

## Original Article

# Cognitive impairment and limited dietary diversity or physical inactivity are conjoint precursors of incident diabetes more so in elderly women than men

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**OBJECTIVES:** To establish whether elderly people with impaired cognition are at greater risk for the development of type 2 diabetes. **DESIGN:** Prospective population-based cohort study. **SETTING:** The Elderly Nutrition and Health Survey in Taiwan (NAHSIT Elderly). **PARTICIPANTS:** One thousand and four hundred ninety-three diabetes-free people  $\geq 65$  years were followed for incident diabetes in relation to cognitive status for up to 8 years. **MEASUREMENTS:** The association between cognitive impairment and diabetes incidence was analyzed with Cox proportional hazards models with exclusion of people who had diabetes within one year of cognitive function assessments. **RESULTS:** Cognitively-impaired women, but not men, had increased diabetes incidence density (DID). Age, gender, ethnicity and personal behavior adjusted hazard ratios (HR) and 95% confidence intervals (CI) for type 2 diabetes with normal cognition as referent were 2.43 (95% CI: 1.27-4.63) for women and 1.55 (95% CI: 0.48-5.07) for men. These gender differences and the HR significances remained with adjustments for age, ethnicity, financial status, dietary quality as a dietary diversity score, physical functioning, physical activity, fasting glucose, indices of body composition, body mass index, waist circumference, mid-arm muscle circumference, perceived and mental health status. There were extensive significant interactions with the covariates in women. **CONCLUSION:** Cognitive impairment in later life is associated with greater risk of type 2 diabetes in women and considerable potential risk enhancement.

**Key Words:** cognitive impairment, type 2 diabetes, dietary, physical activity, body composition

## INTRODUCTION

The prevalences of both cognitive impairment and diabetes increase with age.<sup>1,2</sup> It is clear that diabetes can be an antecedent and risk factor for cognitive impairment,<sup>3,4</sup> dementia<sup>5</sup> and affective disorders<sup>6</sup> associated with neurodegeneration. However, the extent to which impaired cognition might be a risk factor for diabetes is unclear or not canvassed in the observed associations between the two.<sup>7,8</sup> For the neurodegenerative Parkinson's disease<sup>9</sup> and for affective disorders like depression,<sup>6</sup> there would appear to be a bidirectional pathogenesis with diabetes.<sup>10</sup> It is plausible that cognitive impairment might increase the risk of diabetes by way of poor food and activity choices,<sup>11</sup> through neuro-endocrine pathways activated in stress and adversely affecting visceral fat<sup>12</sup> or via a shared underlying pathology which might include stress hormones known both to compromise cognition and increase insulin resistance.<sup>13</sup> At the least, the presence of cognitive impairment might modulate recognized risk factors for diabetes such as pre-diabetes, diet, physical activity, body

composition or mental health (Figure 1).

Our general hypothesis is that elderly people with impaired cognition are at greater risk for the development of type 2 diabetes (T2DM). Therefore, we have assessed in a Taiwanese cohort whether elderly people who have impaired cognition have a higher incidence of diabetes.

## RESEARCH DESIGN AND METHODS

Data used in this study were from the Elderly Nutrition

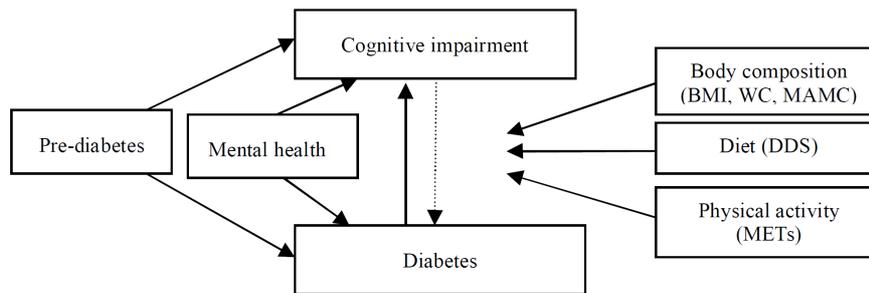
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**Figure 1.** An hypothesis that not only does diabetes increase the risk of cognitive impairment, but that the reverse may also apply or that both may have an underlying pathogenesis, in any case modulated by contributors to energy nutrition (diet and physical activity).

and Health Survey (NAHSIT Elderly) which is a nationally representative sample of the free-living elderly, aged 65 and over, conducted during 1999 and 2000 in Taiwan. A multi-staged, stratified, systematic sampling scheme was used in the survey. The interview information (which included self-reports) was collected in households, face to face.<sup>14</sup> The dataset was linked to the 1999-2006 National Health Insurance to assess T2DM incidence.

### Participants

There were 1,937 participants who completed the household interview; 49 had no cognition or dietary data and were excluded. An additional 395 participants were excluded on account of diabetes diagnosis before or within the first year of interview. Finally, a total of 1,493 elders were studied. All participants signed informed consent. To ensure anonymity, coding was subject to a double-scrambling procedure. The ethics committees of the National Health Research Institutes and of Academia Sinica approved the study protocol.

### Cognitive function

Cognitive function was assessed by the Short Portable Mental Status Questionnaire (SPMSQ) which has been validated in Chinese, in a Taiwanese population.<sup>15</sup> This test has 10 questions dealing with orientation in time and place, personal history, long term and short-term memory and calculation. In this test, total score ranges from zero to ten. Correct answers were coded 1, whereas errors were coded 0. Participants were grouped into normal, those who did not incur errors (SPMSQ score is 10 for intact cognition), and impaired cognition where one or more errors was incurred.

### Type 2 diabetes (T2DM)

The presence of T2DM was recognized by the diagnostic codes A181 (Taiwan), pre-ICD9 use before 2000, or by ICD-9 Code 250, without evidence of insulin dependency (eg, ketoacidosis). At least two diabetes mellitus records within one year were required. Unless otherwise indicated, in this report we mean T2DM when we refer to diabetes.

### Dietary Diversity Score, DDS

Dietary quality was measured by DDS. From a 24-hour recall, a DDS (range 1-6) was derived, a modification of the NHANES method.<sup>16</sup> In accordance with the Taiwanese Food Guides, half a serving per day for one of the six food groups including 'dairy', 'meat', 'staple', 'fruit', 'vegetable' and 'fat and oil' was the minimal intake required for a DDS score of 1. The 'meat' group comprised

protein rich foods, ie eggs, fish and shellfish, soybean products and meats. Higher scores indicate better quality.

### Physical function and mental health

A validated traditional Chinese version (a Short Form, SF-36<sup>®</sup>) was used to assess physical function and mental health. SF-36 contains a total of 36 items with self-assessment questions to measure eight dimensions of health, which included physical functioning (PF) and mental health.<sup>17,18,24</sup> We grouped subjects' responses into eight subscales following the norm-based scoring system ( $\mu=50$ ,  $\sigma=10$ ) and calculated the standardized score for each subscale on the basis of the NAHSIT population.<sup>17,25</sup> We used the physical functioning and mental health scores as our measure of physical function and mental health, respectively. We further classified mental health by tertile, approximations in this population as <48, 48-55, >55.<sup>15</sup>

### Physical activity

Daily physical activity was measured by the number of metabolic equivalents (METs) calculated from sport and leisure time activities, based on activity duration, frequency and intensity, as well as the number of stairs climbed.<sup>19</sup>

### Fasting glucose, FG

Impaired fasting glucose (IFG) was defined by an elevated fasting plasma glucose (FPG) concentration (100-125 mg/dL) in accordance with American Diabetes Association criteria.<sup>20</sup>

### Body composition

After an overnight fast, height and weight were measured without shoes and with a deduction for estimated clothes' weight. Waist circumference (WC in cm) was measured at the level of the natural waist. Mid-arm circumference (MAC in cm) was measured midway between the acromion and the olecranon with the arm parallel to the trunk. With Lange skinfold calipers, triceps skinfold (TSF in mm) thickness was measured midway between the acromion and the olecranon on the mid-line of the posterior of the right upper arm.<sup>14,17</sup> Mid-arm muscle circumference (MAMC in cm) =  $MAC - (\pi \times TSF)$ <sup>21</sup> was used as an index of relative sarcopenia. Central obesity was defined for men as a  $WC \geq 90$  and, for women, a  $WC \geq 80$ , according to Taiwanese criteria based on Asian recommendations by the WHO,<sup>22,23</sup> MAMC was considered as gender-specific distribution tertiles.<sup>17</sup>

**Table 1.** Demographic and personal behavioral variables by cognitive status in NAHSIT Elderly.<sup>†‡</sup> (n=1,493)

Variables	Men (n=767) (%)				Women (n=726) (%)			
	Total	Normal	Cognitive impairment	p value	Total	Normal	Cognitive impairment	p value
Baseline intragender prevalence (%)		90.2	9.84		72.5		27.5	
Baseline whole population prevalence (%)		46.5	4.89		34.4		14.3	
Age, yrs (%)				0.003				<0.001
65-69	28.5	30.6	10.1		30.4	34.9	18.7	
70-74	32.1	33.7	17.5		29.3	31.2	24.0	
75-97	39.4	35.8	72.4		40.3	33.9	57.3	
Education (%)				<0.001				<0.001
Illiterate	21.7	18.8	48.4		59.0	49.8	83.3	
Elementary school and below	47.3	48.0	40.8		29.7	35.1	15.4	
High school and college	30.7	33.2	7.6		10.5	14.0	1.38	
Ethnicity (%)				0.01				0.09
Non indigenous	98.0	98.2	95.6		97.6	98.0	96.7	
Indigenous	2.0	1.76	4.39		2.24	1.86	3.27	
Perceived financial status (%)				0.04				0.002
Enough	75.4	77.6	54.8		70.6	75.4	57.7	
Some difficulty	18.4	17.0	31.1		19.9	17.4	26.3	
Very difficult	3.1	2.86	4.98		6.14	4.18	11.3	
Alcohol drinker (%)				0.126				0.158
No	56.6	56.0	62.3		94.6	93.6	97.4	
Former	12.6	12.3	14.6		0.95	1.10	0.58	
Current	30.3	31.5	19.9		4.16	4.97	2.05	
Smoker (%)				0.714				0.449
Never	33.0	32.7	35.5		95.1	94.5	96.4	
Former	26.6	26.4	27.9		1.49	1.82	0.62	
Current	40.1	40.5	36.4		3.19	3.28	2.96	
DDS (%)				0.003				0.003
≤3	14.9	13.4	28.2		18.5	16.0	25.2	
4	31.8	30.2	46.2		31.3	28.2	39.6	
5-6	53.4	56.4	25.6		50.1	55.8	35.3	
Physical functioning (%)				<0.001				<0.001
<45	16.9	11.8	67.0		32.2	24.5	53.1	
45-53.9	28.7	29.7	18.7		35.6	39.2	25.9	
54-57.9	32.2	34.5	9.38		21.9	23.9	16.6	
≥58	22.2	24.0	4.92		10.2	12.4	4.40	
Leisure time physical activity (METs) (%)				0.004				<0.001
<1.5	52.7	50.2	75.3		61.2	55.3	76.7	
1.5-3	11.3	12.0	4.41		12.1	13.3	9.04	
>3	36.1	37.8	20.3		26.7	31.4	14.3	
Perceived health status (%)				0.008				0.007
Good	58.9	61.1	38.8		58.8	63.5	46.6	
Fair	31.5	31.7	29.0		28.1	27.9	28.5	
Poor	9.04	7.09	26.9		12.0	8.03	22.3	
Fasting glucose, mg/dL, mean		104	102	0.7		104.	110	0.3
BMI, kg/m <sup>2</sup> , mean,		23.3	21.9	0.04		24.0	22.9	0.01
WC, cm, mean		85.2	83.3	0.3		81.1	80.2	0.4
MAMC, cm, mean		23.2	22.2	0.05		21.3	20.8	0.1
Mental health norm based score, mean		52.1	48.7	<0.01		49.8	45.5	<0.001
Duration of diabetes observation, years		7.1	7.4	<0.001		7.0	6.2	0.2
Diabetes incidence density/1000 person-years		257	224	0.09		261	307	<0.001

DM=diabetes.

† % are weighted to reflect their representation in the population.

‡ Chi-square test by SUDAAN program

**Statistical analysis**

All data were weighted for adequate representation of the elderly population in Taiwan during 1999-2000. Chi-square tests were used for categorical variables across cognitive status groups. Cox proportional-hazards models were used to evaluate the effect of cognitive status on risk

of developing diabetes from 1999 to 2006 with relevant covariate adjustments, including gender, age, education, ethnicity, alcohol drinking and smoking status. Relevance was determined with regard to the current literature on risk for cognitive impairment and on the basis of factors significantly related to cognitive impairment in this popu-

**Table 2.** Hazards ratio of cognitive impairment on risk of developing diabetes in NAHSIT elderly (n=1,493)

	HR ratio (95% confidence intervals)		
	Normal <sup>†</sup>	Cognitive impaired	<i>p</i> for trend
Crude	1.00	1.78 (1.05-3.02)*	0.03
Model 1	1.00	2.17 (1.23-3.82)**	0.009
Women	1.00	2.43 (1.27-4.63)**	0.009
Men	1.00	1.55 (0.48-5.07)	0.4
Model 2 (Financial)			
Women	1.00	2.05 (1.08-3.87)*	0.03
Men	1.00	1.67 (0.60-4.64)	0.3
Model 3 (DDS)			
Women	1.00	2.44 (1.28-4.62)**	0.008
Men	1.00	1.38 (0.42-4.53)	0.6
Model 4 (PF)			
Women	1.00	2.52 (1.25-5.11)*	0.01
Men	1.00	1.05 (0.23-4.72)	0.9
Model 5 (METs)			
Women	1.00	2.44 (1.36-4.36)**	0.004
Men	1.00	1.55 (0.46-5.22)	0.5
Model 6 (FG)			
Women	1.00	3.87 (1.47-10.21)**	0.008
Men	1.00	0.94 (0.16-5.56)	0.9
Model 7 (BMI)			
Women	1.00	3.50 (1.21-10.18)*	0.02
Men	1.00	2.17 (0.71-6.67)	0.2
Model 8 (WC)			
Women	1.00	4.26 (1.65-11.04)**	0.004
Men	1.00	2.33 (0.63-8.57)	0.2
Model 9 (MAMC)			
Women	1.00	2.65 (1.28-5.49)*	0.01
Men	1.00	1.69(0.52-5.53)	0.4
Model 10 (Mental health)			
Women	1.00	2.23 (1.22-4.08)*	0.01
Men	1.00	1.69 (0.55-5.20)	0.3
Model 11 (Perceived health status)			
Women	1.00	2.45 (1.28-4.68)**	0.009
Men	1.00	1.61 (0.43-6.06)	0.5

<sup>†</sup> Hazards ratios of developing diabetes were estimated by the Cox proportional-hazards model, "Normal" as reference group.

Model 1 adjusted for age (yr), gender, ethnicity, smoking status and drinking; Model 2 adjusted for Model 1 covariates and financial status; Model 3 adjusted for Model 1 covariates and DDS; Model 4 adjusted for Model 1 covariates and physical function; Model 5 adjusted for Model 1 covariates and METs; Model 6 adjusted for Model 1 covariates and FG; Model 7 adjusted for Model 1 covariates and BMI; Model 8 adjusted for Model 1 covariates and WC; Model 9 adjusted for Model 1 covariates and MAMC; Model 10 adjusted for Model 1 covariates and mental health; Model 11 adjusted for Model 1 covariates and Perceived health status.

\**p*<0.05, \*\* *p*<0.01

lation (Table 1). The models were further adjusted on this background for financial status, DDS, physical functioning, METs, FG, body composition, mental health and perceived health status. All analyses were performed using SAS statistical software (version 9.1.3) and SUDAAN (version 10.0).

## RESULTS

### *Socio-demography and personal behaviors*

A total of 1,493 participants including 767 men and 726 women were involved in this study. Men and women have different cognition status and diabetes incidence even for the same risk factors, so their characteristics are presented separately. Cognitive impairment prevalence for men and women are 9.8% and 27.5% respectively. Cognitive impairment is significantly associated with age, ethnicity (men only), education, perceived financial status, DDS, physical function, leisure time physical activity, mental health, perceived health and BMI. Older people had a higher risk of cognitive impairment, especially those aged over 75 years. People who had a high school

and college education had a lower risk of cognitive impairment. Other characteristics which are risk factors for diabetes, such as DDS,<sup>26</sup> physical function,<sup>27</sup> physical activity,<sup>28</sup> BMI,<sup>29</sup> but not WC,<sup>30,31</sup> were also significantly associated in the present study with cognitive status. For women, cognitive impairment was associated with a higher risk of T2DM than men. (Table 1)

### *Cognitive status, gender and risk of diabetes*

In Table 2 the hazards ratios (HR) and 95% confidence intervals (CI) for the risk with cognitive impairment of diabetes are shown by gender in a crude model and Models 1 to 11 with various adjustments. Model 1 is the basic model with adjustments for age, gender (where all subjects are considered), ethnicity, smoking status and drinking alcohol. Models 2 to 11 represent adjustments to Model 1. Only in women are the HRs significant and this significance persists with adjustments for financial status, DDS, physical functioning, physical activity, fasting glucose, BMI, WC, MAMC, mental health and perceived health status.

### Joint effects on diabetes incidence of ethnicity with cognition

Because of the difference in prevalence of diabetes between indigenous and non-indigenous Taiwanese,<sup>32-34</sup> we considered the joint effect of indigenous status and cognition on risk for diabetes. Compared to non-indigenous without cognitive impairment, non-indigenous women with cognitive impairment had an HR of 2.44 with 95% CI of 1.27-4.68; in indigenous men who were not cognitively impaired the HR was 0.64 with 95% CI 0.42-1.00. (Figure 2)

### Joint effects of diabetes incidence of perceived health status with cognition

Given the functional and integrative health significance of 'perceived health status', we considered whether it might act conjointly with cognition to alter the risk for diabetes (Figure 2). In cognitively impaired women with poor perceived health status, the HR (95% CI) was 5.55 (2.70-11.41) using women with normal cognition and good perceived health status as referent; the interaction was of borderline significance with  $p=0.07$ . In men the interaction was non-significant with  $p=0.13$ .

### Joint effects on diabetes incidence by DDS, physical function and physical activity with cognition

Using non-cognitively impaired individuals with, respectively, the highest DDS, physical functioning and physical activity as referent, their joint effects on the risk of diabe-

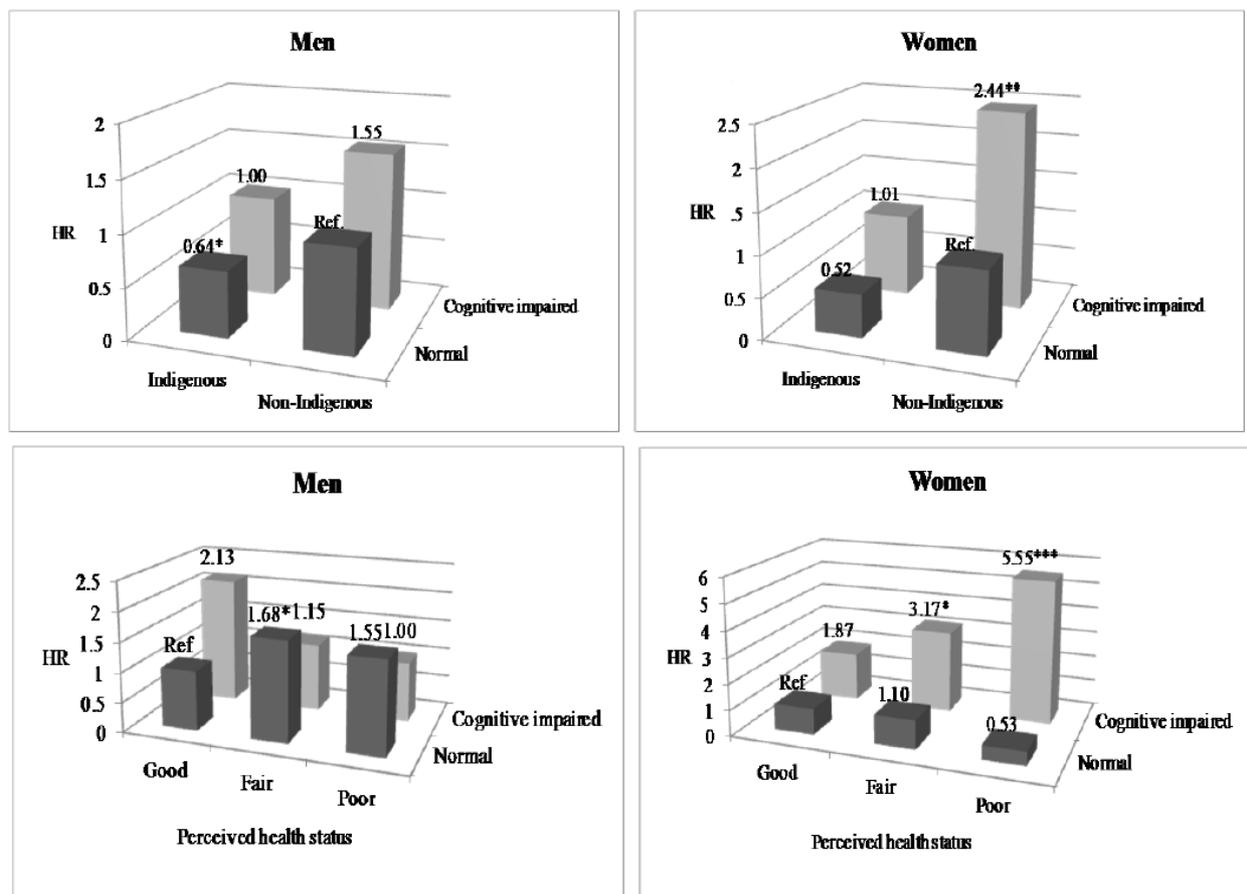
tes over 8 years are shown in Figure 3. In each case, women who were cognitively impaired exhibited a significant or near-significant interaction ( $p$  for DDS is 0.004, for physical functioning is 0.07, and for physical activity is 0.03 with that risk factor such that when it was lowest the risk of diabetes was significantly greatest [HR and 95% CI respectively 13.9 (4.55-42.4), 5.13 (2.06-12.8) and 2.88 (1.12-7.43)]. For men, there were no significant interactions, although, for DDS, intermediate values had the worst risk (HR 3.45, 95% CI: 1.27-9.38), while, for physical functioning, when least the HR was 7.49, 95% CI: 2.22-25.3, in those cognitively impaired.

### Joint effects on diabetes incidence of mental health with cognition

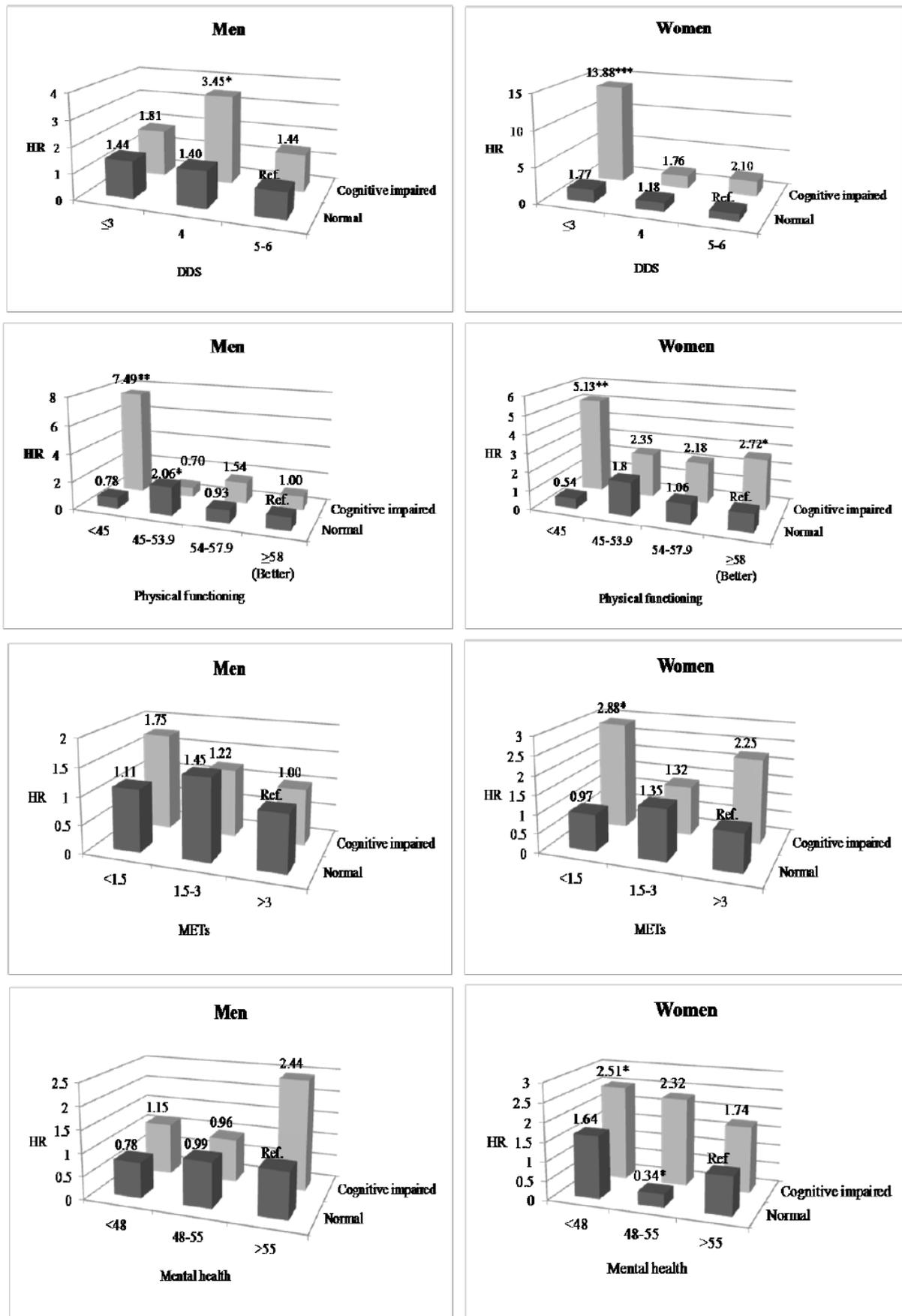
Where mental health is least good it is interactive with cognitive impairment for the risk of diabetes in women ( $p=0.04$ ), but not in men. At the same time the HR (95% CI) when there is cognitive impairment and the least good mental health is 2.51 (1.10-5.70) using best case as referent. (Figure 3)

### Joint effects on diabetes incidence of body composition with cognition

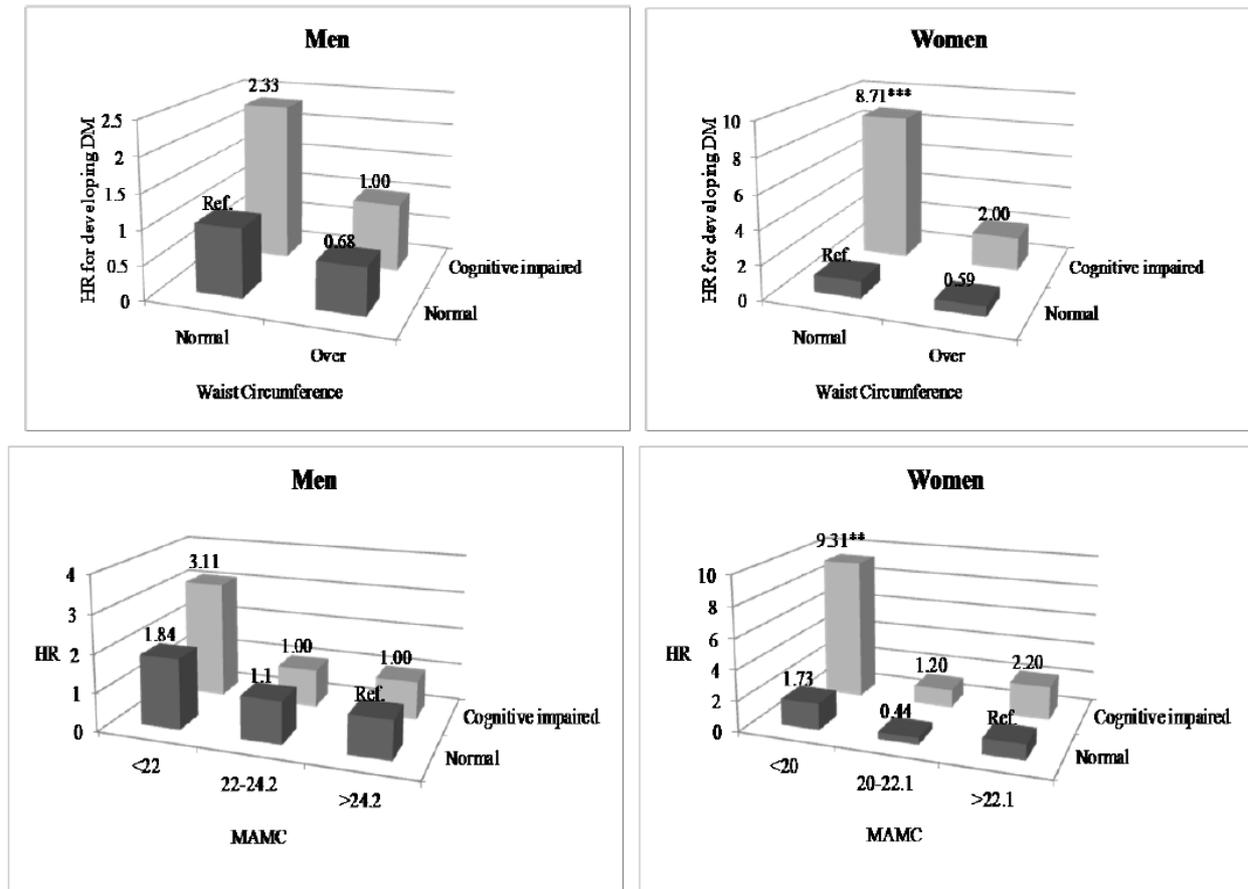
In Figure 4, fat distribution by WC and muscle mass by MAMC as possible joint risk factors with cognitive impairment for diabetes are shown. In women only are the interactions significant, WC  $p=0.02$  and MAMC  $p=0.002$ . In addition, when there is cognitive impairment, the joint



**Figure 2.** Joint hazard ratios (HRs) for developing diabetes in elder Taiwanese after an 8-year follow-up in accordance with cognitive function and in relation to ethnicity. The model has been adjusted for gender, age, education, alcohol drinking, and smoking. Significance is shown by \* $p<0.05$ , \*\* $p<0.01$ , \*\*\* $p<0.001$ . The  $p$  value for interaction for cognitive status and ethnicity in men and women are 0.07 and 0.04; for cognitive status and perceived health status in men and women are 0.13 and 0.07 respectively.



**Figure 3.** Joint hazard ratios (HRs) for developing diabetes in elder Taiwanese after an 8-year follow-up in accordance with cognitive function and in relation to dietary diversity scores (DDS), physical function and metabolic equivalents (METs). The model has been adjusted for gender, age, education, ethnicity, alcohol drinking, and smoking. Significance is shown by \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ . The  $p$  value for interaction for cognitive status and DDS in men and women are 0.5 and 0.004; for cognitive status and METs in men and women are 0.7 and 0.03; for cognitive status and physical function in men and women are 0.2 and 0.07, for cognitive status and mental health are 0.7 and 0.04, respectively.



**Figure 4.** Joint hazard ratios (HRs) for developing diabetes in elder Taiwanese after a 8-year follow-up in accordance with cognitive function and in relation to waist circumference (WC) and Mid-arm muscle circumference (MAMC). The model has been adjusted for gender, age, education, ethnicity, alcohol drinking, and smoking. Significance is shown by \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ . The  $P$  value for interaction for cognitive status and WC in men and women are 0.14 and 0.02; for cognitive status and MAMC are 0.2 and 0.002 respectively.

HRs (95% CIs) are, respectively 8.71 (2.67-28.4) and 9.31 (2.58-33.6) for normal WC and the least muscle mass.

## DISCUSSION

### *Cognitive impairment as an antecedent of diabetes*

The association between cognitive impairment and diabetes is well-established, although most of the evidence points to hyperglycemia or diabetes as a risk factor for cognitive impairment or dementia.<sup>5</sup> What we have found is that cognitive impairment can antedate and constitute a risk factor for T2DM. This means that cognitive function may be part of a vicious cycle in the progression of diabetes and its sequelae. It is possible that the risk of diabetes operates across the SPMSQ range which we have not evaluated. Nevertheless, it maybe of clinical and public health importance to consider lesser degrees of cognitive impairment in relation to risk of diabetes.

### *Gender, being indigenous and joint effects*

Population studies of cognitive impairment vary in gender equivalence or dominance of prevalence.<sup>35-37</sup> A study of elderly Taiwanese in 1990 reported higher prevalences among women than men.<sup>38</sup> There are consistent recognized differences in the type of cognitive ability, however, with men better in spatial and number cognition and women in word fluency.<sup>35,36</sup> In our diabetes-free baseline population, prevalence was greater among women. There

is a gender difference in the risk of incident T2DM when there is cognitive impairment, with an adjusted impact of 2.4-fold in women and no significant impact in men. This raises questions as to the nature of this susceptibility in women. The risk is seen in non-indigenous rather than indigenous women so that ethnicity may play a role. However, we are uncertain as to why there appears to be less susceptibility to diabetes with cognitive impairment among indigenous women, especially since the study design over-sampled minority groups making false negativity less likely. It is noteworthy that the major Taiwanese indigenous communities, the Ami, are matriarchal and matrilineal and this societal strength may play a role.<sup>39</sup>

The gender effect in those who are dominantly Han Chinese women is amplified, as judged by significant joint effects, by poor dietary quality (assessed by DDS), limited physical function and activity, mental health difficulties and the body compositional factors of less abdominal fatness (WC) and sarcopenia (MAMC<22). These findings may point to the mechanisms involved.

### *Mechanisms for cognitive impairment as a risk factor for diabetes*

Cognitive impairment is associated with a number of phenomena which themselves might contribute to an apparent actual biological basis for its association with diabetes. Chief among these may be socio-cultural,<sup>33</sup> mental stress,<sup>12</sup> perceived health problems or illness cognition.<sup>40</sup>

Notwithstanding a well-established National Health Insurance scheme in Taiwan, equity and poverty have been found to be ongoing concerns in the recognition and management of diabetes.<sup>41</sup> Among elderly Taiwanese, education, ethnicity and perceived financial status were less satisfactory in the cognitively impaired than those not. However, adjustments for these in all joint effect models did not alter the gender differences or associations with antecedent cognitive impairment and diabetes.

With cognitive impairment as a risk factor for diabetes in women of dominantly Han Chinese ancestry, it is conceivable that there is a shared underlying basis for the two health problems. Both have their pre-clinical counterparts, moderate cognitive impairment and pre-diabetes or the metabolic syndrome.

Insulin resistance is a candidate for an underlying pathogenesis as it is not only a feature of pre-diabetes, but has been associated with cognitive impairment.<sup>42</sup> These observations might be explained by impaired energy regulation (IER) where the plane of energy nutrition or energy throughput might be sufficiently low in some elderly women as to compromise dietary quality.<sup>43</sup> This problem of energy regulation may be apparent in diabetes dementia given the favorable associations with metformin with its effects on AMP kinase involved in cellular bioenergetics.<sup>5</sup> However, a gender difference has not been reported with this association, albeit for diabetes, metformin and cancer<sup>44</sup> where the energy dysregulatory hepatocellular and colorectal cancers behave differently. Although not significantly conjoint in the present study, poor PF is strongly associated with incident diabetes, as it is in women. Low PF also conjointly with underweight increases the mortality risk in men and women in this elderly Taiwanese population<sup>17</sup> which emphasizes the adverse overall health consequences of impaired energy regulation in the elderly.<sup>43,44</sup>

The more detailed pathogenesis of cognitive impairment and diabetes might be shared through amyloid deposition in brain and pancreatic islets with their beta cells.<sup>45</sup> Evidence for type 3 brain diabetes makes a similar case.<sup>46</sup>

### Limitations

Diagnostic rates may have been higher in women than in men because of differences in health-seeking behavior.<sup>40</sup> In this case, the observed gender differences might not have been so great. However, we have also considered the question of gender discrimination in the Taiwanese health care system and show how it is probably not a major factor in regard to the metabolic syndrome and cardiovascular disease where substantial cost differences are nevertheless incurred by gender.<sup>47</sup>

It is possible that we have not taken into account all possible confounders in our exploration of the associations of antecedent cognitive impairment with T2DM. Thus, these associations may be over-stated, although they have been accentuated in the conjoint models and the resultant relative risks are generally large. We have recorded all 8 dimensions of SF-36 and studied 3 of them (physical functioning, mental health and perceived health status) as covariates. We considered that those omitted would be largely covered by the socio-demographic vari-

ables available to us and included in any case, but acknowledge that a clearer picture of cognitive impairment as a risk for diabetes might emerge from the inclusion of each and every SF-36 dimension.

Finally, it is likely that sub-clinical phenomena which we have not ascertained may clarify what presently seems a possible sequential set of events, with cognition preceding T2DM. This is especially so since, separately, we know that the reverse sequence occurs<sup>5</sup>.

### Implications

It is of interest to consider the implications of the present findings in light of trends in T2DM prevalence and incidence in Taiwan.<sup>48</sup> In later life, this may be relevant even for minor degrees of cognitive impairment. While overall adult prevalence has been increasing, increased incidence is located principally among young men aged 20-40 years. Our study is of elders  $\geq 65$  years where incidence is relatively stable and similar for men and women from 1999-2004, at about 18 per 1000 person-years. It would be useful to establish whether interruption of the cognitive function-diabetes association could decrease the burden of both health problems in later life. Likely candidates for such a strategy include efforts to encourage optimal neuronal energy regulation through enhanced physical function and activity, where energy needs are met with a nutritious diet as judged by its diversity and the emphasis on body compositional health is maintenance of skeletal mass and avoidance of sarcopenia. Although these findings apply to women rather than men in our study, for reasons of general and public health, the same approaches are relevant to men. Moreover, since it is known that insulin resistance may precede both cognitive impairment and diabetes, these strategic steps may abort a shared underlying pathogenesis.

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### AUTHOR DISCLOSURES

No author has a conflict of interest in regard to this paper.

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## Original Article

## Cognitive impairment and limited dietary diversity or physical inactivity are conjoint precursors of incident diabetes more so in elderly women than men

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### 認知功能障礙伴隨單調飲食或缺乏運動是老年女性而非男性罹患糖尿病的前導因子

已有研究發現患有糖尿病的老人易發生認知功能障礙，對於患有認知功能障礙的老人是否更易發生糖尿病，也就是老人糖尿病和認知功能障礙發生是否存在雙向性影響，目前不可知。本研究的目的是為觀察患有認知功能障礙的老人是否更容易發生糖尿病。以參與 1999-2000 年臺灣老人營養和健康調查中 1493 位年齡超過 65 歲，且沒有糖尿病的老人為研究對象，追蹤 8 年，研究糖尿病發生率和認知功能的關係。認知功能障礙和糖尿病的發生率以 Cox 比例風險迴歸模型來分析。結果發現有認知功能障礙的女性其糖尿病發生率顯著提高，但在男性中沒有觀察到這樣的結果。以正常認知功能組做為參照組，在校正年齡，性別，種族和個人行為之後，認知功能障礙老年女性二型糖尿病風險比值(HR)為 2.43 (95%信賴區間: 1.27-4.63)，男性為 1.55 (95%信賴區間: 0.48-5.07)。在分別校正年齡，種族，個人行為和經濟狀況，飲食品質，身體活動功能，運動，空腹血糖值，身體質量指數，腰圍及中臂肌圍等可能影響糖尿病發生的變數後，性別差異和風險比顯著性仍然存在。在女性中，上述共變數對糖尿病的發生存在顯著交互作用。飲食品質差及少運動，會增加認知功能障礙老年女性患糖尿病的風險比。

**關鍵字：**認知功能障礙、第二型糖尿病、飲食、運動、身體組成