Dietary Calcium and Magnesium, Major Food Sources, and Risk of Type 2 Diabetes in U.S. Black Women

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OBJECTIVE — Inverse associations between magnesium and calcium intakes and risk of type 2 diabetes have been reported for studies in predominantly white populations. We examined magnesium, calcium, and major food sources in relation to type 2 diabetes in African-American women.

RESEARCH DESIGN AND METHODS — This is a prospective cohort study including 41,186 participants of the Black Women's Health Study without a history of diabetes who completed validated food frequency questionnaires at baseline. During 8 years of follow-up (1995–2003), we documented 1,964 newly diagnosed cases of type 2 diabetes.

RESULTS — The multivariate-adjusted hazard ratio of type 2 diabetes for the highest compared with the lowest quintile of intake was 0.69 (95% CI 0.59–0.81; P trend <0.0001) for dietary magnesium and 0.86 (0.74–1.00; P trend = 0.01) for dietary calcium. After mutual adjustment, the association for calcium disappeared (hazard ratio 1.04 [95% CI 0.88–1.24]; P trend = 0.88), whereas the association for magnesium remained. Daily consumption of low-fat dairy (0.87 [0.76–1.00]; P trend = 0.04) and whole grains (0.69 [0.60–0.79]; P trend <0.0001) were associated with a lower risk of type 2 diabetes compared with a consumption less than once a week. After mutual adjustment, the hazard ratio was 0.81 (0.68–0.97; P trend = 0.02) for magnesium and 0.73 (0.63–0.85; P trend <0.0001) for whole grains.

CONCLUSIONS — These findings indicate that a diet high in magnesium-rich foods, particularly whole grains, is associated with a substantially lower risk of type 2 diabetes in U.S. black women.

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The prevalence of diabetes is increasing in the U.S. and worldwide (1). It has been estimated that 11% of U.S. blacks aged ≥20 years have diabetes, which is 60% higher than the prevalence in non-Hispanic whites of similar ages (2). Insight into the relation between dietary factors and risk of type 2 diabetes may contribute to the efforts to prevent this chronic condition. In previous studies in predominantly white populations, higher intakes of magnesium (3–6) and calcium (7) and their major food sources, such as whole grains (6,8–10) and low-fat dairy (11), were associated with a lower risk of type 2 diabetes. It is unclear whether these findings can be extrapolated to blacks. In one U.S. cohort study, serum magnesium concentrations were inversely associated with risk of type 2 diabetes in white, but not in black, participants (12). Possible protective effects of magnesium and calcium intake against the development of type 2 diabetes would be particularly relevant for U.S. blacks, who tend to have a substantially lower intake of these minerals than other U.S. ethnic groups (13,14). We therefore examined the association between magnesium, calcium intake, and major food sources in relation to risk of type 2 diabetes in the prospective Black Women's Health Study.

RESEARCH DESIGN AND METHODS

— The Black Women's Health Study of Boston University and Howard University is a prospective cohort study of ~59,000 women who were aged 21–69 years at baseline in 1995. Women were enrolled through questionnaires mailed mainly to subscribers of *Essence* magazine (a national lifestyle magazine whose readership consists almost entirely of African-American women) (15). Participants were from all parts of the U.S., and the education level was only slightly higher than reported for nationally representative data on African-American women (16). Information has been collected using biennial mailed questionnaires, and response rates have been >80% of the original cohort for each follow-up questionnaire. For the current analysis, baseline exclusions included a history of diabetes (including gestational diabetes), cancer (except nonmelanoma skin cancer), myocardial infarction, or stroke (n = 5,424); current pregnancy (n = 956); and ≥10 items on the dietary questionnaire left blank or implausible reported total energy intakes (<500 kcal/day or >3,800 kcal/day) (n = 5,967). We also excluded women who did not reach the age of 30 years during follow-up or had diabetes diagnosed before age 30 years during follow-up (as these cases may include a substantial number of women with type 1 diabetes) (n = 2,034) and those that did not complete any follow-up questionnaires (n = 268). In addition, we excluded women with missing values for BMI, calcium intake, or magnesium intake (n = 3,232). A total of 41,186 women remained for the current analysis. The study was approved by the institutional review boards of Boston University and Howard University.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Baseline characteristics of the study population according to dietary magnesium and calcium intake*

	Magnesium (quintiles)					Calcium (quintiles)				
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5
Median intake	115	144	168	195	244	219	299	377	476	661
Number of participants	8,237	8,237	8,238	8,237	8,237	8,237	8,237	8,238	8,237	8,237
Age (years) (mean)	37.1	37.5	38.0	39.4	41.4	38.7	38.8	38.6	38.4	39.0
Low education level (%)*	21	16	14	13	12	21	17	14	13	12
BMI (kg/m^2) (mean)	28.0	27.9	27.6	27.6	27.0	27.6	27.7	27.6	27.6	27.6
Strenuous activity <1 h/week (%)	62	53	48	44	36	60	52	49	44	38
Current smoker (%)	19	18	17	14	12	21	18	16	14	12
Parental history of diabetes (%)	27	26	26	26	26	27	27	25	26	26
Alcohol (drinks/day)	0.20	0.21	0.21	0.19	0.17	0.25	0.20	0.21	0.19	0.15
Dietary intake (mean)										
Fiber (g/day)	6.0	7.9	9.5	11.3	15.2	7.3	9.4	10.3	10.9	11.6
Magnesium (mg/day)						129	159	176	191	217
Calcium (mg/day)	268	350	411	474	567					
Saturated fat (energy %)	10.9	10.8	10.4	9.6	8.0	9.9	10.1	10.1	10.0	9.5
Linoleic acid (energy %)	6.7	6.5	6.3	5.8	4.9	6.7	6.4	6.2	5.8	5.1
Processed meat (servings/day)	0.44	0.42	0.36	0.29	0.18	0.42	0.38	0.35	0.31	0.23
Other red meat (servings/day)	0.34	0.34	0.30	0.24	0.15	0.33	0.31	0.28	0.25	0.19
Soft drinks (glasses/day)†	1.07	0.65	0.47	0.32	0.17	1.02	0.58	0.46	0.38	0.24
Coffee (cups/day)	0.52	0.69	0.80	0.95	1.17	0.70	0.83	0.88	0.85	0.87
Whole grains (servings/day)	0.16	0.30	0.43	0.62	0.93	0.28	0.43	0.51	0.57	0.64
Dairy (servings/day)	0.67	0.87	1.00	1.10	1.18	0.37	0.60	0.86	1.18	1.79

*<13 years of education. †Only includes sugar-sweetened soft drinks.

Ascertainment of type 2 diabetes

Diabetes was assessed on each biennial follow-up questionnaire by asking whether the women had been diagnosed with diabetes. The accuracy of self-reports of diabetes was examined using questionnaires filled out by the physicians of a random sample of participants who reported having been diagnosed with diabetes. Of 424 women who were sent release forms asking permission to contact their physicians, 184 returned signed releases. Physician questionnaires were obtained for 141 women and indicated a diagnosis of type 2 diabetes for 134 (95%) women. Of seven other women, two had type 1 diabetes, three had metabolic syndrome, one had steroid-induced diabetes, and one did not have diabetes or related conditions.

Information on diet and potential confounders

Diet was assessed using the 68-item baseline Block food frequency questionnaire that inquired about the consumption of foods and drinks during the previous year (17). Questions included nine response categories ranging from "never to <1 per month" to "2 or more per day" for foods and from "never to <1 per month" to "6 or more per day" for drinks. We calculated whole-grain and dairy consumption by adding the daily number of servings of individual items (whole grains: "dark breads, such as wheat, rye, pumpernickel" ["2 slices"] and "high fiber, bran or granola cereals, shredded wheat" ["1 medium bowl"]; dairy: "whole milk" ["8 ounce glass"], "2% milk" ["8 ounce glass"], "skim milk, 1% milk or buttermilk" ["8 ounce glass"], "milk or cream in coffee or tea" ["1 tablespoon"], "yoghurt" ["8 ounces"], "frozen yoghurt" ["1 scoop"], "ice cream" ["1 scoop or 1/2 cup"], "butter on bread or rolls" ["2 pats"], and "cheeses and cheese spreads not including cottage cheese" ["2 slices or two ounces"]). For milk/cream in coffee, we first divided the number of daily servings by 16 to make the serving size comparable with that for other milk items. Low-fat dairy included reduced-fat milk (≤2% fat), reduced-fat yogurt, and reduced-fat frozen yogurt, and high-fat dairy included all other dairy items. Yogurt and frozen yogurt were assumed to be high-fat if women indicated that they rarely used a low-fat version of these. Nutrient intakes were calculated using the National Cancer Institute's DIETSYS software (version 4.01, food database version 3.7c) (18). The dietary questionnaire was validated in 408 cohort members by comparison with one 3-day dietary record and three telephone 24-h recalls (19). The energy-adjusted deattenuated Pearson correlation coefficients for the food frequency data compared with diet records and 24-h recalls were 0.40 and 0.63 for saturated fat, 0.32 and 0.79 for calcium, and 0.57 and 0.67 for fiber, respectively (19).

The baseline questionnaire requested information about age, number of years of school finished, parental history of diabetes, consumption of alcoholic drinks in the past year, cigarette smoking history, average number of hours per week spent on strenuous physical activity in the past year, weight, and height. BMI was calculated as weight in kilograms divided by the square of height in meters.

Statistical analysis

Person-years of exposure were calculated from the year of return of the baseline questionnaire or age 30 for participants who only reached age 30 during follow-up to the year on which the first diagnosis of diabetes was indicated on the questionnaire, the year of the last completed questionnaire, or 2003. Cox proportional hazards regression models using age as the time scale were used to calculate hazard ratios for type 2 diabetes and corresponding 95% CIs comparing categories of dietary intake with the lowest category of dietary intake. Categories for the dietary variables were defined us-

Table 2—*Hazard ratios of type 2 diabetes for dietary calcium intake and magnesium intake*

	Categories of intake					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P* trend
Calcium						
Median (mg/day)	219	299	377	476	661	
Cases (*n*)	436	424	395	345	364	
Person-years	53,240	52,783	53,182	52,836	52,402	
Age-adjusted hazard ratio	1 (ref.)	0.91 (0.80–1.04)	0.84 (0.74–0.97)	0.72 (0.62–0.83)	0.71 (0.62–0.82)	<0.0001
Multivariate hazard ratio*	1 (ref.)	0.96 (0.84–1.10)	0.91 (0.79–1.05)	0.82 (0.70–0.95)	0.86 (0.74–1.00)	0.01
Further adjusted for magnesium intake†	1 (ref.)	1.03 (0.90–1.19)	1.02 (0.88–1.19)	0.95 (0.81–1.12)	1.04 (0.88–1.24)	0.88
Magnesium						
Median (mg/day)	115	144	168	195	244	
Cases (*n*)	430	390	373	386	385	
Person-years	51,658	51,952	53,069	53,387	54,377	
Age-adjusted hazard ratio	1 (ref.)	0.81 (0.71–0.93)	0.69 (0.60–0.79)	0.60 (0.52–0.69)	0.47 (0.41–0.54)	<0.0001
Multivariate hazard ratio*	1 (ref.)	0.87 (0.76–1.01)	0.80 (0.69–0.92)	0.75 (0.64–0.86)	0.69 (0.59–0.81)	<0.0001
Further adjusted for calcium intake†	1 (ref.)	0.86 (0.75–0.99)	0.78 (0.66–0.91)	0.72 (0.61–0.84)	0.65 (0.54–0.78)	<0.0001

Data are hazard ratio (95% CI). Age-adjusted hazard ratios are adjusted for age (years) and total energy intake (kcal/day). *Multivariate hazard ratio adjusted for age (years), total energy intake (kcal/day), BMI (kg/m^2), smoking status (never, past, current <15/day, or current ≥15/day), strenuous physical activity (five categories), alcohol consumption (five categories), parental history of diabetes (yes/no), education level (four categories), coffee consumption (six categories), sugar-sweetened soft drink consumption (five categories), and quintiles of processed meat and other red meat consumption. †Multivariate model with additional adjustment for calcium or magnesium intake (quintiles).

ing quintiles or the cutoff points specified on the questionnaires. Some questionnaire categories were combined to avoid small numbers and lack of precision for estimates of association. All hazard ratios were adjusted for age (years) and total energy intake (kilocalories per day). The multivariate hazard ratios were further adjusted for BMI (weight in kilograms divided by the square of height in meters), smoking status (never, past, current <15/day, or current ≥15/day), strenuous physical activity (0, <1, 1–2, 3–6, or ≥7 h/week), alcohol consumption (0, 0.1–0.4, 0.5–0.9, 1.0–1.9, or ≥2 drinks/day), parental history of diabetes (yes/no), education level (<13, 13–15, 16, or ≥17 years), coffee consumption (none, less than five cups/week, five to six cups/week, one cup/day, two to three cups/day, and four or more cups/day), sugar-sweetened soft drink consumption (none, less than five cups/week, five to six cups/week, one cup/day, or two or more cans/day), and quintiles of processed meat and other red meat consumption. We used baseline (1995) data for all exposure variables and potential confounders. To test for linear trends across categories, we modeled the median of each category of consumption as a continuous variable. Nutrient intakes were adjusted for total energy intake using the residual method (20). We calculated Pearson correlations between dietary intakes with adjustment for total energy intake. All reported *P* values were two tailed, and *P* values <0.05 were considered statistically significant. All analyses were performed using SAS software, version 8.2 (SAS Institute, Cary, NC).

RESULTS — Characteristics of the study population according to dietary magnesium and calcium intakes are shown in Table 1. Women with a higher magnesium intake tended to be older, more highly educated, leaner, more physically active, and nonsmokers. Women with a higher calcium intake tended to be more highly educated, more physically active, and nonsmokers. In addition, higher intakes of magnesium and calcium were associated with higher intakes of fiber, whole grains, dairy, and coffee and lower intakes of alcohol, saturated fat, linoleic acid, red meat, and sugar-sweetened soft drinks. Correlations with dietary magnesium were 0.58 for calcium, 0.25 for dairy, 0.38 for low-fat dairy, −0.08 for high-fat dairy, and 0.54 for whole grains. Correlations with dietary calcium were 0.74 for dairy, 0.73 for low-fat dairy, 0.23 for high-fat dairy, and 0.22 for whole grains.

During 264,443 person-years of follow-up, we documented 1,964 new cases of type 2 diabetes. Higher calcium intakes were associated with a lower risk of type 2 diabetes, but the association was substantially weakened after adjustment for potential confounders (Table 2). For magnesium intake, the multivariate-adjusted hazard ratio for type 2 diabetes was 0.69 (95% CI 0.59–0.81) for the highest compared with the lowest quintile (*P* trend <0.0001). When magnesium and calcium intakes were mutually adjusted, an inverse association with magnesium remained, whereas the association between calcium intake and risk of type 2 diabetes disappeared (Table 2). Magnesium intake was highly correlated ($r = 0.82$) with fiber intake, and after adjustment for fiber intake the multivariate hazard ratio was 0.75 (0.62–0.92) for the highest compared with the lowest quintile of magnesium intake (*P* trend = 0.008). Additional adjustment for intakes of saturated fatty acids and linoleic acid did not appreciably change the results (<10% change in regression coefficients).

Women who used calcium supplements had a lower risk of type 2 diabetes than nonusers (multivariate-adjusted hazard ratio 0.82 [95% CI 0.73–0.91]), and this association was similar for calcium supplements with vitamin D (0.82 [0.69–0.98]) and without vitamin D (0.81 [0.72–0.91]). However, among calcium supplement users neither the amount (1.34 [1.03–1.74] for >600 mg/day vs. ≤250 mg/day) nor the duration of calcium supplement use (0.86 [0.64–1.16] for ≥5 years vs. <1 year) was associated with a lower risk of type 2 diabetes. Exclusion of women who used calcium supplements did not strengthen the asso-

Table 3—*Hazard ratio of type 2 diabetes for whole-grain and dairy consumption*

	Categories of intake				
	Less than one serving per week	One to four servings per week	Five to six servings per week	One or more servings per day	*P* trend
Whole grains					
Median (servings/day)	0.03	0.37	0.79	1.29	
Cases (*n*)	673	746	209	336	
Person-years	81,809	108,021	28,440	46,173	
Age-adjusted hazard ratio	1 (ref)	0.75 (0.68–0.84)	0.65 (0.55–0.76)	0.52 (0.46–0.60)	<0.0001
Multivariate hazard ratio*	1 (ref.)	0.84 (0.75–0.93)	0.76 (0.65–0.89)	0.69 (0.60–0.79)	<0.0001
Low-fat dairy					
Median (servings/day)	0	0.39	0.82	1.22	
Cases (*n*)	937	570	160	297	
Person-years	124,471	78,261	22,248	39,463	
Age-adjusted hazard ratio	1 (ref.)	0.97 (0.87–1.08)	0.87 (0.74–1.03)	0.76 (0.66–0.86)	<0.0001
Multivariate hazard ratio*	1 (ref.)	1.00 (0.90–1.11)	0.93 (0.78–1.10)	0.87 (0.76–1.00)	0.04
High-fat dairy					
Median (servings/day)	0.07	0.33	0.83	1.33	
Cases (*n*)	422	983	208	351	
Person-years	57,156	135,754	28,117	43,416	
Age-adjusted hazard ratio	1 (ref.)	1.10 (0.98–1.24)	1.12 (0.95–1.33)	1.06 (0.91–1.23)	0.77
Multivariate hazard ratio*	1 (ref.)	1.05 (0.94–1.19)	1.05 (0.88–1.25)	1.03 (0.88–1.20)	0.94

Total dairy	Less than one serving per week	One to four servings per week	Five to six servings per week	One serving per day	Two or more servings per day	*P* trend
Median (servings/day)	0.07	0.39	0.85	1.33	2.53	
Cases (*n*)	177	729	249	593	216	
Person-years	21,115	100,997	38,069	78,767	25,495	
Age-adjusted hazard ratio	1 (ref)	0.93 (0.79–1.10)	0.82 (0.68–1.00)	0.83 (0.70–0.98)	0.75 (0.61–0.93)	0.001
Multivariate hazard ratio*	1 (ref)	0.98 (0.83–1.16)	0.87 (0.72–1.06)	0.91 (0.76–1.08)	0.93 (0.75–1.15)	0.31

Data are hazard ratio (95% CI). Whole grains include dark breads, such as wheat, rye, and pumpernickel; high fiber, bran, or granola cereals; or shredded wheat. Dairy includes milk, milk/cream in tea or coffee, yogurt, frozen yogurt, ice cream, butter, and cheese. Low-fat dairy includes reduced-fat milk, reduced-fat yogurt, and reduced-fat frozen yogurt. High-fat dairy includes cheese, butter, ice cream, milk/cream in coffee, and nonreduced fat milk, yogurt, and frozen yogurt. Age-adjusted hazard ratios are adjusted for age (years) and total energy intake (kcal/day). *Multivariate adjusted as described in the footnotes to Table 2 with additional adjustment for low-fat dairy consumption (for calculation of the hazard ratio for whole grains) or for whole-grain consumption (for calculation of hazard ratio for the dairy variables).

ciation between dietary calcium and risk of type 2 diabetes (0.92 [0.78–1.10] for highest vs. lowest quintile).

Higher consumption of whole grains was associated with a lower risk of type 2 diabetes, and this association was independent of other risk factors (Table 3). The inverse association remained after additional adjustment for magnesium intake (hazard ratio 0.73 [95% CI 0.63–0.85] for ≥1/day vs. <1/week; *P* trend <0.0001), suggesting that the results for whole grains could not be explained by its contribution to magnesium intake. Dairy consumption was associated with a lower risk of type 2 diabetes, but in multivariate models only an inverse association for low-fat dairy remained (Table 3) that was further weakened after adjustment for magnesium intake (0.90 [0.78–1.03] for ≥1/day vs. <1/week; *P* trend = 0.13). The inverse association between magnesium intake and risk of type 2 diabetes remained after adjustment for whole grains (0.81 [0.68–0.97] for highest vs. lowest quintiles; *P* trend = 0.02) or low-fat dairy (0.72 [0.61–0.84]; *P* trend <0.0001).

CONCLUSIONS— In this 8-year prospective study of 41,186 U.S. black women, higher dietary magnesium intake was associated with a lower risk of type 2 diabetes. Higher calcium intake was not independently associated with risk of type 2 diabetes. Of the food sources, consumption of whole grains and low-fat dairy, but not high-fat dairy, were associated with a lower risk of type 2 diabetes.

Although African Americans are at increased risk of type 2 diabetes, few studies have examined whether diet may affect diabetes risk in this group (12,21). In the Atherosclerosis Risk in Communities study, low serum magnesium concentrations predicted type 2 diabetes in white, but not in black, participants and no association with dietary magnesium was observed in either group (12). However, serum magnesium concentrations may not accurately reflect magnesium status of other tissues (12). In a cross-sectional study of African Americans without diabetes, higher magnesium intakes were associated with higher insulin sensitivity (22). The low median magnesium intake observed in the current study agrees with that reported for a national sample of African-American women based on 24-h recalls (median 183 mg/day) and is well below the recommended dietary allowance for women aged >30 years (320 mg/day) (13). Effects of poor magnesium status on glucose homeostasis are plausible and may be mediated through oxidative stress, the role of magnesium as cofactor for enzymes involved in glucose metabolism, or the effects of intracellular ion levels on insulin sensitivity and insulin secretion (23). Some short-term intervention studies also provide support for a beneficial effect of magnesium intake on glucose metabolism, but results have not been consistent (24). In the absence of more definitive results on magnesium from larger, longer-term, intervention studies, the recommendation of magnesium-rich foods seems prudent. In adult participants of the National Health and Nutrition Examination Survey 1999–2000, the most important sources of magnesium were vegetables (12.9%), bread and cold cereals (10.7%), and milk (7.5%) (13). In addition to magnesium, many other components of whole grains including fibers, vitamin E, several B vitamins, and lignans may contribute to beneficial effects on glucose metabolism (25).

Dairy consumption was strongly associated with a lower incidence of the metabolic syndrome and hyperglycemia in both white and black participants of the CARDIA study (26). In the current study and a study of male health professionals (11), more modest associations were observed and these associations were limited to low-fat dairy. Calcium intake was inversely associated with risk of type 2 diabetes in female nurses (7). Further studies of calcium and dairy intakes in relation to type 2 diabetes are needed to establish whether effects are independent of other dietary and lifestyle factors.

We controlled for confounding by known risk factors of type 2 diabetes in detail. However, because of the nonrandomized study design, residual confounding cannot be completely excluded as a potential explanation of the observed associations. The assessment of type 2 diabetes relied on self-reports of physician diagnosis. Our validation study indicated that the specificity of self-report was high. Underascertainment of diabetes in the cohort would only have affected hazard ratios if diabetes detection was associated with the studied exposures (27). Measurement error in the assessment of dietary intakes is inevitable and will have led to some misclassification of the studied dietary exposures. We only used dietary intake assessed at baseline, which may have contributed to misclassification because of dietary changes during follow-up. Given the prospective design of the study, this misclassification was unlikely to be associated with the studied outcome and therefore probably led to underestimation of hazard ratios. Furthermore, our results for dietary magnesium and whole grains are consistent with observational data from diverse populations (3–6,8–10) and results of metabolic studies (24,28).

We observed an inverse association between magnesium intake and risk of type 2 diabetes in this cohort of African-American women, whereas no independent association for calcium intake was observed. Because coconstituents of magnesium in foods may contribute to the observed association for magnesium intake, it is not clear whether the results apply to supplemental magnesium intake. These findings indicate that higher consumption of magnesium-rich foods, particularly whole-grain products, is associated with a lower risk of type 2 diabetes in African-American women.

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