Activities of Daily Living – Outcome During Three Years in Donepezil Treated Alzheimer Patients.

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ACTIVITIES OF DAILY LIVING
– OUTCOME DURING THREE YEARS IN
DONEPEZIL TREATED ALZHEIMER PATIENTS

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Objectives

To analyse and present the outcome of longitudinal change in ADL function and cognition in patients treated with donepezil for three years.

Methods and Subjects

The Swedish Alzheimer Treatment Study (SATS) is an open, long-term, multicentre study in a routine clinical setting. Patients with the diagnosis of Alzheimer's disease received the cholinesterase inhibitor donepezil. The 435 patients were assessed with several functional and cognitive rating scales including IADL, PSMS, FAST, MMSE and ADAS-cog at baseline and every 6 months for a total period of three years. A mathematical correction of the sum of the IADL scores was performed to ensure that activities more commonly done by women did not affect the result between genders.

The expected rate of IADL decline in untreated patients was calculated using a linear equation as presented by Green et al.[1, 2]:

$$\Delta IADL = 10,124 - 0,332 * IADL_{Bas}$$

in which $\Delta IADL$ is the annual rate of decline of IADL and $IADL_{Bas}$ is the IADL score at baseline.
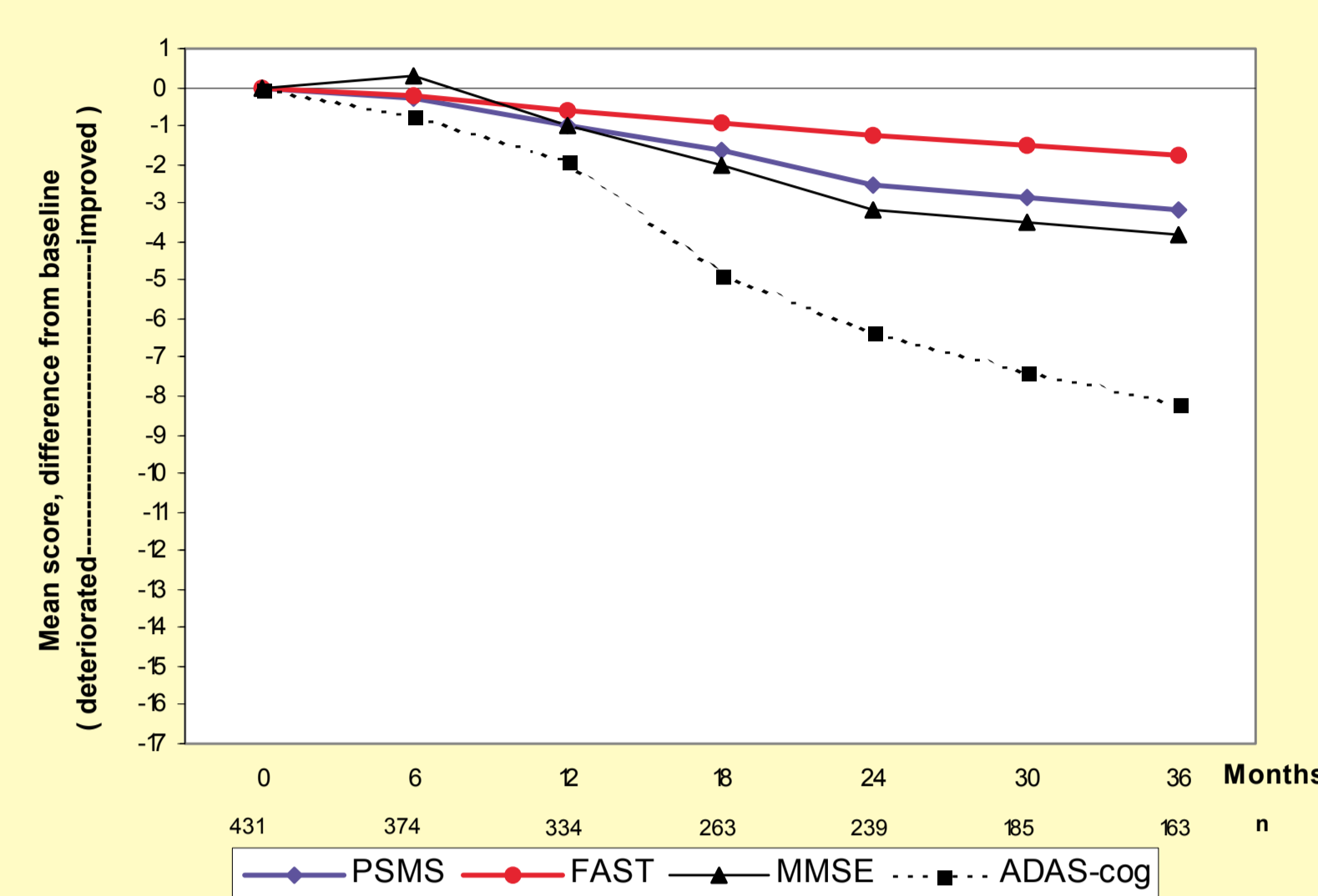
A two-step cluster analysis was performed to reveal any natural groupings (clusters) of the patients based on the ADL scores at baseline.

Baseline characteristics	
Number of patients (n)	435
Gender (males/females)	35 %/65 %
Donepezil mean dose during study, mg/day	6.5 – 8.3
3 year completion rate	38 %
Age at start of donepezil treatment*	74.6 ± 6.5
Illness duration, years*	3.1 ± 2.3
MMSE*	22.0 ± 4.6
ADAS-cog (0-70)*	20.7 ± 10.0
IADL*	15.9 ± 5.8
PSMS*	7.4 ± 2.2
FAST*	4.0 ± 1.3
*mean ± SD	

| IADL – Instrumental activities of daily living scale (8 – 31) |
| PSMS – Physical Self–Maintenance Scale (6 – 30) |
| FAST – Functional assessment staging (0 – 16) |
| MMSE – Mini Mental State Examination (30 - 0) |
| ADAS-cog - Alzheimer's Disease Assessment Scale-cognitive subscale (0 – 70) |

Reference List

[1] Green CR, Mohs RC, Schmeidler J, Aryan M, Davis KL. Functional decline in Alzheimer's disease: a longitudinal study. Journal of the American Geriatrics Society. 1993 Jun;41(6):654-61.

[2] Imbimbo BP, Verdelli G, Martelli P, Marchesini D. Two-year treatment of Alzheimer's disease with eptastigmine. The Eptastigmine Study Group. Dementia and geriatric cognitive disorders. 1999 Mar-Apr;10(2):139-47.

Results

Fig A   PSMS, FAST

After three years of donepezil treatment the total mean decline from baseline in PSMS score was 3,2 ± 3,6 points and in FAST 1,8 ± 2,1 points. Comparisons between efficacy measures showed that the PSMS and FAST mean changes from baseline had a significant correlation with ADAS-cog (p < 0.01) at 6 months. MMSE and ADAS-cog mean changes from baseline showed significant correlations with PSMS (0,000<p<0,01) and FAST (p < 0.001) at all intervals during 12 to 36 months, and the strength of the relationship increased over time.

Fig B   IADL
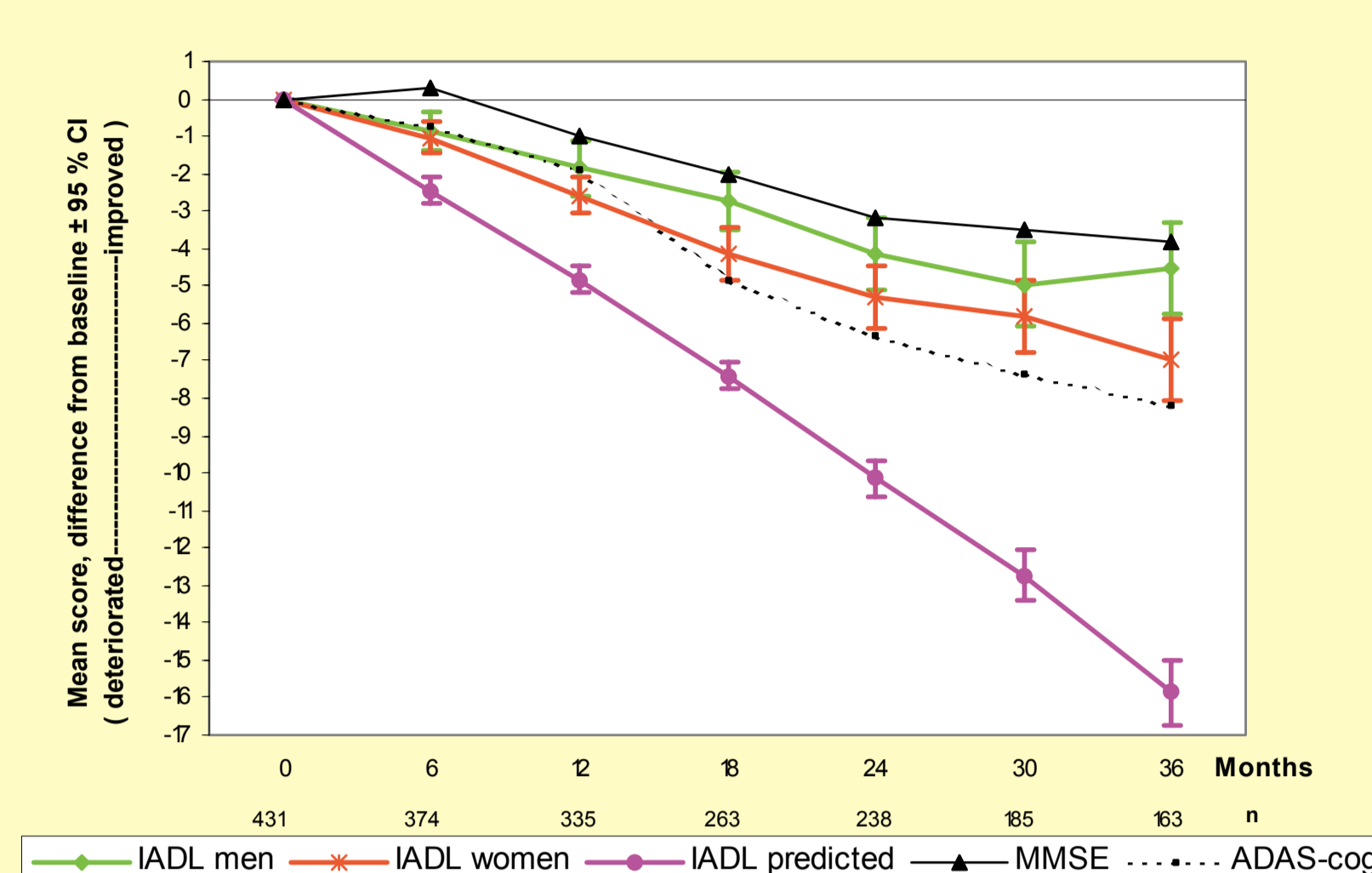
After three years of donepezil treatment the total mean decline from baseline in IADL-score was 6.1 ± 5.4 (mean ± SD) points. Using the mathematical model by Green et al.[1] patients in this study would be expected to decline approximately 15.8 ± 5.6 points on IADL score after 3 years. The IADL changes from baseline show a strong linear relationship (p<0,001) with cognition at all assessments between 12 and 36 months. None of the ADL scales showed significant differences between gender at baseline but after three years the IADL mean decline from baseline was significantly worse among females 7.0 ± 5.7 (p<0,01) compared to males 4.5 ± 4.6.

431 patients with complete items in the three ADL scales at baseline were analysed in a two-step cluster analysis. Two clusters (groups) were identified (p<0,001).

Fig C

The 10 most significant variables between the two groups, in order of significance, were:
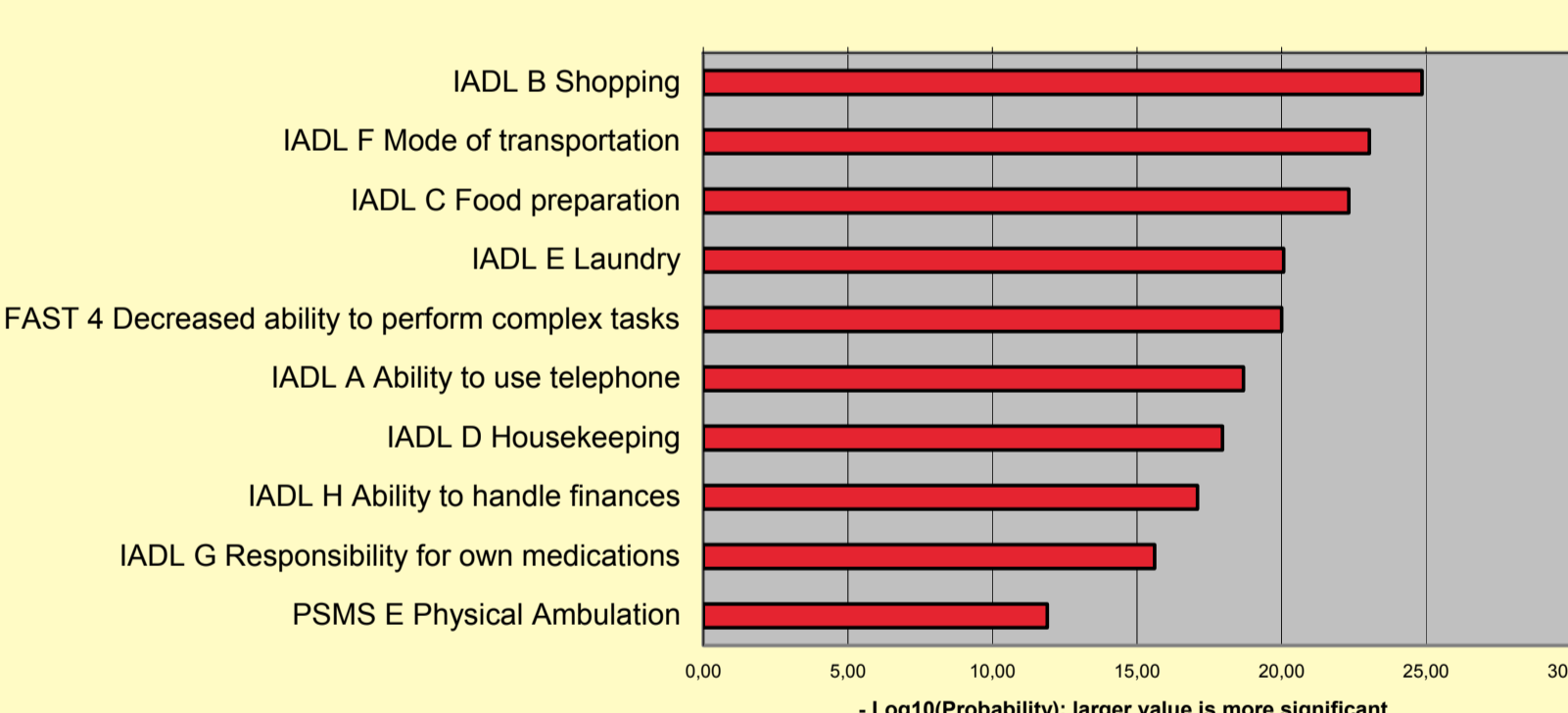
Other significant differences between the two groups

	Cluster 1, n=234 Lower ADL function at baseline, see fig C	Cluster 2, n=197 Higher ADL function at baseline, see fig C	P-value
Age at start of treatment	76.4 ± 5.7	72.5 ± 6.8	p<0,001
Illness duration, years	3.3 ± 2.4	2.9 ± 2.1	p<0,05
MMSE at baseline*	20.1 ± 4.4	24.3 ± 3.5	p<0,001
ADAS-cog at baseline*	25.0 ± 10.1	15.8 ± 7.5	p<0,001
PSMS change between:*			
baseline and 12 months	-1.2 ± 2.6	-0.7 ± 1.9	p<0,01
baseline and 18 months	-2.3 ± 3.3	-1,0 ± 1,8	p<0,001
baseline and 24 months	-2.9 ± 3.3	-2.1 ± 3.6	p<0,001
baseline and 30 months	-3.6 ± 3.4	-2.2 ± 3.3	p<0,001
baseline and 36 months	-4,6 ± 3.5	-2.2 ± 3.3	p<0,001
*mean ± SD			

A cluster analysis showed two subgroups that significantly differed in age (p<0,001), illness duration (p<0,05) and cognition (p<0,001) at baseline. No significant difference in gender, apoE4-carriers or mean dose of donepezil was observed. The cluster 1 patients decline significantly faster in the long-term outcome of PSMS score compared to the other group.

Conclusions

Increasing strength in the linear correlation between the three ADL scales as well as cognition was observed during the three years of the study.
The IADL scale showed a decline of function less than expected compared with untreated patients in a mathematic model.

Long-term instrumental activities scores deteriorated significantly faster in the female gender than in the male, thus the result was mathematically corrected for gender-dependent activities.

Cluster analysis based on ADL scores at baseline, identified two subgroups: with different mean age and cognitive ability and dissimilar rate of change in basic functional decline

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