# Reduced insulin resistance partly mediated the association of high dietary magnesium intake with less metabolic syndrome in a large Chinese population

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**Research**

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# Abstract

Background

High dietary magnesium intake may reduce insulin resistance (IR) and metabolic syndrome (MetS). However, previous studies were inconsistent in Asian population and there have been no study about the mediation of IR in the relationship between dietary magnesium intake and MetS. Thus, this cross-sectional analysis aimed to evaluate the association between dietary magnesium intake, IR and MetS using data from China Health and Nutrition Survey.

Methods

Dietary magnesium intake was defined as daily dietary magnesium intake divided by body weight. Logistic regression analysis was used to calculate the odds ratio (OR) for IRand the prevalence of MetS across the quartile categories of dietary magnesium intake.

Results

8,254 participants were included in final analysis. We found a significant negative association between dietary magnesium intake and IR, the multivariable-adjusted OR for HOMA-IR comparing the highest to the lowest quartile of dietary magnesium intake was 0.435 (95% confidence intervals (CI) 0.376 to 0.502). The prevalence of the MetS was 33.5%, 24.9%, 18.4% and 13.4% for increasing quartiles of dietary magnesium intake ($p < 0.001$). The direct effect and indirect effect of dietary magnesium on MetS was found significant, and the calculated percentage of mediation was 23.0%.

Conclusion

Our study demonstrated a significant and independent negative relationship among weight adjusted dietary magnesium intake, HOMA-IR and MetS in a large Chinese population. IR partly mediated the relationship between dietary magnesium intake and MetS.



Keywords: diet magnesium intake; metabolic syndrome; insulin resistance; Chinese population; mediation effect


# 1. Introduction

Magnesium (Mg), a cofactor required in more than 300 enzymatic reactions, is the fourth most abundant cation in the human body that is involved in both glucose metabolism and insulin homeostasis [1, 2]. Insulin resistance is an early stage marker of diabetes mellitus (DM) [3]. Recent evidence has suggested that dietary Mg intake may play an important role in insulin resistance, but population-based studies have found conflicting evidences regarding the potential effects of dietary Mg intake. Several studies have correlated low dietary Mg intake with increased insulin resistance [3–5]. However, other studies do not

support the proposed protective effect that dietary Mg intake could attenuate the development of diabetes [6–8].

Insulin resistance has been implicated in the development of metabolic syndrome (MetS) [9]. MetS, a highly widespread disease among developed and developing populations, is characterized by a cluster of risk factors that threatens public health and increases disability, mortality, and health-care costs [10, 11]. As mentioned earlier, researches supported the notion that low intakes of dietary Mg may contribute to insulin resistance. Thus, inadequate intake of Mg might also play a role in the pathogenesis of MetS. Results from a meta-analysis estimating the role of Mg intake and risk of MetS have consistently shown that dietary Mg intake was significantly and inversely associated with the risk of MetS [12–14]. However, there were few related studies in the Chinese population.

Despite reports describing the relationship between dietary Mg intake, insulin resistance, and MetS, few investigations have considered dietary Mg intake and insulin resistance in a large Chinese population, and to the best of our knowledge, no study has explored the mediating role of insulin resistance in the effect of dietary Mg intake on MetS. In the present analysis, we evaluated the association between dietary Mg intake, insulin resistance, and MetS, taking into consideration age, sex, energy intake, fiber intake, smoking status, alcohol consumption, and other factors. The purposes of this study were as follows: 1) to verify the relationship between dietary Mg intake, insulin resistance, and MetS in a large national representative sample of Chinese population; and 2) to assess if the insulin resistance mediated the effect of dietary Mg intake on MetS.

## 2. Materials And Methods

# 2.1 Study Population

The China Health and Nutrition Survey (CHNS) was designed to examine how the social and economic transformation in China affects the health and nutritional status of the Chinese population [1]. The survey used a multistage random-cluster sampling process to select samples from nine provinces [11, 15]. We used data from the survey conducted in 2009, when the blood samples were collected for the first time, 9,554 participants had available data obtained from blood samples and anthropometric measures in this survey. Participants were excluded from the study if any of the following criteria were met: missing laboratory data (n = 42), aged < 18 years (n = 849), and pregnant (n = 62). In addition, participants with extreme values for total energy intake [male < 800 or > 4200 kcal/day, female < 500 or > 3500 kcal/day (n = 293)], and fasting blood glucose level of > 3.5 mmol/L, to ensure that the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) values could be calculated (n = 54). Insulin resistance was defined as the upper quartile of HOMA-IR. After applying the exclusion criteria, 8,254 participants (86.4% of 9,554) were finally included in the analyses. All participants gave written informed consent for their participation in the survey.

The study was approved by the institutional review boards of the University of North Carolina at Chapel Hill and the National Institute for Nutrition and Health as well as the Chinese Center for Disease Control and Prevention.

## 2.2 Dietary Mg intake assessment and other relevant variables

The 2009 CHNS combined data from three consecutive days of 24-hour dietary recall and a household food inventory to assess individual consumption [10]. Individual dietary intake for three consecutive days (2 weekdays and 1 weekend day) was collected for every household member. Interviewers were trained to use standard forms for administering the dietary recalls in household interviews. The participants were asked to report all foods and beverages consumed both at home and away from home. In addition, household food intake was determined on a daily basis by calculating the changes in the food inventory. The individuals' daily intake value for each food item was assessed using data from the 24-hour dietary recall, which was enhanced using data from household measures. Additionally, edible oils and other common condiments (sugar, starch soya sauce, salt) consumed in the household by each member were allocated based on the proportion of the reference man. Per capita daily consumption of nutrients was calculated by combining both of these.

Blood samples were collected by venipuncture and tested immediately for glucose and hemoglobin A1c (HbA1c) after an overnight fast for individuals who participated in the 2009 survey. Plasma and serum samples were then frozen and stored at -86 °C for further laboratory analysis [11, 15]. All samples were analyzed in a national central laboratory in Beijing with strict quality control.

The adult's questionnaire provided data on each participant's background information, health history, physical measurement, and health-related behaviors [16]. Standard procedures were followed by the trained interviewers. Weight was measured to the nearest 0.1 kg with lightweight clothing on a calibrated beam scale. Height was measured to the nearest 0.1 cm without shoes using a portable stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Waist circumference (WC) was measured at a midpoint between the lowest rib and the iliac crest in a horizontal plane using a non-elastic tape.

Insulin resistance was determined with HOMA, as described by Matthews et al. [17]. Based on the Adult Treatment Panel III (ATP III) guidelines, MetS was defined as the presence of three or more of the following characteristics: abdominal obesity: WC $\geq$ 90 cm in men or $\geq$ 80 cm in women, elevated triglyceride (TG): TG $\geq$ 110 mg/dL, low high-density lipoprotein cholesterol (HDL): HDL $\leq$ 40 mg/dL. Additionally, elevated blood pressure (BP): BP $\geq$ 130 mmHg) or 85 mmHg diastolic blood pressure (DBP), and elevated fasting glucose level: glucose $\geq$ 110 mg/dL [18].

## 2.3 Statistical analysis

We categorized dietary Mg intake per kilogram body weight into quartiles based on the distribution in the whole population and used the quartiles to compare nutrient intake, metabolic index, and other lifestyle

factors. Summary statistics were presented using frequencies and proportions for categorical data and means (standard deviations) for continuous variables. Baseline characteristics of participants are expressed as mean and SD and percentage, and were compared according to quartiles of Mg intake using analysis of variance (ANOVA) or a $\chi^2$ test as appropriate. HOMA-IR values, insulin, glucose, and TG levels were log-transformed to better approximate a normal distribution before the analysis was conducted. Logistic regression analysis was used to estimate adjusted geometric means and 95% confidence intervals (CIs) for these variables across the categories of dietary Mg intake per kilogram. The first model was adjusted for age (years) and male sex (yes or no), and the second model was further adjusted for smoking status (yes or no), alcohol consumption (yes or no), educational level (high school level or above, level below high school), and residence (urban or rural). The third model was further adjusted for total energy intake (kcal/day), total protein intake (g/day), total carbohydrate intake (g/day) and total fat intake (g/day) [12].

We performed a mediation analysis to quantify the role of insulin resistance in the association of dietary Mg intake per kilogram with MetS. To do so, we used the logistic model as reported by Baron and Kenny[19]. We calculated the indirect effect, which is a measure of the degree of mediation through the mediator, and tested for significance using bootstrapping procedures [20].

All data were analyzed using IBM SPSS Statistics, version 25 (SPSS, Chicago, IL, USA). The authors have full access to and take full responsibility for the integrity of the data. A two-sided p value < 0.05 was used to indicate statistical significance.

# 3. Results

## 3.1 Characteristics of the participants

A total of 8,254 adults were included in this study. Table 1 shows the characteristics of the participants according to daily dietary Mg intake per kilogram body weight (mg/kg). The average quartile of dietary Mg intake was 2.91 ± 0.53, 4.09 ± 0.28, 5.16 ± 0.37, and 7.75 ± 2.13 mg/kg. Participants with a higher quartile of dietary Mg intake were younger (P < 0.001) and had lower HbA1c levels (P < 0.001) and HOMA-IR values (P < 0.001). No significant difference was found in the proportion of men and women in each group (P = 0.207). The group that consumed more Mg also consumed more total energy, protein, fat, and carbohydrate. Participants with a higher quartile of dietary Mg intake were more likely to be with a low educational level, be an urban resident, and be ever smoking. They also had lower BMI, WC, BP, low-density lipoprotein cholesterol (LDL) levels, and higher HDL levels.

Table 1

Baseline characteristics of the study population according to quartiles of dietary magnesium intake per kilogram body weight

| | Magnesium intake/kg (quintiles) | | | | |
|---|---|---|---|---|---|
| | 1(low) | 2 | 3 | 4(high) | P* |
| Age (years) | 52.66 ± 15.81 | 50.67 ± 14.74 | 49.96 ± 14.87 | 50.33 ± 14.78 | < 0.001 |
| Male (%) | 45.1 | 45.5 | 47.4 | 47.8 | 0.207 |
| BMI ( $kg/m^2$) | 24.98 ± 3.65 | 23.84 ± 3.27 | 22.69 ± 2.99 | 21.85 ± 2.96 | < 0.001 |
| Daily dietary intake | | | | | |
| Mg intake/kg (mg/kg) | 2.91 ± 0.53 | 4.09 ± 0.28 | 5.16 ± 0.37 | 7.75 ± 2.13 | < 0.001 |
| Mg intake (mg) | 190.23 ± 46.62 | 254.10 ± 45.55 | 302.78 ± 53.64 | 430.17 ± 127.66 | < 0.001 |
| Energy intake (kcal) | 1614.59 ± 467.14 | 1938.17 ± 477.10 | 2174.98 ± 531.12 | 2632.43 ± 603.69 | < 0.001 |
| Protein intake (kcal) | 49.12 ± 15.39 | 60.86 ± 16.55 | 68.98 ± 17.96 | 86.11 ± 25.88 | < 0.001 |
| Fat intake (kcal) | 59.58 ± 32.24 | 65.51 ± 31.85 | 70.97 ± 34.71 | 80.33 ± 36.18 | < 0.001 |
| Carbohydrate intake (kcal) | 220.23 ± 67.50 | 274.08 ± 76.31 | 312.75 ± 88.22 | 391.85 ± 112.06 | < 0.001 |
| Urban residence (%) | 37.6 | 36.5 | 32.3 | 25.7 | < 0.001 |
| High school education or above (%) | 27.1 | 25.6 | 23.8 | 17.9 | < 0.001 |
| Current drinker (%) | 30.1 | 31.9 | 34.0 | 34.4 | 0.057 |
| Ever smoking (%) | 29.0 | 29.4 | 30.9 | 33.5 | 0.016 |
| HOMA-IR | 4.58 ± 8.58 | 3.91 ± 7.32 | 3.50 ± 6.12 | 3.14 ± 6.33 | < 0.001 |

Data are presented as means ± SD, or %. *P values are for any difference across the quintiles of magnesium intake using ANOVA or $\chi^2$ test as appropriate. Mg intake/kg: dietary magnesium intake per kilogram body weight, Mg intake: dietary magnesium intake, BMI: body mass index, FINS: fasting insulin, FBG: fast blood glucose, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglyceride, HDL: high-density lipoprotein cholesterol, LDL: low-density lipoprotein cholesterol

| | Magnesium intake/kg (quintiles) | | | | |
|---|---|---|---|---|---|
| FINS (uIU/mL) | 16.59 ± 24.71 | 14.68 ± 20.67 | 13.95 ± 24.08 | 12.59 ± 19.90 | < 0.001 |
| FBG (mmol/L) | 5.68 ± 1.73 | 5.43 ± 1.47 | 5.33 ± 1.33 | 5.20 ± 1.17 | < 0.001 |
| WC (cm) | 86.72 ± 10.33 | 83.66 ± 9.96 | 80.76 ± 9.61 | 79.29 ± 9.51 | < 0.001 |
| SBP (mmHg) | 128.36 ± 20.40 | 125.39 ± 18.48 | 123.80 ± 18.85 | 121.91 ± 17.88 | < 0.001 |
| DBP (mmHg) | 82.25 ± 11.59 | 80.91 ± 11.08 | 79.98 ± 11.48 | 78.94 ± 11.04 | < 0.001 |
| TC (mmol/L) | 5.04 ± 1.04 | 4.92 ± 1.00 | 4.78 ± 0.98 | 4.73 ± 0.96 | < 0.001 |
| TG(mmol/L) | 1.87 ± 1.51 | 1.79 ± 1.71 | 1.61 ± 1.40 | 1.45 ± 1.27 | < 0.001 |
| LDL (mmol/L) | 3.13 ± 0.99 | 3.01 ± 0.99 | 2.90 ± 0.93 | 2.88 ± 0.99 | < 0.001 |
| HDL (mmol/L) | 1.38 ± 0.42 | 1.41 ± 0.42 | 1.46 ± 0.65 | 1.50 ± 0.46 | < 0.001 |

Data are presented as means ± SD, or %. *P values are for any difference across the quintiles of magnesium intake using ANOVA or $\chi^2$ test as appropriate. Mg intake/kg: dietary magnesium intake per kilogram body weight, Mg intake: dietary magnesium intake, BMI: body mass index, FINS: fasting insulin, FBG: fast blood glucose, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: total cholesterol, TG: triglyceride, HDL: high-density lipoprotein cholesterol, LDL: low-density lipoprotein cholesterol

## 3.2 Association of dietary Mg intake per kilogram body weight with HOMA-IR

To adjust for confounding factors, a logistic regression analysis was done. The logarithm of dietary Mg intake was negatively associated with HOMA-IR (Table 2). We observed a significant inverse association between dietary Mg intake per kilogram body weight and HOMA-IR ($P < 0.001$), with odds ratio (OR) comparing the top versus bottom quintiles of 0.435 (95%CI: 0.376–0.502). After the additional adjustment for age and male sex, the OR between extreme quintiles was 0.442 (95% CI 0.383–0.511). After further adjustment for other non-dietary covariates, including educational levels, residence, smoking, and alcohol consumption, the ORs between extreme quintiles was 0.435 (95% CI: 0.396–0.529). The ORs remained significant after the addition of dietary variables in the multivariate models ($P < 0.001$), but the estimate of the association did not significantly change (OR comparing extreme quintiles 0.250, 95%CI: 0.204–0.306).

Table 2
Prevalence ratios (95% CI) for Insulin resistance according to quartiles of dietary magnesium intake per kilogram body weight

| | Magnesium intake/kg (quintiles) | | | | |
|---|---|---|---|---|---|
| | 1(low) | 2 | 3 | 4(high) | P* |
| | 1 | 0.690 (0.604, 0.790) | 0.553 (0.481, 0.635) | 0.435 (0.376, 0.502) | < 0.001 |
| Model 1 | 1 | 0.703 (0.614, 0.804) | 0.565 (0.492, 0.649) | 0.442 (0.383, 0.511) | < 0.001 |
| Model 2 | 1 | 0.706 (0.617, 0.807) | 0.573 (0.499, 0.659) | 0.458 (0.396, 0.529) | < 0.001 |
| Model 3 | 1 | 0.589 (0.511, 0.678) | 0.421 (0.360, 0.493) | 0.250 (0.204, 0.306) | < 0.001 |

Data are presented as coefficients (95% CI). Insulin resistance was defined by upper quartile of HOMA-IR. *All models were constructed using the Logistic regression analysis. Model 1: adjustment for age (years) and male (yes or no), model 2: model 1 with additional adjustment for ever smoking (yes or no), current alcohol consumption (yes or no), education level (high school degree or above, degree below high school), and residence (urban or not urban). Model 3 was model 2 with additional adjustment total energy intake (kcal/day), total protein intake (g/day), total carbohydrate intake (g/day), and total fat intake (g/day). Magnesium intake/kg was dietary magnesium intake per kilogram bodyweight and Mets: metabolic syndrome.

# 3.3 Prevalence and distribution of MetS components

A total of 1,861 participants were classified as having MetS according to the NCEP-ATP III definition, which yielded an overall prevalence of 22.5%. Participants with the lowest quartile of dietary Mg intake per kilogram had the highest prevalence of MetS, with a prevalence of 33.5%. The prevalence estimates of elevated fasting glucose, BP, and TG levels, abdominal obesity, and low HDL were all higher in individuals with a low intake of dietary Mg (Table 3).

Table 3

Prevalence of MetS and its components according to quartiles of dietary magnesium intake per kilogram body weight.

| Mg intake/kg | Q1 | Q2 | Q3 | Q4 | P* |
|---|---|---|---|---|---|
| MetS% | 33.5 | 24.9 | 18.4 | 13.4 | < 0.001 |
| WC% | 58.2 | 47.4 | 35.6 | 29.2 | < 0.001 |
| TG% | 39.8 | 34.4 | 30.5 | 24.2 | < 0.001 |
| HDL% | 30.4 | 28.0 | 25.1 | 19.5 | < 0.001 |
| BP% | 46.9 | 40.6 | 35.9 | 31.7 | < 0.001 |
| GLU% | 19.8 | 13.9 | 12.8 | 9.0 | < 0.001 |

Data are %. *P values are for any difference across the quintiles of magnesium intake using $\chi^2$ test. MetS: metabolic syndrome, Mg intake/kg: dietary magnesium intake per kilogram weight, WC: waist circumference, BP: blood pressure, TG: triglyceride, HDL: high-density lipoprotein cholesterol, GLU: glucose.

## 3.4 Association of dietary Mg intake per kilogram body weight with MetS

We observed a significant inverse association between dietary magnesium intake per kilogram body weight and MetS (Table 4), showing an unadjusted OR (95% CI) of 0.658 (0.575–0.753), 0.447 (0.387–0.456), and 0.307 (0.263–0.359) for the second to the highest quartiles as compared with the lowest quartile. The first model was adjusted for age and male sex, the second model was further adjusted for education level, rural residence, smoking status, and alcohol consumption, and the third model was further adjusted for dietary variables. After the three-model adjustment, the association remained significant (P < 0.001)

Table 4
Prevalence ratios (95% CI) for MetS according to quartiles of dietary magnesium intake per kilogram body weight

| | Magnesium intake/kg (quintiles) | | | | |
|---|---|---|---|---|---|
| | 1(low) | 2 | 3 | 4(high) | P* |
| MetS | 1 | 0.658 (0.575, 0.753) | 0.447 (0.387, 0.516) | 0.307 (0.263, 0.359) | < 0.001 |
| Model 1 | 1 | 0.688 (0.599, 0.790) | 0.473 (0.408, 0.547) | 0.320 (0.273, 0.375) | < 0.001 |
| Model 2 | 1 | 0.686 (0.598, 0.788) | 0.473 (0.408, 0.548) | 0.320 (0.273, 0.376) | < 0.001 |
| Model 3 | 1 | 0.491 (0.424, 0.570) | 0.266 (0.224, 0.315) | 0.103 (0.082, 0.130) | < 0.001 |

Data are coefficients (95% CI). A logarithmic transformation was used to improve the normality of distribution for dependent variables. *All models were constructed by the Logistic regression analysis. The adjusted covariates in the models were the same as those listed in Table 2. Mets: metabolic syndrome, Magnesium intake/kg: dietary magnesium intake per kilogram body weight.

## 3.5 The role of HOMA-IR in the association between dietary Mg intake per kilogram weight and MetS

The association between Mg levels, HOMA-IR, and MetS is shown in Fig. 1. We confirmed that dietary Mg intake levels were significantly associated with HOMA-IR and that HOMA-IR was significantly associated with MetS. When studying the direct effect of dietary Mg per kilogram on the MetS adjusted for HOMA-IR, the effect estimates were attenuated, and the association was still statistically significant. The association between dietary Mg, insulin resistance, and MetS was modelled through a mediation analysis, with insulin resistance calculated as loge HOMA-IR levels. The direct effect of dietary Mg on MetS was found significant when adjusting for loge HOMA-IR levels (OR: -0.1882, 95%CI: -0.2212 to -0.1552). The indirect effect, which represents the effect of dietary Mg levels on MetS as mediated by loge HOMA-IR levels, was also found to be significant (OR: -0.0562, 95%CI: -0.0672 to -0.0458); the calculated percentage of mediation was 23.0%.

## 4. Discussion

The present investigation revealed a significant and independent negative relationship between weight-adjusted Mg intake and HOMA-IR in a large Chinese population, independent of age, sex, smoking status, alcohol consumption, educational level, residence, energy intake, protein intake, carbohydrate intake, and fat intake. We also found that group with high Mg intake was less likely to have MetS. To the best of our

knowledge, we first demonstrated that insulin resistance partly mediated the relationship between dietary Mg intake and MetS.

Consistent with the result of our research, previous studies demonstrated an inverse association between dietary Mg intake and insulin resistance and a dose-effect relationship [21–24]. However, there is a lack of relevant research in Asian population and most Asian studies focused on the relationship between dietary Mg and the risk of diabetes, which were inconsistent. Some studies showed high dietary Mg intake could reduce the risk of type 2 diabetes[5, 22, 25], whereas others could not reach a significant result [8]. To fill the gap, our study aimed to explore the relationship between Mg intake and insulin resistance in a national representative sample of Chinese adults. Our study found a significant association between total dietary Mg intake and HOMA-IR, but after adjusting for dietary factors, the results did not stay significant. Then, we decided to adjust the dietary Mg intake by body weight, and we found a significant association before and after the three-model adjustment. A study from Mexico also chose to adjust the Mg intake by body weight and found a significant result showing that the insulin sensitivity assessed by the Matsuda index was higher in the high dietary Mg intake group; however, the sample size of the study was small [26]. Given that the previous studies, which did not show a statistically significant correlation between dietary Mg intake and insulin resistance all used total dietary Mg intake instead of weight-adjusted dietary Mg intake, we assumed that the amount of dietary Mg an individual needed was related to his/her weight. In other words, the heavier the person, the more Mg might be needed in his/her diet. This is consistent with the Dietary Reference Intakes (DRI) from the French Food Safety Agency, which recommended 6 mg/kg body weight Mg intake per day [27]. A study from the United States also demonstrated that the dietary Mg intake requirement was related to body weight, which was 2.36 mg/kg per day [28]. More studies would be necessary to confirm whether weight-adjusted Mg intake was a better indicator for Mg intake.

Our study found that increased intake of dietary Mg was negatively associated with the prevalence of MetS and its five components in the Chinese population. Studies have reported the beneficial effect of dietary Mg intake or Mg supplementation in reducing the prevalence of MetS [12, 29, 30], which was consistent with our findings. In those studies, dietary Mg intake was only relative with one to no more than five components of MetS, and there were few correlation studies involving Chinese individuals. In addition to the abovementioned findings, we also further found that dietary Mg intake was significantly associated with all five components of MetS in a national representative sample of Chinese adults. According to our data, the risk of the metabolic syndrome was nearly 70% lower in the top quintile of the dietary Mg intake than in the bottom quintile.

Insulin resistance is the basis of MetS [9], and Mg has been shown to be a key factor in insulin action through the activation of the b-subunit of the insulin receptor and the activation of substrates and proteins in the insulin-signaling pathway [31]. It is easy to speculate that the effect of Mg on metabolic syndrome was mediated by insulin resistance. In this study, we explored the mediation of insulin resistance in the effect of dietary Mg on MetS, and the calculated percentage of mediation was 23.0%, indicating that there were other mechanisms in the relationship between dietary Mg intake and MetS

besides insulin resistance. It has been previously suggested that higher Mg intake and intracellular Mg might have a role in insulin secretion by preserving pancreatic β-cell function via its effect on calcium homeostasis and oxidative stress [12]. Mg also acts as a cofactor for several critical enzymes involving lipid metabolism. Mg has been reported to raise HDL and reduce LDL cholesterol and TG by limiting the action of lecithin cholesterol acyltransferase and HMG-CoA reductase and by increasing the lipoprotein lipase activity [12]. It has been assumed that Mg, in the intestine, by forming an unabsorbable soap with fatty acids and cholesterol, can decrease their absorption, reduce energy intake from the diet, and may have advantages for weight maintenance because of this tendency [32]. Apart from the abovementioned mechanisms, the relationship between Mg and, MetS might also be affected by genes [33, 34].

The strengths of the present investigation include the following: 1) it is the first large-scale investigation of the relationship between dietary Mg intake, insulin resistance, and MetS in a national representative sample of Chinese population. 2) It is the first study to explore the mediating role of insulin resistance in the relationship between Mg and Mets, 3) in this study, standardized protocols, and data collection procedures were used, data collectors were well trained, and quality control was assured, which can largely avoid measurement bias. Potential perceived limitations would be that we applied a cross-sectional research design to investigate associations; thus, we cannot establish causality in the present study. The 24-hour recall, which was the method we used to calculate Mg intake, is considered to have a similar accuracy to that of semi-quantitative food frequency questionnaires, but it has the disadvantage of recall bias.

# 5. Conclusions

The present study is the first to demonstrate a significant and independent negative relationship between weight-adjusted Mg intake and HOMA-IR with MetS in a large Chinese population. Insulin resistance has a partial mediating role in the relationship between Mg and MetS. However, prospective longitudinal studies are needed to verify this relationship.

# Abbreviations

Mg: Magnesium; DM: diabetes mellitus; MetS: metabolic syndrome; CHNS: China Health and Nutrition Survey; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; HbA1c: hemoglobin A1c; BMI: Body mass index; WC: Waist circumference; TG: triglyceride; HDL: high-density lipoprotein cholesterol; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; CI: confidence intervals; LDL: low-density lipoprotein cholesterol; OR: odds ratio

# Declarations

### Ethics approval and consent to participate

The study was approved by the institutional review boards of the University of North Carolina at Chapel Hill and the National Institute for Nutrition and Health as well as the Chinese Center for Disease Control and Prevention.

## Consent for publication

Not applicable.

## Availability of data and material

The datasets generated and/or analysed during the current study are available in the CHNS repository, http://www.cpc.unc.edu/projects/china.

## Competing interests

The authors declare that they have no competing interests.


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## Authors' contributions

Study concept and design: NY, LYH, HBZ, and YXL. Acquisition of data: NY and LYH. Analysis and interpretation of data: NY, and HBZ. Drafting of the manuscript: NY and HBZ. Critical revision of the manuscript for important intellectual content: NY, HLY, LLX, FP, WL, HBZ, and YXL. Statistical analysis: NY and HBZ. Obtained funding: HBZ. All authors have read and agreed to the published version of the manuscript.


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# Figures




**Figure 1**

Not included with this version.