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Estimating the impact of metabolic syndrome on low back pain and the joint effects of metabolic syndrome and depressive symptoms on low back pain: insights from the China Health and Retirement Longitudinal Study

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Abstract

Background Although metabolic syndrome (MetS) and depressive symptoms (DS) are predictors of low back pain (LBP), their combined effects and relative contributions to LBP have not been well studied. Using the nationally representative data from the China Health and Retirement Longitudinal Study (CHARLS), this study conducted cross-sectional and longitudinal analyses to investigate the impact of MetS on LBP, and the joint effects of MetS and DS on LBP.

Methods This study included a cross-sectional analysis of 8957 participants aged at least 45 years from the CHARLS 2011 dataset and a longitudinal follow-up of 3468 participants without LBP from the CHARLS 2011, tracked over 9.25 years (from June 2011 to September 2020) with 4 times LBP assessment in CHARLS 2013, 2015, 2018, and 2020. To explore the association between MetS on LBP and the joint effects of MetS and DS on LBP, multivariable-adjusted multinomial logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Multivariable-adjusted COX proportional hazards regression models were applied to estimate hazard ratios (HRs) and 95% CIs. All statistical analyses were conducted using STATA (version SE16).

Results In the cross-sectional analysis, MetS was associated with a lower risk of LBP (adjusted OR = 0.85, 95% CI = 0.74–0.97), while there was no significance for this association in the longitudinal analysis. In the joint association of MetS and DS with LBP, participants with NoMetS + DS (adjusted OR = 2.31, 95% CI = 1.94–2.75), and MetS + DS (adjusted OR = 2.16, 95% CI = 1.81–2.59) were risk factors for LBP events, while those with MetS + NoDS (adjusted OR = 0.75, 95% CI = 0.62–0.90) was a protective factor for LBP events than those with NoMetS + NoDS. During the 9.25 years of follow-up, 1708 cases (49.25%) experienced incident LBP events. In the longitudinal analysis, a significantly

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negative association was not found in MetS + NoDS for LBP events. Three sensitivity analyses identified the robustness of the associations. Moreover, the nature of cross-sectional associations differed by age (45–64 and 65 + years).

Conclusions Our study found that MetS was linked to a lower incidence of LBP, but this effect does not persist over time. Importantly, the combination of MetS and DS significantly increased LBP risk, a joint effect not extensively studied before. These findings underscore the novel contribution of our research, advocating for the joint assessment of MetS and DS to enhance LBP risk stratification and inform prevention strategies.

Keywords Joint effect, Metabolic syndrome, Depressive symptoms, Low back pain, CHARLS

Introduction

Low back pain (LBP) is one of the most common musculoskeletal diseases worldwide. LBP was identified as the leading contributor to the global disability burden and was observed across all nations, from developing to developed countries, and affects every age group, from children to the elderly, especially for the developing countries and the elderly [1, 2]. Epidemiological evidence based on the Global Burden of Disease (GBD) suggested that 619 million prevalent cases of LBP in 2021 worldwide [1] and the total number of persons affected by LBP will further increase in the coming decades [3].

Although previous research has well-documented the relationship between individual components of metabolic syndrome (MetS) and LBP, the findings have been somewhat inconsistent. For instance, hypertension has been observed as a protective factor in research conducted in Korean [4] and Norwegian [5], while statistical associations with other MetS components, such as obesity [6], diabetes [7], and dyslipidemia [8], have not been found. Despite these insights, limited research examined the relationship between MetS itself and LBP, based on the population. To the best of our knowledge, only two community-based cross-sectional studies from Japan have explored the relationship [9, 10]. These studies found a significant association between MetS and LBP, but this association was only evident among females. Both studies also emphasized the need for prospective research to explore the potential causal relationships. However, these Japanese studies defined MetS according to adjusted criteria for Japan, which may limit the generalizability of their findings to other populations. Furthermore, there is still a lack of evidence from studies including representative populations outside Japan, like in China. This gap highlights the need for further research, involving studies with diverse populations, to better understand the global relevance of the MetS-LBP relationship.

Importantly, in patients with pain, depressive symptoms (DS) often coexist with metabolic disorders, suggesting a complex interaction role between the two. This can either exacerbate the severity of LBP, amplify pain perception, and contribute to the long-term nature of the disease, increasing the complexity of treatment and management, and impeding recovery [11, 12]. It is worth noting that the mechanism by which metabolic adversities affect LBP may be mediated by factors such as systemic inflammation and altered pain perception [13, 14], which are also affected by mental disorders such as DS [15, 16]. Psychosomatic factors play a critical role in this interaction. For instance, therapies like Short-term Intensive Dynamic Psychotherapy, Acceptance and Commitment Therapy (ACT), and Compassion-Focused Therapy (CFT) are effective in treating conditions where psychological distress exacerbates physical symptoms, such as irritable bowel syndrome and physical symptoms disorder [17, 18]. These therapeutic approaches target the psychological components of chronic pain and somatic symptoms, suggesting that similar interventions might also be beneficial in managing the complex interaction between MetS, DS, and LBP. By addressing the mental health aspects in conjunction with physical symptoms, these therapies could potentially mitigate the severity and chronicity of LBP in patients with MetS and DS. This may imply the combination of MetS and DS was ranked the important contributor to more chronic and severe pain experiences. Therefore, the joint effects of MetS and DS can provide a new perspective into risk stratification and targeted intervention for populations at high risk of pain. However, existing findings did not provide insight into how MetS interacts with DS to influence LBP outcomes.

Given the limited research on how MetS interacts with DS to influence LBP outcomes, this study aimed to address this gap by estimating the effects of MetS on LBP, as well as the joint effect of MetS and DS on LBP, based on data from a prospective national cohort in China. Specifically, we hypothesized that: (1) MetS is associated with a decreased risk of LBP, and (2) the coexistence of MetS and DS reverses this possible protective effect and amplifies the risk of LBP. By providing both cross-sectional and longitudinal evidence, this study not only describes the contribution of these factors to LBP incidents but also enhances our understanding of our understanding of the complex interactions between metabolic and psychological factors in the development of LBP, offering new perspectives on risk stratification and preventive strategies.

Methods

Study design and population

This study was a secondary analysis of the data set of the CHARLS. CHARLS, as a significant component of global ageing cohorts, is a high-quality, nationally representative, large-scale, interdisciplinary survey project with baseline (2011) and subsequent follow-up visits every 2–3 years (2013, 2015, 2018, and 2020) to track the assessment of participants' health status, living habits, socioeconomics, and other aspects among adults aged 45 and older in China, selected using multistage stratified probability-proportionate-to-size sampling. Details of CHARLS have been presented in a previous publication [19].

In this study, we performed both cross-sectional and longitudinal analyses to achieve our research objectives. The objective of the cross-sectional analysis was to examine the association between MetS and LBP at a single point in time, as well as to assess the joint effect of MetS and DS on LBP. The longitudinal analysis aimed to evaluate the effects of baseline MetS, and MetS and DS on the incidence of new-onset LBP over the follow-up period. Specifically, two sections were conducted: (1) **Cross-sectional analysis**: Participants were included if they were aged at least 45 years and had complete information on key variables including MetS indicators and DS. Several exclusion criteria were considered: ① age < 45 years (n = 368); ② missing information on age (n = 26) and sex (n = 12); ③ missing information on MetS (fasting plasma glucose (FPG) = 5903, high-density lipoprotein cholesterol (HDL-C) (n = 2), systolic blood pressure (BP) (n = 1784), diastolic BP (n = 19), and waist circumference (WC) (n = 58); and ④ missing information on DS (n = 576). (2) **Longitudinal analysis**: Based on the cross-sectional analysis, participants were included if they had no LBP at baseline (2011) and had follow-up data available during 2013–2020. We excluded participants with: ① participants with LBP in 2011 (n = 1857); ② lost in follow-up during 2013–2020 (n = 1586); and (3) participants with missing information on LBP during 2013–2020 (n = 2046) (Fig. 1).

This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Assessment of metabolic syndrome

MetS was defined according to the definition of the guidelines of the American Heart Association and the National Heart, Lung, and Blood Institute's adaptation of the National Cholesterol Education Program Adult Treatment Panel III [20]. Additionally, we incorporated the WC criteria provided by the Guidelines for the Prevention and Control of Type 2 Diabetes in China [21]. Specifically, MetS was diagnosed based on the presence of three or more of the following abnormalities at baseline (2011):

1) FPG ≥ 5.6 mmol/L (100 mg/dL) or drug treatment for elevated glucose.
2) Total cholesterol (TC) ≥ 1.7 mmol/L (150 mg/dL) or drug treatment for elevated triglycerides.
3) HDL-C < 1.0 mmol/L (40 mg/dL) for males and < 1.3 mmol/L (50 mg/dL) in females.
4) Elevated BP: systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg or antihypertensive drug treatment.
5) WC ≥ 90 cm in males or ≥ 85 cm for females.

BP was measured three times using an Omron HEM-7200 sphygmomanometer, and the average value was recorded. WC was measured using a tape measure. During the survey, trained staff collected venous blood samples and, following standard procedures, sent them to the Chinese Center for Disease Control and Prevention to obtain information on FPG, TC, and HDL-C. FPG, TC, and HDL-C levels were determined using enzymatic colorimetric tests. All procedures were conducted by trained personnel according to standard protocols [19].

Assessment of depressive symptoms

In the baseline survey (2011) of the CHARLS, the presence of DS was assessed using the 10-item Center for Epidemiological Studies Depression Scale (CESD-10) [22], which has excellent validity and reliability and is widely used in population-based studies [23]. 10 specific items include: (1) bothered by little things, (2) had trouble concentrating, (3) felt depressed, (4) everything was an effort, (5) felt hopeless, (6) felt fearful, (7) sleep was restless, (8) felt unhappy, (9) felt lonely, and (10) could not get going. Each item was scored using a 4-point scale (0: rarely or none of the time, < 1 day; 1: some or little of the time, 1–2 days; 2: occasionally or a moderate amount of the time, 3–4 days; and 3: most or all of the time, 5–7 days), the fifth and eighth were reverse coded, with total possible scores ranging from 0 to 30, with the higher scores indicating greater DS severity. Previous research has suggested that a CESD-10 score of 10 be used as the cutoff for having the presence of DS [24]. The CESD-10 was administered via face-to-face interviews by trained interviewers who ensured that participants understood each item [19].

Definition of combination in metabolic syndrome and depressive symptoms

According to the above definition of MetS and DS, the four combination types of MetS and DS were considered: (1) NoMets+NoDS: No MetS and No DS, (2) NoMetS+DS: No MetS and DS, (3) MetS+NoDS: MetS and No DS, and (4) MetS+DS: MetS and DS. The

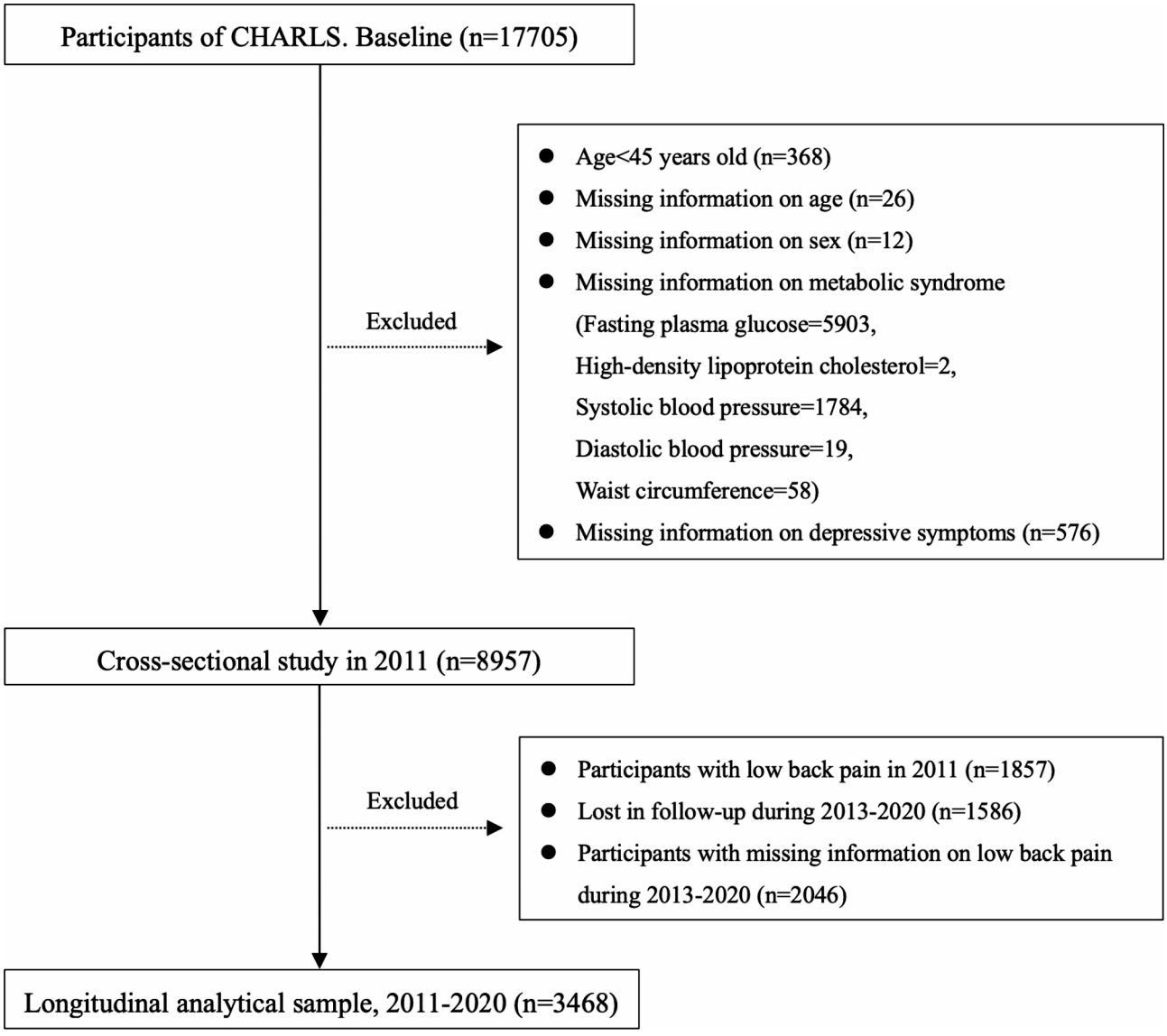

Fig. 1 The screening flowchart for the study population

NoMets+NoDS was the reference group in the current study.

Assessment of low back pain

From 2011 to 2020, the interviewer asked the participant, "On what part of your body do you feel pain? Please list all parts of body you are currently feeling pain (Question Da042 in CHARLS)." At the same time, the interviewer presents a human card for confirmation. If the participant responded affirmatively and marked the lower back on the card as the location of their pain, they were classified as having incident LBP. The date of the interview incident LBP events was recorded as the date of LBP diagnosis. New-onset LBP during follow-up was regarded as the endpoint in longitudinal analysis [19, 25].

Covariates

The following covariates were considered in this study: (1) sociodemographics: age (continuous), sex (male and female), residence (rural and urban), and marital status (married/cohabitated and others), (2) health behaviors: smoking (nonsmokers, light to moderate, and heavy), alcohol consumption (nonsmokers, light to moderate, and heavy), and social activity (none, some, and active), and (3) health status: functional disability (none, mild, and severe), number of chronic diseases (0, 1–2, and ≥ 3), and body mass index (continuous). More detailed information about the above covariates was provided in Table S1 in the supplementary files. All covariates were collected at baseline (2011) through in-person interviews using standardized questionnaires by trained interviewers [19].

Statistical analyses

Statistical analysis was conducted from May 4, 2024, to June 20, 2024. Data were cleaned and preprocessed before analysis. All analytical protocols are as follows. At baseline, participants' characteristics across different combinations types of MetS and DS were described with median (interquartile range) or mean (standard deviation) for non-normal distributed or normal distributed discontinuous variables, and frequency (percentage) for categorical variables. Comparison of differences among combinations types of MetS and DS groups were examined by Analysis of Variance (ANOVA) if they passed Bartlett's test, and otherwise Kruskal-Wallis H test for continuous variables, and χ^2 test and categorical variables.

In the cross-sectional analysis, odds ratios (ORs) and 95% confidence intervals (CIs) of MetS, and jointed MetS and DS for the risk of LBP were estimated by multivariable-adjusted multinomial logistic regression models. In the longitudinal analysis, hazard ratios (HRs) and 95% CIs of MetS, and jointed MetS and DS for the risk of LBP were estimated by multivariable-adjusted COX proportional hazards regression models. The proportional hazards assumption was tested for COX proportional hazards regression models using Schoenfeld residuals, and the proportional hazards assumption was upheld throughout ($P>0.05$). Moreover, these associations were stratified by age, and likelihood ratio tests in models with and without an interaction term were further used to estimate the interaction term's statistical significance.

Two different models were considered: (1) estimating the risk of LBP according to MetS, adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, body mass index, and DS, (2) estimating the risk of LBP according to MetS and DS, adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, and body mass index.

We performed three sensitivity analyses to repeated main analyses: (1) 12 on the CESD-10 scale was considered as the cutoff of the presence of DS; (2) participants with memory-related diseases ($n=103$) at baseline (2011) were excluded to reduce the concern regarding recall bias; (3) covariates in 2011 were assumed to be missing at random ($n=185$ for cross-sectional analysis, $n=59$ for longitudinal analysis), and the "mi estimate" command in STATA software was utilized to pool the results, following the generation of 10 imputed data sets through multiple imputation via chained equations.

All statistical analyses were conducted using STATA (version SE16). Two-tailed $P<0.05$ was set as the threshold for statistical significance.

Results

A total of 8957 persons were included in the cross-sectional analysis, and 3468 persons were included in the longitudinal analysis. As summarized in Tables 1 and 2306 (25.75%) persons had NoMetS+NoDS, 1489 (16.62%) persons had NoMetS+DS, 3222 (36.97%) persons had MetS+NoDS, and 1940 (21.66%) persons had MetS+DS. Compared to participants with NoMetS+NoDS, those with MetS+DS were more likely to be older, female, urban residents, no formal education, not married/cohabitated, nonsmokers, nondrinkers, and none social activity, mild and severe functional disability, ≥1 chronic diseases, and higher body mass index (All $P<0.05$). Table 2 also showed the sample characteristics stratified by combination types of MetS and DS in the longitudinal analysis (***n = 3468***). Moreover, descriptive statistics for subgroups based on MetS and DS status are likewise provided (Table S2-S5).

In the cross-sectional analysis, compared to NoMetS, MetS (adjusted OR=0.85, 95% CI=0.74–0.97, $P<0.05$) was a protective factor for LBP events. Participants with NoMetS+DS (adjusted OR=2.31, 95% CI=1.94–2.75, $P<0.001$), and MetS+DS (adjusted OR=2.16, 95% CI=1.81–2.59, $P<0.001$) were risk factors for LBP events, while those with MetS+NoDS (adjusted OR=0.75, 95% CI=0.62–0.90, $P<0.01$) was a protective factor for LBP events (Table 3).

During a maximum follow-up of 9.25 years (from June 2011 to September 2020), 1708 (49.25%) persons experienced LBP. The incidence rates of LBP were 54.58 per 1000 person-years among participants with NoMetS+NoDS, 106.73 per 1000 person-years among participants with NoMetS+DS, 57.97 per 1000 person-years among participants with MetS+NoDS, and 107.40 per 1000 person-years among participants with MetS+DS. Table 3 also showed the longitudinal association of MetS and DS with incident LBP events. After adjusting for potential confounders, participants with NoMetS+DS and MetS+DS were independently associated with a 74% (adjusted HR=1.74, 95% CI=1.49–2.03, $P<0.001$) and a 55% (adjusted HR=1.55, 95% CI=1.32–1.82, $P<0.001$) increased risk of incident LBP than those with NoMetS+NoDS. All sensitivity analyses were consistent with the main findings (Table 4).

Moreover, Table 5 showed the cross-sectional association of MetS, and MetS and DS with incident LBP did not differ by age (45–64 and 65+years). Our findings found no significant association of MetS, and MetS and DS and incident LBP among participants aged 65+.

Discussion

In cross-sectional evidence including 8957 Chinese adults aged 45 years or above, exposure to MetS was significantly associated with a lower risk of LBP, while

Table 1 Baseline characteristics according to metabolic syndrome and depressive symptoms ($n=8957$)

Characteristics	Total Sample ($n=8957$)	Combination types of MetS and DS				*P*-value [b]
		NoMetS + NoDS ($n=2306$)	NoMetS + DS ($n=1489$)	MetS + NoDS ($n=3222$)	MetS + DS ($n=1940$)	
MetS	5162 (57.6)	0 (0.0)	0 (0.0)	3222 (100.0)	1940 (100.0)	< 0.001
DS	3429 (38.3)	0 (0.0)	1489 (100.0)	0 (0.0)	1940 (100.0)	< 0.001
LBP	1857 (20.7)	296 (12.8)	518 (34.8)	350 (10.9)	693 (35.7)	< 0.001
Age, median (IQR), years	59.4 (9.3)	57.0 (13.0)	59.0 (13.0)	59.0 (13.0)	60.0 (13.0)	< 0.001
Male	4231 (47.2)	1440 (62.5)	700 (47.0)	1478 (45.9)	613 (31.6)	< 0.001
Rural residence	5795 (64.7)	1565 (67.9)	1137 (76.4)	1796 (55.7)	1297 (66.9)	< 0.001
Education level						< 0.001
No formal education	4195 (46.8)	923 (40.0)	800 (53.7)	1328 (41.2)	1144 (59.0)	
Primary school	2035 (22.7)	543 (23.6)	361 (24.2)	726 (22.5)	405 (20.9)	
Middle school	1818 (20.3)	535 (23.2)	248 (16.7)	745 (23.1)	290 (15.0)	
High school or above	909 (10.2)	305 (13.2)	80 (5.4)	423 (13.1)	101 (5.2)	
Married/Cohabitated	7909 (88.3)	2132 (92.5)	1283 (86.2)	2902 (90.1)	1592 (82.1)	< 0.001
Smoking [a]						< 0.001
Nonsmokers	5395 (60.2)	1167 (50.6)	880 (59.1)	2006 (62.3)	1342 (69.2)	
Light to moderate	1963 (21.9)	565 (24.5)	363 (24.4)	665 (20.6)	370 (19.1)	
Heavy	1598 (17.8)	573 (24.9)	246 (16.5)	551 (17.1)	228 (11.8)	
Alcohol consumption						< 0.001
Nondrinkers	6005 (67.0)	1329 (57.6)	1011 (67.9)	2184 (67.8)	1481 (76.3)	
Light to moderate	2492 (27.8)	802 (34.8)	405 (27.2)	887 (27.5)	398 (20.5)	
Heavy	460 (5.1)	175 (7.6)	73 (4.9)	151 (4.7)	61 (3.1)	
Social activity						< 0.001
None	4412 (49.3)	1100 (47.7)	837 (56.1)	1439 (44.7)	1036 (53.4)	
Some	3029 (33.8)	812 (35.2)	445 (29.9)	1123 (34.9)	649 (33.5)	
Active	1516 (16.9)	394 (17.1)	207 (13.9)	660 (20.5)	255 (13.1)	
Functional disability [a]						< 0.001
None	6450 (72.8)	1936 (84.9)	887 (60.2)	2600 (81.7)	1027 (53.5)	
Mild	1577 (17.8)	281 (12.3)	333 (22.6)	460 (14.5)	503 (26.2)	
Severe	831 (9.4)	64 (2.8)	253 (17.2)	123 (3.9)	391 (20.4)	
Number of chronic diseases						< 0.001
0	2732 (30.5)	1054 (45.7)	360 (24.2)	1000 (31.0)	318 (16.4)	
1–2	4508 (50.3)	1068 (46.3)	815 (54.7)	1662 (51.6)	963 (49.6)	
≥ 3	1717 (19.2)	184 (8.0)	314 (21.1)	560 (17.4)	659 (34.0)	
Body mass index, mean (SD) [a]	23.5 (3.7)	21.8 (2.7)	21.3 (2.8)	25.1 (3.6)	24.5 (3.8)	< 0.001

Abbreviation IQR, interquartile range (75th quartile minus 25th quartile); SD, standard deviation; MetS, metabolic syndrome; DS, depressive symptoms; LBP, low back pain

DS: The score of the 10-item Center for Epidemiological Studies Depression Scale is greater than or equal to 10, otherwise NoDS

[a] Missing data: 1 for smoking, 99 for functional disability, and 81 for body mass index

[b] Categorical variables were based on χ^2 test and continuous variables were analyzed by ANOVA if they passed Bartlett's test, and otherwise Kruskal-Wallis *H* test

there was no significance for this association in the longitudinal evidence including 3468 Chinese adults aged 45 years or above. For the joint effects of MetS and DS with LBP, in cross-sectional evidence, compared to those with NoMetS+NoDS, participants with NoMetS+DS and MetS+DS were risk factors for LBP events, and MetS+NoDS was a protective factor for LBP events. Interestingly, the protective role of MetS+NoDS on LBP was not found in longitudinal evidence. The associations persisted in robustness in three sensitivity analyses. Moreover, the nature of cross-sectional associations differed by age (45–64 and 65+years).

LBP survivors often experience metabolic adversities. However, While prior research has extensively explored the link between individual MetS components and LBP and remains controversial, studies examining the influence of MetS itself on LBP are relatively scarce [4, 7, 8]. Therefore, this study explored the association of MetS with LBP and found that MetS is negatively associated with LBP, which is inconsistent with two community-based cross-sectional studies in Japan [9, 10]. The difference may be attributed to different definitions of MetS [9, 10]. Interestingly, our finding aligns with part studies evaluating the association of individual components of MetS and LBP. For example, epidemiological studies in

Table 2 Baseline characteristics according to metabolic syndrome and depressive symptoms ($n=3468$)

Characteristics	Total Sample ($n=3468$)	Combination types of MetS and DS				*P*-value [b]
		NoMetS + NoDS ($n=1077$)	NoMetS + DS ($n=420$)	MetS + NoDS ($n=1479$)	MetS + DS ($n=492$)	
MetS	1971 (56.8)	0 (0.0)	0 (0.0)	1479 (100.0)	492 (100.0)	< 0.001
DS	912 (26.3)	0 (0.0)	420 (100.0)	0 (0.0)	492 (100.0)	< 0.001
Incident LBP	1708 (49.3)	451 (41.9)	278 (66.2)	657 (44.4)	322 (64.5)	< 0.001
Average follow-up duration, month	87.2 (32.1)	92.1 (29.3)	74.4 (35.3)	92.0 (29.0)	73.1 (36.6)	< 0.001
Age, median (IQR), years	58.0 (8.4)	57.0 (11.0)	57.0 (14.0)	58.0 (13.0)	59.0 (11.0)	< 0.001
Male	1749 (50.4)	688 (63.9)	195 (46.4)	689 (46.6)	177 (36.0)	< 0.001
Rural residence	2249 (64.9)	751 (69.7)	315 (75.0)	845 (57.1)	338 (68.7)	< 0.001
Education level						< 0.001
No formal education	1422 (41.0)	397 (36.9)	198 (47.1)	551 (37.3)	276 (56.1)	
Primary school	811 (23.4)	257 (23.9)	104 (24.8)	343 (23.2)	107 (21.8)	
Middle school	812 (23.4)	268 (24.9)	87 (20.7)	377 (25.5)	80 (16.3)	
High school or above	423 (12.2)	155 (14.4)	31(7.4)	208 (14.1)	29 (5.9)	
Married/Cohabitated	3175 (91.6)	1008 (93.6)	372 (88.6)	1381 (93.4)	414 (84.2)	< 0.001
Smoking						< 0.001
Nonsmokers	2058 (59.3)	537 (49.9)	245 (58.3)	939 (63.5)	337 (68.5)	
Light to moderate	747 (21.5)	264 (24.5)	105 (25.0)	292 (19.7)	86 (17.5)	
Heavy	663 (19.1)	276 (25.6)	70 (16.7)	248 (16.8)	69 (14.0)	
Alcohol consumption						< 0.001
Nondrinkers	2230 (64.3)	608 (56.5)	281 (66.9)	978 (66.1)	363 (73.8)	
Light to moderate	1061 (30.6)	393 (36.5)	120 (28.6)	436 (29.5)	112 (22.8)	
Heavy	177 (5.1)	76 (7.1)	19 (4.5)	65 (4.4)	17 (3.5)	
Social activity						0.008
None	1647 (47.5)	512 (47.5)	220 (52.4)	666 (45.0)	249 (50.6)	
Some	1173 (33.8)	384 (35.7)	124 (29.5)	500 (33.8)	165 (33.5)	
Active	648 (18.7)	181 (16.8)	76 (18.1)	313 (21.2)	78 (15.9)	
Functional disability [a]						< 0.001
None	2841 (83.0)	956 (89.6)	311 (75.1)	1242 (85.2)	332 (68.3)	
Mild	467 (13.6)	102 (9.6)	76 (18.4)	184 (12.6)	105 (21.6)	
Severe	117 (3.4)	9 (0.8)	27 (6.5)	32 (2.2)	49 (10.1)	
Number of chronic diseases						< 0.001
0	1381 (39.8)	578 (53.7)	139 (33.1)	539 (36.4)	125 (25.4)	
1–2	1674 (48.3)	441 (41.0)	233 (55.5)	748 (50.6)	252 (51.2)	
≥ 3	413 (11.9)	58 (5.4)	48 (11.4)	192 (13.0)	115 (23.4)	
Body mass index, mean (SD) [a]	23.7 (3.7)	21.9 (2.7)	21.6 (2.8)	25.2 (3.6)	24.6 (3.9)	< 0.001

Abbreviation IQR, interquartile range (75th quartile minus 25th quartile); SD, standard deviation; MetS, metabolic syndrome; DS, depressive symptoms; LBP, low back pain

DS: The score of the 10-item Center for Epidemiological Studies Depression Scale is greater than or equal to 10, otherwise NoDS

[a] Missing data: 43 for functional disability, and 17 for body mass index

[b] Categorical variables were based on χ^2 test and continuous variables were analyzed by ANOVA if they passed Bartlett's test, and otherwise Kruskal-Wallis *H* test

Korean [4] and Norwegian [5] populations have shown that hypertension is associated with a low prevalence of LBP, potentially due to an increased pain threshold from elevated plasma endorphins in hypertensive individuals [4]. However, no negative association has been observed in obesity [6], diabetes [7], and dyslipidemia [8]. Moreover, the significant negative association between MetS and LBP observed in the cross-sectional analysis might also be attributed to healthier behaviors in the MetS group than the NoMetS group, such as a higher proportion of nonsmokers (cross-sectional: 64.9% vs. 54.0%; longitudinal: 64.7% vs. 52.2%) and nondrinkers (cross-sectional: 71.0% vs. 61.7%; longitudinal: 68.0% vs. 59.4%) (Table S2-S3). That is, the higher-risk behaviors prevalent among individuals without MetS could increase their risk of LBP incidence, thus leading to a comparatively lower risk of LBP among individuals with MetS. However, this significant negative association was not observed in the longitudinal analysis. The disparity might be attributed to the long follow-up period of 9.25 years, during which the adverse effects of physical aging likely surpassed the benefits of health-related behaviors. Cross-sectional, age-stratified subgroup analyses support this hypothesis, revealing that this negative association

Table 3 The risk of low back pain according to metabolic syndrome, and metabolic syndrome and depressive symptoms

	Cross-sectional	Longitudinal		
	OR (95% CI)	Cases, No.	Incidence Rate, per 1000 person-Years	HR (95% CI)
MetS [a]				
No	1.00 [Reference]	729	67.08	1.00 [Reference]
Yes	0.85 (0.74–0.97) *	979	68.31	0.91 (0.82–1.02)
Combined MetS and DS [b]				
NoMetS + NoDS	1.00 [Reference]	451	54.58	1.00 [Reference]
NoMetS + DS	2.31 (1.94–2.75) ***	278	106.73	1.74 (1.49–2.03) ***
MetS + NoDS	0.75 (0.62–0.90) **	657	57.97	0.92 (0.81–1.06)
MetS + DS	2.16 (1.81–2.59) ***	322	107.40	1.55 (1.32–1.82) ***

Abbreviation DS, depressive symptoms; OR, odds ratio; HR, hazards ratio; CI, confidence interval; MetS, metabolic syndrome; DS, depressive symptoms

[a] Adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, body mass index, and depressive symptoms

[b] Adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, and body mass index

*P <0.05, **P <0.01, ***P <0.001

persisted only in participants aged 45–64 years, but not in those aged 65 years or above. Moreover, because changes in health-related behaviors over the follow-up period were not monitored in this study, it is unclear whether participants adopted new habits such as smoking or drinking. Future studies should consider exploring the impact of health-related behaviors on the relationship between MetS and LBP.

Increasing evidence demonstrated that DS was associated with an increased risk of LBP [26–29]. Depression is known to affect the perception of pain. It can lower pain thresholds and alter the pain processing pathways, making individuals more sensitive to pain. Therefore, in the context of DS, the association of MetS with LBP is more complex. As implied by our findings, the risk of experiencing LBP with exposure to DS (cross-sectional: adjusted HR=2.31, 95% CI=1.94–2.75; longitudinal: adjusted HR=1.74, 95% CI=1.49–2.03) and co-exposure to MetS and DS (cross-sectional: adjusted HR=2.16, 95% CI=1.81–2.59; longitudinal: adjusted HR=1.55, 95% CI=1.32–1.82). Although no studies based on population data have investigated the joint effects of MetS and DS on LBP, several hypotheses regarding the association between MetS and DS, and incident LBP have been proposed. Firstly, inflammation plays a critical role: both MetS and DS are linked with elevated levels of systemic inflammation [30, 31]. Moreover, DS is associated with an increase in pro-inflammatory cytokines [32]. These inflammatory processes may intensify degenerative changes in the spine and other musculoskeletal structures, thereby elevating the risk or severity of LBP [33]. Second, metabolic changes: MetS, characterized by factors such as hyperglycemia and dyslipidemia, can alter the body's metabolic state. For instance, high blood sugar levels can lead to the formation of advanced glycation end-products (AGEs), which can damage collagen in spinal discs and joints [34, 35]. Similarly, DS can disrupt the hypothalamic-pituitary-adrenal (HPA) axis, leading to cortisol dysregulation [36, 37]. Elevated cortisol levels may exacerbate metabolic disorders, increasing insulin resistance and adversely affecting fat distribution, potentially heightening physical stress on the lower back [38]. Third, behavioral factors: Individuals experiencing DS often exhibit reduced frequency of physical activity [39], contributing to obesity and other components of MetS [40]. Sedentary behavior, for example, can lead to muscle weakness and poor core stability, increasing the risk of developing LBP [41]. Additionally, both MetS and DS are related to unhealthy behaviors such as smoking and poor diets, which can independently impact spinal health and pain perception [42, 43]. Fourth, disease management stress: The presence of DS can impair an individual's ability to manage MetS. Additionally, chronic diseases are often linked to significant socioeconomic burdens, which can increase the risk of DS, creating a self-perpetuating cycle of worsening health conditions.

It is important to note the challenges in determining the temporal sequence between MetS and LBP in cross-sectional studies, which may lead to issues of reverse causality. Specifically, older adults with LBP may be more inclined to report higher metabolic adversity [33], which in turn may have influenced our analysis results. Thus, the protective effect of MetS + NoDS on LBP observed in cross-sectional studies may be partially attributed to this reverse causality. This possibility was further explored in our longitudinal analyses, which did not confirm the causality of this protective effect. Meanwhile, the omission of certain key covariates could lead to misleading conclusions. For example, the failure to account for factors such as body posture, occupation, history of trauma, and prior spinal surgery may create spurious associations in cross-sectional analyses, where relationships between certain variables appear to exist but cannot be substantiated in longitudinal studies. These unmeasured covariates could

Table 4 Sensitivity analyses of the risk of low back pain according to metabolic syndrome, and metabolic syndrome and depressive symptoms

	Cross-sectional	Longitudinal
	OR (95% CI)	HR (95% CI)
Sensitivity 1[c]		
Combined MetS and DS [b]		
No MetS + NoDS	1.00 [Reference]	1.00 [Reference]
No MetS + DS	2.26 (1.90–2.70) ***	1.75 (1.48–2.037 ***
MetS + NoDS	0.79 (0.67–0.93) **	0.91 (0.80–1.03)
MetS + DS	2.11 (1.76–2.52) ***	1.61 (1.36–1.92) ***
Sensitivity 2[d]		
MetS [a]		
No	1.00 [Reference]	1.00 [Reference]
Yes	0.85 (0.75–0.97) *	0.91 (0.82–1.02)
Combined MetS and DS [b]		
No MetS + NoDS	1.00 [Reference]	1.00 [Reference]
No MetS + DS	2.32 (1.95–2.77) ***	1.76 (1.51–2.05) ***
MetS + NoDS	0.75 (0.62–0.90) **	0.93 (0.82–1.07)
MetS + DS	2.18 (1.82–2.61) ***	1.55 (1.32–1.81) ***
Sensitivity 3[e]		
MetS [a]		
No	1.00 [Reference]	1.00 [Reference]
Yes	0.84 (0.73–0.95) **	0.93 (0.83–1.03)
Combined MetS and DS [b]		
No MetS + NoDS	1.00 [Reference]	1.00 [Reference]
No MetS + DS	2.28 (1.92–2.71) ***	1.74 (1.49–2.03) ***
MetS + NoDS	0.73 (0.61–0.88) **	0.93 (0.82–1.07)
MetS + DS	2.10 (1.76–2.51) ***	1.59 (1.35–1.86) ***

Abbreviation DS, depressive symptoms; OR, odds ratio; HR, hazards ratio; CI, confidence interval; MetS, metabolic syndrome; DS, depressive symptoms

[a] Adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, body mass index, and depressive symptoms

[b] Adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, and body mass index

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

[c] Cut point of depressive symptoms was defined as a score greater than or equal to 12 on the 10-item Center for Epidemiological Studies Depression Scale

[d] After excluding participants with memory-related diseases ($n = 8854$ in cross-sectiona analysis; $n = 3449$ in longitudinal analysis)

[e] Pooled results based on 10 imputed data sets

obscure or distort the true relationships between MetS, MetS + DS, and LBP, thereby impacting the accuracy of the study's findings. Therefore, it is crucial to consider the potential influence of confounding factors and the risk of reverse causality when interpreting these associations. This also highlights the complexity and challenges inherent in analyzing and interpreting data across different time points.

Given the high prevalence and public health burden DS [44] and its potential to influence the relationship between MetS and LBP through changes in inflammatory [33], metabolic [36, 37], behavior, and disease management stress. This potential relationship makes DS essential to LBP clinical practice and public health strategies. We recommend that general practitioners consider the possibility of depression and MetS in patients with LBP, particularly in primary care settings. Screening for MetS and DS in these patients may lead to early interventions that could improve prognosis, enhance quality of life, and reduce healthcare costs. This integrated approach underscores the need for holistic management strategies that address both physical and mental health issues in a coordinated manner. This is particularly important in the context of China's basic public health services, which only manage patients with severe mental disorders.

In this study, several strengths were identified. First, this study innovatively explored the joint effects of MetS and DS on incident LBP based on the data derived from a large and representative sample of Chinese adults aged 45+, which had a positive impact on this study. Second, the application of both cross-sectional and longitudinal designs was utilized to estimate the association of MetS, MetS and DS with incident LBP. Third, three sensitivity analyses were considered to ensure the stability of our findings.

Nevertheless, certain limitations of the study must also be acknowledged. First, findings based only on middle-aged and older adults in China raise questions about the generalizability to younger and different ethnic groups. Future research should extend validation to multi-cohort studies, such as the Health and Retirement Study (HRS), the English Longitudinal Study of Ageing (ELSA), and UK biobank studies. Second, self-reported can introduce recall bias. However, excluding participants with baseline memory-related diseases reduced this concern, suggesting a minimal impact on our results. Third, assessments of MetS, DS, and potential confounders were conducted only at baseline. While this is feasible, it failed to capture their changes during follow-up. This limitation may underestimate or overestimate the long-term effects of exposure to LBP. Fourth, despite the widespread use of the CHARLS definition of LBP [19, 25], which is based solely on self-reported binary questions, this approach has notable limitations. It lacks detailed information regarding the duration, intensity, and characteristics of LBP. Additionally, due to the constraints of the CHARLS dataset, key co-covariates related to trunk pain—such as body posture, occupation, history of trauma, and spinal surgery—were not included in this study. The absence of these factors could compromise the reliability of the findings and, consequently, the external validity of the study. Future research, as well as the CHARLS study team, should aim to incorporate these variables to enhance the robustness of the analysis. Finally, the observational nature of this study limits to determining a causal association of MetS, and MetS and DS with LBP. Despite the

Table 5 The risk of low back pain according to metabolic syndrome, and metabolic syndrome and depressive symptoms stratified by age

Subgroups		Cross-sectional		Longitudinal	
		OR (95% CI)	*P* for interaction	HR (95% CI)	*P* for interaction
Age					
45–64 years	MetS [a]		1.000		1.000
	No	1.00 [Reference]		1.00 [Reference]	
	Yes	0.78 (0.67–0.91) **		0.90 (0.80–1.02)	
65 + years	MetS [a]				
	No	1.00 [Reference]		1.00 [Reference]	
	Yes	0.95 (0.74–1.22)		0.89 (0.70–1.12)	
Age			1.000		0.177
45–64 years	Combined MetS and DS [b]				
	No MetS + NoDS	1.00 [Reference]		1.00 [Reference]	
	No MetS + DS	2.21 (1.81–2.70) ***		1.61 (1.35–1.92) ***	
	MetS + NoDS	0.69 (0.56–0.85) ***		0.89 (0.76–1.03)	
	MetS + DS	1.92 (1.56–2.37) ***		1.50 (1.26–1.80) ***	
65 + years	Combined MetS and DS [b]				
	No MetS + NoDS	1.00 [Reference]		1.00 [Reference]	
	No MetS + DS	2.71 (1.87–3.94) ***		2.40 (1.69–3.40) ***	
	MetS + NoDS	0.86 (0.58–1.27)		1.05 (0.77–1.43)	
	MetS + DS	2.72 (1.88–3.94) ***		1.72 (1.20–2.44) **	

Abbreviation DS, depressive symptoms; OR, odds ratio; HR, hazards ratio; CI, confidence interval; MetS, metabolic syndrome; DS, depressive symptoms

[a] Adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, body mass index, and depressive symptoms, except itself

[b] Adjusted for age, sex, residence, education level, marital status, smoking, alcohol consumption, social activity, functional disability, number of chronic diseases, and body mass index, except itself

**$P < 0.01$, ***$P < 0.001$

limitations, our study provides important insights into the relationship between MetS, DS, and LBP among middle-aged and older adults in China. These findings suggest the need for further research across different populations to confirm the generalizability of these results. Specifically, our study highlights the importance of considering both physical and mental health factors in the management of LBP, which could have significant implications for clinical practice. Future studies may consider the above limitations.

Conclusions

MetS was found to be inversely associated with a higher incidence of LBP. Additionally, our findings underscore the combined effect of concurrent exposure to MetS and DS on LBP events. This study suggested the joint assessment of MetS and DS to stratify risk for LBP more effectively and provided clinical guidelines for its primary prevention.

Abbreviations

MetS	Metabolic syndrome
LBP	Low back pain
DS	Depressive symptoms
ACT	Acceptance and commitment therapy
CFT	Compassion-focused therapy
CHARLS	The China Health and Retirement Longitudinal Study
ORs	Odds ratios
CIs	Confidence intervals
HRs	Hazard ratios
GBD	Global Burden of Disease
WC	Waist circumference
FPG	Fasting plasma glucose
TC	Total cholesterol
BP	Blood pressure
CESD-10	The 10-item Center for Epidemiological Studies Depression Scale
ANOVA	Analysis of Variance
AGEs	Advanced glycation end-products
HPA	Hypothalamic-pituitary-adrenal
HRS	Health and Retirement Study
ELSA	English Longitudinal Study of Ageing

Supplementary Information

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Supplementary Material 1

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Author contributions

JH: Conceptualization, Methodology, Software, Validation, Formal analysis, Resources, Data curation, Writing-original draft, Writing-review & editing, and Visualization. DP: Writing-review & editing. XW: Writing-review & editing , Supervision, Project administration, and Funding acquisition.

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Data availability
The data supporting this study's findings are available from the CHARLS website: http://charls.pku.edu.cn/articles/news/608/zh-cn.html. To obtain the data, you must register as a user on the website. Once your registration has been verified and approved, you can follow the instructions provided to download the dataset.

Declarations

Ethics approval and consent to participate
This study is a secondary analysis based on the CHARLS, which was approved by the Biomedical Ethics Review Committee of Peking University (IRB001052-11015). All participants provided written informed consent to participate in the study.

Consent for publication
None.

Competing interests
The authors declare no competing interests.

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