Diabetes and Nutrition

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This is the first in a series of articles covering the 2002 American Diabetes Association Annual Meeting, which was held San Francisco, 14–18 June 2002.

Nutrition recommendations

Marion Franz (Minneapolis, MN) discussed the process used for the "evidence basing" approach for current American Diabetes Association (ADA) nutrition recommendations (1). "We have made some progress," she pointed out, comparing the starvation treatment used in 1917 (composed of whiskey mixed with black coffee) with our current approaches. "There are many ways of approaching medical nutrition therapy" for persons with diabetes, she stated, which requires assessment of the individual's goals and her/his ability to comply with a given recommendation. "The gold standard of research in nutrition has generally been a study in which food is provided to the subjects so that you can know what is being consumed," she stated, but such studies are necessarily short in duration, and therefore may not be completely applicable to the "real world," and must be extended by studies implemented in free-living subjects. Also, many questions have not been addressed in persons with diabetes and must be extrapolated from studies in persons with other conditions.

Franz referred to the studies on fiber as examples. Early studies showed a great deal of benefit, but "there are many variables. People lost weight, they changed the percentage of macronutrients, medications were changed, and yet all the benefit was ascribed to fiber." More recent studies of high–fiber load approaches show only equivocal evidence, with benefit at fiber levels exceeding 50 g daily, far above the level of ~20 g daily that can be attained in realistic circumstances, that has not been shown to be associated with improvement in lipids, glycemia, or insulin resistance. With newly diagnosed type 2 diabetes, she stated, lifestyle change leads to a fall in HbA_{1c} of ~2%, and with existing type 2 diabetes, falls of ~1% can be expected. These changes can be seen over 6–12 weeks, a realistic timeframe for intervention. As Franz pointed out, "At three months, if an individuals had made all the changes that they were willing or able to make [and had not a shown fall in glycemia], then, obviously, medications would need to be changed." She recommended this approach rather than using one "ADA diet," since "handing out these diet sheets to people is rarely effective"; more individualized medical nutrition therapy should be undertaken. Furthermore, although weight loss is the ideal, we should not consider this essential, and we should realize that changes in eating habits and exercise without weight loss may be beneficial. Additionally, even small amounts of weight loss, by 5–7%, can improve metabolic parameters in the short term, and "we don't know what happens in the long term." It appears that the "total quantity of carbohydrate [CHO] is more important than the source of the CHO," and that sugars are not less desirable than starches. "Adding protein does not slow the rate of absorption," she stated, and protein also does not prevent late hypoglycemia, so that this common recommendation is no longer accepted. Micronutrient supplementation is now considered "unlikely to be beneficial," with the exceptions of calcium and folic acid. One should not consider a patient to "fail" with diet and exercise, but simply that at a given point medications need to be added or changed. Finally, nutrition therapy is now reimbursed by most health insurers, and this should not be seen as a barrier to nutrition counseling for patients.

Madelyn Wheeler (Indianapolis, IN) discussed nutritional approaches to dyslipidemia. The "primary target" is reduction of risk for cardiovascular disease (CVD) by lowering LDL cholesterol levels to <100 mg/dl, with lowering triglyceride and raising HDL cholesterol levels as secondary aims. Nonpharmacologic treatment includes reduction in saturated fat for LDL lowering. Decreasing weight, increasing physical activity, and smoking cessation increase HDL cholesterol, and weight loss, physical activity, and decreasing alcohol consumption lower triglycerides. The focus of medical nutrition therapy is on saturated and "trans" fats, which comprise 11 and 3%, respectively, of the typical diet, raise LDL cholesterol levels, and should be limited to <7–10% of energy. Wheeler reviewed data suggesting that reduction of saturated and trans fat to <10 and to <7% of calories, respectively, which requires a decrease in fat intake by ~10 and 15 g daily, will reduce LDL cholesterol by 18 and 25 mg/dl. Caveats include the need for a period of observation of at least 6 weeks to assess the response to such an intervention, and the recognition that the magnitude of response is related to the initial LDL cholesterol level. The optimal approach involves reduction of dairy and animal fats and high-fat baking products and fried foods. Thus, using one glass of fat-free rather than low-fat milk eliminates ~2.5 g; exchanging 1 oz of low-fat cheddar cheese for regular cheese eliminates 2.5 g; and having a very lean ground round burger rather than a lean hamburger saves 4 g of fat. Hard margarine has hydrogenated fats and is higher in trans fats than soft margarine, and use of this rather than butter may eliminate 5 g of saturated fat. Eating an apple rather than a pastry eliminates 6 g of saturated and 2 g of trans fats.

Wheeler suggested, then, that achieving fat reduction goals need not be difficult. For those persons who are at goal weight, rather than adding CHO, monounsaturated fats may be desirable, although CHO from grains amounting to <60% of total calories do not have the undesirable effects on triglycerides seen with high levels of refined CHO. "A tablespoon [of fat] is a lot of calories," she stated, so that adding CHO to diet is certainly important. Another option is the

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Abbreviations: ADA, American Diabetes Association; CHD, coronary heart disease; CHO, carbohydrate; CVD, cardiovascular disease; DPP, Diabetes Prevention Project; UKPDS, U.K. Prospective Diabetes Study.

use of plant stanols, which have fewer calories than fat; consumption of 2–3 g daily reduces LDL cholesterol by ~10%. Viscous (previously referred to as "soluble") fiber, made from oat products, psyllium, or pectin, may be associated with LDL reduction of 2.2 mg/dl per g fiber (2). Soy products may also reduce cholesterol levels, with 25 g per day reducing LDL by as much as 10%. Garlic and antioxidants would theoretically be useful, but "unfortunately, so far no clinical trials have found significant benefits." Weight loss and increased physical activity can increase HDL by 10%, fish (and fish oils) can decrease triglycerides, and moderate alcohol use appears to decrease CHD risk. "Sometimes, despite our best efforts and despite our patients' best efforts, medical nutrition therapy does not have desired results," Wheeler stated, but, overall, "medical nutrition therapy is effective."

Christine Beebe (Lincolnshire, IL) reviewed nutrition recommendations as they relate to obesity. She termed this "one of the most controversial areas the committee had to deal with." Obesity prevalence is increasing, "a frightening and challenging opportunity." She discussed the areas of prevention of obesity (and hence of the development of type 2 diabetes), the prevention of progression from obesity to type 2 diabetes, and the treatment of obese persons with diabetes. Approaches to prevention of diabetes have considered the question of fat versus CHO. There is epidemiologic evidence that dietary fat is associated with obesity and that elimination of dietary fat leads to weight loss. In the Finn Risk Study, high fat intake was the strongest predictor of weight gain, while vegetable and modest alcohol intake and physical activity exceeding 150 min/week were the strongest predictors of lower weights. Restriction of fat need not lead to weight loss. Over the past decade, fat intake has decreased from 38 to 32% of total calories, but total caloric intake has increased by 100–200 kcal/day (soft drink consumption is a predominant cause). Decreasing the ratio of simple to complex CHO may be of some benefit in dietary approaches to weight loss, particularly in persons with the metabolic syndrome, although Beebe suggested that decreasing fat intake is of more importance.

"Once an individual develops obesity," Beebe asked, "is there consensus on an optimal diet?" A 53 vs. 25% fat diet on a metabolic ward did not affect the degree of weight loss for a given calorie deficit. Reducing fat intake by 10% in free-living persons does appear of benefit, however, particularly in obese persons. Low-calorie diets with low and moderate fat content may have little short-term difference, although there may be benefit of reduction in fat in maintaining weight loss long-term. Furthermore, maintenance of weight loss is more manageable with fat restriction. These findings of adverse effects of fat ingestion have been demonstrated to some extent in persons with diabetes. There is interest in the protein content of diet, with 25 vs. 12% protein diets (the difference mainly in CHO) beneficial in some but not in all studies in promoting weight loss. "We really don't know for sure" what is the optimal macronutrient content of diet, but reducing fat by 10% and giving ~20% of calories as protein may be optimal. Beebe noted, however, that a relatively high 100-g protein diet could comprise 4 servings of vegetables, 10 servings of whole grains, 1 serving of dairy, and 2 4-oz servings of meat, fish, or poultry; thus, it is not necessary to make major efforts to increase meat intake.

Diet and exercise are both helpful, but most studies have been short in duration and have used very low–calorie approaches, which may not lead to long-term weight loss. The U.S. National Weight Control Registry follows persons who have maintained weight loss, showing that low fat intake and high frequency of exercise are major associations. The best approaches, then, emphasize lifestyle change, low-fat diets, regular physical activity, and regular contact with healthcare providers. The U.K Prospective Diabetes Study (UKPDS) showed that dietary intervention during the first 3 months after diagnosis of diabetes was effective in lowering fasting glucose, particularly during the initial month of intervention, although there was a great deal of intrapatient variability. Beebe characterized diet as more important than weight change per se, suggesting that "we shouldn't be hammering home the weight loss issue all the time" in our discussion with patients. She stated that weight gain occurred with pharmacologic treatment throughout the study, perhaps 70% of which could be explained by decreased glycosuria with consequent retention of calories and that 30% of weight gain might have been related to a decrease in metabolic rate. Analyzing the effect of initiation of insulin treatment in type 2 diabetes, after 6–12 months, mean weight gain of 6 kg occurs, two-thirds due to increase in fat, without relationship to pre-existing obesity. Weight gain with insulin secretagogues and, particularly, with thiazolidinediones is also expected. Bebee recommended an approach to obesity and overweight with monitoring physical activity and diet to attempt to create a 250-kcal daily deficit, focusing on portion control.

Lea Ann Holtzmeister (Tempe, AZ) discussed pediatric and adolescent nutrition recommendations. There is an increasing prevalence of type 2 diabetes in youth paralleling the increasing prevalence of childhood obesity. Little evidence, however, exists to guide the nutrient recommendations for such children, with current approaches extrapolated from those for children in general. She noted that few U.S. children meet guidelines for fruits, grains, dairy, and total and saturated fat. Children with diabetes should strive to achieve these recommendations, but studies suggest that children aged 4–9 years with type 1 diabetes have adequate energy, vitamin, and mineral intake, but higher saturated fat and lower fiber intake than recommended. The initial weight loss at onset of type 1 diabetes can be restored with initiation of insulin treatment. The use of growth charts allows assessment of dietary adequacy. Energy requirements fluctuate and should be regularly re-evaluated. It is important to assess the family's willingness to make changes. Children and adolescents with diabetes should have lipid screening, with LDL cholesterol <110 mg/dl and total cholesterol <170 mg/dl as goals. The two-step National Cholesterol Education Program approach involves *1*) a population approach with saturated and total fat <10 and 30% of calories and dietary cholesterol <300 mg/day, and *2*) an individual approach, particularly if parents have coronary disease and hypercholesterolemia, but useful for all children with diabetes. Dietary fiber in childhood may be associated with health benefits, and the sum of the child's age plus 5 in g/day is recommended. Such foods should be introduced gradually as fruits, vegetables, and grains and should be accompanied by increases in water intake. Twenty percent of children and adolescents have BMI

>85th percentile, with more sedentary behavior patterns, and increases in activity and fitness are associated with lipid lowering in children with type 1 diabetes. The level of activity needs to be maintained.

In the Diabetes Control and Complications Trial (DCCT) and the UKPDS, the importance of glycemic control has been demonstrated. Achieving glucose goals without hypoglycemia, then, is important, recognizing that there is little evidence pertaining to specific nutrient requirements. Children with type 1 diabetes before puberty do have increased hypoglycemia risk, and cognizance of this should be incorporated into the nutrition recommendations for these children. Flexibility for irregular meals, exercise, etc., must be considered. For children with type 2 diabetes, cessation of excessive weight gain with preservation of normal linear growth should be the goal, along with prevention of comorbidities and normalization of glycemia. Behavior modification to decrease high fat and calorie intake in a fashion appropriate to the family's resources is important. For adolescents whose parents already have type 2 diabetes, the risk of type 2 diabetes is increased and typical features of the metabolic syndrome are common, and such children should be screened for diabetes and dyslipidemia and included in the lifestyle intervention offered to the parent.

Regarding Atkins-type low-CHO diets, the discussants noted that these 25–30% protein diets have in general been studied in healthy populations, and "we don't know how that could be extrapolated to diabetes." This diet "restricts many healthful foods [and] hardly seems fair to persons with diabetes," particularly with an increase in saturated fats, and, although "without a doubt they lose weight," there is substantial subsequent weight regain after discontinuation with these approaches. Although it had been assumed that high protein diets would lead to slow increase in glucose entry to the circulation, it has not been possible to show this in human studies. Some amino acids are used by the gastrointestinal tract and liver as fuel, but it is noteworthy that protein is a stimulus of insulin to as great an extent as CHO, and perhaps to a greater extent in persons with type 2 diabetes, and so would not be expected to offer insulin-sparing effects. In a study presented at the ADA meeting, Seshadri et al. (256-OR) randomized 12 vs. 13 obese persons with type 2 diabetes to a low-calorie/low-fat diet, with a 500-kcal daily deficit versus a <30-g CHO non–calorie-restricted diet for 6 months (abstract numbers refer to the abstracts of the 62nd ADA Scientific Sessions, *Diabetes* 51 [Suppl. 2], 2002) . HbA_{1c} fell 0.75 vs. 1.6%, BMI fell from 43 to 38 kg/m^2 (vs. from 42 to 38 kg/m^2), and neither group showed significant change in lipids, suggesting the low-CHO diet to be feasible for use in persons with diabetes. An interesting point raised in discussion is that with high protein and fat intake it may be necessary to adjust the bolus insulin dose formula for patients using insulin pumps. Of course, many approaches to diet can be effective. Lanou et al. (252-OR) reported improvement in insulin sensitivity and a decrease in fasting glucose accompanied by a decrease in total and fat weight with a low-fat vegan diet, but not with a National Cholesterol Education Step II diet, in 59 overweight postmenopausal women in a 14-week intervention.

CHO in diabetes risk

At a symposium addressing the role of CHO in diabetes risk, David Jenkins (Toronto, Canada) discussed the evolution of the concept of "slow-release" CHO, comparing those absorbed rapidly with those absorbed slowly, the former "causing high rises and undershoots." The latter can be achieved with addition of fiber, particularly viscous fiber, with low–glycemic index foods, with enzyme inhibitors such as acarbose, and with higher food ingestion frequency. Comparing normal volunteers who "nibbled," with slow ingestion of a liquid oral glucose load over 180 min, as opposed to "gorging" by ingesting the glucose load over 5 min, he showed that the usual rise in blood glucose seen with rapid glucose ingestion can be completely prevented by the slow ingestion approach. The latter is associated with considerably greater increase in insulin and, subsequently, in counter-regulatory hormones such as glucagon, cortisol, and catecholamines and then in free fatty acids, and with decreased glucose tolerance following a second glucose load. This observation predicts that delaying the absorption of CHO would improve glucose metabolism in persons with diabetes. In type 1 diabetes, such an approach decreases the likelihood of nocturnal hypoglycemia. Lipid metabolism appears to be favorably influenced by "nibbling," and LDL cholesterol and apolipoprotein B levels are decreased by ~20% with such an approach. Unfortunately, the recommendation of more frequent meals may lead to an increase in total caloric intake and therefore may not be generally advisable. Slow-release CHO, such as oats and legumes, are more slowly digested than grains as in breads and breakfast cereals. White bread shows glycemic excursion more than twice as great as that with spaghetti, suggesting the importance of food preparation. In analysis of effects of various foods on glycated hemoglobin and fructosamine levels, the glycemic index of foods calculated from such data shows association with mean glycemia in persons with diabetes. The risk of development of diabetes has been shown to be associated with the product of glycemic index and calories, with cereal fiber and whole grain foods being particularly noteworthy in reducing this risk. Use of foods with lower glycemic index also reduces triglyceride and cholesterol levels in patients with dyslipidemia, high glycemic index diets may be associated with higher HDL cholesterol levels, and levels of plasminogen activator inhibitor 1 decrease in individuals with type 2 diabetes ingesting low–glycemic index diets. CVD risk in women with BMI >23 kg/m^2 increases with higher glycemic load in population studies. There is also evidence of an association between higher glycemic load and colon cancer risk, and higher levels of ingestion of bread may be particularly associated with higher risk.

David Jacobs (University of Minnesota) discussed the role of CHO-containing foods in the prevention of diabetes and in the clinical management of diabetes, pointing out that a number of other nutrients are present in such foods and may be relevant to this topic (3). Digestible and nondigestible CHO should be distinguished, and we have little information about long-term physiologic effects of the differing chemicals comprising CHO. The term "fiber" refers to nondigestible material in foods, but fiber may also be a marker of cell wall phytochemicals contained in foods, and fiber may also be added to foods. The potential benefit may differ for these different groups of substances, with Jacobs referring to a recent study showing that adding a nonnutritive fiber increased rather than decreased the appearance of colonic polyps. The diabetes risk associated with CHO-containing foods may relate to the interaction of their various components. Refined wheat has lost ~80% of its biochemical constituents, and fiber from whole grain foods is more highly associated with protection against CVD and diabetes than is fiber from refined wheat. The various diets that can be classified as being "high fiber," then, may greatly differ, including wheat bran only, oatmeal, oat bran, legumes, high-fruit, and vegetable diets, etc. An audience member, however, pointed out that what we refer to as "whole wheat" flour is actually manufactured by reconstitution of refined flour with bran and other products, so that it may not be useful to contrast fiber additives from "true" high-fiber grain products. Furthermore, foods with low glycemic index can be manufactured by addition of fat or of fructose. Another interesting issue raised was whether highly processed rice, which has high glycemic index, may be related to the increasing rates of diabetes in Asian populations. "It is only partially known which kinds of foods and [. . .] which combinations," Jacobs pointed out, are associated with decreasing rates of CVD and diabetes.

Lifestyle interventions that have been shown to reduce diabetes include those of the Finnish Diabetes Prevention Study of 522 persons, with whole grain, vegetables, fruit, low fat milk, and meat as part of the program, and of the 3,200-person DPP, which did not specify the fiber content of its dietary approach. Both of these studies showed a >50% decrease in the development of diabetes with lifestyle change. The Nurses' Health Study of 85,000 women showed that cereal fiber, glycemic load, higher polyunsaturated-to-saturated fat ratio, and trans-fat diets were protective, with high-fiber diets reducing risk by 26–27%. The Iowa Women's Health Study utilized a dietary questionnaire in ~40,000 women, suggesting that greater ingestion of whole grain was strongly associated with other lifestyle characteristics and was associated with lower body weight. When correcting for body weight, there remained a 20% reduction in diabetes risk with whole grain ingestion. The Health Professional's Study similarly showed that cereal fiber was associated with decreased diabetes risk. Fasting insulin levels and body weight decreased with increasing whole grain intake in these and other studies. In clinical studies, overweight persons treated with diets high in whole grain improved insulin sensitivity, with decreases in fasting blood glucose levels and improvement in glucose tolerance as well; wheat bran had a lesser effect than other dietary fiber sources. Similar benefits have been reported in subjects with diabetes.

David Ludwig (Boston, MA) presented additional information pertaining to dietary approaches for diabetes, pointing out that there is actually little association between dietary fat and the development of obesity and diabetes, and that low-fat diets are only modestly effective, which suggests that calories from CHO may be associated with development of obesity. The concept of glycemic index addresses this to some extent, "with some refined starch products equivalent to glucose." High–glycemic index foods "elicit a series of metabolic changes," Ludwig stated, which may be associated with obesity. He also pointed out that over- and underfeeding are associated with compensatory changes in energy expenditure to blunt the change in body weight. Diets with high glycemic load may also be associated with proteolysis and negative nitrogen balance, "which might over time cause a change in body composition." There are no long-term controlled studies in humans to show that dietary starch content is beneficial, but animal studies do appear to support this idea. In obese persons, weight loss and, in particular, reduction in body fat appear to be greater with low–glycemic index foods. Retrospective analysis of children given low–glycemic index diets suggests greater weight loss as well. Ludwig speculated that high–glycemic index diets may increase β-cell work and may contribute to development of diabetes. In the EURODIAB study, there was a correlation between glycemic index and HbA_{1c} in persons with type 1 diabetes (4). Given the potential benefits of such diets, he suggested that a grain-based diet may be "extremely high in glycemic index," and that use of "abundant quantities of fruits, vegetables, nuts, and legumes [and] grain in their least refined form possible" constitute the optimal diet for persons with and at risk for developing diabetes.

Shah et al. (253-OR) analyzed factors affecting adherence to ADA dietary recommendations among 252 insulin-treated persons with type 2 diabetes. Only a minority of these patients met the seven recommendations for fat, saturated and polyunsaturated fat, fiber, CHO, cholesterol, and sodium, with each person meeting a mean of 2.9 recommendations. Being married and working longer hours were correlated with meeting fewer dietary objectives, while age and diabetes duration were associated with meeting more objectives. Gregg et al. (916-P) used data from the 1989 National Health Interview Survey of 1,400 individuals with self-reported diabetes aged >35 years with BMI >25 kg/m^2, with 463 deaths over the subsequent 9 years. Those who reported that they were trying to lose weight had a 26% lower mortality risk, whether or not they actually reported weight change, suggesting benefit of efforts at improved diet. Leibson et al. (941-P) studied 1,290 Rochester, Minnesota, residents who developed diabetes as adults between 1970 and 1989. Of these subjects, 76% were overweight at diabetes onset, with 19% having a 5% or more weight gain (particularly in those who were middle-aged and higher fasting glucose and lower BMI at onset) and 50% having a 5% or more weight reduction (particularly in those who were older with lower fasting glucose and higher BMI). Leibson et al. suggest that effective weight loss intervention is most important among younger and middle-aged adults.

A number of specific dietary components may be beneficial for persons with diabetes. Whitham et al. (1654-P) administered 5 g Salba, produced from seeds of the plant source *Salvia hispanica*, which contains high concentrations of omega-3 fatty acids, as well as high polyunsaturated fat levels, to 18 subjects with type 2 diabetes with an HbA_{1c} level of 6.8%, and showed a 7-mmHg decrease in blood pressure, although no change in lipids or blood glucose. Liu et al. (1648-P) described data from 74,090 women in the Nurses' Health Study followed from 1984 to 1996. Women who were in the highest quintile of whole grain intake weighed about 1 kg less at baseline and through the study than those in the lowest quintile of intake, while refined grain was associated with higher weight, controlling for age, follow-up interval, physical activity, cigarette smoking, alcohol intake, caffeine use, use of hormone replacement therapy, and multiple dietary factors that included all different types of fats, protein, and total energy intake.

Jianget al. (1644-P) evaluated 83,818 women from the study. Compared with those who never ate nuts, those who ate nuts <1 time weekly, 1–4 times weekly, and 5 or more times weekly decreased diabetes risk by 7, 16, and 28%, controlling for intakes of vegetables, fruits, whole grain, and a composite diet score composed of trans fat, cereal fiber, glycemic load, marine omega-3 fatty acids, folate, and polyunsaturated fat-to-saturated fat ratio. However, Kasim et al. (1645-P) reported effects of eating 48 g walnuts daily among 17 women with the polycystic ovary syndrome, reporting a fall in 15-deoxyprostaglandinJ2, the natural ligand for peroxisome proliferator–activated receptor (PPAR)-γ, and an increase in fasting and post-oral glucose blood glucose levels. Hu et al. (251-OR) reported data from 5,179 diabetic participants in the Nurses' Health Study, showing significant inverse associations between fish intake and incidence of coronary heart disease (CHD), with those eating fish 1–3 times per month, once per week, 2–4 times per week, and 5 or more times per week having 33, 35, 37, and 60% decreases in CHD rates; the latter group also had 48% lower mortality.

Lifestyle intervention for diabetes prevention

At a symposium on prevention of diabetes, Rena Wing gave an overview of the DPP lifestyle intervention, Andrea Kriska discussed changing exercise behaviors, Bonnie Gillis discussed changing nutrition behaviors, and Linda Siminerio discussed implications of diabetes education. Wing (Providence, RI) discussed the results of the DPP (5). The DPP required screening of ~150,000 persons and performedg ~30,000 glucose tolerance tests; 4,500 persons participated in the run-in program, with 3,819 persons assigned to one of the four arms of the program. The troglitazone arm was subsequently discontinued and therefore the main study population comprised 3,234 subjects. Of this population, 68% were women, randomized to intensive lifestyle intervention or to standard lifestyle intervention plus metformin 850 mg twice daily or placebo; 70–80% took their assigned medication. Three previous studies, the Malmo, Da Qing, and Finnish Diabetes Prevention Studies, suggested efficacy of such intervention, all leading to 42–58% reductions in diabetes risk. She described the concern of the investigators that the intervention be maintained long-term in a variety of ethnic groups.

A "goal-based intervention" was used, with all participants sharing the same goals of 7% body weight loss, 150 min of physical activity (equivalent to brisk walking) weekly, and the same intensive intervention with frequent ongoing contact throughout the trial, and with a "toolbox" of various approaches to be used with a case manager assigned to each participant. Each participant had a 16-session core curriculum over a 16- to 24-week period, followed by monthly or alternate monthly visits and monthly telephone contact throughout the trial. Participants reported actually performing ~90 min/week of physical activity, while those in the placebo and metformin groups did not increase exercise. At the end of the core curriculum and at the end of the study, 50 and 38%, respectively, achieved the 7% weight loss goal. Metformin produced a 2-kg weight loss; placebo resulted in no weight loss; and lifestyle resulted in a 4-kg weight loss over the course of the study. Of the placebo, metformin, and lifestyle groups, 11, 7.2, and 4.8% developed diabetes annually; thus, 13.9 and 6.9 persons would need to be treated for 3 years to prevent one case of diabetes. There was no difference between sexes and ethnic groups in development of diabetes with lifestyle, suggesting the broad applicability of the approach. Metformin was not effective in individuals over 60 years of age, while lifestyle was effective in this group, which was particularly able to implement behavioral change, and in the younger groups. Metformin was only effective in heavier participants, while lifestyle intervention was effective regardless of the BMI category. Wing stated that the effect of metformin was independent of the degree of weight loss with this agent.

The question, Wing stated, is how can this be implemented. For every kilogram of weight loss, the diabetes risk was reduced 13%, while self-reported improvement in diet and physical activity not resulting in weight loss did not reduce risk, suggesting this to be the most important aspect of the study. The predictors of weight loss were changes in percent of calories from dietary fat and changes in physical activity (which was more related to weight loss maintenance), suggesting these to be the major important components of the intervention.

Andrea Kriska (Pittsburgh, PA) discussed the physical activity component of the lifestyle intervention of the DPP. Physical activity improves insulin sensitivity, with particular reduction in visceral fat. The simple goal was 150 min of modest activity weekly, with lifestyle participants significantly more likely to achieve exercise goals. Of the participants, 74% reported that they had achieved this goal following the core curriculum, with 55–75% achieving this goal at subsequent time points. She noted that the "participants were among the least active groups," suggesting this to be a particularly noteworthy achievement.

Lifestyle routines and goals are considerably more effective than just telling the person to attend a gym or to be more active. Kriska stated that participants were encouraged to exercise "when you want to, with whom you want to." Neighborhood walks were started, and participants became involved in community fitness centers. A gradual increase in activity was recommended, and participants were given recommendations about proper foot wear, to start exercising slowly, to be careful about exercise in cold weather, etc. Participants were allowed up to $100 annually for "rewards" of their own choice, such as T-shirts. Each participant was assigned to a lifestyle coach "to help through [the] barriers" with frequent contacts.

These exercise approaches built on findings of earlier studies. In the Malmo study, 47 men (mean age 49 years) participated in two 60-min sessions weekly, with walking the most frequent activity. Maximum oxygen uptake improved in the exercising group but not in men who chose not to exercise; the latter group showed a 50% reduction in diabetes (6). In the Da Qing study, 110,000 persons from 33 health clinics were screened, with 577 classified as having imparied glucose tolerance (IGT) and randomized by clinic into diet, diet and exercise, exercise, or control. The activity goal for walking, the most common activity, was 140 min/week, with the intervention leading to a reduction in diabetes (7). In the Finnish study, the exercise goal was 30 min/day, again with brisk walking the most commonly employed exercise; 86% of the intervention subjects vs. 71% of control subjects increased activity, resulting in a 58% decrease in diabetes (8). Kriska discussed the "Walking Women" study of 229 postmenopausal women randomized to walk ~150 min weekly or to a noexercising group. Activity increased in the intervention group, and the 10-year follow-up indicated that those assigned to exercise continued this behavior, "so it seems that 150 minutes can be maintained" (9). Similar follow-up of participants in the DPP is planned.

Bonnie Gillis (Pittsburgh, PA) discussed nutritional components of the DPP. Weight loss in the lifestyle group averaged 14.5 pounds at conclusion of the core curriculum with 50% losing 7% of weight, and by the end of the study, mean weight loss was 12.3 pounds and 35% had maintained at least 7% weight loss. Caloric and fat intake decreased 450 kcal and 6.6% at the end of 1 year in the lifestyle group. The "interventionist" (a "coach" or "case manager") was typically a registered dietitian, with others being social workers, exercise physiologists, or psychologists, most having Master's degrees. Gillis described the 16 sessions of the core curriculum. In the first session, participants "built a commitment" to the study, assigning weight and exercise goals and beginning self-monitoring their food intake. In session 2, participants began monitoring their weight, were assigned a fat goal of 25% of calories, as a goal of 33, 42, 50, or 55 g fat/day, depending on the starting weight, and began monitoring fat intake using a pocket-sized "fat counter" book. This was based on the concept that lowering fat intake might increase insulin sensitivity, as fat reduction is associated with reduction of calorie intake and weight loss. In session 3, participants were taught to weigh and measure foods and addressed approaches to reduction in calorie intake. In session 4, participants reviewed the importance of regular meals, of eating slowly, and of following the low-fat low-calorie choices of the food guide pyramid (in differing ethnic versions). In sessions 5 and 6, exercise was the major focus. Session 7 defined energy balance and assigned a calorie goal, using the formula 12 × [starting weight] − 500–1,000 calories depending on starting weight, recommending goals of 1,200–2,000 calories for participants who had not made progress in weight loss. Session 8 introduced the idea of cues, or stimuli for problem behavior. Session 9 reviewed steps to problem solving, first describing the problem (antecedents, behaviors, and consequences ["A-B-C's"]) and then developing action plans, which was used as the paradigm for the entire intervention. The interventionist and participant developed a written action plan at this and every session to help achieve goals. Session 10 addressed strategies to be used in "eating out," using examples from restaurants the participants frequented. Session 11 developed the idea of "talking back to negative thoughts." Session 12 emphasized that "slips or lapses are normal" and focused on approaches to getting "back on track." Session 13 involved exercise. Session 14 addressed problems in social settings, learning how to "ask for help," and planning ahead for parties and holidays. Session 15 taught coping strategies for stresses and reviewed skills that were introduced in earlier sessions. Session 16 gave a menu of strategies and "ways to stay motivated," and outlined personal goals for the next phase of the study.

Behavioral, nutrition, and physical activity classes, as well as motivational campaigns that lasted 4–8 weeks, were offered every year during the remainder of the study period, with participants "winning" rewards and recognition and being challenged to improve their personal performance as a contribution to the national goal. Approximately 2 years into the study, the most used "tools" were problem solving, review of self monitoring, recommending increased activity, and increasing frequency of contact. Slim Fast or coupons for Slim Fast and actual foods for periods of ~1 week were also provided for some of the participants. Additional information for the intervention is located at the DPP Web site (http://www.preventdiabetes.com), though some is in preliminary form.

Linda Siminerio (Pittsburgh, PA) further reviewed aspects of the DPP intervention and reviewed aspects of diabetes education relevant to this discussion. A meta-analysis discussed a variety of approaches to delivery of diabetes education that had effects on knowledge but no effect on weight or on HbA_{1c} (10). Therefore, "it's not about giving knowledge, it's about behavior change." The DCCT, Siminerio stated, "gave us such a powerful message" of the value of teamwork in patient care. The UKPDS showed "that diabetes is a progressive disease and it's not the fault of the patient," an important lesson for diabetes education, which requires frequent contact and a variety of approaches. She stated that the development of professional standards has been extremely important in allowing reimbursement, which will be critical in offering care of the sort given in the DPP. Professional service codes now allow reimbursement for diabetes education of approximately $35 per half hour for individual sessions and approximately $17 per half hour for group services, and this will be crucial in allowing such ongoing care.

"If you go to see a dietitian you are not reimbursed for anything unless you have diabetes or renal disease." Such services are not reimbursed prior to surgical treatment for morbid obesity, but will be reimbursed after such surgery. She suggested that it is illogical for an insurance company to pay $18,000 for obesity surgery but not to pay $50 for nutritionist services. "We've got to increase our advocacy efforts," she stated.

Another barrier, Siminerio stated, is the recognition of the importance of primary prevention. Managed care has limited the availability of time for patient-contact, and health care providers have limited care in prevention and counseling. Patients trust their physicians, and this is an important opportunity for "teachable moments" when high cholesterol or blood pressure is discovered. Tracking the outcome of primary prevention will be important in documenting accomplishments. "We've got to start thinking about exploring incentives" for health care providers to improve their preventative efforts. Outreach to minority communities and Internet interactive approaches, she suggested, will be particularly important.

The DPP Research Group (115-OR) analyzed various factors that potentially determine efficacy of the lifestyle intervention. None of the measures of physical activity or diet were associated with risk of diabetes above and beyond the effect of weight, with on average a 13.4% reduction in risk of diabetes per kilogram of weight loss. A further report from the DPP (972-P) was that change in diet, but not activity, was related to weight loss at 1 year and that changes in both diet and physical activity were associated with weight loss at 2 and 3 years in the DPP lifestyle participants. Delahanty et al. (1836-P) interviewed 274 of 1,079 lifestyle participants, finding that the most important determinants of meeting the 7% DPP weight loss goal at 6 months were greater dietary restraint ($P = 0.035$) and less frequent emotional eating ($P = 0.002$) at baseline and greater improvements in dietary restraint ($P = 0.0002$) and low-fat diet efficacy ($P = 0.013$) from baseline to 6 months. A history of weight cycling was a positive predictor, and frequency of previous weight loss programs was a negative predictor of weight loss at 1 year. In a cost-effectiveness analysis (301-OR), the DPP group reported that both the lifestyle and metformin interventions cost approximately $2,600 more per participant per year than the placebo (costs of $15,800 and $31,300 per case prevented). Assuming considerably lower costs, "as they might be implemented in clinical practice," they estimated that these costs would be reduced to $4,000 and $11,100 per case prevented. Considering direct medical costs, direct nonmedical costs, and indirect costs, the latter costs increased to $10,600 and $14,300 per case prevented.

Saremi et al. (998-P) studied the relationship between physical activity and incidence of type 2 diabetes in a high-risk Native American population; 346 of 1,728 individuals without diabetes at baseline developing the disease over a 6-year follow-up. Among women, regardless of BMI, high physical activity levels were associated with lower rates of developing diabetes. Tanasescu et al. (970-P) reported the relationship between physical activity and cardiovascular disease and total mortality among 2,648 men with type 2 diabetes in the Health Professionals' Follow-up Study. Compared with those in the lowest physical activity quintile, CVD risks with increasing activity were 26, 37, 31, and 37% lower, and mortality risks were 30, 47, 53, and 49% lower in the higher activity quintiles. In particular, walking was associated with reduced mortality, and the pace of walking was inversely associated with CVD and mortality risks independent of the time spent on this activity. Burge et al. (1001-P) described an effective exercise intervention for 30 individuals with type 2 diabetes. These subjects were given a pedometer and instructed to walk at least 10,000 steps per day at least 5 days a week for 6 weeks. The 15 persons receiving the pedometer walked 10,690 steps per day, as compared with those who did not receive a pedometer, who walked 6,410 steps per day; this discrepancy is the equivalent to walking ~2 extra miles per day. However, no change in glycemia, lipids, or body weight could be demonstrated.

It may, however, be difficult for persons with diabetes to exercise, both early and late in the course of the disease. Regensteiner et al. (241-OR) performed right heart catheterization and bicycle ergometry in seven women with type 2 diabetes, which was diagnosed a mean of 3 years earlier, and in nine control subjects, all with normal resting echocardiogram and without macro- or microvascular complications. The results showed a greater increase in pulmonary capillary wedge pressure and lower maximal oxygen consumption, suggesting that cardiac function was abnormal during exercise, despite there being no evidence of coronary disease in the diabetic group. Murata et al. (995-P) assessed exercise levels among 284 men with diabetes for a mean duration of 14.9 years; diabetic complications, disabilities, and cognitive dysfunction interfered with the ability of many of this group to exercise. Such conditions included peripheral vascular disease in 38%, foot ulcers in 17%, amputation in 8%, and prior myocardial infarction in 31%. Of the patients, 6% reported no physical activity whatsoever.

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