

Focused and Unfocused Transcranial Ultrasound Stimulation in Alzheimer’s Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Abdelrahman I. Abdellatif^{1,6}, Asmaa Elsharab^{2,6}, Elsayed S. Moubarak³, Khalid Radwan Alsaadany^{4,6}, Youssef W. Ayad^{5,6}

1. Faculty of Medicine, Minia University, Minia, Egypt.
2. Clinical Pharmacy Department, Faculty of Pharmacy, Tanta University, Tanta, Egypt.
3. Faculty of Medicine, Cairo University, Cairo, Egypt
4. Faculty of Medicine, Mansoura University, Mansoura, Egypt
5. Faculty of Medicine, Badr University in Cairo, Cairo 11829, Egypt
6. Medical Research Group of Egypt (MRGE), Negida Academy, Arlington, MA, USA.

INTRODUCTION

Transcranial ultrasound stimulation (TUS) is a non-invasive method that allows deep brain structures to be targeted, and it may benefit individuals with Alzheimer's disease (AD).

AIM

We conducted a systematic review and meta-analysis to assess the effect of TUS on global cognitive function in mild-to-moderate AD, comparing focused transcranial pulse stimulation (TPS) with unfocused low-intensity pulsed ultrasound (LIPUS).

METHOD

We searched PubMed, Scopus, Cochrane, and Web of Science for randomized controlled trials (RCTs) comparing TUS with sham stimulation. The primary outcome was the change in global cognitive function. Secondary outcomes included functional status, depressive symptoms, and safety.

CONCLUSION

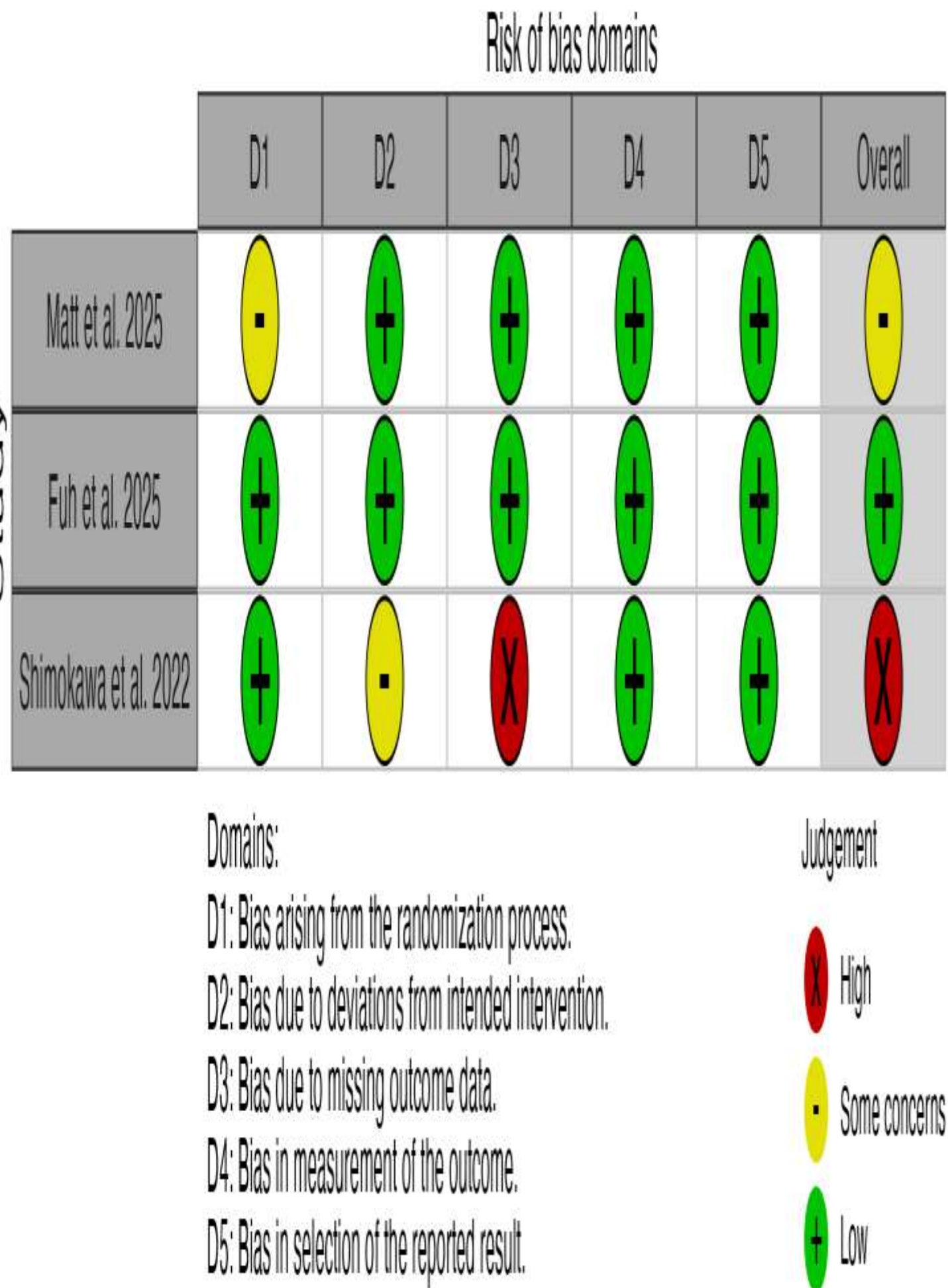
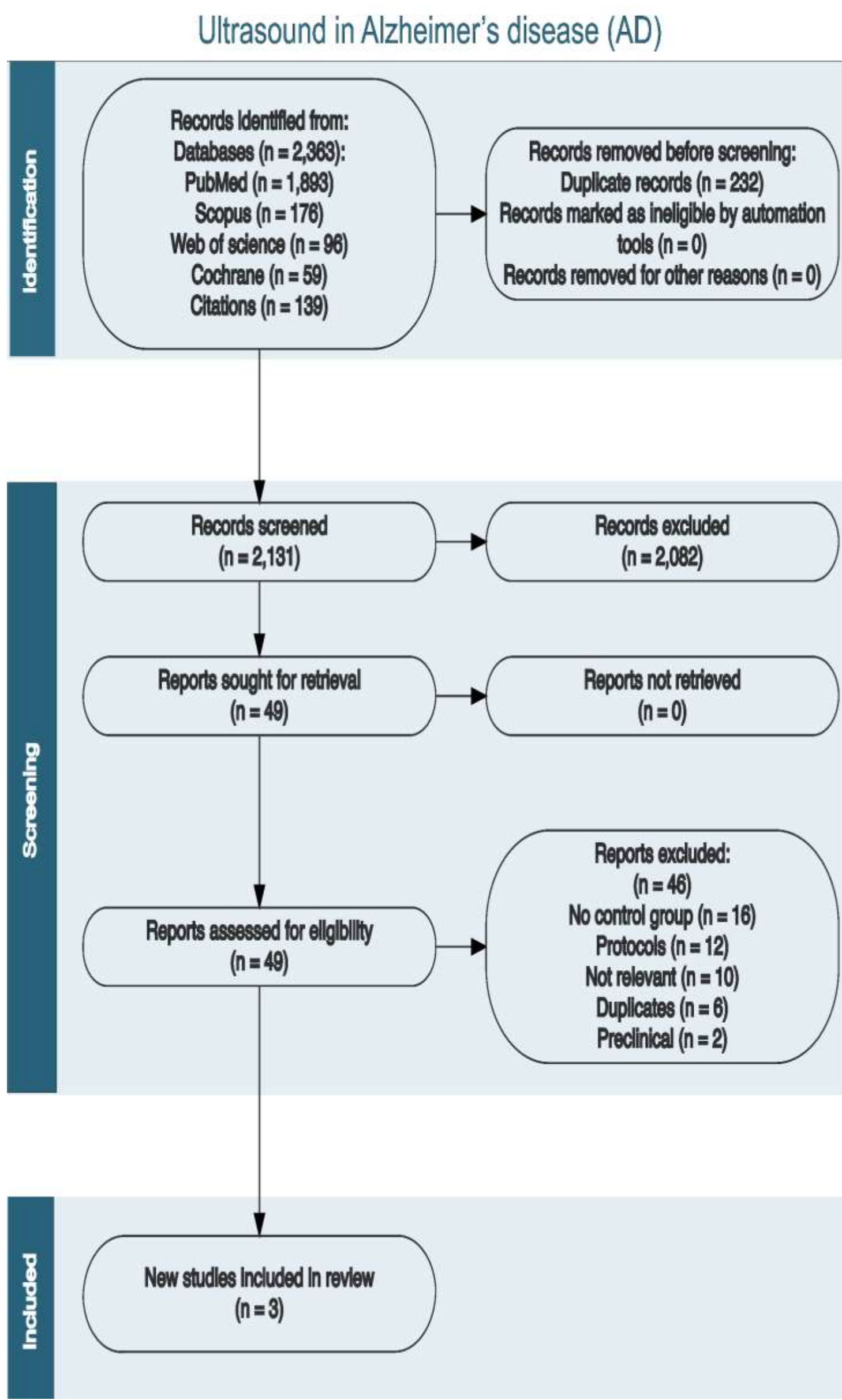
While pooled analyses did not show a global cognitive benefit, the results favoured unfocused LIPUS over focused TPS, TUS had an excellent safety profile and higher disease stabilization rates; the potential benefits in younger populations and the biological effects suggest that TUS is a promising adjunct that should be further optimized for stimulation.

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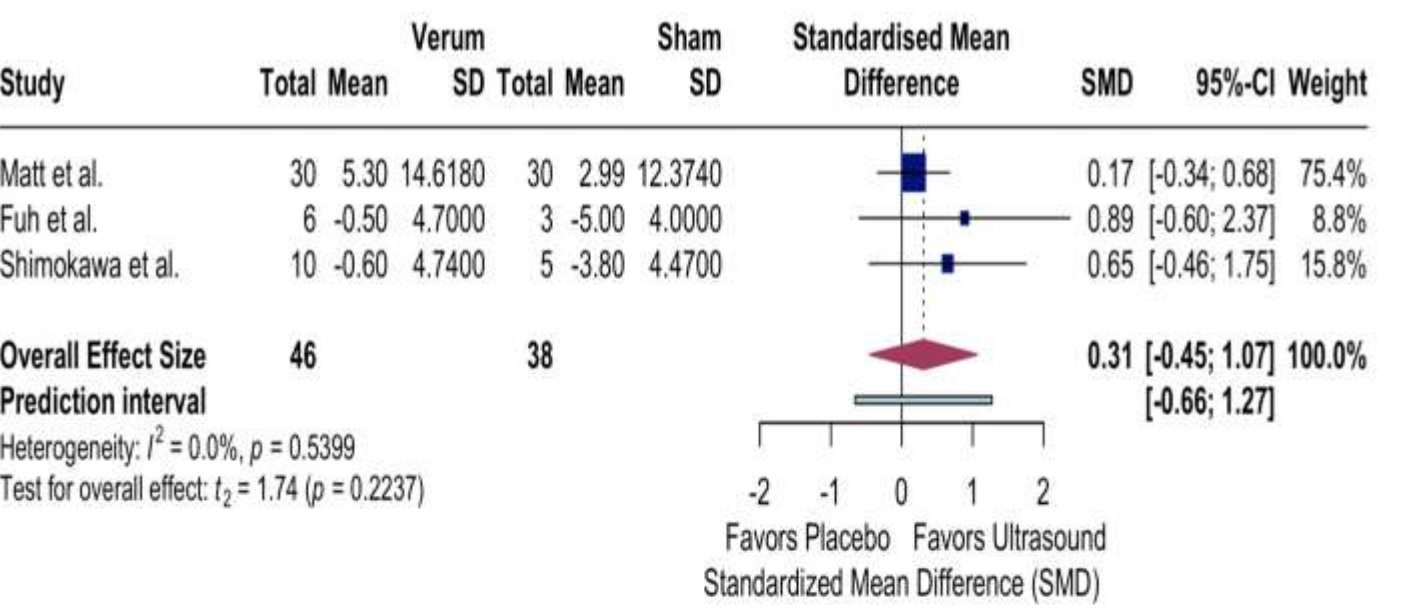
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RESULTS

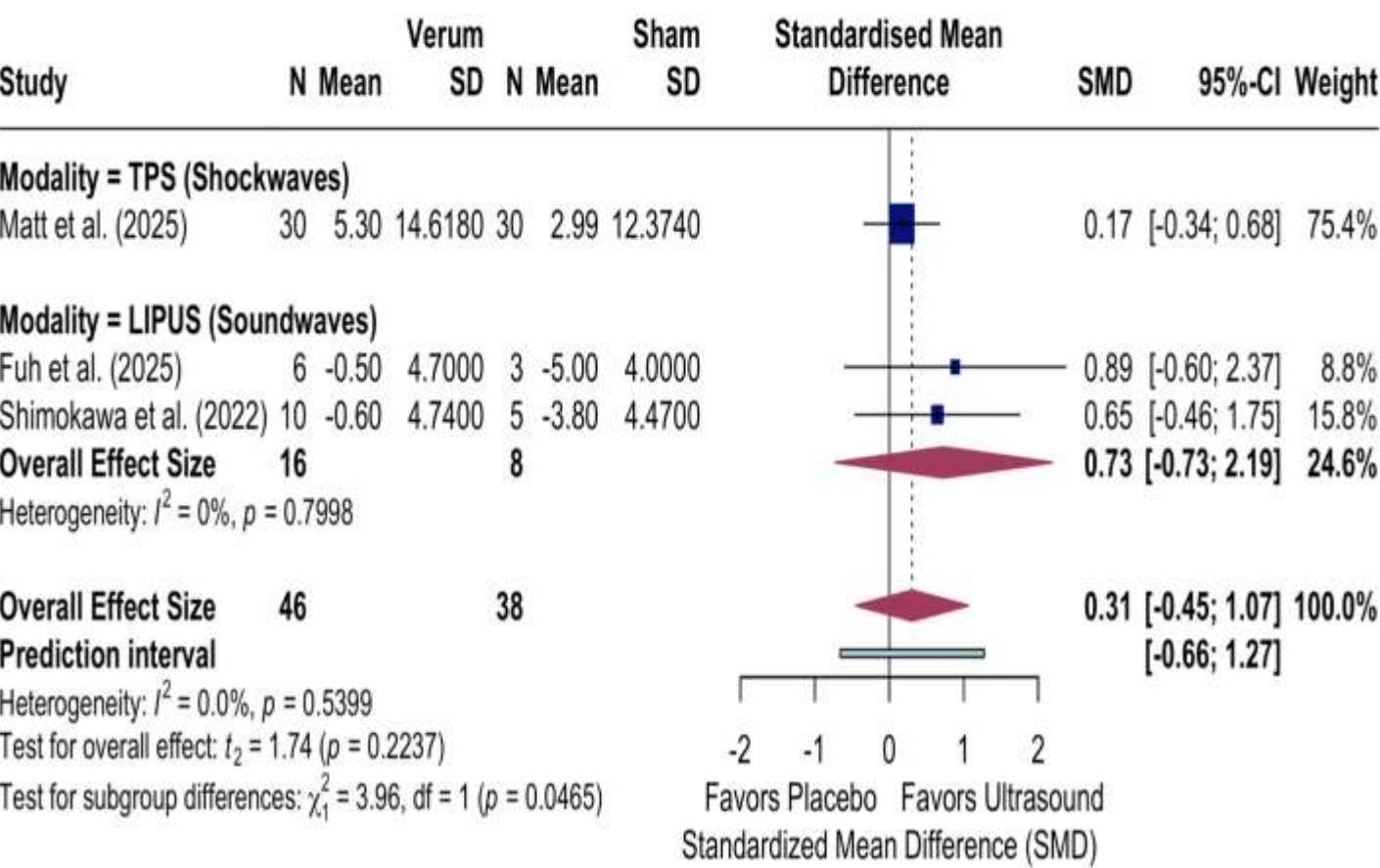
Three RCTs (N=84) were included. Pooled analysis showed that TUS did not significantly improve global cognition compared with sham (SMD=0.31, p=0.54). However, subgroup analysis showed a significant difference between modalities (p=0.047): unfocused LIPUS had a larger effect size (SMD=0.73) than focused TPS (SMD=0.17). Notably, significant cognitive improvement was observed in patients <70 years. Active treatment showed higher disease stabilization rates ("responders"), reduced depressive symptoms (specifically TPS, p=0.008), and improved cerebral perfusion without amyloid-related imaging abnormalities (ARIA).



(A)



(B)



CONTACT INFORMATION

Asmaa Elshafey Abdeltawab Elsharab
E-mail: asmaa94.elshafey@gmail.com