

# Reason to Treat

: Benefits of early and continuous therapy in AD



**Aricept**<sup>®</sup>

Donepezil HCl 5mg & 10mg Tablets

아주의대 정신과  
홍창형



Eisai Korea Inc.

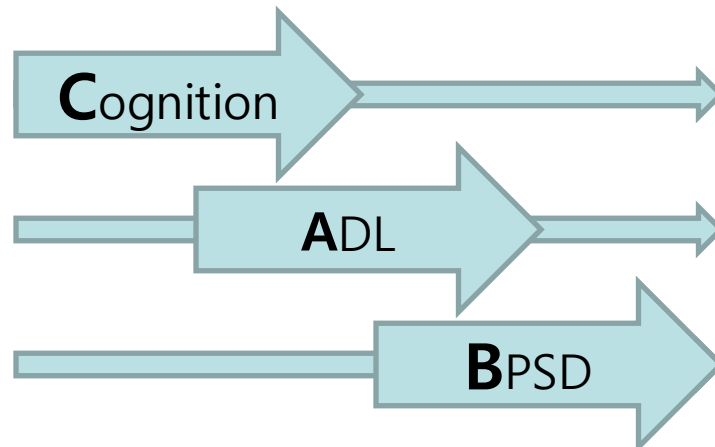
# 치매평가

## CAB

- 명사
  - 택시 (taxi) ; (옛날의) 승객용 마차
    - take a cab 택시 [마차] 를 타다
  - (공항의) 관제탑
- 동사
  - (~bed;~·bing) vi. 택시 [마차] 를 타다



Brain damage



# 치매의 진행과정



-기억력 감퇴  
-방향감각저하



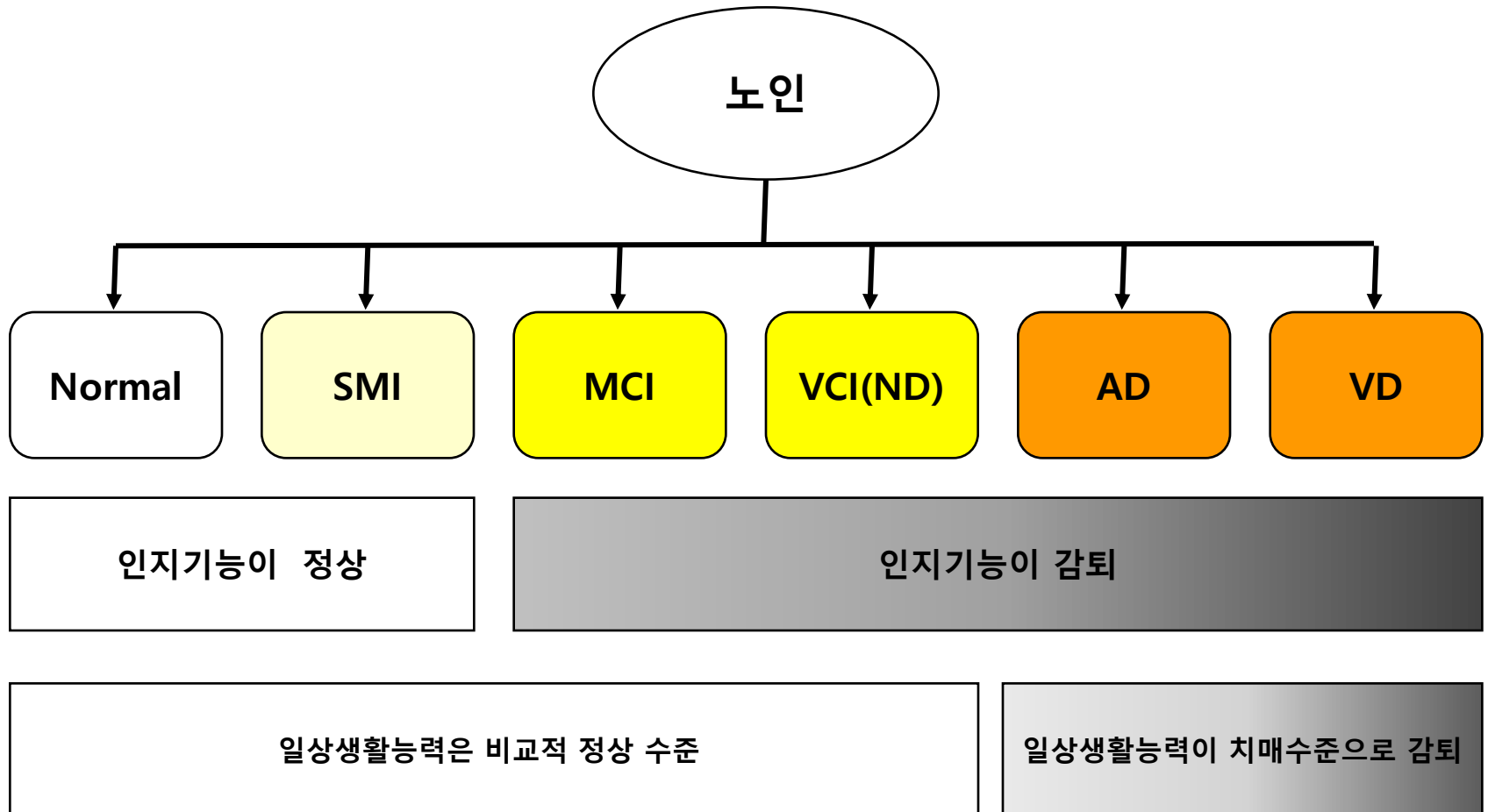
-집안일, 사회생활 등  
-일상생활 수행의 장애



-문제심리행동: 며느리에게 욕하고 의심  
-낮 밤이 바뀌고 집밖으로 배회함

대소변 못 가림, 자식을 못 알아봄.  
24시간 간병인이 필요함

# Simple Classification



# 치매 평가도구

	선별 검사	정밀 검사
<b>C</b>	<b>MMSE</b> , 3MS 개정 하세가와 치매척도(HDS-R) 7분 치매선별검사(7MS) Short Blessed Test (SBT) 시계그리기(CDT), CAMCOG-R 몬트리얼 인지평가(MoCA)	CERAD-K (신경심리평가집) SNSB <b>ADAS-Cog</b> K-DRS  <b>SIB</b>
<b>A</b>	K-ADL, S-ADL, B-ADL K-IADL, S-IADL K-DAD	
<b>B</b>	<b>NPI</b> BEHAVE-AD GDS(30문항, 15문항)	

## 치매선별설문지(Questionnaire-Self report)

S-DSQ, K-DSQ, IQ-CODE, SIRQD, AD8

## 치매단계평가

GDS (Global Deterioration Scale), CDR (Clinical Dementia Rating), **CIBIC-plus**

# 치매 평가도구

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GDS (Global Deterioration Scale), CDR (Clinical Dementia Rating), **CIBIC-plus**

**CLINICIAN INTERVIEW BASED IMPRESSION OF CHANGE  
SUMMARY SHEET**

***THREE – SIX MONTH VISIT***

**Subject's Interview – Clinical Impression of Change:**

- Very Much Improved
- Much Improved
- Minimally Improved
- No change
- Minimal worsening
- Moderate worsening
- Marked worsening

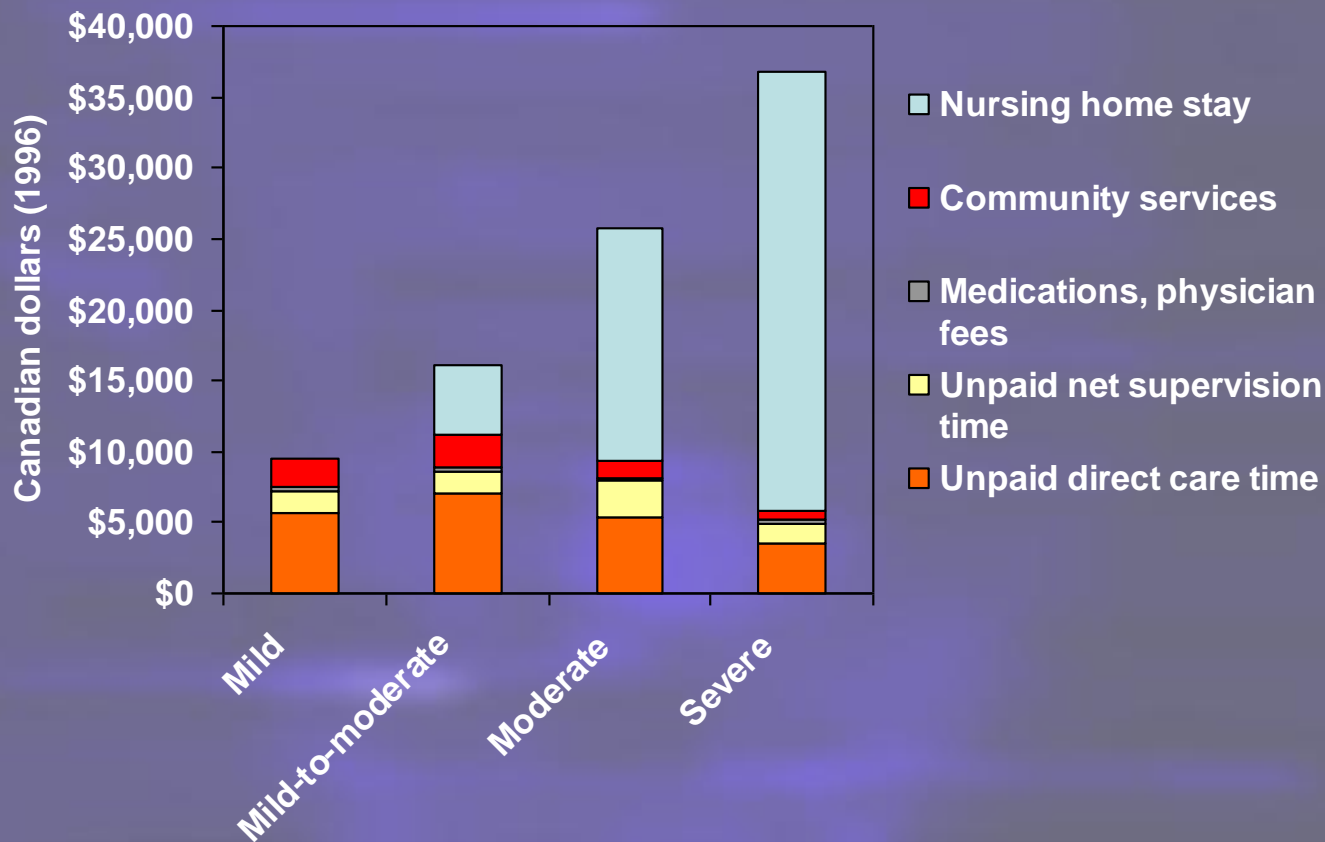
**Informant's Interview – Clinical Impression of Change:**

- Very Much Improved
- Much Improved
- Minimally Improved
- No change
- Minimal worsening
- Moderate worsening
- Marked worsening

**Overall Score – Clinical Impression of Change:**

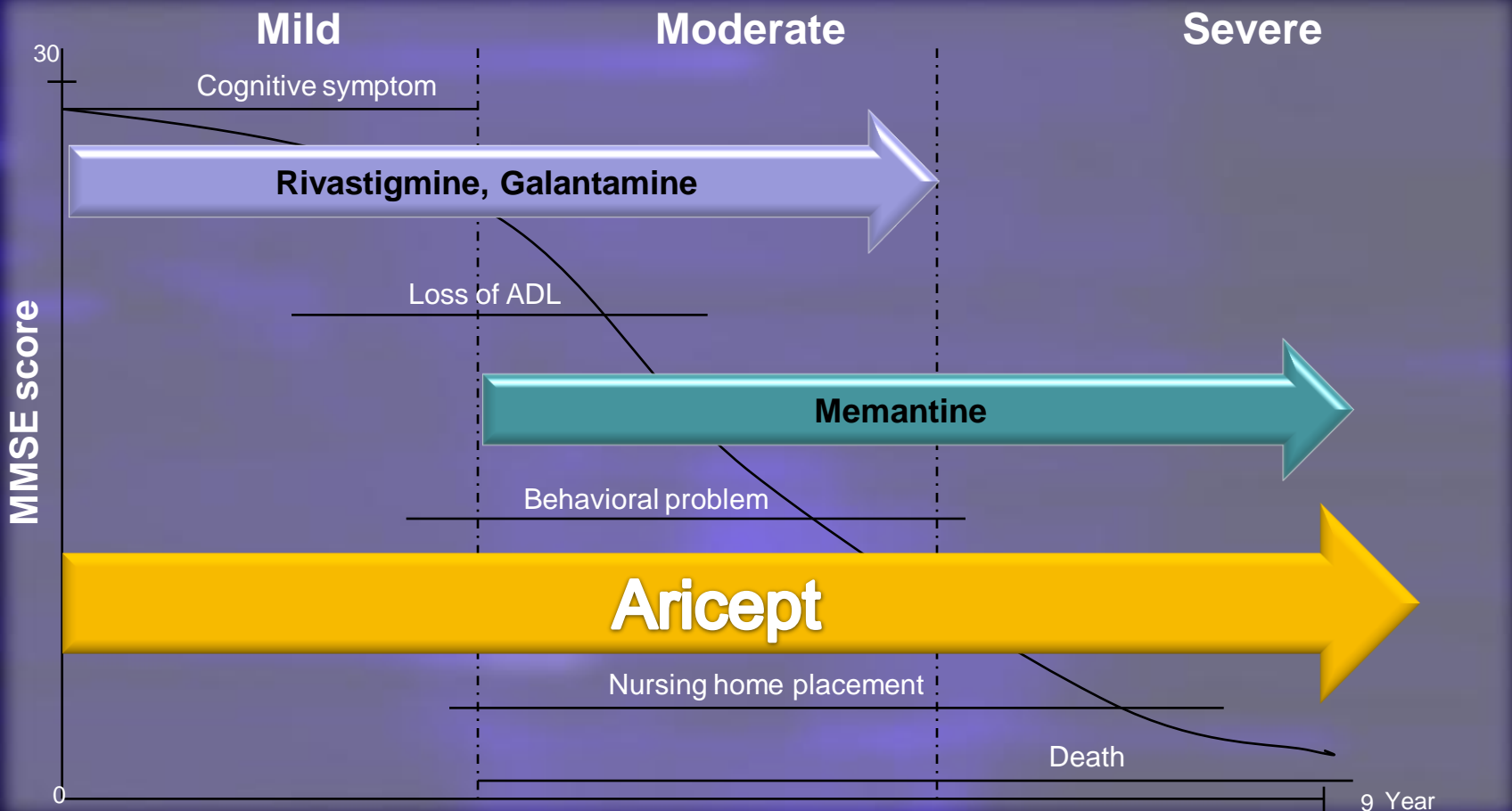
- Very Much Improved
- Much Improved
- Minimally Improved
- No change
- Minimal worsening
- Moderate worsening
- Marked worsening

# Mean Annual Cost of AD by Disease Severity





# ARICEPT is the only AChE-I for all stage of AD



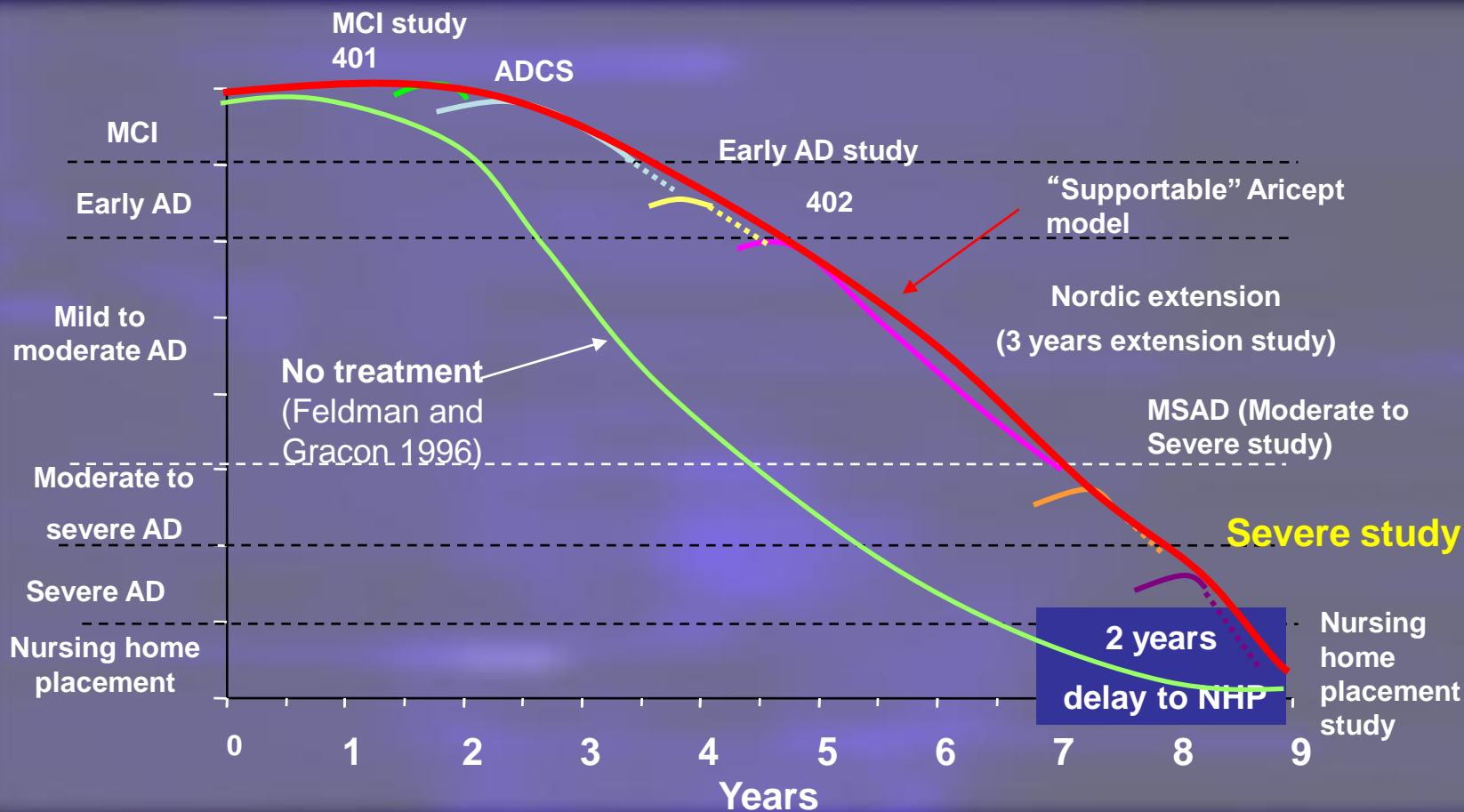
# Proven efficacy of ARICEPT through all dementia course



— Projection

— From data

Disease progression



# MCI study (Neurology 2004;63:651-657)



CME

## Efficacy of donepezil in mild cognitive impairment

### A randomized placebo-controlled trial

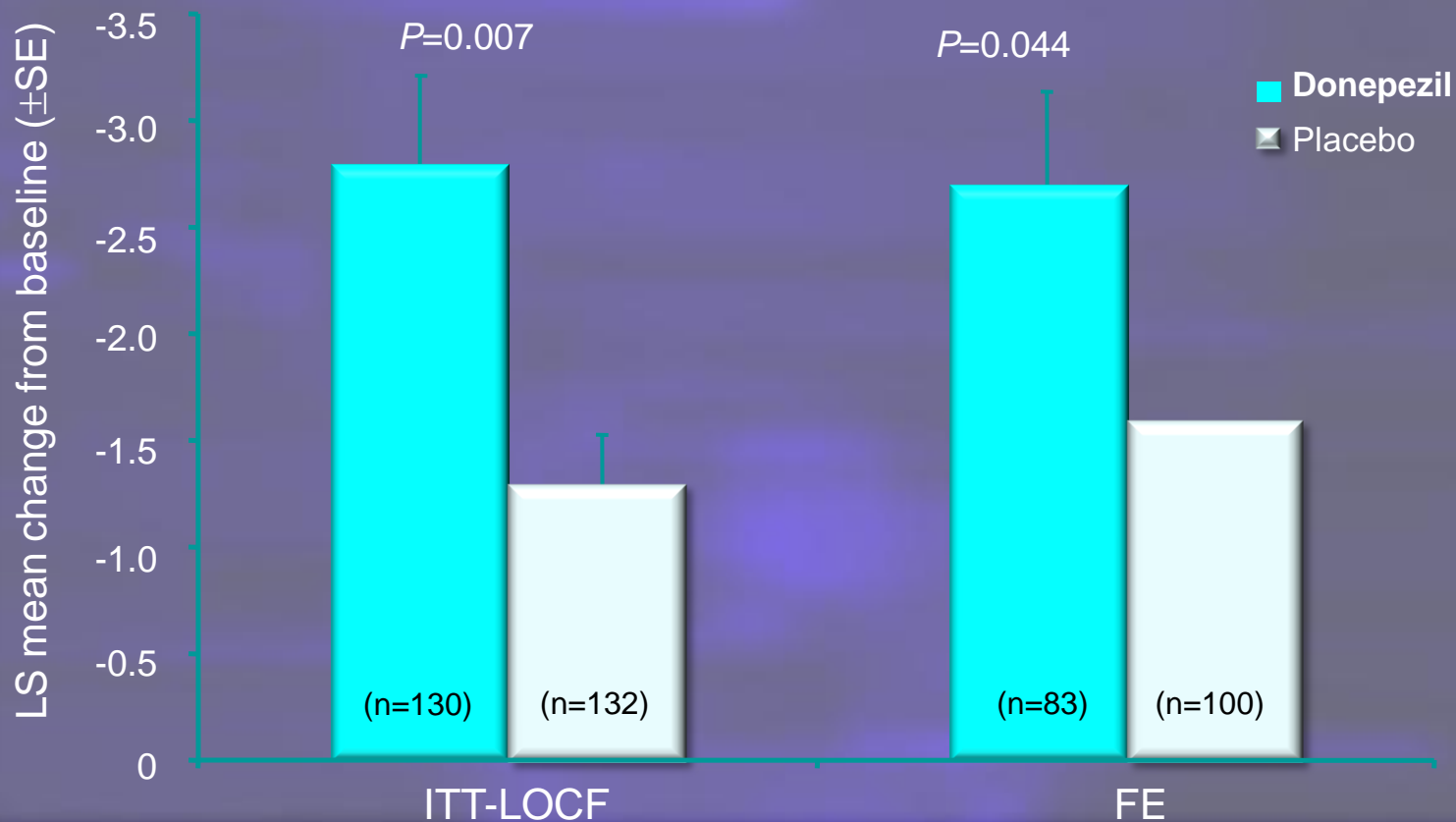
S. Salloway, MD, MS; S. Ferris, PhD; A. Kluger, PhD; R. Goldman, PhD; T. Griesing, PhD; D. Kumar, MS;  
and S. Richardson, PhD, for the Donepezil "401" Study Group\*

- Design: 24-week, multicenter, randomized, double-blind, placebo-controlled study
- Patients: A total of 270 patients with MCI ( $24 \leq$ MMSE score) were enrolled and randomized to receive either donepezil or placebo

# Result of MCI study (1)



## Modified ADAS-cog Score at Week 24





# MCI long term study (comparison with VitE & Placebo)



*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

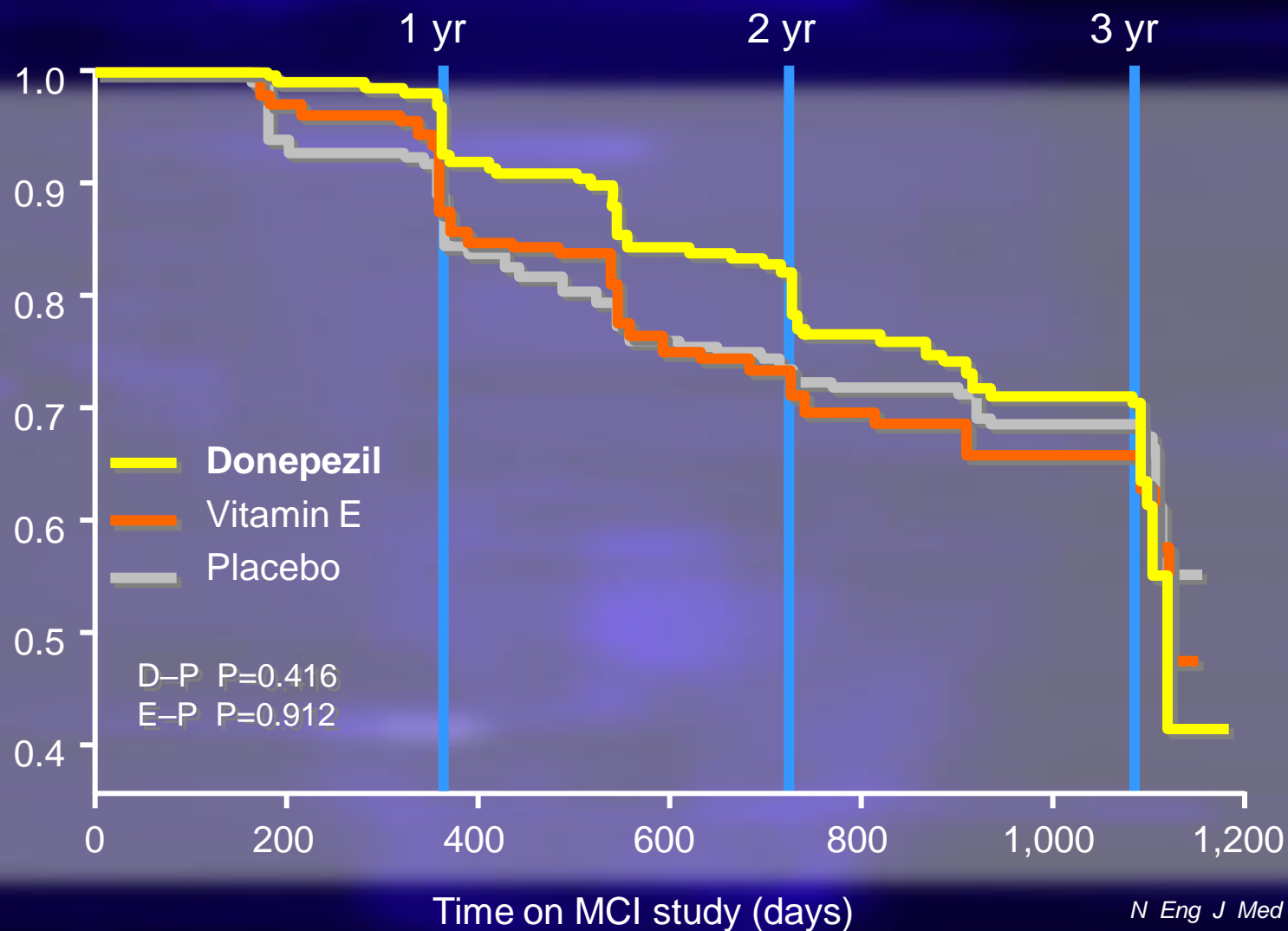
JUNE 9, 2005

VOL. 352 NO. 23

Vitamin E and Donepezil for the Treatment  
of Mild Cognitive Impairment

- Design: 3 years, randomized, multicenter, randomized, double-blind, placebo-controlled, parallel study  
(→ *Open-label donepezil after conversion to AD*)

# ARICEPT delays conversion to dementia



# Benefit for early stage AD patients



## Efficacy of Donepezil in Early-Stage Alzheimer Disease

### *A Randomized Placebo-Controlled Trial*

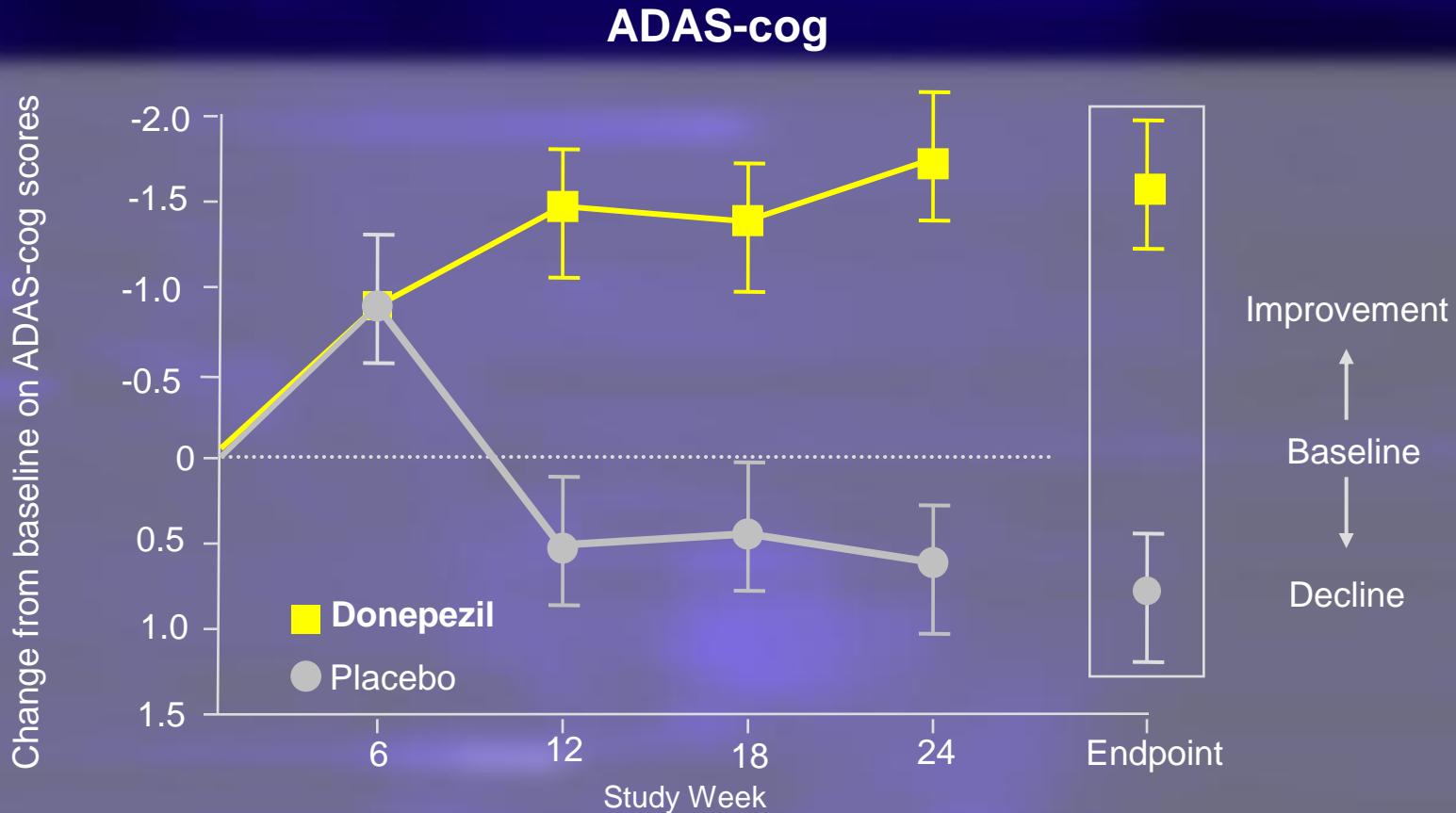
*Ben Seltzer, MD; Parvaneh Zolnouri, MD; Margarita Nunez, MD; Robert Goldman, PhD; Dinesh Kumar, MA; John Ieni, PhD; Sharon Richardson, PhD; for the Donepezil "402" Study Group*

*Arch Neurol. 2004;61:1852-1856*

- *Design*: 24-week, multicenter, randomized, double-blind, placebo-controlled study
- *Patients*: A total of 153 patients with early AD ( $21 \leq$  MMSE score  $\leq 26$ ) were enrolled and randomized to receive either donepezil or placebo



# Result of Early AD study (1)



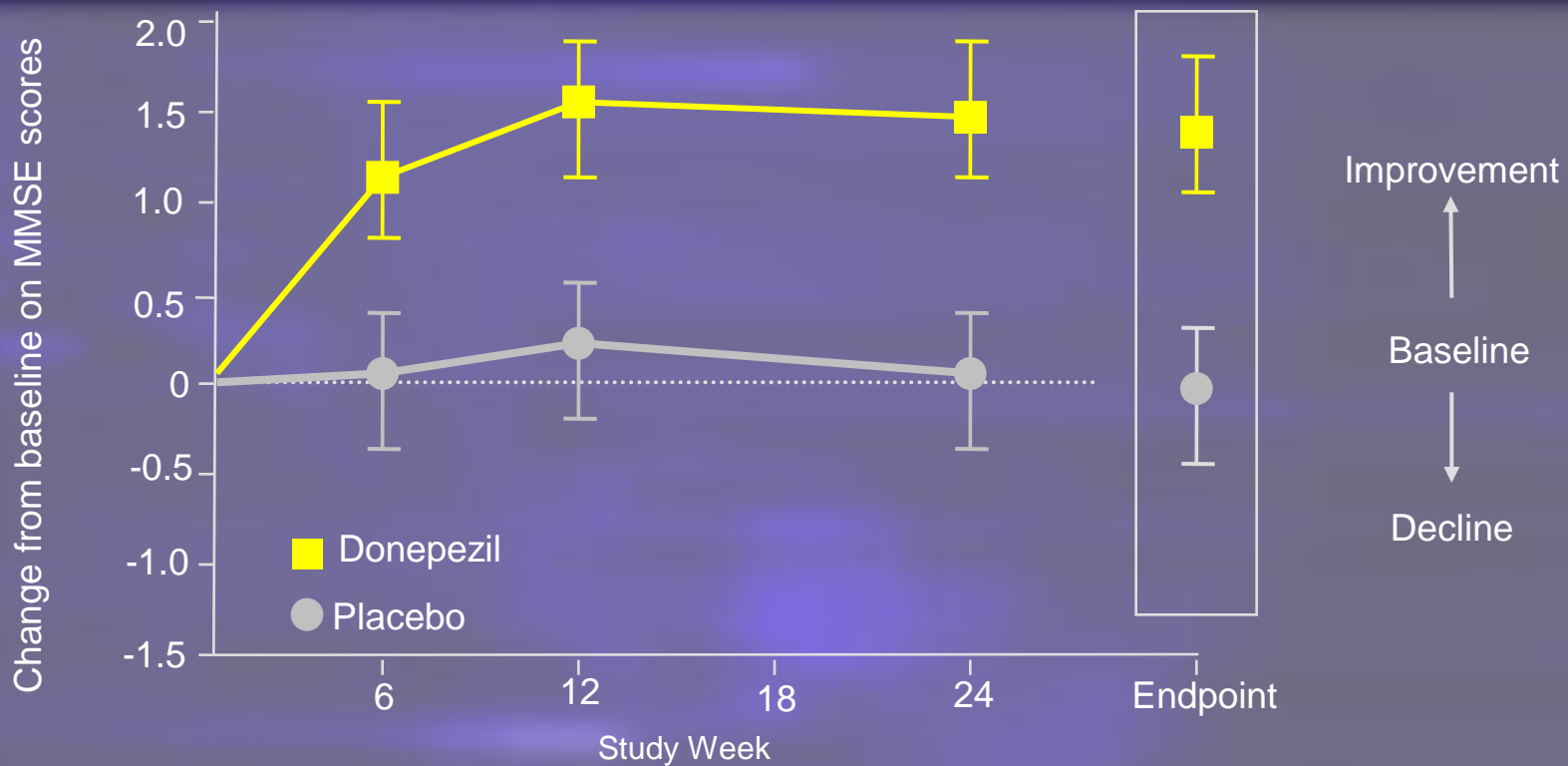
**\*Improvement  $\geq 4$  points : 16% placebo, 37% donepezil**

**\*Improvement  $\geq 7$  points : 7% placebo, 10% donepezil**

# Result of Early AD study (2)



## MMSE



\* Improvements from week 6 ( $P=.02$ ) through week 24 ( $P=.03$ )

\* Difference 1.8 points ( $P = .002$ ) at the end point

# Mild to Moderate AD (Nordic study 2001)

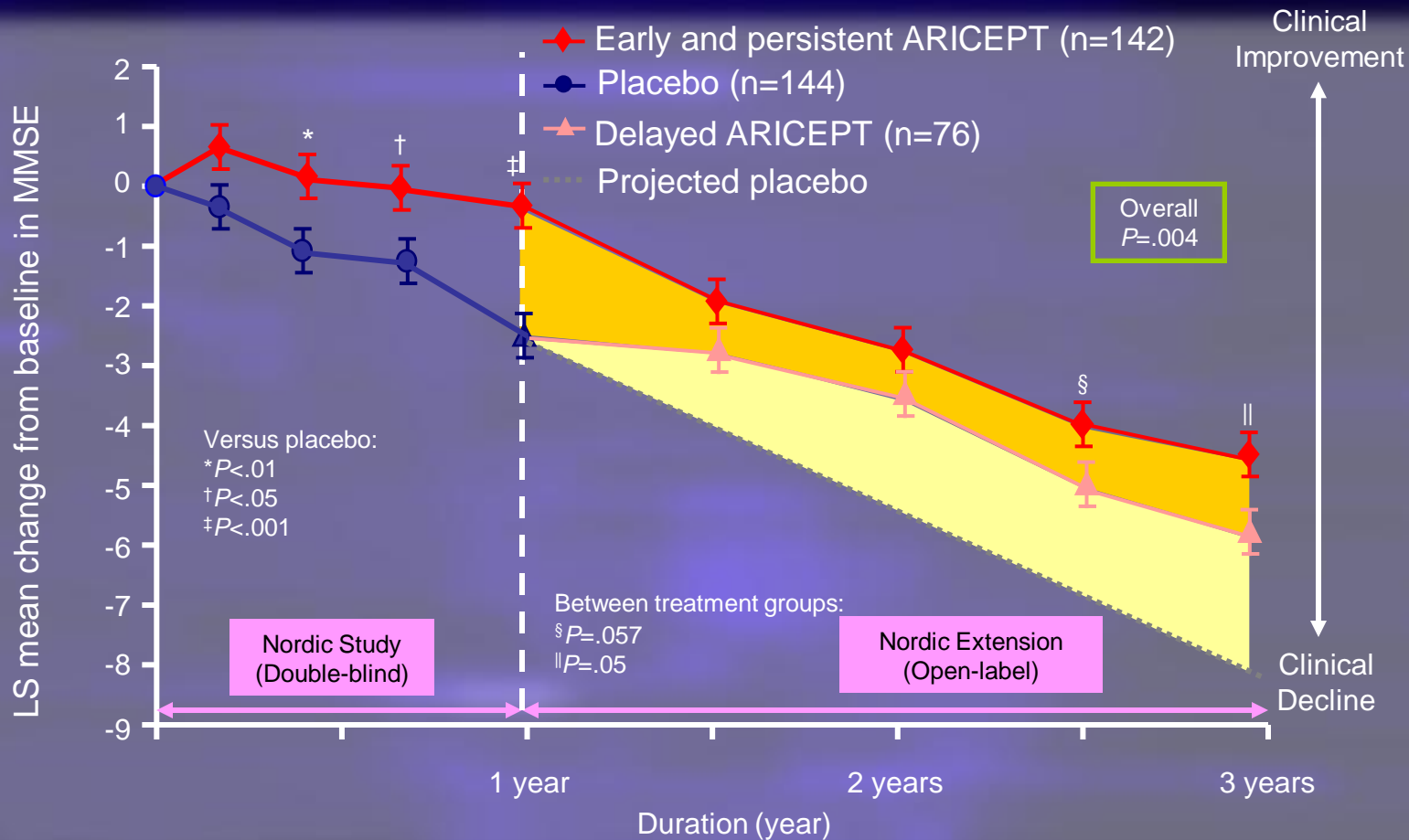


## 3-Year Study of Donepezil Therapy in Alzheimer's Disease: Effects of Early and Continuous Therapy

B. Winblad<sup>a</sup> A. Wimo<sup>b</sup> K. Engedal<sup>c</sup> H. Soininen<sup>d</sup> F. Verhey<sup>e</sup>  
G. Waldemar<sup>f</sup> A.-L. Wetterholm<sup>g</sup> A. Haglund<sup>g</sup> R. Zhang<sup>h</sup> R. Schindler<sup>h</sup>  
for the Donepezil Nordic Study Group

- Design: 52-week, double-blind phase (1 year)→ open-label extension (2 year)  
☞ total 3 year nordic extension study
- Patients: N=286 with possible or probable AD (MMSE 10~26)  
- donepezil 5mg/day for 4 weeks, followed by 10mg/day

# Benefit of early and persistent treatment



# Efficacy of ARICEPT for Moderate to Severe AD



## A 24-week, randomized, double-blind study of donepezil in moderate to severe Alzheimer's disease

H. Feldman, MD; S. Gauthier, MD; J. Hecker, MD, B. Vellas, MD, PhD; P. Subbiah, MD; E. Whalen, PhD,  
and the Donepezil MSAD Study Investigators Group\*

NEUROLOGY 2001;57:613-620

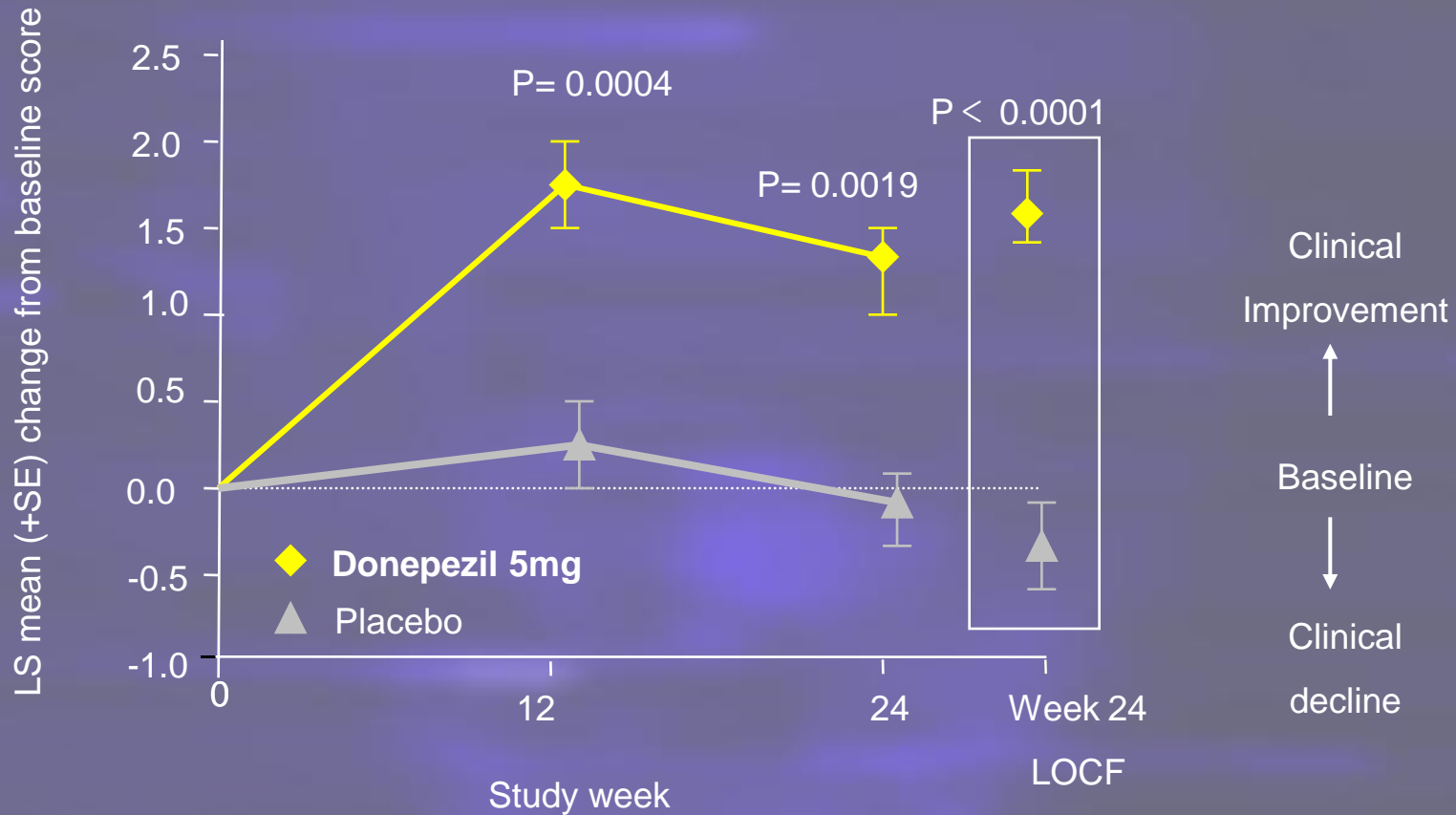
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- Design: 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study
- Patients: 290 patients ( sMMSE 5 to 17) were randomized to receive either donepezil or placebo

# Result of Moderate to Severe AD (1)



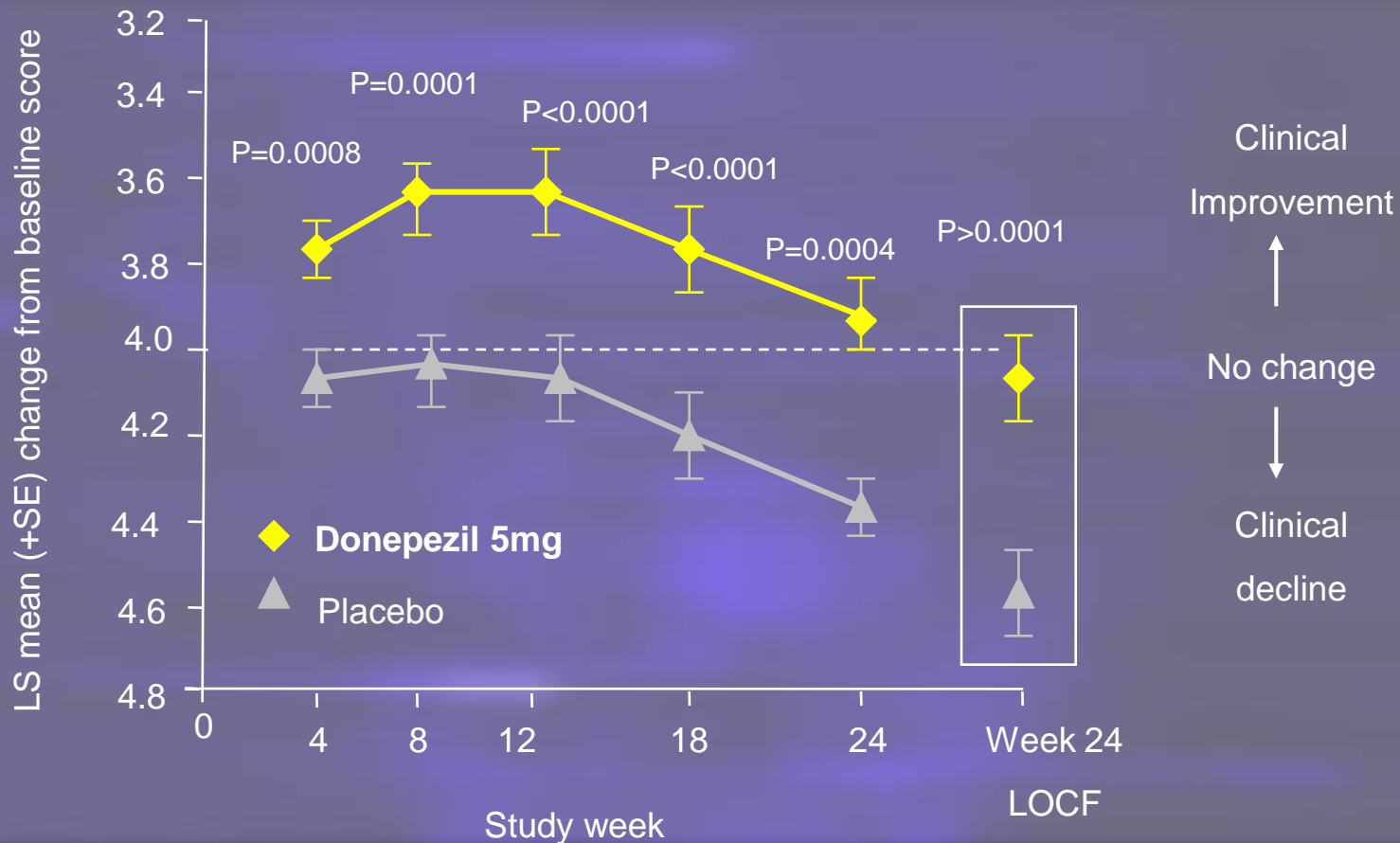
## sMMSE



# Result of Moderate to Severe AD (2)



## CIBIC-plus



# Efficacy of ARICEPT for Severe AD



Efficacy and safety of donepezil in patients with more severe Alzheimer's disease: a subgroup analysis from a randomized, placebo-controlled trial

Howard Feldman<sup>1\*</sup>, Serge Gauthier<sup>2</sup>, Jane Hecker<sup>3</sup>, Bruno Vellas<sup>4</sup>, Yikang Xu<sup>5</sup>, John R. Ieni<sup>6</sup>, Elias M. Schwam<sup>7</sup> and the Donepezil MSAD Study Investigators Group

*Int J Geriatr Psychiatry 2005; 20: 559-569*

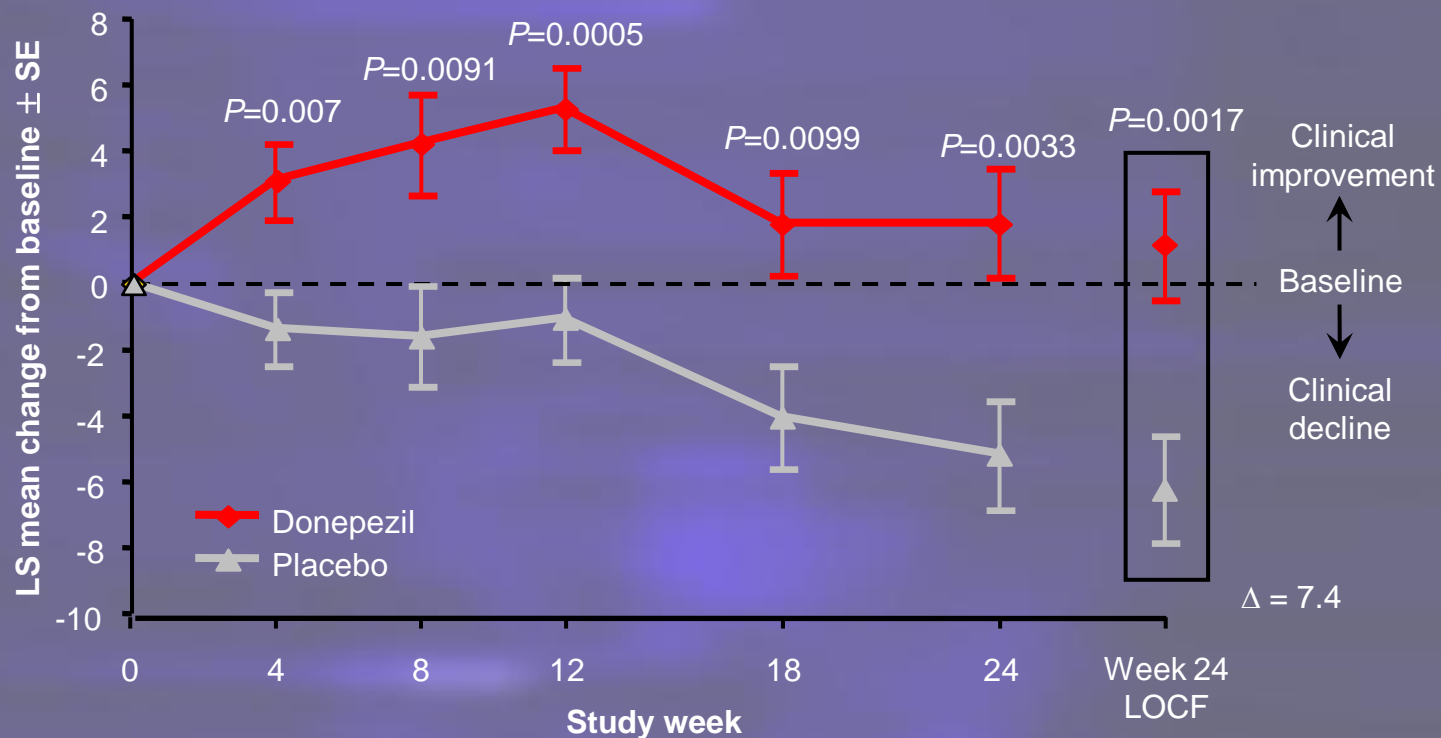
- **Design**: 24-week, multicenter, randomized, double-blind, placebo-controlled study
- **Patients**: A total of 145 patients with more severe AD ( sMMSE 5 to 12) were enrolled and randomized to receive either donepezil or placebo





# Result: SIB

## SIB



Donepezil  
Placebo

n=71  
n=73

67  
70

61  
61

Study week

66  
62

63  
65

62  
63

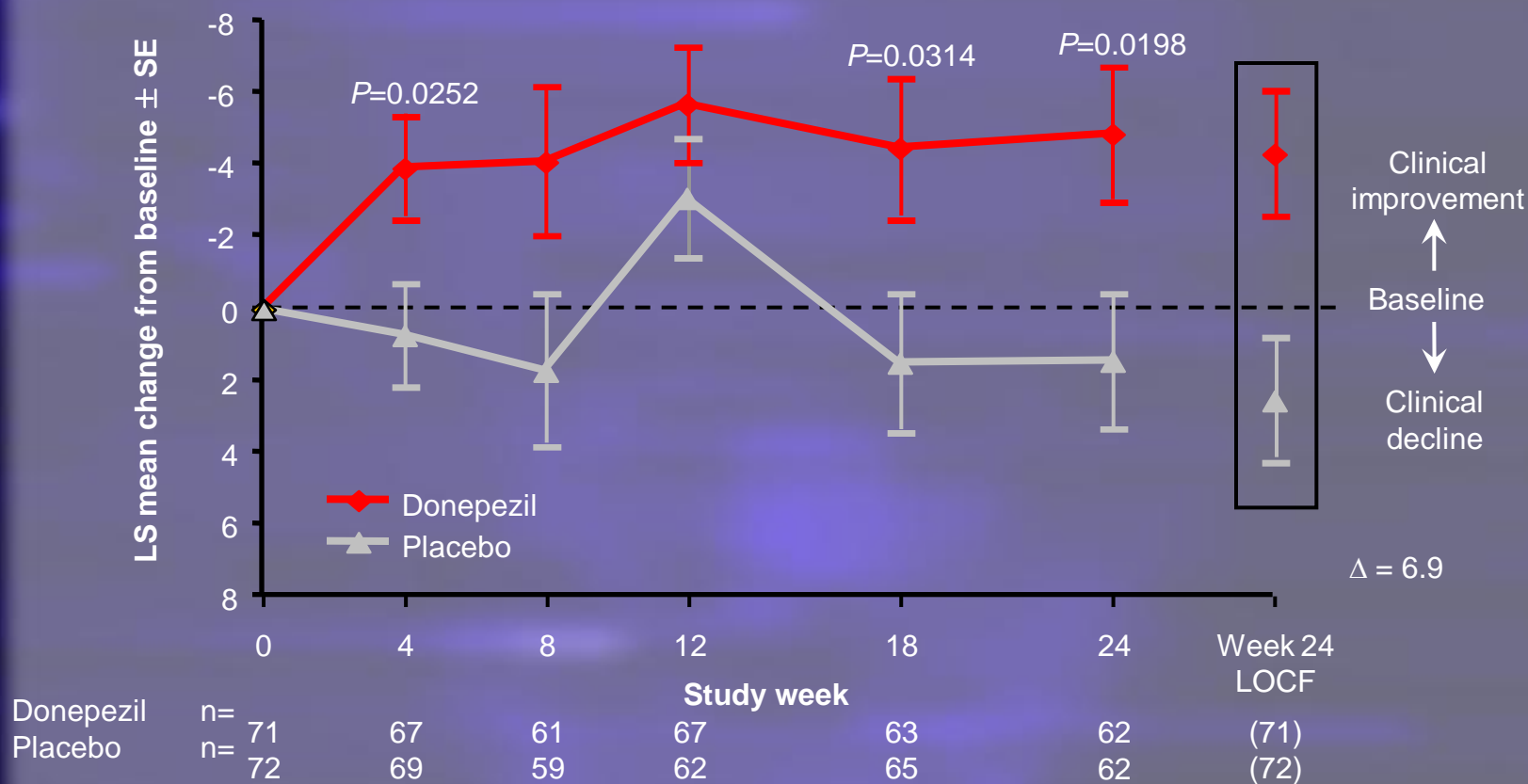
Week 24  
LOCF

(71)  
(73)



# Result: NPI

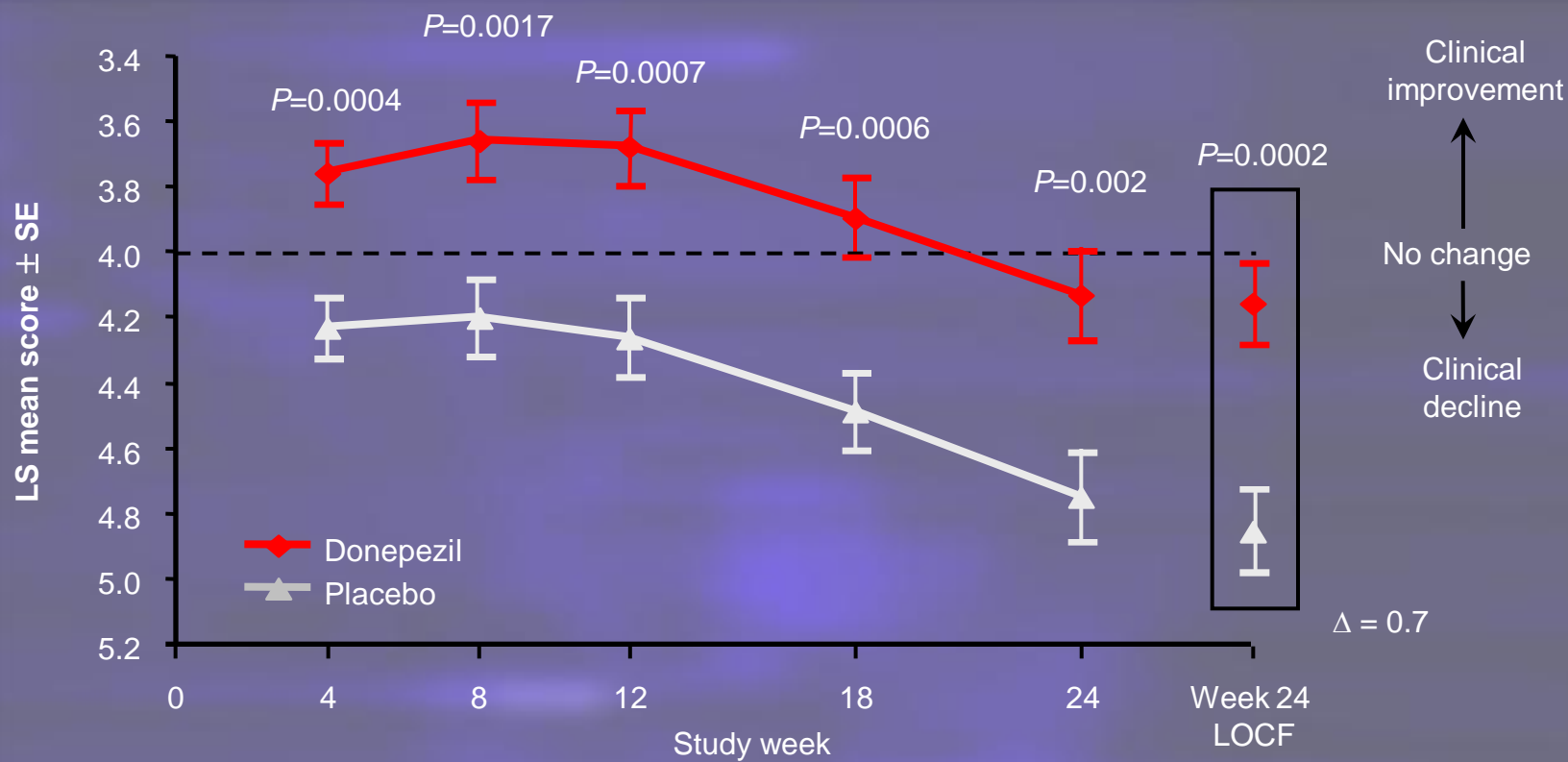
## 12-Item NPI Total





# Result: CIBIC-plus

## CIBIC-plus



Donepezil  
Placebo

n=69

61

68

64

62

(72)

n=70

61

62

64

63

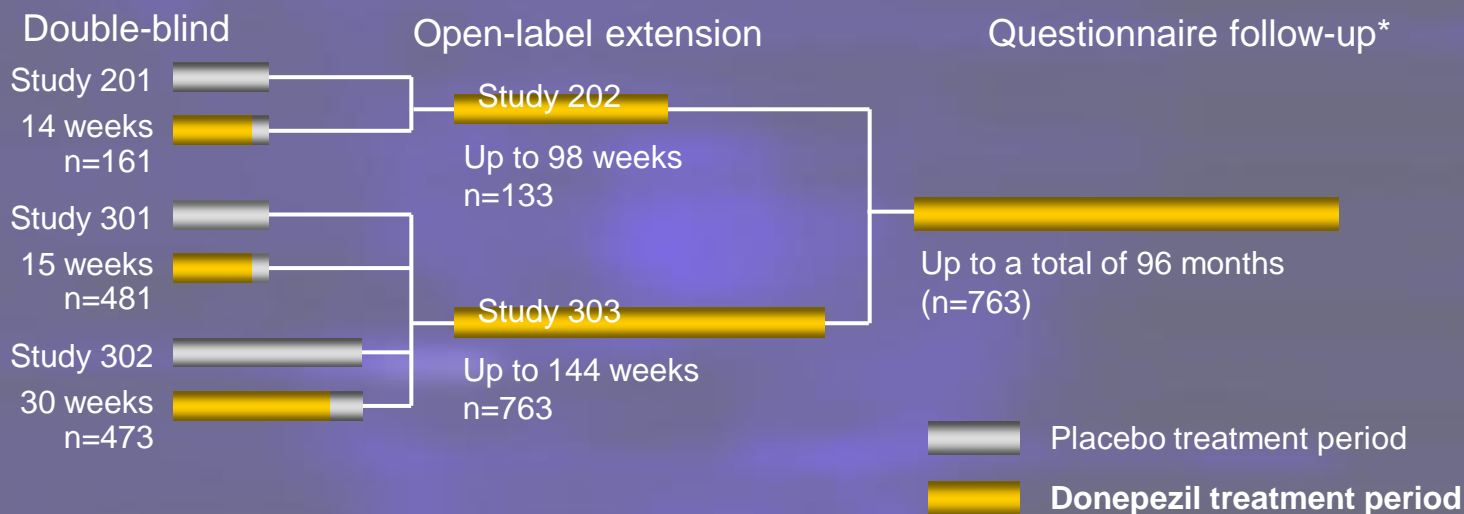
(73)



# Efficacy of ARICEPT for DNHP

## Donepezil Is Associated with Delayed Nursing Home Placement in Patients with Alzheimer's Disease

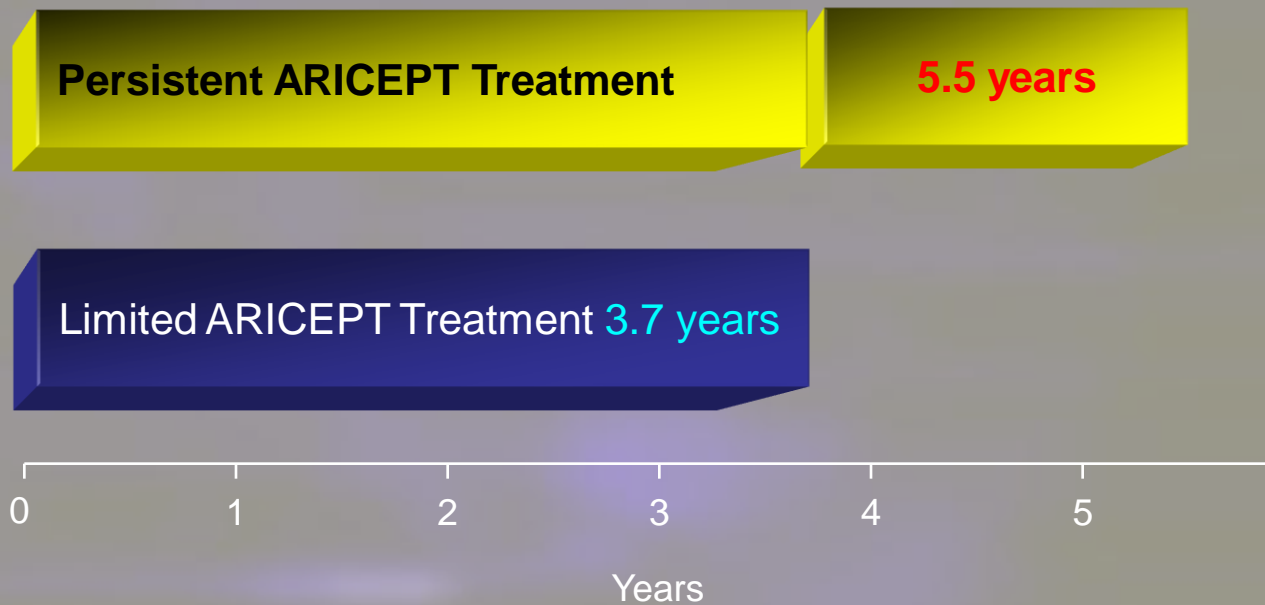
David S. Geldmacher, MD,<sup>\*†</sup> George Provenzano, PhD,<sup>‡</sup> Thomas McRae, MD,<sup>§</sup>  
Vera Mastey, MS,<sup>||</sup> and John R. Ieni, PhD<sup>¶</sup>





# 2 year delay to NHP

Median time to first dementia-related nursing home placement



**Keep patients in the community for more than 5 years**



# Long-term efficacy of ARICEPT



ELSEVIER

European Neuropsychopharmacology 10 (2000) 195–203

EUROPEAN NEURO-  
PSYCHOPHARMACOLOGY

[www.elsevier.com/locate/euroneuro](http://www.elsevier.com/locate/euroneuro)

Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: final analysis of a US multicentre open-label study

S.L. Rogers<sup>a,\*</sup>, R.S. Doody<sup>b</sup>, R.D. Pratt<sup>c</sup>, J.R. Ieni<sup>c</sup>

- Design: for up to cumulative 254 weeks (4.9 years)

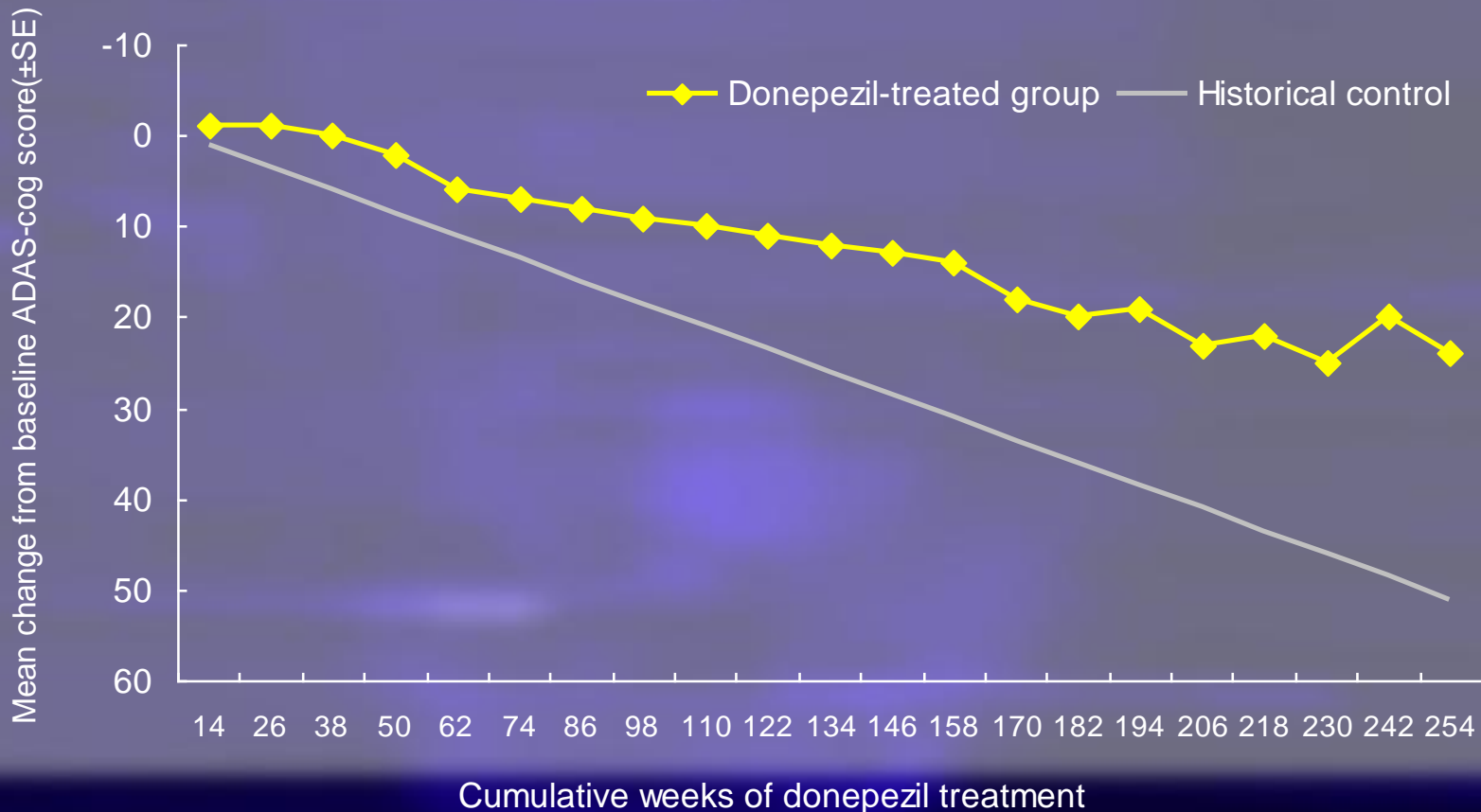


# Result of long-term efficacy of ARICEPT



## ADAS-cog

→ over 254 cumulative weeks



# ARICEPT for severe BPSD



## Effects of Donepezil on Neuropsychiatric Symptoms in Patients With Dementia and Severe Behavioral Disorders

*Jeffrey L. Cummings, M.D., Thomas McRae, M.D.,  
Richard Zhang, Ph.D., The Donepezil–Sertraline Study Group*

*Am J Geriatr Psychiatry 2006; 14: 605*

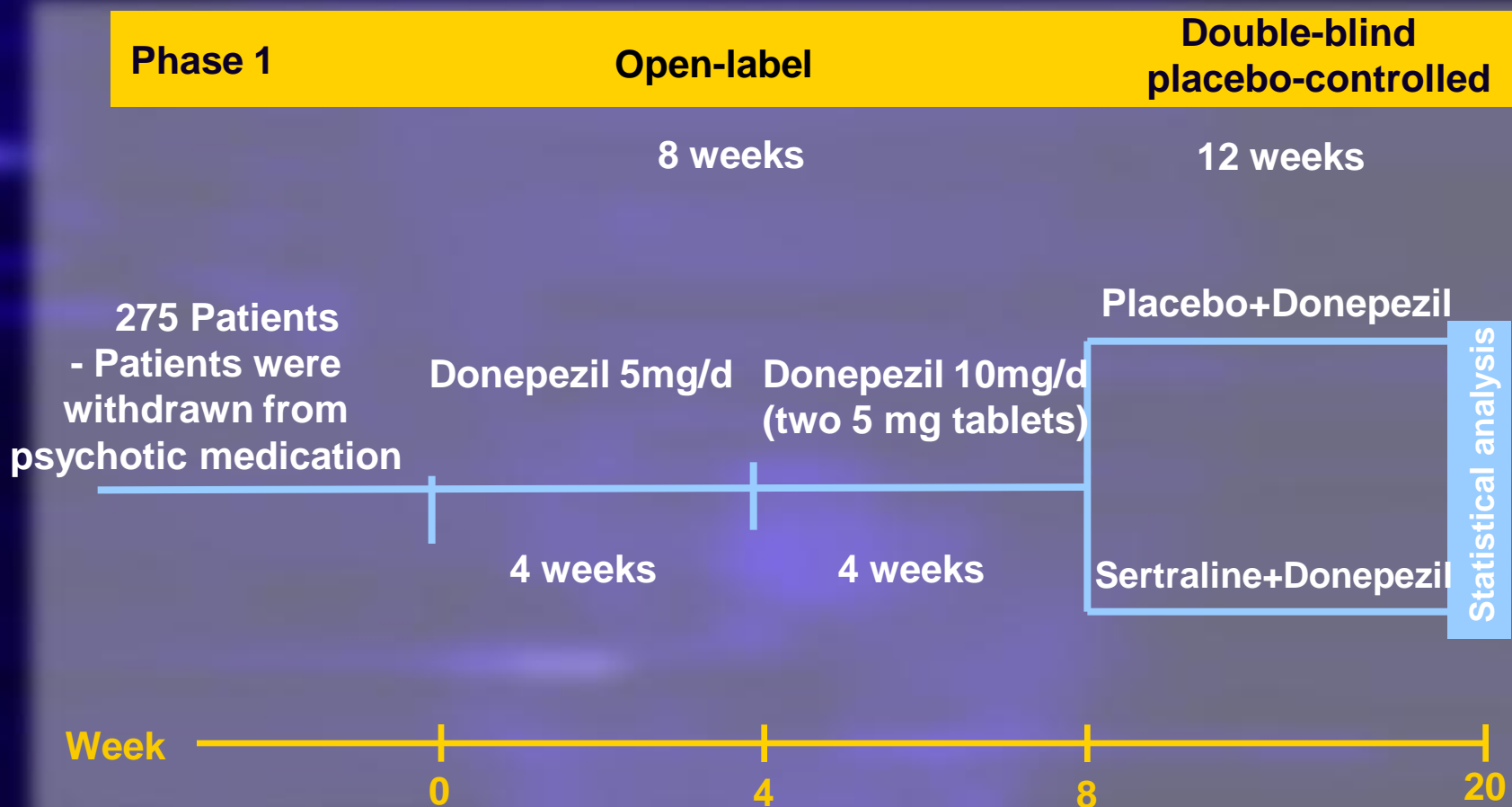
**Design** : 8-week open-label,  
12-week double-blind, placebo-controlled study

**Patients** : Probable or possible AD, according to NINCDS-ADRDA criteria, NPI  $\geq 5$   
Open-label (n=275; mean age, 76.3 years)  
Double-blind (n=120; mean age, 76.9years)





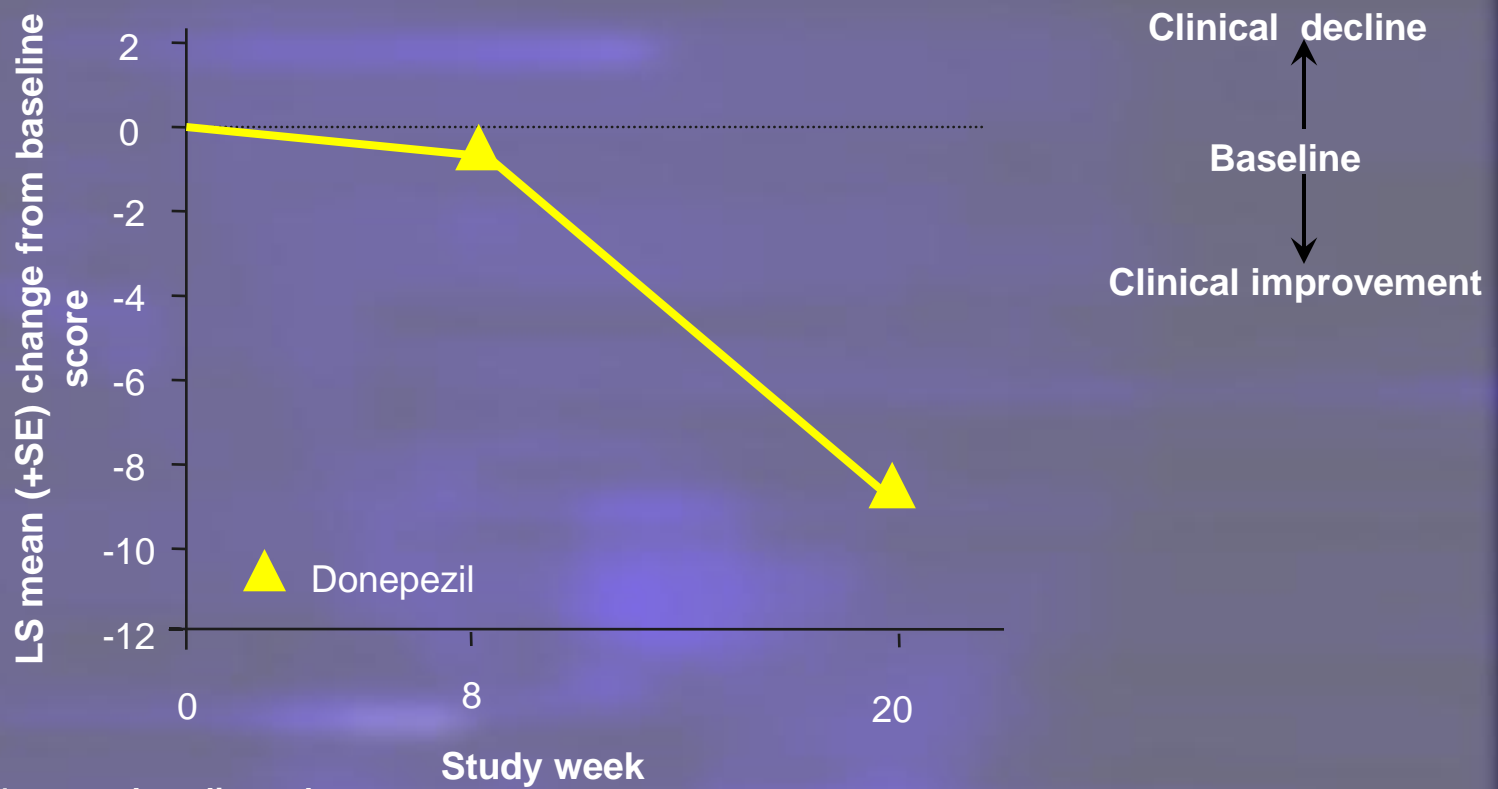
# Study Design



# Result: NPI



## NPI-12



<sup>a</sup>p 0.001 versus baseline value.

<sup>b</sup>p 0.05 versus baseline value.

# Pubmed Search (2009.11.27)

- Donepezil(Aricept)..... 1818 (400)
- Galantamine(Reminyl)..... 1188 (222)
- Rivastigmine(Exelon)..... 900 (263)
- Memantine(Ebixa)..... 1469 (336)



# Summary

- **ARICEPT® significantly improved cognition, global function and behavioral symptoms in patients with mild to severe AD.**
- **ARICEPT® shows the benefit in all course of AD patients**
- **ARICEPT® is safe and well tolerate in severe AD patients**
- **ARICEPT® is a only approved AChE-Inhibitors in severe AD and VaD**

**Aricept is the first choice of dementia treatment**