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Allergic disorders and risk of depression: A systematic review and meta-analysis of 51 large-scale studies

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ABSTRACT

Background: Previous studies have suggested that allergic disorders are associated with an increased risk of depression. However, the results are conflicting.
Objective: To determine the association between allergic disorders and depression based on large-scale studies.
Methods: We reviewed relevant articles obtained from PubMed and Embase. Studies were eligible if they reported an association between allergic disorders and depression and provided available data. Study selection, data extraction, and analyses were undertaken. Pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated.
Results: Of 1,827 studies identified, 51 including more than 2.5 million participants met our inclusion criteria. Overall, the results showed that allergic disorders were associated with a significant increased risk of depression (pooled RR 1.59, 95% CI 1.48–1.71). A higher risk of depression also was observed in patients with asthma (RR 1.59, 95% CI 1.46–1.74) and those with allergic rhinitis (RR 1.57, 95% CI 1.27–1.93). Subgroup analyses were conducted based on sex and age. Children (RR 1.66, 95% CI 1.41–1.96) and adults (RR 1.58, 95% CI 1.44–1.74) with allergic disorders had a higher risk of depression than controls. However, no significant association was found between allergic disorders and risk of depression in male subjects (RR 1.37, 95% CI 0.98–1.91), but a positive association was detected in female subjects (RR 1.65, 95% CI 1.44–1.89).
Conclusion: The results from our study showed that allergic disorders significantly increased the risk of depression.

Introduction

Allergic disorders have become major worldwide public health issues, causing severe social and economic burdens and significant quality-of-life impairment.[1] Moreover, the prevalence of allergic disorders, such as asthma and allergic rhinitis, which are estimated to affect 300 million and 400 million people, respectively, around the world, has continued to escalate over time.[2] Equally detrimental is depression, another major global public health issue. As one of the major psychiatric diseases, depression severely affects patients and society. In total 4% to 20% of the population around the world have had major depression during their lifetime, and it is forecast to be the second leading cause of disability by 2020.[3] Therefore, depression, allergic disorders, and especially their association have become worldwide subjects of current research and clinical interest.

An association between allergic disorders and risk of depression has been hotly debated, but the relation is inconsistent rather than conclusive. A large population-based epidemiologic study reported an association between allergic disorders and a significantly higher risk of depression.[4] Further, the temporal association in adolescents in Taiwan suggested the atopic cohort had an increased risk of major depression compared with the nonatopic cohort after a 10-year duration.[5] However, Brunner et al[6] found no significant association between allergic disorders and risk of depression in a prospective study.

Therefore, we carried out this systematic review and meta-analysis based on large-scale studies to examine the association between allergic disorders and risk of depression.

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Methods

Search Strategy

We selected relevant studies by searching PubMed and Embase from inception until November 2016. Allergic disorders were identified using the following search terms: *asthma, allergic rhinitis, hay fever,* and *allergy* or *atopy.* The search terms *depression* or *depressive disorders* were used to identify citations relevant to depression. The search was limited to articles published in the English language and conducted in humans. Case reports, reviews, editorials, comments, practice guidelines, historical articles, news, and meta-analyses were excluded.

Study Selection

We screened titles and abstracts against the inclusion criteria to identify potential relevance, and then the full-text copies of potentially relevant articles were retrieved and reviewed to confirm eligibility. To enhance the reliability of the results, we specified a minimum sample of 100 participants for all epidemiologic studies. In cohort studies, the exposure was allergic disorders and the end point was depression. In cross-sectional studies, we selected articles or abstracts that assessed the prevalence of depression in patients with allergic disorders compared with a nonallergic group. Studies were eligible if they reported odds ratios (ORs) or relative risks (RRs) or raw data from which we could derive RRs with 95% confidence intervals (CIs) for the potential effect of allergic disorders on risk of depression.

Data Extraction

We extracted the surname of the first author, year of publication, country of study origin, participants' characteristics including age group (children or adults), sex and number of participants, types of allergic disorders, criteria of allergic disorders and depression diagnosis, duration of follow-up (for cohort studies), and risk estimates from enrolled studies. When studies reported ORs or RRs with different degrees of adjustment for several risk factors, we used the maximum adjusted estimate. For studies presenting with several categories, the highest vs lowest category was used to calculate the pooled RR. For studies with different criteria of allergic disorder diagnosis (such as the association between self-reported asthma and risk of depression or between register-based asthma and risk of depression), we selected the RRs for the best diagnosis method (register-based asthma). For cohort studies, if studies reported depression at several intervals, we selected the longest period for this meta-analysis.

Data Analysis

The RRs and corresponding 95% CIs were used to assess the association between allergic disorders and risk of depression. We extracted dichotomous data from studies reporting the number of patients with events and total participants and pooled them to calculate RRs and 95% CIs. In addition, subgroup analyses by sex, age, and diseases (asthma and allergic rhinitis) were performed. In analyses, we assessed heterogeneity with the Cochran *Q* statistic, with a *P* value less than .10 suggesting evidence of heterogeneity. Then, the magnitude of heterogeneity was measured using the I^2 statistic, with values of 25% to 49% representing low heterogeneity, values of 50% to 75% representing moderate heterogeneity, and values greater than 75% representing high heterogeneity.[7] The funnel plot was used to evaluate the possibility of publication bias. We used the Begg test and Egger test to test for the asymmetry of funnel plots. All statistical analyses were conducted with Review Manager 5.3 (Cochrane Collaboration, London, United Kingdom) and STATA 12 (StataCorp, College Station, Texas). Statistical results were deemed significant if the 2-sided *P* value was less than .05.

Results

Study Selection

Figure 1 shows the flow diagram of study identification and selection. We identified 721 articles from the PubMed database and 3,335 articles from the Embase database. After removing duplicates, we identified 1,827 unique citations from the electronic database. After initial screening, based on titles and abstracts, 81 articles or abstracts remained for further assessments. After detailed evaluation, 30 more articles were excluded according to our inclusion criteria. Therefore, 51 studies were included in our systematic review and meta-analysis.[4–6,8–55]

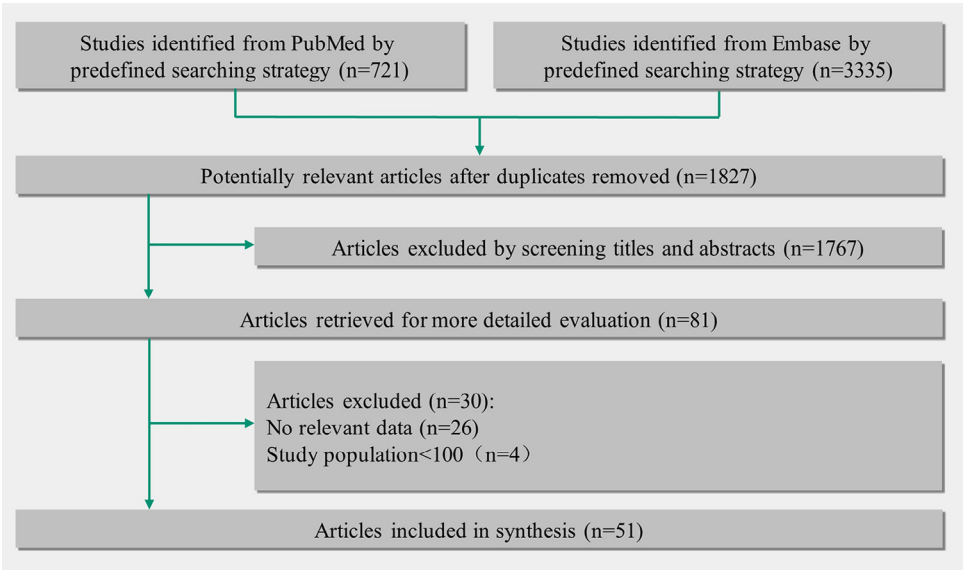

Figure 1. Details of literature search and study selection.