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# Nutrition Recommendations for the Treatment and Prevention of Type 2 Diabetes and the Metabolic Syndrome: An Evidenced-Based Review

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## INTRODUCTION

Nutritional recommendations for the prevention and management of diabetes and other diseases were in the past based principally upon the opinion of "expert" committees. Leading clinicians and researchers who served on such committees were expected to base their advice on their own clinical experience or research, or on that of others known to them. More recently, in parallel with the development of evidence-based medicine,[1] nutritional management is required to be based on evidence-based nutrition. This involves a prescribed method for searching the relevant literature using an agreed set of descriptors and relevant data banks (e.g., Medline, Embase). Individual studies are evaluated according to specified criteria and assigned to one of five evidence classes according to the type and quality of the study (Table 1). Recommendations themselves are graded according to the strength of the evidence. Grade A recommendations are based on evidence of class Ia or Ib, which require meta-analyses of randomized, controlled clinical trials, or at least one appropriately conducted randomized, controlled trial. Ideally, evidence-based guidelines are based upon trials with fatal or nonfatal clinical endpoints.

Given the complexities of large-scale nutritional intervention studies, which are required to produce such clinical endpoints, it is often necessary to base recommendations on surrogate endpoints. Surrogate endpoints relevant to the management of diabetes are shown in Table 2. In the past 4 years, there have been several randomized, controlled trials that have examined the role of lifestyle modification in the prevention of diabetes among persons at high risk who have already developed impaired glucose tolerance. It has thus been possible to generate evidence-based recommendations for the prevention and the management of type 2 diabetes. Randomized, controlled trials that have examined potential agents for the prevention of type 1 diabetes have not confirmed the potential of any of the agents tested to reduce risk. The Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD) has recently published its guidelines derived from evidence-based nutritional approaches to the treatment and prevention of diabetes mellitus,[2] upon which this review is largely based.

## ENERGY BALANCE AND BODY WEIGHT

An overwhelming body of evidence justifies grade A recommendations to reduce energy intake and increase energy expenditure among those who are overweight, and to prevent weight regain once weight loss has been achieved. Insulin sensitivity is reduced and most of the metabolic abnormalities associated with diabetes are exaggerated in those who are overweight.[3] Even modest weight loss (of less than 10% body weight) improves insulin sensitivity and glucose tolerance and reduces lipid levels and blood pressure.[4]

There is evidence to suggest that for European populations the appropriate body-mass index (BMI) range for people with diabetes should be the same as that for nondiabetic persons (18.5–25 kg/m$^2$),[5,6] although for other population groups a somewhat different range may be more appropriate[7] (e.g., for those of Indian descent, a lower range may apply). The life expectancy of overweight people with diabetes is improved in those who lose weight and may even be normalized without the

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**Table 1.** Evidence Classes and Grades of Recommendations Suggested by the Scottish Intercollegiate Guidelines Network (SIGN)

| SIGN Statements of Evidence | | SIGN Grades of Recommendations | |
|---|---|---|---|
| Ia | Evidence obtained from meta-analysis of randomized, controlled trials | A | Requires at least one randomized, controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendations (evidence levels Ia, Ib) |
| Ib | Evidence obtained from at least one randomized, controlled trial | | |
| IIa | Evidence obtained from at least one well-designed, controlled study without randomization | B | Requires the availability of well-conducted clinical studies but no randomized, controlled trials on the topic of recommendation (evidence levels IIa, IIb, and III) |
| IIb | Evidence obtained from at least one other type of well-designed, quasi-experimental study | | |
| III | Evidence obtained from well-designed, non-experimental, descriptive studies such as comparative studies, correlation studies, and case studies | | |
| IV | Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities | C | Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities; indicates an absence of directly applicable clinical studies of good quality (evidence level IV) |

patient's achieving a BMI of less than 25 kg/m$^2$.[8] Overweight patients with type 1 diabetes may also become insulin resistant, and weight loss may lead to a reduction in insulin dose and improved glycemic control.[9] Other recommendations regarding the most appropriate ways of achieving weight loss are graded as C (Table 1), since they are based on expert opinion rather than on sound experimental evidence.

**Table 2.** Surrogate Endpoints Used in Nutritional Studies Involving People with Diabetes

| | |
|---|---|
| Glycemia | Fasting plasma glucose |
| | Postprandial plasma glucose |
| | Glycated hemoglobin ($HbA_{1C}$) |
| Body composition | Adiposity |
| | Body weight |
| | Body-mass index (BMI) |
| | Waist circumference |
| Lipoprotein profile | Total cholesterol |
| | LDL cholesterol |
| | HDL cholesterol |
| | Triglyceride |
| Blood pressure | |
| Insulin sensitivity | Fasting insulin |
| | Postprandial insulin |
| | Insulin sensitivity index (ISI) |
| | Whole-body glucose disposal |
| Renal function | Microalbuminuria |
| | Proteinuria |
| | Glomerular filtration rate |

## DIETARY PROTEIN

Recommendations regarding dietary protein have long been controversial, with conflicting advice regarding amount and quality from different authorities. A meta-analysis[10] of randomized, controlled trials of up to 3 years' duration in patients with type 1 diabetes and nephropathy[11-14] found that a low-protein diet significantly slowed the development of albuminuria and the decrease of glomerular filtration rate. The most recent randomized, controlled trial published subsequent to the meta-analysis involved 82 patients with nephropathy, and was the longest carried out thus far (4 years). In this trial, patients with type 1 diabetes assigned to the low-protein treatment (target intake, 0.6 g/kg/d; achieved intake, 0.89 g/kg/d) had a strikingly improved outcome (relative risk for end-stage renal disease or death after adjustment for cardiovascular risk factors, 0.23) compared with those assigned to the usual protein intake (1.2 g/kg/d).[15]

Thus, restriction of protein intake to the lower end of the acceptable range (0.8 g/kg normal body weight/d) is recommended for diabetic nephropathy in type 1 diabetes (grade A recommendation). Severe protein restriction is not recommended, since patients with diabetes, especially those whose diabetes is poorly controlled or who

are on hemodialysis, have increased protein turnover, and their protein requirements may be greater than the Recommended Dietary Allowance (RDA).[16] Thus, protein intake should not be reduced below 0.6 g/kg normal body weight/d, because such reduction may lead to malnutrition.

For patients with type 1 diabetes and incipient nephropathy (microalbuminuria) and those with type 2 diabetes and established or incipient nephropathy, there is insufficient evidence to make a firm recommendation regarding protein restriction. For these patients, and for all patients with diabetes without nephropathy, it seems appropriate for protein to contribute between 10% and 20% of total energy, the range for most Western populations. Replacing red meat with chicken, fish, or vegetable protein is associated with reduced rates of glomerular filtration and albumin excretion in patients with elevated glomerular filtration. However, the studies have been relatively short term and the results inconsistent, and they are therefore not a basis for making recommendations.[2]

## DIETARY FAT

Given the appreciably increased risk of cardiovascular disease in diabetics, it is hardly surprising that recommendations regarding dietary fat are similar for people with diabetes and those at risk for cardiovascular disease for other reasons.[2] However, a grade A recommendation to reduce saturated fatty acids and *trans*-unsaturated fatty acids to below 10% of total energy (or below 8% if low-density lipoprotein [LDL] cholesterol is raised) is justified not only because of the established benefit in terms of reducing cardiovascular risk,[17] but also because of the effects of these fatty acids on insulin resistance and the increased insulin sensitivity noted when saturated fatty acids are replaced by *cis*-unsaturated fatty acids.[18-20] Although the recommendation that a wide range of monounsaturated fatty acids is acceptable achieves only grade B status, this advice is important because it permits considerable flexibility in terms of both carbohydrate and total fat intake, provided that total fat intake does not exceed 35% of total energy. The maximum total fat intake is based upon the energy density of high-fat diets and possible adverse effects on insulin sensitivity.

N-6 polyunsaturated fatty acids have beneficial effects on lipids and lipoproteins when substituted for saturated fatty acids, but as in the case for nondiabetic persons, it is recommended (grade C recommendation) that intake not exceed 10% of total energy because of the increased risk of lipid peroxidation possibly associated with higher levels of intake. Regular consumption (at least twice weekly) of fish (preferably oily) and plant sources of n-3 fatty acids (e.g., rapeseed oil, soybean oil, nuts, and some green leafy vegetables) helps to ensure an adequate intake of n-3 polyunsaturated fatty acids (grade B recommendation). Restriction of dietary cholesterol to 300 mg or less per day, especially in the presence of raised LDL cholesterol (grade A recommendation), is based on evidence from diabetic[17,21] and nondiabetic persons.

## TOTAL CARBOHYDRATE, GLYCEMIC INDEX, DIETARY FIBER, AND FREE SUGARS

Advice regarding carbohydrates has varied over the years, ranging from carbohydrate restriction to the recommendation of high-carbohydrate diets. It is now clear that the quality rather than the quantity of carbohydrate is what really matters. Vegetables, legumes, fruits, and whole-grain cereals are the most appropriate sources of carbohydrate; a meta-analysis[22] suggested that a wide range of intakes (45%–60% of total energy) is compatible with comparable glycemic control. Naturally occurring foods that are rich in dietary fiber are strongly recommended, with a total dietary fiber intake of 40 g/d (or 20 g/1000 kcal/d) or more being ideal. This grade A recommendation is based on randomized, controlled trials in type 1 and type 2 diabetes.[23,24] However, beneficial effects are also obtained with lower and, for some, more acceptable amounts.

About half of total dietary fiber should be soluble. Such diets not only improve glycemic control but also result in reduced levels of total and LDL cholesterol[25] and increased levels of high-density-lipoprotein (HDL) cholesterol.[26] Many foods that are high in dietary fiber, especially soluble fiber, also have a low glycemic index. However, regardless of fiber content, a meta-analysis[27] has reported that among subjects with diabetes, the percentage of hemoglobin A1c is, on average, 0.43% lower in those consuming a diet of low-glycemic-index foods than in those consuming a diet of high-glycemic-index foods. Although this effect is smaller than that which has been observed with some other dietary interventions, it should not be considered trivial, since it was achieved over and above the other dietary changes aiming to improve glycemic control, such as increased dietary fiber and reduction in body weight. Thus, it is appropriate to make a grade A recommendation that carbohydrate-rich, low-glycemic-index foods are suitable as carbohydrate-rich choices provided other attributes of these foods are appropriate. This caveat is essential, since some low-glycemic-index foods (e.g., ice cream) may be energy dense because they are high in fat and sugars.

Moderate intakes of free sugars (up to 50 g/d) may be incorporated, if desired, within the diets of persons

with type 1 or type 2 diabetes (grade A recommendation), provided blood glucose levels are acceptable and the person is not overweight.[28-30] Randomized, controlled trials suggest that glycemic control, lipids, and lipoproteins are not adversely affected by such amounts of sugar. In persons with insulin resistance, a high intake of free sugars may be associated with hypertriglyceridemia.[31] The wide acceptable range of intakes of total carbohydrate means that personal and cultural preferences can play an important role in determining intakes, which in turn enhances compliance. However, for some, metabolic characteristics may also suggest the most appropriate intake within this range. For those who are insulin resistant and hypertriglyceridemic, intakes at the lower end of the range might help to lower triglyceride levels and improve glycemic control. It is also particularly important for such persons to emphasize foods that are rich in dietary fiber and have a low glycemic index.[32-34] A range of grade C recommendations helps to facilitate the choice of carbohydrate-containing foods of appropriate quality.

## ANTIOXIDANT NUTRIENTS, VITAMINS, MINERALS, AND TRACE ELEMENTS

Sodium restriction has been shown to produce substantial reduction in systolic blood pressure in hypertensive patients[35] and to enhance the blood pressure-lowering effect of other dietary manipulations (low-fat dairy products, fruits, and vegetables), hence the grade A recommendation to restrict salt to under 6 g/d, with the possibility of further restriction for those with elevated blood pressure. Although no conclusive evidence exists for people with diabetes, grade C recommendations are offered regarding the encouragement of foods naturally rich in dietary antioxidants, trace elements, and other vitamins. This is achieved by daily consumption of a range of vegetables and fruits and regular consumption of whole-grain breads, cereals, and oily fish. There is no convincing evidence for the benefit of dietary supplements.

## PREVENTION OF DIABETES

Prospective studies have shown an increased risk of developing type 2 diabetes in those who have a high proportion of saturated fatty acids in their plasma lipid esters compatible with a high dietary intake of saturated fat.[36] Conversely, those who exercise regularly, are not overweight,[37] and have a high proportion of linoleic acid[38] have a reduced risk of developing type 2 diabetes. High intakes of dietary fiber (especially cereal fiber) and low-glycemic-index foods are also associated with a lower risk of developing type 2 diabetes. Several randomized, controlled trials in China,[39] Finland,[40] India (A. Ramachandran, personal communication), and the United States[41] have shown that a lifestyle intervention program involving dietary modification and increased physical activity can substantially reduce the risk of progression from impaired glucose tolerance to type 2 diabetes. Weight reduction of 5% to 7% of initial body weight or a weight loss of 5 to 10 kg, depending upon the degree of obesity, appears to be the pivotal component of the protective lifestyle regimen, hence the grade A recommendation regarding weight reduction and maintenance of weight loss in overweight persons.

All of the intervention trials were based on a macronutrient composition that included a relatively low intake of total and saturated fat (less than 30% and 10% of total energy, respectively) and a moderate to high intake of dietary fiber (more than 15 g/1000 kcal/d), and therefore such a dietary composition is also strongly recommended (grade A). Reduction of intake of energy-dense foods and frequent ingestion of whole-grain products, vegetables, fruits, low-fat meat and milk products, and soft margarines and vegetable oils rich in mono-and polyunsaturated fats are the means of facilitating such a macronutrient composition and achieving weight reduction.

Physical activity of at least moderate intensity (e.g., brisk walking) for at least 30 minutes each day is an important component of lifestyle modification aimed at reducing the risk of type 2 diabetes, and together with an increased intake of dietary fiber has been shown to make a contribution to risk reduction that is independent of weight loss. A similar exercise and dietary regimen has been shown to improve insulin sensitivity in insulin-resistant persons prior to the development of impaired glucose tolerance.[42] It seems highly likely that the traditional Mediterranean diet and other traditional dietary patterns may also be appropriate for achieving risk reduction if weight loss in those who are overweight or obese is achieved, although these diets have not been tested in randomized, controlled trials.

Regular vitamin D supplementation or a high dietary intake of vitamin D[43] among young children, a high intake of magnesium,[44] and treatment with nicotinamide have been linked with a reduced risk of developing type 1 diabetes. However, clinical trials have not confirmed the beneficial effect of nicotinamide,[45] and the absence of clinical trials relating to increasing intakes of vitamin D and magnesium precludes recommendations.

Given the existence of nutritional recommendations firmly based on experimental evidence, the challenge now is to develop strategies that will facilitate their implementation in those at risk for diabetes to reduce their chances of developing full-blown disease, and to reduce the risk of complications in those who have already developed diabetes.

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