

## Original Article

# Magnesium status and association with diabetes in the Taiwanese elderly

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The average dietary intake of magnesium is below recommended dietary allowances in many affluent Western countries. Prolonged low magnesium intake tends to result in hypomagnesaemia which might increase the risk of chronic diseases in elderly people. A national population-based cross-sectional nutrition survey, the Elderly Nutrition and Health Survey in Taiwan (1999-2000), was used to investigate the magnesium status and association with diabetes in the Taiwanese elderly. Dietary magnesium intake was based on 24-hour dietary recalls. Blood biochemical parameters including plasma magnesium and blood glucose were also measured. Average magnesium intake was 250mg in men and 216mg in women, which is equivalent to 68-70% of relevant Taiwanese Dietary Reference Intakes. The mean plasma magnesium concentration was 0.903 mmol/L in men and 0.906 mmol/L in women. The prevalence of a plasma magnesium level of <0.7 mmol/L was 0.7 - 0.9% in the elderly, and that of <0.8 mmol/L was 8.0-9.1%. Elderly vegans had a significantly lower magnesium intake than ovo-lacto vegetarians and non-vegetarians. Diabetic men and women had significantly higher blood glucose levels than non-diabetics. The risk of diabetes was elevated 3.25 times at plasma magnesium levels <0.863mmol/L. There was an inverse association between plasma magnesium concentration and the prevalence of diabetes. However, no association was found between diabetes and low dietary magnesium. Taiwanese elderly persons had suboptimal levels of dietary magnesium intake, which although may be sufficient to avoid overt magnesium deficiency, may not be sufficient to reduce the risk of diabetes in the elderly. Further prospective study is required to help explain the differential results between dietary and plasma magnesium levels.

**Key words:** magnesium intake, plasma magnesium, the elderly, diabetes mellitus, nutrition survey, Taiwan, Elderly Nutrition and Health Survey in Taiwan (1999-2000)

## Introduction

Magnesium is the second most abundant intracellular cation in the body, and is a cofactor in more than 300 enzymatic reactions involved in energy metabolism, protein and nucleic acid synthesis, transport of potassium and calcium ions, signal transduction and cell proliferation.<sup>1-3</sup> The net absorption rate of magnesium from a typical diet is approximately fifty percent and can be inhibited by high levels of dietary fiber, phosphorus, oxalic acid and phytic acid.<sup>4-8</sup> The plasma level of magnesium is maintained remarkably constant in healthy individuals by a poorly understood homeostatic mechanism.<sup>9</sup> Although magnesium is found in a variety of foods and beverages, magnesium depletion is not uncommon among the general population.<sup>9,10</sup>

Inadequate magnesium intake has been found to be associated with chronic diseases including diabetes, hypertension, and atherosclerosis.<sup>11-14</sup> Epidemiological and experimental studies support a role for magnesium deficiency in the pathogenesis of hypertension, with reports demonstrating an inverse correlation between magnesium levels and blood pressure involving a hypotensive action of dietary magnesium supplementation and a hypertensive effect of magnesium deficiency.<sup>14-18</sup> Epidemiological studies also

indicate a direct relationship between atherosclerosis and serum magnesium, which in turn depends on dietary intake.<sup>15</sup> Oral magnesium supplementation has beneficial effects on plasma lipids<sup>19</sup> and an inverse association between serum magnesium concentration and mortality from ischemic heart disease has been documented.<sup>20,21</sup> Furthermore, hypomagnesaemia has been demonstrated in 25-38% of patients with type 2 diabetes, especially in those without good metabolic control.<sup>22,23</sup> Low magnesium intake may reduce glucose tolerance and increase insulin resistance.<sup>23-27</sup> The American Diabetes Association has already endorsed magnesium supplementation for diabetics who are at high risk of magnesium deficiency.<sup>28</sup>

Some short-term metabolic studies suggest that magnesium supplementation has a beneficial effect on insulin action and glucose metabolism.<sup>26-29</sup> Several large observational studies have demonstrated a strong cross-sectional

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association between the incidence of type 2 diabetes and serum Mg as well as dietary Mg.<sup>12,15</sup> Recently, results from prospective studies have also supported a protective role for higher magnesium intake in reducing the risk of developing type 2 diabetes.<sup>30-32</sup>

Diabetes, hypertension and cardiovascular disease are among the ten leading causes of death in Taiwan and inadequate magnesium intake has been linked to these adverse health outcomes. As a result, we assessed dietary intake of magnesium, plasma magnesium levels and the population distribution of magnesium status and compared these with associated health effects in the Taiwanese elderly.

## Subjects and Methods

### Subjects and data source

The Elderly Nutrition and Health Survey in Taiwan (1999-2000) (Elderly NAHSIT) was a government-sponsored survey that included 24-h dietary recall and health status assessment by interviewer-administered questionnaires. The complex sampling scheme used in this survey is reported in detail in another publication in this issue<sup>33</sup> as is the assessment of dietary intake.<sup>34</sup> Estimates of dietary magnesium intake were taken from 1911 subjects aged 65 years and older who had completed the dietary assessment. Estimates of the population distribution of plasma magnesium concentrations were calculated from 2225 subjects aged 65 years and older who had participated in the physical examination which included measurement of anthropometric and blood biochemical parameters. A subgroup of subjects who provided complete data for both dietary recall and blood parameters were used in the analysis of the association between magnesium parameters and the prevalence of diabetes.

### Statistical analyses

All variables were weighted to represent the population in Taiwan.<sup>23</sup> Values were expressed as mean  $\pm$  standard error and differences between groups were tested using the t-test. Trends across quartiles were evaluated by linear regression. Logistic regression analysis was performed to evaluate the association between low plasma magnesium and diabetes mellitus. Statistical analysis was performed using SAS version 8.2<sup>35</sup> and SUDAAN version 9.0.<sup>36</sup> The level for statistical significance was set at  $P < 0.05$ .

### Results

Dietary intake of magnesium by gender and age is listed in Table 1. Daily magnesium intake averaged  $250 \pm 13$  mg in men and  $216 \pm 11$  mg in women, which is equivalent to 69.4% and 68.6% of the DRIs (Dietary Reference Intakes) for men and women, respectively. Daily calorie intake averaged  $1833 \pm 72$  kcal in men and  $1477 \pm 63$  kcal in women, which is equivalent to 108 % and 100 % of the DRIs for men and women, respectively.<sup>34</sup> Mg density was 142.7 mg/1000 kcal in men and 153.5 mg/1000 kcal in women. Men had a significantly higher intake than women at every age interval from 65 to 79 years old, but there was no difference in the over 79 age range.

Plasma magnesium concentrations by gender and age are listed in Table 2. The mean concentration was  $0.903 \pm 0.007$  mmol/L in men and  $0.906 \pm 0.004$  mmol/L in women; it increased with age and the trend was significant for men but not for women. Plasma magnesium concentrations did not differ among vegans, ovo-lacto vegetarians and non-vegetarians, but dietary magnesium intake was significantly lower in vegans versus non-vegetarians (Table 3).

**Table 1.** Daily dietary intake of magnesium by gender and age in the Taiwanese elderly\*

Age (yr)	Men		Women		Gender difference <i>P</i> trend
	Subject <i>N</i>	Mg intake mg/day	Subject <i>N</i>	Mg intake mg/day	
All	955	$250 \pm 13$	956	$216 \pm 11$	<0.0001
65-69	356	$253 \pm 8$	392	$222 \pm 10$	0.0042
70-74	326	$246 \pm 15$	302	$216 \pm 12$	0.0490
75-79	185	$256 \pm 22$	154	$222 \pm 25$	0.0203
$\geq 80$	88	$246 \pm 31$	108	$197 \pm 19$	0.1347
<i>P</i> trend for age		0.8909		0.3559	

\*Values are expressed as mean  $\pm$  SE and weighted. Gender difference was tested using the Student's t test and significance was set at  $P < 0.05$ .

**Table 2.** Plasma magnesium concentrations by gender and age in the Taiwanese elderly\*

Age (yr)	Men		Women		Gender difference <i>P</i> trend
	Subject <i>N</i>	Plasma Mg (mmol/L)	Subject <i>N</i>	Plasma Mg (mmol/L)	
All	1127	$0.903 \pm 0.007$	1098	$0.906 \pm 0.004$	0.4816
65-69	427	$0.895 \pm 0.007$	456	$0.903 \pm 0.006$	0.2307
70-74	390	$0.901 \pm 0.006^*$	339	$0.902 \pm 0.006$	0.9659
75-79	203	$0.915 \pm 0.012$	189	$0.913 \pm 0.007$	0.8318
$\geq 80$	107	$0.913 \pm 0.011$	114	$0.916 \pm 0.009$	0.8476
<i>P</i> trend		0.0290		0.1488	

\*Values are expressed as mean  $\pm$  SE. Gender difference was tested using the Student's t test and significance was set at  $P < 0.05$ .

**Table 3.** Comparison of magnesium intake and plasma magnesium concentrations among vegans, ovo-lacto vegetarians and non-vegetarians\*

Dietary types	Men		Women		Men		Women	
	N	Plasma Mg (mmol/L)	N	Mg Intake (mg/d)	N	Plasma Mg (mmol/L)	N	Mg Intake (mg/d)
Vegan	17	0.915 ± 0.012	18	196 ± 17 <sup>a</sup>	92	0.906 ± 0.011	102	193 ± 17 <sup>a</sup>
Ovo-lacto vegetarian	42	0.918 ± 0.015	44	244 ± 16 <sup>ab</sup>	192	0.911 ± 0.008	211	225 ± 14 <sup>ab</sup>
Non-vegetarian	611	0.902 ± 0.007	680	263 ± 15 <sup>b</sup>	379	0.903 ± 0.007	403	233 ± 21 <sup>b</sup>

\*The vegan diet excluded all animal products; the ovo-lacto vegetarian diet excluded all animal flesh but included dairy products and eggs. Values are expressed as mean ± SE. Groups not sharing the same superscript letters "a, b" are significantly different based on the t-test significant at  $P < 0.05$ .

**Table 4.** Prevalence of magnesium deficiency by age and gender in the Taiwanese elderly

Gender	Subjects (N)	Proportion (%) by plasma Mg concentration*				
		< 0.7 (mmol/L)	0.7 - < 0.8 (mmol/L)	0.8 - < 0.9 (mmol/L)	0.9 - < 1.0 (mmol/L)	> 1.0 (mmol/L)
Men	1127	0.9	9.1	31.7	50.8	8.3
Women	1098	0.7	8.0	31.6	50.3	10.1

The distribution of plasma magnesium concentrations in the elderly is shown in Figure 1. The median value of plasma magnesium was 0.905 mmol/L for both men and women. The prevalence of magnesium deficiency defined as serum Mg values <0.7mmol/L was 0.9% in men and 0.7% in women (Table 4). The prevalence of low plasma magnesium defined as values <0.8 mmol/L was 9.1% in men and 8.0% in women (Table 4).

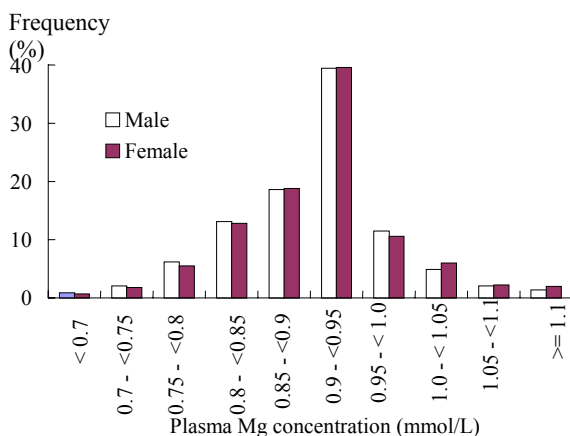
Table 5 compares the magnesium intake and plasma magnesium concentrations in diabetic and non-diabetic subjects, which were identified according to a physician's diagnosis. In both men and women, dietary intake of magnesium did not differ between diabetic and non-diabetic subjects, but plasma magnesium concentrations were significantly lower in diabetic subjects than in non-diabetics. The prevalence risks for diabetes by quartile of plasma magnesium concentration according to logistic regression analysis are listed in Table 6. Compared to the highest quartile of plasma magnesium concentration, the odds ratios of diabetes prevalence in elderly men and women were 5.27 and 2.66, respectively, for the lowest quartile with a plasma magnesium level lower than 0.863 mmol/L. Table 7 compares several predictors of diabetes across three different plasma magnesium ranges. There

was no difference in age, waist-to-hip ratio or magnesium intake, but low plasma magnesium levels were associated with higher fasting blood glucose concentrations ( $P = 0.0042$  and  $0.0040$ ) and a higher prevalence of diabetes ( $P = 0.0015$  and  $0.0365$ ) in both men and women.

## Discussion

Recent dietary surveys have shown that the average magnesium intake is slightly below the appropriate RDAs in Western countries.<sup>10</sup> The dietary magnesium intake for US men and women aged 71 years and older from the NHANES III was 314 mg/d and 230 mg/d, which is equivalent to 90% and 84% of the RDAs, respectively.<sup>9,15,37</sup> The average magnesium intake in the Dutch elderly was 311mg/d.<sup>38</sup> The true intake of magnesium in a German diet has been found to be about 200mg for women and 260mg for men.<sup>39</sup> The mean magnesium intakes in adult men and women based on the results of the SU.VI.MAX cohort in France were 369 and 280mg, respectively.<sup>40</sup> In Belgium, a mean magnesium intake of 271mg/day was found.<sup>41</sup> In Switzerland, an estimate based on disappearance data from 1994/1995 was 406 mg/d for subjects aged 15 years and above,<sup>42</sup> and the mean intake in Swiss elderly was 421 mg/d in men and 383 mg/d in women.<sup>43</sup> The Taiwanese DRI of magnesium is 360 and 315 mg/d for adult men and women, respectively.<sup>44</sup> According to this study, the average magnesium intake of 250 and 216 mg/d in elderly Taiwanese men and women, respectively, is suboptimal and is comparatively lower than that found in Western countries. Our study agrees with others with respect to a gender-related difference, with men having a higher magnesium intake than women.

Magnesium intake may vary with different types of diets. Compared to the data from the US, Swiss elderly had higher magnesium intake because of their higher consumption of cereal products, which contribute 23% of magnesium intake in the Swiss diet in contrast to only 17-18% in the US diet.<sup>43</sup> A population of Mexicans eating a more plant-based diet had magnesium intakes of 301 mg/d in women and 318 mg/d in men.<sup>39</sup> In Germany, magnesium intake for lacto-ovo vegetarians was 376 mg/d

**Figure 1.** Distribution of plasma magnesium concentrations in the Taiwanese elderly.

**Table 5.** Comparison of magnesium intake and plasma magnesium concentration between diabetic and non-diabetic elderly in Taiwan

Variables	Men		Women	
	Diabetics (N)	Non-diabetics (N)	Diabetics (N)	Non-diabetics (N)
Mg intake (mg/d)	243 ± 38 (67)	263 ± 14 (594)	212 ± 18 (86)	224 ± 13 (573)
	<i>P</i> = 0.5230		<i>P</i> = 0.5805	
Plasma Mg (mmol/L)	0.875 ± 0.007 (67)	0.907 ± 0.007 (603)	0.882 ± 0.012 (86)	0.909 ± 0.006 (577)
	<i>P</i> = 0.0028		<i>P</i> = 0.0440	

\*The diabetic subjects were diagnosed clinically by physicians. The difference between diabetic and non-diabetic groups was tested using a t-test, significant level set at *P* < 0.05.

**Table 6.** Odds ratio of diabetes mellitus by quartile of plasma magnesium in the Taiwanese elderly

Gender	Odds ratio by quartile of plasma Mg concentration*		
	I < 0.863 mmol/L	II, III 0.863 - 0.946 mmol/L	IV > 0.946 mmol/L
All	3.25 (1.67 - 6.34)	1.94 (0.91 - 4.12)	1
Men	5.27 (1.69 - 16.47)	4.06 (1.01 - 16.39)	1
Women	2.66 (1.24 - 5.67)	1.30 (0.68 - 2.4)	1

\*Logistic regression analysis was used. Numbers in parentheses indicate 95% confidence intervals adjusted for age, waist-hip ratio, blood pressure, BMI, and supplements for both men and women. In men, drinking and smoking were also adjusted for. Interval classes for adjustment were: age (65 - 69, 70 - 74, 75 - 79, 80+), waist-hip ratio ( $\geq 0.9$  or  $< 0.9$  for men,  $\geq 0.85$  or  $< 0.85$  for women), SBP ( $\geq 140$ ,  $< 140$  mmHg), DBP ( $\geq 90$ ,  $< 90$  mmHg), drinking ( $\geq 1$  time/wk, N), smoking (Y, N), supplements (regular intake, N), BMI ( $< 19.8$ ,  $\geq 19.8$ ).

in women and 474 mg/d in men, which was significantly higher than the intake of 205 mg/d and 266 mg/d in omnivorous women and men, respectively.<sup>39</sup> However, findings in Taiwan are contrary to those of Western countries.<sup>39,43</sup> Elderly vegans in Taiwan had a lower magnesium intake than non-vegetarians, and the differences in magnesium intake between ovo-lacto vegetarians and non-vegetarians was not significant (Table 3). This disagreement is most likely related to food choices as Chinese vegetarians tend to use more soy products made of processed soy proteins rather than whole legumes and whole grains. This supports the idea that a beneficial vegetarian diet requires an appropriate combination of a range of plants as food.<sup>34</sup>

The inadequate magnesium intakes observed in various countries including Taiwan may reflect similar trends in dietary patterns. The "Western diet" is considered relatively deficient in magnesium, while the "Oriental diet" is traditionally characterized by a greater intake of fruits and vegetables and therefore is richer in magnesium.<sup>34</sup> However, dietary patterns in Taiwan have been gradually westernized as the nation has become more affluent. We have noted that the analyzed magnesium content in meals prepared by some registered Taiwanese dietitians was only 258 mg/d,<sup>45</sup> which is below the Taiwanese DRI of magnesium for adults.<sup>44</sup> The top-ranked source of magnesium was rice/rice products (14.5% of total intake) for males and green vegetables for females (15.8% of total intake).<sup>34</sup> The consumption of magnesium-rich foods such as whole grains, legumes and nuts is below the recommended quantities.

The normal range of plasma magnesium concentration is 0.75-1.00 mmol/L.<sup>10</sup> The prevalence of magnesium deficiency in developing countries such as India has been found to be as high as 11.8%.<sup>46</sup> The prevalence of low serum magnesium concentration ( $< 0.8$  mmol/L) was estimated to be 23% in U.S. adults aged 25-74 years.<sup>21</sup> In Germany, low serum magnesium concentrations were found in about 5-8% of the overall population of various ages,<sup>47</sup> and plasma magnesium concentrations below 0.76 mmol/L were observed in 14.5% of an unselected population.<sup>48</sup> According to the results of this study, overt magnesium deficiency (0.7-0.9%) and low serum magnesium (8.0-9.1%) in the elderly were both less prevalent in Taiwan than in some developing and developed countries.

Low serum magnesium levels in patients with type 2 diabetes and an inverse association between magnesium status and risk of type 2 diabetes have been reported in Caucasian populations.<sup>15,22,43</sup> The association has been further supported by cross-sectional studies that have observed an inverse association between plasma or erythrocyte magnesium levels and fasting insulin levels in diabetic patients and apparently healthy individuals.<sup>15,23,49,50</sup> Strong support also comes from several prospective dietary studies, including the Atherosclerosis Risk in Communities Study,<sup>30</sup> the Women's Study,<sup>31</sup> the Nurses' Health Study,<sup>32</sup> and the Health Professionals Follow-up Study.<sup>32</sup> This study of Taiwanese elderly persons is the first to demonstrate an inverse association between serum magnesium concentration and the prevalence of diabetes in a non-Caucasian population. The findings are consistent with the results found for Western countries, but

**Table 7.** Comparison of blood glucose and selected predictors for diabetes mellitus by quartile of plasma magnesium concentration\*

Variables	Plasma Mg concentration (mmol/L)			P trend
	<0.863	0.863-0.946	>0.946	
<b>Men</b>				
Subjects (N)	176	376	118	
Age (yr)	72.6 ± 0.7	72.0 ± 0.4	73.7 ± 0.8	0.2366
Waist-to-hip ratio	0.913 ± 0.005	0.908 ± 0.004	0.921 ± 0.009	0.3701
Mg intake (mg/d)	257 ± 20	252 ± 13	281 ± 24	0.3237
Blood glucose (mg/dL)	124 ± 5 <sup>a</sup>	112 ± 2 <sup>b</sup>	105 ± 4 <sup>b</sup>	0.0042
Prevalence of diabetes (%)	14.0 <sup>a</sup>	10.3 <sup>a</sup>	2.5 <sup>b</sup>	0.0015
<b>Women</b>				
Subjects (N)	169	372	122	
Age (yr)	72.0 ± 0.6	72.4 ± 0.5	73.4 ± 0.9	0.2003
Waist-to-hip ratio	0.876 ± 0.009	0.861 ± 0.005	0.865 ± 0.010	0.3545
Mg intake (mg/d)	213 ± 14	219 ± 13	245 ± 19	0.1156
Blood glucose (mg/dL)	126 ± 5 <sup>a</sup>	111 ± 2 <sup>b</sup>	110 ± 2 <sup>b</sup>	0.0040
Prevalence of diabetes (%)	19.9 <sup>a</sup>	10.0 <sup>b</sup>	10.0 <sup>b</sup>	0.0365

\*Values are mean ± SE. Differences between groups were evaluated using the t-test. A different superscript letter indicates significant difference at  $P < 0.05$ .

the causal relationship is not clear as magnesium depletion might induce insulin resistance, alternatively hyperinsulinemia and glucosuria might also contribute to magnesium depletion.<sup>12</sup> Taken together, our data seem to indicate a plasma magnesium concentration at the lower end of the reference range might not be sufficient to reduce the risk or ameliorate the symptoms of diabetes in the elderly. However, a prospective study is required to confirm the temporal nature of this relationship.

The elderly are probably susceptible to magnesium depletion due to several reasons. Firstly, aging is associated with increased intracellular calcium and decreased intracellular magnesium levels.<sup>51</sup> Secondly, magnesium intake from dietary sources would seem to be suboptimal throughout life. In addition, the elderly might not be able to benefit from magnesium-rich foods due to their hard texture and inappropriate physical properties. An improvement of glucose metabolism and/or insulin sensitivity by magnesium supplements has been demonstrated in diabetic and apparently healthy elderly persons.<sup>26,52,53</sup> Therefore, increased everyday consumption of whole grains, legumes, and vegetables rich in magnesium and the use of supplements may help to improve the magnesium status of the elderly.

This study is the first to demonstrate an inverse association between plasma magnesium concentration and the prevalence of diabetes in a non-Caucasian population. In addition, this report describes the magnesium status of the elderly in Taiwan. The average daily intake of dietary magnesium in both men and women was below the Taiwanese DRIs for adults. A vegetarian diet did not increase magnesium intake and had no significant effect on plasma magnesium concentrations. Overt magnesium deficiency rarely occurred, and the prevalence of low serum magnesium levels was comparatively lower than that found in other developed countries. However, diabetic subjects had significantly lower plasma magnesium and higher blood glucose concentrations than non-diabetic subjects. An increased prevalence of diabetes was significantly associated with plasma magnesium concentrations less than 0.863 mmol/L. Both dietary modification and magnesium supplementation may need to be considered for the elderly

when this relationship is confirmed.

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However, no association was found between diabetes and low dietary magnesium. Taiwanese elderly persons had suboptimal levels of dietary magnesium intake, which although may be sufficient to avoid overt magnesium deficiency, may not be sufficient to reduce the risk of diabetes in the elderly. Further prospective study is required to help explain the differential results between dietary and plasma magnesium levels.<sup>23</sup> However, its association with total usual nutrient intakes, inclusive of dietary supplements, and biomarkers of nutritional status among US children remains unknown. Subclinical magnesium deficiency increases the risk of numerous types of cardiovascular disease, costs nations around the world an incalculable amount of healthcare costs and suffering, and should be considered a public health crisis. That an easy, cost-effective strategy exists to prevent and treat subclinical magnesium deficiency should provide an urgent call to action. magnesium. cardiovascular disease. deficiency. mineral. This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. However, no association was found between diabetes and low dietary magnesium. Taiwanese elderly persons had suboptimal levels of dietary magnesium intake, which although may be sufficient to avoid overt magnesium deficiency, may not be sufficient to reduce the risk of diabetes in the elderly. Further prospective study is required to help explain the differential results between dietary and plasma magnesium levels.<sup>23,24</sup> The inverse association between Mg intake and DM risk in our study and relatively poor Mg status in the Taiwanese population<sup>25</sup> suggest that poor Mg status may be critical in DM etiology in Taiwan and future intervention studies are warranted. Lower intake of magnesium and dietary fiber increases the incidence of type 2 diabetes in Taiwanese.