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- CMAJ. 2004 Nov 9;171(10):1174-5.
- Evid Based Ment Health. 2004 Nov;7(4):112.
- Lancet. 2004 Jun 26;363(9427):2100-1.
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- Lancet. 2004 Oct 2;364(9441):1214-5; author reply 1216-7.
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- Lancet. 2004 Oct 2;364(9441):1215-6; author reply 1216-7.

Long-term donepezil treatment in 565 patients with Alzheimer's disease (AD2000): randomised double-blind trial.

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BACKGROUND: Cholinesterase inhibitors produce small improvements in cognitive and global assessments in Alzheimer's disease. We aimed to determine whether donepezil produces worthwhile improvements in disability, dependency, behavioural and psychological symptoms, carers' psychological wellbeing, or delay in institutionalisation. If so, which patients benefit, from what dose, and for how long? METHODS: 565 community-resident patients with mild to moderate Alzheimer's disease entered a 12-week run-in period in which they were randomly allocated donepezil (5 mg/day) or placebo. 486 who completed this period were rerandomised to either donepezil (5 or 10 mg/day) or placebo, with double-blind treatment continuing as long as judged appropriate. Primary endpoints were entry to institutional care and progression of disability, defined by

loss of either two of four basic, or six of 11 instrumental, activities on the Bristol activities of daily living scale (BADLS). Outcome assessments were sought for all patients and analysed by logrank and multilevel models. FINDINGS: Cognition averaged 0.8 MMSE (mini-mental state examination) points better (95% CI 0.5-1.2; p<0.0001) and functionality 1.0 BADLS points better (0.5-1.6; p<0.0001) with donepezil over the first 2 years. No significant benefits were seen with donepezil compared with placebo in institutionalisation (42% vs 44% at 3 years; p=0.4) or progression of disability (58% vs 59% at 3 years; p=0.4). The relative risk of entering institutional care in the donepezil group compared with placebo was 0.97 (95% CI 0.72-1.30; p=0.8); the relative risk of progression of disability or entering institutional care was 0.96 (95% CI 0.74-1.24; p=0.7). Similarly, no significant differences were seen between donepezil and placebo in behavioural and psychological symptoms, carer psychopathology, formal care costs, unpaid caregiver time, adverse events or deaths, or between 5 mg and 10 mg donepezil. INTERPRETATION: Donepezil is not cost effective, with benefits below minimally relevant thresholds. More effective treatments than cholinesterase inhibitors are needed for Alzheimer's disease.

Publication Types:
- Clinical Trial
- Multicenter Study
- Randomized Controlled Trial

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