BMJ Open

Inverse association between body mass index and all-cause mortality in rural chinese adults: 15-year follow-up of the Anqing cohort study

Jie Yang,[1] Nannan Cheng,[1] Yue Zhang,[1] Lijing Ye,[1] Jingyi Li,[1] Ziyi Zhou,[2] Zhuo Wang,[2] Lishun Liu,[2] Xiao Huang ,[3] Xinglong Liang,[4] Tianchi Ling,[5] Yongcheng Xu,[6] Yun Song,[7] Binyan Wang,[7] Genfu Tang,[8] Xianhui Qin ,[9] Pierre Zalloua,[10] Huisheng Zhang,[11] Fangrong Yan ,[12] Xiping Xu[7]

To cite: Yang J, Cheng N, Zhang Y, *et al*. Inverse association between body mass index and all-cause mortality in rural chinese adults: 15-year follow-up of the Anqing cohort study. *BMJ Open* 2021;**11**:e045495. doi:10.1136/bmjopen-2020-045495

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-045495).

Received 02 October 2020
Accepted 05 July 2021

For numbered affiliations see end of article.

Correspondence to
Dr Fangrong Yan;
f.r.yan@outlook.com

ABSTRACT

Objective To investigate the association between body mass index (BMI) and all-cause mortality in a Chinese rural population.

Design Prospective cohort study.

Setting This study was conducted from 2003 to 2018 in Anqing, Anhui Province, China.

Participants 17 851 participants aged 25–64 years (49.4% female) attending physical examinations and questionnaire were included in this study. The inclusion criterion was families having a minimum of three participating siblings. The exclusion criteria included participants without family number and BMI data at baseline.

Outcome measures The outcome measure was all-cause mortality. Generalized estimating equation (GEE) regression analysis was performed to determine the association between baseline BMI and all-cause mortality.

Results During a mean follow-up period of 14.1 years, 730 deaths (8.0%) occurred among men, and 321 deaths (3.6%) occurred among women. The mean BMI for males was 21.3±2.5 kg/m^2, and for female it was 22.1±3.1 kg/m^2. Baseline BMI was significantly inversely associated with all-cause mortality risk for per SD increase (OR, 0.79 (95% CI, 0.72 to 0.87) for males; OR, 0.88 (95% CI, 0.76 to 1.01) for females). When BMI was stratified with cut points at 20 and 24 kg/m^2, compared with the low BMI group, a significantly lower risk of death was found in the high BMI group (BMI ≥24: OR, 0.57 (95% CI, 0.43 to 0.77) in males; 0.65 (95% CI, 0.46 to 0.93) in females) after adjustment for relevant factors.

Conclusions In this relatively lean rural Chinese population, the risk of all-cause mortality decreased with increasing BMI. The excess risk of all-cause mortality associated with a high BMI was not seen among this rural population.

Strengths and limitations of this study

- The main strength of this study might be that the findings was a prospective, population-based cohort study among Chinese rural population with a large sample size and with 15-year follow-up.
- Generalized estimating equation regression analysis was performed to explore the relationship between body mass index (BMI) and the risk of all-cause mortality among Chinese rural population.
- The association between BMI and all-cause mortality was unclear and comprehensively assessed in this study.
- The time of death was not collected precisely although we conducted four follow-up visits.
- BMI measurements were only obtained on baseline, without being obtained at follow-ups.

INTRODUCTION

Over the past few decades, obesity has become one of the most serious public health problems in the world.[1 2] The association between body mass index (BMI) and all-cause mortality has been widely explored,[3 4] but it remains controversial. Recently, results from a meta-analysis involving 3.6 million people suggested a J-shaped association between BMI and all-cause mortality among British adults.[4] Similarly, studies have shown that overweight and obesity increased the risk of all-cause mortality among white adults.[5] However, in a young metabolically healthy adult cohort in Asia, underweight was associated with increased all-cause mortality, and overweight/obesity was associated with decreased all-cause mortality.[6] Data from another study suggested that the risk of mortality significantly decreased with increasing BMI for Chinese hypertensive adults[7].

Since most of the studies have been conducted in populations of Western origin; however, the dose–response relationship between BMI and the risk of all-cause mortality among Chinese rural population remains unclear. We aimed to examine the

association between BMI and all-cause mortality for rural Chinese, using up to 15 years of longitudinal data from a rural community-dwelling Chinese cohort at baseline.

METHODS

Study design and participants

This study is part of a large community-based cohort initiated in 2003 among residents of Anhui Province, China.[8] All participants aged 25–64 years old were from a family of at least three siblings. The major exclusion criteria included history of type 1 diabetes; renal failure; chronic infections such as tuberculosis or other infectious diseases; malignancies; rickets or other metabolic bone diseases; chronic glucocorticoid use; viral cirrhosis; and thyrotoxicosis. Premenopausal women who were uncertain of their pregnancy status at baseline were also excluded. All participants provided written informed consent and underwent a questionnaire survey at baseline, administered by professionally trained investigators, that included information on demographic data, lifestyle and medical history. As part of the baseline study, weight and height measurements, and blood samples were obtained (as detailed below).

The current analysis was designed to investigate the relationship between BMI and all-cause mortality in this cohort. All-cause mortality included death due to any reason. There were 18 237 participants enrolled in the baseline, after 15-year follow-up, we excluded 386 participants who were missing weight or height data, family member number at baseline and who have not been collected the outcome; finally, a total of 17 851 participants with 1051 deaths (from baseline to 2018) were included for the further analysis.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Assessment of BMI

BMI was calculated as weight in kilograms divided by height in metres squared. Height and weight were measured by trained health technicians following standardised procedures. Height and weight were measured with participants wearing light indoor clothing and no shoes. At the initial study visit, trained research staff measured and recorded height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) for each participant.

Follow-up and outcomes

Follow-up visits including interviews and data collection were conducted in 2010, 2014, 2017 and 2018. The study had a high rate of follow-up, due to the fact that this rural population remained stable and homogeneous with respect to ethnicity, dietary habits, lifestyle and environmental factors. Subjects who participated in the baseline study were resurveyed with a mean follow-up interval of 14.1 years. The data on death incidence were obtained by telephone or through face-to-face interviews with family members, neighbours or village doctors. During the follow-up period, 730 deaths (8.1%) occurred among men, and 321 (3.6%) deaths occurred among women.

Laboratory assays

At baseline, fasting blood samples were collected and stored in aliquots at −80°C. Serum lipids and fasting glucose (GLU) were measured enzymatically with a Cobas Integra Roche analyzer (Roche, Indianapolis, IN)

Statistical analysis

Initially, we categorised baseline BMI into six categories : BMI<18.5, 18.5 to <20, 20 to <22, 22 to <24, 24 to <26 and ≥26 kg/m^2. In addition, for the further analysis, we use the BMI cut-off points of 20 and 24 kg/m^2.

Our analysis was performed on different sexes in order to detect possible sex differences. Baseline characteristics are presented as the mean±SD for continuous variables or percentages for categorical variables according to the categories of BMI (kg/m^2). Comparison of characteristics was performed by χ^2 test for categorical variables or analysis of variance for continuous variables. Generalized estimating equations (GEE) models were used to analyse the association between baseline BMI and all-cause mortality risk. First, we estimated ORs and 95% CIs for every SD of BMI change. Then using the lowest BMI group as the reference, we estimated ORs and 95% CIs for the other BMI ranges, after adjusting for potential confounders, including baseline age, sex, age, blood pressure, smoking status, drinking status, GLU, total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C).

In sensitivity analyses, to limit reverse causality, the outcome which collected in the first follow-up were excluded. GEE models also were used to analyse the association between baseline BMI and all-cause mortality risk.

Further stratified analyses by subgroups including age, smoking and alcohol drinking status, hypertensive status, glucose levels, and lipid levels were also explored by GEE regression models to test for consistency of results. A two-tailed p<0.05 was considered to be statistically significant in all analyses. R software, V.3.6.1 (http://www.R-project.org/), were used for all statistical analyses.

RESULTS

Patient characteristics

Baseline characteristics by BMI groups of all participants are presented in table 1. Of the 17 851 participants, 9033 (50.6%) were male, and 8818 (49.4%) were female. The mean BMI for males was 21.3±2.5 kg/m^2, and for female it was 22.1±3.1 kg/m^2. For males, the percent distributions of the lowest group (BMI <20), middle group (BMI 20 -<24) and highest (BMI≥24 kg/m^2) were 32.0%, 53.6% and 14.3%, respectively; for females, the percentages were 23.0%, 54.2% and 22.8%, respectively. Higher

Table 1 Baseline characteristics of the study participants by BMI

	Male				Female			
Variables	**BMI <20**	**BMI 20 to <24**	**BMI ≥24**	**P value**	**BMI <20**	**BMI 20 to <24**	**BMI ≥24**	**P value**
No. (%)	2894	4843	1296		2030	4781	2007	
Death, n (%)	303 (10.5)	349 (7.2)	78 (6.0)	<0.001	93 (4.6)	162 (3.4)	66 (3.3)	0.035
Age, year*	47.6±8.0	46.7±7.5	46.0±7.6	<0.001	45.2±7.9	44.6±7.3	45.3±7.1	<0.001
SBP, mm Hg*	118.2±17.5	121.7±18.0	129.0±20.2	<0.001	115.5±17.2	120.0±18.6	126.9±20.8	<0.001
DBP, mm Hg*	76.0±11.1	78.5±11.5	84.9±12.5	<0.001	73.3±10.1	76.0±10.9	81.2±11.9	<0.001
BMI, kg/m^2*	18.8±0.9	21.6±1.1	25.9±1.7	<0.001	18.7±1.0	21.9±1.1	26.1±3.4	<0.001
Fasting glucose, mmol/L†	5.3 (4.9, 5.7)	5.3 (5.0, 5.7)	5.4 (5.1, 5.8)	<0.001	5.3 (5.0, 5.8)	5.3 (5.0, 5.7)	5.4 (5.1, 5.8)	<0.001
Total cholesterol, mmol/L†	4.2 (3.7, 4.7)	4.3 (3.8, 4.8)	4.7 (4.1, 5.2)	<0.001	4.2 (3.8, 4.8)	4.3 (3.8, 4.9)	4.6 (4.0, 5.1)	<0.001
Triglycerides, mmol/L†	0.9 (0.7, 1.1)	1.0 (0.7, 1.3)	1.5 (1.0, 2.1)	<0.001	1.0 (0.8, 1.3)	1.1 (0.9, 1.5)	1.4 (1.1, 2.0)	<0.001
HDL cholesterol, mmol/L†	1.4 (1.2, 1.7)	1.4 (1.1, 1.6)	1.2 (1.0, 1.4)	<0.001	1.4 (1.2, 1.6)	1.3 (1.1, 1.6)	1.2 (1.1, 1.4)	<0.001
Smoking status, n (%)				<0.001				0.012
Never	515 (17.9)	1031 (21.4)	372 (28.8)		1932 (95.6)	4615 (96.8)	1944 (97.2)	
Ever	2364 (82.1)	3786 (78.6)	920 (71.2)		89 (4.4)	154 (3.2)	56 (2.8)	
Drinking status, n (%)				<0.001				0.413
Never	1695 (59.0)	2568 (53.3)	702 (54.3)		1978 (97.9)	4640 (97.4)	1946 (97.3)	
Ever	1179 (41.0)	2254 (46.7)	591 (45.7)		43 (2.1)	123 (2.6)	55 (2.7)	
Hypertension, n (%)				<0.001				<0.001
No	2528 (87.4)	3937 (81.3)	841 (64.9)		1826 (90.0)	4074 (85.2)	1428 (71.2)	
Yes	365 (12.6)	904 (18.7)	455 (35.1)		204 (10.0)	707 (14.8)	578 (28.8)	
Diabetes, n (%)				<0.001				<0.001
No	2804 (97.1)	4715 (97.5)	1240 (95.8)		1971 (97.3)	4664 (97.6)	1928 (96.2)	
Yes	83 (2.9)	121 (2.5)	55 (4.2)		54 (2.7)	114 (2.4)	77 (3.8)	

*For continuous variables, values are presented as mean±SD.
†Values are presented as median (IQR).
BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; SBP, systolic blood pressure.

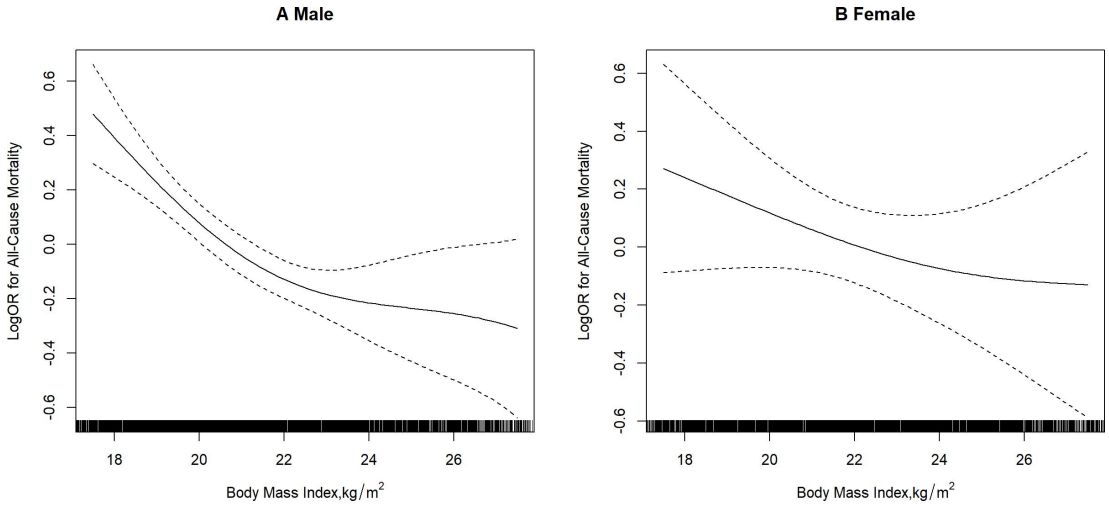

Figure 1 Smooth curves between body mass index and all-cause mortality for male (A) and female (B) adjusted for age, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, smoking status and drinking status.

BMI groups were associated with lower mortality, younger age and higher levels of systolic blood pressure, diastolic blood pressure, TC and TG. Lower BMI groups were associated with higher HDL-C levels and smoking rate for both males and females.

BMI and all-cause mortality

As shown in figure 1, as BMI increases, the smoothing curves show a decrease in all-cause mortality risks after adjustment for both males and females. Consistently, in the GEE regression models, for every SD (2.5 kg/m^2) increase in BMI, the risk of mortality decreased by 21% (OR, 0.79; 95% CI, 0.72 to 0.87; p<0.001) after adjusting for potential confounders for males. And for females, for every SD (3.1 kg/m^2) increase in BMI, the risk of mortality decreased by 12% (OR, 0.88; 95% CI, 0.76 to 1.01; p=0.079) (table 2).

Initially, we divided BMI into six groups:<18.5, 18.5 to <20, 20 to <22, 22 to <24, 24 to <26, and ≥26 kg/m^2. Among males, compared with the lowest BMI group (BMI <18.5), from the second group to the last group, the risk of death decreased by 7% (OR, 0.93; 95% CI, 0.71 to 1.21; p=0.568), 31% (OR, 0.69; 95% CI, 0.53 to 0.89; p=0.004), 33% (OR, 0.67; 95% CI, 0.50 to 0.91; p=0.009), 45% (OR, 0.55; 95% CI, 0.37 to 0.80; p=0.002) and 47% (OR, 0.53; 95% CI, 0.33 to 0.86; p=0.009), respectively. For females, the ORs were 1.26 (95% CI, 0.80 to 1.99; p=0.328), 0.82 (95% CI, 0.53 to 1.27; p=0.385), 0.96 (95% CI, 0.61 to 1.52; p=0.872), 0.78 (95% CI, 0.47 to 1.30; p=0.343) and 0.75 (95% CI, 0.42 to 1.34; p=0.344), respectively.

As no significant difference was found for the risk of all-cause mortality when comparing the second BMI group (18.5 to <20 kg/m^2) to the lowest group (<18.5 kg/m^2), we defined the BMI cut-off points of 20 and 24 kg/m^2. For males, with BMI less than 20 kg/m^2 as the reference, among middle BMI group (20-<24 kg/m^2) and highest group (≥24 kg/m^2), the risk of all-cause mortality decreased by 28% (OR, 0.72; 95% CI, 0.61 to 0.85; p<0.001), and 43% (OR, 0.57; 95% CI to 0.43 to 0.77; p<0.001), respectively. The results for females followed the same trend, with a 25% (OR, 0.75; 95% CI, 0.57 to 0.99; p=0.043), and 35% (OR, 0.65; 95% CI, 0.46 to 0.93; p=0.020) decrease, respectively.

Sensitivity analyses

To limit reverse causality, the outcome that collected in the first follow-up(n=329) were excluded. Then, 17 522 participants with 727 deaths (from 2011 to 2018) were included for the further analysis. The result shows in table 3. And we find the result is similar with table 2. For every SD (2.5 kg/m^2) increase in BMI, the risk of mortality decreased by 21% (OR, 0.79; 95% CI, 0.70 to 0.89; p<0.001) after adjusting for potential confounders for males. And for females, for every SD (3.1 kg/m^2) increase in BMI the risk of mortality decreased by 12% (OR, 0.88; 95% CI, 0.75 to 1.02; p=0.110) (table 3).

Stratified analyses on BMI and all-cause mortality

Further stratified analyses were performed with important covariables including age, smoking status, alcohol drinking status, hypertensive status and GLU, TC, TG, and HDL-C levels for males (table 4); age, hypertensive status and GLU, TC, TG, and HDL-C levels for females (table 5).

Among males, none of the following variables, including age, smoking status, drinking status, GLU, TC and HDL-C, significantly modified the association between BMI and all-cause mortality. However, there was a significant interaction between BMI and TG level on mortality. (P for interaction=0.044). For men with higher TG levels, compared with those in the lowest BMI group, for those in the middle group and the highest group, the risk of mortality decreased slightly (ORs: 0.85 (0.65 to 1.11) and 0.55 (0.38 to 0.81), respectively). Otherwise, for those in the lower TG group, the ORs were 0.63 (0.50 to 0.80) and 0.81 (0.49 to 1.33) for the middle and high BMI groups,

Table 2 The association between all-cause mortality and body mass index (BMI)

	N	Case (%)	Crude model OR (95% CI)	P value	Adjusted model* OR (95% CI)	P value
BMI, kg/m^2						
Males						
BMI to per SD	9033	730 (8.1)	0.77 (0.71 to 0.84)	<0.001	0.79 (0.72 to 0.87)	<0.001
<18.5	879	103 (11.7)	Ref		Ref	
18.5 to <20	2015	200 (9.9)	0.83 (0.65 to 1.07)	0.158	0.93 (0.71 to 1.21)	0.568
20 to <22	3066	226 (7.4)	0.60 (0.47 to 0.77)	<0.001	0.69 (0.53 to 0.89)	0.004
22 to <24	1777	123 (6.9)	0.56 (0.43 to 0.74)	<0.001	0.67 (0.50 to 0.91)	0.009
24 to <26	825	51 (6.2)	0.50 (0.35 to 0.70)	<0.001	0.55 (0.37 to 0.80)	0.002
≥26	471	27 (5.7)	0.46 (0.30 to 0.71)	<0.001	0.53 (0.33 to 0.86)	0.009
<20	2894	303 (10.5)	Ref		Ref	
20 to <24	4843	349 (7.2)	0.66 (0.57 to 0.78)	<0.001	0.72 (0.61 to 0.85)	<0.001
≥24	1296	78 (6)	0.55 (0.42 to 0.71)	<0.001	0.57 (0.43 to 0.77)	<0.001
Females						
BMI, per SD	8818	321 (3.6)	0.90 (0.79 to 1.02)	0.123	0.88 (0.76 to 1.01)	0.079
<18.5	719	30 (4.2)	Ref		Ref	
18.5 to <20	1311	63 (4.8)	1.16 (0.74 to 1.81)	0.517	1.26 (0.80 to 1.99)	0.328
20 to <22	2636	85 (3.2)	0.77 (0.50 to 1.17)	0.225	0.82 (0.53 to 1.27)	0.385
22 to <24	2145	77 (3.6)	0.86 (0.56 to 1.32)	0.485	0.96 (0.61 to 1.52)	0.872
24 to <26	1235	40 (3.2)	0.77 (0.47 to 1.25)	0.292	0.78 (0.47 to 1.30)	0.343
≥26	772	26 (3.4)	0.80 (0.47 to 1.37)	0.428	0.75 (0.42 to 1.34)	0.344
<20	2030	93 (4.6)	Ref		Ref	
20 to <24	4781	162 (3.4)	0.73 (0.56 to 0.95)	0.018	0.75 (0.57 to 0.99)	0.043
≥24	2007	66 (3.3)	0.71 (0.51 to 0.98)	0.040	0.65 (0.46 to 0.93)	0.020

*Adjusted for age, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, HDL cholesterol, smoking status and drinking status.

respectively, compared with the low BMI group. Among females, there was no significant interaction between BMI and other variables on all-cause mortality.

DISCUSSION

Our analysis of this rural Chinese population in this cohort showed that BMI was significantly and inversely associated with all-cause mortality. Compared with the lowest BMI group (BMI <20 kg/m^2), the risk of all-cause mortality decreased for those in the middle group (BMI20-<24 kg/m^2) and the highest group (BMI ≥24 kg/m^2) for both males and females.

Most studies conducted in European or American populations have shown a U-shaped or J-shaped association between BMI and all-cause mortality.[3 4 9] Our findings are not consistent with these results. In contrast, a reverse J-shaped relationship has been observed in most studies in Asian populations.[6 7 10] This contradiction may be due to differences in weight distribution and leading causes of death among different populations. A number of researchers have reported that the risk of death from respiratory causes was higher among subjects with a lower BMI,[11] and the risk of death from atherosclerotic cardiovascular disease or cancer was higher among subjects with a higher BMI.[12] In European or American populations, obesity is highly prevalent, and cardiovascular disease is the leading cause of death.[13] Therefore, a U-shaped or J-shaped relationship is more likely to be observed.[3] However, in East Asia, underweight-related morbidities, such as respiratory disease and kidney disease, are the major causes of death.[14 15] Therefore, it is more likely to find an L-shaped or reversed J-shaped relationship between BMI and all-cause mortality in Chinese rural population.[16]

Our study is a large prospective cohort study of a Chinese rural community population. Participants were lean and people with obesity (BMI >28 kg/m^2) were only 2.2%. And the mean BMI was 21.4 kg/m^2 for males, 22.1 kg/m^2 for females, while which was 25 kg/m^2 or more for western origins.[9 17] In our study, the risk of all-cause mortality decreased with increasing BMI in both sexes. Even after adjusting for potential confounders, the results

Table 3 Results of sensitivity analyses for the association between all-cause mortality and body mass index (BMI)†

	N	Case (%)	Crude model OR (95% CI)	P value	Adjusted model* Or (95% CI)	P value
BMI, kg/m^2						
Males						
BMI to per SD	8779	479 (5.5)	0.78 (0.71 to 0.86)	<0.001	0.79 (0.70 to 0.89)	<0.001
<18.5	845	70 (8.3)	Ref		Ref	
18.5 to <20	1940	125 (6.4)	0.76 (0.56 to 1.03)	0.093	0.85 (0.62 to 1.17)	0.330
20 to <22	2987	148 (5.0)	0.58 (0.43 to 0.78)	<0.001	0.65 (0.47 to 0.88)	0.006
22 to <24	1738	85 (4.9)	0.57 (0.41 to 0.79)	<0.001	0.66 (0.47 to 0.95)	0.024
24 to <26	809	35 (4.3)	0.50 (0.33 to 0.76)	0.001	0.52 (0.33 to 0.83)	0.005
≥26	460	16 (3.5)	0.40 (0.23 to 0.70)	0.001	0.45 (0.25 to 0.82)	0.009
<20	2785	195 (7.0)	Ref		Ref	
20 to <24	4725	233 (4.9)	0.69 (0.57 to 0.84)	<0.001	0.73 (0.59 to 0.90)	0.003
≥24	1269	51 (4.0)	0.56 (0.41 to 0.76)	<0.001	0.55 (0.39 to 0.79)	0.001
Females						
BMI, per SD	8743	248 (2.8)	0.88 (0.76 to 1.02)	0.111	0.88 (0.75 to 1.02)	0.110
<18.5	710	21 (3.0)	Ref		Ref	
18.5 to <20	1296	48 (3.7)	1.26 (0.75 to 2.13)	0.387	1.41 (0.82 to 2.40)	0.219
20 to <22	2620	69 (2.6)	0.89 (0.54 to 1.46)	0.646	0.98 (0.58 to 1.63)	0.926
22 to <24	2130	62 (2.9)	0.98 (0.60 to 1.63)	0.950	1.15 (0.68 to 1.94)	0.619
24 to <26	1227	32 (2.6)	0.88 (0.50 to 1.54)	0.657	0.92 (0.51 to 1.66)	0.789
≥26	760	16 (2.1)	0.71 (0.37 to 1.36)	0.307	0.70 (0.35 to 1.40)	0.327
<20	2006	69 (3.4)	Ref		Ref	
20 to <24	4750	131 (2.8)	0.80 (0.59 to 1.07)	0.136	0.83 (0.61 to 1.14)	0.259
≥24	1987	48 (2.4)	0.69 (0.48 to 1.01)	0.059	0.66 (0.44 to 0.99)	0.050

*Adjusted for age, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, HDL cholesterol, smoking status and drinking status.
†Analyses exclude the outcome data which collected in the first follow-up.

were similar. Compared with the lowest BMI group, from the middle group to the highest group, the risk of all-cause mortality decreased by 28% and 43% for males, respectively, and 25% and 35% for females, respectively.

These results can be attributed to multiple factors, including manual labour diet and lifestyle, and more. On the one hand, it is important to recognise that participants in this study come from an under-developed area. Among this population, having a high BMI may represent having a higher socioeconomic status, allowing for better access to healthcare than having a lower BMI. And participants in this study with low BMI at baseline may have had certain ailments that caused weight loss, supporting the theory that those with high baseline BMI may have had better health. Reverse causality is a major problem in observational studies. But in sensitivity analyses, to limit reverse causality, the outcome that collected in the first follow-up were excluded. And we find the result is the similar with table 2. In this relatively lean rural Chinese population, the risk of all-cause mortality decreased with increasing baseline BMI for both males and females after excluded the outcome data, which collected in the first follow-up. On the other hand, It is known that the risk of death for some diseases, such as respiratory diseases, decreases with increasing BMI[11 18] Although many studies reported that the risk of cardiovascular disease increases with increasing BMI. It is also important to recognise that, in general, the Chinese rural population engages in more manual labour than their urban counterparts, and tend to be more physically active, which is a protective factor for death of cardiovascular disease.[19 20] Therefore, with increasing BMI, death from cardiovascular disease may have less impact on this population than urban population. Although some researchers believe that this negative association between BMI and all-cause mortality is caused by confounders, the most discussed point is smoking. Some studies have shown that obesity paradox can only be observed in smokers. And for non-smoking people, this phenomenon cannot be observed.[21 22] But in the stratified analysis of smoking for males, the results did not change substantially. We did not conduct it for females because the number of female smokers is very small. In

Table 4 Risk factors-stratified analyses of body mass index (BMI) on all-cause mortality for males

		BMI<20		BMI 20 to <24		BMI 24		P for interaction
	N	Events (%)	OR (95% CI)	Events (%)	OR (95% CI)	Events (%)	OR (95% CI)	
Age, years								0.320
<45	3640	48 (4.6)	Ref	76 (3.8)	0.84 (0.57 to 1.23)	21 (3.6)	0.71 (0.39 to 1.29)	
45	5393	255 (13.9)	Ref	273 (9.6)	0.67 (0.55 to 0.81)	57 (8.1)	0.50 (0.36 to 0.70)	
Smoking status								0.908
Never	1918	37 (7.2)	Ref	55 (5.3)	0.83 (0.52 to 1.33)	14 (3.8)	0.63 (0.30 to 1.30)	
Ever	7070	264 (11.2)	Ref	292 (7.7)	0.71 (0.59 to 0.85)	63 (6.8)	0.58 (0.42 to 0.80)	
Drinking status								0.464
Never	4965	173 (10.2)	Ref	170 (6.6)	0.66 (0.52 to 0.83)	41 (5.8)	0.57 (0.38 to 0.85)	
Ever	4024	126 (10.7)	Ref	178 (7.9)	0.81 (0.62 to 1.05)	36 (6.1)	0.59 (0.38 to 0.91)	
Fasting glucose, mmol/L								0.144
<5.6	6196	212 (10.5)	Ref	226 (6.7)	0.66 (0.54 to 0.82)	53 (6.4)	0.65 (0.46 to 0.93)	
5.6	2822	89 (10.2)	Ref	123 (8.3)	0.83 (0.61 to 1.14)	25 (5.3)	0.47 (0.28 to 0.80)	
Total cholesterol, mmol/L								0.212
B1 (<4.3)	4482	182 (10.9)	Ref	166 (6.9)	0.63 (0.50 to 0.80)	31 (7.3)	0.59 (0.38 to 0.91)	
B2 (4.3)	4536	119 (9.7)	Ref	183 (7.5)	0.82 (0.64 to 1.07)	47 (5.4)	0.58 (0.39 to 0.87)	
Triglycerides, mmol/L								0.044
B1 (<1.0)	4466	192 (10.8)	Ref	162 (6.6)	0.63 (0.50 to 0.80)	23 (9.1)	0.81 (0.49 to 1.33)	
B2 (1.0)	4552	109 (9.8)	Ref	187 (7.8)	0.85 (0.65 to 1.11)	55 (5.3)	0.55 (0.38 to 0.81)	
HDL-C, µmol/L								0.136
B1 (<1.3)	4441	134 (11.2)	Ref	160 (6.8)	0.62 (0.48 to 0.80)	51 (5.8)	0.53 (0.36 to 0.77)	
B2 (1.3)	4577	167 (9.9)	Ref	189 (7.6)	0.80 (0.64 to 1.01)	27 (6.6)	0.56 (0.35 to 0.90)	
Hypertension								0.448
No	7306	236 (9.3)	Ref	257 (6.5)	0.76 (0.63 to 0.93)	38 (4.5)	0.56 (0.38 to 0.82)	
Yes	1724	67 (18.4)	Ref	92 (10.2)	0.60 (0.41 to 0.87)	40 (8.8)	0.55 (0.34 to 0.89)	

Adjusted, if not stratified, for age, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, hdl cholesterol, smoking status anddrinking status.
HDL-C, high-density lipoprotein cholesterol.

our study, BMI was inversely associated with all-cause mortality risk for both smokers and non-smokers. Also, age is an important confounding factor. Studies also have shown that obesity paradox only exists in older people.[23] We analysed in two age groups, and the results did not change substantially. Whether in young people or older people, the risk of death decreased with increasing BMI.

In this study, stratified analyses were consistent in all important covariables. Our results suggest that male participants with low TG levels may be at increased risk of all-cause mortality. For male, in the high TG group, the relationship between BMI and death is the same as that of the total male population; compared with the low BMI group, the risk of all-cause mortality from the middle group to the high group decreased by 15% and 45%, respectively. However, in the low TG group, the risk of all-cause mortality was higher in the high BMI group than that of the middle BMI group, differing from the trend shown in the total population. TG is a component of lipids, formed by glycerol and three fatty acids. The lipid composition is complex. In addition to TG, it also includes cholesterol, phospholipids, fatty acids and a small number of other lipids. The blood level of TG is regulated by homeostatic mechanisms that balance the rates of secretion from the intestines and liver as well as the rates of catabolism.[24] Usually, TG in the plasma maintain a dynamic balance. There are two primary sources of TG in plasma. The first being exogenous: when fat ingested from food is in the intestine, it is absorbed by the intestinal mucosa under the action of bile acids and lipases, and TG are synthesised in the intestinal epithelial cells. The second is endogenous: TG synthesised in the body are mainly stored in the liver, followed by adipose tissue.[25] Therefore, there may be two reasons for low TG levels. First, low TG levels may be due to malnutrition, and previous studies have shown that malnutrition is a risk factor for death.[26 27] Second, low TG levels may be caused by certain metabolic diseases. Further analyses are needed on similar study populations to confirm this finding.

Our study also has several limitations. First, although we conducted four follow-up visits, we did not collect the time

Table 5 Risk factors-stratified analyses of body mass index on all-cause mortality for females

		BMI<20		BMI 20 to <24		BMI 24		
	N	Events (%)	OR (95% CI)	Events (%)	OR (95% CI)	Events (%)	OR (95% CI)	P for interaction
Age, years								0.924
<45	4552	25 (2.5)	Ref	46 (1.8)	0.63 (0.38 to 1.05)	17 (1.7)	0.51 (0.26 to 1.01)	
45	4266	68 (6.5)	Ref	116 (5.2)	0.76 (0.56 to 1.05)	49 (4.9)	0.66 (0.44 to 1.00)	
Fasting glucose, mmol/L								0.630
<5.6	5834	63 (4.7)	Ref	108 (3.3)	0.68 (0.49 to 0.95)	37 (2.9)	0.53 (0.34 to 0.84)	
5.6	2974	30 (4.4)	Ref	54 (3.5)	0.89 (0.55 to 1.43)	29 (3.9)	0.92 (0.52 to 1.64)	
Total cholesterol, mmol/L								0.183
B1 (<4.4)	4389	43 (3.7)	Ref	66 (2.7)	0.76 (0.50 to 1.15)	28 (3.5)	0.80 (0.47 to 1.38)	
B2 (4.4)	4419	50 (5.8)	Ref	96 (4.1)	0.72 (0.49 to 1.04)	38 (3.2)	0.53 (0.33 to 0.86)	
Triglycerides, mmol/L								0.088
B1 (<1.2)	4366	63 (5.0)	Ref	75 (3.0)	0.64 (0.44 to 0.91)	16 (2.5)	0.50 (0.27 to 0.90)	
B2 (1.2)	4442	30 (3.9)	Ref	87 (3.8)	0.99 (0.63 to 1.55)	50 (3.7)	0.88 (0.53 to 1.46)	
HDL-C, µmol/L								0.177
B1 (<1.3)	4305	37 (4.5)	Ref	67 (2.9)	0.74 (0.48 to 1.15)	43 (3.6)	0.89 (0.54 to 1.49)	
B2 (1.3)	4502	56 (4.7)	Ref	95 (3.8)	0.73 (0.52 to 1.04)	23 (2.8)	0.42 (0.25 to 0.70)	
Hypertension								0.601
No	7328	76 (4.2)	Ref	112 (2.7)	0.72 (0.53 to 0.98)	38 (2.7)	0.70 (0.46 to 1.06)	
Yes	1489	17 (8.3)	Ref	50 (7.1)	0.93 (0.50 to 1.74)	28 (4.8)	0.70 (0.35 to 1.41)	

Adjusted, if not stratified, for age, systolic blood pressure, diastolic blood pressure, fasting glucose, total cholesterol, triglycerides, hdl cholesterol, smoking status anddrinking status.
BMI, body mass index; HDL-C, high-density lipoprotein cholesterol.

of death precisely. Second, no BMI measurements were obtained at follow-up, therefore the association between changes in BMI and risk of death over the 15-year period could not be assessed. Third, we conducted household or telephone interviews at follow-up visits and recall bias could exist. Last, specific cause of death was not available, therefore further explorations on the association between BMI and specific causes of death could not be conducted.

CONCLUSIONS

In conclusion, the risk of death decreased with increasing baseline BMI in this relatively lean rural Chinese population for both males and females. For males, low TG levels may be associated with an increased risk of death. These results indicate optimal BMI ranges for health in different populations may be different and further studies are needed to illustrate the relationships between weight, BMI and health in different populations.

Author affiliations
[1]State Key Laboratory of Natural Medicines, Research Center of Biostatistics and Computational Pharmacy, China Pharmaceutical University, Nanjing, China
[2]Beijing Advanced Innovation Center for Food Nutrition and Human Health, College of Food Science and Nutritional Engineering, China Agricultural University, Beijing, China
[3]Department of Cardiovascular Medicine, Nanchang University Second Affiliated Hospital, Nanchang, China
[4]Health Center of Xigang Center, Tengzhou, China
[5]Hami Central Hospital, Hami, China
[6]Putian College Affiliated Hospital, Putian, China
[7]National Clinical Research Study Center for Kidney Disease, State Key Laboratory for Organ Failure Research, Renal Division, Nanfang Hospital, Southern Medical University, Guangzhou, China
[8]Institute for Biomedicine, Anhui Medical University, Hefei, China
[9]National Clinical Research Study Center for Kidney Disease; the State Key Laboratory for Organ Failure Research; Renal Division, Nanfang Hospital, Southern Medical University Nanfang Hospital, Guangzhou, China
[10]School of Medicine, Lebanese American University, Beirut, Lebanon
[11]Guangdong Key Laboratory for Biomedical Measurements and Ultrasound Imaging, School of Biomedical Engineering, Health Science Center, Shenzhen University, Shenzhen, China
[12]China Pharmaceutical University, Nanjing, China

Acknowledgements We thank the investigators and participants of the osteoporosis cohort study, the parent study, who made this report possible. XX, the PI of the osteoporosis cohort study, has full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Contributors XX, XQ and BW designed the study. ZZ, ZW, LL, XL, TL, YX and YS contributed significantly to analysis. JY, NC, YZ, LY and JL performed the data analyses and writing of the article. GT, LL and XH helped perform the collect data. PZ, HZ, FY and XX helped perform the analysis with constructive discussions.

Funding The study was supported by funding from the following: the National Key Research and Development Program (2016YFE0205400, 2018ZX09739010, 2018ZX09301034003); the Science and Technology Program of Guangdong (2020B121202010); the Science and Technology Planning Project of Guangzhou (201707020010); the Science, Technology and Innovation Committee of Shenzhen (GJHS20170314114526143, JSGG20180703155802047); the Economic, Trade and Information Commission of Shenzhen Municipality (20170505161556110, 20170505160926390, 201705051617070); the National Natural Science

Foundation of China (81730019, 81973133, 81960074, 81500233); Jiangxi Outstanding Person Foundation (20192BCBL23024) and the Major projects of the Science and Technology Department, Jiangxi (20171BAB205008).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved by the Institutional Review Boards of the Harvard School of Public Health Anhui Medical University, approval ID is 1005 2003-8-11.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data described in the manuscript, code book, and analytic code will be made available from the corresponding authors on request, after the request is submitted and formally reviewed and approved by the Ethics Committee of the Institute of Biomedicine, Anhui Medical University, Hefei, China.

ORCID iDs
Xiao Huang http://orcid.org/0000-0003-0686-6318
Xianhui Qin http://orcid.org/0000-0001-7812-7982
Fangrong Yan http://orcid.org/0000-0002-3284-6647

REFERENCES

1 Ng M, Fleming T, Robinson M, *et al*. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the global burden of disease study 2013. *The Lancet* 2014;384:766–81.
2 Collaboration NRF. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. *The Lancet* 2016;387:1377–96.
3 Prospective Studies Collaboration, Whitlock G, Lewington S, *et al*. Body-Mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009;373:1083–96.
4 Bhaskaran K, dos-Santos-Silva I, Leon DA, *et al*. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. *The Lancet Diabetes & Endocrinology* 2018;6:944–53.
5 Zheng W, McLerran DF, Rolland B, *et al*. Association between body-mass index and risk of death in more than 1 million Asians. *New England Journal of Medicine* 2011;364:719–29.
6 Sung K-C, Ryu S, Lee J-Y, *et al*. All cause mortality and body mass index in a young Asian occupational cohort without baseline metabolic syndrome components. *Int J Cardiol* 2016;224:271–8.
7 Yang W, Li J-P, Zhang Y, *et al*. Association between body mass index and all-cause mortality in hypertensive adults: results from the China stroke primary prevention trial (CSPPT). *Nutrients* 2016;8:384.
8 Feng Y, Hsu Y-H, Terwedow H, *et al*. Familial aggregation of bone mineral density and bone mineral content in a Chinese population. *Osteoporos Int* 2005;16:1917–23.
9 Berrington de Gonzalez A, Hartge P, Cerhan JR, *et al*. Body-Mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010;363:2211–9.
10 Murayama H, Liang J, Shaw BA, *et al*. Age and gender differences in the association between body mass index and all-cause mortality among older Japanese. *Ethn Health* 2020;25:1–14.
11 Yang L, Zhou M, Smith M, *et al*. Body mass index and chronic obstructive pulmonary disease-related mortality: a nationally representative prospective study of 220,000 men in China. *Int J Epidemiol* 2010;39:1027–36.
12 Jee SH, Sull JW, Park J, *et al*. Body-Mass index and mortality in Korean men and women. *N Engl J Med Overseas Ed* 2006;355:779–87.
13 Centers for Disease Control and Prevention (CDC). Vital signs: state-specific obesity prevalence among adults - United States, 2009. *MMWR Morb Mortal Wkly Rep* 2010;59:951–5.
14 Zheng W, McLerran DF, Rolland B, *et al*. Association between body-mass index and risk of death in more than 1 million Asians. *N Engl J Med* 2011;364:719–29.
15 GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the global burden of disease study 2016. *Lancet* 2017;390:1211–59.
16 Chen Y, Yang Y, Jiang H, *et al*. Associations of BMI and waist circumference with all-cause mortality: a 22-year cohort study. *Obesity* 2019;27:662–9.
17 Nordström P, Pedersen NL, Gustafson Y, *et al*. Risks of myocardial infarction, death, and diabetes in identical twin pairs with different body mass indexes. *JAMA Intern Med* 2016;176:1522.
18 Hong J-S, Yi S-W, Yi J-J, *et al*. Body mass index and cancer mortality among Korean older middle-aged men: a prospective cohort study. *Medicine* 2016;95:e3684.
19 FB H, Willett WC, Li T. Adiposity as compared with physical activity in predicting mortality among women. *New England Journal of Medicine* 2004;351:2694–703.
20 Katzmarzyk PT, Janssen I, Ardern CI. Physical inactivity, excess adiposity and premature mortality. *Obesity Reviews* 2003;4:257–90.
21 Badrick E, Sperrin M, Buchan IE, *et al*. Obesity paradox and mortality in adults with and without incident type 2 diabetes: a matched population-level cohort study. *BMJ Open Diabetes Res Care* 2017;5:e000369.
22 Preston S, Stokes A. Obesity paradox: conditioning on disease enhances biases in estimating the mortality risks of obesity. *Epidemiology* 2014;25:454–61.
23 Oreopoulos A, Kalantar-Zadeh K, Sharma AM, *et al*. The obesity paradox in the elderly: potential mechanisms and clinical implications. *Clin Geriatr Med* 2009;25:643–59.
24 Kohli P, Cannon CP. Triglycerides: how much credit do they deserve? *Medical Clinics of North America* 2012;96:39–55.
25 Ginsberg HN. New perspectives on atherogenesis: role of abnormal triglyceride-rich lipoprotein metabolism. *Circulation* 2002;106:2137–42.
26 Söderström L, Rosenblad A, Adolfsson ET, *et al*. Nutritional status predicts preterm death in older people: a prospective cohort study. *Clin Nutr* 2014;33:354–9.
27 Correia MITD, Waitzberg DLIsabel T. D. Correia M, Isabel TD. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clin Nutr* 2003;22:235–9.