Web-only Commentary

Whithead et al present a meta-analysis of donepezil for the treatment of patients with mild to moderate Alzheimer’s disease, including 10 studies that met appropriate criteria. While there are a number of meta-analyses and less systematic reviews considering the efficacy of various cholinesterase inhibitor therapies, this paper has a clear methodological advantage as individual patient data were used. In addition, the similarity of inclusion criteria and the assessment measures for the individual studies facilitate the meta-analysis approach.

For a total of more than 2300 patients, the data indicate clear advantages for donepezil treatment compared with placebo on cognition and global clinician rating after both 12 and 24 weeks of treatment, with only modest adverse events. Importantly, the meta-analysis indicated greater efficacy for the 10mg than the 5mg dose of donepezil.

This study confirms, in a more robust evaluation, the meaningful clinical benefits of donepezil in people with mild to moderate Alzheimer’s disease. However, the study was completed before the publication of the much discussed AD 2000 study,1 which concluded that despite significant efficacy upon cognitive and global performance, donepezil treatment was not cost effective. This has triggered widespread debate regarding the usefulness of donepezil. It is unfortunate that the AD 2000 study could not be included in the meta-analysis, which as a result is already out of date, particularly as it is unlikely that the inclusion of these data would have changed any of the conclusions.

Despite the considerable ethical issues raised with respect to the current emphasis placed by the National Institute of Clinical Excellence and others on the cost effectiveness of cholinesterase inhibitor therapy, a robust meta-analysis of the health economic evaluations from randomised placebo controlled trials of cholinesterase inhibitors is now the main priority to inform current thinking regarding the place of these treatments in the therapeutic armoury.

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Reference