Systematic Review and Meta-Analysis

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Prevalence of and risk factors for anxiety after coronary heart disease

Systematic review and meta-analysis

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Abstract

Background: As the most important component of cardiovascular disease, coronary heart disease (CHD) is closely related to psychological factors such as anxiety. Anxiety, whether present before or after the onset of illness, can lead to many serious consequences. The aim of this systematic review and meta-analysis was to assess the prevalence of and potential risk factors for anxiety after coronary heart disease (post-CHD anxiety).

Method: Systematic searches were performed in electronic databases including China National Knowledge Infrastructure (CNKI), Wanfang, Technology Journal database (VIP), PubMed, Web of Science, Embase and Medline.

Result: Thirteen studies were included. With regard to cross-sectional studies, the prevalence of post-CHD anxiety was $P = .37$, 95% CI (0.26–0.49). The overall analysis among cohort studies revealed that the prevalence of post-CHD anxiety was $P = .50$, 95% CI (0.05–0.95). Among the 11 potential risk factors, low education level [OR = 1.46, 95% CI (1.05–2.02)] and long duration of disease [OR = 2.05, 95% CI (1.05–4.00)] were statistically significant.

Conclusion: There is high heterogeneity between studies and many defects; thus, further research is required to support these results. Attention should be paid to post-CHD anxiety, and clinical caring should include psychological counselling and imparting disease-related knowledge to patients with a long disease duration and low educational background.

Abbreviations: CHD = cardiovascular disease, CI = confidence interval, CNKI = China National Knowledge Infrastructure, OR = odds ratio, P-rate = the prevalence of post-CHD anxiety, RCT = randomized controlled trial, SE = standard error, VIP = Technology Journal Database.

Keywords: anxiety, coronary heart disease, meta-analysis, Risk factors

1. Introduction

The prevalence and mortality of cardiovascular diseases (CHDs) rank first among urban and rural residents in China with an increasing trend.[1] As the most important component of cardiovascular disease, CHD is closely related to psychological factors such as anxiety. Studies have shown that in patients with CHD, the prevalence of anxiety disorders is as high as 40% to 70%.[2,3] Anxiety, whether present before or after the onset of illness, can lead to limited physical function, decreased quality of life[4] and premature death of patients while increasing the cost of primary and secondary healthcare.[5] Therefore, the complexity and bidirectionality of the causal relationship between psychological factors and CHD are gaining increasing attention.

Post-CHD anxiety means that anxiety occurs after the onset of coronary heart disease. CHD patients might be vulnerable to anxiety for many reasons. For example, some studies[6,7] have found that women with CHD are more likely to experience anxiety than men, whereas other studies have found no significant gender difference in anxiety.[8] Given the various mechanisms and hypotheses of the interaction between CHD and anxiety, we have summarized the following potential risk factors.

1.1. Female

Gender differences in anxiety among patients with CHD have been reported. Females are more likely to experience anxiety.[9] Olsen et al reported that the risk of anxiety and mood disorders is significantly higher in females than in males.[7]

1.2. Low education

Low education classifies an individual who has not finished or has finished only the 9-year obligatory education. Some studies have

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found that low education is associated with more frequent depression and anxiety.[10] Therefore, we assume that education affects the psychology and mood of patients by influencing the cognitive level of their disease.

1.3. Single

Single refers to individuals who are unmarried, divorced, separated or widowed. One study[11] showed that a higher level of perceived social support in individuals with CHD was associated with lower levels of depressive symptoms and anxiety. In addition, a previous study[12] performed in the Netherlands showed that the absence of a partner exacerbated the risk of anxiety and depression symptoms in already distressed Type D patients. However, we believe that married status may be a risk factor for post-CHD anxiety.

1.4. High hospitalization costs

Liu[13] found that individuals who spent more money on CHD treatment were inclined to think that the disease was more serious, leading to negative emotions such as anxiety or depression. Furthermore, the high cost of CHD after onset increases economic pressure in self-paying patients, who are apt to experience a distressed emotional state.[14] However, the negative emotions of patients with CHD can be alleviated by a medical insurance policy.[15] Therefore, we take economic factors into account.

1.5. Smoking and alcohol consumption

Previous studies[10,16] have shown that in men and women, anxiety scores are directly related to smoking, which moderates the sensitivity to anxiety. Wolitzky-Taylor et al found that patients with alcohol problems can be effectively treated for anxiety disorders in primary care.[17] It seems that alcohol use can be conducive to easing anxiety. Further evidence[18] suggests that alcohol consumption in combination with cigarette smoking reduces anxiety.

1.6. Hypertension and diabetes

Evidence[19,20] shows that anxiety sensitivity is linked to cardiovascular disease and adverse cardiovascular health behaviours. One study found that sympathetic overactivity may be a contributing factor to the development of diabetes,[21] and sympathetic overactivity has been strongly associated with anxiety disorders.[22,23] Therefore, we hypothesize that there is a potential correlation between anxiety and hypertension and diabetes.

1.7. Previous myocardial infarction

There are some studies[24] of the relationship of previous myocardial infarction (MI) and post-CHD anxiety. One of these studies reported that the death anxiety level was affected by a history of hospitalization for CHD.

1.8. Long duration of CHD

Regarding the interval between the first diagnosis of CHD and its treatment, recent studies[25,26] on chronic diseases in China have found a positive correlation between the mental health status score and the length of illness.

1.9. Severity of coronary atherosclerosis

The number of blocked or narrow coronary arteries was evaluated. There was a positive correlation between the incidence of coronary artery disease and postoperative anxiety, and this correlation was more obvious 6 to 9 months after surgery.[27] We hypothesize that patients with severe coronary artery disease are likely to think that the disease is serious, resulting in increased anxiety.

With this background information in mind, our first step was to evaluate the overall prevalence of anxiety in Chinese adults with CHD before planning treatment provision. Second, the risk factors for anxiety after CHD were investigated for reference in clinical work.

This review consists of three sections: *Part 1)* Incidence of cross-sectional studies; *Part 2)* Incidence of cohort studies, and *Part 3)* Analysis of potential risk factors.

2. Methods

2.1. Ethics approval

Because all of the data used in this systematic review and meta-analysis has been published, this review does not require ethical approval. Furthermore, all data will be analyzed anonymously during the review process Trial.

2.2. Search strategy

This meta-analysis was conducted, analyzed and written in accordance with the requirements of the MOOSE statement. A protocol has not been published. A systematic search of the China National Knowledge Internet (CNKI), Wanfang database, Technology Journal database (VIP), PubMed, Web of Knowledge, and Embase and Medline databases was performed to obtain the global prevalence data for post-CHD anxiety (search date: 2018.6.8; update: 2018.11.26). See supplementary table 1, http://links.lww.com/MD/D206, which lists the appropriately keywords used in different databases: coronary heart disease/CHD, anxiety, and risk factor* (there is no "risk factor" in the English database retrieval strategy to expand the retrieval scope). The results were limited to human studies published in English and Chinese. No limitations were set for the year of publication.

2.3. Study eligibility

2.3.1. Population. The population included adult (18 years and older) participants with verified CHD from the clinical or general population. The inclusion criteria were CHD, including myocardial infarction, unstable angina or acute-coronary syndrome, and angina due to verified coronary artery disease; previous percutaneous coronary intervention or coronary artery bypass grafting; and diagnosis by a physician or cardiologist.

2.3.2. Exclusions.

1. Republished data, incomplete data or unavailable full text;
2. appearance of anxiety symptoms before CHD;
3. patients with other diseases, such as cerebrovascular disease and pulmonary disease;

4. literature with unclear exposure factors or existing interventions without available baseline data on prevalence rates of anxiety; and
5. studies in which the included patients were not from mainland China.

2.4. Study selection and data extraction process

The eligibility of studies was independently determined by 2 reviewers using the aforementioned search strategy. Data and information (the name of the first author, year of publication, study design, participant demographics and diagnoses, questionnaires or tools used for evaluation, outcome measures, outcomes and exposures) were extracted separately. If there was disagreement between the reviewers regarding a study's eligibility and data extraction, a third reviewer was consulted.

2.5. Study quality and risk of bias

The methodological quality of cross-sectional studies was evaluated using the Newcastle-Ottawa quality assessment scale (NOS),[28,29] which gives a score out of a possible total of 9 stars. Studies with a score higher than 6 were classified as high- or medium-quality studies, while studies with a score lower than 6 were classified as low-quality studies. Each reviewer independently rated the studies individually. Again, disagreement between the reviewers was resolved by a third reviewer.

2.6. Data synthesis and analysis

2.6.1. Primary outcome. The prevalence of anxiety (P-rate) and the confidence interval (CI) of the prevalence rates of anxiety disorders were extracted where reported. We used random-effects models to calculate the summary P-rate and 95% CIs associated with exposure. If not reported, the SE was calculated using $SE = \frac{\sqrt{p \times (1-p)}}{N}$, where P is the proportion of cases and N is the denominator.[30]

The rate was converted to log, logit, arcsine and Freeman-Tukey Double arcsine[31] using the Shapiro-Wilk test[32] to verify that the distribution of the rate was normal. Then, the most appropriate transformation method to calculate the effect size was chosen (ESp).

The heterogeneity test was conducted by Cochran's Q statistic, and the I^2 test was used to conduct a chi-square-based test (P value less than .05 indicates heterogeneity). Subgroup analysis and meta-regression analysis were conducted based on the potential confounding factors of heterogeneity.

A mixed-effects meta-regression model for identifying sources of heterogeneity in the prevalence of anxiety was developed through an iterative process of model building and testing. Univariate and multivariate models were calculated for potential confounding factors. Inter-study variance (τ^2) was estimated using the residual maximum likelihood (REML) method to produce an adjusted R^2 statistic.

2.6.2. Secondary outcome. For studies from which data on the total and positive patients in the exposed and control groups could be extracted, the OR and SE were calculated using the Miettinen method. The OR and CI of the prevalence rates of anxiety disorders were extracted where reported.

The leave-one-out approach was used to perform the sensitivity analysis for the outcomes of the clinical trial. Egger and Begg tests for outcome were used to assess publication bias as well as to calculate the fail-safe number.

2.7. Potential confounding factors

By reading the included literature and analyzing the relevant literature, we made the prior assumption that methodological factors and clinical demographic characteristics may be confounding factors leading to heterogeneity.

2.7.1. Methodological factors.

(1) *Coverage:* Coverage describes the geographical scope covered by the study and was categorized as 'national' or 'regional' (e.g., based on a state or province).
(2) *Sample size:* The categories for sample size were dichotomized into studies 'below the median' ($n < 216$) and 'median or greater' ($n \geq 216$).
(3) *Length:* Based on the time intervals between treatment of CHD by a specialist and data collection, studies were defined as 'long term' (>3 months) and 'short term' (<3 months).
(4) *Survey instruments:* Our classification of survey instruments was partly conceptual, e.g., 'SAS'/'BAI'/'HAMA'/'HAD-A'.
(5) *NOS score* The NOS score was dichotomized into '<6' and '≥ 6'.

2.7.2. Demographic factors.

(1) *Geographical location*. Geographical location describes the geographical region in which the patients were recruited and was categorized as 'north' (large area north of the Qinling-Huaihe line) and 'south' (large area south of the Qinling-Huaihe line).
(2) *Percentage*. The percentage of patients undergoing coronary therapy (e.g., PCI, coronary artery bypass grafting) from the total number of participants in a study was categorized as 'none' (100%), 'partly' (<100%), 'all' (100%) and 'unclear' (not described).

3. Results

3.1. Search results

The PRISMA flow chart describing study selection and inclusion is shown in Fig. 1. The initial search resulted in 1095 articles. After excluding duplicate titles and abstracts and screening the full text, 13 articles[33–45] met the inclusion criteria and were included in the review.

3.2. Study characteristics

Table 1 presents the characteristics of the included articles. The sample included 5794 patients with CHD from mainland China. Sample sizes ranged from 91 to 1144, with a median of 216.1839 patients diagnosed with anxiety symptoms 2–180 days after receiving a diagnosis of CHD. All potential exposures were reported. The patient population consisted of 2085 females (36.0%) and 3709 males (64.0%). To avoid the co-promotion effect of depression and anxiety, we considered the depression group as the non-exposure group.

Regarding potential risk factors for post-CHD anxiety, we extracted 11 factors from the following included studies: gender information was extracted from 9 studies;[33–36,38,39,41,44,45]

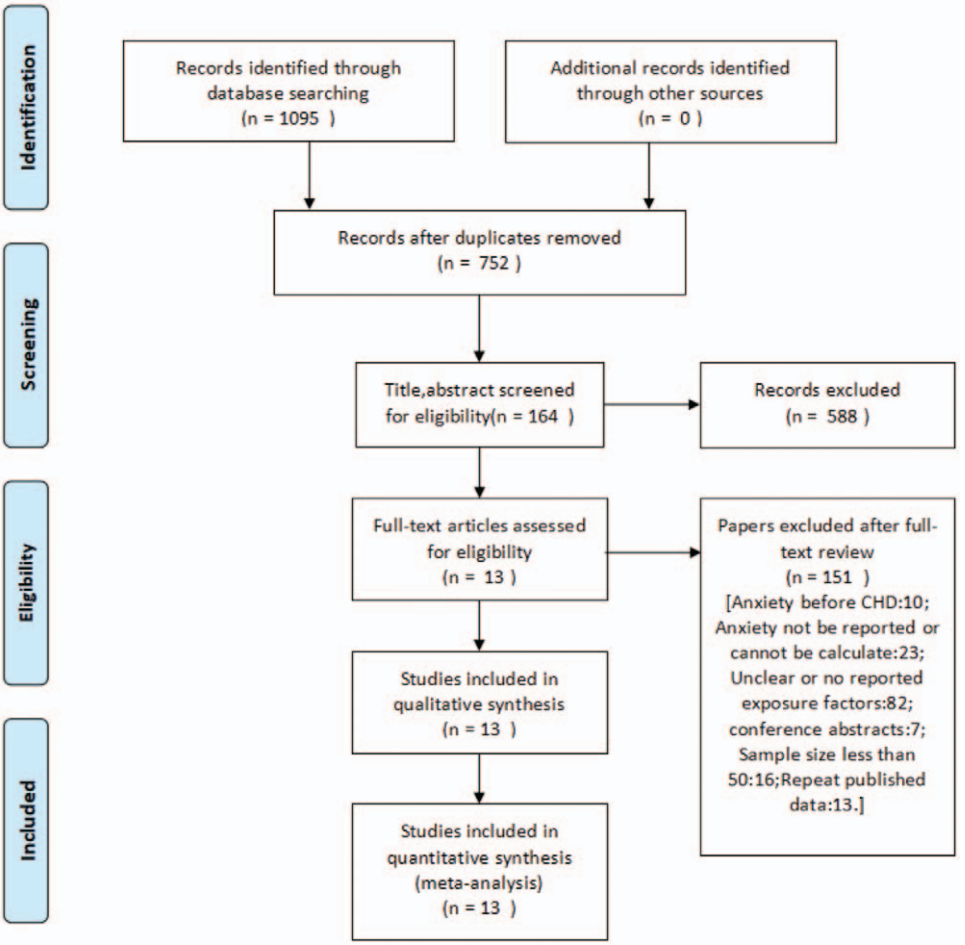

Figure 1. PRISMA flow chart of article selection. A: Illustration of how eligible articles were selected. B: The initial search resulted in 1095 articles. After excluding duplicate titles and abstracts and screening the full text, 13 articles met the inclusion criteria and were included in the review.

Table 1

Summary of study design and study characteristics.

Study	Publication Year	Study Design	Coverage	Control	Information collection	Tool	Rate of anxiety (positive/Total)	Factors recorded for exposure
Deng[43]	2010	Cross-sectional	Regional	Negative anxiety diagnosis	Hospital (Within 2d of postoperative)	SAS	240/1083	2
Fu[40]	2006	Cross-sectional	National	Negative anxiety diagnosis	Hospital	HAD-A	22/359	2
Guo[33]	2012	Cohort study	Regional	Negative anxiety diagnosis	Hospital	HAMA	177/216	1,2,3,5,6,7,9,11
Li[41]	2008	Cross-sectional	Regional	Negative anxiety diagnosis	Hospital	HAD-A	195/647	1,5,6,7,
Liang[36]	2012	Cross-sectional	National	Negative anxiety diagnosis	Home	SAS	381/1144	1,2,10
Wang [34]	2013	Cohort study	Regional	Negative anxiety diagnosis	Hospital (Within 2d of postoperative)	SAS	187/1007	1,2,3,5,6,7,8,11
Wang[45]	2018	Cross-sectional	Regional	Negative anxiety diagnosis	Outpatient Center or telephone (180d of postoperative)	HAMA	65/120	1,2,5,6,7,9,11,
Xia[35]	2013	Cross-sectional	Regional	Negative anxiety diagnosis	Hospital	SAS	354/521	1,2,3,4,5,6,10
Xue[44]	2018	Cross-sectional	Regional	Depression diagnosis+ Comorbid anxiety and depression	Hospital	HAD-A	68/200	1,2,4,5,6,
Zhang[37]	2011	Cross-sectional	Regional	Negative anxiety diagnosis	Hospital	BAI	51/100	2,5,6,7,9,
Zhang[38]	2012	Cross-sectional	Regional	Negative anxiety diagnosis	CCU	SAS	42/91	1,2,3,5,6,7,8,
Zhou[42]	2015	Cross-sectional	Regional	Negative anxiety diagnosis	Outpatient Center or telephone (12m of postoperative)	HAD-A	29/170	7,8
Zhu[39]	2017	Cross-sectional	Regional	Negative anxiety diagnosis	Hospital	SAS	91/136	1,2,4,9,10

Note: 1, Female; 2, Low education level; 3, Single; 4, High hospitalization costs; 5, hypertension; 6, diabetes mellitus; 7, smoking; 8, alcohol consumption; 9, Severity of coronary atherosclerosis; 10, Long duration of CHD; 11, Previous myocardial infarction.

Table 2

Quality assessment of cross-sectional studies.

	Selection				Comparability	Outcome		
Study	1	2	3	4	1	1	2	Total
Deng	☆	☆		☆☆		☆	☆	6☆
Fu	☆	☆		☆☆		☆	☆	6☆
Li	☆	☆			☆	☆	☆	5☆
Liang	☆	☆		☆☆		☆	☆	6☆
Wang	☆	☆		☆☆	☆	☆	☆	7☆
Xia	☆			☆☆	☆	☆	☆	6☆
Xue	☆	☆		☆☆		☆	☆	6☆
Zhang	☆	☆		☆☆	☆	☆	☆	7☆
Zhang	☆	☆		☆☆		☆	☆	6☆
Zhou	☆	☆		☆☆	☆	☆	☆	7☆
Zhu	☆	☆		☆☆		☆	☆	6☆

11 studies[33–40,43–45] mentioned education level; patients with hypertension and diabetes mellitus were obtained from 8 studies;[33–35,37,38,41,44,45] 7 studies[33,34,37,38,41,42,45] reported on smoking; 4 studies[22,33,34,38] reported on living alone; 4 studies[33,37,39,45] reported on the severity of coronary atherosclerosis; and 3 studies mentioned 'hospitalization costs',[35,39,44] 'drunk',[34,38,42] 'previous myocardial infarction',[33,34,45] or 'long duration of CHD'.[35,36,39]

3.3. Quality assessment

Risks of bias analyses were performed using NOS. Tables 2 and 3 show the quality evaluation results. The supplemental table S2a, http://links.lww.com/MD/D206 and S2b, http://links.lww.com/MD/D206, represents the assessed outcomes for the 13 included studies.

3.4. Prevalence of anxiety

Because both cross-sectional and cohort studies are included, we will discuss the incidence rates separately.

After conversion and conducting the Shapiro-Wilk normal test for the 13 included studies, the Freeman-Tukey double arcsine conversion was selected to treat the incidence of P-rate. The fixed-effects model and random-effects model were selected for the combination and heterogeneous Q tests, respectively (Fig. 2A and B). The figure shows the pooled prevalence incidence rate for persons with anxiety.

The I^2 was 98% and 100%, respectively, and there was large heterogeneity. Considering the diversity of clinical practice and methodology in the study, the effect size (ESp) was analyzed by subgroup analysis and sensitivity analysis using the random-effects model, and the data were analyzed by regression analysis using the mixed-effects model.

3.4.1. Part 1. Cross-sectional study

3.4.1.1. Tendency to change. In a cross-sectional study, the prevalence of post-CHD anxiety was between 0.06 and 0.67 between 2006 and 2018, with the highest incidence in 2013 [P-rate = 0.68, 95% CI (0.64–0.72)] and the lowest in 2010 [P-rate = 0.06, 95% CI (0.04–0.09)]. There was no characteristic change in morbidity. There was large heterogeneity of each year (2012: 95%, 2018: 0.92%, I^2 could not be calculated for other year groups).

With regard to the cross-sectional studies, the prevalence of post-CHD anxiety was P-rate = 0.37, 95% CI (0.26–0.49), and I^2 was 98%. We will analyze the sources of heterogeneity based on the following aspects according to the prior hypothesis.

3.4.1.2. Potential confounding factors. A subgroup analysis of 7 potential regulatory variables was unable to determine the source of heterogeneity. The internal heterogeneity of different subgroups was large ($I^2 > 80\%$) (Fig. 3). The data results for each subgroup analysis are shown in Supplemental table S3, http://links.lww.com/MD/D206. The above variables were taken as covariables, and the p-value was included in the univariate mixed regression model as the dependent variable (Table 4). The regression models of *Coverage*, *Survey instruments, Percentage of PCI* and *Geographical location* were statistically significant. Of the potential confounding factors, survey instruments and percentage explained the greatest variance in estimates [1.1%, 19.0%, 52.9% and 37.9%, respectively]. Taking the above 4 variables as covariables in the multivariable mixed regression model fitting (Table 5), the variance between studies was 0.67, and the heterogeneity reduced from 98% to 96.6%. The heterogeneity may be related to the above four aspects, but not all sources of heterogeneity were fully explained.

3.4.2. Part 2. Cohort study.

The overall analysis among cohort studies revealed that the prevalence of post-CHD anxiety was P-rate = 0.50, 95% CI (0.05–0.95), and I^2 was 100%. As only 2 articles were included, the source of heterogeneity and the characteristics of prevalence could not be further analysed.

Table 3

Quality assessment of cohort studies.

	Selection				Comparability	Outcome			
Study	1	2	3	4	1	1	2	3	Total
Guo	☆	☆	☆	☆	☆				5☆
Wang	☆	☆	☆	☆	☆		☆	☆	7☆

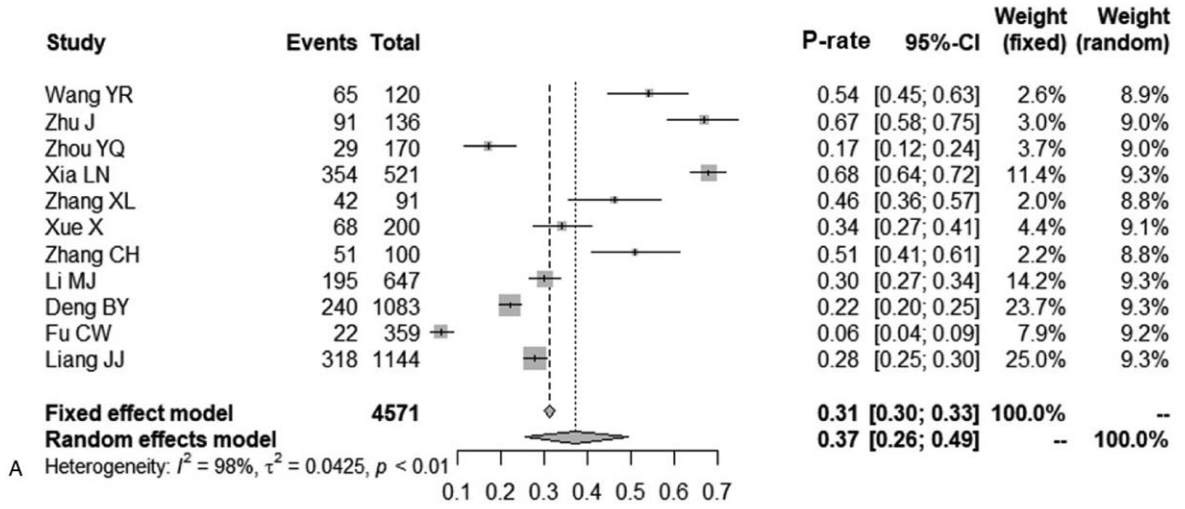

Figure 2. A: Prevalence of post-CHD anxiety rate (Fixed and random-effects) in cross-sectional study. A: Figure showing the pooled prevalence incidence rate for persons with an anxiety. B: The prevalence incidence rate of the included cross-sectional studies were combined using a fixed effect model and a random effect model, and the results showed considerable heterogeneity. The pooled prevalence incidence was 37%. B: Prevalence of post-CHD anxiety rate (Fixed and random-effects) in cohort study. A: Figure showing the pooled prevalence incidence rate for persons with an anxiety. B: The prevalence incidence rate of the included cohort studies were combined using a fixed effect model and a random effect model, and the results showed considerable heterogeneity. The pooled prevalence incidence was 50%.

Subgroup	Term	Case	P-rate(95%CI)	Heterogeneity test I-squared	P-value
Coverage	National	2	0.14(0.03,0.48)	98%	<0.01
	Regional	9	0.42(0.29,0.57)	98%	<0.01
Median	Lower	6	0.44(0.30,0.59)	94%	<0.01
	Median or greater	5	0.27(0.15,0.45)	99%	<0.01
Information collection	Short term	9	0.37 (0.21,0.64)	99%	<0.01
	Long term	2	0.21(0.17,0.50)	96%	<0.01
Tool	HAMA	1	0.54 (0.45,0.63)	-	<0.01
	SAS	5	0.45(0.26,0.66)	99%	<0.01
	HAD-A	4	0.19 (0.10,0.34)	96%	<0.01
	BAI	1	0.51 (0.41,0.61)	-	<0.01
Percentage of PCI	0	1	0.51 (0.41,0.61)	-	<0.01
	<100%	2	0.62(0.48,0.75)	88%	<0.01
	100%	3	0.42 (0.16,0.73)	97%	<0.01
	N.A	5	0.22 (0.16,0.30)	95%	<0.01
Location	North	6	0.50 (0.34,0.66)	96%	<0.01
	South	3	0.28(0.22,0.36)	90%	<0.01
	N.A	2	0.14(0.03,0.48)	98%	<0.01
NOS	<6*	1	0.30(0.27,0.34)	-	<0.01
	≥6*	10	0.36(0.24,0.51)	98%	<0.01
Total	-	11	0.37(0.26,0.49)	98%	<0.01

Figure 3. The forest plot of prevalence of anxiety in subgroup analysis (Cross-sectional study). A: Figure shows 7 subgroup analyses of cross-sectional studies. B: After subgroup analysis of 7 potential moderating variables, the heterogeneity was still large, and the source could not be determined clearly ($I^2 > 80\%$).

Table 4

Univariate mixed regression model univariate associations between Potential confounding factors and disorder prevalence (Cross-sectional study).

Covariate	Term	Case	Unadjusted ES (95%CI)	R^2	I^2	τ^2	*P* value
Coverage	National	2	1.50 (0.08, 2.93)	0.00%	98.0%	0.70	.04
	Regional	9	−1.81 (−3.11, −0.53)				
Sample size	Lower	6	0.74 (−1.73, 0.29)	0.00%	98.1%	–	.15
	Median or greater	5	−0.98 (−0.72, 1.76)				
Length	Short term	8	0.27 (−0.99, 1.54)	0.00%	98.2%	–	.67
	Long term	3	−0.78 (−1.87, 0.29)				
Survey instruments	HAMA	2	0.80 (0.36, 2.96)	9.24%	98.3%	0.57	.01
	SAS	6	−0.45 (−2.35, 1.45)				
	HAD-A	4	−1.48 (−3.45, 0.49)				
	BAI	1	0.04 (−1.73, 1.81)				
Percentage	=0%	1	−0.11 (−0.47, 0.26)	55.02%	96.6%	0.33	.01
	<100%	2	0.90 (0.70, 0.11)				
	=100%	3	−0.08 (−0.34, 0.17)				
	N.A	5	−0.41 (−0.65, −0.17)				
Geographical location	North	6	1.80 (0.70, 2.89)	37.49%	96.0%	0.44	.03
	South	3	0.88 (−0.34, 2.09)				
	N.A	2	0.40 (0.12, 0.69)				
NOS score	<6*	1	0.27 (−1.65, 2.21)	0.00%	98.3%	–	.77
	≥6*	10	−0.84 (−2.67, 0.99)				

Note: -The variance is analyzed only if the model makes sense.

3.4.3. Part 3. Potential risk factors for post-CHD anxiety. A total of 11 potential risk factors included in 13 studies were combined in the effect volume OR value and confidence interval. The results showed that among 11 exposure factors, only the factors of low education [OR = 1.46, 95% CI (1.05–2.02)] and long duration of CHD [OR = 2.05, 95% CI (1.05–4.00)] were

Table 5

Multivariate mixed regression model multivariate associations between potential confounding factors and disorder prevalence (Cross-sectional study).

Covariate	Term	Case	Unadjusted ES (95%CI)	*P* value	R^2	τ^2	I^2
Survey instruments	HAMA	1	0.60 (0.21, 0.92)	.02	29.65%	0.66	96.6%
	SAS	5	−0.17 (−0.18, 0.52)	.35			
	HAD-A	4	−1.50 (−3.70, 0.69)	.59			
	BAI	1	(Reference)	–			
Percentage	=0%	1	(Reference)	–			
	<100%	2	0.49 (−0.03, 0.95)	.04			
	=100%	3	−0.10 (−0.34,0.41)	.45			
	N.A	5	−0.38 (−0.70, 0.06)	.02			
Geographical location	North	6	0.38 (−1.77, 2.49)	.51			
	South	3	0.82 (−0.06, 2.26)	.25			
	N.A	2	(Reference)	–			
Coverage	National	2	(Reference)	–			
	Regional	9	0.62 (−0.62, 1.86)	.72			

Table 6

Potential risk factors of post-CHD anxiety.

Risk Factors	Case	ES (95%CI)	I^2	τ^2	Z test (P-value)	fail-Safe Number (*P* < .05)
Female	9	1.55 (0.31, 7.86)	99.1%	–	0.60	105.77
Low Education	11	1.46 (1.05, 2.02)	63.1%	0.16	0.02	188.77
Single	4	0.35 (0.01, 9.29)	98.4%	–	0.53	6.76
Hypertension	8	1.55 (0.31, 7.86)	99.1%	–	0.60	33.90
Diabetes mellitus	8	0.61 (0.19, 2.01)	69.3%	–	0.42	−0.25
High hospitalization costs	3	0.12 (0.67, 1.57)	94.3%	–	0.89	−2.12
smoking	7	1.25 (0.30, 5.30)	97.4%	–	0.76	25.12
alcohol consumption	3	0.25 (0.05, 1.33)	94.6%	–	0.14	−1.67
Severity of coronary atherosclerosis	4	1.08 (0.62, 1.54)	98.3%	–	0.56	−0.84
Long duration of CHD	3	2.05 (1.05, 4.00)	87.3%	0.29	0.03	55.78
Previous myocardial infarction	3	0.27 (0.04, 1.83)	92.7%	–	0.18	−0.58

Note: Only the factors with significant differences were analyzed for variance.

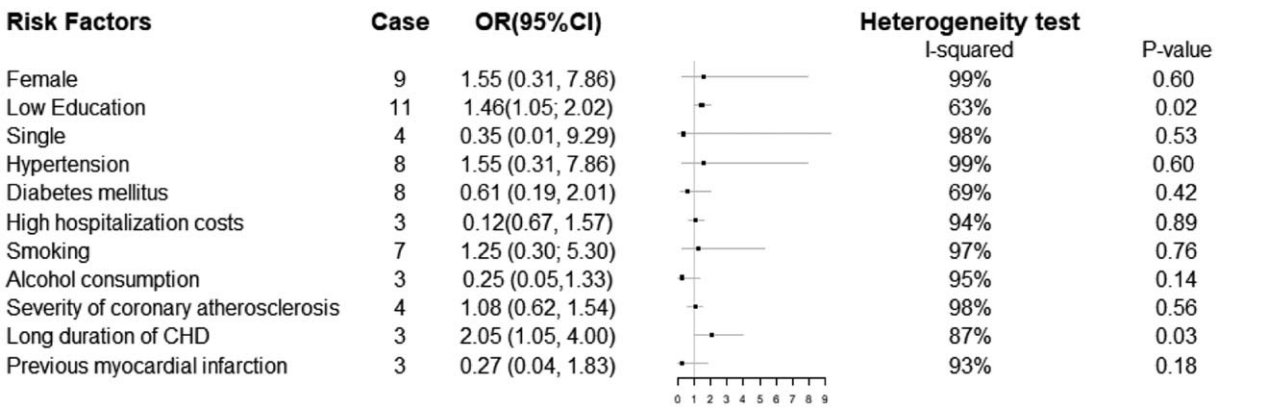

Figure 4. The forest plot of potential risk factors of post-CHD anxiety (Odds Ratio value). A: A total of 11 potential risk factors included in 13 studies were combined in the effect volume OR value and confidence interval. B: The results showed that among 11 exposure factors, only the factors of low education [OR = 1.46, 95% CI (1.05–2.02)] and long duration of CHD [OR = 2.05, 95% CI (1.05–4.00)] were statistically significant. The heterogeneity was 63.1% and 87.3%, respectively.

statistically significant. The heterogeneity was 63.1% and 87.3%, respectively (Table 6, Fig. 4).

To explore the clinical heterogeneity between the primary studies, we conducted subgroup analyses. The methodological and demographic factors of the above 2 factors were analyzed in subgroups. 1.) The factors for low education level in each subgroup analysis, heterogeneity were all decreased to different degrees; therefore, the interference factors could be affected by various confounding factors. 2.) Subgroup analysis of a long duration of CHD did not reveal a significant decline in the study of the disease in groups due to insufficient inclusion in this study. The supplemental table S4, http://links.lww.com/MD/D206, represents the data results of the above analysis. Similarly, due to the small number of primary studies, statistical procedures such as subgroup analyses did not seem to be meaningful.

3.4.4. Publication bias assessment. Both Egger linear regression test and Begg and Mazumdar's rank correlation test reported non-significant results [Egger $P = .14$, Begg $P = .32$]. Due to insufficient literature, the risk factors were tested by calculating the fail-safe number, which indicates the risk factors for diabetes, alcohol consumption, high hospitalization costs, severity of coronary atherosclerosis, and previous myocardial infarction. The fail-safe number of the severity of coronary atherosclerosis was less than 0. In addition, the publication bias of all other factors was greater than the number of included studies (N = 13); thus, publication bias was small.

3.4.5. Sensitivity analysis. There was no significant change in the results of the cross-sectional studies combined effect after removing the included studies via the leave-one-out approach (Fig. 5A). However, the sensitivity analysis results of the cohort study showed that the combined effect size changed significantly (Fig. 5B).

4. Discussion

This systematic review examined the prevalence of post-CHD anxiety in individuals from mainland China with a meta-analysis of published studies. After the evaluation of conference papers, randomized control trials, case-control studies and cross-sectional studies, only 11 cross-sectional studies and 2 cohort studies were included.

First, we evaluated the study quality using the NOS. Only 4 studies[34,37,42,45] were classified as high quality; the medium-quality[35,36,38–40,43,44] and low-quality studies[33,41] exhibited bias mainly due to the choice of cases and potential bias in the control group. Only 1 study[41] controlled for confounding factors, and uncontrolled confounding factors could have masked or exaggerated the association between potential risk factors and post-CHD anxiety. In addition, there was a lack of description of the response rate of the exposed group and the non-exposed group. If the response rate was low, the bias of the results was enhanced, and the representativeness was diminished. The quality assessment highlighted some shortcomings in the research methods, so the internal effectiveness of the research was weakened.

Regarding methodology, although we attempted to make the criteria as strict as possible to reduce heterogeneity, the heterogeneity was still high, so the conclusions should be considered carefully. First, although all the included studies were conducted in hospitals in mainland China, due to geographical and institutional reasons, the study adopted a variety of diagnostic methods for patients with CHD and did not elaborate on the treatment methods adopted by patients. To a certain extent, this could affect the occurrence of anxiety. Second, during or after hospitalization, the patients' life events were not controlled and recorded, which could greatly influence the results of the study. In addition, due to the absence of original literature, we could not assess the age of the exposure group or the age of the non-exposure group. Therefore, analysis of various age groups was not possible, potentially leading to a certain degree of heterogeneity.

4.1. Prevalence of anxiety

The prevalence of psychiatric comorbidity observed in this study was 36.0% (50% in cohort studies). Several studies reported a different prevalence of post-CHD anxiety in China.[2,46,47] Ji et al[46] reported a prevalence of post-CHD anxiety of 23.0%, while Gu et al.[2] reported a prevalence of 54.7% in male and female patients in Hebei with a mean age of 58 years. Ying et al[47] reported a prevalence of 43.2% in male and female patients with a mean age of 68.8 ± 10.9 years. The differences between the prevalence of anxiety among studies might be due to

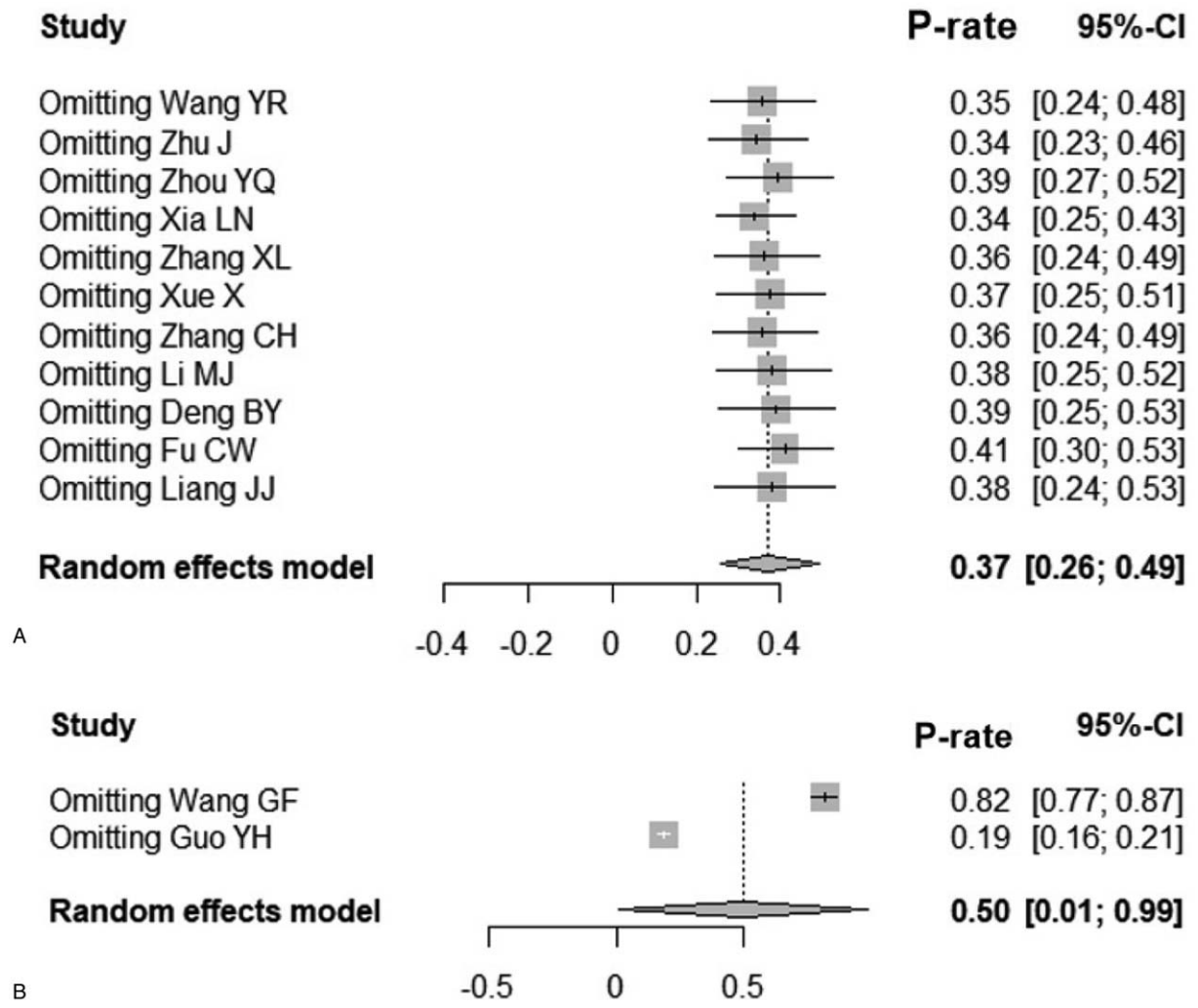

Figure 5. A. Sensitivity analysis of the prevalence of post-CHD anxiety (Cross-sectional studies). A: The leave-one-out approach was used to perform the sensitivity analysis for the outcomes of the cross-sectional studies. B: There was no significant change in the results of the cross-sectional studies combined effect after removing the included studie. B. Sensitivity analysis of the prevalence of post-CHD anxiety (Cohort studies). A: The leave-one-out approach was used to perform the sensitivity analysis for the outcomes of the cohort studies. B: The sensitivity analysis results of the cohort study showed that the combined effect size changed significantly.

geographic regions or the subjects' gender. There was great heterogeneity in the amount of combined effects [$I^2 = 98\%$]. After univariate and multivariate meta-regression, possible sources of methodological heterogeneity, namely, the differences in survey instruments and the number of patients treated, were found. However, these factors did not fully explain all the sources of heterogeneity.

4.1.1. Survey instruments. In terms of the survey instruments, the Hamilton anxiety scale[33,45] was most commonly used [P-rate = 0.54 95%CI (0.45–0.63)]. However, the Hamilton anxiety scale cannot diagnose the presence of anxiety concomitant with other pathologies or problems,[48] so the reality and reliability of the reported incidence is uncertain. The incidence rate was lowest in the HAD-A subgroup. From the perspective of sociology, three of the 4 studies were conducted in economically developed cities in the south. Missed diagnosis may have occurred because the Hospital Anxiety and Depression Scale (HADS) does not include all of the diagnostic criteria for depression.[4]

4.1.2. Percentage. Differences in the number of PCI therapy patients included in the study may have resulted in differences in morbidity. Previous studies have shown that patients with PCI have a higher risk of anxiety, which is associated with relatively high costs,[49] fears of surgery, uncertainty about the illness, death, pain, unfavourable clinical findings and lying flat in bed.[50] However, in this study, the incidence of anxiety after CHD onset was lower when all subgroups[51] were treated with PCI than when only some subgroups[35,45] were treated with PCI [P-rate = 0.42 (0.16–0.73); P-rate = 0.62 (0.48–0.75), respectively] (Appendix 3). The differences are likely related to the economic development level of the region in which the study was conducted. Both studies were located in the outlying areas of northern China. Compared with those in inland areas, the economy is less developed, the health care system is not yet sound, and patients have limited access to effective economic and medical support in the outlying areas. Thus, there is a high risk of anxiety after the onset of CHD in patients from the outlying areas of northern China.

4.2. Potential risk factors for post-CHD anxiety

In this study, 11 potential risk factors were included in the random-effects model. Education level and the course of disease were identified as possible risk factors, while the other 9 combined OR values were not statistically significant. The probable causes and credibility of the results are as follows.

4.2.1. Low education. According to the statistical analysis, low education was considered a possible risk factor [OR = 1.46, 95% CI (1.05–2.02)]. The results suggest that the lower the level of education, the higher the likelihood of anxiety. A high level of education can correlate to a certain extent with high social status and good economic income, which may alleviate some anxiety.[35,45] In addition, more-educated patients are better at finding effective social support than less-educated patients, and their understanding of diseases may be more objective, thus preventing negative emotions.[25] The fail-safe number is 188.77, and the probability of publication bias is small. There is a high degree of heterogeneity, and the source of heterogeneity could not be determined after subgroup analysis due to the lack of studies. Thus, although we consider low education a possible risk factor, this conclusion should be considered with caution.

4.2.2. Long duration of CHD. In this review, a long duration of CHD was a possible risk factor for anxiety after CHD [OR = 2.05, 95% CI (1.05–4.00)]. The fail-safe number was 55.78, suggesting that there was a low possibility of publication bias. However, subgroup analysis did not reveal the source of heterogeneity. In a related study, Luo et al[25] found that patients with CHD needed to take expensive drugs for a long time, and economic pressure may lead to an increased incidence of anxiety and depression in patients with CHD compared with those without CHD. Other studies of elderly patients with CHD have found that the risk of anxiety in patients with CHD gradually increased with the extension of the disease course, which may be related to the long-term risk of complications and the poor physical condition of patients with short disease durations.[5] Therefore, it is reasonable to consider a long duration of CHD as a risk factor.

There was insufficient evidence to suggest that other potential risk factors were statistically significant as there were years of medical progression and a change in the health care system and labor market. These factors may have resulted in inconsistent findings.

Some positive results can be explained by demographic factors. Some evidence shows that the incidence of anxiety is related to drinking and smoking,[26] but after controlling for demographic factors, the presence of a lifetime of anxiety disorders was not significantly associated with an increased risk of CHD. Furthermore, the small number of recruited patients in some studies[38] (particularly the number of women[34]) could have caused the relationship between females and post-CHD anxiety to be not statistically significant. In addition, as some young participants were included in the present study,[1] symptoms of anxiety after CHD may not have been adequately detected.

Some studies have found that patients who have experienced an MI display a similar increase in cortisol after awakening compared to patients without previous myocardial infarction. However, the total level of cortisol output is significantly lower in patients without previous myocardial infarction, so cortisol could be a predictor of anxiety in CHD patients.[52] However, this study did not find a significant correlation. Because most studies did not focus on the effect of previous myocardial infarction on post-CHD anxiety and relevant data were not reported, the relationship may have been partially obscured.

Several study limitations must be considered in the interpretation of our findings. First, this study did not take into account other potential confounding factors, such as religious beliefs[53] and self-esteem levels,[53] which may influence anxiety after CHD. Second, only one study analyzed changes in the trend of anxiety; the rest were cross-sectional studies or short-term case-control studies limited to time points or short periods. Therefore, more longitudinal studies are needed to analyze the changes and influencing factors of anxiety after CHD. Third, because the diagnosis of anxiety in the included studies was obtained based on the self-reports of patients, there may be deviations in the diagnoses. In addition, most studies did not record the follow-up methods for patients, and different follow-up environments may influence the measures of anxiety.[54]

5. Conclusion

Within the limits of this study, it can be concluded that the prevalence of post-CHD anxiety in mainland China is 38%, and low education levels and long duration of disease are potential risk factors. This type of research has many deficiencies with regard to sample selection, research design and control of confounding factors, which will be improved in future studies. In addition, due to the lack of long-term and continuous studies, it is impossible to determine the dynamic changes of morbidity and the strength of correlations between some risk factors. Future research should focus on longitudinal studies of morbidity and direct studies of risk factors.

Regarding risk factors for post-CHD anxiety, clinical care should include psychological counselling and imparting disease-related knowledge to patients with a long disease duration and low educational background.

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