

## Preplanned Studies

# The Association Between Depression and All-Cause, Cause-Specific Mortality in the Chinese Population — China, 2010–2022

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## Summary

### What is already known about this topic?

Depression is linked to higher all-cause and cardiovascular mortality rates, but its effects on specific subgroups and non-cardiovascular mortality in the Chinese population remain unclear.

### What is added by this report?

Both severe and mild to moderate depression were found to elevate mortality rates among the Chinese population. The impact was particularly notable among males, urban residents, younger individuals, and those with higher education levels. Depression exhibited a stronger connection with fatalities related to suicide and non-suicidal injuries.

### What are the implications for public health practice?

Individuals experiencing mild depression require healthcare attention to avoid negative consequences. Enhanced physical and psychological support is particularly crucial for high-risk subgroups.

Depression is a pressing global health concern affecting populations worldwide. By 2015, the number of individuals affected globally reached 320 million, with a prevalence rate of 4.4% (1). Recent research in China (2) reported an 8.29% prevalence of moderate to severe depression in 2021, indicating a significant burden. While studies worldwide have linked depression to increased mortality rates (3–4), limited evidence exists specifically for China. This study utilized a population-based cohort in China to assess the 12-year mortality risk for individuals with depression in 2010. The findings revealed a notable positive correlation between depression and all-cause and cause-specific mortality among the Chinese population, indicating diverse effects across various demographics such as gender, age, and education level. Our results emphasize the necessity for enhanced physical and psychological support for all individuals

with depression, with particular attention to males, urban residents, younger individuals (below 60 years), and those with higher education levels.

The China Chronic Disease and Risk Factor Surveillance (CCDRFS) is an enduring national survey overseen by the National Centre for Chronic and Non-communicable Disease Control and Prevention. The CCDRFS 2010 survey was conducted in 162 disease surveillance points (DSP) across China. It included over 100,000 participants aged 18 years and above. This study was ethically reviewed and approved by the institutional review board of China CDC under approval number 201010, with written consent obtained from all participants.

Individual data was collected from the CCDRFS 2010 and was cross-referenced with the National Mortality Surveillance System (NMSS) records until 2022 using unique ID numbers, establishing a 12-year cohort. The recorded death data contained the date of death and causes classified according to the ICD-10 system. Causes of death were grouped into categories including cardiovascular diseases (I21–I25, I60–I69), cancers (C00–C97), suicide (X60–X84), non-suicide injuries (V01–X59, X85–Y89), and other causes.

In the CCDRFS 2010 study, depression was evaluated using the Patient Health Questionnaire-9 (PHQ-9), comprising 9 questions on depression symptoms experienced in the previous two weeks, scoring from 0 (not at all) to 3 (nearly every day). Individuals with over 4 missing responses in the 9 questions were excluded, and multiple imputation was used to manage these missing values. Depression severity was classified into three levels: none (PHQ-9 ≤ 5), mild to moderate (5 < PHQ-9 ≤ 15), and severe (PHQ-9 > 15). Additionally, various covariates such as demographic, behavioral, metabolic factors, and medical history were considered.

To ensure comparability, we standardized the proportion of baseline characteristics based on the age distribution of the total studied population, as the age

distribution varied among individuals with different levels of depression. We utilized the cumulative incidence function (CIF) and performed a log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CI) were calculated through three Cox models adjusting for various covariates. Subgroup analyses were carried out using Cox models in different subgroups. HRs for cause-specific mortality were determined using a competitive risk model. Statistical analyses were conducted using SAS (version 9.4; SAS Institute Inc., Cary, USA) and R (version 4.1.2; the R Core Team, R Foundation for Statistical Computing, Vienna, Austria).

Out of the total 98,658 participants, 288 were excluded due to having more than 4 missing values in the PHQ-9. Among the remaining 98,370 individuals, 5,683 (5.78%) had mild to moderate depression, while 341 (0.35%) had severe depression. The baseline characteristics can be found in Table 1.

After a mean follow-up of 11.60 years, the study identified 7,333 deaths. Participants with depression had a higher cumulative mortality compared to those without (Figure 1). Table 2 presents overall and subgroup results for all-cause mortality. After adjusting for covariates, individuals with mild to moderate depression (HR=1.12, 95% CI: 1.03, 1.23) and severe depression (HR=1.88, 95% CI: 1.46, 2.43) showed increased risks. Among those with severe depression, males (2.60 *vs.* 1.49), urban dwellers (2.34 *vs.* 1.56), younger individuals (<60 years, 2.02 *vs.* 1.79), highly educated individuals (2.98 *vs.* 1.57), and those with low weight (2.16 *vs.* 1.62) had higher HRs. Mild to moderate depression also significantly affected most subgroups. Additionally, age-standardized mortality among men with severe depression was three times higher than that among women (25.98 *vs.* 8.66 per 1,000 person-years) (Table 2).

Severe depression was linked to an increased risk of death from suicide (HR=5.13, 95% CI: 1.15–22.81), non-suicide injuries (HR=3.23, 95% CI: 1.21, 8.60), and cardiovascular diseases (HR=1.71, 95% CI: 1.14, 2.55) as shown in Table 3.

## DISCUSSION

Utilizing data from a population-based cohort, we discovered a direct correlation between depression and mortality. This association was particularly significant among males, urban residents, younger individuals, and those with higher education levels. Individuals with depression faced an elevated risk of mortality

from both injuries and cardiovascular diseases.

The results aligned with a prior UK Biobank (UKB) study (4) that found a correlation between lifetime depression and overall mortality (HR=1.46, 95% CI: 1.40, 1.52). Additionally, a US study (3) indicated that a 5-point rise in PHQ-9 score was associated with increased mortality in individuals with and without CVD risk (HR=1.33, 95% CI: 1.14, 1.55; HR=1.26, 95% CI: 1.02, 1.56, respectively).

One potential explanation for the impact of depression is its correlation with unhealthy habits like smoking and limited physical activity (6). Additionally, we observed a similar association in the baseline characteristics. Another plausible mechanism is depression's influence on metabolic functions, particularly lipid metabolism, which may contribute to the development of ischemic heart disease (7).

It is concerning that among individuals with severe depression, the mortality rate for men was three times higher than that of women despite a higher prevalence of depression among women. Urban, younger, and highly educated individuals were more significantly impacted by depression despite belonging to relatively advantaged subgroups that have been less studied in the past. These disparities may stem from distinct psychological and behavioral responses to depression among different subgroups; for instance, men were less likely to seek help compared to women (8), and younger individuals experienced higher levels of depression-related stigma than older individuals (9). Our findings highlight the importance of addressing the mental health needs of these individuals, even though they may be perceived as having better physical and socio-economic circumstances.

Depression is significantly linked to mortality from cardiovascular diseases and injuries, indicating the need for tailored interventions. While prior research has mainly concentrated on the connection between depression and suicide, it is essential to recognize that depression influences non-suicidal injuries as well. Individuals with depression face an elevated risk of fatalities due to accidents and interpersonal violence (10).

The findings suggest strategies to mitigate negative health consequences in individuals with depression. It is recommended to offer psychological interventions to all individuals with depression, regardless of symptom severity. Specifically, increased physical and psychological support is advised for men, urban residents, younger individuals, and those with higher education levels. Moreover, beyond averting suicide

TABLE 1. Baseline characteristics of participants with and without depression, by sex.

Characteristics	PHQ-9 score					
	Men			Women		
	0–5 years	6–15 years	>15 years	0–5 years	6–15 years	>15 years
Number (n, %)	42,895 (95.35)	1,984 (4.41)	108 (0.24)	49,451 (92.63)	3,699 (6.93)	233 (0.44)
Age (mean, s)	46.40 (15.24)	47.38 (16.24)	50.15 (15.49)	46.38 (14.63)	48.94 (15.16)	52.70 (15.16)
Urban (%)	43.85	47.67	53.46	46.73	47.00	52.63
Education level (%)						
Less than primary	16.81	18.83	23.75	31.68	35.19	33.38
Primary	20.62	22.13	21.68	20.35	18.52	22.66
Junior secondary	36.60	29.30	26.11	27.92	24.42	20.17
Senior secondary	17.80	17.93	20.85	14.02	14.94	18.17
University and above	8.17	11.81	7.61	6.02	6.93	5.62
Marital status (%)						
Unmarried	5.90	8.72	15.93	3.17	4.86	6.23
Married	88.59	81.29	71.11	88.28	83.14	79.82
Divorced	1.68	4.41	8.55	1.41	2.31	4.79
Widowed	3.56	5.43	4.40	6.94	9.50	9.17
Other	0.27	0.16	<0.01	0.20	0.19	<0.01
Smoking (%)						
Current smoking, everyday	50.48	50.08	61.14	2.65	3.85	6.55
Current smoking, not everyday	5.29	6.62	1.24	0.53	1.00	0.93
Past smoking	11.20	15.75	14.93	0.77	1.52	1.85
Never smoking	33.02	27.55	22.69	96.05	93.63	90.67
Alcohol consumption (%)						
Frequent drinking	27.58	25.13	24.73	2.93	3.06	2.60
Light drinking	31.24	35.09	30.26	12.54	18.19	17.99
No drinking	41.18	39.78	45.01	84.53	78.75	79.41
Diet (%)						
Excessive intake of red meat	30.78	27.00	32.34	20.97	17.24	19.57
Insufficient intake of vegetable	42.90	41.64	40.90	43.13	43.15	43.54
Insufficient intake of fruit	90.19	89.54	88.05	86.11	85.67	87.64
Physical activity (%)						
Low	28.42	33.31	37.83	26.52	24.97	32.39
Medium	37.76	34.05	32.70	46.53	43.28	37.58
High	33.82	32.64	29.47	26.95	31.76	30.03
Insufficient sleep	17.20	28.79	46.83	17.02	31.33	39.55
BMI (%)						
Low weight	3.08	4.26	5.92	3.16	3.94	6.89
Normal	49.90	51.05	59.38	48.10	49.64	50.38
Overweight	34.23	31.21	26.88	33.97	31.62	27.81
Obesity	12.78	13.48	7.82	14.77	14.80	14.92

Note: All characteristics were age-standardized except number of participants and age.  
Abbreviation: PHQ=patient health questionnaire; BMI=body mass index.

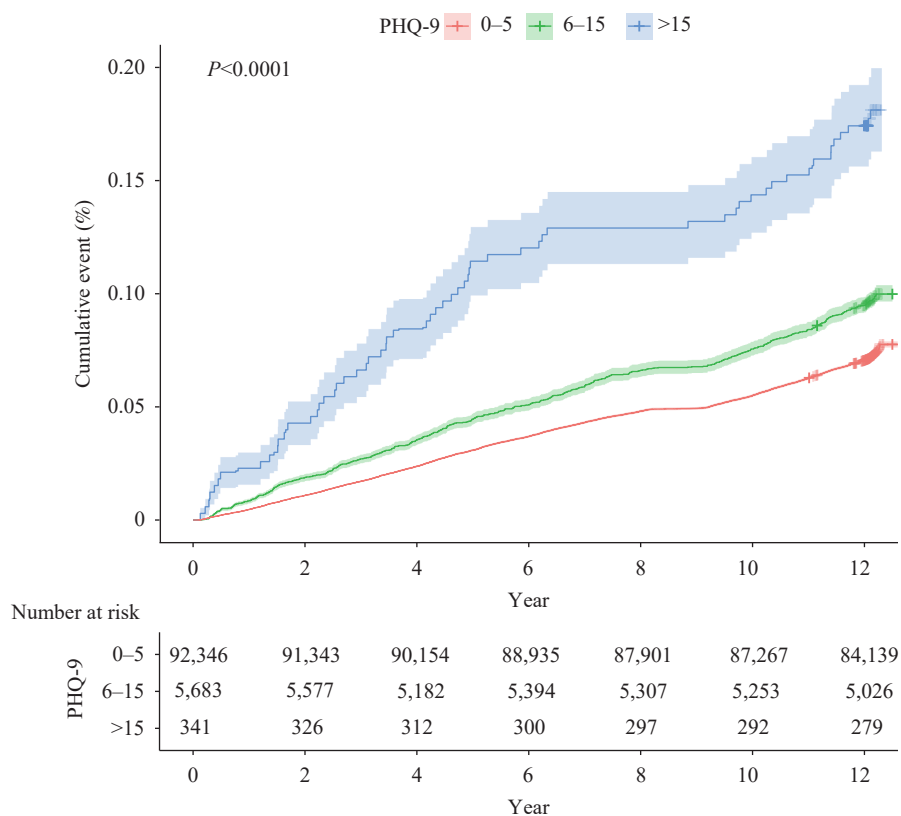


FIGURE 1. Cumulative mortality rate (%) throughout the study period, categorized by level of depression.

TABLE 2. HRs and 95% CI for the risk of all-cause mortality by depression level: overall and in different subgroups.

Subgroups	Number of death (n)	ASMR (per 1,000 person-year)	Model 1 (HR, 95% CI)	Model 2 (HR, 95% CI)	Model 3 (HR, 95% CI)
Overall					
PHQ $\leq$ 5	6,716	6.61	1.00	1.00	1.00
5<PHQ $\leq$ 15	556	7.84	1.20 (1.10, 1.31)	1.18 (1.08, 1.29)	1.12 (1.03, 1.23)
PHQ>15	61	12.64	2.05 (1.59, 2.64)	2.00 (1.55, 2.58)	1.88 (1.46, 2.43)
Sex					
Men					
PHQ $\leq$ 5	3,863	8.10	1.00	1.00	1.00
5<PHQ $\leq$ 15	242	10.40	1.19 (1.04, 1.35)	1.17 (1.03, 1.34)	1.09 (0.95, 1.24)
PHQ>15	29	25.98	2.89 (2.00, 4.17)	2.75 (1.90, 3.97)	2.60 (1.80, 3.77)
Women					
PHQ $\leq$ 5	2,853	5.33	1.00	1.00	1.00
5<PHQ $\leq$ 15	314	6.63	1.20 (1.07, 1.35)	1.19 (1.05, 1.34)	1.15 (1.02, 1.30)
PHQ>15	32	8.66	1.59 (1.11, 2.26)	1.56 (1.09, 2.22)	1.49 (1.05, 2.13)
Urban-rural					
Urban					
PHQ $\leq$ 5	2,727	5.61	1.00	1.00	1.00
5<PHQ $\leq$ 15	209	6.65	1.22 (1.06, 1.41)	1.21 (1.05, 1.39)	1.16 (1.01, 1.35)
PHQ>15	34	13.86	2.61 (1.86, 3.66)	2.56 (1.82, 3.60)	2.34 (1.66, 3.31)

Continued

Subgroups	Number of death (n)	ASMR (per 1,000 person-year)	Model 1 (HR, 95% CI)	Model 2 (HR, 95% CI)	Model 3 (HR, 95% CI)
Rural					
PHQ $\leq$ 5	3,987	7.51	1.00	1.00	1.00
5<PHQ $\leq$ 15	348	8.85	1.19 (1.07, 1.33)	1.19 (1.06, 1.33)	1.12 (1.00, 1.26)
PHQ>15	28	11.08	1.66 (1.14, 2.42)	1.61 (1.11, 2.35)	1.56 (1.06, 2.28)
Age (year)					
$\leq$ 60					
PHQ $\leq$ 5	2,916	3.31	1.00	1.00	1.00
5<PHQ $\leq$ 15	242	4.37	1.41 (1.24, 1.61)	1.40 (1.23, 1.60)	1.31 (1.14, 1.50)
PHQ>15	20	6.33	2.13 (1.37, 3.30)	2.14 (1.37, 3.32)	2.02 (1.29, 3.15)
>60					
PHQ $\leq$ 5	3,799	21.41	1.00	1.00	1.00
5<PHQ $\leq$ 15	315	23.37	1.07 (0.96, 1.20)	1.05 (0.93, 1.18)	1.01 (0.90, 1.14)
PHQ>15	41	40.63	1.99 (1.46, 2.70)	1.89 (1.39, 2.57)	1.79 (1.31, 2.44)
Education					
Less than lower secondary					
PHQ $\leq$ 5	4,522	7.53	1.00	1.00	1.00
5<PHQ $\leq$ 15	424	9.05	1.19 (1.07, 1.31)	1.17 (1.06, 1.30)	1.12 (1.01, 1.25)
PHQ>15	42	10.80	1.71 (1.26, 2.33)	1.64 (1.21, 2.24)	1.57 (1.15, 2.13)
Lower secondary and above					
PHQ $\leq$ 5	2,194	5.19	1.00	1.00	1.00
5<PHQ $\leq$ 15	132	5.74	1.26 (1.06, 1.51)	1.26 (1.05, 1.50)	1.17 (0.97, 1.40)
PHQ>15	19	17.14	3.47 (2.21, 5.44)	3.47 (2.21, 5.45)	2.98 (1.88, 4.70)
BMI (kg/m <sup>2</sup> )					
<24.0					
PHQ $\leq$ 5	3,789	7.17	1.00	1.00	1.00
5<PHQ $\leq$ 15	282	7.48	1.05 (0.93, 1.18)	1.03 (0.91, 1.17)	0.97 (0.86, 1.10)
PHQ>15	37	14.37	2.30 (1.64, 3.21)	2.22 (1.59, 3.11)	2.16 (1.55, 3.02)
$\geq$ 24.0					
PHQ $\leq$ 5	2,927	6.00	1.00	1.00	1.00
5<PHQ $\leq$ 15	274	8.30	1.41 (1.24, 1.59)	1.38 (1.22, 1.57)	1.33 (1.16, 1.51)
PHQ>15	24	10.94	1.74 (1.16, 2.61)	1.70 (1.14, 2.56)	1.62 (1.07, 2.44)

Note: Model 1: adjusted by demographic factors (sex, age, urbanity, marital status, and education). Model 2: adjusted by behavioral factors (smoking status, alcohol intake, diet, physical activity, and sleep time) based on model 1. Model 3: adjusted by metabolic factors (BMI, blood pressure, lipids, and glucose) and history of diseases (myocardial infarction, stroke, chronic obstructive pulmonary disease, and cancer) based on model 2.

Abbreviation: PHQ=patient health questionnaire; HR=hazard ratio; CI=confidence interval.

and cardiovascular issues, implementing safety precautions is crucial for the prevention of accidental injuries.

This study is subject to some limitations. First, self-reported depression may introduce reporting bias. Second, using PHQ-9 for depression screening is less reliable than clinical diagnosis, though a PHQ-9 score

>15 showed 95% specificity in depression diagnosis (5). Third, the limited number of individuals with depression led to wide confidence intervals in some subgroups. Additionally, the survey lacked data on medication usage and genetic factors.

In conclusion, our study identified a direct correlation between depression and mortality rates.

TABLE 3. HRs and 95% CI for the risk of cause-specific mortality based on depression level, in comparison to individuals with no depression (PHQ≤5).

Cause	5<PHQ≤15	PHQ>15
Vascular	1.09 (0.94, 1.25)	1.71 (1.14, 2.55)
Cancer	1.12 (0.94, 1.34)	1.19 (0.63, 2.25)
Non-suicide injury	0.92 (0.58, 1.46)	3.23 (1.21, 8.60)
Suicide	1.03 (0.44, 2.37)	5.13 (1.15, 22.81)
Other	1.16 (0.98, 1.39)	1.84 (1.12, 3.01)

Note: HRs was adjusted by demographic factors (sex, age, urbanity, marital status and education), behavioral factors (smoking status, alcohol intake, diet, physical activity, and sleep time), metabolic factors (BMI, blood pressure, lipids and glucose) and history of diseases (myocardial infarct, stroke, chronic obstructive pulmonary disease and cancer).

Abbreviation: ASMR=age-standardized mortality rate; BMI=body mass index; PHQ=patient health questionnaire; HR=hazard ratio; CI=confidence interval.

This association was notably stronger among male individuals residing in urban areas, younger age groups, and those with higher education levels. Moreover, the impact was particularly significant concerning fatalities from injuries and cardiovascular conditions. Enhanced physical and psychological support should be prioritized for individuals with depression, with a heightened attention to those belonging to high-risk subgroups.

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