BIOMEDICAL AND ENVIRONMENTAL SCIENCES 15, 245-252 (2002)

Effect of Body Mass Index on All-cause Mortality and Incidence of Cardiovascular Diseases — Report for Meta-Analysis of Prospective Studies on Optimal Cut-off Points of Body Mass Index in Chinese Adults[1]

ZHOU BEI-FAN

Cooperative Meta-Analysis Group of the Working Group on Obesity in China[*]

Objective To verify the optimal cut-off points for overweight and obesity in Chinese adults based on the relationship of baseline body mass index (BMI) to all-cause mortality, and incidence of cardiovascular diseases from pooled data of Chinese cohorts. **Methods** The prospective study data of existing cohort studies in China were collected, and the age-adjusted all-cause mortality stratified by BMI were estimated. The similar analysis was repeated after excluding deaths within the first three years of follow-up and after excluding smokers. The incidence of age-adjusted coronary heart disease (CHD) and stroke stratified by BMI were also analyzed. Multiple Cox regression coefficients of BMI for the incidence of CHD and stroke after controlling other risk factors were pooled utilizing the methods of weighting by inverse of variance to reveal whether BMI had independent effect and its strength on the incidence of CHD and stroke. **Results** The data of 4 cohorts including 76 227 persons, with 745 346 person-years of follow-up were collected and analyzed. The age-adjusted all-cause mortality stratified by BMI showed a U-shaped curve, even after excluding deaths within the first three years of follow-up and excluding smokers. Age-adjusted all-cause mortality increased when BMI was lower than 18.5 and higher than 28. The incidence of CHD and stroke, especially ishemic stroke increased with increasing BMI, this was consistent with parallel increasing of risk factors. Cox regression analysis showed that BMI was an independent risk factor for both CHD and stroke. Each amount of 2 kg/m^2 increase in baseline BMI might cause 15.4%, 6.1% and 18.8 % increase in relative risk of CHD, total stroke and ischemic stroke. Reduction of BMI to under 24 might prevent the incidence of CHD by 11% and that of stroke by 15 % for men, and 22 % of both diseases for women. **Conclusion** BMI ≤ 18.5, 24-27.9 and ≥28 (kg/m^2) is the appropriate cut-off points for underweight, overweight and obesity in Chinese adults.

Key works: Body mass index (BMI); All-cause mortality; Coronary heart disease; Stroke

INTRODUCTION

The first international recommendation for cut-off point of normal body weight was based on the range of lower all-cause mortality as an indicator, and the data used to derive this criterion were from studies in Western Caucasian. Hereafter, scientists recommended to take the incidence of related diseases or relevant risk factors as useful indicators to define the cut-off point of overweight and obesity for preventing the related chronic diseases at earlier stage[1]. The Working Group on Obesity in China had recommended the cut-off points

[1] Biographical note of the author: Professor on epidemiology of cardiovascular diseases, female, working in Institute of Cardiovascular Diseases, Chinese Academy of Medical Sciences.

[*] This project is supported by China Roche Pharmaceuticals.

0895-3988/2002
CN 11-2816

for overweight and obesity in Chinese adults based on meta-analysis of cross-sectional data[2]. The objective of meta-analysis on prospective data is to explore the quantitative relation between BMI and all-cause mortality as well as incidence of cardiovascular diseases in Chinese adult to verify the above recommendations on overweight and obesity.

PARTICIPANTS AND METHODS

Criteria for Eligible Cohorts

1. Baseline data: at least included variables of age, gender and BMI.
2. End points of follow-up: at least included all cause of death.
3. Average time of follow-up: $\geqslant$ 4 years.
4. With fairly good measures for quality control

End Points of Follow-up

The classification of deaths was in accordance with the ICD.9

Death—death of all-cause, death of cardiovascular disease (including CHD and stroke only), CHD death, stroke death (haemorrhagic, ischemic), cancer death.

Incidence—CHD (acute myocardial infarction, coronary sudden death, other CHD death). Stroke (ischemic, haemorrhagic—excluding transient ischemic attack and cerebral bleeding caused by cancer or wound, etc.).

Methods of Data Collection and Statistics

1. Baseline gender and age groups—stratification of samples by gender- and ten-years age group, from 30, 40, 50, 60 to 70 years and over (overall, 5 age-specific groups in men and 5 age-specific groups in women).
2. Means and standard deviations of BMI and other risk factors by specific gender-age group of baseline study cohorts were summed by weighted average method.
3. The number of person-years of follow-up and number of deaths or incident cases by strata of BMI of gender-age specific groups in each cohort were summed directly, the mortality or incidence per 100 000 person-years were estimated. Age-adjusted mortality or incidence of age combined groups for men and women stratified by BMI were calculated based on the standard composition of age-gender combined groups of total cohort.
4. In order to minimize the confounding effects of existed potential diseases or smoking led to decrease of body weight and increase in mortality, repeated analysis for mortality by strata of BMI after excluding deaths within the first 3 years of follow-up and excluding smokers were done to compare the age-adjusted mortality curves.
5. Set BMI of 24 as cut-off points, calculating the population attributable risk percent [PAR (%)] for incidence of CHD and stroke according to the following equation:

$$\text{PAR}(\%) = \frac{(\text{Age-adjusted incidence of total cohort} \ \ \text{Age-adjusted incidence of cohort below a certain cut-off point}) \times 100}{\text{Age-adjusted incidence of total cohort}}$$

6. Taking the incidence of CHD or stroke as dependent variable, and age, gender, BMI, diastolic blood pressure, serum total cholesterol and smoking as the independent variables, the Cox regression coefficients and standard errors for each independent variable were estimated for cohort with complete data separately. The sum of regression

coefficients were calculated utilizing the method of weighting by inverse of variance, the relative risks and its 95% CI of BMI was estimated to reveal whether BMI had independent effect on the incidence of cardiovascular diseases.

RESULTS

A total of 4 cohorts accord with the eligible criteria for BMI and all-cause mortality data, 3 of them had incidence data, and 2 cohorts possessed of complete data on end points and baseline risk factors. A total of 76 227 persons (39 905 men and 36 322 women) aged 30 to 70 years and over entered into the analysis. The means and standard deviations of BMI, and means or percentages of related risk factors of pooled cohort are shown in Tables 1 and 2.

TABLE 1

Mean and Standard Deviation of Body Mass Index at Baseline of Pooled Cohort

	Number of Persons	Height (cm)		Body Weight (kg)		BMI (kg/m²)	
		Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Men							
30-	9 004	168.1	5.7	62.7	8.9	21.9	2.5
40-	14 611	167.7	5.8	62.9	9.4	22.4	3.0
50-	12 529	166.8	6.0	63.5	9.6	22.7	3.0
60-	2 933	167.9	6.0	64.9	10.0	23.1	3.0
70-	778	166.4	6.6	60.8	10.0	21.5	3.0
Total	39 905	167.5	5.9	63.2	9.4	22.4	2.9
Women							
30-	8 949	157.3	5.4	54.7	8.4	21.9	2.8
40-	14 496	156.3	5.4	55.7	9.0	22.9	3.0
50-	9 920	155.3	5.8	55.1	9.6	22.5	3.6
60-	2 225	155.4	6.0	54.9	10.3	22.6	4.0
70-	732	153.0	6.0	51.0	10.0	22.0	4.0
Total	36 322	156.2	5.5	55.2	9.1	22.5	3.2

TABLE 2

Mean or Percentage of Risk Factors of Cardiovascular Diseases for Pooled Cohort[a]

	30-	40-	50-	60-	70-	Total
Average Age (years)	37	45	54	63	75	47
Percentage of Women (%)	50	50	44	43	48	48
Percentage of Smokers (%)	36	39	40	34	28	38
Mean of SBP (mm Hg)	114	119	127	134	141	122
Mean of DBP (mm Hg)	75	77	81	82	82	78
Mean of TC (mg/dL)	190	191	200	211	185	194

[a]Abbreviations: SBP: systolic blood pressure, DBP: diastolic blood pressure, TC: (serum) total cholesterol.

The average time of follow-up for different cohorts varied from 3.5 to 15.2 years, if taking death as the end point, the total follow-up was 745 346 person-years, and there were 5 411 cases of deaths. If taking the incidence of cardiovascular diseases as end points, the total follow-up was 665 940 person-years, and 445 cases of CHD and 1 564 cases of stroke, (612 haemorrhagic and 912 ischemic strokes) emerged during the period of follow-up.

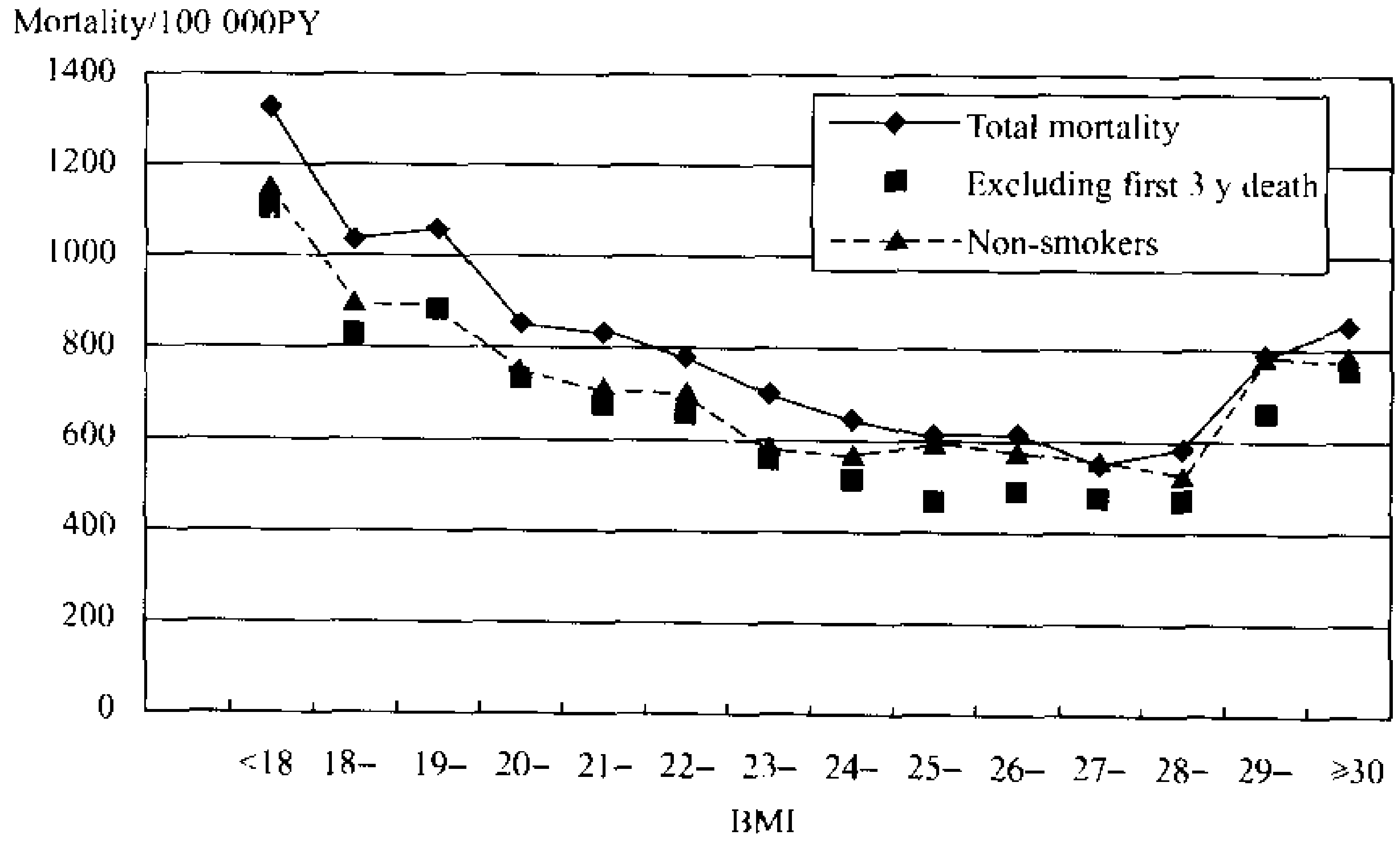

FIG. 1. Age-adjusted all-cause mortality / 100 000 person-years stratified by BMI (men).

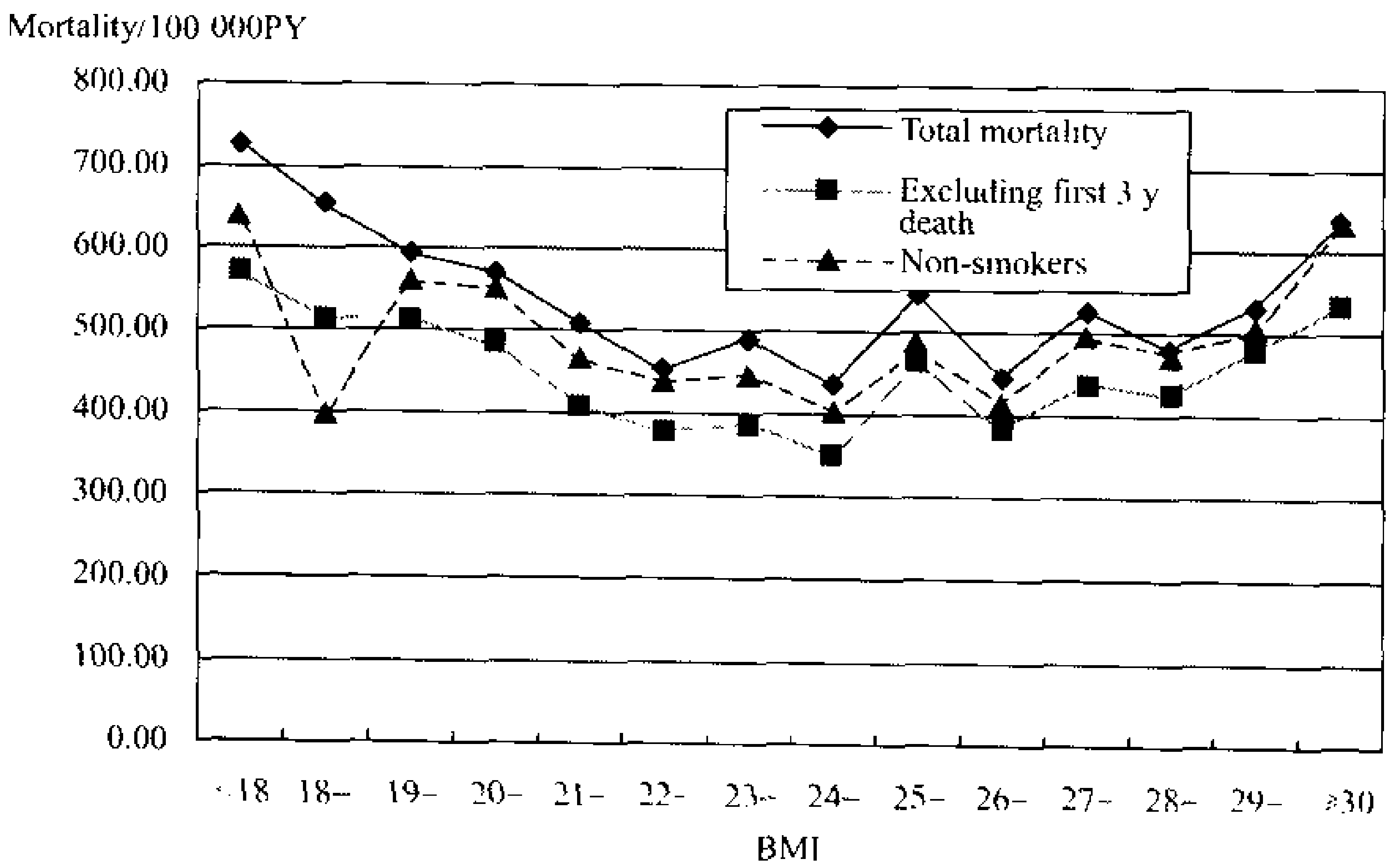

FIG 2. Age-adjusted all-cause mortality / 100 000 person-years stratified by BMI (women).

The curves of age-adjusted all-cause mortality stratified by BMI of men and women and after excluding the deaths within the first 3 years of follow-up and after excluding smokers, are shown in Fig. 1 and Fig. 2. The figures showed U-shaped curves of age-adjusted all-cause mortality stratified by gender-specific BMI, the maximun mortality for men was at BMI < 18, with a significant increasing point below BMI 18.5, and became flattened at BMI 24 or 25, then increased again at BMI 28 and above. The maximum mortality for women was at BMI < 18 also, then decreased gradually at BMI 24, and increased significantly again at BMI of 28 and above. Results illustrated that the U-shaped curves of relationship between all-cause mortality and BMI in Chinese adults was not caused by the confounding effects of potential diseases or smoking.

The incidence of age-adjusted CHD, strokes and ischemic stroke stratified by BMI increased with increasing levels of BMI. Results of Cox regression analysis indicated that after controlling of age, gender, blood pressure, serum total cholesterol and smoking, BMI associated with CHD, strokes and ischemic stroke independently, each amount of increase by 2 kg/m^2 of BMI, the relative risks of CHD, strokes and ischemic stroke increased by 15.4%, 6.1% and 18.8% respectively (Table 3). The population attributable risk percent for CHD and strokes at BMI ⩾ 24 are shown in Table 4.

TABLE 3

Results of Multifactor Cox Regression Analysis of BMI for Incidence of CHD and Stroke

End of Observation	BMI (kg/m^2)			
	Regression Coefficient, β	Standard Error, SE	RR/2 kg/m^2	95% CI
CHD (445)	0.0715	0.0165	1.154	1.081-1.231
Stroke (1564)	0.0297	0.0096	1.061	1.022-1.102
Haemorrhagic (612)	-0.0377	0.0163	0.927	0.870-0.988
Ischemic (912)	0.0864	0.0121	1.188	1.094-1.292

TABLE 4

Population Attributable Risk Percent (PAR, %) of BMI⩾24 for Incidence of CHD and Stroke

	Men BMI⩾24	Women BMI⩾24
CHD	11.0	22.3
Stroke	6.6	12.6
Haemorrhagic	-0.03	1.9
Ischemic	15.1	21.5

DISCUSSION

In early period, all-cause mortality was the basis for appropriate range of normal BMI, most of the studies indicated that BMI and all-cause mortality showed a U-shaped or J-shaped relationship, i.e. the all-cause mortality was increased at extremely low or high level of BMI. However, some scientists considered that very low body weight and high mortality were confounded by potential diseases during baseline and smokers, for instance, the follow-up study of American nurses[3] showed that after exclusion of the deaths within the first 4 years of follow-up and smokers, the J-shaped curve disappeared and a linear relationship between all-cause mortality and BMI appeared. However, many articles illustrated that after excluding possible confounding factors, the all-cause mortality and BMI remained a J-shaped relationship, such as the study of 5 cohorts in Italy[4], a twelve-year prospective study in Korea[5], the seven countries follow-up study[6], mortality and optimal

BMI study in the US (NHANESI follow-up study) [7], and the prospective evaluation of the middle-aged men cohort in Shanghai[8], etc. This meta-analysis collected the study data of 4 cohorts in China, the results illustrated that after excluding the deaths within the first 3 years of follow-up and smokers, a U-shaped relationship between BMI and all-cause mortality still existed. These results pointed out that while pay attention to prevention and treatment of obesity in Chinese population, one must concern about the health risk caused by very low level of BMI. Very low BMI and high mortality in Chinese population were not caused by confounding factors, but conformed to the profile in cause of death of Chinese population, though cardiovascular diseases have become the leading cause of death in China, however, the death among cardiovascular diseases were as follows: CHD about 15%, hypertansion 4%, strokes 41% (in which, about 30-40% was haemorrhagic stroke), pulmonary heart disease 25%, and other cardiovascular diseases 15%. This meta-analysis illustrated that the incidence of CHD, ischemic stroke increased with increasing BMI, however, haemorrhagic stroke showed a negative correlation with BMI. Pulmonary heart disease and other cardiovascular diseases such as rheumatic heart disease, etc. were possibly correlated with low level of BMI and worse status of health. This meta-analysis also demonstrated that cancer deaths was associated negatively with BMI, even after excluding deaths within the first 3 years of follow-up and excluding smokers (data not shown). These might explain the cause of high mortality occurred a very low level of BMI . Analysis of BMI and all-cause mortality indicated that all-cause mortality increased at BMI < 18.5 and ≥28 (kg/m^2).

Multiple Cox regression analysis indicated that the increase of BMI was an independent risk factor for the incidence of CHD, total strokes and ischemic stroke, this was consistent with the increasing of risk factors with increasing level of BMI illustrated by the cross-sectional analysis. For each increment of 2 kg/m^2 of BMI, the relative risks of CHD, total stroke and ischemic stroke were increased by 15.4%, 6.1% and 18.8% respectively. Persons with BMI ≥24 account for 29% of the cohorts , population attributable risk percent showed that reduction of BMI to below 24 might prevent the incidence of CHD and ischemic stroke by 11% and 15% respectively in men, and prevent 22% of the incidence of both diseases in women.

CONCLUSION

The meta-analysis of prospective cohort data further verified the results of cross-sectional analysis[3], indicating that the recommendation on cut-off points of BMI for overweight (24-27.9) and obesity (≥28) in Chinese adults by the Working Group on Obesity in China is scientifically acceptable and feasible in practice.

APPENDIX

Organization of the project:

Working Group on Obesity in China, International Life Science Institute, Focal point in China

Institutions responsible for data analysis:

Department of Epidemiology, Fu Wai Hospital ZHOU Bei-Fan, WU Yang-Feng, ZHAO

Lian-Cheng, LI Xian, WANG Xin

Institutions and personnel responsible for data contribution:

Department of Epidemiology, Fu Wai Hospital WU Yang-Feng
Department of Epidemiology, An Zhen Hospital WU Zhao-Su
Department of Epidemiology, Neurosurgery Institute of Beijing Municipality LI Shi-Zhuo
Department of Epidemiology, Institute of Elderly Diseases, 301 Hospital HE Yao

Collaborative institutions and persons in charge:

Department of Epidemiology, Guangdong Cardiovascular Diseases Institute LI Yi-He, LIU Xiao-Qing
General Hospital of Capital Iron and Steel Co. YU Xue-Hai
Shi-Jing-Shan Chronic Diseases Prevention and Treatment Institute, Beijing Municipality TIAN Xiu-Zhen
Second Affiliated Hospital of Zhejiang University LIU Li-Min, XIA Shun-Ying
People's Hospital of Jiangsu Province WANG Hai-Yan, QIAN Wei-Chong
Affiliated Hospital of Guangxi Medical University ZHU Li-Guang
People's Hospital of Yu-xian County, Shanxi Province YANG Rui-Xiang, GUO Dong-Shuang
Hanzhong Cardiovascular Diseases Institute, Shaanxi Province FU Xi-Han, YANG Jun
Cardiovascular Diseases Institute of Putuo District, Zhou Shan City, Zhejiang Province RUAN Lian-Sheng
Sanitation and Anti-epidemic Station of Jintan City, Jiangsu Province ZHANG Wen-Sheng, GUO Jian-Tao
Qian-an Worker's Hospital of Capital Iron and Steel Co. ZHANG Yu-Zhuo, YIN Qi-Yun
Neurosurgery Institute of Beijing Municipality CHEN Xue-Ming
Tianjin Medical University YANG Lu-Chun, WANG Jing-Hua
Hospital of Inner Mongolia Autonomous Region ZHOU Jing-Chun
Shengyang Red Cross Hospital GUO Bao-Xia
Office of Cardiovascular Diseases Prevention and Treatment, Anshan Iron and Steel Co. WANG A-Ling
Dalian Medical University LI Dong-Guang
China Medical University ZHENG Ding-Yin
Harbin Medical University HE Hou-Qi
Daqing First Affiliated Hospital of Heilongjiang Province HU Ying-Hua
Cardiovascular Diseases Insititute of Shanghai PAN Xin-Wei
Second Military Medical University WANG Gui-Qing
Office of Cardiovascular Diseases Prevention and Treatment, Zhejiang Province WANG Bing-Huan
College of Medicine, Henan University SU Fang-Zhong
Guangzhou Medical University LU Xue-Fen
Huaxi Medical University LUO Zu-Ming
Ningxia Medical University DAI Xiu-Ying
Bethune Medical University WU Ying-Quan, RAO Ming-Li
Hunan Medical University YANG Qi-Dong, LIU Yun-Hai

Huashan Hospital, Medical Univesity of Shanghai HONG Zhen

REFERENCES

1. Committee report (1994). Report of the American Institute of Nutrition Steering Committee on Healthy Weight. *J. Nutri.* **124**, 2240-2243.
2. Zhou, B.F., (Cooperative Meta-Analysis Group of the Working Group on Obesity in China) (2002). Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults-Study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomedical and Environmental Sciences* **15**, 85-95.
3. Manson, J.E., Willet, W.C., Stampfer, M.J., Colditz, G.A., Hunter, D.J., Hankinson, S.E., Hennekens, C.H., and Speizer, F.E. (1995). Body weight and mortality among women. *N. Engl. J. Med.* **383**(11), 677-665.
4. Menotti, A, Deacovich, G.C., Lanti, M., Spagnolo, A., Dormi, A., and Seccareccia, F. (1993). Index of obesity and all-cause mortality in Italian. *Epidemiological Date Prev. Med.* **22**, 293-303.
5. Song, Y.M. and Sung, J. (2001). Body mass index and mortality a twelve-year prospectives study in Korea. *Epidemiology* **12**(2), 173-179.
6. Visscher, T.L.S., Seidell, J.C., Menotti, A., Blackburn, H., Nissinen, A., Feskens, E.J.M., and Kromhout, D. (2000). Underweight and overweight in relation to mortality among men and women aged 40-59 and 50-69 years, The seven countries study. *Am. J. Epidemiol.* **151**, 660-666.
7. Duraza-Arvizu, R.A, Mc Gee, D.L., Cooper, R.S., Liao, Y., and Luke, A. (1998). Mortality and optimal body mass in a sample of the US population. *Am. J. Epidemiol.* **147**(8), 739-749.
8. Yuan, J.M., Ross, R.K., Gao, Y.T., and Yu, M.C. (1998). Body weight and mortality: a prospective evaluation in a cohort of middle-aged men in Shanghai. *China Internat. J. Epidemial.* **27**, 824-832. (In Chinese)

(*Received January* 10, 2002 *Accepted July* 26, 2002)