

# A meta-analysis of emotional disorders as possible risk factors for chronic periodontitis

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## Abstract

The aim of the present meta-analysis was to evaluate scientific evidence on the association between emotional disorder (depression and anxiety) and chronic periodontitis. An overall electronic literature search in PubMed, ISI Web of Science, Cochrane Library, and China National Knowledge Infrastructure was undertaken up to November 2017. Newcastle–Ottawa scale was applied to ascertain the validity of each eligible study. Stata statistical software was used to perform meta-analysis. The strength of the association between periodontitis and emotional disorder was measured by odds ratios (ORs) with their 95% confidence intervals (95% CIs). Subgroup analysis and sensitivity analysis were performed. Publication bias was assessed through funnel plots and Begger's test. A total of 14 eligible articles were included in the meta-analysis, 6 of them were focused exclusively on depression, whereas 8 studies investigated both depression and anxiety. There was significant association between emotional disorder and chronic periodontitis (OR = 1.54, 95% CI = 1.27–1.86). Sensitivity analyses confirmed the stability of the present results. No evidence of asymmetry was observed in Begger's test. This meta-analysis demonstrates significant association between emotional disorder (including anxiety and depression) and chronic periodontitis. Nevertheless, the result should be interpreted with caution because of the potential bias and confounding in the included studies.

**Abbreviations:** CI = confidence interval, OR = odds ratio.

**Keywords:** anxiety, chronic periodontitis, depression, emotional disorders, meta-analysis

## 1. Introduction

Periodontal diseases, including gingivitis and periodontitis, are inflammatory conditions surrounding the teeth. They are highly prevalent and affect up to 90% of the worldwide population.<sup>[1]</sup> Periodontitis is an irreversible process that leads to periodontal

attachment loss, alveolar bone loss, and ultimately increased tooth mobility and tooth loss.<sup>[1]</sup> According to the Global Burden of Disease 2010 Study, periodontitis has been identified as the sixth most prevalent condition worldwide.<sup>[2]</sup> However, the pathogenesis of periodontitis is elusive and multifactorial. Specific subgingival microorganisms clustered in microbial biofilms are considered as the determinant agents of periodontal diseases.<sup>[3]</sup> Besides, the role of coinfections and comorbidities, such as herpesviruses<sup>[4]</sup> and diabetes,<sup>[5]</sup> has been confirmed in the initiation and progression of periodontitis. In addition, cigarette smoking,<sup>[6]</sup> reduced serum 25-hydroxy vitamin D,<sup>[7]</sup> low serum insulin-like growth factor-binding protein-3 levels,<sup>[8]</sup> worsen host-immune response,<sup>[9]</sup> and low socioeconomic profile have been identified as risk factors for the development of periodontitis.<sup>[10,11]</sup>

Psychological stress has been recognized as the pathophysiological origin of many chronic diseases, and periodontitis is no exception.<sup>[12]</sup> The biologic mechanism for this association is explained by studies indicating that psychosocial conditions might alter the host-immune response<sup>[13–15]</sup> and thus predispose individuals to periodontal disease.<sup>[13–15]</sup> Nevertheless, controversy exists as to whether psychological stress should be regarded as a potential risk factor of periodontitis. In 2007, a review of 14 studies (7 case-control, 6 cross-sectional, and 1 prospective clinical trial) showed that 57.1% of eligible studies suggested a positive association between psychosocial factors and periodontal diseases, 28.5% reported correlations between several aspects of psychosocial factors and periodontal diseases, while 14.2% indicated no association.<sup>[16]</sup> Thus, a systematic review and meta-analysis covering this topic is necessary.

Emotional disorders, including depression/depressive state and anxiety/anxiety state, are the most frequent symptoms resulting from psychological stress.<sup>[17]</sup> In 2016, major depressive disorder ranked in the top 10 of years lived with disability (YLDs) in all

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195 countries and territories except only 4 countries.<sup>[18]</sup> Anxiety disorders also ranked in the top 10 of YLDs in more than half of the countries and territories.<sup>[18]</sup> Meanwhile, depression and anxiety disorders present pronounced comorbidity, with 50 to 60% of depressed individuals meeting lifetime criteria for an anxiety disorder,<sup>[19]</sup> and anxiety disorders might act as a causal risk factor for later depression.<sup>[20,21]</sup>

In a recent meta-analysis, Araujo et al<sup>[22]</sup> failed to affirm an association between depression and periodontitis. However, there is scope for improvement in that study. We conducted an updated meta-analysis to evaluate scientific evidence on the association between emotional disorder (depression and anxiety) and chronic periodontitis. Moreover, the data from Chinese population was also adopted.

## 2. Materials and methods

This review was conducted according to a predetermined protocol that included all aspects of the review methods: search strategies, inclusion criteria for studies, quality assessment by 2 independent reviewers, data extraction, and data synthesis.

### 2.1. Data sources and search strategies

An overall electronic literature search in PubMed, ISI Web of Science, Cochrane Library, and China National Knowledge Infrastructure (CNKI) was undertaken for all the potentially relevant studies focusing on the association between anxiety or depression and chronic periodontitis up to November 2017. The language was restricted to English and Chinese. The following search strategy was used in Pubmed and Cochrane Library: ((periodontal disease[Mesh] OR periodontitis [Mesh] OR chronic periodontitis [Mesh]) AND (emotional disorder [Mesh] OR anxious [Mesh] OR anxiety [Mesh] OR depression [Mesh] OR depressive disorder [Mesh])); in Web of Science: ((periodontal disease OR periodontitis OR chronic periodontitis) AND (emotional disorder OR anxiety OR anxious OR depression OR depressive disorder)); in CNKI: (periodontitis (in Chinese)) AND (emotional disorder (in Chinese) OR anxiety (in Chinese) OR depression (in Chinese)).

### 2.2. Inclusion and exclusion criteria

The inclusion criteria of studies in the present review are as follows: case-control studies, cross-sectional studies, and cohort studies; clinical trials; studies in adult human beings; studies with adequate diagnostic criteria of periodontitis (such as bleeding on probing, probing depth, and clinical attachment loss etc.); studies with adequate criteria for emotional disorder (such as psychometric instrument); studies focusing on the presence of emotional disorder (anxiety or depression) in patients with periodontitis, with periodontally healthy individuals as control.

The exclusion criteria of studies in the present review are as follows: case reports, review or comments; basic studies; other oral diseases other than chronic periodontitis such as dental caries, gingivitis, and aggressive periodontitis; other neurological and psychotic disorders rather than emotional disorder (anxiety or depression); absence of healthy controls.

### 2.3. Quality assessment

Newcastle-Ottawa scale (NOS) was applied to ascertain the validity of each eligible study. The scale for cross-sectional and

case-control studies consists of 8 items that cover 3 dimensions: selection (adequate definition of cases, representativeness of cases, selection of controls, and definition of controls); comparability (control for the most important or any additional confounder); exposure (ascertainment of exposure, same method of ascertainment for cases and controls, and non-response rate). The scale for cohort study also consists of 8 items that cover 3 dimensions: selection (representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure, and demonstration that outcome of interest was not present at start of study); comparability (control for 1 confounder or does not control for confounder); outcome (assessment of outcome; enough long follow-up for outcomes; adequacy of follow-up cohorts). A point is awarded for each item that is satisfied by the study, with the exception of the comparability part of the scale, which is assigned a maximum of 2 points. A full score is 9 points, and a score  $\geq 6$  is considered as high quality, while a score  $< 6$  as low quality.<sup>[23]</sup> The NOS score was assessed independently by 2 reviewers and discrepancies were resolved after discussion.

### 2.4. Data extraction

Two reviewers independently extracted the following information from all selected articles: first author, year of publication, study classification, country of origin, language, sample size, age of individual at examination, diagnostic criteria of periodontitis, diagnostic criteria of emotional disorder, and exposure to risk factors.

### 2.5. Statistical analysis

Stata, version 12.1, statistical software (StataCorp; StataCorp LP, College Station, Texas) was used to perform meta-analysis. The strength of the association between periodontitis and emotional disorder was measured by odds ratios (ORs) with their 95% confidence intervals (95% CIs).

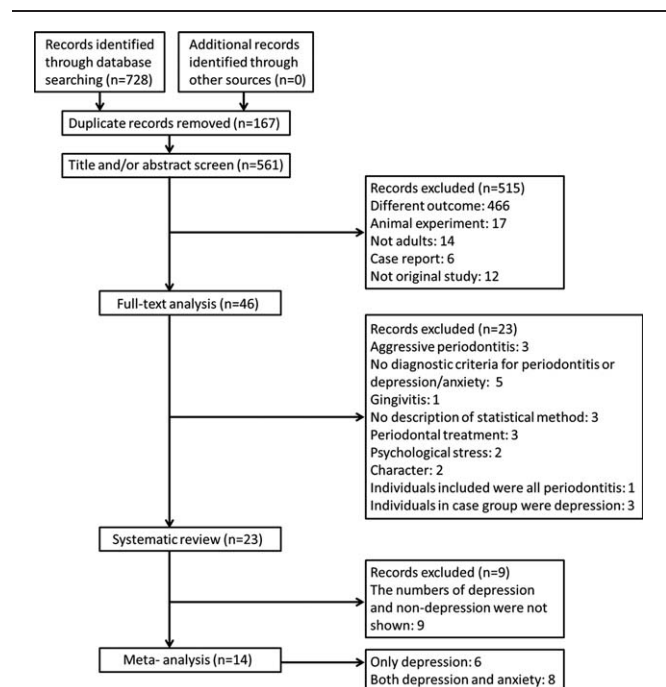


Figure 1. Flow diagram of study selection.

**Table 1**  
**Studies characteristics.**

Author	Year	Language	Country	N (case/control)	Age (years)	Periodontitis measure	Emotional disorder measure	Summary of results	Classifications	NOS score
Moss et al	1996	English	USA	148 (71/77)	25–74	Supragingival plaque, GB, Subgingival calculus, PD, CAL	Daily strains scale, BSI, COPE	Depression (OR: 1.28; 95% CI: 0.56–2.95) and anxiety (OR: 1.34; 95% CI: 0.55–3.27) trait was not different between cases and controls	Cohort	6
Genco et al	1999	English	USA	1426	25–74	Supragingival plaque, gingival bleeding, PD, CAL at 6 sites, radiographic ACH	Life event scale, measures of chronic stress, BSI, coping styles and strategies	Periodontitis was significantly associated to depression (OR: 1.51, 95% CI: 1.02–2.2)	Cross-sectional	7
Persson et al	2003	English	USA	701 (340/361)	60–75	The frequencies of mesial and distal vertical bone defects $\geq 3$ mm; PD $\geq 5$ mm	GDS and depression self-reported	Depression was not associated with periodontitis (OR: 0.85; 95% CI: 0.58–1.23)	Cross-sectional	7
Solis et al	2004	English	Brazil	153 (106/47)	19–67	Two or more interproximal sites from different teeth with a clinical CAL $\geq 6$ mm; at least 1 additional site with a PD $\geq 5$ mm	BDI, STAI	No evidence was found for an association between depression and established periodontitis (OR: 0.57, 95% CI: 0.15–2.21)	Cross-sectional	8
Castro et al	2006	English	Brazil	165 (96/69)	35–60	PD, CAL, BOP	LES, BAI, STAI, BDI	No association between depression and periodontal disease: BDI: (OR: 0.96; 95% CI: 0.88–1.05); neither for anxiety state (OR: 1.044; 95% CI: 0.98–1.11)	Case-control	7
Ng et al	2006	English	China	1000 (724/276)	25–64	Number of standing teeth; calculus; BOP; recession; PD; CAL	LEQ, SRRS, problems of everyday living scale of pearl and schooler SCL-90; DASS-S; COPE	Periodontitis was statistically associated with anxiety trait (OR: 1.51, 95% CI: 1.09–2.27) and depression trait (OR: 1.62; 95% CI: 1.15–2.35)	Cross-sectional	8
Abahneh et al	2010	English	Jordan	666 (583/83)	15–62	PD, CAL, GI	ZSDS	There was no significant association between depression and periodontal parameters CAL (OR adjusted: 0.71, 95% CI: 0.48–1.05)	Cross-sectional	7
Abahneh et al	2010	English	Jordan	181 (100/81)	14–71	PI, CAL $\geq 4$ mm on more than 1 tooth	HAD	Periodontitis was associated with anxiety (OR: 2.06, 95% CI: 1.131–3.751) and depression (OR: 2.251; 95% CI: 1.104–4.594)	Case-control	6
Wang et al	2010	Chinese	China	65 (36/29)	24–55	CI, BOP, CAL $\geq 3$ mm	HAMD, HAMA	Findings showed periodontal disease was associated between depression (OR: 15.6; 95% CI: 4.038–60.267) and anxiety (OR: 21.938; 95% CI: 4.564–104.974)	Case-control	7

(continued)

**Table 1**  
(continued).

Author	Year	Language	Country	N (case/control)	Age (years)	Periodontitis measure	Emotional disorder measure	Summary of results	Classifications	NOS score
Wang et al	2011	Chinese	China	100 (50/50)	26–60	CAL $\geq$ 2 mm, bone loss over 30%	SDS	Findings showed association between depression and periodontal disease (OR: 12.667; 95% CI: 4.902–32.733)	Case-control	6
Khambaty et al	2013	English	USA	1979 (125/1854)	20–39	One or more tooth sites with loss of attachment $\geq$ 4 mm	CIDI-Auto	Depressive disorder (OR adjusted: 0.92, 95% CI: 0.42–2.02) or anxiety (OR adjusted: 0.68, 95% CI: 0.21–2.21) were not related to periodontal disease	Cross-sectional	9
Mendes et al	2013	English	Brazil	72 (15/57)	$\geq$ 60	CPI, CAL (at least 1 site with PD $\geq$ 4 mm, and at last 1 site with CAL $\geq$ 4 mm)	GDS	Findings showed no significant association between depression and periodontal disease (OR: 0.837; 95% CI: 0.317–2.207)	Cross-sectional	8
Shi et al	2015	Chinese	China	375 (175/200)	25–60	CAL	SAS, SDS, TCSQ	Findings showed association between depression (OR: 4.090; 95% CI: 1.901–8.800) and anxiety (OR: 3.311; 95% CI: 1.586–6.912) with periodontal disease	Case-control	6
Laforgia et al	2015	English	Italy	108 (54/54)	24–67	BI, plaque record control, PD, interradicular lesions, dental mobility, gingival recession	IRLE, SOL-90, BDI	Significant correlation could be observed between depression (OR: 1.288, 95% CI: 1.228–5.813) and anxiety (OR: 1.796, 95% CI: 0.748–4.315) with periodontal disease	Case-control	6

ACH = radiographic alveolar crestal height, auto version 2.1, BAI = beck anxiety inventory, BDI = beck depression inventory, BOP = bleeding on probing, BSI = brief symptom inventory, CAL = clinical attachment level, CIDI-Auto = World Health Organization Composite International Diagnostic Interview, COPE = COPE inventory, CPI = community periodontal index, DASS-S = depression anxiety stress scales-state, GB = gingival bleeding, GDS = geriatric depression scale, GI = gingival inflammation, HAD = depression subscale of the hospital anxiety and depression scale, HAMA = Hamilton Anxiety Scale, HAM-D = Hamilton depression scale, IRLE = interview for recent life events, LEQ = life event questionnaire, LES = life events scale, PD = probing depth, SAS = self-rating anxiety scale, SOL-90 = Symptom Checklist-90, SDS = self-rating depression scale, SRRS = social readjustment rating scale, STAI = state-trait anxiety inventory, TCSQ = trait coping style questionnaire, ZSDS = Zung Self-Rating Depression Scale.

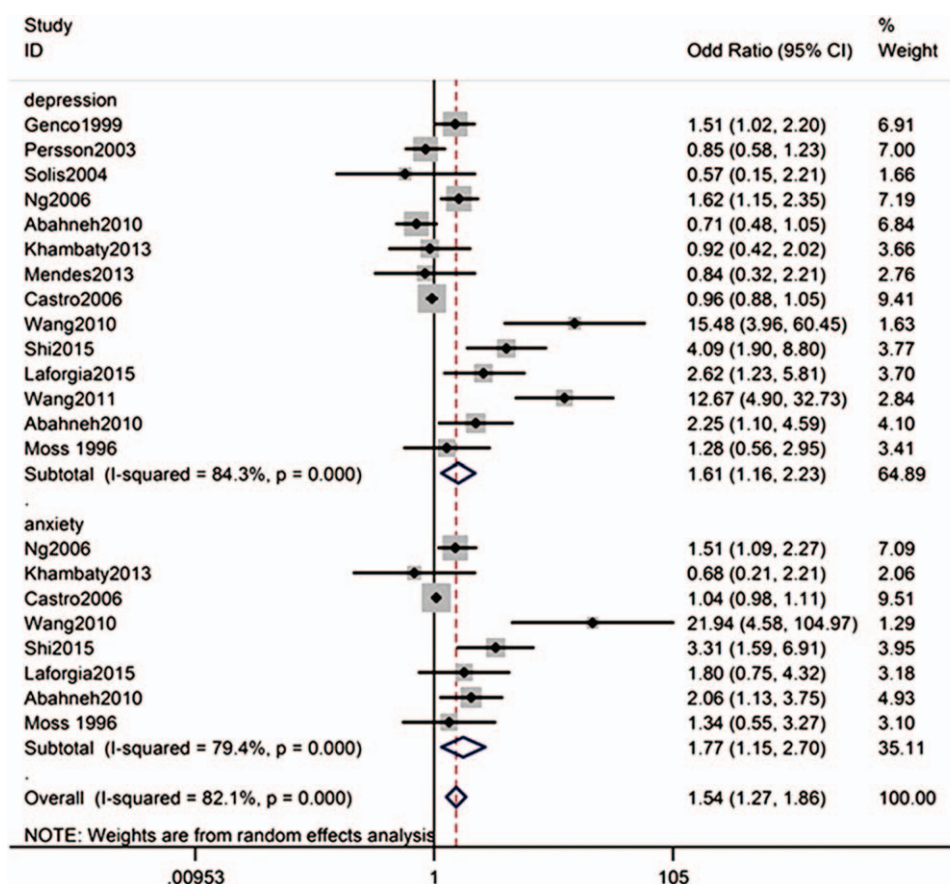


Figure 2. Forest plot for association between emotional disorder (depression and anxiety) and chronic periodontitis.

Heterogeneity was assessed by the  $I^2$  statistic, which was documented for the percentage of the observed between-study variability due to heterogeneity rather than chance with the ranges of 0 to 100%. When  $I^2 < 50\%$ , the fixed-effects model (Mantel-Haenszel method) was used; when  $I^2 > 50\%$ , a random-effects model (the DerSimonian & Laird method) was used to account for study heterogeneity. Then subgroup analysis stratified by study classification, country of origin, language, and sample size was performed. Finally, publication bias was assessed through funnel plots and Begger's test.

## 2.6. Ethical considerations

No ethical approval or patient consent was required, because all the analyses in the present study were based on previously published articles.

## 3. Results

### 3.1. Literature search and study characteristics

Figure 1 summarizes the process of study identification and selection. We identified 728 records, of which 167 were duplicates. Based on the title and/or abstract of these, 515 were excluded as they were not relevant to the objectives of this systematic review. Of the 46 studies whose full-texts were retrieved, another 23 studies were excluded for reasons given in Fig. 1. Finally, 14 eligible articles were included in the meta-analysis, 6 of them were focused

exclusively on depression, whereas 8 studies investigated both depression and anxiety.

Characteristics of the 14 eligible articles for meta-analysis are detailed in Table 1. There were 1 cohort study, 7 cross-sectional studies, and 6 case-control studies. The year of publication ranged from 1996 to 2015. Three studies were in Chinese and other 11 were in English. Four studies were conducted in USA, 3 in Brazil, 4 in China, 2 in Jordan, and 1 in Italy. These studies covered 7139 subjects, and the sample size ranged from 65 to 1979 individuals. Only in the study of Mendes et al,<sup>[24]</sup> was the age criteria defined as above 60 years. Other studies all defined the specific age ranges.

### 3.2. Quality assessment

Of the 14 eligible articles included in analysis, scores of these studies ranged from 6 to 9 (Table 1). Major source of bias of cross-sectional and case-control studies came from the selection part. All the studies had adequate definition for cases and controls, with independent validation. Only 1 study chose a representative sample from National Health and Nutrition Examination Survey of USA,<sup>[25]</sup> while others used convenience samples from hospitals, advertisement recruitment, or neighborhoods. In exposure part, no study mentioned blinding of examiners and only 1 study reported non-response rate (Wang et al, 2010). Bias of the cohort study by Moss et al<sup>[26]</sup> was mainly in outcome part. There was no statement that the outcome of interest (chronic periodontitis) was not present at the start of

**Table 2****Subgroup analyses of the association between depression and chronic periodontitis.**

		N	OR	95% CI Low	95% CI High	% Weight
Classification	Cross-sectional	7	1.032	0.754	1.414	53.26
	Case-control	6	3.726	1.458	9.523	40.42
	Cohort	1	1.28	0.558	2.938	6.32
Language	English	11	1.154	0.916	1.454	83.89
	Chinese	3	8.395	3.488	20.206	16.11
Sample size	<1000	11	1.755	1.138	2.707	74.65
	≥1000	3	1.487	1.16	1.906	25.35
Country	USA	4	1.115	0.8	1.554	31.56
	Brazil	3	0.957	0.876	1.045	19.89
	China	4	5.433	1.775	16.627	25.56
	Jordan	2	1.215	0.393	3.753	16.33
	Italy	1	2.617	1.203	5.694	6.66

CI = confidence interval, OR = odds ratio.

study. The follow-up period might not be long enough for outcome (depression) to occur.

### 3.3. Data synthesis and meta-analysis

Figure 2 shows the meta-analysis of 14 articles. In those 14 articles, 6 of them focused exclusively on depression and 8 focused on both depression and anxiety. Therefore, actually 8 substudies of anxiety and 14 substudies of depression were synthesized for meta-analysis. There was significant association between depression and chronic periodontitis (OR = 1.61, 95% CI = 1.16–2.23), so was anxiety (OR = 1.77, 95% CI = 1.15–2.70). In addition, the association between emotional disorder (combined depression and anxiety) and chronic periodontitis was also statistically significant (OR = 1.54, 95% CI = 1.27–1.86).

### 3.4. Subgroup analyses

To reduce the impact of common risk factors, several subgroup analyses have been performed. The subgroup analyses of association among depression, anxiety or emotional disorders, and chronic periodontitis were shown in Table 2, Table 3, and Table 4, respectively.

For depression, enhanced ORs and significant associations were estimated when case-control studies (OR = 3.726, 95% CI = 1.458–9.523), Chinese studies (OR = 8.395, 95% CI = 3.488–20.206), studies with sample size less than 1000 (OR =

1.755, 95% CI = 1.138–2.707), and studies conducted in China (OR = 5.433, 95% CI = 1.775–16.627) and Italy (OR = 2.617, 95% CI = 1.203–5.694) were put in the analyses. The association was still significant when the sample size was equal or more than 1000 (OR = 1.487, 95% CI = 1.16–1.906).

For anxiety, enhanced ORs and significant associations were estimated when case-control studies (OR = 2.461, 95% CI = 1.179–5.136), Chinese studies (OR = 7.473, 95% CI = 1.193–46.826), studies with sample size less than 1000 (OR = 2.186, 95% CI = 1.173–4.071), and studies conducted in China (OR = 3.754, 95% CI = 1.204–11.704) and Jordan (OR = 2.06, 95% CI = 1.131–3.752) were put in the analyses.

For emotional disorders, enhanced ORs and significant associations were estimated when case-control studies (OR = 2.287, 95% CI = 1.71–3.058), Chinese studies (OR = 7.564, 95% CI = 3.629–15.552), studies with sample size less than 1000 (OR = 1.625, 95% CI = 1.295–2.039), and studies conducted in China (OR = 4.38, 95% CI = 2.269–8.453) and Italy (OR = 2.217, 95% CI = 1.24–3.966) were put in the analyses. The associations were still significant when English studies (OR = 1.172, 95% CI = 1.021–1.345) or studies with sample size equal or more than 1000 (OR = 1.46, 95% CI = 1.192–1.787) were put in the analyses.

### 3.5. Sensitivity analysis

Sensitivity analyses were performed via sequential deletion of each individual study to determine the relative influence of each

**Table 3****Subgroup analyses of the association between anxiety and chronic periodontitis.**

		N	OR	95% CI Low	95% CI High	% Weight
Classification	Cross-sectional	2	1.243	0.635	2.433	25.6
	Case-control	5	2.461	1.179	5.136	63.66
	Cohort	1	1.34	0.55	3.267	10.74
Language	English	6	1.321	0.986	1.77	81.95
	Chinese	2	7.473	1.193	46.826	18.05
Sample size	<1000	6	2.186	1.173	4.071	74.4
	≥1000	2	1.243	0.635	2.433	25.6
Country	USA	2	1.046	0.514	2.13	18.69
	Brazil	1	1.044	0.981	1.111	20.23
	China	3	3.754	1.204	11.704	35.7
	Jordan	1	2.06	1.131	3.752	14.48
	Italy	1	1.796	0.748	4.314	10.91

CI = confidence interval, OR = odds ratio.

**Table 4**  
**Subgroup analyses of the association between emotional disorder and chronic periodontitis.**

		N	OR	95% CI Low	95% CI High	% Weight
Classification	Cross-sectional	9	1.081	0.827	1.414	45.17
	Case-control	11	2.287	1.71	3.058	48.32
	Cohort	2	1.308	0.712	2.401	6.51
Language	English	17	1.172	1.021	1.345	86.52
	Chinese	5	7.564	3.679	15.552	13.48
Sample size	<1000	17	1.625	1.295	2.039	73.09
	≥1000	5	1.46	1.192	1.787	26.91
Country	USA	6	1.107	0.859	1.427	26.14
	Brazil	4	1.012	0.957	1.07	23.34
	China	7	4.38	2.269	8.453	27.76
	Jordan	3	1.434	0.633	3.25	15.88
	Italy	2	2.217	1.24	3.966	6.88

CI = confidence interval, OR = odds ratio.

individual dataset on the pooled ORs. The results showed that pooled ORs for the association of depression, anxiety, and emotional disorders with chronic periodontitis and the corresponding 95% CIs did not alter substantially by removing any 1 study, confirming the stability of the present results (Fig. 3).

### 3.6. Publication bias

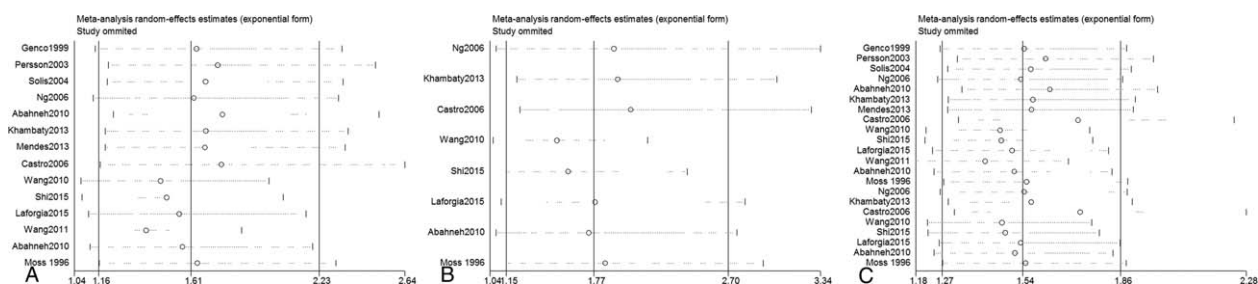
In Fig. 4, Begger's test was conducted to assess publication bias. No evidence of asymmetry was observed in the association among depression ( $P=0.324$  by Begger's test), anxiety ( $P=0.711$  by Begger's test) or emotional disorders ( $P=0.284$  by Begger's test), and chronic periodontitis (Fig. 4A, B, and C, respectively).

## 4. Discussion

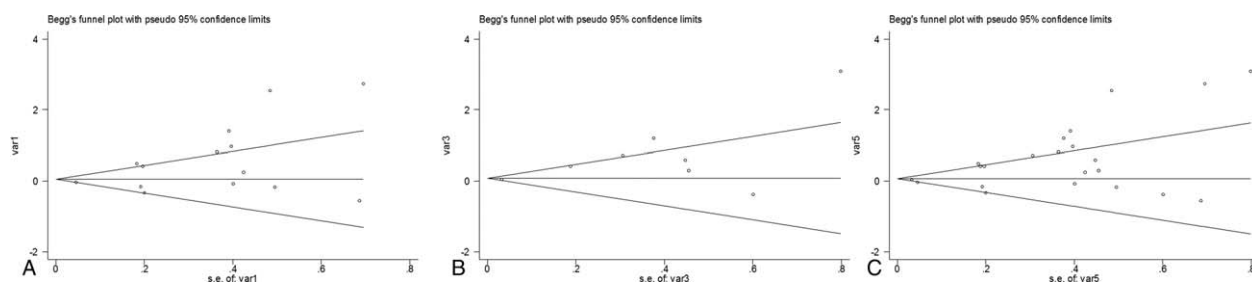
In the past decades, bacteria have been concluded as the primary etiological factor of periodontal diseases.<sup>[16]</sup> Besides, environmental risk factors which could modify host immune response may help carriers adapt to bacteria and affect progression, severity, and outcome of periodontitis.<sup>[27]</sup> Although a few studies focused on the potential impact of anxiety and (or) depression on periodontitis, the association between them has not been well-established yet. To our knowledge, this is the first meta-analysis of the association between emotional disorder (including anxiety and depression) and chronic periodontitis. The results in our meta-analysis suggest that the association between emotional disorder and chronic periodontitis was statistically significant. In addition, the association was consistently found in most subgroup analyses.

Although emotional disorder may increase the risk of chronic periodontitis, the mechanism remains unclear. On one hand, the altered emotional status would change the health-related behaviors, such as oral hygiene, oral health examination, smoking, and diet, which might increase the risk of periodontitis.<sup>[28]</sup> On the other hand, the emotional disorder has been hypothesized to deteriorate the already damaged periodontal tissues, through comprehensive immunosuppression or elevated susceptibility to inflammatory. One potential hypothesis is that the activated hypothalamic-pituitary-adrenal axis in anxiety and depression results in continued release of glucocorticoids and thereby leading to inflammation.<sup>[29]</sup> Another hypothesis is that in emotional disorder patients, sympathetic nervous system releases adrenaline and noradrenaline from the adrenal medulla, which exerts an immunosuppressive effect.<sup>[16]</sup> What's more, emotional disorder also regulates immune response by altering release of cytokines.<sup>[30]</sup> These could directly or indirectly provoke periodontal tissue breakdown.

Our findings are of clinical significance to some extent. Controlling inflammation and counteracting microbial subversion are therapeutic principles of chronic periodontitis. Besides, the association between chronic periodontitis and systemic conditions highlights the importance of effective treatment of comorbidities. For example, diabetes, as another risk factor of chronic periodontitis, has received substantial attention. Glycemic control is as important as periodontal therapy for treatment of chronic periodontitis in patients with diabetes mellitus.<sup>[31]</sup> Similarly, we have reasons to believe that for the chronic periodontitis patients with emotional disorder, the psychiasis would contribute to therapeutic efficacy combined with



**Figure 3.** Sensitivity analysis. The pooled odds ratio and 95% confidence interval were stability after deletion of each individual study, no matter in the in the association between depression (A), anxiety (B) or emotional disorders (C), and chronic periodontitis.



**Figure 4.** Funnel plot analysis to detect publication bias. (A) the association between depression and chronic periodontitis ( $P=0.324$  by Begger's test). (B) the association between anxiety and chronic periodontitis ( $P=0.711$  by Begger's test). (C) the association between emotional disorders and chronic periodontitis ( $P=0.284$  by Begger's test).

periodontal therapy. Such assumption has also been confirmed by animal experiments. In rats receiving olfactory bulbectomy, which is a model of depression, chronic treatment of tianeptine significantly attenuated susceptibility to experimental periodontitis.<sup>[32]</sup> Aguiar et al<sup>[33]</sup> found that fluoxetine inhibited progression of experimental periodontal disease in a conditioned fear stress rat model.

Strengths of this meta-analysis included the high quality of the eligible studies, with an average NOS score of 7. Not only articles on PubMed, ISI Web of Science, and Cochrane Library, but also the Chinese articles published on CNKI were undertaken for all the potentially relevant studies. Sensitivity analysis revealed that no single study qualitatively changed the pooled ORs, indicating that the results of this meta-analysis were stable. Moreover, we did not observe any publication bias in the present study, which also demonstrating stability of this meta-analysis.

However, several limitations of this meta-analysis merit consideration. First, only articles published in English or Chinese were selected, potentially causing a language bias. Second, all of our results may be influenced by casualness due to the small number of studies included and the limited sample size of each study. Larger sample sizes are necessary to accurately clarify the association between emotional disorder and chronic periodontitis. Third, the characteristics of populations, severity of the illness, and the adjusted confounding factor were not strictly described in some trials. And the instruments used to detect emotional disorder varied among the studies. Fourth, the public health system, medical care system, cultures are quite varied among these countries, which might result in the discrepant outcomes in different countries. These factors might be the resources of heterogeneity and have a potential impact on our results. Accordingly, we used a random-effects model throughout to incorporate heterogeneity into our analyses.

In summary, this meta-analysis demonstrates significant association between emotional disorder (including anxiety and depression) and chronic periodontitis. Nevertheless, the result should be interpreted with caution because of the limited number of published articles, the potential bias, and confounding in the included studies.

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