

# A Comparative Analysis of Long-Term Experience With Cholinesterase Inhibitors in a Memory Disorders Clinic

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## BACKGROUND

- Cholinesterase inhibitors (ChEIs) are the most commonly prescribed medications for Alzheimer's disease (AD).
- Four ChEIs have been approved in the United States. Donepezil, rivastigmine, and galantamine are commonly used. Tacrine is disfavored because of its dosing regimen and potential hepatotoxicity.
- There is no compelling clinical evidence that any one ChEI is superior over the others in short-term studies of 1 year or less.<sup>1,2</sup>
- We wished to explore if long-term clinical experience of 2.5 or more years with ChEIs might reveal evidence for advantage of one compound over the others.

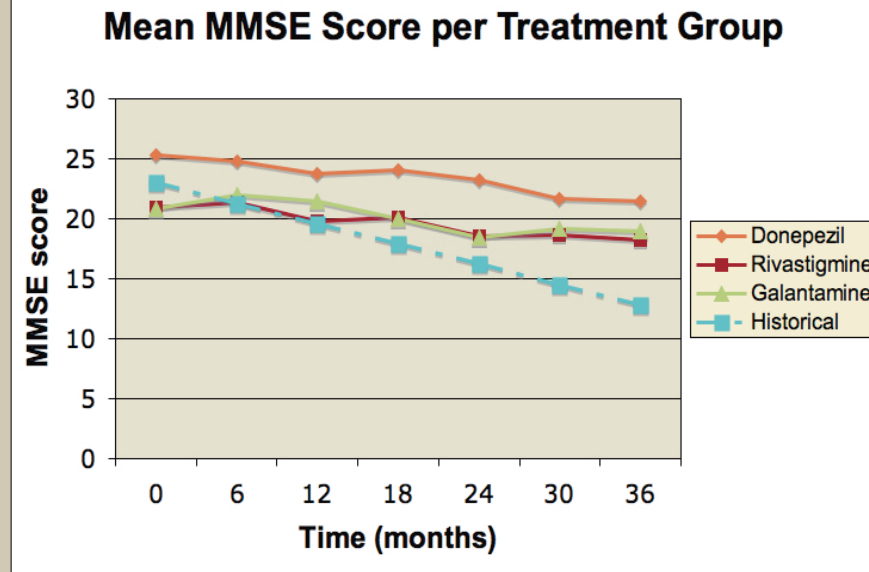
## OBJECTIVE

Evaluate real-life long-term experience with ChEIs in a memory disorders clinic over a minimum of 2.5 years

## METHODS

- We performed a retrospective chart review of patients seen at the University of Alabama at Birmingham (UAB) Memory Disorders Clinic over the past 8 years. Patients with a diagnosis of possible or probable AD by NINCDS-ADRDA criteria<sup>3</sup> or with a diagnosis of MCI according to Petersen criteria<sup>4</sup> who had received a ChEI for at least 2.5 years were included in the analysis.
- Cognitive ability was assessed on average every 6 months using the Mini-Mental State Examination (MMSE).
- The trajectories of the patients were followed for 36 months, when there was continued follow-up of at least 60% of the original patients who remained on the same drug in each group.
- We compared our results to the trajectory reported in three previous studies.<sup>5,6,7</sup> The rate of decline on the MMSE in these historical controls ranged from 2.8 to 3.8 points, with a weighted average decline of 3.4 points per year.

## Mean MMSE Score per Treatment Group



## RESULTS

- Out of 3,388 total patients seen at the UAB Memory Disorders Clinic over the previous eight years, 314 individuals had a diagnosis of AD or MCI and had taken the same ChEI for at least 2.5 years.
- Of these 314 patients, we randomly selected 49 who were treated with donepezil for at least 2.5 years, and we included all available patients treated for at least 2.5 years with rivastigmine (N=22) or galantamine (N=46).
- In part, the number of patients on rivastigmine or galantamine is smaller than the number of patients on donepezil because these drugs were approved several years later than donepezil. This limited the opportunity for patients to have long-term experience with these drugs.

## RESULTS

	Aricept	Exelon	Reminyl	p
Age, mean (std)	72 (10)	68 (9)	71 (8)	0.2268
Female, N (%)	35 (71%)	8 (37%)	26 (57%)	
Male, N (%)	14 (29%)	14 (63%)	20 (43%)	0.0192
MMSE T0, mean (std)	25.2 (3.4)	20.9 (4.6)	20.6 (6.3)	0.0006
MMSE T36, mean (std)	20.6 (6.2)	19.6 (5.2)	19.3 (9.5)	0.8506

- There was no statistically significant difference between ChEIs in slope of decline after adjusting for age, sex, and initial MMSE score,  $p = 0.8152$ .
- Scores decline with time ( $p < .0001$ ), and initial MMSE scores affect the slope ( $p < 0.0001$ ).

## CONCLUSIONS

This study extends previously conducted shorter term studies showing that ChEIs overall have similar efficacy. Benefits of ChEIs, as a class, appear to extend beyond 2.5 years, and are significant when compared to historical controls. Despite the retrospective nature of the study, the knowledge gained from this real-life experience indicates that other factors such as tolerance and cost may be more important when selecting a ChEI.

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