturated fats reduced to 7 percent. So just to give an idea of the modelings within the nutritionally adequate ranges.

Why don't we move on to the cholesterol modeling, and we'll take all the modeling at the end here. What we also had was looking at food choices and nutrient adequacy if you were to limit dietary cholesterol to less than 200 milligrams a day.

Again this is some recommendations for a high-risk patients with coronary disease, hypolipidemia obviously has this recommendation.

Here you can see the methods that were used. The amount of cholesterol at the base food patterns in each calorie level; the amounts of cholesterol in each food group, then selecting the foods to modify, revising the amounts in the food groups to reduce the cholesterol, identify levels of cholesterol and calories in the revised food patterns. And looking at what nutrients changed and what didn't change, and which nutrient goals were met or not met.

And the next slide is just the calorie levels again with the energy and cholesterol contents with each of the patterns. And the USDA food patterns then includes only nutrient dense forms without excess solid fats. And across those caloric patterns from - that raises from 92 at 1,000

to 290 at 3,200 calories per day, and therefore cholesterol levels can be reduced to less than 200 milligrams per day by limited eggs to less than two per week; reducing meats and poultry; and substituting some oils for solid fats.

So certainly the suggestion is that this would be doable. If you give them that there would be reductions in protein; also choline. I might see even at the baseline that this did not meet the allowance recommendations from the IOM. Also Vitamin A and Vitamin D, the fat soluble vitamins, would be reduced, and EPA and DHA. Those same changes would increase Vitamin E with the increased oils in nuts, which would still be below the RDA for most foods.

So I think the point with choline and Vitamin D, they are below the recommended levels to begin with, and this would take them even lower. So a diet can be constructed at less than 200 milligrams per day of

cholesterol. The low cholesterol diet would have further reductions in several nutrients, particularly choline, vitamin D. And the restrictions in cholesterol intake to less than 200 milligrams per day should target subgroups at high risk of cardiovascular disease or type 2 diabetes, given the limited general population data on benefits.

Okay, and Roger, do you want to talk about the seafood modeling?

DR. RIMM: I think it's me. Eric.

DR. THOMAS PEARSON: I'm sorry, right.

DR. RIMM: So this is another what-if scenario given the fact that we think there is strong evidence to suggest that 250 milligrams per day of n-3 fatty acids is beneficial. We wanted to look at what is the impact on nutrient adequacy of increasing seafood in the USDA food patterns data. And we had three scenarios.

And thanks to several of the staff including Kelly for bringing together the food safety people with the fatty acids people with a few other groups to look at this. And here are the three patterns we looked at, where four ounces per week of seafood high in n-3 fatty acids, that's EPA and DHA, so call it the HI3 group.

And what happens if you have 8 ounces per week of seafood, including seafood both in a low n-3 and high n-3 classes? And in this we looked at the distribution based on NHANES data, and we used that same proportion. So assuming that people had 8 ounces per week, or two servings per week of low and high n-3 fatty acids.

And our final choice was, what if individuals had 12 ounces per week of seafood low in n-3 fatty acids? So that is three servings per week. Ironically we're coming upon lunch, so I'm sure we are all hungry.

For this we used amounts of

seafood and the USDA food patterns were increased at four, eight and 12 ounces using the 2000-calorie reference level by substituting for meat and poultry. So four ounces of HI3, all the seafood is HI3, and low three fish is set to zero.

For the second scenario, 8 ounces of LO3 and HI3, using the current ratio of LO3 to HI3 in the population.

The third scenario is 12 ounces of LO3. All seafood is LO3, and HI3 is set to zero. The amounts of eggs, nuts, seeds and soy products are held constant. And the amounts of solid fats in the patterns were not modified either. Next slide, please.

So the amounts of food subgroups in patterns adjusted using the same proportions as in the 2000 kcal patterns. And we then assessed the nutrient adequacy of food patterns, compared to the RDAs from the IOM report of 2006, and there is no RDA for EPA or DHA, so the amounts were compared to base

patterns. Next slide.

And you can see here there are several different scenarios. The first column is the base USDA pattern, and then we have the servings of meat, poultry, high-fish, low-fish, eggs, soy products, nuts and seeds, and then there is a total at the bottom.

And each column then -- columns two, three and four, are what happens when we substituted the seafood at the three different levels. And you can see the ounce equivalents per day for each of these. So meat went down a little for column one, more so for two and three. Same for poultry. And then you can see the other things are not changed. Eggs, soy, nuts and seeds are not changed. So overall at the bottom you get the same ounce equivalence. It's just that we are consuming more fish that has differing levels of n-3 fatty acids.

Next slide. So what results of this found is that we didn't get substantial

change in energy, protein, carbohydrates, or total fat, nor was there substantial changes in cholesterol, saturated fat, MUFUs and PUFAs.

We did, because fish contain selenium, vitamin D, and B-12, we do get a slight increase in those metals and micronutrients. Next. So overall for the seafood modeling summary, the amounts of seafood in the USDA food patterns could be increased to the levels specified without any negative impact on nutrient adequacy, and overall using these patterns what we've found is that we would achieve that level of DHA plus EPA per day of 296 milligrams in the high-3 group; on average we have 259 milligrams in the middle group; and even those people who had three servings of low-3 fish we would achieve the levels of 250 milligrams per day EPA and DHA. Next.

Ah, yes, so for this particular analysis we did not include methyl mercury.

Contaminants are not part of the NHANES nutrient composition database, so we are going to have to rely on Rafael's report on that. The seafood species of interest could not be identified, and the amounts of these species in the patterns were estimated to come to the low-3 fish and the high-3 fish. And of course the analysis did not address vegetarian diets. That would take a bit more work and be focused on the vegetable sources of n-3 fatty acids. And I believe that is it. Are there any questions for any of us?

DR. THOMAS PEARSON: And the modeling questions, open for brief discussion?

Okay. I think we are a little bit past our time. I want to thank everybody for their good comments and lively discussion, and I think we can turn this back to Linda.

DR. VAN HORN: Excellent job, Tom, Eric, and your whole group; that was really wonderful. And I suspect that discussion was just halted by the confluence

of peoples' stomachs at this point. I'm sure there will be more discussion, but it was great to hear and see the deliberations of your group. Really excellent.

So with that I just want to thank everyone for your patience thus far. We are now ready to take our lunch break, and we will return in one hour. We are supposed to start again at 2:15 Eastern time. So please be back by then. Thank you.

(Whereupon, at 1:25 p.m., the proceedings in the above-entitled matter went off the record and returned at 2:18 p.m.)

DR. FUKAGAWA: In the interest of time, I'd like to just launch into the next reports from the Energy subcommittee that was chaired by Dr. Xavier Pi-Sunyer.

Xav?

ENERGY BALANCE SUBCOMMITTEE

DR. PI-SUNYER: Yes, hello. So we are going to divide this presentation, and each of us on the subcommittee is going to

take a different portion of it. I think what we should do in the interest of time is let whoever is talking go through all of their questions, and then we'll open it up for questions after each - at the end of each speaker, but not in the middle of it.

These are the questions that we've addressed. And the first one is, what effects do the food environment and dietary behaviors have on body weight? And the chair of that particular question was Miriam Nelson, and she will come on now to discuss that question.

Mim.

DR. NELSON: Sure, thank you. So this is the series of questions that we are going to be addressing today are ones that we haven't addressed before, so it complements the full chapter.

So my charge, working with the very able USDA staff, Eve and Julia and others, was to look at the food environment, body weight and we put in vegetable and fruit

intake here although the main focus is on body weight, but this came out of the review.

So a little, just a tiny bit of background. As we all know the overall food environment has changed. There are many more places to buy and consume food. And in fact the number of commercial eating places has gone up about 90 percent since 1972. The number of fast food restaurants has gone up by 147 percent. The percentage of meals eaten away from home is about 150 percent up. So things have really changed. There is less availability of healthy foods in urban and low income areas, the so-called food deserts. Foods are consumed in a variety of different places, and the food supply is quite different, and we've spoken about that in many of the other sessions.

But increased availability of calories, sweeteners, refined grains, processed vegetables and fruits, cheese and chicken, those are the things that have really

increased, with a decrease in fluid milk, and fresh vegetables and fruit. Next slide.

So for the environment the proposed conclusion is with a Grade of II for BMI and a Grade of II (moderate) for vegetable and fruit intake around the food environment. There is substantial evidence that indicates that the food environment is associated with dietary intake, especially less consumption of vegetables and fruits and higher body weight. Availability of healthy foods including vegetables and fruits is associated with improved dietary intake and weight status, especially in economically disadvantaged areas. The presence of supermarkets and other sources of fruits and vegetables is associated with lower BMI, while lack of supermarkets and long distances to supermarkets is associated with higher BMI, and increased density of fast food restaurants and convenience stores is related to increased BMI, and this last sentence is, stronger relationships tend to be

seen between the environment and vegetable and fruit intake than with body weight. It's more - it's not - it's just that we have a few more studies, not that there is a stronger relationship; I just wanted to clarify that.

And fast food is defined as foods designed for ready availability, use and consumption, and sold at eating establishments for quick and available -- availability and take out. So the implication of the environment and food question is that policy and private sector efforts must be made to increase the availability of healthy foods for all Americans, especially low income Americans, so greater access to grocery stores, produce trucks, farmers' markets, and greater financial incentives to purchase and prepare healthy foods, as the healthier foods tend to be more expensive than the cheap and processed foods.

Next slide. We looked at for - with the NEL we only reviewed systematic

reviews. We didn't go back to the original literature as there was enough to look at here. All 10 studies found a relationship between the environment and body weight and dietary intake. Three found neighborhood-level measures of economic disadvantage were associated with obesity and poor dietary intake. Eight reviews found that the availability of healthy food or lack thereof -- supermarkets, vegetable gardens -- is associated with weight status and dietary intake, especially fruit and vegetable intake, and two reviews found that higher density of fast - systematic reviews found a higher density of fast food restaurants and convenience stores in association with higher rates of obesity.

So I think this is very much in line with what we expected to see. We didn't dive all that much deeper into things like sidewalks and some other sort of built environment questions. It was more around

food availability and food environment that we looked at, and we kept it at a fairly high level for this first time, because this hasn't been reviewed yet by the Dietary Guideline. Next slide.

So then turning towards behaviors - if I could go back to the last slide just for a second, the only thing I would say is that in the Integration and Translation chapter, we - a fair amount of this work will be considered in that chapter just because it seems to be when you think of the sort of systems-related aspect of food availability both on the negative and the positive, that is where we need to be focusing on, a lot more than just individual behavior change. But moving on to behavior, looking at it in both children and adults, we looked at a number of different behaviors related to body weight, and many of these were also addressed in the 2005 Guidelines, and so we've updated the review, but looking at eating out, portion

sizes, screen time, breakfast consumption, snacking, eating frequency, and diet self-monitoring.

We focused on 2000 to present, children two to 18 and adults 19 and up, and we excluded cross-sectional studies.

The proposed conclusion for what is the relationship between eating out and body weight, we proposed that this is a Grade I (strong) evidence, there is strong and consistent evidence that children and adults who eat fast food are at increased risk for weight gain, overweight and obesity, the strongest relationship between fast food and obesity is seen when one or more fast food meals are consumed per week. There was not enough evidence at this time to evaluate whether eating out at other restaurants and the relationship between risk of weight gain and overweight and obesity, so it was focused mostly -- exclusively on fast food restaurants.

The proposed implication is that if people do choose to eat fast food they are encouraged to choose lower calorie options and smaller portions. The restaurant industry is also encouraged to offer healthier foods in appropriate portion sizes that are low in calories, added sugar and solid fat.

Looking at the evidence, these were - there was one systematic review and several prospective cohort studies. This is not a topic that I think is possible at this point in time to look at an RCT, because this is really a relationship with body weight at the moment, and I think there are some issues with a number of these behavior and environment questions, with the design, and I think that this is what we are going to have to be looking at.

And then there were several prospective cohort studies, of which, all were strong in terms of relationship with the exception of one that was a negative

association with girls and no association with boys. But all the other studies were very strong. Next.

With adults, similarly the systematic review plus the prospective cohort studies, with the exception of one, which was positive for fast food, but there was no relationship with other restaurant food; all were strong and positive. Next slide.

What is the relationship between portion size and body weight? And this has been - this is more just an update of the 2005 DGAC. The proposed conclusion is that there is strong evidence there's a positive relationship between larger portion sizes and body weight. The conclusion from 2005 is “the amount of food offered to a person influences how much he or she eats, and, in general, more calories are consumed when a large portion is served rather than a small one.”

The proposed implication is that individuals are encouraged to prepare, serve

and consume smaller portions at home, and to choose smaller portions of food while eating foods away from home. Next slide.

These are the studies that we looked at. There were a number of RCTs, and there were no studies in children, because we didn't focus on weight loss. It was more on weight maintenance over time, and one case-control study.

So what is the relationship between screen time and body weight? This is also Grade I, and this is also an update from 2005. There is strong and consistent evidence in both children and adults that screen time is associated with increased overweight and obesity. The strongest association is with television screen time. And the proposed implication is that children and adults should limit screen time, especially, here we are sitting for 14 hours over the next two days watching our screens, but children and adults should limit screen time, especially

television viewing, and to not eat food while watching television. We propose in terms of the implication to support the American Academy of Pediatrics guideline of no more than one to two hours of total media time for children and adolescents. And to discourage television viewing for children less than two years of age, and then to also support the Healthy People 2010 objective to increase the proportion of adolescents who view television two or fewer hours on a school day. So we propose to use those as implications to be in concert with other guidelines. Next slide.

With this update these are a number of - there is a meta-analysis we looked at for children. We didn't do a full NEL search, and there was a positive relationship between screen time and adiposity, and in adults, with the update you can see there are eight cohort, prospective cohort studies all with a strong relationship between screen time and weight. I don't think any of this is very

new; it was more of an update for the literature. Next slide.

What is the relationship between breakfast consumption and body weight? And I will say that we have been working, and it will be presented tomorrow to coordinate this question with the Nutrient Adequacy subcommittee. And I would say at the moment there is a Grade II (moderate) for children, Grade III (limited) for adults. There is modest evidence that children who do not eat breakfast are at increased risk for overweight and obesity. The evidence is stronger for adolescents. There is inconsistent evidence both for the positive and the negative for adults who skip breakfast, that it puts them at increased risk for overweight and obesity, and I think a fairly simple, straightforward proposed implication is that children and adults are encouraged to consume a nutrient-dense breakfast, and we will be defining nutrient-dense much more tomorrow. Next

slide.

You can see this is for children. You can see that, so a negative relationship is that it means - a positive one is that it puts them at risk for overweight and obesity, so a negative is in the right direction. You can see that with an RCT, breakfast consumption only with nutrition education was positive. Eve, are you on the call here? I'm thinking actually the positive here, or Julie are you on the call? Because I think there is - this positive, this study, the positive actually is in the direction we would want, correct?

DR. OBBAGY: No, the negative. So if you increase your breakfast. Yes, you want the inverse in this case.

DR. NELSON: We want the inverse in this case. So positive means a relationship with more breakfast, more obesity, or not?

DR. PI-SUNYER: No.

DR. OBBAGY: The positive is if you increase your breakfast intake you increase your body weight, whereas the negative is if you increase breakfast intake you decrease body weight.

DR. NELSON: Body weight. So here breakfast is associated with an increase in body weight with the Rosado study. I thought the nutrition education actually reduced obesity rates. In the Rosado.

DR. PI-SUNYER: Yes, these are reduced.

DR. OBBAGY: I think that first one is supposed to be a negative association.

DR. NELSON: I think it is too. I think that is a typo, because otherwise they are not in concert, and that was why I was - okay. So that should be a negative, because it was only with nutrition education where they saw a decrease in body weight. Then you can see with these other trials there was either no association or there was a

association the way we would expect with breakfast being protective of body weight.

And a couple of these studies show differences between girls and boys, but it's not universal here, and that's why I gave it a Grade II. Next slide.

With adults, there was also a negative relationship in the direction that we had expected, although one study didn't show - it's just that there weren't as many studies here in adults as there were in children.

Next slide. In terms of snacking, this was a real nightmare, because of - if you actually I think the NEL search was very difficult to do with this, because all the different studies actually define snacking in a different way. I'm happy that there is a new study, large study, looking at snacking trends over time since the `70s to now, done out of UNC. It has done more definition of what snacking is, and I think that that will be a help for the literature,

so at the moment I think mostly because of the methodology, there is inconsistent evidence to suggest that snacking is associated with increased body weight, and I think the reason is the inconsistency in the variability in design and definitions for snacking. I think that it's fine to have a proposed implication that when snacking, Americans are encouraged to choose foods that help meet their nutrient needs while staying within calorie limits. Next slide.

Here, so it's a little complicated because there's also with television viewing, but three found a positive relationship between snacking and adiposity, one only found the positive relationship in front of the television, and three didn't find a relationship between snacking and adiposity. So there is really quite a variability here, so I just think it's inconsistent at the moment. Next slide.

With adults, two studies found a

positive relationship, but we only have two studies, so I think we have insufficient data at this point, although it seems like there is a positive relationship. Next slide.

So what is the relationship? If snacking was difficult to look at, this one was even more difficult, which is, what is the relationship between eating frequency and body weight? Here, I think there is limited evidence, or insufficient evidence, that frequency of eating has an effect on overweight and obesity in children and adults. Some of this also was methodologically very difficult to feather out in terms of is this in addition to three meals a day, or is it with all meals in the day? There is still some definitions that need to be determined, and the implication is that children and adults are encouraged to follow a frequency of eating that provides nutrient-dense foods throughout the day. Caution must be taken that the frequency of eating helps children

and adults stay within daily caloric requirements. I will say for the snacking, breakfast and body weight questions, or rather, and frequency of eating, we did not look at - we didn't include weight loss studies. These were all in terms of relationship with body weight or weight maintenance over time. I should clarify that.

So, in children, there was one prospective study that showed a negative relationship between eating frequency and adiposity in girls, and in adults there was a positive. So I just don't think we have enough data to say much about this at the moment. Next slide.

The only place that we did look at weight loss and weight control was in people in terms of self-monitoring, and here this is an update from 2005 and some other reports that there is a strong evidence that for adults who need or desire to lose weight or who are maintaining body weight following

weight loss, that self-monitoring of food intake improves outcomes. So adults are encouraged to self-monitor food intake to improve outcomes when actively losing weight or maintaining body weight following weight loss, and in addition there is also evidence that self-monitoring of body weight and physical activity improves outcomes, when actively losing weight or maintaining body weight following loss.

Here are the trials. So this is, positive is that they had better outcomes. So there are quite a few RCTs of which only one RCT did not show an improvement; the others showed an improvement. I will mention that several of these were studies done overseas, but this just adds to the literature of studies that have been done in the past. Next slide.

So research recommendations: more research is needed to understand both positive and negative environmental influences that

affect body weight, and how change in the environment impacts dietary intake and health outcomes and body weight. This is a very new field, and I think it deserves a lot more good research. Macro level research on the effects of local and national food systems on dietary intake and health outcomes is necessary to better understand the relative contributions of different sectors on dietary intake and health.

More research on the influence of snacking and meal frequency on body weight and obesity is needed. Better definitions for snacking will need to be developed, and I believe they are being. Research is needed on how best to influence fast food and restaurant manufacturers and retailers to reduce portion sizes and to improve the quality of food.

And I might also add, and how we can also influence consumers' choices within those establishments. And then more research is needed on other behaviors that might

influence eating practices such as child feeding practices and other family influences and peer influences.

And I think that might be my last slide. Is that correct?

DR. PI-SUNYER: That is correct. So questions for Mim?

DR. NELSON: I know that was a lot, but I know we have a lot to cover today.

DR. APPEL: This is Larry. First of all, that was terrific. I learned a lot myself. But the fast food. I think this could become a lightning rod. These are all observational studies. Were they able to control for other aspects, either at the neighborhood or individual level, related to like SES or income or these other factors that people will probably argue are more important than the fast foods?

DR. NELSON: Yes, they all - I'd have to go back and look at each of the individual studies, but most of them really

did control for income and SES, education. I must say, when we were looking at that, that we were surprised at the strength of the relationship and the consistency in both adults and children. We weren't expecting that. And there were quite a few trials - not trials but prospective studies - in which the design was really strong. Eve and Julie were really helpful with this. And we really, because we are aware that this could be a lightning rod. But the strength of the relationship was pretty strong. And then, again we also we saw it on the flip side when we looked at the food environment and its relationship, because we saw it two different ways, when we looked at the food environment, the number of fast food restaurants in an area was also related to obesity rates. So it was supportive in both directions.

DR. APPEL: I think you should actually mention that, because I think it is going to come up.

DR. NELSON: Yes, I think - I'm going to make a note of that.

DR. RIMM: Mim, this is Eric Rimm. Can I pile on there? I think this really is spectacular, and I too learned lots. And I wonder, can we take your first two conclusions and sort of merge them? If the number of fast food restaurants are associated with obesity in a given population, can we say that is also the case for kids? It seems like your second conclusion was that fast food restaurants cause obesity. And an implication of this is that fast food restaurants shouldn't be allowed to be in high-density, in places where there are a lot of kids, like in schools or around schools. Is that a potential implication of your first two conclusions?

DR. NELSON: I think it is. I think it is. I think that different towns zone differently, but I think that could be an implication. I'm making a note of that as

well.

DR. RIMM: I know there are some progressive cities that do this, but this would be a fantastic implication if we really think that is a cause of obesity in kids.

DR. NELSON: Well, a contributor.

DR. RIMM: Sorry.

DR. NELSON: But I'm not sure that we can merge the two. I think in the discussion and the chapter we can make note of that.

Let's go with other questions and I can come back to my thought.

DR. PI-SUNYER: Any other questions for Mim?

DR. APPEL: This is Larry again. The diet self-monitoring, is this a - I wasn't quite sure - is this a calorie measure, assessment? I am just wondering if you need to be a little more specific.

DR. NELSON: They did it in a variety of ways. It wasn't just calories. It

was also just monitoring the different studies, not all did it the same. It was just monitoring food intake, size - they were done in a couple of different ways. But let me also take a look closer at that which may have been the strongest.

DR. APPEL: Because I think it's a little bit vague when you say food monitoring. I mean, at least in contemporary trials, they are really trying to either correctly measure calories or to measure indirectly calories by proxy. So I would actually, if you feel comfortable, I would add calories to that.

DR. NELSON: Yes, I'm comfortable doing that. Eve or Julie, if you could make note of that, and I will make note of that as well. But we will add calories. What I was going to add is that actually with Eve and Julie and Trish were very helpful - what I haven't presented because we don't have time is, we actually have a fairly detailed

historical look at the change in the food environment from the 1970s to current in terms of eating establishments, portion sizes, just sort of how things have changed, and I think that will be helpful as sort of the basis for the whole report, because it shows the historical perspective, not just what we are eating right now. And that will help to set up these massive changes in the food environment that have happened.

DR. NICKOLS-RICHARDSON: This is Shelly. And just to add to what Larry talked about before, the Food Away From Home report that was published in February 2010 by the ERS they, in their estimation approach, count some of the things like food preferences, knowledge, time constraints, so forth, and there are a couple of quotes from this report, quote: "For the average consumer eating one meal away from home each week translates directly to two extra pounds per year." And then the other quote that I think is pretty

striking is that one additional meal eaten away from home increases daily intake by about 134 calories.

So if there is a way to incorporate their report into the text and the background, I think obviously they have done a good job and it would be important to include that.

DR. NELSON: Yes, and that is part of the sort of background that we've got. But those two quotes we can add.

DR. FUKAGAWA: This is Naomi. Also look at differences in, sort of, socioeconomic - I may have missed that.

DR. NELSON: Well, it did come out as a factor. And it's in the proposed conclusion. It keeps coming out. And I think what we need to do, and this will come also up, even more so in the Integration and Translation chapter, as we proposed in the environment conclusion or implication is that we need to have greater financial incentives,

or figure out a price structure for the healthier foods to be cheaper than the non-healthier foods, however we want to define them, and because the socioeconomic piece keeps coming up.

DR. FUKAGAWA: That doesn't get broken down into ethnic or cultural --

DR. NELSON: Not at the moment.

DR. FUKAGAWA: Okay.

DR. PI-SUNYER: Any other questions for Mim?

DR. SLAVIN: This is Joanne. I have a question about the breakfast in adults. This is very consistent for a Grade III. Was that just because of the number of studies?

DR. NELSON: Yes. It was the number and I believe it was primarily the number of studies that we just didn't feel like there was enough there. And I think I can - while the next presenter is presenting I can just dig into that a little bit and maybe come back and answer that question. Would

that be helpful?

DR. SLAVIN: That would be great, thanks.

DR. PI-SUNYER: Okay, let's move on to breastfeeding and maternal and postpartum weight reduction -- retention. And Rafael Perez-Escamilla is going to talk about that.

DR. PEREZ-ESCAMILLA: Hello, good afternoon.

The question that I will be addressing is what is the relationship between breastfeeding and maternal weight change, a question that was not addressed in the 2005 report.

The NEL search strategy was based on identifying literature reviews addressing this question published between 2000 and 2010.

The Committee's proposed conclusion is that breastfeeding may be associated with moderate maternal postpartum weight loss, and we assigned this a Grade II

even though it is based on two randomized controlled trials and several prospective studies. Several of them did not control for key confounders or had enough statistical power.

It is important to note that weight loss associated with breastfeeding is small, transient and depends on breastfeeding intensity and duration. As discussed later on in this presentation, implications of these findings for women in the U.S. need to take into account that only a third of them are breastfeeding extensively at three months postpartum when the recommendation is for women to breastfeed exclusively for six months, endorsed by both the World Health Organization and the American Academy of Pediatrics.

Lactation increases energy demands, but at the same time it increases appetite substantially, without evidence that lactation increases levels of physical

activity. For this reason it is important to establish the net effect of lactation on maternal postpartum weight loss.

The Committee initially identified four reviews, but based its conclusions mostly on the reviews by Dewey and the Agency for Health Care Research and Quality, or AHRQ. This is because the AHRQ review builds upon on the Fraser review, and the Kramer review only discussed two randomized controlled trials also addressed by Dewey in her review.

Dewey based her review on 15 studies, two randomized controlled trials conducted in Honduras by her group, showing that exclusive breastfeeding for six months vis-à-vis four months led to greater weight loss between four and six months postpartum.

In one of the trials the weight loss was of -0.6 kg, and in the second one it was -0.2 kg. The difference in weight loss across trials was explained by the between-group differences in breast milk energy output

among women participating in both studies.

Dewey classified the 13 prospective studies that met the initial inclusion criteria into those that actually measured versus those that estimated weight changes. Six out of the seven studies that had the best methodology found an inverse association between breastfeeding and postpartum weight change. By contrast only one out of the six studies with poor methodology detected the association.

Here we concluded that there is a dose/response relationship between breastfeeding duration or intensity and postpartum weight loss, and that weight loss differences attributed to breastfeeding were transient, being more evident between three and six months postpartum, and she also identified the need to improve study design in future studies, especially the need to control for key confounders and improve the clarity of breastfeeding definitions used.

AHRQ identified eight prospective studies that met their inclusion criteria, most of which were published after the review by Dewey. From three studies that examined return to pre-pregnancy weight, one found that exclusive breastfeeding was not associated with weight retention at one to two years postpartum.

A second study found that breastfeeding at one year was associated with -1.2 kg of weight retention versus +2 kg of weight retention among formula-feeding women at one year postpartum.

A third study found that breastfeeding was associated with reaching pre-pregnancy weight six months earlier vis-à-vis formula-feeding. However, consistent with the weight loss associated with intensive proceedings, and reported by Dewey, two prospective studies found that postpartum weight change was inversely associated with breastfeeding intensity and duration.

The remaining three studies that classified women according to different infant feeding categories did not find significant between-group differences in total postpartum weight changes. However, consistent with the conclusion from Dewey, one study did find more rapid weight loss between three and six months postpartum among exclusively breastfed women. The AHRQ review concluded that the effect of breastfeeding on postpartum weight loss is unclear, and that if an association was present, the effect size is likely to be small. They also make the very important point that postpartum weight changes vary enormously among women. And you can see the range, how huge it is, just from one of the studies conducted by Ohlin and Rossner.

So, future studies need in addition to control for key confounders to ensure that they are adequately powered to detect the relatively small differences in weight changes that have been found to be

associated with breastfeeding.

In sum, the evidence supports the conclusion that breastfeeding may be associated with moderate maternal postpartum weight loss. This relatively small effect is linked with breastfeeding intensity.

And lastly given the very low rate of exclusive breastfeeding and short breastfeeding durations among women in the U.S., the Committee does not recommend simply issuing a blanket statement advertising breastfeeding as an effective tool for maternal weight loss among women in the U.S.

And that's the last slide.

DR. PI-SUNYER: Okay, thank you very much, Rafael. Questions for Rafael?

DR. VAN HORN: Rafael, this is Linda, can you hear me?

DR. PEREZ-ESCAMILLA: Yes, I can.

DR. VAN HORN: That was excellent. Wonderful job. In our interest in looking for ways to prevent obesity starting

in childhood, are there data yet to document offspring and any benefit in terms of weight and weight gain in children of breastfeeding mothers?

DR. PEREZ-ESCAMILLA: The evidence is mixed, about 80 percent of cross-sectional studies have found an association between breastfeeding and less likelihood of childhood obesity, and also several retrospective studies. However, the randomized trial conducted in Belarus, and the [inaudible] trial by Kramer and colleagues does not confirm that finding, and there is now another prospective study that does not confirm the findings. So I would say the jury is still out regarding that point.

DR. VAN HORN: Okay, thank you.

DR. PI-SUNYER: Any other questions for Rafael?

DR. NELSON: No, but this is - we will keep going with Rafael - I had a 30-second update on breakfast consumption.

DR. PI-SUNYER: Okay, let's finish with Rafael. Any other questions for Rafael?

Okay, well, thank you, Rafael.

Go ahead, Mim.

DR. NELSON: Okay, so there were seven trials for the breakfast consumption in adults, one trial but it was with freshmen, college age, that the more breakfast they ate the greater weight gain, so that might be a little tricky one to look at. And then four out of the seven did show reduction in body weight with breakfast consumption or relationship with lower body weight. Then the other two didn't show any association. So it's kind of mixed, and so that's why it was a Grade III as opposed to a Grade II. But I'm happy to change that grade if people - four do show a relationship with breakfast consumption and lower body weight. It was just that one showed a higher, but it was freshman young adults, and two didn't show an association, so

that was the reason for Grade III. But suggestions?

DR. SLAVIN: I'm not sure in Nutrient Adequacy, Shelly, we did, I'm trying to think if there is any overlap with other committees on breakfast eating. Probably not, right?

DR. NICKOLS-RICHARDSON: This is Shelly. I think we are the only other subcommittee that looked at breakfast intake. And for us, for Nutrient Adequacy, the Grade is a II which we will present tomorrow.

DR. NELSON: I think we are okay with this, unless, Joanne, if you feel strongly. It's just they are inconsistent and I think some of it has to do with the quality of the breakfast more than anything.

DR. VAN HORN: Right. I was just going to say, I think in what we'll hear tomorrow there are more issues related to the qualitative nature rather than the behavior of eating breakfast.

DR. NELSON: Exactly, that's what I think. And as long as the implication is such that, you know, high quality breakfast, I think we are okay.

DR. PI-SUNYER: Okay, thank you Mim and thank you Rafael. And let's go on to Christine. She has a whole lot of questions. We will let her go through them and then ask questions. So Christine, you're on.

DR. WILLIAMS: I'd like to thank Eve Essery and Jean Altman for all their contributions to these questions. The overarching question for this family of questions is, how is dietary intake associated with childhood adiposity? And of course, the background for this question is the dramatic increase in the prevalence of obesity among U.S. children and adolescents over the past several decades. Since the early 1970s obesity has quadrupled among six to 11-year-olds, tripled among 12 to 19-year-olds, and more than doubled among preschool children.

We know the dietary patterns among U.S. children have changed significantly over the past several decades concurrent with the obesity epidemic. So the research questions that we have chosen to address represent dietary factors that have often been hypothesized to promote or protect against increased adiposity in children.

Since obesity results from a positive energy balance it seems natural that the first question relates to total energy: Is intake of total energy (caloric) associated with adiposity in children?

We conducted a full NEL review for this question with a search for the NEL review from 2004 to July 2009. And also distilled the data from the previous ADA review, again, children 0 to 18. We included cross-sectional studies and studies from underdeveloped countries. And we only included studies that included some measure of adiposity as an outcome variable.

This review led to the proposed conclusion that the preponderance of evidence from a review of the recent scientific literature tends to support a positive association between total energy intake and adiposity in children with a Grade III (limited).

This conclusion was based on a review of four studies published between 2004 and 2009. All four of them were longitudinal cohort studies, and three of the four longitudinal studies found a positive association between total energy intake and adiposity, and one found no association. However, this study did not adequately assess or adjust for implausible reports of energy intake.

And these are the four studies that were included in this review. All four of the studies were conducted in the United States, and all four earned a positive quality ratings. And again three of the four found a

positive association between total energy intake and adiposity in children. Two of the studies that saw the positive association, all distinguish between plausible and implausible reports of energy intake on an individual basis, and the final study, Stunkard study, measured total energy expenditure directly by doubly labeled water.

The fourth study by Fulton did not find a positive association. However, this study didn't assess the plausibility of energy intake, and also used less frequent measures of dietary intake and measure by food frequency questionnaire, whereas the others were by food records with more frequent measurements.

Some of the earlier ADA evidence review were energy intake and overweight in children included 45 studies, however, two-thirds of them were cross-sectional studies, and of the 15 longitudinal studies four found a positive association between total energy

intake and adiposity and ten did not, one found a negative association.

These studies were all published prior to 2004, and did not assess or adjust the plausible reports of energy intake on an individual basis.

So the ADA review concluded that total energy intake measured using current dietary assessment tools at that time which may not accurately assess total energy intake does not appear to have a strong association with overweight in children. And again two-thirds of those studies were cross-sectional in nature.

And if you look at the data related to plausible reports of energy intake in studies in children you can see that, for example, Huang was actually the first one to look at this in any detail in a nationally representative cross-section study of U.S. children. And 55 percent of the children had implausible energy intake. Then several other

investigators have looked at this, again all since 2004. And the percentage of children with implausible energy intake varies from about 36 to 38 percent, except for the Johnson studies which were a little bit lower in younger children.

So a significant number of children with implausible energy intake. Next slide. So before 2004 there was little evidence that obese children consume more energy than normal weight children. However, studies since then have demonstrated that unless the plausibility of energy intake is assessed and accounted for in data analysis, the link between energy intake and adiposity is often masked.

Results from these methodologically stronger studies contribute to a growing body of evidence that, one, overweight children, especially adolescents, underreport energy intake to a much greater extent than youth of normal weight; and two,

that total energy intake among obese children is greater than among normal weight children.

The NEL conclusion statement was based on a small number of studies. However, several were methodologically very strong, and assessed and adjusted for implausible energy intake reports. Overall, they provided evidence that there is a positive association between total energy intake and greater adiposity in children. In view of the small number of studies, however, the evidence was assigned a Grade III or limited.

The evidence suggests that strategies to prevent childhood obesity should include efforts to reduce surplus energy intake, especially energy from foods and beverages that provide empty calories from added sugars and solid fats.

The second sub-question that we addressed had to do with dietary fat. Is intake of dietary fat associated with adiposity in children? And again this was

based on a review, an NEL review that covered January 2004 to 2009, and an ADA review, from 1982 to September 2004, with the same inclusion/exclusion criteria.

And a review of the evidence led to the proposed conclusion that a review of the evidence suggests that increased intake of dietary fat is associated with greater adiposity in children, with a Grade II.

A review of the NEL evidence, overall, there were six included studies. Five were longitudinal and one was a clinical trial. Of the five longitudinal studies there were reports on three cohorts. Two of the reports involved the STRIP cohort studied at different ages, and two reports involved the DONALD cohort study at different ages.

Three of the reports found a positive association between total fat intake, or intake of high fat foods and adiposity, in all or a subsample of the population studied. And two reports found no association.

The one randomized clinical trial found no association between total fat intake and adiposity in children.

And these are more details from the six included studies in the NEL review. One is a randomized controlled trial; and five longitudinal. For the STRIP study you can see the Hakanen study in the middle, a 2006 study of children at 10 years of age, and they found that after two years of age there were continuously fewer overweight girls in the low fat, low saturated fat, low cholesterol diet intervention group than in the control group.

And then, Niinikoski in the bottom also studied children at 14 years of age, and found that at that time there was no difference between the intervention and the control group in both BMI or pubertal development. And the other studies, you can see that the three with positive outcomes, and three with no association.

When you look at the ADA evidence,

there were 21 longitudinal studies in the ADA evidence review, and 12 of those studies found a positive association between total fat intake or intake of high fat foods and adiposity, in all or a subsample of the population, and nine found no association.

And their conclusion was that dietary fat intake is associated with higher adiposity in children with a Grade II. Their review also included 34 cross-sectional studies. However we did not consider these in the NEL combined review process.

And this is a very busy slide, but just to give you a flavor for the 21 longitudinal studies in the ADA review, and the top ones in green were the ones that found a positive association for the most part between dietary fat and adiposity. The lower -- the ones at the bottom found no association. And one of the things that differentiated the positive studies was that more of them had multiple measures of

adiposity, and not just BMI. Which I think is important because BMI has been found to be a relatively poor surrogate measure of adiposity in children as based on the Friedman report of 2009.

So when you combine the evidence from the NEL and the ADA evidence review, you are left with 27 methodologically stronger studies that were RCTs or longitudinal studies, and 15 of the 27 studies, all longitudinal, found a positive association between total fat intake or intake of high fat foods and adiposity in all or a subsample of the population studied. And 12 found no association.

Again the proposed conclusion was that the review of the evidence suggests that increased intake of dietary fat is associated with greater adiposity in children, with a Grade II. Next slide.

The implications, diets high in total fat can theoretically result in passive

over-consumption of energy, since fat is so palatable and energy-dense, yielding more than twice the calories per gram as carbohydrate or protein. Although the percent of energy from total fat has decreased over the past several decades, currently one-fourth of U.S. children still have average daily intakes that exceed the IOM acceptable macronutrient range for age.

After consumption of MyPyramid core foods for nutrient requirements at recommended energy levels, there are few discretionary calories remaining, only about 8 to 20 percent before energy needs are exceeded. Unfortunately about 40 percent of the total energy intake for 2- to 18-year-old children comes from empty calories, of which about half comes from solid fats, which contribute to energy surpluses as well as elevated blood cholesterol.

Evidence from both NEL and the ADA reviews support a positive association between

total fat intake and increased adiposity in children, thus total fat should not exceed the IOM acceptable ranges and should consist primarily of mono- and polyunsaturated fats that promote heart health and provide essential fatty acids for growth and development.

The third sub-question that we will review at this time has to do with calorically-sweetened beverages, and the question is, is intake of calorically-sweetened beverages associated with adiposity in children? And again, this evidence was based on the NEL review from 2004 to 2009, and on a previous ADA review from 1982 to 2004, with similar exclusion/inclusion criteria.

The proposed conclusion: a moderate amount of evidence supports the conclusion that greater intake of calorically-sweetened beverages is associated with increased adiposity in children, with a Grade II.

And the NEL review was based on 11 included studies, 10 are longitudinal and one was an RCT. Of the 10 longitudinal studies, seven found a positive association between intake of calorically-sweetened beverages and adiposity in all or a subsample of the population studied. Three found no association. And the one randomized controlled trial by Ebbeling found some evidence for a positive association between intake of calorically-sweetened beverages and adiposity.

These are the 11 primary studies and the one trial in the NEL review. You can see the top seven that have a positive association with adiposity in children; and the bottom three that had no association.

In review of the ADA evidence which goes back to 1982, there were six longitudinal studies in this review, three of the six found a positive association between intake of calorically-sweetened beverages and

adiposity, and three studies found no association. One RCT found evidence of a positive association. And their conclusion statement was that intake of calorically-sweetened beverages is positively associated with adiposity in children with a Grade II.

The ADA Evidence Review also included 13 cross-sectional studies. However, again, these were not considered in the NEL combined review process. Next slide.

And for the combined review of the NEL and the ADA evidence, there were 18 included studies, randomized controlled trials and longitudinal studies. And, overall, of those 18 studies 12 of them found a positive association between calorically-sweetened beverage intake and adiposity in all or a subsample of the population studied, and six found no association.

Of the randomized controlled trials there were two, in the combined review, one by Ebbeling which was among 13 to 18-year-

old children, and in this study, only for the heaviest children in the top tertile the increase in BMI was less than in the intervention group compared to the controls, and this was with home delivery of non-caloric beverages to displace sugar-sweetened beverages. And in the James study a one-year-based nutritional education program in schools focused on decreasing intake of carbonated beverages.

The percent of overweight and obese children increased in the control group, but decreased slightly in the intervention group. So there was a significant difference between the treatment groups. Next slide.

For implications: the principal sources of energy among children are intended to be the MyPyramid core foods - grains, meats, fruits, vegetables and dairy - in order to meet recommended intakes of essential nutrients within estimated energy requirements.

And again after consumption of core foods for nutrient requirements, there are few discretionary calories remaining, only about 8 to 20 percent, before energy needs are exceeded. Unfortunately about 40 percent of children's total energy intake comes from less nutritious sources of energy - added sugars and solid fats - contributing to energy surplus and risk of obesity. Calorically-sweetened beverages are a major source of added sugar among children; most providing energy without other nutrients.

Evidence from both the NEL and the ADA reviews, especially data from the larger, methodologically stronger and higher quality studies, supports a positive association between calorically-sweetened beverage intake and increased adiposity in children.

Thus consumption of calorically-sweetened beverages in children should be discouraged. One, because of the positive association with increased adiposity, and two,

because of the need to replace empty calories with nutrient-rich energy sources for optimal growth and development.

So again the proposed conclusion is that there is a positive association between intake of calorically-sweetened beverages and adiposity in children with a Grade II.

The next question we reviewed has to do with calcium and dairy, milk and milk products. Is intake of calcium and/or dairy (milk and milk products) associated with adiposity in children?

And, again, this is based on a combined review of the NEL review from 2004 to 2009, and the ADA review which goes back to 1982. Next slide.

And the proposed conclusion: the NEL review provides little convincing evidence that intake of calcium and/or dairy - milk and milk products - plays a significant role in regulating adiposity in children and

adolescents, with a Grade III.

And the NEL review identified 13 articles that were included in this review, five were longitudinal studies, and five were randomized controlled trials, and three were systematic reviews. Next slide.

The randomized controlled trial, one randomized controlled trial found evidence for a negative protective association between intake of calcium or dairy and adiposity for the children studied. And two trials found no association between intake of calcium/dairy and adiposity.

And two trials found mixed results.

Of the trials that found mixed results, one found that higher habitual dietary calcium intake was inversely associated or protective body fat, however, calcium supplement had no effect on weight, height or body fat in girls.

And the other study by DeJongh

found no differences in fat mass between calcium supplemented and placebo groups, and no association between percent body fat and fat mass changes and dietary calcium intake or total calcium. However, for children with the lowest dietary calcium intakes, that net gain was lower in the calcium-supplemented versus placebo group. Next slide.

For the longitudinal study there were five in the NEL review, and two of the five longitudinal studies found evidence for a negative or protective association between intake of calcium and dairy and adiposity in children. One found no association and one large longitudinal study of adolescents reported a positive association - increased weight gain - between intake of calcium/dairy and adiposity.

And the final study found mixed findings, in the study, with hypercholesterolemic or non-hypercholesterolemic children. Next slide.

We also considered the evidence from -- actually that should be three - three systematic reviews, one by Barr, one by Lanou and one by Winzenberg. And, overall, they all three concluded that there was insufficient evidence that calcium or dairy was protective against adiposity in children. I won't go through all the details. Next slide.

This summarizes the ten primary studies in the NEL review for calcium, dairy and adiposity in children. The five RCTs at the top and the five longitudinal studies on the bottom. And you can see that the results were quite mixed between positive, no association and negative. Mostly no association for - or weakly protective. Next slide. In reviewing the earlier ADA evidence that goes back to 1982, they reviewed them separately, although many of the same articles were included in both reviews. There were four longitudinal studies that looked at calcium and adiposity in children, and there

were three cross-sectional studies. Two of the four longitudinal studies found a positive association, and two found a positive and one found a negative association, and they concluded that a low intake of calcium may be associated with increased adiposity.

Both for dairy and adiposity in children there were 15 studies, ten of these were cross-sectional however, and only four were longitudinal studies -- five were longitudinal, sorry -- and of the five longitudinal studies four of them found no association between intake of dairy and adiposity and one found a negative protective association.

Again they concluded that research indicates that a low intake of dairy may be associated with increased adiposity among children. However, their conclusions were based on a significant number of cross-sectional studies.

If you combine the NEL and ADA

reviews, and only look at the randomized controlled trials and the longitudinal studies, there were five randomized controlled trials in the combined review, and again, primarily no association or mixed association, with one, primarily the bottom one, protective against adiposity in children. Next slide.

The 12 longitudinal studies, five from the NEL review, and seven from the ADA review. There were primarily either no association or for a few studies, a negative protective association or mixed. Next slide.

So for the combined reviews of NEL and ADA, the 12 longitudinal studies, six found no association between calcium and/or dairy and adiposity, four found a negative protective association, one found mixed results, and one found a positive association between weight gain over four years.

Thus when you look at the combined evidence, there are 17 studies of either controlled trials or longitudinal studies, and

of these 17 studies 8 found no association, five found inverse protective effect, three found mixed results, and one found a positive association.

Thus we felt that the preponderance of evidence of these studies was greatest for no association, although there was some evidence for a weak protective association.

The NEL review also included the three systematic review articles, and these reviews concluded that the preponderance of evidence did not support a protective association between intake of dairy/calcium and adiposity.

Next slide. So although the NEL review provides insufficient evidence that intake of calcium and/or dairy, milk and milk products, plays a significant role in regulating adiposity in children and adolescents, milk and milk products have traditionally been a source of nutrient-rich

foods and beverages for children and adolescents. Besides providing energy, they are a concentrated source of highly bioavailable calcium, providing about three-fourths of the calcium in the U.S. diet.

In addition, they are a rich source of essential amino acids, have a good balance of macronutrients, and are rich sources of riboflavin and contain high quality protein. Although some studies suggest a protective effect of dairy intake against obesity in adults and children, others have found no association or in some cases even a positive association with adiposity.

But, regardless of evidence for or against the role of regulating adiposity, children should be encouraged to consume recommended servings of low fat dairy products daily in order to meet recommended dietary intake levels for key nutrients such as calcium. Next slide.

The final sub-question that we

will review today is, is intake of dietary fiber associated with adiposity in children? And again this is not a question that was reviewed by ADA, so this was only an NEL review that extended back to 1980 through July of 2009.

And the proposed conclusion: since so few clinical trials and longitudinal cohort studies have examined the association between dietary fiber intake and changes in adiposity in children, there is insufficient evidence at the present time to support the hypothesis that dietary fiber may protect against increased adiposity with a Grade III (limited).

The NEL review identifies five included studies. Two of them were trials and three were longitudinal studies. Of the two randomized controlled trials, Ventura found an inverse, protective effect of dietary fiber on adiposity in the 16-week trial of 54 overweight Latino adolescents aged 15. The

increased dietary fiber intake had an improvement in BMI which decreased, and visceral adipose tissue, minus 10 percent versus no change in the control group.

And the other study by Vido found no benefit of a dietary fiber supplement on weight change in 60 overweight Italian children. At the end of the intervention weight decreased in both treatment groups, no significant difference between the groups.

And for the last three longitudinal studies, Berkey et al. studied dietary intake and physical activity among a large number of U.S. children 9 through 14, and found no significant associations between energy-adjusted dietary fiber or dietary fat and BMI.

And Cheng assessed dietary intake and adiposity in a cohort of 215 German adolescents. And, again, they found that neither dietary fiber intake, whole grain intake, dietary glycemic intake nor glycemic

load were associated with changes in percent body fat or BMI Z-score throughout puberty.

Newby measured dietary intake and adiposity at baseline and again six to 12 months later in a cohort of low-income U.S. preschool children enrolled in the WIC program. In this population, intake of total dietary fiber was not associated with weight change, however, intake of WIC-defined breads and grains was associated with a lower weight change per year. Next slide.

And this is a summary of the five studies included in this review. Again, four of them showing no association, and the one trial, by Ventura, showing negative protective effect.

Dietary fiber is often a marker for a healthy, nutrient-rich diet in childhood, it's associated with greater intakes of Vitamin A, B-6, B-12, C, and niacin, thiamin, riboflavin, folate, magnesium, iron, zinc and calcium, and an

increased number of servings of Food Guide Pyramid food groups. Children with higher fiber intake have also been shown to have lower total fat, saturated fat, mono-unsaturated fat, and sucrose intake and higher protein intake compared with children with lower fiber intake.

Higher dietary fiber is also associated with lower serum cholesterol concentrations in children and adolescents, in a recent paper from the STRIP study. And dietary fiber also plays an important role in supporting healthy gastrointestinal function and normal laxation in children.

The role of dietary fiber in weight management in children and adolescents however is less clear. Theoretically, high fiber diets could promote a healthy weight since high fiber foods require more time to chew, slowing down the rate at which food is eaten and allowing more time for satiety signals; fiber absorbs fluid, increasing the

bulk of ingested food and promoting a feeling of fullness. High fiber foods are generally lower in energy density, having fewer calories than the same weight of low fiber foods.

Unfortunately, very few studies have examined the association between dietary fiber intake and adiposity in children. Thus, at the present time, there is insufficient evidence for a protective role.

Higher dietary fiber intake however, as part of a healthy dietary pattern that also includes lower intake of dietary fat and reduced energy density has been shown to be associated with decreased adiposity in young children.

At present, the majority of U.S. children consume far less than the recommended 14 grams of dietary fiber per 1000 calories. Thus, regardless of evidence for or against the role in regulating adiposity, children should be encouraged to consume greater amounts and varieties of high fiber foods in

order to increase nutrient density and promote healthy lipid profiles, glucose tolerance, and normal gastrointestinal function.

DR. PI-SUNYER: Okay, thank you very much, Christine, for this incredible piece of work. These are now open for discussion. Any comments for Christine?

DR. PEREZ-ESCAMILLA: Christine, this is Rafael, and I have first of all to congratulate you for a most comprehensive presentation. My question is related to the grade level that you gave to the calcium and dairy question in relationship to childhood adiposity, because you gave it a Grade III, and it seems to me that you have a very substantial number of well designed studies, randomized controlled trials, longitudinal studies, systematic reviews and so on, that would lead me to believe that the grade should be stronger than that. I'm not sure that doing 20 more studies in that area is going to change the distribution of results that you

have. If I do a mental meta-analysis of what you just presented it seems there is no relationship between calcium/dairy and childhood adiposity.

DR. WILLIAMS: That is a good question, Rafael. I think we found it a Grade III mostly because the evidence is so mixed, but you're right that there are a significant number of included studies, so I'm willing to revisit that.

DR. PI-SUNYER: It seems to me that you do have enough evidence that you have shown us for a II rather than a III.

DR. NELSON: This is Mim. I would agree with that.

DR. CLEMENS: Christine, this is Rog. Really nice work, thank you so much. Question: did your team examine various dairy components that may impact satiety signaling therefore have an impact on food intake?

DR. WILLIAMS: No, we didn't.

DR. CLEMENS: I think to Rafael's

point there might be - you might get a stronger signal, no pun intended, as you look at various dairy components. It may well be the composition of those dairy components that would have an overall effect versus the entire category.

DR. WILLIAMS: There could be. I don't think there was enough information in the studies that we reviewed to look at that.

DR. APPEL: This is Larry. I have two questions, or actually one suggestion and one question. The total energy section, you don't mention in your implications or in the conclusion that these studies, unless I'm really off-base, did not measure physical activity particularly well. So in that setting I think it's really quite hard to discuss total energy as opposed to energy balance or deficit or difference. And I was just suggesting that you add something about the inadequate measurement of physical

activity being a major hindrance to understanding intake.

DR. WILLIAMS: That's a good point, Larry. It was measured better in some studies than others, and I didn't include it in this writeup but some of them did measure it with accelerometers or questionnaires, but some did better than others.

DR. APPEL: But even with accelerometers, it's pretty weak, and most questionnaires don't do a good job, so I think it really needs to be a strong caveat in the implications.

DR. WILLIAMS: Okay. Thank you.

DR. APPEL: The other, it's a question, and I don't know if there is a subtle distinction here. But in the sweetened beverages, you put "calorically-sweetened beverages" as opposed to "sugar-sweetened beverage". That's what we talked about in adults; this is what is the term [inaudible] switched. And I don't know if there was some

reason for that, or if it's accidental.

DR. WILLIAMS: I think that was the way it was phrased in the original ADA review, but I think a lot of people use the terms interchangeably, so we should probably be consistent and use it one way or the other.

DR. NELSON: I think we are mostly using "sugar-sweetened beverages".

DR. WILLIAMS: So we could change that.

DR. NELSON: This is Mim, I have two questions. One, is the lack of strength with dietary fiber, is that because just everybody is so low that nobody is sort of meeting a threshold that would make a difference?

DR. WILLIAMS: Well, that's possible. I think there were just so few studies.

DR. NELSON: Okay, because it seems like one of the issues just might be literally, children the intake is so low, that

was just a comment. And then back to the sugar-sweetened beverages, it seems like when you add - I might argue for even a Grade I - there is a lot - between all the years of study of this, it seems like it may be stronger than a Grade II. I just might argue for - I know that like every single study doesn't show it but there is a lot of evidence there both in RCTs and prospective trials. I wonder what the rest of the Committee thinks.

DR. PI-SUNYER: Well, there aren't many RCTs.

DR. NELSON: Two, but yes but a few decades.

DR. PI-SUNYER: And they are not very good, most of them are carried out over a very long period of time.

DR. WILLIAMS: It was kind of limited, even in those trials. It could possibly be a I to II, but I kind of lean toward the II.

DR. VAN HORN: One of the rate-

limiting steps in all of the literature related to children appears to be the variability in the diet assessment methodology. For example there are studies especially related to dietary fiber where, for example, in the one study that discusses a fiber supplement, there is no assessment of the rest of the fiber in the diet. So obviously one has ask yourself, what does that really mean? So I think unfortunately, especially earlier on, many of these studies which involve food frequency questionnaires or other less precise methods leave you wondering about, not only the fact that just as in adults overweight children underreport their intake et cetera, but the methods used to assess it are even more difficult in children than they are in adults, so I think we suffer a little bit from that.

But one of the aspects that I find especially intriguing is - and perhaps we will address some of this tomorrow when we discuss

the modeling issues. But when you look at the NHANES data and you begin to put patterns together, and Chris mentioned this in her magnificent overview of all these factors, which is just unbelievable, that there is an interesting finding in that those children who consume dietary fiber, increased dietary fiber is associated with lower total fat, lower saturated fat, lower sugar, added sugars, lower sugar-sweetened beverages. In other words, I believe as we go forward and take the best of what the evidence provides, we can also look at the actual eating behavior of American children today and get some ideas about patterns that lend themselves to more nutritious as well as less obesity-associated types of eating patterns. I think once our research data run out then we are left to look at exactly what kind of eating patterns might protect and promote a healthier outcome. Would you agree with that, Chris?

DR. WILLIAMS: That's a good

point. I think also, when you look at a lot of the studies, they use multiple measures of diet assessment, multiple measures of adiposity, and stratify by different variables, and often measure intake both in absolute terms, gram intake, or percent of energy, so there were so many different variables in the study to kind of sort through. But in the end I think the body of evidence was strong for many of the questions.

DR. APPEL: This is Larry again. You know, in this section, I think there is an important piece of the puzzle that should come out in the implications but doesn't, and it's the amount of calories and the percent of calories from explicitly sugar-sweetened beverages. And where you have it now, it's sort of buried as a percent of calories from added sugars and solid fats, which doesn't hit the point head on from what - at least in 2005 when we looked at calorie sources, it was like 20 percent of calories came from sugar-

sweetened beverages in certain subgroups of children, and I think that really needs to come out as part of the puzzle; it's not directly cohort studies, but I think that is contextual material that is incredibly important.

DR. WILLIAMS: I agree.

DR. VAN HORN: And along that line the fact that up to 40 percent of calories are coming from what one would consider snacks and desserts and foods of that nature is really quite disturbing. The idea of again focusing attention on the need to consume proper food, as snacks and as desserts et cetera, really has to come out loud and clear.

DR. RIMM: This is Eric. Can I raise my point for the third time. I guess we should talk about it once again, the issue of the dietary fat proposed conclusion. I guess my reading, and I think the way Christine has put together the implications which are very

nice, which essentially says that children should not be eating above the IOM report recommendations for fat for children, which is, if I can recall, is 25 - 35 percent of calories from fat. I think that is consistent with what we are saying for adults in terms of fat composition, but the way I read this conclusion is that, all kids should be on a low fat diet. I am concerned that a low fat diet will increase the sugar-sweetened beverages and the refined grains. So I don't know - I know that we talked about this before in our previous subcommittee call, and I think Joanne and Larry and a few others agreed that, I think the evidence doesn't necessarily point to the fact that a lower fat diet is beneficial, and in a few of the studies where it was lower saturated fat it was beneficial, but that the evidence doesn't support necessarily that there is a difference in what we should give for guidelines between children and adults.

DR. PI-SUNYER: Well, how would you like to fix that, Eric, by putting an actual range in here?

DR. RIMM: The implications do say that, and I think several of the cohort studies that you cite where there is an association between fat and weight gain, it is at levels above 35 percent of calories from fat, but I think if we are going to say something here, and say that the evidence is Grade II, which to me is pretty strong given what's here, is that we maybe should try to quantitate it so that people see that it is not different than what we are saying for adults.

DR. PI-SUNYER: I think that is a good idea. I think that would clarify things.

DR. WILLIAMS: I think we did put that in the implications though, that children should stay within the recommended range.

DR. RIMM: But right now the conclusion, if I was a food service provider

looking at the conclusion in dietary fat, it would say, eat low fat foods. Or if I was a parent or if I was someone trying to interpret this, it does suggest eating low fat foods. And I am concerned that that is what we said in the `70s to adults, and everybody went to low fat foods and ate nonfat yogurt, and I think that contributed to some of our weight gain issues, because we didn't follow the rest of the guidelines, and get our fruits and vegetables, but instead ate processed carbohydrates. And that's what all of us are concerned about and have been talking about with the fiber guideline.

DR. WILLIAMS: I think the key thing is to be careful about not overconsuming fat in the diet because it is so energy dense.

DR. RIMM: But our energy conclusion is only Grade III. So I understand the reason why we don't want to eat energy dense foods. It's just that in all the trials for humans where you look at a high fat versus

low fat diet it doesn't work. So there is no evidence here to me that says, trials among kids, where you are focusing just on total fat, that it did work. All we have is a trial, the STRIP study, which is a low saturated fat, high exercise, make sure your parents don't smoke, trial. And at age nine it only worked in the girls, and in age 14 there is no weight difference. So I'm not convinced that the evidence should really be different between kids and adults, and I am worried that we are going to give the wrong - I think we should have kids not eating at fast food restaurants, rather than trying to guide them into low fat foods.

DR. NELSON: This is Mim. I completely agree. But, so, it's more the way this is presented in the conclusion, isn't it, that it should be a range as opposed to lower intake of dietary - like lower intake of dietary fat.

DR. PI-SUNYER: I think Chris can

fix this very easily by just putting in that IOM range.

DR. WILLIAMS: That is no problem. I think that is a good suggestion.

DR. VAN HORN: I think that the point really is also that no one is suggesting a low fat diet of 30 percent of calories is not low fat. So I think the data that document a higher fat, and especially a higher saturated fat intake, it really does come out loud and clear. So an emphasis on reducing saturated fat seems totally appropriate, and again, perhaps emphasis on the foods that should be eaten, i.e., the complex carbohydrates, higher fiber foods appear to help achieve the recommended nutrient composition that is really being advertised --

DR. RIMM: I wonder if that could be one of the implications, what you just said, Linda, specifically focusing on saturated fat, because right now I think it's just on total fat, and I think there are

benefits to kids from the healthy fats. And so again I don't see any demarcation that says, adolescents are different than adults in terms of what we should be advising here. And I think we should have something in the implications that maybe specifically focuses on saturated fat so we are in line with fast food restaurants and all the other guidance we are giving.

DR. NELSON: And that would be complementary to the rest of the report, too.

DR. RIMM: Right, it's consistent.

DR. PI-SUNYER: Yes, I think we could include that.

DR. RIMM: The last implication is about the benefits of monos and polys, but maybe we should put upfront about the detrimental effects of saturated fats.

DR. PI-SUNYER: Okay, thank you, Eric. Thank you very much, Chris.

I think we need to move on,

because we don't have much time. The next session is on macronutrient proportion and body weight. And Joanne and I worked on this particularly but all of the subcommittee somewhat. So the overall question is what is the relationship between macronutrient proportion and body weight and other questions are, what is the optimal macronutrient proportion to maintain a health weight? To lose weight if overweight or obese? And for weight loss maintenance? And then, are low carbohydrate hypocaloric diets safe and effective for long term weight loss and maintenance, and are high protein hypocaloric diets safe and effective for long term weight loss and maintenance? Next slide please.

The search strategy you see here, we went back to June of 2004, included adults 19 and older and had the outcome measures you see there, overweight, obesity, BMI, percent fat, waist-to-hip ratio, weight gain and weight loss.

The overall research question: what is the relationship between macronutrient proportion and body weight? Next slide.

Proposed conclusion: when calorie intake is controlled the macronutrient proportion of the diet is not related to maintaining a healthy body weight, losing weight or avoiding weight gain. Weight loss can be achieved through changing macronutrient proportions. But this effect does not last. Dietary patterns with macronutrient proportions that are outside the Dietary Reference Intakes are difficult to maintain over the long term and also raise some safety questions.

Next question: what is the optimal proportion of dietary fat, carbohydrate and protein to maintain a healthy body weight? The conclusion, the limited number of studies that address this suggest that carbohydrate intake is negatively associated with BMI, and that normal body weight is associated with a

carbohydrate intake at the level of 40 to 65 percent of total calories. Next slide.

The two studies that lead to this conclusion particularly are these two, and unfortunately, they are both cross-sectional studies. Both studies found that normal weight subjects were more likely to consume a diet higher in carbohydrates than overweight or obese individuals. Next slide.

What is the optimal proportion of dietary fat, carbohydrate and protein to lose weight if one is overweight or obese? And the conclusion: when overweight/obese persons attempt to lose weight with reduced calorie intake, there are no differences in weight loss with differing macronutrient proportions if diets are followed for longer than six months. In shorter-term studies low-calorie, high-protein diets may result in greater weight loss, but these differences are not sustained over time.

With regard to loss of weight, you

can see, we looked at 36 articles. Five systematic reviews, 31 RCTs, and one non-RCT. Twenty studies found no relationship between macronutrient proportion and weight loss; 13 studies found that low carbohydrate diets are more effective than low fat diets, or higher carbohydrate diets. Four studies found that high protein diets are more effective than low or moderate protein diets.

These are the trials. I'm not going to go through them. You can see most of them are randomized controlled trials which is pretty good. But you can see on the right that most of them have a zero with a slash through them showing no difference in effect.

What is the optimal proportion of dietary fat, carbohydrate and protein to avoid regain in weight reduced persons? There are no data to suggest that any one macronutrient proportion is more effective for avoiding weight regain in weight reduced persons.

This, we looked at 12 articles.

Two systematic reviews, nine RCTs and one prospective cohort study. Ten studies found no relationship between macronutrient proportion and weight loss. One study found that a low carbohydrate diet was more effective than a low fat diet, and one study found that a higher protein diet resulted in better weight maintenance than a lower protein diet.

And here you see again randomized controlled trials showing little relationship between - no relationship between macronutrient proportion and weight loss maintenance. Next slide.

Are low carbohydrate hypocaloric diets safe and effective for long-term, greater than six months, weight loss/maintenance? Diets with less than 45% of calories as carbohydrates are not more successful for long-term weight loss, that is, followed up to 12 months. There is also some evidence that they may be less safe. Next

slide.

And here we looked at 15 articles, 3 systematic reviews, 9 RCTs and 4 prospective cohort studies. Nine of the studies found no relationship between macronutrient proportion and weight loss. Two studies found that low carbohydrate diets are more effective than low fat diets. And two studies found that low carbohydrate diets were associated with increased mortality, especially cardiovascular disease mortality.

Here you can see the list of studies, most of them RCTs showing no effect with regard to differences. The last two trials, the Lagiou trial and the Trichopoulou trial, are two trials that were done in Greece, and they followed patients for a longer period of time, and reported that with a lower carbohydrate, higher protein diet there was a higher cardiovascular disease mortality and increased total mortality.

It's on the basis of only these

two trials that we put in the thing about safety, that they might be less safe. Next slide, please.

Are high protein hypocaloric diets safe and effective for long term weight loss/ maintenance? Intake of diets higher in protein than accepted standards, greater than 35 percent of total calories, provide no advantages for weight loss or weight maintenance or for improved health biomarkers compared to other diets with differing macronutrient composition. Also such diets may be less safe than diets within the DRI ranges for macronutrients.

And here you see there are less studies available, three RCTs and one cohort study. The three studies, the three RCTs, found no relationship between macronutrient proportion and weight loss, and one study found that diets lower in carbohydrate and higher in protein were associated with increased mortality, especially cardiovascular

disease mortality. And that Trichopoulou study is the same one I quoted earlier for the low carbohydrate, high protein diets.

What is the relationship between macronutrient proportion and body weight? So, the overall conclusion is that when calorie intake is controlled the macronutrient proportion of the diet is not related to maintaining a healthy body weight, losing weight or avoiding weight gain. Weight loss can be achieved through changing macronutrient proportions, but this effect does not last. Dietary patterns with macronutrient proportions that are outside the Dietary Reference Intakes are difficult to maintain over the long term, and also raise some safety questions. Next slide, please.

I will go on and deal with this and then ask for questions. This is the effect of weight loss in older adults on health outcomes. And the research question is, for older adults, those aged 65 and over,

what is the effect of weight loss versus weight maintenance on selected health outcomes, cardiovascular disease, type 2 diabetes, cancer, and mortality?

This question was not addressed in the 2005 Dietary Guidelines Report. We searched back further because it wasn't addressed in 2005, so we went back to 1995, included older adults above age 65, and looked at cardiovascular disease, type 2 diabetes, cancer and mortality. The proposed conclusion, which is a Grade II, in older adults mortality associated with BMI is U-shaped, increasing below 18.5 and also rising beginning at BMI 27 to 34, depending on the study. Weight loss in older adults is associated with increased risk of mortality. Most studies have not differentiated between intentional versus unintentional weight loss--

DR. VAN HORN: Okay, this is just an announcement to everyone. We have decided due to technical difficulties today that we

will go ahead and end our session and pick it up again tomorrow morning at 9:00 a.m. Eastern time by concluding the rest of this particular report, and then picking up with the next subcommittee report after that.

We appreciate your patience, and we look forward to talking with you in the morning. Thank you.

(Whereupon at 4:07 p.m. the proceedings in the above-entitled matter was adjourned.)

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