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METABOLIC SYNDROME & TYPE 2 DIABETES: DAIRY'S POTENTIAL PROTECTIVE ROLE

SUMMARY

Emerging research suggests a potential protective role for dairy foods and/or dairy food nutrients (e.g., calcium, vitamin D) in metabolic syndrome and type 2 diabetes. Metabolic syndrome is generally diagnosed when three of the following five metabolic disorders are present: elevated fasting glucose, low high density lipoprotein (HDL) cholesterol, high triglyceride levels, abdominal obesity, and hypertension. Persons with metabolic syndrome are at risk for type 2 diabetes and cardiovascular disease. Metabolic syndrome is reported to affect more than one-third of U.S. adults and this syndrome is being diagnosed more frequently among children and adolescents.

Although genetic and environmental factors influence the development of metabolic syndrome and type 2 diabetes, the focus is on lifestyle choices, including diet, to help prevent these diseases. Because overweight/obesity increases the risk of metabolic syndrome and type 2 diabetes, achieving and maintaining a healthy body weight is recommended. Increasing physical activity and consuming a diet consistent with the 2005 *Dietary Guidelines for Americans* are also encouraged. Recently, scientists have begun to explore the possible beneficial role of dairy foods and/or dairy food nutrients in metabolic syndrome and type 2 diabetes.

Findings from epidemiological studies demonstrate a relatively consistent inverse association between consumption of dairy foods and metabolic syndrome in various populations. When data from several cross-sectional studies were combined, researchers reported that the prevalence of metabolic syndrome was 29% lower among adults who consumed three to four servings of dairy foods a day compared to those who consumed 0.9 to 1.7 dairy servings/day. Prospective studies in large populations of adults also support an inverse association between dairy food consumption and metabolic syndrome.

Although few clinical studies have examined the relationship between dairy foods and metabolic syndrome, intervention trials have shown a beneficial effect of dairy foods on components of the metabolic syndrome such as hypertension and obesity/adiposity. Also, studies demonstrate that several dairy food nutrients are inversely associated with metabolic syndrome and that they favorably affect its components.

The relationship between dairy foods and type 2 diabetes has been examined primarily by epidemiological studies. Based on a meta-analysis of prospective studies, researchers reported that the incidence of type 2 diabetes was 14% lower for adults consuming three to five servings of dairy foods a day compared to those consuming less than 1.5 dairy food servings a day. Dairy food nutrients such as calcium, vitamin D, and magnesium may contribute to dairy foods' potential protective effect against type 2 diabetes.

Additional studies, particularly randomized controlled trials, are needed to substantiate the beneficial role of dairy foods and dairy food nutrients such as calcium and vitamin D in the prevention and management of metabolic syndrome and type 2 diabetes. However, findings to date are promising and provide another reason to consume three cups of low-fat or fat-free milk or equivalent milk products (cheese, yogurt) a day as part of a healthful diet recommended by the 2005 *Dietary Guidelines for Americans*.

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INTRODUCTION

Metabolic syndrome (also known as Syndrome X or insulin resistance syndrome) refers to a cluster of metabolic abnormalities that predispose an individual to increased risk of developing cardiovascular disease and type 2 diabetes (1). Persons with metabolic syndrome are approximately twice as likely to develop cardiovascular disease and five times more likely to develop type 2 diabetes than those without this syndrome (2).

Although several different definitions are used to describe metabolic syndrome (3-5), the National Cholesterol Education Program's definition has been most commonly used in the United States (3,6,7). According to this definition, metabolic syndrome is diagnosed when three or more of the following five risk factors are present: elevated fasting blood glucose (≥ 100 mg/dL), low HDL cholesterol (<40 mg/dL in men or <50 mg/dL in women), high triglyceride levels (≥ 150 mg/dL), abdominal obesity (waist circumference ≥ 40 inches in men or ≥ 35 inches in women), and hypertension (blood pressure ≥ 130 mm Hg systolic or 85 mm Hg diastolic) (1,3). Individuals with these characteristics also commonly have elevated markers of inflammation and abnormalities in the blood coagulation system (5,7).

Based on data from the National Health and Nutrition Examination Survey 1999-2002, the age-adjusted prevalence of metabolic syndrome for adults is 34.6% (76 million Americans) (1). The prevalence increases with age and is higher among some ethnic minority groups (e.g., Hispanics, African American women, Native Americans) than among Caucasians (1,2). Worldwide, approximately 20% to 30% of the adult population has metabolic syndrome (2). Metabolic syndrome has been reported in 9.4% (2.9 million) of adolescents aged 12 to 19 (1). However, because of the lack of a universally accepted definition of metabolic syndrome in children and adolescents (8,9), prevalence rates in this population vary widely (1).

Metabolic syndrome, a cluster of metabolic abnormalities, is a risk factor for type 2 diabetes and cardiovascular disease. The increasing prevalence of metabolic syndrome and type 2 diabetes in the U.S. in recent decades parallels the increase in overweight/obesity.

Diabetes, 90 to 95% of which is type 2 diabetes (previously called non-insulin-dependent diabetes mellitus or adult-onset diabetes), affects nearly 24 million Americans (nearly 8% of the population) and an additional 57 million people have pre-diabetes (10). Type 2 diabetes, which typically was diagnosed in adults aged 40 and over, is being diagnosed in an increasing number of children (1).

Although genetics influences the development of metabolic syndrome and type 2 diabetes, lifestyle choices and behaviors also play a major role (1,11,12). The prevalence of metabolic syndrome and type 2 diabetes appears to be increasing parallel to the rise in obesity among both adults and children (1-4,9,13,14). Key recommendations for preventing and managing metabolic syndrome and type 2 diabetes include achieving and maintaining a healthy body weight, increased physical activity, and dietary changes that are consistent with the 2005 *Dietary Guidelines for Americans* (3,6,7,11,15,16).

The role of specific categories of foods, and/or nutrients, as well as dietary patterns in the prevention and management of metabolic syndrome and type 2 diabetes is an emerging area of research. This *Digest* reviews the growing body of scientific evidence suggesting that consumption of dairy foods and/or dairy food nutrients may help reduce the risk of metabolic syndrome and type 2 diabetes, which is a frequent consequence of metabolic syndrome.

DAIRY FOODS, DAIRY FOOD NUTRIENTS & METABOLIC SYNDROME

Epidemiological Studies of Dairy Foods. While epidemiological studies do not establish a cause and effect relationship, these types of studies provide insights into possible associations between food/nutrients and health outcomes. Findings from a number of cross-sectional and prospective epidemiological studies demonstrate an inverse association between dairy food consumption and metabolic syndrome in various populations (17,18). In a cross-sectional study of 827 Iranian adults

aged 18 to 74 years, the prevalence of metabolic syndrome was lower in the group which consumed the highest intake of dairy foods (i.e., ≥ 3.1 servings/day of milk, yogurt, cheese, milk-based dessert) compared to the group with the lowest dairy food intake (<1.7 servings/day) (19). This relationship was also highlighted in another cross-sectional investigation involving 4,811 Iranian students which showed that increased frequency of dairy food intake was associated with decreased risk of metabolic syndrome (20).

A cross-sectional study of 2,375 men aged 45 to 59 years in the United Kingdom found that regular consumption of two or more cups of milk/day was associated with a 62% reduced risk of metabolic syndrome and that increased total dairy food (i.e., milk, cheese, yogurt) consumption reduced the risk of metabolic syndrome by 60% (21). A study of men aged 45 to 64 years in France demonstrated similar findings (22).

When the association between calcium and dairy products and metabolic syndrome was examined in 10,006 U.S. women aged 45 years and older participating in the Women's Health Study, those who consumed the most total dairy foods (i.e., >3.0 servings/day) had a 34% reduced risk of metabolic syndrome compared to those with the lowest dairy intake (<0.91 servings/day) (23). Total fluid milk, high-fat and low-fat dairy foods, and total, dietary, and supplemental calcium were all inversely associated with the prevalence of metabolic syndrome (23). Other cross-sectional studies in U.S. adults have demonstrated an inverse association between calcium-rich foods (24), some (i.e., whole milk and yogurt) but not other (i.e., cheese or low-fat milk) dairy foods (25) and metabolic syndrome.

Based on a meta-analysis of data from cross-sectional studies (19,23,26), researchers reported that the prevalence of metabolic syndrome was 29% lower among those who had consumed the highest dairy food intake (3 to 4 servings/day) vs. the lowest (0.9 to 1.7 servings/day) (27). A cross-sectional study of 3,177 adults aged 26 to 82 years found that consumption of a dietary pattern consistent with the 2005 *Dietary Guidelines* (i.e., a diet containing low-fat dairy foods, fruits, vegetables, and whole grains, and low in saturated fat, *trans* fat, and cholesterol) was associated with a lower prevalence of metabolic syndrome and several of its components (28).

Observational studies in various populations show a relatively consistent association between increased dairy food consumption, vitamin D status, and calcium intake and reduced risk of metabolic syndrome and type 2 diabetes.

Some prospective studies also support a potentially beneficial effect of dairy foods against metabolic syndrome (29,30). According to the Coronary Artery Risk Development in Young Adults study that involved 3,157 adults aged 18 to 30 years, the 10-year incidence of metabolic syndrome was 72% lower among overweight individuals who consumed five or more servings of dairy foods a day compared to those who consumed less than 1.5 servings/day (29). Increased dairy food consumption was also associated with significant reductions in components of metabolic syndrome, such as obesity, hypertension, abnormal blood glucose levels, and dyslipidemia (i.e., low serum HDL cholesterol and high blood triglyceride levels) in individuals who were overweight or obese at baseline (29). In a multicenter, nine-year prospective study of 9,514 adults aged 45 to 64 who participated in the Atherosclerosis Risk in Communities Study, the highest vs. lowest quintile of dairy consumption (i.e., 3.3 vs. 0.28 servings/day) was associated with a significant 13% lower risk of developing metabolic syndrome (30).

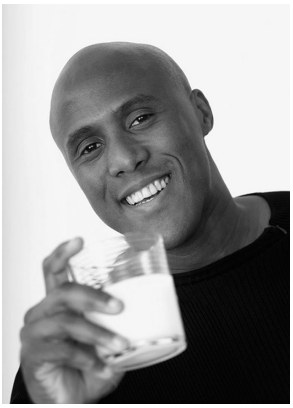
Despite the above findings, not all epidemiological studies support a protective effect of dairy foods against metabolic syndrome (25,31-33). For example, in an elderly Dutch population followed for 6.4 years, dairy consumption was not associated with the incidence of metabolic syndrome or its components (33). Among possible explanations, the researchers suggest that the usual intake of dairy foods in this relatively healthy population may have already been high.

Intervention Studies. Few clinical trials have directly examined dairy food consumption and metabolic syndrome (18). However, several intervention studies have shown that dairy foods influence components of metabolic syndrome (e.g., blood pressure, blood lipids, adiposity). Clinical trials (as well as numerous

observational studies) demonstrate a beneficial effect of dairy foods on blood pressure (34). The well-known, U.S. government-sponsored intervention study called the Dietary Approaches to Stop Hypertension (DASH) trial provides compelling support for a blood pressure-lowering effect of dairy foods (35). This study demonstrated that a low-fat eating plan high in fruits and vegetables (eight to ten servings/day) and dairy foods (two to three servings/day) (i.e., the DASH diet) was more effective than a similar diet low in dairy foods in reducing blood pressure in adults with pre-hypertension or hypertension (35). In a randomized controlled trial of 116 patients with metabolic syndrome, the DASH diet favorably affected several components of metabolic syndrome (i.e., increased HDL cholesterol and weight loss and lowered triglyceride levels, systolic and diastolic blood pressure, and fasting blood glucose levels) (36).

As reviewed by several authors (18,37-39), clinical trials demonstrate that diets moderately restricted in calories (-500 kcal/day) and that include three servings of dairy foods a day increase losses of body weight and fat in overweight/obese individuals when dairy/calcium intakes are increased from inadequate to adequate.

Dairy Food Nutrients. Studies demonstrate that dairy food nutrients beneficially impact individual components of metabolic syndrome (17,23,27,40-42). As reviewed by several researchers, dairy nutrients such as calcium, protein, and medium chain fatty acids favorably affect body weight/adiposity during weight loss; calcium, magnesium, potassium, and bioactive peptides may reduce blood pressure; and calcium has been shown to increase blood levels of HDL cholesterol and decrease total and LDL cholesterol (17,40-42). In epidemiological studies, calcium intake (23), vitamin D status (43), and magnesium intake (44) have shown inverse associations with metabolic syndrome.



Clinical intervention trials have demonstrated that dairy foods or dairy food nutrients have beneficial effects on hypertension and obesity/adiposity, which are risk factors for metabolic syndrome and type 2 diabetes.

DAIRY FOODS & TYPE 2 DIABETES

Although relatively few epidemiological studies have examined the relationship between dairy food consumption and type 2 diabetes, emerging evidence from these studies indicates that consumption of dairy foods and/or dairy food nutrients is associated with reduced risk of type 2 diabetes (18,27,45-50). In a prospective study of more than 41,000 men participating in the Health Professionals Follow-up Study, each additional daily serving of dairy foods was associated with a 9% lower risk of developing type 2 diabetes over 12 years (45). Similarly, in a prospective study of more than 37,000 middle-aged or older women who participated in the Women's Health Study, each additional serving of dairy foods was associated with a 4% lower risk of type 2 diabetes in women followed for 10 years (46). In both these studies, the relationship between dairy food intake and reduced risk of type 2 diabetes was mainly attributed to low-fat dairy foods (45,46).

In the Nurses Health Study, the risk of type 2 diabetes was 11% lower in women who consumed three or more servings of dairy foods a day compared to those who consumed less than one serving (47). However, after adjusting for total vitamin D and calcium intake, there was essentially no effect of dairy foods on risk of type 2 diabetes (47). A healthy dietary pattern containing low-fat dairy foods, fruits, vegetables, and whole grains has been shown to reduce the risk of type 2 diabetes in a prospective analysis of more than 7,700 adults followed for 15 years (49).

Based on a meta-analysis of prospective studies, researchers reported that the incidence of type 2 diabetes was 14% lower for adults consuming three to five servings of dairy foods a day compared to those who consumed less than 1.5 dairy food servings/day (27). Recent epidemiological studies also report an inverse relationship between milk consumption and insulin resistance in young school-aged children (51,52).

Dairy food nutrients such as calcium, vitamin D (if fortified), and magnesium may favorably modify the risk of type 2 diabetes. In epidemiological studies such as the Women's Health Study (23) and the Nurses Health Study (47) increased calcium intake was associated with lower risk of type 2 diabetes after adjusting for confounding factors such as vitamin D.

Several epidemiological studies and a meta-analysis have shown an inverse association between vitamin D status and type 2 diabetes or measures of insulin resistance (a risk factor for type 2 diabetes) (27,53-55). According to a systematic review and meta-analysis, the prevalence of type 2 diabetes was 64% lower among nonblacks for highest vs. lowest 25-hydroxyvitamin D levels (27).

Epidemiological findings from the Nurses Health Study showed that women who consumed the highest combined calcium (>1,200 mg/day) and vitamin D (>800 IU/day) intake had a 33% reduced risk of type 2 diabetes compared to those with the lowest intakes (i.e., <600 mg calcium/day and <400 IU vitamin D/day) (47). However, increased calcium (1,000 mg/day) plus vitamin D_3 (400 IU/day) failed to reduce the risk of developing type 2 diabetes over seven years of follow-up in healthy postmenopausal women aged 50 to 79 who participated in the Women's Health Initiative randomized placebo-controlled trial (56). The researchers suggest that, among other possible reasons, higher intakes of vitamin D may have been necessary to influence diabetes risk (56). The current recommended intake for vitamin D is 400 IU/day for adults aged 51 to 70 and 600 IU/day for those older than 70 years (57). Researchers have suggested that an intake of ~1,000 IU of vitamin D/day is needed to achieve optimal vitamin D status (58,59), and that a calcium intake higher than the current recommendation of 1,200 mg/day for adults 51 years and older (57) may be optimal for protection against type 2 diabetes (27).

Emerging scientific evidence suggests that daily consumption of at least three servings of low-fat or fat-free milk or equivalent milk products (cheese, yogurt) as part of a healthful diet consistent with the 2005 Dietary Guidelines for Americans may help reduce the risk of metabolic syndrome and type 2 diabetes.

Few intervention studies have examined the relationship between calcium, vitamin D, or their combination and type 2 diabetes (27). According to *post hoc* analyses of a study designed for bone-related outcomes in older adults, the beneficial effect of combined vitamin D and calcium on type 2 diabetes was significant for those with impaired fasting glucose levels at baseline, but not for participants with normal glucose tolerance (60).

Other dairy food nutrients such as magnesium (50,61-63) may contribute to dairy foods' inverse association with type 2 diabetes. An inverse association between calcium and magnesium intakes and type 2 diabetes was observed after seven years of follow-up in a large, prospective study of more than 64,000 middle-aged women in Shanghai, China (63). Milk intake was also inversely associated with type 2 diabetes in this study.

As discussed above, dairy foods and dairy food nutrients such as calcium and vitamin D may play a beneficial role in hypertension and obesity/adiposity, each of which is a risk factor for type 2 diabetes (18,34-39). A diet rich in calcium, particularly from low-fat dairy foods, has been demonstrated to enhance weight reduction in overweight type 2 diabetic patients, according to ancillary analyses of data from a six-month randomized clinical trial (64). Because modest weight loss improves insulin resistance, weight loss is recommended for all overweight/obese individuals who have or are at risk for diabetes (11).

CONCLUSION

Emerging evidence, primarily from epidemiological studies, suggests that consumption of dairy foods or dairy food nutrients such as calcium and vitamin D is inversely associated with metabolic syndrome and type 2 diabetes. Few clinical studies have directly examined the role of dairy foods in metabolic syndrome or type 2 diabetes. However,

these studies have demonstrated that dairy foods/dairy food nutrients alone or as part of a healthful diet reduce the risk of hypertension and adiposity, which are risk factors for metabolic syndrome and type 2 diabetes.

Future studies, including intervention trials with sufficient numbers of participants, are needed to clarify the role of dairy foods and dairy food nutrients in the prevention and treatment of metabolic syndrome and type 2 diabetes, and to elucidate the mechanism(s) involved. To date, findings related to dairy food intake and metabolic syndrome or type 2 diabetes are promising and provide another reason to consume three cups of low-fat or fat-free milk or equivalent milk products (cheese, yogurt) a day as part of a healthful diet recommended by the 2005 *Dietary Guidelines for Americans* (16). D

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