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Magnesium intake is inversely associated with risk of obesity in a 30-year prospective follow-up study among American young adults

Liping Lu[1,2], **Cheng Chen**[1,2], **Kefeng Yang**[3,4], **Jie Zhu**[5], **Pengcheng Xun**[6], **James M. Shikany**[7], **Ka He**[1,2,*]

[1]Department of Obstetrics and Gynecology, Columbia University Irving Medical Center, New York, USA

[2]Department of Epidemiology, Columbia University Mailman School of Public Health, New York, USA

[3]Department of Clinical Nutrition, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China

[4]Department of Nutrition, Shanghai Jiao Tong University School of Medicine, Shanghai, China

[5]Nutrition and Foods Program, School of Family and Consumer Sciences, Texas State University, San Marcos, Texas, USA

[6]Department of Epidemiology and Biostatistics, School of Public Health-Bloomington, Indiana University, Bloomington, Indiana, USA

[7]Division of Preventive Medicine, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA

Abstract

Purpose—Although laboratory studies suggest a potential role of magnesium (Mg) in weight regulation, human studies relating Mg intake to body weight are limited. This study sought to prospectively examine the association between Mg intake and incidence of obesity and related anthropometric and biochemical indicators.

Methods—The Coronary Artery Risk Development in Young Adults (CARDIA) study recruited 5,115 American young adults, aged 18–30 years, at baseline in 1985–6, and re-examined them in 8 follow-ups. Incident obesity was defined as body mass index (BMI) ≥ 30 kg/m^2. Dietary Mg intake was collected using the CARDIA Diet History at baseline and exam years 7 and 20.

*Corresponding Author: Ka He, kk3399@cumc.columbia.edu.

Conflicts of Interest

None of the authors had any conflicts of interest to disclose.

Results—During the 30-year follow-up, 1,675 incident cases of obesity were identified. After adjustment for potential confounders, Mg intake was inversely associated with incidence of obesity. The multivariable-adjusted hazards ratios (95% confidence interval) from quintile 1 (Q1) (lowest intake group) to quintile 5 (Q5) (highest intake group) were 1 (referent), 0.86 (0.74, 1.00), 0.83 (0.71, 0.97), 0.55 (0.46, 0.66), and 0.49 (0.40, 0.60); *P* for trend < 0.01. Consistently, Mg intake was inversely associated with the levels of BMI, triceps skinfold, suprailiac skinfold, subscapular skinfold, fasting insulin, and C-reactive protein. The observed associations were not materially modified by age, sex, race, or BMI at baseline. In addition, the intakes of foods rich in Mg, including whole grains, nuts and seeds, legumes and dark-green vegetables, were associated with lower incidence of obesity.

Conclusions—This longitudinal study suggests that Mg intake is inversely associated with incidence of obesity.

Keywords

Magnesium; Obesity; Body mass index; Diet; Young adults

Introduction

Obesity is a major risk factor for a variety of comorbid conditions, including type 2 diabetes [1], cardiovascular diseases [2], certain types of cancer [3], gastrointestinal disorders [4], respiratory problems [5], and psychological issues [6]. Although these comorbidities are multifactorial, even a small weight reduction is associated with a significantly lower risk of obesity-related diseases and may act as a catalyst for further weight reduction [7].

Magnesium (Mg) is an essential mineral needed by the human body. Besides being a cofactor in hundrds of key metabolic reactions, it plays an important role in glucose metabolism and insulin homeostasis [8]. Although evidence from laboratory studies supports a potential role of Mg in weight regulation [9], human studies relating Mg intake to body weight are limited. Some cross-sectional studies found that obese individuals were more likely to have low Mg status as compared with non-obese people [10–12]. One cohort study reported an inverse association between dietary Mg intake and waist circumference [13]. The intakes of whole grains [14,15], nuts [16] and seeds [17], legumes [18] and dark-green vegetables [19], which are the major foods contributing to Mg intake [20], have also been suggested to be inversely related to body weight. However, no published study has examined the associations between Mg intake and long-term weight maintenance and incidence of obesity. In addition, studies on Mg and weight status or obesity-related comorbidities were mainly conducted in middle-aged or older adults. Since middle-aged or older individuals are likely to have already had disease onset, their dietary choices and health conditions may be affected by perceived illness or treatment for existing health conditions that are related to obesity.

Therefore, we prospectively examined the association between Mg intake and incidence of obesity in a cohort of American young adults in the Coronary Artery Risk Development in Young Adult (CARDIA) study with a follow-up of 30 years. We hypothesized that Mg

intake during young adulthood would be inversely associated with obesity incidence later in life in the general US population.

Methods

Study population

The CARDIA study is a multi-center longitudinal cohort study designed to examine cardiovascular risk factors in Africa American and Caucasian men and women with various socioeconomic statuses [21]. In 1985–86, 5,115 participants aged 18–30 years were enrolled and completed the baseline examination from four clinical centers in the US including Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California. To date, eight follow-up examinations have been completed at exam years 2 (1987–8), 5 (1990–1), 7 (1992–3), 10 (1995–6), 15 (2000–1), 20 (2005–6), 25 (2010–1), and 30 (2015–6). Examination rates of the surviving cohort were 91%, 86%, 81%, 79%, 74%, 72%, 72% and 71%, respectively. One person dropped out after recruitment and was not included in any analysis.

After excluding participants who had obesity at baseline (n = 598), whose obesity status could not be determined during follow-up (n = 145), who had implausible energy intake (< 600 or > 6000 kcal/day for women; < 800 or > 8000 kcal/day for men, n = 59), or pregnant women at any examination (n = 215), a total of 4,097 participants were included in this analysis. The institutional review boards of the CARDIA participating institutions approved the study protocol. Written informed consent was received from all participants.

Dietary assessments

The CARDIA Diet History questionnaire was used to assess the dietary intake of participants in 1985–6 (baseline), 1992–3 (exam year 7), and 2005–6 (exam year 20) by trained interviewers. This questionnaire inquired about the average food consumption in the past month. Nutrient intake was estimated by using the food and nutrient content databases from the Minnesota Nutrition Coordinating Center (NCC Nutrient Database, version 10 at baseline and version 20 at exam years 7 and 20). The validity and reproducibility of the questionnaire has been previously reported [22,23]. Mg intake from supplements was also assessed. Thus, the Mg intake in this study is the sum of intakes from diet and supplements. To further validate the magnesium intake, a pilot study has been conducted and reported [13]. To reduce within-person variation and to best represent long-term dietary intakes, food consumption and energy-adjusted nutrient intake including Mg were calculated by cumulatively averaging the corresponding measurements at baseline and exam years 7 and 20 depending on the time of incident obesity [24]. The A Priori Diet Quality Score, which represents a diet pattern that protected against oxidative stress- and inflammation-related diseases [25–27], was calculated at baseline, and exam years 7 and 20. This score was derived from 46 foods groups with a higher score indicating better diet quality as previously described in the CARDIA study [28]. The corresponding scores by the time of incident obesity or end of follow-up was used in the analyses.

Assessment of obesity and anthropometric measurements

Anthropometric indicators were measured at baseline and each follow-up based on standard protocols. A centralized training prior to the exam cycle was completed [29]. Body weight and height were measured in light clothes without shoes, and body mass index (BMI) was calculated as weight (kg) divided by height-squared (m^2). Weight was rounded to the nearest 0.2 kg using a calibrated scale and height was rounded to the nearest 0.5 cm using a vertical ruler [30]. Incident obesity was defined as having a BMI equal to or greater than 30 kg/m^2 for the first time since baseline examination [31]. Waist circumference was measured in duplicate to the nearest 0.5 cm around the minimal abdominal girth identified laterally midway between the iliac crest and the lowest portion of the rib cage and anteriorly midway between the xiphoid process and the umbilicus [32]. Hip circumference was measured at the level of the symphysis pubis anteriorly and posteriorly at the level of the maximal protrusion of the gluteal muscles [33]. Skinfold measurements were obtained at subscapula, suprailium, and triceps using Harpenden Callipers.

Other covariate assessments

Information on age, sex, race, field center, education level, smoking status, alcohol consumption, physical activity, and medical history was obtained through self- and interviewer-administered questionnaires at each examination. Age and BMI at baseline and smoking status at the time of incident obesity or last follow-up were used in the analyses. For other covariates, cumulative average statistics were calculated by averaging the corresponding repeated measurements at each exam through incident obesity occurrence or last follow-up. Resting blood pressure was measured by using a random-zero sphygmomanometer at the baseline exam through exam year 15 and the Omron HEM907XL sphygmomanometer (Omron Corporation, Kyoto, Japan) at exam years 20, 25, and 30. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or taking antihypertensive medications. Fasting glucose and insulin were measured by the hexokinase [30] and immunoassay [34] method, respectively, at baseline and exam years 7, 10, 15, 20, 25, and 30. Diabetes was defined if any of the following conditions were met: a fasting glucose ≥ 126 mg/dL; a non-fasting glucose ≥ 200 mg/dL; a blood hemoglobin HbA1c ≥ 6.5%; use of antidiabetic medications. Plasma total cholesterol, HDL-cholesterol, and triglyceride concentrations were measured by enzymatic methods at baseline and each follow-up [35]. HDL-cholesterol concentrations were measured after dextran-sulfate-magnesium precipitation of other lipoprotein. LDL-cholesterol concentrations were estimated with the Friedewald equation for individuals with fasting triglyceride values less than 400 mg/dL [36]. Serum C-reactive protein was measured using a BNII nephelometer (Dade Behring, Deerfield, Ill) at baseline and each follow-up [37]. Extensive quality control has been implemented by CARDIA to reduce variability in longitudinal laboratory data [38].

Statistical analysis

Characteristics of participants were presented as mean values with standard deviations or medians with inter-quartile ranges for continuous variables and proportions for categorical

variables. The overall differences across quintiles of Mg intake were tested by using the analysis of variance (ANOVA), Kruskal-Wallis test, or chi-squared test, as appropriate.

Cox proportional hazards regression models were used to estimate the association between cumulative Mg intake and incidence of obesity. Using the lowest Mg intake quintile as the referent, hazard ratios (HRs) and 95% confidence intervals (95% CIs) were presented in 3 sequential models. Model 1 was adjusted for age, sex, race, and field center. Model 2 was additionally adjusted for education level, smoking status, alcohol consumption, physical activity, total energy intake, Mg supplement use, and BMI at baseline. Model 3 was further adjusted for systolic blood pressure, total cholesterol, HDL/LDL-cholesterol ratio, triglycerides, fasting glucose, and history of diabetes and hypertension. *P* for linear trend was examined by using the median values of Mg quintiles as a continuous variable. The proportional hazards assumption was assessed with graphical methods visually[39] and with testing for a non-zero slope in a generalized linear regression of the scaled Schoenfeld residuals against functions of time[40]. Mg supplement non-users and users were examined separately to explore the potential modification of supplementation.

To test the robustness of our findings, several sensitivity analyses were performed. First, model 3 was additionally adjusted for intakes of fiber at baseline and cumulative average intakes of polyunsaturated fatty acids, saturated fat, and total carbohydrates to reduce the confounding by other nutrients related to body weight. In CARDIA, crude fiber was measured at baseline, while dietary fiber was measured at exam years 7 and 20. Because the combination of crude and dietary fibers may bias the results in either direction, only intake of crude fiber at baseline was adjusted for in the model. Second, model 3 was additionally adjusted for the A Priori Diet Quality Score to examine if high Mg intake is a marker of healthy diet quality. Third, the model was further adjusted for the nutrients highly correlated with Mg in this cohort, including calcium (Spearman correlation, r = 0.60), potassium (r = 0.80), folate (r = 0.72), and vitamins A (r = 0.66), C (r = 0.54), and E (r = 0.54). Fourth, the associations between the intakes of whole grains, nuts and seeds, legumes, and dark-green vegetables - the major food sources of Mg - with incidence of obesity were tested using the same model (model 3).

In stratified analyses, the potential effect modification by pre-specified factors including sex, race, and age and BMI at baseline on the association of interest were examined based on model 3. *P* for linear trend and *P* for interaction were tested using the median value of each Mg quintile as a continuous variable.

In addition, we examined the associations between Mg intake and some anthropometric indicators including BMI, waist circumference, hip circumference, triceps skinfold, suprailiac skinfold, and subscapular skinfold. To explore the underlying mechanisms by which Mg may protect against obesity, we examined the associations between Mg intake and available indicators of glucose metabolism and chronic inflammation including fasting insulin, fasting glucose, and C-reactive protein. Multivariable-adjusted general linear regression models were used. All analyses were performed by using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Two-sided *P* values ≤ 0.05 were considered statistically significant.

Results

During the 30-year follow-up, 1675 of 4097 participants (40.9%) became obese. The total person-years of follow-up is 81,564 person-years. The characteristics of the study population across quintiles of Mg intake are presented in Table 1. Among 4,097 participants, 51% were females and 48% were blacks with an average age of 25 years [standard deviation (SD) = 3.6] at baseline. The Recommended Dietary Allowances (RDAs) in the US are 400 mg for men and 310 mg for women who are 19–30 years old [41]. In the present study, 44.7% of men and 54.0% of women had Mg intake at baseline below the RDAs. Participants with higher cumulative average Mg intake levels were more likely to be Mg supplement users, older, females, and whites. They were more likely to have higher levels of education, alcohol consumption, and physical activity. They were also more likely to have higher concentrations of total cholesterol, HDL/LDL-cholesterol ratio, and fasting glucose, but lower BMI at baseline, blood pressure levels and triglyceride concentrations. Mg intake was positively associated with the intakes of whole grains, nuts and seeds, legumes, and dark-green vegetables, as well as the A Priori Diet Quality Score. In addition, those with greater Mg intake were less likely to be current smokers or have hypertension.

After adjustment for potential confounders, Mg intake was inversely associated with incidence of obesity (Table 2). Compared to the lowest quintile (Q1) of Mg intake level, the incidence of obesity was reduced by 51% among participants in the highest quintile (Q5) [HR = 0.49, 95% CI = (0.40, 0.60), P for trend < 0.01]. The proportional hazards assumption was met (P=0.78). The inverse associations were similar among Mg supplement non-users [Q5 vs. Q1: HR = 0.61, 95% CI = (0.48, 0.78), P for trend < 0.01] and users [Q5 vs. Q1: HR = 0.49, 95% CI = (0.36, 0.66), P for trend < 0.01].

In the stratified analyses (Online Resource 1), the inverse association between Mg intake and incidence of obesity was not significantly modified by sex (P for interaction = 0.10), race (P for interaction = 0.10), age at baseline (P for interaction = 0.11), or BMI at baseline (P for interaction = 0.90).

In the sensitivity analyses, the inverse association between Mg intake and incidence of obesity was not materially altered with additional adjustment for intakes of fiber, polyunsaturated fatty acids, saturated fat acids, and total carbohydrates, A Priori Diet Quality Score, or nutrients highly correlated with Mg, including calcium, potassium, folate, and vitamins A, C and E (Online Resource 2). In addition, intakes of major food sources of Mg, including whole grains, nuts and seeds, legumes and dark-green vegetables, were inversely related to obesity incidence (Table 3).

Mg intake was inversely associated with some relevant anthropometric indicators, such as BMI, and triceps, suprailiac, and subscapular skinfolds (Table 4), but not with waist and hip circumference. In addition, Mg intake was inversely related to fasting insulin [Q5 vs. Q1: mean difference (MD) = −1.93, 95% CI = (−3.50, −0.36), P for trend = 0.04] and C-reactive protein [Q5 vs. Q1: MD = −1.29, 95% CI = (−2.31, −0.28), P for trend = 0.14], but not to fasting glucose (Table 4).

Discussion

Findings from this longitudinal study reveal an inverse association of Mg intake with incidence of obesity and some related anthropometric and biochemical indicators independent of major lifestyle factors. These inverse associations persisted across sub-groups of age, sex, race, or BMI status at baseline.

Although data directly relating Mg intake to incidence of obesity are sparse, our findings are consistent with some other relevant observational studies. A cross-sectional study found that Mg intake was inversely associated with BMI and prevalence of obesity among middle-aged or older American women [42]. Similarly, according to the National Health and Nutrition Examination Survey (NHANES) 1999–2004, dietary Mg intake was inversely associated with BMI and waist circumference [43]. In addition, our findings are consistent with some studies of metabolic syndrome [37–39], which includes a central obesity component [44]. In our sensitivity analyses, we found that the intakes of foods rich in Mg were consistently associated with lower risk of obesity, which further supports the potential beneficial influence of Mg on weight regulation. Similar to the present study, increasing evidence from observational studies and clinical trials suggest that the intakes of whole grains [14,15], nuts [16], seeds [17], legumes [18] and dark-green vegetables [19] were associated with lower risk of obesity.

The potential beneficial effects of Mg intake on body weight are biologically plausible. Mg is a cofactor in a number of key enzymatic reactions in the body. Since Mg is indispensable to ATP metabolism, it has played an important role in many metabolic processes including glucose and energy utilization, as well as synthesis of lipid, protein, and nucleic acids [45]. Theoretically, Mg could have an anti-obesity effect because of its capability of forming soaps with fatty acids in the intestine and thus reducing the digestible energy content of the diet [46,47]. In addition, Mg is involved in the metabolism of glucose in insulin homeostasis. Animal studies indicated that Mg administration was beneficial for significantly reducing fasting and fed-stated blood glucose concentrations and improving glucose disposal, consequently delaying the development of spontaneous type 2 diabetes mellitus in rats [48]. Similarly, a cohort study of 12,128 non-diabetic middle-aged adults found that low serum Mg concentration was a strong and independent predictor of incident type 2 diabetes among Caucasian participants after a 6-year follow-up [10]. Therefore, high intake of Mg may protect against the development of insulin resistance and type 2 diabetes, which may subsequently affect adiposity. In the present study, we found that Mg intake was inversely associated with fasting insulin concentrations, which supports this hypothesis. Moreover, Mg may regulate chronic and low-grade inflammation, and thus lower the risk of obesity. In concordance with a meta-analysis of 7 cross-sectional studies including 32,918 participants [49], we found that Mg intake was inversely related to the concentration of serum C-reactive protein. Furthermore, Mg may be involved in the pathogenesis of obesity as an antioxidant, participating in cell membrane stabilization and mitigating the effects of oxidative stress [50]. Thus, alterations in the homeostasis of Mg may affect these functions and promote the pathogenesis of obesity.

Some limitations of the study need to be acknowledged. First, objective measurements of Mg biomarkers were not available for the longitudinal analysis. However, the interviewer-administered CARDIA Diet History has been validated [23,22]. High-quality publications have been generated using Mg intake data in CARDIA [13]. In addition, a validation study for Mg intake was conducted among a random sample of 99 participants. The correlation coefficient was reasonably good ($r = 0.37$) between toenail Mg measured at exam year 2 and the mean Mg intake of exam years 0 and 7 given the different time frames of these measurements [51]. Second, similar to other observational studies, the possibility of residual confounding from dietary and non-dietary factors cannot be completely ruled out. But the consistent results from main and sensitivity analyses suggest that our findings should not be substantially biased.

To the best of our knowledge, this study is the first longitudinal study that examined the association of Mg intake with incident obesity. Because long-term randomized clinical trials may not be feasible, a well-designed longitudinal study such as the present one provides important data to the literature. Also, this apparently healthy young adult cohort, followed from age 20s to 50s, is unique for studying the risk of obesity. In addition, comparing to other studies that only have baseline intake data, the repeated dietary intake of Mg in the present study reduced the possibility of results being biased by variation of diet over time.

The present study suggests that Mg intake is inversely and longitudinally associated with incidence of obesity and related anthropometric indicators. Findings from the present study further support a diet recommendation on foods rich in Mg such as whole grains for human well-being and disease prevention. Because of the observational study design and possible measurement error in diet, Mg intake may be a surrogate of healthy diet. Thus, further studies are needed to establish the causal inference.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors' responsibilities were described as follows: KH designed the research; LL and CC performed statistical analysis, and wrote the manuscript; KY, JZ, PX, and JMS contributed to critical revision of the manuscript for important intellectual content; KH had primary responsibility for final content. All authors read and approved the final manuscript.

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Table 1

Characteristics of the study population by quintiles of magnesium intake levels: the CARDIA study, 1985–86 to 2015–16[a,b]

Characteristics	Quintiles of Mg intake levels (mg/1,000 kcal)					Total	*P* value
	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)		
n	819	820	819	820	819	4,097	NA
Mg intake	99.8	121.7	143.6	167.4	208.1-	143.6	NA
(mg/1,000 kcal)	(91.7–105.9)	(116.8–126.7)	(137.8–149.0)	(161.0–174.3)	(193.6–238.2)	(116.8–174.3)	
Mg supplementation use (yes, %)	14.7	23.7	39.8	48.2	74.0	40.1	<0.01
Age at YO (year)	23.5±3.8	24.3±3.7	25.013.6	25.5±3.4	26.0±3.2	24.9±3.6	<0.01
Female (%)	49.2	42.4	42.7	53.2	65.9	50.7	<0.01
Blacks (%)	82.2	64.9	43.6	30.6	20.0	48.3	<0.01
Education levels (year)	13.01±1.81	13.75±2.12	14.42±2.33	15.25±2.35	15.57±2.23	14.40±2.37	<0.01
Current smokers (%)	33.3	28.2	21.5	14.1	13.5	22.1	<0.01
Alcohol consumption (ml/day)	4.86 (0.41–16.10)	6.09 (1.01–19.05)	6.72 (1.12–16.43)	7.12 (1.42–17.40)	6.09 (1.39–14.64)	6.28 (1.09–16.38)	0.03
Physical activity (EU)	275.2 (160.5–434.8)	307.9 (186.0–501.3)	339.9 (213.8–502.6)	368.4 (240.9–523.1)	401.8 (279.6–559.7)	339.8 (212.5–509.1)	<0.01
BMI at YO (kg/m^2)	23.27±3.29	23.32±3.19	23.18±2.75	23.10±2.73	22.73±2.72	23.12±2.95	<0.01
SBP (mmHg)	111.97±9.62	111.82±9.53	110.77±9.23	109.73±9.28	107.90±9.58	110.44±9.56	<0.01
DBP (mmHg)	70.62±7.77	70.36±8.12	70.09±7.42	69.40±7.29	68.13±7.32	69.72±7.64	<0.01
Total cholesterol (mg/dL)	175.2±29.8	181.7±31.0	183.7±30.3	182.9±28.2	181.3±26.9	181.0±29.4	<0.01
HDL/LDL cholesterol ratio	0.56±0.27	0.52±0.23	0.51±0.26	0.53±0.21	0.58±0.22	0.54±0.24	<0.01
Triglycerides (mg/dL)	81.88±39.92	88.34±57.81	88.18±50.25	87.26±62.33	79.27±43	84.99±51.48	<0.01
Glucose (mg/dL)	87.31 ±12.83	89.68±16.51	89.76±18.16	90.03±11.28	89.07±12.00	89.17±14.44	<0.01
Diabetes ever (yes, %)	5.4	6.1	5.3	6.1	3.44	6.4	0.09
Hypertension ever (yes, %)	51.2	49.8	47.4	46.1	38.6	46.6	<0.01
Intake of whole grain (servings/day)	0.83±0.91	1.29±1.10	1.68±1.42	1.83±1.31	2.13±1.47	1.55±1.34	<0.01
Intake of nuts and seeds (servings/day)	0.39±0.70	0.62±1.13	0.79±1.20	0.98±1.44	1.20±1.61	0.80±1.29	<0.01
Intake of legumes (servings/day)	0.21 ±0.41	0.24±0.34	0.22±0.35	0.22±0.30	0.27±0.40	0.23±0.36	0.02
Intake of dark-green vegetables (servings/day)	0.18±0.22	0.30±0.41	0.40±0.52	0.60±0.58	0.88±0.95	0.47±0.64	<0.01
A Priori Diet Quality Score (points)	54.9±9.0	61.9±10.2	67.6±10.4	75.1±10.6	79.4±10.5	68.0±13.4	<0.01

Abbreviations: BMI, body mass index; CARDIA, Coronary Artery Risk Development in Young Adults; DBP, diastolic blood pressure; EU, exercise unit; IQR, inter-quartile range; Mg, magnesium; NA, not applicable; Q, quintile; SBP, systolic blood pressure; SD, standard deviation, Y, exam year.

[a]Blood pressure and lipid profile were measured at Y0 and each follow-up exam. Glucose was measured at Y0, 7, 10, 15, 20, 25, and 30. Values of covariates, if not specified, were calculated as the cumulative averages of repeated measurements by incident obesity or last follow-up.Smoking status at the time of incident obesity or last follow-up was used.

[b] Results are presented by means ± SDs, medians (IQRs), or proportions. *P* values are for any difference across quintiles of Mg intake levels using analysis of variance, Kruskal Wallis test, or chi-squared test, as appropriate.

Table 2

Multivariable-adjusted HRs and 95% CIs of incident obesity by quintiles of magnesium intake levels: the CARDIA study, 1985–86 to 2015–16[a–e]

	Quintiles of Mg intake levels (mg/1,000 kcal)					*P* for trend
	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	
All participants (*n* = 4,097)						
Range (mg/1,000 kcal)	<111.49	111.49–132.39	132.39–154.33	154.33–184.73	≥184.73	NA
No. of cases/participants	408/819	385/820	342/819	295/820	245/819	NA
Model 1	1 (Ref.)	0.88 (0.77, 1.02)	0.76(0.65, 0.88)	0.58 (0.49, 0.68)	0.45 (0.38, 0.54)	<0.01
Model 2	1 (Ref.)	0.83 (0.72, 0.96)	0.81 (0.70, 0.95)	0.53 (0.44, 0.63)	0.45 (0.37, 0.55)	<0.01
Model 3	1 (Ref.)	0.86(0.74, 1.00)	0.83 (0.71, 0.97)	0.55 (0.46, 0.66)	0.49 (0.40, 0.60)	<0.01
Mg supplementation non-users (*n* = 2,456)						
Range (mg/1,000 kcal)	<105.00	105.00–120.86	120.86–139.31	139.31–162.11	≥162.11	NA
No. of cases/participants	234/491	220/491	212/492	191/491	173/491	NA
Model 3	1 (Ref.)	0.93 (0.76, 1.12)	0.79(0.65, 0.96)	0.76(0.61, 0.94)	0.61 (0.48, 0.78)	<0.01
Mg supplementation users (*n* = 1,641)						
Range (mg/1,000 kcal)	<133.17	133.17–155.74	155.74–179.02	179.02–209.14	≥209.14	NA
No. of cases/participants	192/328	141/328	118/329	93/328	101/328	NA
Model 3	1 (Ref.)	0.79(0.63, 1.00)	0.48 (0.37, 0.62)	0.41 (0.31, 0.54)	0.49 (0.36, 0.66)	<0.01

Abbreviations: BMI, body mass index; CARDIA, Coronary Artery Risk Development in Young Adults; CI, confidence interval; HR, hazard ratio; Mg, magnesium; Q, quintile; Ref., reference.

[a]All models were constructed using Cox proportional hazards regression model. *P* for trend was examined using the medians of Mg quintiles. The values of covariates, if not specified, were calculated as the cumulative averages of repeated measurements by incident obesity or last follow-up.

[b]Model 1 was adjusted for age at Y0 (continuous), sex (female or male), race (blacks or whites), and study center.

[c]Model 2 was additionally adjusted for education (<12.0, 12.0, 15.9, or ≥16.0, year), smoking status (never, past, or current), alcohol consumption (never, 0.1, 11.9, 12.0, 23.9, or ≥24 ml/day), physical activity (quintiles), total energy intake (quintiles), Mg supplementation use (yes or no) and BMI at Y0 (continuous).

[d]Model 3 was additionally adjusted for systolic blood pressure (quintiles), total cholesterol (quintiles), HDL/LDL-cholesterol ratio (quintiles), triglycerides (quintiles), fasting glucose (quintiles), and medical histories of diabetes and hypertension (yes or no).

[e]In stratified analyses, Mg intake quintiles were calculated separately for each subgroup (Mg supplementation non-users and users).

Table 3

Multivariable-adjusted HRs and 95% CIs of incident obesity by intake quintiles of foods rich in magnesium: the CARDIA study, 1985–86 to 2015–16[a]

	Food intake[mean (SD)]	Intake quintiles of foods					*P* for trend
		Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	
Whole grains (servings/day)	1.55 (1.34)	1 (Ref.)	0.70(0.61, 0.81)	0.63 (0.54, 0.73)	0.59(0.50, 0.69)	0.58 (0.49, 0.69)	<0.01
Nuts and seeds (servings/day)	0.80(1.29)	1 (Ref.)	0.85 (0.73, 0.98)	0.88 (0.76, 1.03)	0.59(0.51, 0.70)	0.70(0.59, 0.83)	<0.01
Legumes (servings/day)	0.23 (0.36)	1 (Ref.)	0.82(0.71, 0.96)	0.89(0.77, 1.04)	0.77 (0.66, 0.90)	0.71 (0.60, 0.83)	<0.01
Dark-green vegetables (servings/day)	0.47 (0.64	1 (Ref.)	0.76(0.66, 0.88)	0.64 (0.55, 0.75)	0.62 (0.53, 0.73)	0.56(0.47, 0.66)	<0.01

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults; CI, confidence interval; HR, hazard ratio; Q, quintile; Ref., reference; SD, standard deviation.

[a]All models were constructed by using Cox proportional hazards regression model with adjustment for the covariates listed in model 3 in Table 2. *P* for trend was examined by using the medians of food intake quintiles.

Table 4

Multivariable-adjusted mean differences (95% CI) in indicators of anthropometry, glucose metabolism, and chronic inflammation according to quintiles (Q) of magnesium intake levels: the CARDIA study, 1985–86 to 2015–16[a]

	Quintiles of Mg intake levels (mg/1,000 kcal)					*p* for trend
	Q1(lowest)	Q2	Q3	Q4	Q5(highest)	
Indicators of anthropometry						
BMI at Y30 (*n*=2,792)	0 (Ref.)	−0.30 (−0.90, 0.30)	−0.34 (−0.98, 0.29)	−0.66 (−1.35, 0.02)	−0.90 (−1.65, −0.15)	0.02
Waist circumstance at Y30 (cm, *n*=2,789)	0 (Ref.)	−0.87 (−2.08, 0.35)	−0.29 (−1.58, 0.99)	−1.51 (−2.89, −0.13)	−1.35 (−2.87, 0.16)	0.08
Hip circumstance at Y30 (cm, *n*=2,789)	0 (Ref.)	−0.36 (−1.42, 0.71)	−0.18 (−1.31, 0.95)	−0.69 (−1.90, 0.51)	−0.48 (−1.82, 0.85)	0.50
Triceps skinfold at Y10 (mm, *n*=3,230)	0 (Ref.)	−0.24 (−0.88, 0.40)	0.11 (−0.57, 0.79)	−0.63 (−1.35, 0.09)	−0.86 (−1.63, −0.08)	0.01
Suprailiac skinfold at Y10 (mm, *n*=3,198)	0 (Ref.)	−0.46 (−1.39, 0.48)	0.20 (−0.79, 1.18)	−0.59 (−1.63, 0.45)	−1.27 (02.40, −0.15)	0.02
Subscapular skinfold at Y10 (mm, *n*=3,226)	0 (Ref.)	−0.12 (−0.80, 0.56)	−0.22 (−0.94, 0.50)	−0.74 (−1.50, 0.02)	−0.95 (−1.77, −0.13)	<0.01
Indicators of glucose metabolism						
Fasting insulin at Y30 (*n*=2,753)	0 (Ref.)	−1.55 (−2.82, −0.27)	−1.00 (−2.35, 0.35)	−2.24 (−3.66, −0.81)	−1.93 (−3.50, −0.36)	0.04
Fasting glucose at Y30 (*n*=2,761)	0 (Ref.)	0.97 (−1.95, 3.89)	0.10 (−3.00, 3.21)	−0.58 (−3.88, 2.72)	−0.93 (−4.56, 2.71)	0.39
Indicators of chronic inflammation						
C-reactive protein at Y25 (*n*=2,885)	0 (Ref.)	−1.40 (−2.22, −0.58)	−1.33 (−2.20, −0.46)	−1.38 (−2.30, −0.46)	−1.29 (−2.31, −0.28)	0.14

Abbreviations: BMI, body mass index; CARDIA, Coronary Artery Risk Development in Young Adults; CI, confidence interval; Mg, magnesium; Q, quintile; Ref., reference; Y, exam year.

[a]All models were constructed by using general linear regression models. *P* for trend was examined by using the medians of Mg intake quintiles. Models were adjusted for baseline level of corresponding indicator, age at Y0, sex, race, study center, education, smoking status at Y0, alcohol consumption, physical activity, total energy intake, Mg supplementation use, BMI (when BMI is not the investigated outcome), systolic blood pressure, total cholesterol, HDL/LDL, cholesterol ratio, triglycerides, fasting glucose (when glucose is not the investigated outcome, and medical histories of diabetes and hypertension. All values of covariates, if not specified, were presented as the cumulative averages by the time of last indicator measurement.