

## Original Article

# Association between rice intake and all-cause mortality among Chinese adults: findings from the Jiangsu Nutrition Study

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**Background and Objectives:** The few studies that have assessed the association between rice intake and mortality have generated inconsistent results. We assessed whether rice intake was associated with cardiovascular disease (CVD) mortality, cancer mortality and all-cause mortality in a prospective cohort of the Chinese population. **Methods and Study Design:** We prospectively studied 2,832 adults aged 20 years and above with a mean follow up of 10 years. Rice intake was measured by a 3-day weighed food record (WFR) in 2002. Hazard ratios (HRs) and 95% CI were calculated by competing risks regression (CVD and cancer mortality) and Cox proportional hazards analysis (all-cause mortality). **Results:** We documented 184 deaths (including 70 CVD deaths and 63 cancer deaths) during 27,742 person-years of follow-up. No association between rice intake and all-cause mortality was found. After adjusting for sociodemographic and lifestyle factors as well as energy and fat intake, HRs for CVD mortality across tertiles of rice intake were 1.00, 0.47 (95% CI 0.25-0.87), and 0.49 (95% CI 0.21-1.13) (*p* for trend 0.049). **Conclusions:** There was no association between rice intake and all-cause mortality.

**Key Words:** rice intake, mortality, Chinese, cohort study, epidemiology

## INTRODUCTION

Rice is the main staple food in many countries especially in Asia.<sup>1</sup> Despite a substantial decline in rice intake over the past several decades, the mean rice intake was still as high as 280 g/day in China in 2004.<sup>2</sup> In Japan, rice provides 43% of carbohydrate and 29% of energy intake.<sup>3</sup> Based on the degree of processing, rice is categorized into two groups (brown rice and white rice). The refining process associated with white rice destroys the structure of the grain kernel and removes dietary fibre and other essential micronutrients. Currently the majority of rice consumed in China is white rice.

White rice has a high glycaemic index but is low in sodium and is free of cholesterol. A recent systematic review showed that white rice intake was positively associated with the risk of diabetes.<sup>4</sup> However, when compared with wheat consumption, rice consumption was inversely related to weight gain.<sup>5</sup> In general, rice consuming nations (e.g. China, Japan) have a low prevalence of overweight/obesity. A rice diet has been used to treat hypertension<sup>6</sup> and an inverse association between rice intake and blood pressure and triglycerides has also been found.<sup>5</sup> Previously we have found that there was no association between rice consumption and the risk of incident metabolic syndrome.<sup>5</sup>

Because diabetes increases the risk of cardiovascular disease (CVD) and cancer mortality, of interest is whether the positive association between rice and diabetes leads to

an increased risk of mortality especially from CVD and cancer. Currently, only two population studies have assessed such association but found inconsistent results.<sup>7,8</sup> In the Japanese Collaborative Cohort (JACC) Study, rice intake was associated with a reduced risk of CVD mortality in Japanese men but not women.<sup>7</sup> However, findings from the Japan Public Health Centre-based (JPHC) study showed that rice intake was not related to all-cause mortality or CVD mortality among Japanese adults.<sup>8</sup> In addition, another study suggests that rice intake was associated with an increased risk of stomach cancer mortality in Japanese.<sup>9</sup>

There is no study assessing the association between rice intake and mortality in the Chinese population. Using data from Jiangsu Nutrition Study, we aimed to assess the association between rice intake and 10-year mortality among adults aged 20 years and above.

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## METHOD

### *Study population*

The Jiangsu Nutrition Study (JIN) is an ongoing cohort study investigating the association of nutrition and other factors with the risk of non-communicable chronic disease.<sup>10-12</sup> The sample was based on a subsample of the Chinese national nutrition and health survey representing Jiangsu province and the year 2002 was used as a base line. The rural sample was selected from six counties (Jiangyin, Taichang, Shuining, Jurong, Sihong and Haimen) (Figure 1). From each of the six counties, three smaller towns were randomly selected. The urban sample was selected from the capital cities of the two prefectures, Nanjing and Xuzhou; and from each capital city three streets were randomly selected. The six counties and the two prefectures represented a geographically and economically diverse population. In each town/street, two villages/neighbourhoods were randomly selected, and 90 households were further selected randomly from each village/neighbourhood. All the members in the households were invited to take part in the study. In addition, one third of the households were interviewed regarding dietary intake. In 2002, 2,832 adults aged 20 and above supplied dietary information and had fasting blood measured for glucose and haemoglobin.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by Jiangsu Provincial Centre for Disease Control and Prevention. Written informed consent was obtained from all participants.

### *Data collection and measurements*

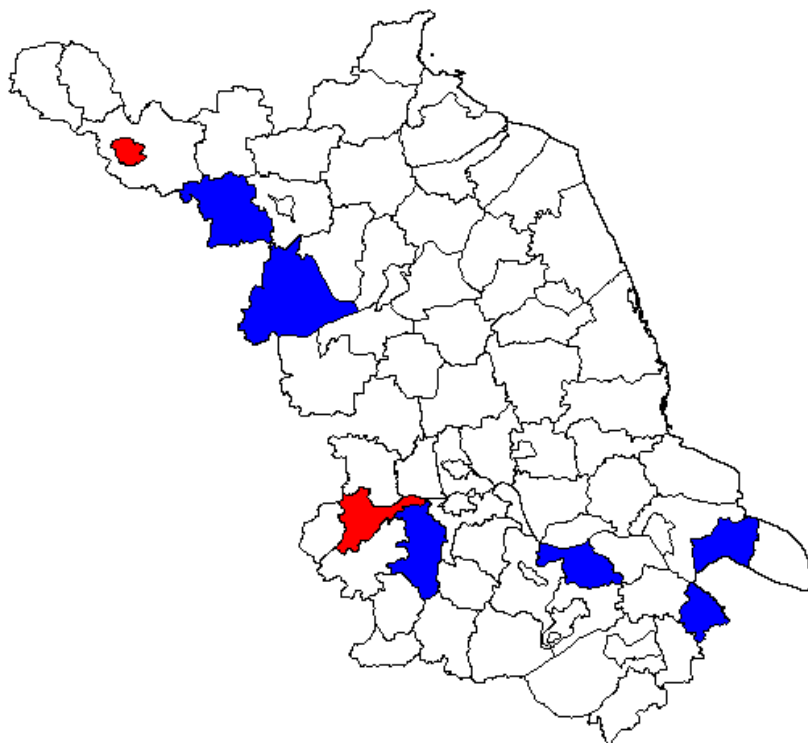
Participants were interviewed at their homes by health workers using a standard questionnaire. All health workers were intensively trained before the survey.

### **Independent variables (dietary measurements)–3-day weighed food records (WFR)**

Food intake including rice intake were assessed using a 3-day weighed food diary which recorded all foods consumed by each individual, on three consecutive days (including one weekend). At the beginning and end of the 3-day survey, health workers weighed all the food stocked in the household. Each day, all purchases, home production, and processed snack foods were weighed and recorded. Food intakes of each individual in the household were recorded in detail each day. During the interview, the health workers would check any intake value for a particular food that fell below or above the usual intake value by the population in the region. For the current study, rice intake (presented as raw rice, g/d) for each individual was calculated based on the 3-day records. We did not consider under- and over-reporting of energy intake as an issue of concern because any unreliable data were checked by the health workers during the survey. Food consumption data were analysed using the Chinese Food Composition Table.<sup>13</sup>

### **Covariates**

Cigarette-smoking was assessed by asking frequency of daily cigarette smoking. Alcohol consumption was assessed by asking the frequency and amount of alcohol/wine intake. Information on physical activity was collected using a validated physical activity questionnaire covering a time period of one year.<sup>14</sup> Questions on the daily commuting return journey were categorized into three categories: (1) using motorized transportation, or no work (0 minute of walking or cycling); (2) walking or bicycling 1-29 minutes; and (3) walking or bicycling for  $\geq 30$  minutes. Daily leisure time physical activity was classified into three categories: 0, 1-29 and  $\geq 30$  minutes. Education was recoded into three categories based on a



**Figure 1.** Map of study sites in Jiangsu province

six categories of education levels in the questionnaire: 'Low'- illiteracy, primary school; 'Medium'- junior middle school; 'High'- high middle school or higher. Occupation was recoded into manual or non-manual based on a question with 12 occupational categories. We defined diabetes as fasting plasma glucose (FPG)  $>7.0$  mmol/L or having known diabetes (self-reported doctor diagnosed). Hypertension was defined as systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg, or using antihypertensive drugs. Overweight was defined as BMI  $\geq 24$  kg/m<sup>2</sup>. Anaemia was defined as a Hb level below 13 g/dL for men and 12 g/dL for women.<sup>15</sup>

### Death ascertainment

The underlying cause of mortality was defined according to the World Health Organization International Classification of Disease, 10th revision (ICD-10). Death information was collected in 2012 during the household visit as well as by linking with the death registry database in the local Centre for Disease Control and Prevention. Thus, the identification of death of the participants was virtually complete. CVD mortality included ICD-10 codes I00–99. Cancers mortality was defined as ICD-10 C00–97.

### Statistical analysis

The chi square test was used to compare differences in categorical and ANOVA in continuous variables. The cohort was divided into tertiles on the basis of rice intake. For each participant, person-years of follow-up were calculated from the date of baseline survey to the date of death or the date of last follow-up (1 December 2012), whichever came first. The association between rice intake and the risk of CVD and cancer mortality was analysed using competing risks regression (*stcrreg* syntax in Stata) and the association between rice intake and all-cause mortality was analysed using Cox proportional hazard models, adjusting for multiple covariates, with the first tertile as the reference category. Two models assessed the association between rice intake and mortality. The first model controlled for age (continuous), gender, and intake of energy and fat; and the second model further adjusted for sociodemographic and lifestyle factors, chronic diseases (anaemia, diabetes, overweight, and hypertension), energy intake and selected food intake (total meat, fruit and vegetable). As the sample size in the full model was 2,771 (97.8% of the whole sample), we did not impute for missing data. In the sensitivity analyses, we excluded those who died within three years of the baseline survey. The proportional hazards assumption in the Cox model was assessed with graphical methods and with models including time-by-covariate interactions. In general, all proportionality assumptions were appropriate.

In the sensitivity analysis, we excluded those with rice intakes of 0 or  $\geq 500$  g/d and used restricted cubic spline regressions<sup>16</sup> to graphically model the associations between rice intake (continuous) and the risk of CVD mortality. Three knots were put at the 5, 50 and 95 percentiles of rice intake.

Sensitivity analysis was conducted by excluding participants with diabetes. Interactions between rice intake and

gender, overweight and anaemia were conducted by adding a multiplicative term with gender, overweight, and anaemia as a binary variable and the tertile of consumption of rice as a categorical variable in fully adjusted models. Because there was no significant gender by rice interaction, we only presented the combined results. We tested for linear trends across categories of rice intake by assigning each participant the median value for the category and modelling this value as a continuous variable. We used a cluster-robust variance estimator [stata command: *vce(cluster clustvar)*] to account for the clustering at the household level in the estimation of the variance. Statistical significance was considered when  $p < 0.05$  (two-sided). All analyses were performed using Stata 13 (Stata Corp., College Station, TX, USA).

### RESULTS

At baseline, compared with participants in the lowest tertile of rice intake, those in the highest tertile of rice intake were older and more likely to have hypertension and anaemia, and to live in the south (Table 1). Across the tertiles of rice intake, fat intake increased. Income was inversely related to rice intake.

Among the 2,832 adults aged 20 years and above at the baseline, there were 184 deaths (including 70 CVD deaths and 63 cancer deaths) during on average 9.8 years follow up (in total 27,742 person-years). No association between rice intake and all-cause mortality was found. In the fully adjusted model, across tertiles of rice intake, HR (95% CI) for all-cause mortality was 1.00, 0.99 (95% CI 0.65–1.51) and 0.96 (95% CI 0.59–1.55), respectively (Table 2).

There was a dose-response inverse association between rice intake and CVD mortality. In the fully adjusted model, the HRs (95% CI) for CVD mortality across tertiles of rice intake were 1.00, 0.47 (95% CI 0.25–0.87), and 0.49 (0.21–1.13) ( $p$  for trend 0.049). The inverse association became stronger when we further excluded those who died within three years of follow-up. There was a marginally significant gender by rice intake interaction ( $p$  for interaction 0.08), where the inverse association appeared stronger in women: HR (95% CI) for CVD mortality across quartiles of rice intake was 1.00, 0.22 (0.07–0.69), and 0.23 (0.05–1.18) in women; 1.00, 0.89 (0.33–2.38) and 0.98 (0.32–2.94) in men. No interaction between rice intake and anaemia, overweight, diabetes, and hypertension was found (data not shown). In the sensitivity analysis, after excluding those with extreme rice intake (0 or  $\geq 500$  g/d), there was a linear inverse association between rice intake and CVD mortality (Figure 2). Excluding those with diabetes did not change the findings (data not shown).

There was a borderline significant trend of increased risk of cancer mortality across tertiles of rice intake.

### DISCUSSION

In this Chinese cohort study, we found no association between rice intake and all-cause mortality. However, rice consumption was inversely related to CVD mortality and marginally associated with an increased risk of cancer mortality.

In line with a large study in China,<sup>17</sup> we found CVD and cancer deaths contributed to the highest proportion of

**Table 1.** Sample characteristics according to tertiles of rice intake among Chinese adults (n=2832)

	Rice intake			p value
	T1	T2	T3	
n	960	931	941	
Raw rice intake (g/day), mean (SD)	92.3 (58.4)	246.2 (36.5)	414.6 (81.6)	<0.001
Age (years), mean (SD)	46.0 (15.0)	47.7 (15.3)	47.6 (12.9)	0.018
BMI (kg/m <sup>2</sup> ), mean (SD)	23.6 (3.5)	23.5 (3.6)	23.5 (3.4)	0.880
Sex, n (%)				<0.001
Men	400 (41.7)	396 (42.5)	504 (53.6)	
Women	560 (58.3)	535 (57.5)	437 (46.4)	
Income, n (%)				<0.001
Low	531 (55.5)	229 (24.8)	152 (16.4)	
Medium	234 (24.5)	264 (28.5)	406 (43.8)	
High	191 (20.0)	432 (46.7)	368 (39.7)	
Education, n (%)				<0.001
Low	451 (47.0)	417 (44.8)	482 (51.2)	
Medium	357 (37.2)	327 (35.2)	344 (36.6)	
High	152 (15.8)	186 (20.0)	115 (12.2)	
Region, n (%)				<0.001
South	183 (19.1)	608 (65.3)	701 (74.5)	
North	777 (80.9)	323 (34.7)	240 (25.5)	
Manual, n (%)	519 (54.2)	373 (40.1)	612 (65.0)	<0.001
Hypertension, n (%)	243 (25.3)	303 (32.6)	279 (29.6)	0.002
Diabetes, n (%)	42 (4.4)	39 (4.2)	21 (2.2)	0.022
Anemia, n (%)	165 (17.3)	278 (30.1)	274 (29.3)	<0.001
Urban, n (%)				<0.001
Urban	351 (36.6)	276 (29.6)	81 (8.6)	
Rural	609 (63.4)	655 (70.4)	860 (91.4)	
Smoking, n (%)	241 (25.3)	218 (23.9)	296 (32.1)	<0.001
Alcohol drinking, n (%)	239 (24.9)	208 (22.4)	247 (26.3)	0.14
Energy intake (kcal/d), mean (SD)	2246 (730.4)	2179 (630.1)	2628 (606.8)	<0.001
Fat intake (g/d), mean (SD)	74.7 (37.2)	80.9 (35.3)	86.8 (37.8)	<0.001
Protein intake (g/d), mean (SD)	68.8 (23.3)	70.0 (22.6)	79.0 (24.0)	<0.001
Carbohydrate intake (g/d), mean (SD)	315 (118.5)	285 (96.7)	372 (84.1)	<0.001

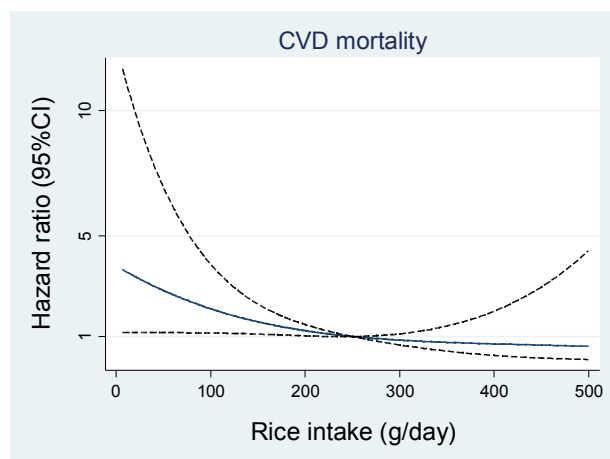
**Table 2.** HRs (95% CI) of mortality from all-cause, CVD and cancer according to tertiles of rice consumption (n=2832)

	Q1	Q2	Q3	p for trend
Participants at risk (n)	960	931	941	
Person-years	9405	9072	9265	
All-cause mortality				
Cases	66	67	51	
Model 1, HR (95% CI) <sup>†</sup>	1.00 (reference)	0.96 (0.66-1.39)	0.83 (0.56-1.22)	0.367
Model 2, HR (95% CI) <sup>‡</sup>	1.00 (reference)	0.99 (0.65-1.51)	0.96 (0.59-1.55)	0.862
Model 3, HR (95% CI) <sup>§</sup>	1.00 (reference)	1.08 (0.64-1.82)	1.15 (0.64-2.07)	0.632
CVD mortality				
Cases	33	23	14	
Model 1, HR (95% CI) <sup>†</sup>	1.00 (reference)	0.61 (0.34-1.09)	0.48 (0.23-0.98)	0.032
Model 2, HR (95% CI) <sup>‡</sup>	1.00 (reference)	0.47 (0.25-0.87)	0.49 (0.21-1.13)	0.049
Model 3, HR (95% CI) <sup>§</sup>	1.00 (reference)	0.55 (0.25-1.21)	0.30 (0.11-0.81)	0.015
Cancer mortality				
Cases	20	20	23	
Model 1, HR (95% CI) <sup>†</sup>	1.00 (reference)	0.98 (0.51-1.89)	1.08 (0.58-2.00)	0.815
Model 2, HR (95% CI) <sup>‡</sup>	1.00 (reference)	1.32 (0.58-3.02)	1.36 (0.57-3.25)	0.484
Model 3, HR (95% CI) <sup>§</sup>	1.00 (reference)	1.18 (0.44-3.16)	2.16 (0.74-6.25)	0.158

<sup>†</sup>Model 1 adjusted for age, gender, intake of energy and fat.

<sup>‡</sup>Model 2 further adjusted for smoking (0, 1-19, ≥20 cigarettes/day), alcohol drinking (no, 1-2 times/wk, 3-4 times/wk, daily), active commuting (no, 1-29 minutes/day, ≥30 minutes/day), leisure time physical activity (no, 1-29 minutes/day, ≥30 minutes/day), sedentary activity (<1 hrs/day, 1-1.9 hrs/day, 2-2.9 hrs/day, ≥3 hrs/day), education (low, medium, high), occupation (manual/non-manual), overweight, selected food intake (fruit, vegetable, and total meat), total energy and fat intake, anemia, diabetes, and hypertension.

<sup>§</sup>Model 3, further excluded those who died within three years.



**Figure 2.** Rice intake and CVD mortality. Multivariable analysis adjusted for variables cited in model 2 of Table 2. Those with rice intakes of 0 ( $n=147$ ) or  $\geq 500$  g/d ( $n=149$ ) were excluded. Solid line represents HR and dash line represents 95% CI.

mortality (in total more than 70%). There was a significant geographic difference in rice intake with the south having much higher consumption than the north. Overall, rice intake in our study was higher than western countries and Japan.

The inverse association between rice intake and CVD mortality in our study is consistent with findings from the JACC study, though inconsistent with those from the JPHC study. In the JACC study, an inverse association between rice intake and CVD mortality was found in men but not women.<sup>7,8</sup> Comparing extreme quintiles of rice intake, the HR for CVD mortality in Japanese men was 0.82 (95% CI 0.70-0.97).<sup>7</sup> However, in our study, we found a significant reduced risk of CVD mortality in women with high rice intake. Although there was no significant interaction between gender and rice intake, the inverse association between rice intake and CVD mortality appeared stronger in women than men. As the prevalence of smoking is much higher in Chinese men than women (52.9% in men vs 2.4% in women),<sup>18</sup> the association between rice intake and CVD mortality could be confounded by smoking. Although we adjusted in the analysis for smoking, residual confounding might possibly exist. We did not have information on the long term smoking history (i.e. pack-years).

We have previously reported that high rice consumption is related to less weight gain and a lower risk of hypertension despite a positive association with diabetes.<sup>19</sup> Overall rice intake has been shown not to be associated with the risk of metabolic syndrome.<sup>5</sup> Although rice has a high glycemic index, it has a low level of cholesterol and sodium.<sup>5</sup> A rice diet has previously been used to treat hypertension.<sup>6</sup> In USA, findings from a pooled analysis of 3 cohorts suggested that rice intake was not associated with the risk of incident CVD.<sup>20</sup> It could be due to these mixed beneficial and adverse aspects of rice that we did not see any association between rice intake and all-cause mortality. It is well known that both diabetes and hypertension are positively related to CVD mortality. In our study sample, impaired fasting glucose and diabetes were related to an increased risk of all-cause mortality and

CVD mortality.<sup>21</sup> As the prevalence of hypertension is much higher than diabetes in the Chinese population,<sup>22,23</sup> if rice intake is beneficial for hypertension, it may partly explain the inverse association between rice and CVD mortality.

Although statistically not significant, there was a trend of positive association between rice intake and cancer mortality in the sample. This finding is supported by existing observational studies. In Japan, rice intake was positively associated with stomach cancer mortality: comparing extreme tertiles of rice intake, the HR for stomach cancer mortality was 1.81 (95% CI 1.06-3.08).<sup>9</sup> According to data from the Chinese National Program of Cancer Registry, the incidence of stomach cancer was the highest among all the cancers and the mortality of stomach cancer ranked second among all cancer mortality in 2009 in rural China.<sup>24</sup> Whether there is a causal relationship and what may be the mechanisms underlying the association, warrant further investigations. Other factors including diabetes,<sup>25</sup> and environmental pollution (e.g. irrigation water used in growing rice) in regions where rice is grown should also be explored given the known link with cancer. The level of arsenic in rice is of increasing concern especially in Asia. In China, the majority of arsenic in rice is inorganic and toxic.<sup>26</sup> A study in the same province showed that 6.7% of the adults had a dietary intake of arsenic exceeding the proposed reference limit.<sup>27</sup> The urine arsenic level in East China is 14.14  $\mu\text{g/L}$ ,<sup>28</sup> which is much higher than in USA (8.09  $\mu\text{g/L}$ ).<sup>29</sup> A study from USA found that when water arsenic is low, 93% of total arsenic exposure is from diet.<sup>29</sup> A study from a neighbouring province found that rice arsenic levels different by regions substantially (as high as five times).<sup>30</sup>

Several limitations in our study should be acknowledged. Firstly, although we had a 5-year follow-up, due to the high attrition rate, we were not able to incorporate the food intake data at follow up. Secondly, due to the small number of deaths, we could not further analyse mortality due to specific CVD outcomes or cancer. Further research with larger sample sizes is needed. Thirdly, as participants with a low rice intake are usually poor, access to health services may be limited. This may confound the association between rice intake and CVD mortality. It may also partly explain the difference between our study and the Japanese studies, where no difference in rice intake was found among different SES groups. However, in the sensitivity analysis, after excluding those with extreme rice intake, the inverse association between CVD mortality remained.

The strength of the study is the use of 3-day WFR to measure rice intake as well as its detailed information on a variety of confounding factors including biomedically measured chronic diseases. As rice is a staple food, seasonal variations of rice intake may be smaller than other food items like vegetables and fruit. WFR-measured rice intake may provide a more robust estimate than the commonly used food frequency questionnaire (FFQ) method. Further, the study included both urban and rural participants and its results can be generalized in the study population in the province. However, whether the findings can be generalized in the whole Chinese population remains to be further studied.

In conclusion, rice intake was not associated with all-cause mortality. An inverse association between rice intake and CVD mortality was found in women but not in men.

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#### AUTHOR DISCLOSURES

No competing interests are reported.

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