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SYSTEMATIC REVIEW
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Systematic Review and Meta-analysis of the Association Between Malnutrition and Risk of Depression in the Elderly

ABSTRACT

Objective: To explore the association between malnutrition and risk of depression in the elderly.

Methods: Relevant studies were searched in PubMed, Web of Science, the Cochrane Library, Scopus, and Embase from the establishment of the database to August 17, 2023. Two researchers independently screened the literature, extracted data, and evaluated the risk of bias in the included studies. Stata16.0 software was used for meta-analysis.

Results: A total of 8 observational studies were identified with 11 112 participants, of which 2771 elderly patients had depression. The meta-pooled results showed a significant correlation between nutritional status and depression risk (odds ratio (OR) = 2.03, 95% CI = (1.47, 2.81), $P < 0.001$). Subgroup analysis found that the malnutrition scores of different study types and the diagnostic methods of depression and malnutrition were correlated with the risk of depression.

Conclusion: Malnutrition was associated with depression risk in the elderly. Further large-scale multicenter studies should be conducted to test and verify the results.

Keywords: The elderly, malnutrition, depression, association, systematic review, meta-analysis

Introduction

The mental health of the elderly has gained increasing attention by the society and the government due to the aging of the population, and depression is an important index for mental health evaluation.[1] Research on depression, both domestic and abroad, shows that mental health problems such as depression and anxiety not only have important effects on quality of life and daily functioning, and increase suicide rates, but also increase the risk of Alzheimer's disease.[2-5] These influences seriously reduce the life satisfaction and happiness of middle-aged and older individuals elderly and cause a heavy economic burden to families and even society.[6,7] Depression is related to multiple factors, including genetic, environmental, psychological, and social factors. Domestic and foreign research shows that depression is related to a number of complications, including diet structure, hormone level changes, eating habits, unbalanced dietary nutrition intake, and other factors.[8-12] In vulnerable groups, such as older people, malnutrition and depression often coexist.[13] Epidemiological studies were conducted to explore the relationship between malnutrition and depression risk, but the results are mixed. Over the past 20 years, several works have reported that poor nutrition increases the risk of depression.[14,15] However, only systematic reviews have found a relationship between vitamin D and depression. To objectively evaluate the correlation between malnutrition and risk of depression, the present work summarized existing observational studies and evaluated them strictly according to the Cochrane systematic review method. Results will provide references for clinical depression prevention decisions and related studies.

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Materials and Methods

This review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[16]

Search Strategy

PubMed, Web of Science, Scopus, and Embase were searched from their establishment date to August 17, 2023. The search terms mainly included the following: depression, malnutrition, nutrition disorders, nutritional deficiency, subnutrition, undernutrition, aged, elderly, and elderly. The references of the included literature were traced back to supplement the acquisition of relevant literature. The specific search strategy is shown as the following by using PubMed as an example.

#1 depression OR depress
#2 malnutrition OR nutrition disorders OR nutritional deficiency OR subnutrition OR undernutrition
#3 aged OR elderly OR senior OR late-life
#4 #1 AND #2 AND #3

Inclusion Criteria

Study Type: Observational study.

Subjects: Elderly population (older than 60 years).

Exposure: Malnutrition was diagnosed either based on an established nutritional status scale or scored above a threshold on the nutritional status rating scale as specified by the study authors.

Outcomes: Clinically significant depression was diagnosed as major depressive disorder (MDD) according to an established diagnostic system [e.g., Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD)] or scored above a threshold according to an established psychopathology Rating Scale for Depression as specified by the study authors. Diagnoses may be based on assessment rating scales, standardized interviews (e.g., WHO-CIDI), or registers that include hospital data with record reliability.

Exclusion Criteria

Language and Publication: Studies not written in Chinese or English.

Publication Status: Duplicate publications.

Data Quality: Literature with incomplete data or data insufficient to calculate the odds ratio (OR) value and 95% confidence interval (CI).

MAIN POINTS

- *A total of 8 observational studies were identified, and they comprised 11112 participants, of which 2771 elderly patients had depression.*
- *The meta-pooled results showed a significant correlation between nutritional status and depression risk (OR = 2.03, 95% CI = (1.47, 2.81), P < .001).*
- *Subgroup analysis found that the malnutrition scores of different study types and the diagnostic methods of depression and malnutrition were correlated with the risk of depression.*

Literature Screening and Data Extraction

Two reviewers independently screened the literature, extracted, and cross-checked the data. In case of disagreement, a third reviewer was consulted to assist in judgment. In terms of lacking data, authors were contacted. Literature screening was performed by reading titles and abstracts first. After excluding obviously irrelevant literature, the full text was further read to determine final inclusion. The data extraction mainly included: (1) basic information of the studies, including research title, first author, publication time, etc.; (2) the baseline characteristics of the subjects, including the number of samples in each group, age, and gender; (3) key elements of risk of bias assessment; and (4) outcome indicators and measures of interest.

Quality Evaluation

The Newcastle–Ottawa Scale (NOS) was used to assess the risk of bias in the included studies.[17] If the evaluation was inconsistent, then disagreements were resolved by discussion. The NOS included 8 items in 3 categories, including selection of research subjects, comparability of cases and controls, and exposure factors, with a total point of 9. Studies with ≥6 points were considered to be of high quality.[17]

Statistical Analysis

Stata version 12.0 (StataCorp LP, College Station, TX, USA) software was used for statistical analysis. The adjusted OR value and its 95% CI were extracted from each study. Odds ratios were pooled using inverse variance method for meta-analysis, and the level of significance was $\alpha = 0.10$ Heterogeneity was considered acceptable when $P > .10$, and a fixed-effect model was used for analysis. The parameters $P < .10$ and $I^2 > 50\%$ indicated large heterogeneity.[18] In the presence of large heterogeneity, a random effect model was used for analysis. All outcome measures were also subjected to subgroup analysis to minimize the influence of potential factors. Funnel plots were used to assess the presence of publication bias. Using the Begg's and Egger's test, we set funnel plot asymmetry and defined significant publication bias as $P < .05$.

Results

Results of Literature Screening

Literature screening was carried out according to the PRISMA flowchart (Figure 1). A total of 4017 studies were retrieved initially. After eliminating duplications and screening the titles and abstracts of the remaining literatures, 73 studies were evaluated for full text according to the inclusion criteria, and 65 were then excluded. The 8 remaining studies consisted of 2771 (24.9%) individuals diagnosed with depression.

Features and Quality Evaluation of Included Documents

Of the 8 studies included, 3 were from Bangladesh, 2 from China, and 1 each from Israel, South Korea, and Portugal. In terms of exposure factors, 3 studies used Mini Nutritional Assessment—Short Form (MNA-SF), 3 studies used MNA, and the remaining studies used meal adequscy ratio (MAR) and BMI and body weight. In terms of outcome measures, 3 studies used Geriatric Depression Scale (GDS)-15, 2 studies used GDS, 2 studies used Ccenter for Epidemiological Studies-Depression (CES-D), and 1 study used Patient Health Questionnaire-9 (PHQ-9). The characteristic information and quality evaluation of the included literatures are shown in Table 1.The table displays the basic information, population characteristics, outcome measures, and quality assessment of the 8 observational studies that were included in the meta-analysis. The studies varied in terms of country, sample

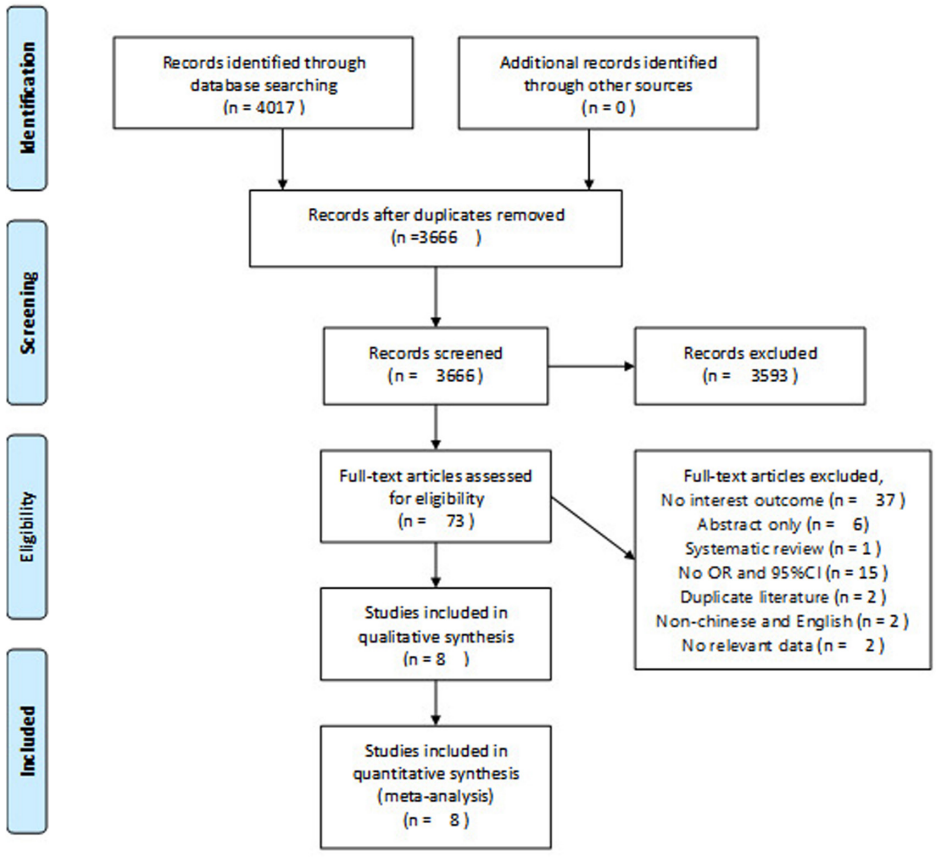

Figure 1. Literature screening results.

size, diagnostic methods of malnutrition and depression, and risk of bias. NOS stands for Newcastle–Ottawa Scale, a tool for assessing the quality of nonrandomized studies.

Meta-analysis

Eight studies examined the association between malnutrition and depression, and significant heterogeneity was found among these studies ($I^2 = 76.1\%$, $P < .001$). The random-effects model showed that malnutrition was significantly associated with the occurrence of depression (OR = 2.03, 95% CI: 1.47-2.81, $P < .001$; Figure 2).

Sensitivity Analysis

Sensitivity analysis was performed by leave-one-out analysis, and the heterogeneity was significantly reduced when the study of Alam et al[20] was excluded ($I^2 = 24.4\%$, $P = .243$). The combined results were still relatively stable (OR = 1.62, 1.34-1.97), $P < .001$).

Subgroup Analysis

Subgroup analysis was performed on the included studies by study type and diagnostic methods for depression and malnutrition to reduce the possibility of the above potential influencing factors. The malnutrition scores in different study types and diagnostic methods for depression and malnutrition were correlated with the risk of depression (Figure 3). However, a robust assessment of publication bias was not possible as only 8 studies were included in this meta-analysis.

Discussion

Studies have described a causal relationship between malnutrition and depression in older adults, but the results are inconclusive.[24,27,28] The present study found a significant association between depression and malnutrition in the elderly. Depression can lead to psychological anorexia, reducing the intake of protein and other nutritional energy sources, causing sympathetic nerve stimulation, and inhibiting gastrointestinal peristalsis and digestive juice secretion. Insufficient dietary nutrient intake leads to malnutrition, which can also increase the occurrence of depression. Akyuz et al[29] conducted a study on elderly patients in a tertiary hospital and found a significant negative correlation between Geriatric Depression Scale—Short Form and MNA scores. Castel et al[30] also studied older adults admitted to the emergency department and found that women had a higher risk of malnutrition, which was associated with depression. However, Yoshimura et al[31] found that younger, malnourished older adults were at risk of depression, but no significant difference was found when the study population was expanded to include all older adults.

The relationship between malnutrition and depression remains controversial, and a threshold effect may exist when depression score and nutritional status score are used as continuous variables. The present meta-analysis explored the correlation between malnutrition and depression by extracting relevant information from the literature. The results showed that malnutrition was an independent risk factor for depression in the elderly.

Although the exact mechanism remains unclear, the significant protective effect of nutrients on depression is biologically plausible. Firstly, as an indicator of depression, folic acid can directly or indirectly participate in the synthesis of neurotransmitters.

Table 1 Characteristic Information and Quality Evaluation of the Included Studies

Study	Research Type	Country	Case Group	Control Group	Male vs Female_ Case Group	Male vs Female_ Control Group	Age_Case Group	Age_Control Group	Diagnosis of Malnutrition	Diagnosis of Depression	Populations	NOS
Alam 2023[19]	Cross-section	Bangladesh	249	181	142/107	87/94	>60		MNA-SF	GDS-15	Community	6
Alam 2021[20]	Cross-section	Bangladesh	120	65	60/60	45/20	71.6 ± 6.0	72.3 ± 8.1	MNA <17	GDS >10	Community	7
German 2008[21]	Cross-section	Israel	54	141	24/30	93/48	74.8 ± 5.9	73.3 ± 5.5	MNA <17	GDS > 10	Community	6
Islam 2021[22]	Cross-section	Bangladesh	300	300	138/132	162/168	>60		MNA-SF <7	GDS-15 >5	Village	6
Kim 2022[23]	Cross-section	Korea	277	3423	1622/2078 (total)		72.6 ± 5.0 (total)		MAR >100%	PHQ-9 ≥10	Nationwide	6
Noronha 2015[24]	Cross-section	Portugal	53	31	13/40	18/13	82.5 ± 6.9	81.4 ± 5.2	MNA <17	CES-D > 16	Nursing home	8
Song 2022[25]	Cohort	China	286	716	31/255	146/567	102 (101, 104)	102(101, 104)	MNA-SF <7	GDS15 >6	Whole province	7
Zhang 2017[26]	Cohort	China	1372	3544	2603/2313 (total)		67.29 ± 6.15 (total)		BMI and weight	CES-D > 10	Nationwide	6

BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric Depression Scale; GDS-15, Geriatric Depression Scale—Short Form; MNA, Mini Nutritional Assessment; MNA-SF, Mini Nutritional Assessment—Short Form; MAR, meal adequacy ratio; NOS, Newcastle–Ottawa scale; PHQ-9, Patient Health Questionnaire 9.

Folate deficiency causes irregular synthesis of neurotransmitters and leads to depression. Huang et al[32] reported that the degree of depression was negatively correlated with the level of folate, and this relationship was significant in women. Secondly, high doses of B vitamins may slow the progression of cognitive decline. People with a healthy diet pattern have a reduced risk of depression due to their increasing levels of serum folate and vitamin B12; by contrast, those with an unhealthy diet have an increased risk of depression due to the low levels of serum folate and vitamin B12.[33] A community survey in South Korea found that vitamin B6 was the only nutrient that could predict depression in elderly women and that increasing the vitamin B6 intake could improve depressive symptoms.[34] In addition, some studies found a significant inverse association between 25(OH)D level and depressive symptoms.[35] This association between low 25(OH)D concentration and worsening depressive symptoms suggests that vitamin D deficiency may be a risk factor for depression in later life.[36] Thirdly, depression is also associated with oxidative stress. Omega-3 fatty acids can reduce oxidative stress and affect cell structure and anti-inflammation. Unsaturated fatty acids are also involved in the regulation of the structure and function of neurons, glial cells, and endothelial cells in the brain. Supplementation with Omega-3 fatty acids may prevent the worsening of subclinical depression.[37,38] Fourthly, zinc, copper, and manganese are negatively correlated with the prevalence of depression in Japanese employees, and those with clinically significant depressive symptoms have low levels of zinc. Oral administration of zinc can increase the effectiveness of antidepressant treatment. Zinc can also protect brain cells from free radical damage.[39] Lastly, studies suggest that certain bacteria or their metabolites may be associated with depression. Intestinal microorganisms are destroyed because of the effect of the brain–gut axis, and the central nervous system function will be impaired.[40] The gut receives signals from the central nervous system and, similarly, transmits the signals to the brain. This bidirectional transmission involves not only neural pathways but also endocrine and immune systems. Animal studies have shown that the metabolism of tryptophan and 5-hydroxytryptamine (also known as serotonin) in mice is affected by *Lactobacillus reuteri (L. reuteri)*.[40] The absence of the gut microbiota during development negatively affects the hypothalamic–pituitary–adrenal axis. Nutrients in food, such as folic acid, VB, VD, and trace elements, have a good relieving effect on depression. Therefore, depression can be prevented and improved by changing the dietary structure and increasing the intake of nutrients.

The reasons for the differences in the effect sizes of the included studies were shown as follows: (1) sample size: some studies had relatively small sample sizes, which may lead to differences in the effect sizes of the effect of malnutrition on depression. (2) Population characteristics: the study population of Islam et al[22] was the rural elderly population, which may affect the association between malnutrition and depression. Most of the other study populations were representative of a whole population, and the disease background and gender differences may lead to differences in the results. (3) The diagnostic methods of malnutrition used in the studies of Kim et al[23] and Zhang et al[26] are different from those in other studies. The diagnostic criteria of depression used in the studies of Kim,[23] Noronha,[24] and Zhang[26] differ from those in other works, which may affect the authenticity of the outcome.

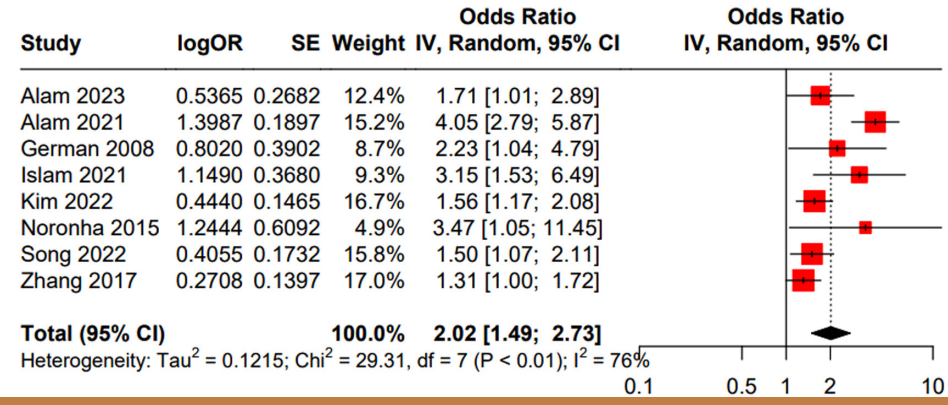

Figure 2. Meta-analysis Results. OR, odds ratio; CI, confidence interval.

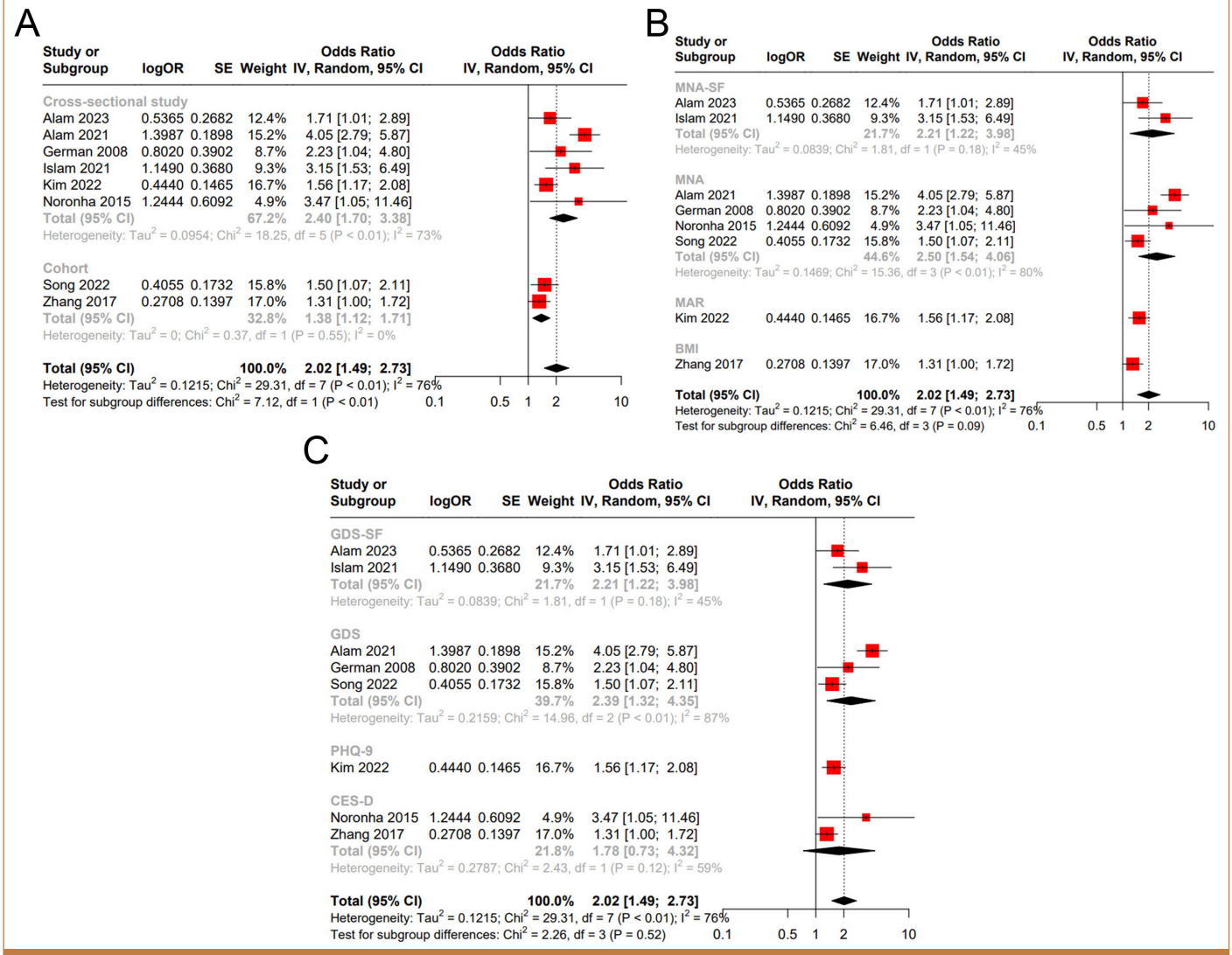

Figure 3. Sensitivity analysis (A) Subgroup analysis for type of study. (B) Subgroup analysis for diagnosis of malnutrition. (C) Subgroup analysis for diagnosis of depression. OR, odds ratio; CI, confidence interval; MNA, Mini Nutritional Assessment; MNA-SF, Mini Nutrtional Assessment-Short Form; MAR, meal adequacy ratio; BMI, body mass index; GDS, Geriatric Depression Scale; GDS-SF, Geriatric Depression Scale-Short Form; PHQ-9, Patient Health Questionnaire-9; CES-D, Center for Epidemiologic Studies Depression Scale; SE, Standard Error.

Nutritional status was found to be associated with the risk of depression. These results help to better understand the important role of abnormal nutritional status in the occurrence and development of depression and provide a basis for the early screening of depression in the elderly population. However, the conclusions should be further verified by large prospective, multi-center, and high-quality studies.

Limitations

The limitations of this study are as follows: (1) the number of included articles is small, and their representative lines need to be further verified; (2) all the included studies were observational, which may have selection bias, and the ability of causal inference may be limited; (3) the heterogeneity of this paper is high (I^2 of 76.1% in the overall analysis), which may have a certain effect on the meta-analysis; (4) the included studies were all in English and small, hence resulting in possible publication bias.

Availability of Data and Materials: *Data are available on request from the authors.*

Peer-review: *Externally peer-reviewed.*

Author Contributions: *Concept – W.H., H.M., D.X.; Design – W.H., S.G., J.J.; Supervision – W.H.; D.X., H,M.; Resources – S.G.; Materials – W.H.; Data Collection and/or Processing – W.H., H.M., J.J.; Analysis and/or Interpretation – J.J., H.M., D.X.; Literature Search –W.H.; Writing – W.H., H.M., D.X., S.G.; Critical Review – D.X., W.H., S.G., J.J.*

Declaration of Interests: *The authors have no conflicts of interest to declare.*

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