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Dietary zinc and iron intake and risk of depression: A meta-analysis

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ABSTRACT

The associations between dietary zinc and iron intake and risk of depression remain controversial. Thus, we carried out a meta-analysis to evaluate these associations. A systematic search was performed in PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure (CNKI) and Wanfang databases for relevant studies up to January 2017. Pooled relative risks (*RRs*) with 95% confidence intervals (*CIs*) were calculated using a random effects model. A total of 9 studies for dietary zinc intake and 3 studies for dietary iron intake were finally included in present meta-analysis. The pooled *RRs* with 95% *CIs* of depression for the highest versus lowest dietary zinc and iron intake were 0.67 (95% *CI*: 0.58–0.76) and 0.57 (95% *CI*: 0.34–0.95), respectively. In subgroup analysis by study design, the inverse association between dietary zinc intake and risk of depression remained significant in the cohort studies and cross-sectional studies. The pooled *RRs* (95% *CIs*) for depression did not substantially change in the influence analysis and subgroup analysis by adjustment for body mass index (BMI). The present meta-analysis indicates inverse associations between dietary zinc and iron intake and risk of depression.

1. Introduction

Depression is a common mental disorder in the general population (Doris et al., 1999). World Health Organization (WHO) has reported that more than 350 million people worldwide suffer from depression. Depression remains the leading cause of disability worldwide, and contributes significantly to the global burden of disease (Ferrari et al., 2013; Murray and Lopez, 1997). Hence, treatments and preventive methods of depression are critical.

Several evidences suggest that depression is a multifactorial disease. Genetic (Caspi et al., 2003), aging (Richardson et al., 2012), sedentary behavior (Zhai et al., 2015) and many other factors contribute to the development of depression in humans (Yary et al., 2010). Evidence shows that depression is also associated with dietary factors, including, fish, fruit, vegetables and coffee (Li et al., 2016; Liu et al., 2016; Wang et al., 2016). Dietary components play important roles in depression, such as vitamin B_{12}, vitamin D and folate (Anglin et al., 2013; Petridou et al., 2016). As essential microelements, zinc and iron are often present in similar dietary sources and deficiencies in iron and zinc often co-occur (Gibson et al., 2002; Lim et al., 2013). Zinc and iron are important in regulating of cellular function and neuromodulation (Momcilovic et al., 2010). Some studies found zinc may also have an influence on the neural transmission involved in depression, such as the serotonergic, dopaminergic and glutamatergic systems (Piotrowska et al., 2013; Toth, 2011). The antidepressant properties of zinc may be explained by modulating the functions of serotonergic and N-methyl-D-aspartate (NMDA) receptors and increasing levels of brain derived neurotrophic factor (BDNF) (Bitanihirwe and Cunningham, 2009; Bresink et al., 1995). Many epidemiological studies have reported the associations of dietary zinc and iron intake and risk of depression. However, the results of these studies were inconsistent. For instance, an inverse association between dietary zinc intake and risk of depression was found in some studies (Amani et al., 2010; Jacka et al., 2012; Kim et al., 2015; Miki et al., 2015), whereas no significant association was found in other studies (Lehto et al., 2013; Maserejian et al., 2012; Vashum et al., 2014). For dietary iron intake, while a significantly association with a decreased risk of depression was reported in two studies (Kim et al., 2015; Miki et al., 2015), the significant association was not found in one study (Woo et al., 2006). Therefore, we conducted a meta-analysis to systemically evaluate the associations between depression and dietary zinc and iron intake.

2. Materials and methods

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline in this meta-analysis (Moher et al., 2009).

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2.1. Search strategy

We searched PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure (CNKI) and Wanfang databases up to January 2017, with the following search terms 'zinc', 'iron', and 'depression', 'depressive disorder', 'depressive symptoms' without restrictions. We also reviewed the reference lists from retrieved articles to identify additional studies not captured by our database search.

2.2. Inclusion criteria

We included studies that met the following criteria: (1) an observational study (cohort, case-control, cross-sectional) published as an original article; (2) the exposure of interest was dietary zinc or iron intake; (3) the outcome of interest was depression; (4) available relative risk (*RR*) or odds ratio (*OR*) with 95% confidence interval (*CI*) (or data to calculate these) was provided (we presented all results with *RR* for simplicity); and (5) the study was conducted within the general population (postpartum depression, depression in pregnancy, diabetes, hypertension and other related diseases population were excluded). The most recent and complete article was chosen if a study had been published more than once.

Two investigators searched articles and reviewed all retrieved studies independently. If the two investigators disagreed about the eligibility of an article, it was resolved by dialogue with a third investigator.

2.3. Data extraction

The following data were extracted from each study by two investigators independently: the first author's name, publication year, country where the study was performed, study design, age range or mean age at baseline years, sex, sample size, the number of depression cases, dietary zinc or iron intake assessment methods, depression assessment methods, variables adjusted for in studies and the most adjusted *RR*s with 95% *CI*s of depression for dietary zinc or iron intake.

2.4. Statistical analysis

Pooled measurement was calculated as the inverse variance-weighted mean of the logarithm of study-specific *RR*s to assess the associations between dietary zinc and iron intake and risk of depression. The I^2 of Higgins and Thompson was used to assess heterogeneity among studies (Higgins and Thompson, 2002) and I^2 values of 0%, 25%, 50%, and 75% represent no, low, moderate, and high heterogeneity, (Higgins et al., 2003) respectively. The DerSimonian and Laird random effects model (REM) was selected as the pooling method (Higgins et al., 2003). Meta-regression analyses were conducted to explore potential sources of heterogeneity. The influence analysis was performed with one study removed at a time to assess whether the results could have been affected markedly by a single study. Subgroup analyses by the continent, study design, dietary zinc assessment methods, depression assessment methods and adjustment for body mass index (BMI) were conducted. Publication bias was evaluated with visual inspection of the funnel plot and Egger's linear regression test. All statistical analyses were performed with Stata V.12.0 (Stata Corp, College Station, Texas, USA). All reported probabilities (*P* values) were two-sided with $P < 0.05$ considered statistically significant.

3. Results

3.1. Literature search and study characteristics

We identified 1625 articles from PubMed, 3571 articles from the Web of Science, 3455 articles from Embase, 481 articles from CNKI and 1463 articles from Wanfang database. After removing duplicates and reviewing the titles or abstracts, 183 articles were retrieved. For the remaining articles, 175 were excluded after reviewing the full text. Ten studies from 8 available articles were finally included in our meta-analysis (Jacka et al., 2012; Kim et al., 2015; Lehto et al., 2013; Maserejian et al., 2012; Miki et al., 2015; Vashum et al., 2014; Woo et al., 2006; Yary and Aazami, 2012). The selection process was shown in Fig. 1.

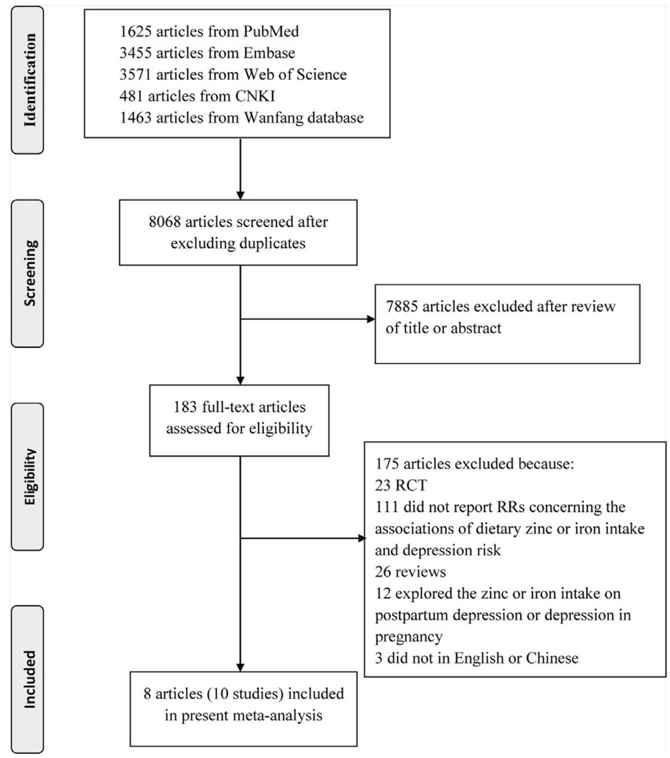

Fig. 1. Flow diagram of literature search.

The characteristics of the included studies were presented in Table 1. Among the 10 studies, 9 studies from 7 articles evaluated the association between dietary zinc intake and risk of depression (Jacka et al., 2012; Kim et al., 2015; Lehto et al., 2013; Maserejian et al., 2012; Miki et al., 2015; Vashum et al., 2014; Yary and Aazami, 2012) and 3 studies provided data of depression for the highest vs the lowest dietary iron intake (Kim et al., 2015; Miki et al., 2015; Woo et al., 2006). One study (Kim et al., 2015) was conducted among adolescents and 9 studies were conducted among adults. The major adjustment confounding factors included age, sex, race, education, marital status, BMI, smoking, alcohol use, and energy intake.

3.2. Quantitative synthesis

3.2.1. Dietary zinc intake and risk of depression

Among the 9 studies, 3 were cohort studies (Lehto et al., 2013; Vashum et al., 2014), 1 was case-control study (Kim et al., 2015) and 5 were cross-sectional studies (Jacka et al., 2012; Maserejian et al., 2012; Miki et al., 2015; Yary and Aazami, 2012). With regard to the study continent, 1 study was conducted in Europe (Lehto et al., 2013), 2 in America (Maserejian et al., 2012), 3 in Asia (Kim et al., 2015; Miki et al., 2015; Yary and Aazami, 2012) and 3 in Oceania (Jacka et al., 2012; Vashum et al., 2014). Among these studies, 6 studies showed a significant association between dietary zinc intake and depression (Jacka et al., 2012; Kim et al., 2015; Maserejian et al., 2012; Miki et al., 2015; Vashum et al., 2014; Yary and Aazami, 2012), while the other 3 studies indicated no significant association (Lehto et al., 2013; Maserejian et al., 2012; Vashum et al., 2014). Six studies assessed depression using Center for Epidemiological Studies Depression (CES-