

No association between C-reactive protein and depressive symptoms among the middle-aged and elderly in China

Evidence from the China Health and Retirement Longitudinal Study

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Abstract

The depressive symptoms have been associated with increased disabilities, and the depressive symptoms-related elevation of high C-reactive protein (CRP) has been proposed as a possible mechanism. We examined the relations between CRP and depressive symptoms among the middle-aged and elderly in China.

A longitudinal sample of the middle-aged and elderly (4404 men and 5055 women) who were interviewed in the 2011 China Health and Retirement Longitudinal Study was used. A multivariate logistic regression analysis was used to examine the effects of sociodemographic characteristics, lifestyle, activity status, physical exercise, systolic blood pressure, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, body mass index (BMI), and CRP levels on depressive symptoms.

The mean age in the study was 60.26 years [standard deviation (SD) \pm 9.25; 46.56% men]. The mean CPR level was 2.79 mg/L (range, 0.01–178.10; SD \pm 7.80). Depression scores ranged from 0 to 30 with a mean 8.65 (SD \pm 6.33). The prevalence of depressive symptoms was 38.49% in the total population, 31.04% in men and 44.99% in men. Compared with baseline CRP levels (\leq 1.00 mg/L), the depressive symptoms are only weakly correlated with CRP levels among women [CRP 1.01–3.00 mg/L: odds ratio (OR) = 0.85, 95% confidence interval (CI) = 0.73–0.98; CRP 3.01–10.00 mg/L: OR=1.25, 95% CI=1.03–1.51; CRP >10 mg/L: OR=1.41, 95% CI=1.06–1.88]. After adjusting for age, education, marital status, hukou, residence, cigarette smoking, alcohol drinking, eating meals, activity status, major accidental injury, diseases, health status, physical exercise, systolic blood pressure, LDL, HDL, triglycerides, and BMI, depressive symptoms were not associated with subsequent high CPR levels among the middle-aged and elderly (CRP 1.01–3.00 mg/L: OR=0.93, 95% CI=0.83–1.03; CRP 3.01–10.00 mg/L: OR=0.95, 95% CI=0.82–1.10; CRP >10 mg/I: OR=1.11, 95% CI=0.88–1.39).

Our data do not support an association between CRP and depressive symptoms in both middle-aged and elderly men and women among china.

Abbreviations: BMI = body mass index, CES-D = Center for Epidemiologic Studies-depressive symptoms scale, CHARLS = China Health and Retirement Longitudinal Study, CI = confidence interval, CRP = C-reactive protein, HDL = high-density lipoprotein, LDL = low-density lipoprotein, OR = odds ratio, SD = standard deviation.

Keywords: body mass index, C-reactive protein, depressive symptoms, mid-aged and elderly

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1. Background

Recently, depressive symptoms have become an important public health concern in general population in most countries. The Chinese population has begun aging and will continue to age rapidly in the future. In China, the prevalent of depressive symptoms is highly prevalent in elderly people,^[1–3] and lead to increased risk of disabilities and mortality associated with chronic diseases.^[4,5] The underlying mechanisms for depressive symptoms in elderly people remain unclear, but it is also possible that depressive symptoms may affect the development of chronic diseases through high sensitivity C-reactive protein (CRP). Depressive symptoms promote and maintain inflammatory responses by diminishing the immune system sensitivity.^[6]

Several previous studies have examined the relationship between CRP and depressive symptoms.^[7] However, the relationship between CRP and depressive symptoms is controversial, with several studies showing positive or null associations. Elovainio et al^[8] conducted a study to investigate the correlation between depression and CRP in a representative sample of adults aged \geq 30 years in Finland and found that inflammatory processes may induce depressive symptoms in men. Using a cross-sectional dataset of 641 healthy adults people aged 20 to 70 years enrolled at American Fallon Healthcare System, Ma et al^[9] found that depression was correlated to hs-CRP levels in women, but not in men. Another research study conducted by Elovainio et al^[10] showed that higher levels of depressive symptoms are associated with higher levels of CRP. Similar evidences of the positive associations have been found in other studies.^[11-18] However, contradictory evidences have been found in several studies. Chaiton et al,^[19] Douglas et al,^[20] and Au et al^[21] found no significance association between CRP and depressive symptoms in the general population.

Much of the literature has been limited by retrospective design and potential uncontrolled confounding. In addition, few studies have examined the association between CRP and depressive symptoms among general population in china. Therefore, this article focused on the relationship between CRP and depressive symptoms among the middle-aged and elderly in China after adjusting for potential confounders.

2. Methods

2.1. Study sample

The 2011 Wave1of China Health and Retirement Longitudinal Study (CHARLS) sample (N=9459) consists of 46.56% men [M=60.26 years, standard deviation (SD)=9.25; range, 45–93 years] and 53.44% women (M=58.89 years, SD=9.42; range, 45–96 years) participants; 6.64% and 3.18% of the respondents have completed high school and above vocational school education, respectively. By contrast, 28.83% of the respondents are illiterate or 61.35% received less than elementary school education; 64.72% of the participants live in rural, whereas 35.28% live in urban currently. Table 1 presents baseline characteristics of the sample for all variables in the research, and most variables based on our previous study.^[22]

2.2. CRP measures

Venous blood samples were taken by the Center for Disease Control (CDC) station, and then immediately stored frozen at -20° C and transported to the Chinese CDC in Beijing within 2 weeks where they were placed in a deep freezer and stored at

 -80° C until assay at CMU laboratory. Low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides were analyzed by the Youanmen Center for Clinical Laboratory at Capital Medical University using the enzymatic colorimetric test, and CRP was measured with immunoturbidimetric assay. We categorized CRP into 4 categories of CRP levels: ≤ 1.00 , 1.01 to 3.00, 3.01 to 10.00, and >10 mg/L, the categorization has been used widely in previous studies.^[17,23,24]

2.3. Depressive symptoms measures

The Chinese version of the Center for Epidemiologic Studies-Depression scale (CES-D) with a high reliability and validity has been widely used to measure depressive symptoms among Chinese.^[25–28] It is a self-reported questionnaire that consists of 10 questions. Participants with a score of 10 or higher on the CES-D were classified as depressed.^[29] The construct validity was 0.61 and the Cronbach alpha coefficient was 0.80.

2.4. Statistical analysis

Our data were used mean \pm SD (continuous data) and number and percentage (categorical data) to express. Differences between men and women, or between the depressive symptoms and those with the normal or CRP categories were evaluated by *t* test or chisquare test, and chi-square test was followed by Bonferroni adjustment. The associations of depressive symptoms and CRP levels were first used binary logistic regression models, as appropriate. Then binary logistic regression models adjusting for 18 potential confounders [age, education, marital status, hukou, residence, cigarette smoking, alcohol drinking, eating meals, activity status, major accidental injury, diseases, health status, physical exercise, systolic blood pressure, LDL, HDL, triglycerides, and body mass index (BMI)]^[30] were conducted to examine the odds ratio (OR) for depressive symptoms across a range of CRP. All data were analyzed by using SPSS version 17.0.

3. Results

The characteristics of our study subjects are shown in Table 1. 4404 (46.56%) of the participants were men, and 5055 (53.44%) of the participants were women. The average ages of the male and female participants were 60.26 ± 9.25 and 58.89 ± 9.42 years, respectively. Among all of the participants, 6.82% were underweight, 29.35% were overweight, and 11.75% were obese. Furthermore, regarding the men, 7.18% were underweight, 25.48% were overweight, and 8.16% were obese, whereas 6.51%, 32.60%, and 14.64% of the women were underweight, overweight, and obese, respectively. The mean value of the CRP was 2.79 ± 7.80 mg/L. The prevalence of depressive symptoms was 38.49% in the total population, 31.04% in men and 44.99% in women. Significant differences in distribution were observed between men and women in all of the variables, except eating habits, activity status, regular physical exercise, and systolic blood pressure.

Tables 2 and 3 show the relationship of various characteristics and BMI in the participants. Only marital status, eating habits, activity status, major accidental injury, and physical exercise were not significantly different between the CRP groups in males (Table 2), and in females, only education, alcohol consumption, eating habits, major accidental injury, self-report health status, physical exercise, and CES-D categories were not significantly different between the CRP groups (Table 3). Table 4 shows the

Baseline characteristics with full samples (N=9459).

	Male	Female	Total		
Variables	N (%)	N (%)	N (%)	t/χ^2	Р
N	4404 (46.56)	5055 (53.44)	9459 (100)		
Age, y	60.26 ± 9.25	58.89 ± 9.42	59.53 ± 9.36	7.158	.000
Average hours for 1 night	6.45 ± 1.81	6.25 ± 1.96	6.34 ± 1.89	5.183	.000
Diseases (0-14)	1.35 ± 1.37	1.49 ± 1.41	1.43 ± 1.39	-4.781	.000
LDL cholesterol, mg/dL	112.16 ± 34.35	120.49 ± 35.32	116.61 ± 35.11	-11.573	.000
HDL cholesterol, mg/dL	50.63 ± 16.22	51.55 ± 14.46	51.12 ± 15.31	-2.906	.000
Triglycerides, mg/dL	128.58 ± 119.4	138.23 ± 99.9	133.74 ± 109.51	-4.280	.000
CES-D	7.60 ± 5.89	9.55 ± 6.55	8.65 ± 6.33	-15.125	.000
BMI	22.99 ± 3.68	24.03 ± 4.12	23.55 ± 3.96	-12.833	.000
C-reactive protein (CRP), mg/L	3.11 ± 9.17	2.52 ± 6.36	2.79 ± 7.80	3.702	.000
Age, y				00 500	
45–49	678 (15.40)	1052 (20.81)	1730 (18.29)	62.598	.000
50–54	623 (14.15)	752 (14.88)	1375 (14.54)		
55–59	922 (20.94)	1063 (21.03)	1985 (20.99)		
60–64	828 (18.80)	895 (17.71)	1723 (18.22)		
65–69	568 (12.90)	553 (10.94)	1121 (11.85)		
≥70	785 (17.82)	740 (14.64)	1525 (16.12)		
Education					
Illiterate	576 (13.08)	2151 (42.55)	2727 (28.83)	1018.135	.000
Less than elementary school	3250 (73.80)	2553 (50.50)	5803 (61.35)		
High school	369 (8.38)	259 (5.12)	628 (6.64)		
Above vocational school	209 (4.75)	92 (1.82)	301 (3.18)		
Marital status	200 (02 (1102)	661 (6116)		
Single	3989 (90.58)	4290 (84.87)	8279 (87.53)	70.286	.000
Married	415 (9.42)	765 (15.13)	1180 (12.47)	10.200	.000
	415 (9.42)	700 (10.10)	1160 (12.47)		
Hukou		40.40 (0.4.00)	7700 (00 45)	10.005	000
Nonagricultural hukou	3550 (80.61)	4249 (84.06)	7799 (82.45)	19.325	.000
Agricultural hukou	854 (19.39)	806 (15.94)	1660 (17.55)		
Current residence					
Rural	2905 (65.96)	3217 (63.64)	6122 (64.72)	5.561	.006
Urban	1499 (34.04)	1838 (36.36)	3337 (35.28)		
Smoke					
NO	1086 (24.66)	4645 (91.89)	5731 (60.59)	4455.396	.000
Former smoke	754 (17.12)	104 (2.06)	858 (9.07)		
Current smoke	2564 (58.22)	306 (6.05)	2870 (30.34)		
Drinking					
NO	1928 (43.78)	4433 (87.7)	6361 (67.25)	2141.412	.000
Less than once a month	486 (11.04)	255 (5.04)	741 (7.83)		1000
More than once a month	1990 (45.19)	367 (7.26)	2357 (24.92)		
Eating meals	1990 (43.19)	307 (7.20)	2337 (24.32)		
0	590 (12 27)	669 (12 21)	1057 (12.00)	0 170	010
≤ 2 Meals per day	589 (13.37)	668 (13.21)	1257 (13.29)	0.172	.918
3 Meals per day	3754 (85.24)	4321 (85.48)	8075 (85.37)		
\geq 4 Meals per day	61 (1.39)	66 (1.31)	127 (1.34)		
Taking activities					
No	2162 (49.09)	2521 (49.87)	4683 (49.51)	0.572	.449
Yes	2242 (50.91)	2534 (50.13)	4776 (50.49)		
Ever been in major accidental injury					
No	3835 (87.08)	4702 (93.02)	8537 (90.25)	94.296	.000
Yes	569 (12.92)	353 (6.98)	922 (9.75)		
Self-report health status					
Very poor	635 (14.42)	949 (18.77)	1584 (16.75)	59.926	.000
Poor	1587 (36.04)	1942 (38.42)	3529 (37.31)		
Fair	1468 (33.33)	1524 (30.15)	2992 (31.63)		
Good	550 (12.49)	510 (10.09)	1060 (11.21)		
Very good	164 (3.72)	130 (2.57)	294 (3.11)		
, ,	104 (3.72)	100 (2.07)	234 (0.11)		
Having regular physical exercises		0000 (01 00)	5000 (01 50)	4 4 6 6	
No physical exercise	2738 (62.17)	3088 (61.09)	5826 (61.59)	1.166	.558
Less than regular physical exercises	827 (18.78)	976 (19.31)	1803 (19.06)		
Regular physical exercises	839 (19.05)	991 (19.60)	1830 (19.35)		
Systolic blood pressure, mm Hg					
<90.00	20 (0.45)	25 (0.49)	45 (0.48)	3.552	.169
90.00-140.00	3166 (71.89)	3549 (70.21)	6715 (70.99)		

(continued)

Variables	Male N (%)	Female N (%)	Total N (%)	t/χ^2	Р
>140	1218 (27.66)	1481 (29.30)	2699 (28.53)		
BMI					
Underweight	316 (7.18)	329 (6.51)	645 (6.82)	189.104	.000
Average	2589 (58.79)	2338 (46.25)	4927 (52.09)		
Overweight	1128 (25.61)	1648 (32.60)	2776 (29.35)		
Obese	371 (8.42)	740 (14.64)	1111 (11.75)		
C-reactive protein (CRP), mg/L					
<1.00	2091 (47.48)	2517 (49.79)	4608 (48.72)	10.7867	.013
	1479 (33.58)	1689 (33.41)	3168 (33.49)		
3.01-10.00	613 (13.92)	650 (12.86)	1263 (13.35)		
>10	221 (5.02)	199 (3.94)	420 (4.44)		
CES-D					
CES-D <10	3037 (68.96)	2781 (55.01)	5818 (61.51)	193.316	.000
CES-D ≥10	1367 (31.04)	2274 (44.99)	3641 (38.49)		

BMI = body mass index, CES-D = Center for Epidemiologic Studies-depressive symptoms scale, CRP = C-reactive protein, HDL = high-density lipoprotein, LDL = low-density lipoprotein.

significantly different variables among the CES-D groups. The prevalence of depressive symptoms, assessed by the CES-D, differed among the variables except systolic blood pressure.

To examine the association between CRP and depressive symptoms, we estimated depressive symptoms equation using binary logistic regression. The crude ORs and the associated 95% confidence intervals (CIs) are shown in Table 5. We controlled for the sociodemographic characteristics (age, education, marital status, hukou, residence), health behaviors (cigarette smoking, alcohol drinking, eating meals, activity status, physical exercise), health conditions (major accidental injury, diseases, health status), systolic blood pressure, and metabolic measures (LDL, HDL, triglycerides, and BMI), the estimation results of the depressive symptoms equation are reported in Table 6. Compared with baseline CRP levels (CRP $\leq 1.00 \text{ mg/L}$), the depressive symptoms are only weakly correlated with CRP levels among women (CRP 1.01-3.00 mg/L: OR = 0.85, 95% CI = 0.73-0.98; CRP 3.01-10.00 mg/L: OR = 1.25, 95% CI = 1.03-1.51; CRP >10 mg/L: OR = 1.41, 95% CI = 1.06-1.88). Several potential confounding factors were associated with CRP. After adjusting for age, sex, education, marital status, hukou, current residence, smoking habit, alcohol consumption, eating habits, activity status, major accidental injury, chronic diseases, health status, physical exercise, systolic blood pressure, LDL, HDL, triglycerides, and BMI, no association between CRP and depressive symptoms were observed in secondary analyses that stratified by sex (male, female).

4. Discussion

In our study, we investigated the association between CRP and depressive symptoms among the middle-aged and elderly in China. Based on the Chinese version of the CES-D, the prevalence of depressive symptoms was 31.04% in men and 44.99% in women. The prevalence of depressive symptoms was higher compared with previous survey results. In the sample collected from the 1999 and 2003 Surveys of Health and Living Status of the Elderly in Taiwan,^[30] the prevalence of depressive symptoms as measured by the CES-D (above the cutoff of 10) was 27.9% in men and 36.2% in women in 2003. The prevalence of depressive symptoms in the Elderly Health Centers between July 1998 to December 2000, in a study

conducted in a population aged 65 or older using the Geriatric Depressive Symptoms Scale criteria, was 4.9% in men and 7.9% in women.^[31] The rates estimated were slightly higher than the respective rates of 29.2% and 41.1% reported by Woo et al.^[32] Such discrepancies between our results and the previous studies may be a result of methodological differences in diagnosis and the healthy worker effect.

In our results a high level of CRP at baseline was associated with depressive symptoms in men, but not in women. However, it was no longer significant after adjustment for sociodemographic characteristics (age, education, marital status, hukou, residence), health behaviors (cigarette smoking, alcohol drinking, eating meals, activity status, physical exercise), health conditions (major accidental injury, diseases, health status), systolic blood pressure, and metabolic measures (LDL, HDL, triglycerides, and BMI). Previous studies have shown that the association between CRP and depressive symptoms is often attenuated by controlling confounders such as BMI.^[33-35] It is likely due to the confounder in the CPR-depressive symptoms relationship. However, most studies support a positive association between CRP and depressive symptoms both in men and women.^[11-18,36,37] The mechanisms for the association between CRP and depressive symptoms are unclear, but various hypotheses have been develop to explain the relationship since CRP cannot cross the bloodbrain barrier, and directly affect emotion regulating area in the brain.^[21]

4.1. Strengths and limitations

There are several limitations of our study. First, the relationship between CRP-depressive symptoms in the elderly becomes seriously more complex, we only consider the confounders as possible as we can, but there are some unknown factors. Secondly, the relationship between CRP and depressive symptoms should be studied prospectively. Our study investigated depressive symptoms in the mid and elderly participant through a cross-sectional study. Follow-up study was relatively short to comprehensively observe changes in the next step. The last, most of the exposure and outcome measures of the study were based on a subjective report and the self-reported questionnaire. Our study has several strengths. Firstly, the study was based on a nationwide survey. Secondly, we conducted the analyses

Variables	CRP ≤1.00 (%)	CRP 1.01-3.00 (%)	CRP 3.01-10.00 (%)	CRP>10 (%)	χ^2	Р
Age, y						
45–49	367 (17.55)	224 (15.15)	74 (12.07)	13 (5.88)	68.156	.000
50–54	303 (14.49)	197 (13.32)	95 (15.5)	28 (12.67)		
55–59	464 (22.19)	303 (20.49)	118 (19.25)	37 (16.74)		
60–64	378 (18.08)	292 (19.74)	110 (17.94)	48 (21.72)		
65–69	251 (12.00)	211 (14.27)	77 (12.56)	29 (13.12)		
≥70	328 (15.69)	252 (17.04)	139 (22.68)	66 (29.86)		
Education	020 (10.00)	202 (17.04)	100 (22.00)	00 (20.00)		
Illiterate	265 (12.67)	180 (12.17)	92 (15.01)	39 (17.65)	38.309	.000
Less than elementary school	1566 (74.89)	1064 (71.94)	448 (73.08)	172 (77.83)	00.000	.000
High school	181 (8.66)	137 (9.26)	44 (7.18)	7 (3.17)		
Above vocational school	79 (3.78)	98 (6.63)	29 (4.73)	3 (1.36)		
Marital status	13 (3.10)	30 (0.03)	23 (4.73)	5 (1.50)		
Single	1907 (91.20)	1342 (90.74)	547 (89.23)	193 (87.33)	5.022	.170
Married	184 (8.80)	137 (9.26)	66 (10.77)	28 (12.67)	0.022	.170
Hukou	104 (0.00)	137 (9.20)	00 (10.77)	20 (12.07)		
	1740 (00.01)	1140 (77.01)	400 (70 77)	177 (00 00)	00.070	000
Nonagricultural hukou	1742 (83.31)	1142 (77.21)	489 (79.77)	177 (80.09)	20.972	.000
Agricultural hukou	349 (16.69)	337 (22.79)	124 (20.23)	44 (19.91)		
Current residence	1404 (00 10)	0.40 (00.70)		140 (00 07)		000
Rural	1424 (68.10)	943 (63.76)	390 (63.62)	148 (66.97)	9.054	.029
Urban	667 (31.90)	536 (36.24)	223 (36.38)	73 (33.03)		
Smoke						
NO	528 (25.25)	366 (24.75)	145 (23.65)	47 (21.27)	13.580	.035
Former smoke	316 (15.11)	270 (18.26)	123 (20.07)	45 (20.36)		
Current smoke	1247 (59.64)	843 (57.00)	345 (56.28)	129 (58.37)		
Drinking						
No	866 (41.42)	664 (44.90)	292 (47.63)	106 (47.96)	13.943	0.030
Less than once a month	250 (11.96)	164 (11.09)	54 (8.81)	18 (8.14)		
More than once a month	975 (46.63)	651 (44.02)	267 (43.56)	97 (43.89)		
Eating meals						
<2 Meals per day	265 (12.67)	205 (13.86)	91 (14.85)	28 (12.67)	3.883	.693
3 Meals per day	1800 (86.08)	1250 (84.52)	513 (83.69)	191 (86.43)		
≥4 Meals per day	26 (1.24)	24 (1.62)	9 (1.47)	2 (0.9)		
Taking activities		(-)				
No	1049 (50.17)	704 (47.60)	291 (47.47)	118 (53.39)	4.566	.206
Yes	1042 (49.83)	775 (52.40)	322 (52.53)	103 (46.61)		1200
Ever been in major accidental injury	1012 (10.00)	110 (02.10)	022 (02.00)	100 (10.01)		
No	1802 (86.18)	1301 (87.96)	538 (87.77)	194 (87.78)	2.891	.409
Yes	289 (13.82)	178 (12.04)	75 (12.23)	27 (12.22)	2.001	.+05
Self-report health status	200 (10.02)	170 (12.04)	10 (12.20)	21 (12.22)		
	273 (13.06)	201 (13.59)	116 (18.92)	45 (20.36)	34.300	.001
Very poor	(/	532 (35.97)			34.300	.001
Poor	741 (35.44)		228 (37.19)	86 (38.91)		
Fair	719 (34.39)	490 (33.13)	193 (31.48)	66 (29.86)		
Good	278 (13.30)	201 (13.59)	53 (8.65)	18 (8.14)		
Very good	80 (3.83)	55 (3.72)	23 (3.75)	6 (2.71)		
Having regular physical exercises						
No physical exercise	1277 (61.07)	930 (62.88)	388 (63.30)	143 (64.71)	4.259	.642
Less than regular physical exercises	412 (19.70)	272 (18.39)	110 (17.94)	33 (14.93)		
Regular physical exercises	402 (19.23)	277 (18.73)	115 (18.76)	45 (20.36)		
Systolic blood pressure, mm Hg						
<90.00	8 (0.38)	8 (0.55)	4 (0.66)	0 (0.00)	33.062	.000
90.00-140.00	1609 (76.11)	998 (68.12)	409 (67.60)	150 (68.18)		
>140	497 (23.51)	459 (31.33)	192 (31.74)	70 (31.82)		
BMI						
Underweight	146 (6.98)	91 (6.15)	53 (8.65)	26 (11.76)	111.627	.000
Average	1358 (64.95)	773 (52.27)	325 (53.02)	133 (60.18)		
Overweight	476 (22.76)	449 (30.36)	157 (25.61)	46 (20.81)		
Obese	111 (5.31)	166 (11.22)	78 (12.72)	16 (7.24)		
CES-D	(0.01)					
CES-D <10	1441 (68.91)	1069 (72.28)	392 (63.95)	135 (61.09)	21.207	.000
		1000 (12.20)	UUL 100.001	100 101.001	61.601	.000

BMI=body mass index, CES-D=Center for Epidemiologic Studies-depressive symptoms scale, CRP = C-reactive protein.

Variables	CRP \leq 1.00 (%)	CRP 1.01-3.00 (%)	CRP 3.01-10.00 (%)	CRP >10 (%)	χ 2	Р
Age, y						
45–49	625 (24.83)	308 (18.24)	94 (14.46)	25 (12.56)	109.534	.000
50–54	399 (15.85)	238 (14.09)	91 (14.00)	24 (12.06)		
55–59	547 (21.73)	361 (21.37)	116 (17.85)	39 (19.60)		
60–64	409 (16.25)	323 (19.12)	123 (18.92)	40 (20.10)		
65–69	239 (9.50)	197 (11.66)	87 (13.38)	30 (15.08)		
≥70	298 (11.84)	262 (15.51)	139 (21.38)	41 (20.60)		
Education				(/		
Illiterate	1050 (41.72)	699 (41.39)	305 (46.92)	97 (48.74)	15.794	.071
Less than elementary school	1292 (51.33)	876 (51.87)	299 (46.00)	86 (43.22)		
High school	136 (5.40)	78 (4.62)	32 (4.92)	13 (6.53)		
Above vocational school	39 (1.55)	36 (2.13)	14 (2.15)	3 (1.51)		
Marital status	00 (1.00)	00 (2.10)	11 (2.10)	0 (1.01)		
Single	2179 (86.57)	1433 (84.84)	520 (80.00)	158 (79.40)	22.318	.000
Married	338 (13.43)	256 (15.16)	130 (20.00)	41 (20.60)	22.010	.000
Hukou	000 (10.40)	200 (10.10)	100 (20.00)	41 (20.00)		
Nonagricultural hukou	0151 (05 46)	1200 (02 24)	E27 (00 G0)	170 (06 40)	9.706	001
6	2151 (85.46)	1389 (82.24)	537 (82.62)	172 (86.43)	9.706	.021
Agricultural hukou	366 (14.54)	300 (17.76)	113 (17.38)	27 (13.57)		
Current residence	1000 (07.00)	1004 (50 44)	000 (00 00)	104 (00.01)	00.055	000
Rural	1693 (67.26)	1004 (59.44)	396 (60.92)	124 (62.31)	29.355	.000
Urban	824 (32.74)	685 (40.56)	254 (39.08)	75 (37.69)		
Smoke						
No	2340 (92.97)	1551 (91.83)	572 (88.00)	182 (91.46)	24.935	.000
Former smoke	42 (1.67)	40 (2.37)	22 (3.38)	0 (0.00)		
Current smoke	135 (5.36)	98 (5.80)	56 (8.62)	17 (8.54)		
Drinking						
No	2178 (86.53)	1498 (88.69)	574 (88.31)	183 (91.96)	11.786	.067
Less than once a month	132 (5.24)	89 (5.27)	28 (4.31)	6 (3.02)		
More than once a month	207 (8.22)	102 (6.04)	48 (7.38)	10 (5.03)		
Eating meals						
≤ 2 Meals per day	334 (13.27)	227 (13.44)	86 (13.23)	21 (10.55)	3.728	.713
3 Meals per day	2150 (85.42)	1441 (85.32)	557 (85.69)	173 (86.93)		
≥4 Meals per day	33 (1.31)	21 (1.24)	7 (1.08)	5 (2.51)		
Taking activities			. ()	- ()		
No	1274 (50.62)	819 (48.49)	324 (49.85)	104 (52.26)	2.302	.512
Yes	1243 (49.38)	870 (51.51)	326 (50.15)	95 (47.74)	2.002	.012
Ever been in major accidental injury	12-10 (-10.00)	010 (01.01)	020 (00.10)	30 (11.14)		
No	2344 (93.13)	1563 (92.54)	606 (93.23)	189 (94.97)	1.858	.602
Yes	173 (6.87)	126 (7.46)	44 (6.77)	10 (5.03)	1.000	.002
Self-report health status	175 (0.07)	120 (1.40)	44 (0.77)	10 (0.00)		
	443 (17.60)	327 (19.36)	126 (19.38)	53 (26.63)	18.160	.111
Very poor	999 (39.69)	()			10.100	.
Poor		623 (36.89)	248 (38.15)	72 (36.18)		
Fair	751 (29.84)	521 (30.85)	205 (31.54)	47 (23.62)		
Good	258 (10.25)	172 (10.18)	60 (9.23)	20 (10.05)		
Very good	66 (2.62)	46 (2.72)	11 (1.69)	7 (3.52)		
Having regular physical exercises						
No physical exercise	1530 (60.79)	1035 (61.28)	399 (61.38)	124 (62.31)	0.929	.988
Less than regular physical exercises	483 (19.19)	327 (19.36)	126 (19.38)	40 (20.10)		
Regular physical exercises	504 (20.02)	327 (19.36)	125 (19.23)	35 (17.59)		
Systolic blood pressure, mm Hg						
<90.00	18 (0.72)	4 (0.24)	1 (0.15)	2 (1.01)	75.606	.000
90.00-140.00	1891 (75.13)	1124 (66.55)	417 (64.15)	117 (58.79)		
>140	608 (24.16)	561 (33.21)	232 (35.69)	80 (40.20)		
3MI						
Underweight	209 (8.30)	72 (4.26)	38 (5.85)	10 (5.03)	300.971	.000
Average	1374 (54.59)	658 (38.96)	230 (35.38)	76 (38.19)		
Overweight	729 (28.96)	648 (38.37)	207 (31.85)	64 (32.16)		
Obese	205 (8.14)	311 (18.41)	175 (26.92)	49 (24.62)		
CES-D	200 (0.17)		110 (20.02)	10 (27.02)		
CES-D <10	1363 (54.15)	943 (55.83)	375 (57.69)	100 (50.25)	4.921	.178

BMI = body mass index, CES-D = Center for Epidemiologic Studies-depressive symptoms scale, CRP = C-reactive protein.

Relationship of various characteristics and depressive symptoms, chi-square test analyses of variance followed by Bonferroni adjustment (N = 9459).

Variables	CES-D <10 N (%)	CES-D ≥10 N (%)	χ^{2}	Р
Sex				
Male	3037 (68.96)	1367 (31.04)	193.316	.000
Female	2781 (55.01)	2274 (44.99)		
Age, y		E 10 (01 E0)		
45-49	1181 (68.27)	549 (31.73)	66.339	.000
50-54	875 (63.64)	500 (36.36)		
55–59	1243 (62.62)	742 (37.38)		
60-64	1006 (58.39)	717 (41.61)		
65–69	655 (58.43)	466 (41.57)		
≥70	858 (56.26)	667 (43.74)		
Education	1404 (50.00)	1202 (47 79)	237.876	000
Illiterate	1424 (52.22)	1303 (47.78) 2151 (37.07)	237.070	.000
Less than elementary school	3652 (62.93) 494 (78.66)	134 (21.34)		
High school Above vocational school	248 (82.39)	53 (17.61)		
Marital status	240 (02.39)	55 (17.01)		
Single	5250 (63.41)	3029 (36.59)	101.821	.000
Married	568 (48.14)	612 (51.86)	101.021	.000
Hukou	000 (40.14)	012 (01.00)		
Nonagricultural hukou	4603 (59.02)	3196 (40.98)	116.114	.000
Agricultural hukou	1215 (73.19)	445 (26.81)	110.114	.000
Current residence	1210 (10.10)	110 (20.01)		
Rural	3546 (57.92)	2576 (42.08)	94.218	.000
Urban	2272 (68.09)	1065 (31.91)	011210	.000
Smoke	2212 (00.00)	1000 (01.01)		
NO	3356 (58.56)	2375 (41.44)	54.130	.000
Former smoke	556 (64.80)	302 (35.20)	0.1100	1000
Current smoke	1906 (66.41)	964 (33.59)		
Drinking				
No	3711 (58.34)	2650 (41.66)	85.928	.000
Less than once a month	482 (65.05)	259 (34.95)		
More than once a month	1625 (68.94)	732 (31.06)		
Eating meals				
<2 Meals per day	651 (51.79)	606 (48.21)	57.853	.000
3 Meals per day	5086 (62.98)	2989 (37.02)		
≥4 Meals per day	81 (63.78)	46 (36.22)		
Taking activities				
No	2687 (57.38)	1996 (42.62)	66.813	.000
Yes	3131 (65.56)	1645 (34.44)		
Ever been in major accidental injury				
No	5316 (62.27)	3221 (37.73)		.000
Yes	502 (54.45)	420 (45.55)		
Self-report health status				
Very poor	570 (35.98)	1014 (64.02)	881.716	.000
Poor	1978 (56.05)	1551 (43.95)		
Fair	2142 (71.59)	850 (28.41)		
Good	875 (82.55)	185 (17.45)		
Very good	253 (86.05)	41 (13.95)		
Having regular physical exercises				
No physical exercise	1193 (65.19)	637 (34.81)	13.117	.000
Less than regular physical exercises	1087 (60.29)	716 (39.71)		
Regular physical exercises	3538 (60.73)	2288 (39.27)		
Systolic blood pressure, mm Hg				_
<90.00	32 (71.11)	13 (28.89)	1.847	.397
90.00-140.00	4134 (61.56)	2581 (38.44)		
>140	1652 (61.21)	1047 (38.79)		
BMI			04.050	
Underweight	322 (49.92)	323 (50.08)	64.353	.000
Average	2959 (60.06)	1968 (39.94)		
Overweight	1806 (65.06)	970 (34.94)		
Obese	731 (65.80)	380 (34.20)		

BMI=body mass index, CES-D=Center for Epidemiologic Studies-depressive symptoms scale.

Estimated crude odds ratios of depressive symptoms.

			Male			Female				
Variables	OR	95% CI	Р	OR	95% CI	Р	OR	95% CI	Р	
CRP, mg/L	≤1.00	1.00			1.00			1.00		
	1.01-3.00	0.85	(0.73,0.98)	.030	0.93	(0.83,1.06)	.283	0.89	(0.81,0.98)	.018
	3.01-10.00	1.25	(1.03,1.51)	.021	0.87	(0.73,1.03)	.106	1.01	(0.88,1.14)	.937
	>10	1.41	(1.06,1.88)	.018	1.17	(0.88,1.56)	.288	1.22	(1.00,1.50)	.050

BMI = body mass index, CI = confidence interval, CRP = C-reactive protein, OR = odds ratio.

Table 6 adjusting odds ratios and 95% confidence interval for C-reactive protein and depressive symptoms.

		Male		Female			Total		
Variables	OR	95% CI	Р	OR	95% CI	Р	OR	95% CI	Р
Age, y	1.00	(0.99,1.01)	.844	1.00	(0.99,1.01)	.726	1.00	(0.99,1.00)	.196
education		()			()			()	
Illiterate	1.00			1.00			1.00		
Less than elementary school	0.48	(0.3,0.79)	.004	0.78	(0.45,1.33)	.360	0.50	(0.35,0.71)	.000
High school	0.53	(0.37,0.77)	.001	0.58	(0.42,0.81)	.002	0.49	(0.39,0.62)	.000
Above vocational school	0.89	(0.72,1.11)	.311	0.94	(0.81,1.08)	.348	0.83	(0.74,0.93)	.001
Marital status	0100	(011 2,111 1)	1011	0.01	(0101)1100)	1010	0.00	(011 1,0100)	
Single	1.00			1.00			1.00		
Married	0.53	(0.42,0.67)	.000	0.70	(0.58,0.85)	.000	0.60	(0.52,0.70)	.000
Hukou	0.00	(0.12,0.01)	.000	0.10	(0.00,0.00)	.000	0.00	(0.02,0.1 0)	.000
Nonagricultural hukou	1.00			1.00			1.00		
Agricultural hukou	1.41	(1.11,1.78)	.004	1.55	(1.24,1.93)	.000	1.49	(1.27,1.75)	.000
Current residence	1.41	(1.11,1.70)	.004	1.00	(1.24,1.00)	.000	1.40	(1.27,1.70)	.000
Urban	1.00			1.00			1.00		
Rural	1.10	(0.92,1.31)	.286	1.20	(1.03,1.40)	.023	1.14	(1.01,1.28)	.031
Smoke	1.10	(0.32,1.31)	.200	1.20	(1.00,1.40)	.025	1.14	(1.01,1.20)	.031
No smoke	1.00			1.00			1.00		
Former smoke	1.18	(0.98,1.41)	.077	0.87	(0.67,1.13)	.295	0.78	(0.70,0.88)	.000
Current smoke	1.06		.609			.295	0.78		.000
	1.00	(0.84,1.34)	.009	1.01	(0.65,1.58)	.905	0.74	(0.62,0.89)	.001
Drinking	1.00			1.00			1.00		
NO	1.00	(0.70.1.01)	071	1.00	(0.00.1.50)	100	1.00	(0.74.0.05)	005
Less than once a month	0.86	(0.73,1.01)	.071	1.19	(0.93,1.52)	.160	0.84	(0.74,0.95)	.005
More than once a month	0.86	(0.67,1.1)	.224	1.36	(1.02,1.82)	.035	0.96	(0.80,1.15)	.653
Average hours for 1 night	0.82	(0.78,0.85)	.000	0.81	(0.78,0.83)	.000	0.81	(0.79,0.83)	.000
Eating meals	1 00			1 00			1.00		
3 Meals per day	1.00	(1 1 0 1 70)	000	1.00		000	1.00	(1.00.1.00)	
≤ 2 Meals per day	1.46	(1.18,1.79)	.000	1.42	(1.18,1.71)	.000	1.44	(1.26,1.66)	.000
\geq 4 Meals per day	0.87	(0.46,1.62)	.650	0.91	(0.53,1.57)	.730	0.87	(0.58,1.31)	.515
Taking no activities									
No	1.00			1.00			1.00		
Yes	0.76	(0.66,0.88)	.000	0.84	(0.74,0.95)	.007	0.82	(0.74,0.90)	.000
Ever been in major accidental injury									
NO	1.00			1.00			1.00		
Yes	1.74	(1.42,2.14)	.000	1.26	(0.98,1.61)	.067	1.48	(1.26,1.73)	.000
Diseases (0-14)	1.29	(1.22,1.37)	.000	1.31	(1.24,1.37)	.000	1.31	(1.26,1.35)	.000
Self-report health status									
Very poor health	1.00			1.00			1.00		
Poor	0.17	(0.10,0.30)	.000	0.16	(0.10,0.27)	.000	0.17	(0.12,0.24)	.000
Fair	0.16	(0.11,0.22)	.000	0.22	(0.17,0.29)	.000	0.19	(0.16,0.24)	.000
Good	0.32	(0.26,0.4)	.000	0.34	(0.28,0.41)	.000	0.33	(0.29,0.38)	.000
Very good	0.55	(0.45,0.68)	.000	0.55	(0.46,0.66)	.000	0.55	(0.49,0.63)	.000
Having regular physical exercises									
No physical exercise	1.00			1.00			1.00		
Less than regular physical exercises	0.82	(0.68,0.99)	.041	0.87	(0.74,1.03)	.098	0.85	(0.75,0.96)	.009
Regular physical exercises	0.96	(0.79,1.16)	.662	1.05	(0.89,1.23)	.567	1.00	(0.89,1.13)	.960
Systolic blood pressure (mmHg)									
90.00-140.00	1.00			1.00			1.00		
<90.00	0.77	(0.26,2.31)	.644	0.47	(0.18,1.23)	.123	0.62	(0.30,1.26)	.185
>140	0.81	(0.69,0.96)	.013	0.87	(0.75,1.01)	.060	0.85	(0.76,0.94)	.002
								,	ontinued)

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Variables		Male			Female			Total		
	OR	95% CI	Р	OR	95% CI	Р	OR	95% CI	Р	
LDL cholesterol, mg/dL	1.00	(1.00, 1.00)	.314	1.00	(1.00,1.00)	.574	1.00	(1.00,1.00)	.468	
HDL cholesterol, mg/dL	1.00	(1.00,1.01)	.345	1.00	(1.00,1.01)	.172	1.00	(1.00,1.01)	.021	
Triglycerides, mg/dL	1.00	(1.00, 1.00)	.762	1.00	(1.00,1.00)	.799	1.00	(1.00, 1.00)	.363	
BMI										
Normal weight	1.00			1.00			1.00			
Underweight	1.26	(0.96,1.65)	.094	1.00	(0.76,1.30)	.979	1.15	(0.95,1.38)	.160	
Overweight	0.74	(0.61,0.89)	.002	0.82	(0.70,0.95)	.007	0.81	(0.72,0.90)	.000	
Obese	0.74	(0.55,1.00)	.047	0.71	(0.58,0.87)	.001	0.73	(0.62,0.86)	.000	
CRP, mg/L										
<u>≤</u> 1.00	1.00			1.00			1.00			
1.01-3.00	0.88	(0.74,1.03)	.119	0.96	(0.83,1.11)	.578	0.93	(0.83,1.03)	.157	
3.01-10.00	1.12	(0.90,1.39)	.303	0.83	(0.68,1.01)	.068	0.95	(0.82,1.10)	.486	
>10	1.15	(0.83,1.58)	.404	1.08	(0.77,1.51)	.648	1.11	(0.88,1.39)	.383	

BMI=body mass index, CI = confidence interval, CRP = C-reactive protein, HDL = high-density lipoprotein, LDL = low-density lipoprotein, OR = odds ratio.

according to sex. Thirdly, it is interesting that the study has shown the null result which provides an opportunity to understand the other underlying mechanism between inflammation and depressive symptoms.

5. Conclusions

The result recently conducted studies demonstrate a high level of CRP at baseline was associated with depressive symptoms in men, but not in women. However, after adjusting the potential confounders, our data do not support the association between CRP and depressive symptoms in both men and women in China. Paying more attention to the role of CRP in depressive symptoms provides an opportunity to understand the underlying mechanisms between inflammation and depressive symptoms.

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Author contributions

LZ conceived and drafted the manuscript. J-lL, L-lZ, L-Lg, HL, and DL helped revise the manuscript.

- Formal analysis: Lin Zhang.
- Writing original draft: Lin Zhang.
- Writing review and editing: Jin-long Li, Li-li Zhang, Lei-lei Guo, Hong Li, Dan Li.

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