

THE ASSOCIATION BETWEEN ANTICHOLINERGIC MEDICINE AND COGNITION DECLINE IN OLDER ADULTS: A SYSTEMIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objectives

Some randomized clinical trials indicated the increasing risk of cognition decline by anticholinergic medicine, while the association did not found by other clinical trials. The meta-analysis studies have been made by scholars, but this controversy has not been resolved by them. The goal of this systemic review and meta-analysis was to confirm the association between anticholinergic medicine and cognition decline in older adults by using additional RCTs and further analyses.

Methods

Following the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA), electronic databases (PubMed, EMBase, and Cochrane) were searched for all clinical trials and observational studies till August 15, 2019. The outcome of interest was cognition decline in older adults with anticholinergic medicine exposure. We used MMSE (mini-mental state examination) as an outcome variable. Figure 1 shows the flow diagram of the study selection. The JADAD quality score was applied to evaluate bias in randomized controlled trials (RCTs) (Table 1). Heterogeneity was assessed using I² tests. Subgroup analysis were furtherly performed. Five RCTs were divided into 2 subgroups as inpatient + outpatient individuals and nursing home residents. Publication bias was assessed using Funnel plot.

Results

A total of 5 RCTs were included for full article review, and the meta-analysis was performed based on these 5 RCTs with 225 individuals. Both of fixed effect and random effect were performed, and the results showed no association between anticholinergic medicine exposure and cognition decline (fixed effect, $p=0.036$, 95% CI; random effect, $p=0.413$, 95% CI) (Figure 2). High heterogeneity among studies ($I^2=84.94\%$) were found, and subgroup analysis was performed (Figure 3). Heterogeneity among studies with inpatient + outpatient individuals was low ($I^2=20.45\%$), and heterogeneity among studies with nursing home residents was high ($I^2=88.28\%$). Figure 4 reveals the funnel plot of publication bias, and there was no significant publication bias (Egger's regression intercept, $p=0.95$).

Conclusions

In conclusion, the present study did not find the association between anticholinergic medicine exposure and cognition decline in older adults.

Keywords

meta-analysis, anticholinergic medicine, cognition decline, older adult

Key Findings and Strengths of This Study

- We did a comprehensive systemic review and meta-analysis, and we did not find the association between anticholinergic medicine exposure and cognition decline in older adults. The result was compatible with previous systemic review and meta-analysis.
- There were significant heterogeneities in our meta-analysis and previous meta-analysis, and we tried to deal with heterogeneity by performing subgroup analysis. Heterogeneity among studies with inpatient + outpatient individuals was low ($I^2=20.45\%$), and heterogeneity among studies with nursing home residents was high ($I^2=88.28\%$).
- The subgroup analysis showed that heterogeneity was majorly from the studies of nursing home residents, and we should be cautious in interpreting the results regarding to nursing home residents.
- We believed that it is very difficult to perform another meta-analysis for this topic in the near future, because there were few randomized clinical trials with small numbers. We included 5 RCTs for final meta-analysis, and 5 RCTs are the most we could include to date. In addition, most studies used different tools in cognition assessment, and reports of cognition changes as continuous or categorical variables were inconsistent. We used MMSE as an outcome variable, because it was the gold standard in cognition assessment.

Figure 1. Flow chart

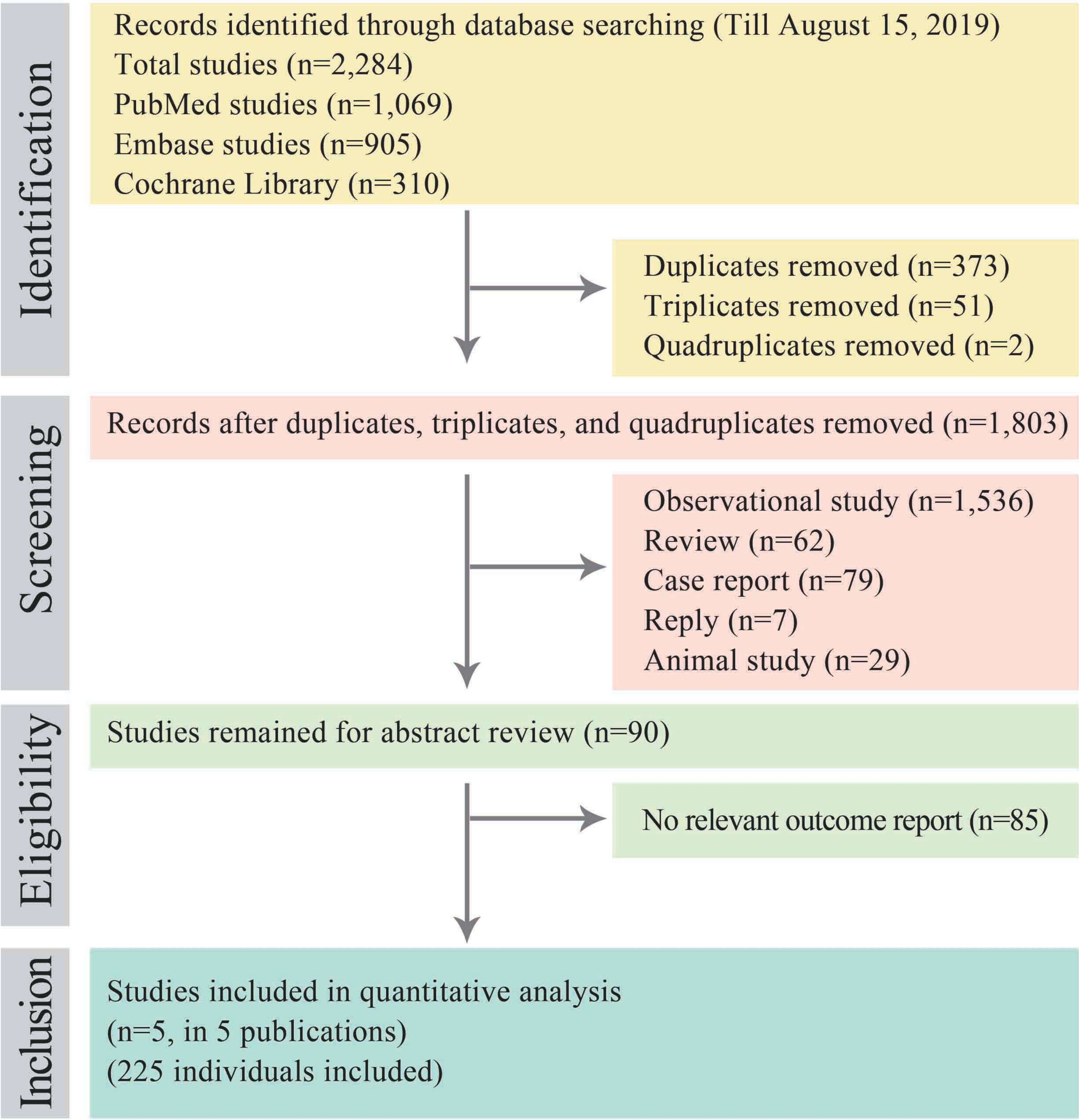


Table 1. Characteristics and quality evaluation of selected studies

Study	Year	Outcome	Anticholinergic		Control		JADAD
			N	Mean (S.D.)	N	Mean (S.D.)	
Miller	1988	MMSE	16	26.7 ± 3.5	16	26.7 ± 3.5	1+1+1=3
Tollefson	1991	MMSE	15	23.03 ± 4.92	15	23.03 ± 4.92	1+1+1=3
Lackner	2008	MMSE	26	15.2 ± 0.8	26	15.2 ± 0.8	2+2+1=5
Kersten	2013	MMSE	34	14.46 ± 5.92	34	14.46 ± 5.92	2+0+1=3
Geller	2017	MMSE	21	28.1 ± 1.9	21	28.1 ± 1.9	2+2+1=5

Figure 2. Forest plot of standardized differences in means between anticholinergic medicine and mini-mental state examination scores

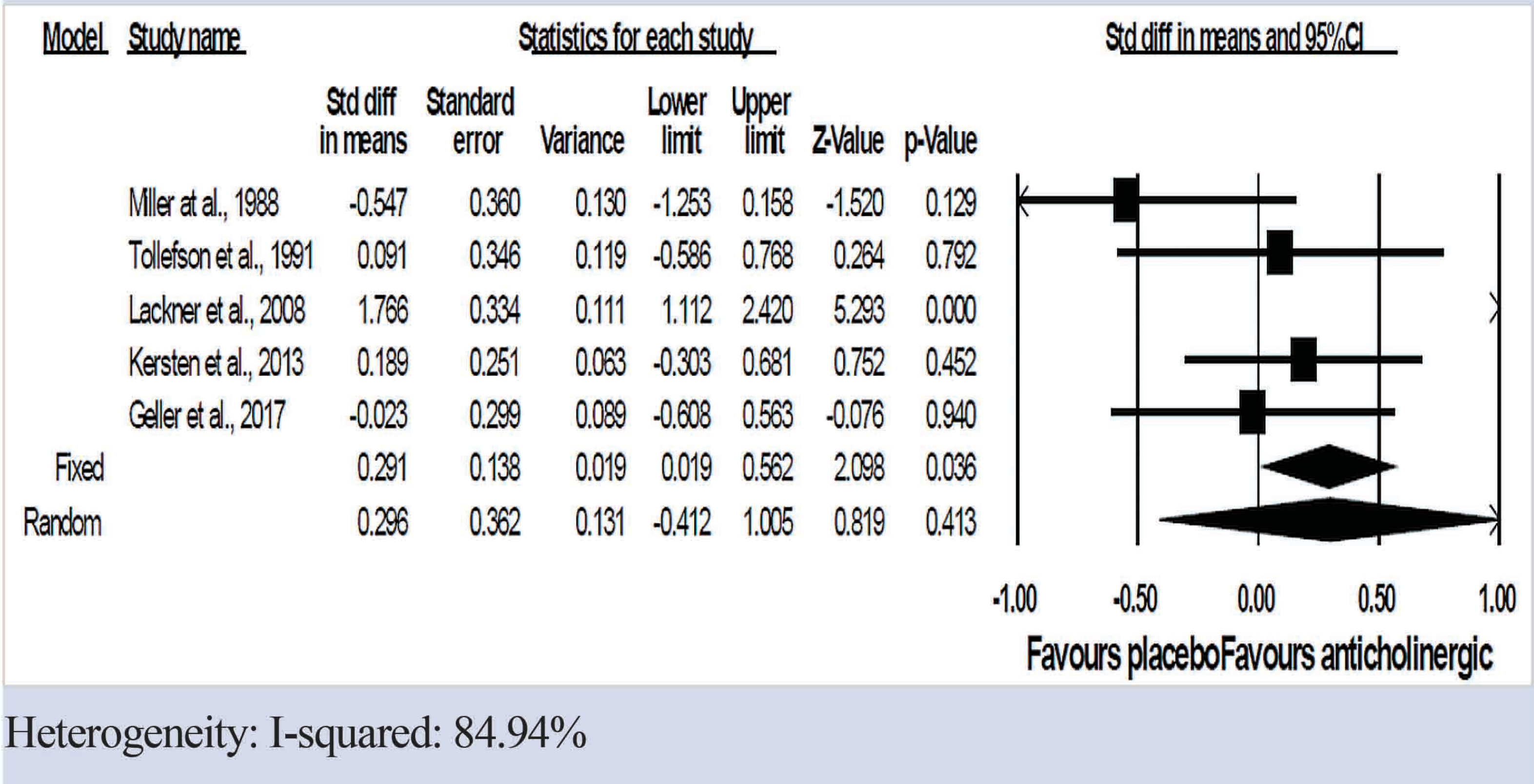


Figure 3. Forest plot of standardized differences in means between anticholinergic medicine and mini-mental state examination scores by subgroup analysis

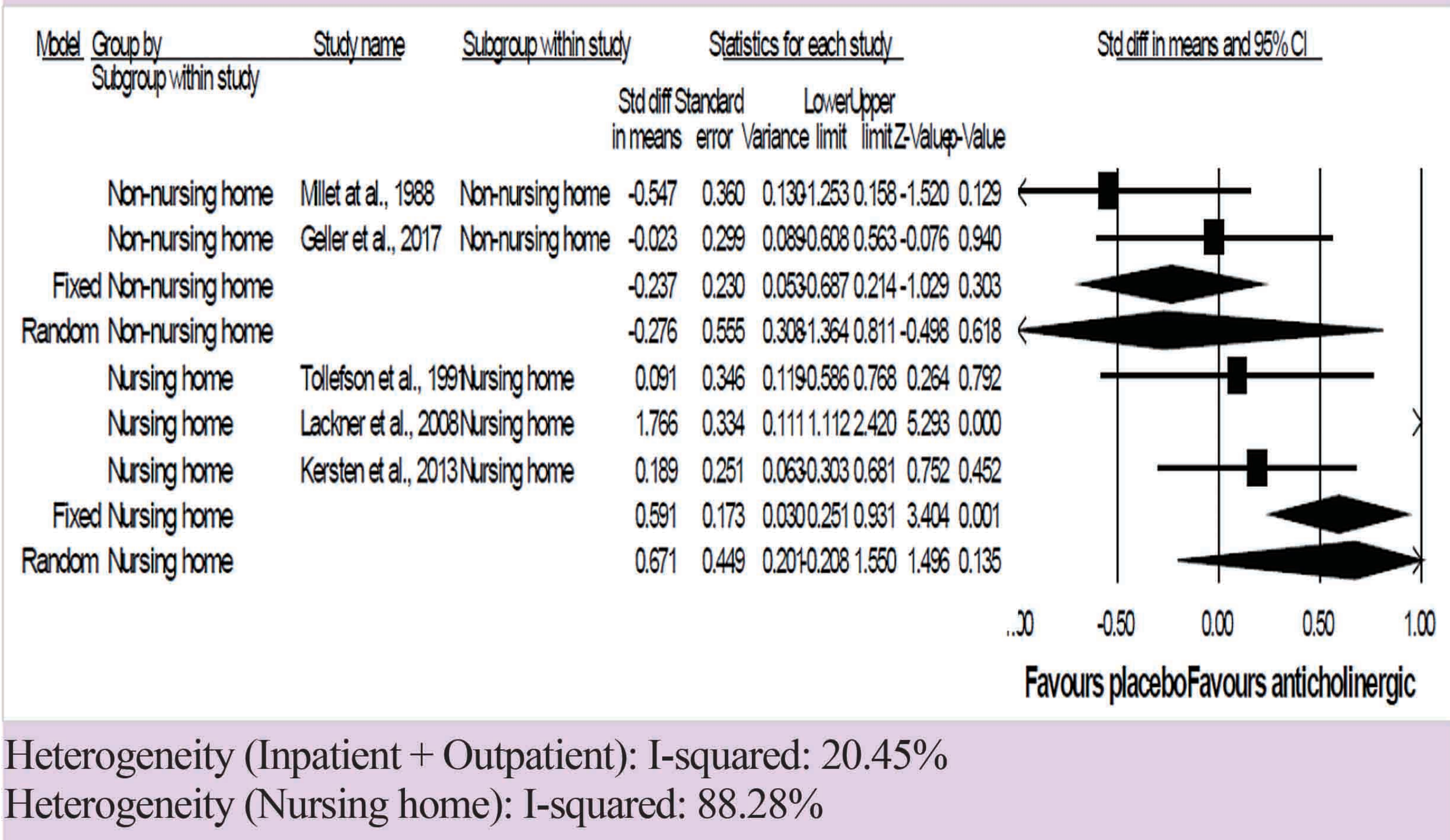


Figure 4. Funnel plot of publication bias

