Schizophrenia and Aging: Myths and Reality

Dilip V. Jeste, M.D.

University of California, San Diego &

VA San Diego Healthcare System

Pre-Lecture Exam
Question 1

1. **True or False:** By the year 2030, it is estimated that the number of people over 65 years of age with psychiatric disorders in the USA will equal the number of people between ages 30 and 44 years of age with psychiatric disorders.

Question 2

2. The course of schizophrenia in late life is characterized by all of the following EXCEPT:

A. Relatively stable course

B. Persistence of negative symptoms

C. Improvement of positive symptoms

D. Severe cognitive deterioration

E. Relatively non-deteriorating course

Question 3

3. **MAOS (middle-age-onset schizophrenia) resembles EOS (early onset schizophrenia) in all but which of the following characteristics?**

A. Positive family history of schizophrenia is common.

B. Response to neuroleptics is often good.

C. Much lower rate of mortality is seen with MAOS.

D. Nonspecific MRI abnormalities are typical in both syndromes.

E. Chronic course is typical.

Question 4

4. **MAOS differs from EOS in all but which of the following characteristics?**

A. MAOS is less common among women.

B. Negative symptoms in MAOS tend to be less severe.

C. A greater percentage of patients with MAOS than EOS never have been married.

D. Lower dose of neuroleptics than in EOS may be effective in MAOS.

E. Learning and abstraction are less severely impaired in MAOS than in EOS.

Question 5

5. **Which of the following is NOT true of very late-onset schizophrenia-like psychosis?**

A. It is a heterogeneous group of disorders including medically-induced and other psychotic states.

B. It should not be treated with antipsychotic medications.

C. Patients with this disorder should receive appropriate psychotherapeutic help, e.g., with CBSST (cognitive behavioral social skills training)

D. Treatment with antipsychotic medication can produce TD.

E. Treatment with antipsychotic medication can result in increased weight gain, hyperprolactinemia, and changes in eye and/or heart functioning.

Question 6

6. Late-onset schizophrenia (LOS) differs from early-onset schizophrenia (EOS) in all of the following ways EXCEPT:

A. LOS is common in women.

B. LOS patients generally have less severe negative symptoms.

C. LOS is predominantly of the paranoid subtype.

D. LOS patients have a need for lower doses of antipsychotics.

Question 7

7. **Of the following statements regarding similarities between EOS and LOS, choose the one that is TRUE:**

A. Positive symptoms are less severe in LOS.

B. Both EOS and LOS have a chronic course.

C. LOS is not a true psychotic illness.

D. LOS patients have a better qualitative response to antipsychotics.

Question 8

8. Which one of the following statements about controlled studies of typical antipsychotics in dementia is correct?

A. Conventional antipsychotics are no better than placebo.

B. Improvement rates with conventional antipsychotics were more than double that of placebo.

C. Improvement rates with conventional antipsychotics were more than triple that of placebo.

D. No single conventional agent was better than others.

Question 9

9. Which of the following are adverse effects of conventional antipsychotics in the elderly?

A. Anticholinergic toxicity

B. Sedation and confusion

C. Extrapyramidal side effects

D. All of the above

Question 10

10. Which of the following is most commonly the appropriate dosage range of risperidone for the treatment of psychosis and agitation in dementia, considering both safety and efficacy?

A. 0.25 – 0.5 mg/day
B. 1 – 2 mg/day
C. 2 – 4 mg/day
D. 4 – 6 mg/day

Question 11

11. Which of the following are risk factors for tardive dyskinesia in older patients?

A. Baseline duration of antipsychotic use

B. History of alcohol abuse/dependence

C. Cumulative amount of antipsychotics used (especially high-potency conventional agents)

D. All of the above

E. Two of the above

Question 12

12. Which of the following is generally considered the most appropriate dosage range of olanzapine for the treatment of psychosis and agitation in dementia, considering both safety and efficacy?

A. 5 – 10 mg/day

B. 15 – 20 mg/day

C. 2.5 – 5.0 mg/day

D. 7.5 – 15 mg/day

Question 13

13. For which of the following medications have randomized controlled trials for agitation in dementia been conducted?

A. Valproate
B. Trazodone
C. Citalopram
D. Two of the above
E. All of the above

Question 14

14. Choose the one statement regarding tardive dyskinesia (TD) that is true:

A. Severity of TD is not associated with quality of well-being or everday functioning scores.

B. The cumulative annual incidence of TD in older patients treated with conventional agents is 5-10%.

C. In general, the risk of developing TD in older patients is reduced with the use of atypical antipsychotics compared to conventional agents.

D. TD risk is only slightly increased on older versus younger individuals.

Question 15

15. Read the following statements regarding the management of psychosis in the elderly and choose the correct statement(s):

I. Pharmacotherapy should be combined with supportive therapy and caregiver education.

II. Pharmacotherapy should always be the initial treatment of agitation in dementia.

III. Atypical antispsychotics are safer than conventional agents, but have their own limitations.

IV. Clear communication, consistent daily routines and a modified environment are all examples of nonpharmacologic management techniques for patients with dementia.

Please see next slide for choices

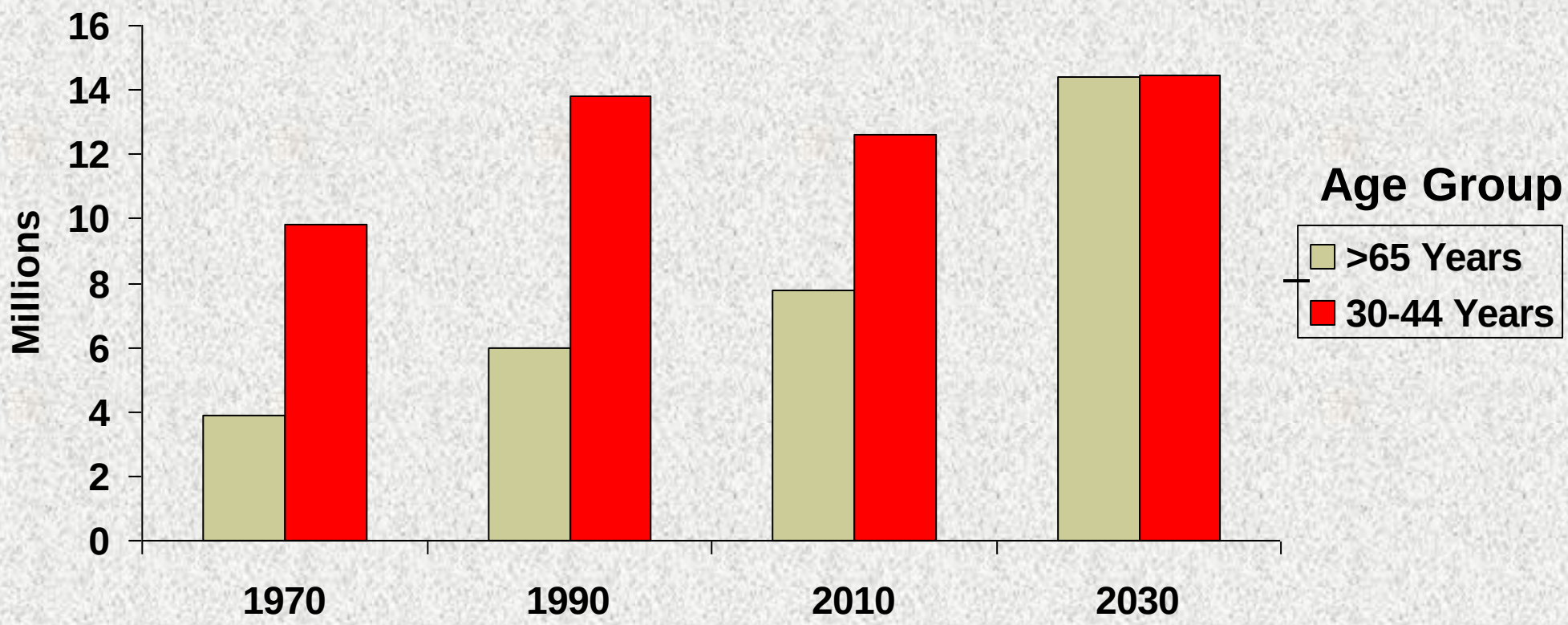
Question 15 (continued)

A. I only
B. II only
C. I, II, and III
D. I, III, and IV
E. I, II, III, and IV

OUTLINE

- Introduction
- Course of Schizophrenia in Late Life
- Middle-Age-Onset Schizophrenia
- Very Late-Onset Schizophrenia-like Psychosis
- Pharmacologic & Psychosocial Treatments

Estimated Numbers of People with Psychiatric Disorders in USA



(Jeste et al., Arch Gen Psychiatry, 1999)

UCSD Studies of Late-Life Schizophrenia

- Over 400 middle-aged and elderly patients with schizophrenia and related psychoses, and over 150 normal comparison subjects.
- Longitudinal follow-up with comprehensive clinical, neuropsychological, and functional evaluations.

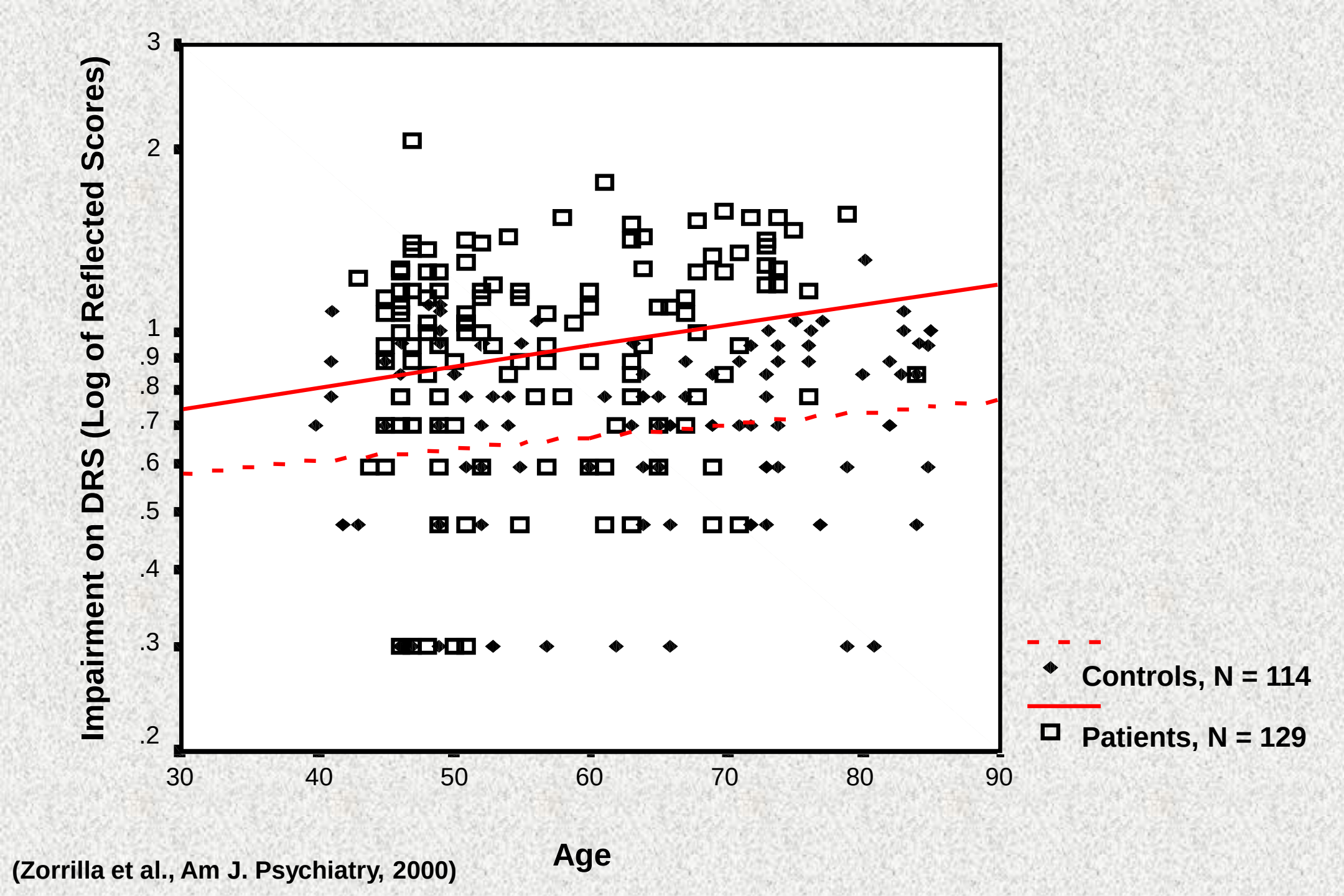
Course of Schizophrenia in Late Life

- Relatively stable and non-deteriorating course
- Negative symptoms persist while positive symptoms show a modest improvement
- The rate of age-related cognitive decline is similar in patients and normal subjects

Correlations with Age in Schizophrenia Patients Aged 40-85 (N=192)

Positive Symptoms:	**SAPS**	**-0.19***
Negative Symptoms:	**SANS**	**-0.15**
Daily Neuroleptic Dose:		**-0.31****
Cognitive Impairment:	**DRS**	**0.21***

***p<0.05; **p<0.01**



(Zorrilla et al., Am J. Psychiatry, 2000)

Late-Onset Schizophrenia: A Controversial Entity

Age of onset and diagnosis of schizophrenia in USA:

DSM-III (1980)
DSM-III-R (1987)
DSM-IV (1994)

European terminology:

Paranoia
Paraphrenia
Late paraphrenia

Questions

1. **Can schizophrenia manifest after age 45?**

   If it can,

2. **Why do these patients develop schizophrenia?**

   and

3. **What protects them from developing schizophrenia until late in life?**

Diagnosis

DSM-III-R or DSM-IV diagnosis with SCID

Age of onset of prodromal symptoms of schizophrenia

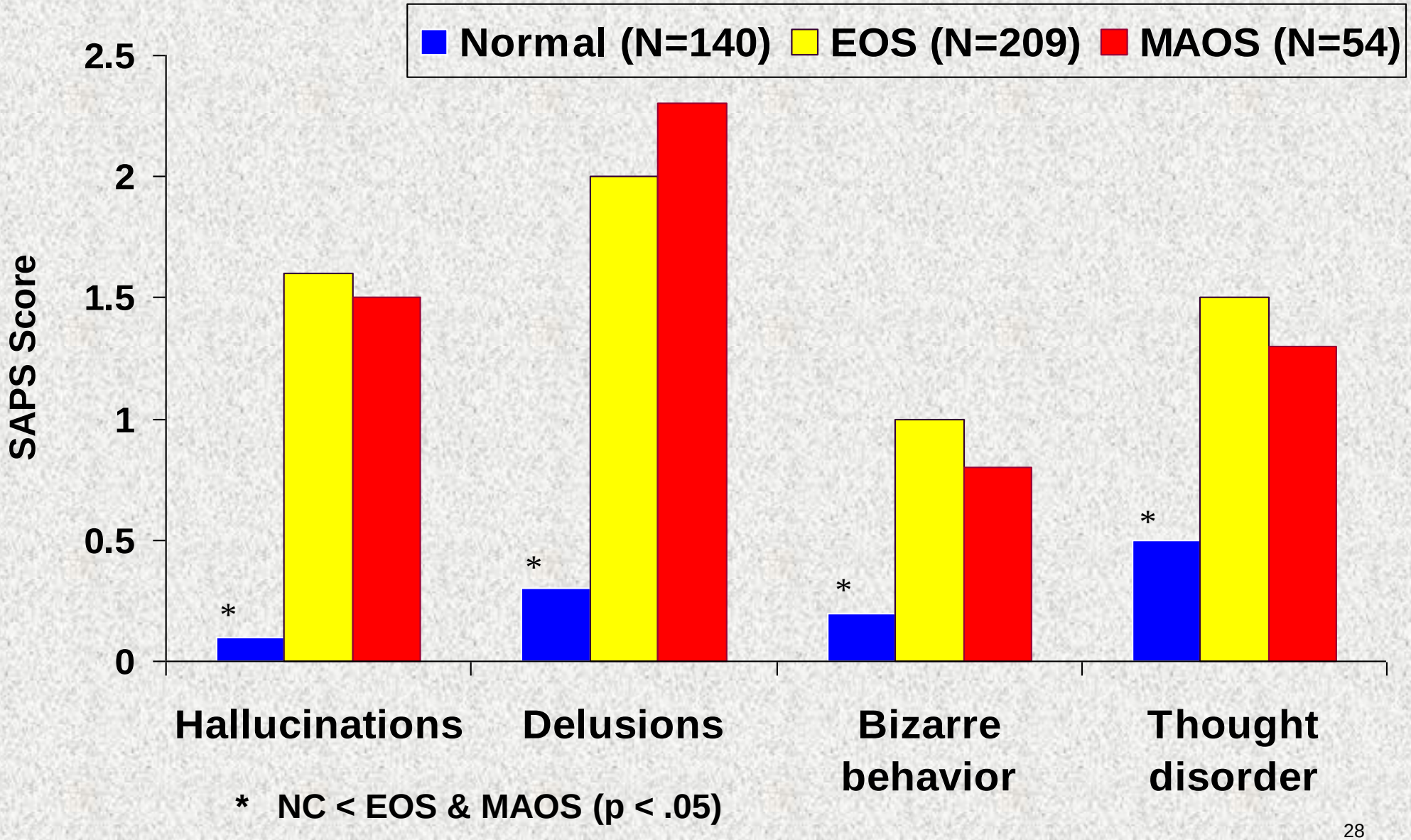
Specific inclusion and exclusion criteria

Diagnostic stability over follow-up period

Patient Characteristics

	EOS (N=253)	MAOS (N=65)
Age of onset of schizophrenia	25 (7)	51 (8)
Duration of illness	31 (11)	10 (8)
Neuroleptic dose (mg CPZE/day)	250	126 *

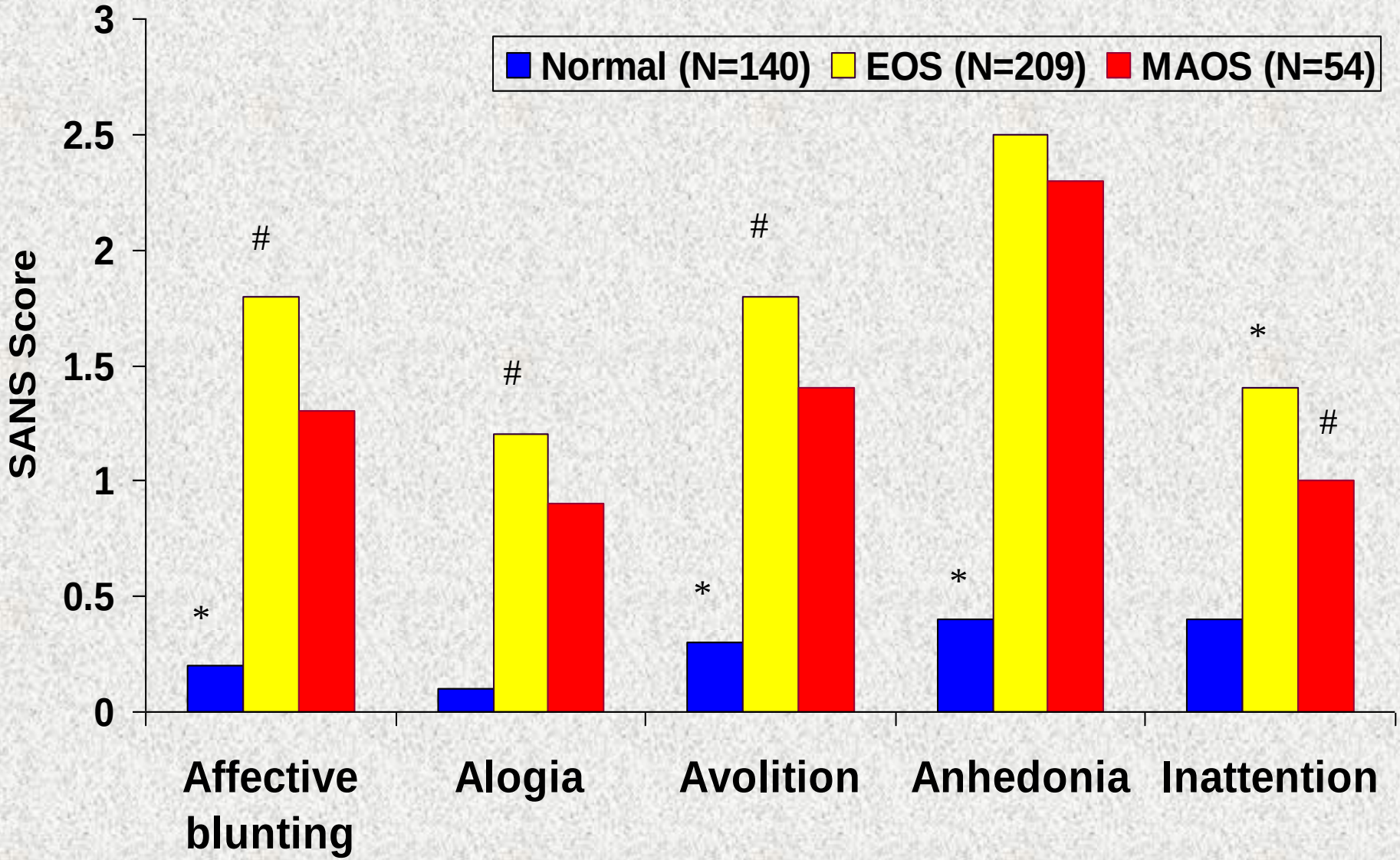
SAPS Subscale Scores



* NC < EOS & MAOS ($p < .05$)

(Palmer et al., Harv Psychiat Rev, 2001)

SANS Subscale Scores



* NC < EOS & MAOS (p < .05) # EOS > MAOS (p < .05)

(Palmer et al., Harv Psychiat Rev, 2001)

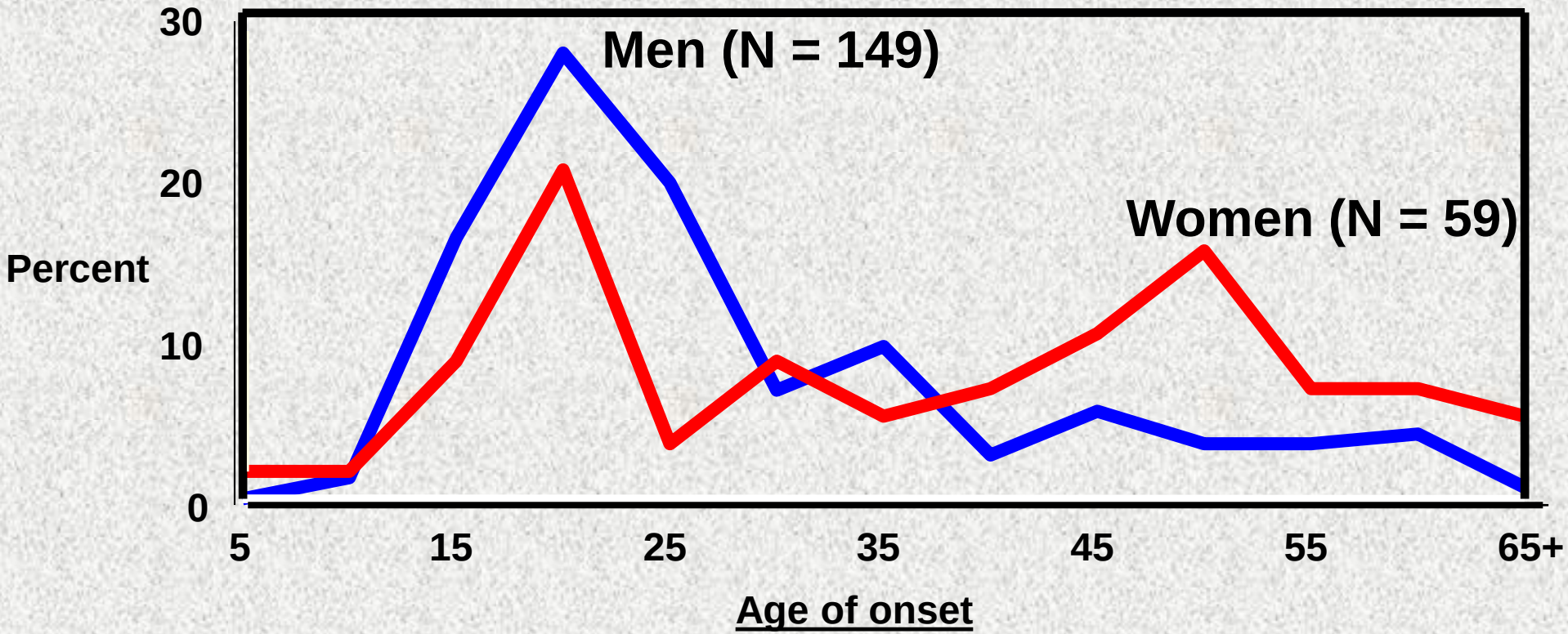
MAOS: Similarities with EOS

(I) Clinical

1) Severity of positive symptoms
2) Family history of schizophrenia
3) Minor physical anomalies
4) Childhood maladjustment
5) Sensory impairment

(Jeste et al., Am Psychiatry, 1995; Am J Geriat Psychiatry, 1997)

Age of Onset of Schizophrenia by Gender (Age > 45)



Kolmogorov-Smirnov pvalue < .0001

(Lindamer et al., Psychopharm. Bull., 1997)

MAOS: Differences from EOS

(I) Clinical

1) More common in women
2) Less severe negative symptoms
3) Mostly paranoid subtype
4) Greater % of patients ever married

(Jeste et al., Am J Psychiatry, 1995; Am J Geriat Psychiatry, 1997)

Psychosocial Factors

- **Premorbid Functioning: Suboptimal without being grossly psychopathological. Premorbid personality may show paranoid or schizoid traits but not disorder.**

- **Psychosocial Stressors: Retirement, bereavement, financial loss, physical disability, etc. may serve as precipitants and/or maintainers of psychosis.**

Neuropsychological Assessment

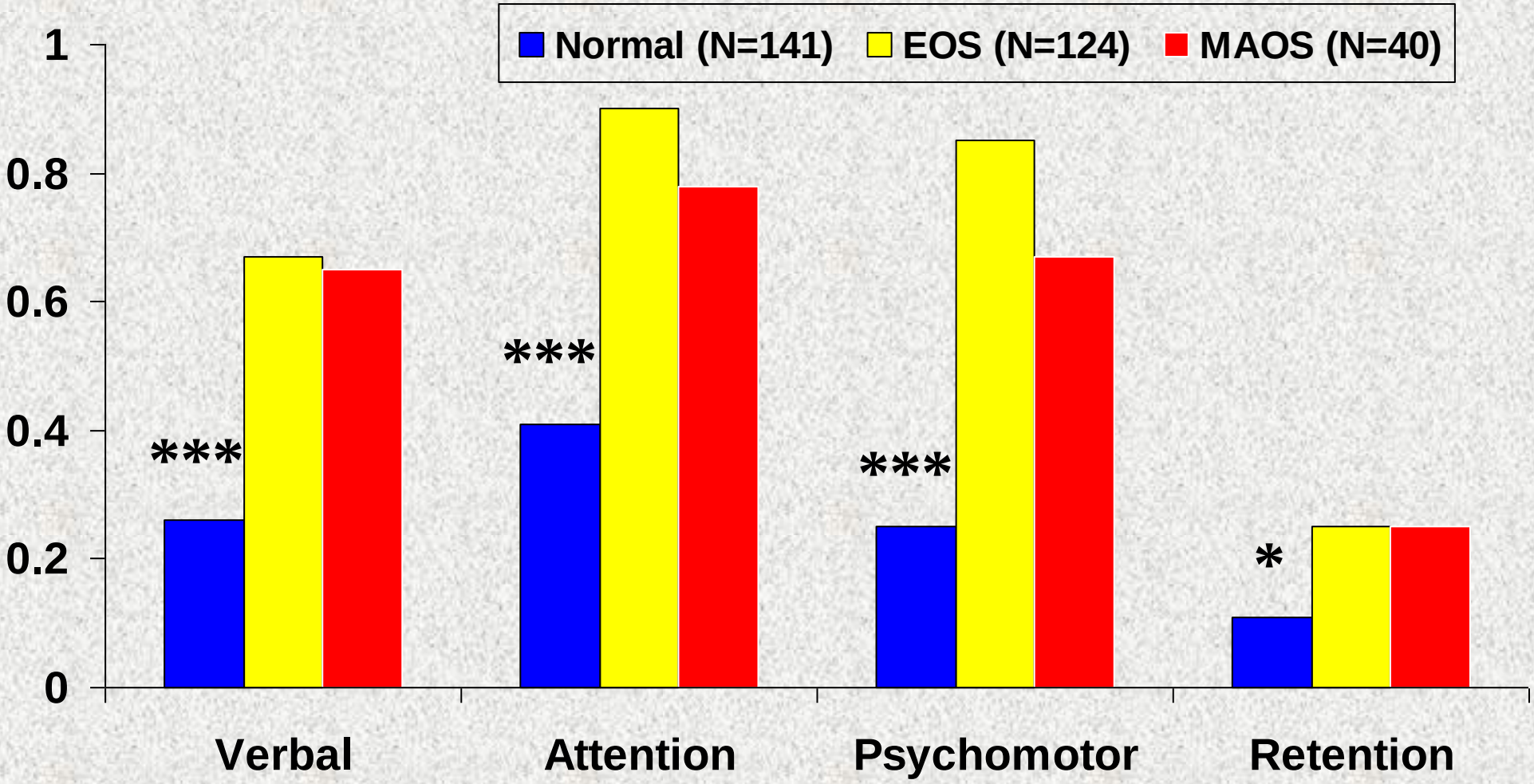
- **Expanded Halstead-Reitan battery, Age-, gender-, and education-corrected, T-, and deficit-scores for 7 ability areas:**

1) Verbal, 2) Attention, 3) Psychomotor,

4) Memory (retention), 5) Learning,

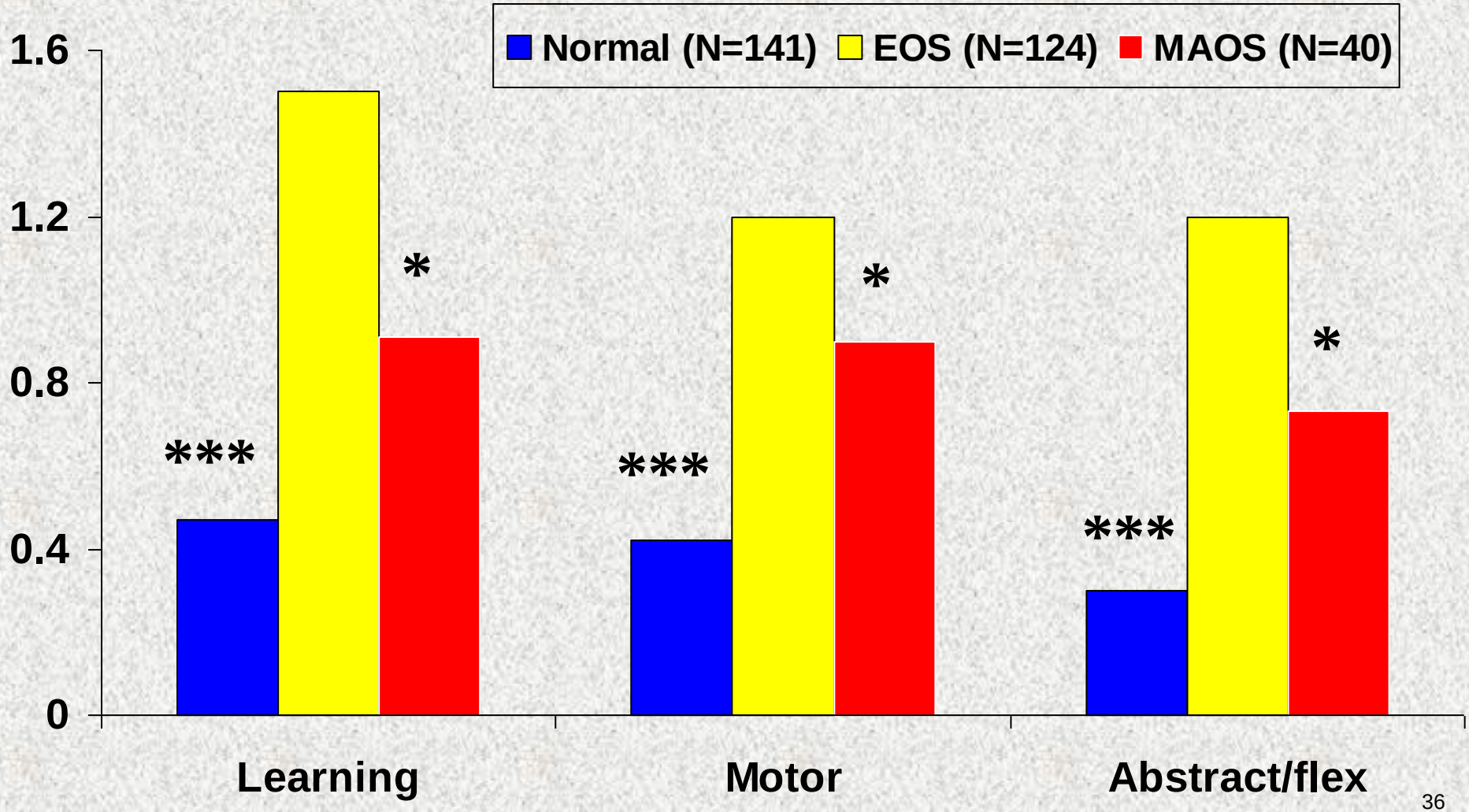
6) Motor, and 7) Abstraction.

Neuropsychological Deficit Scores



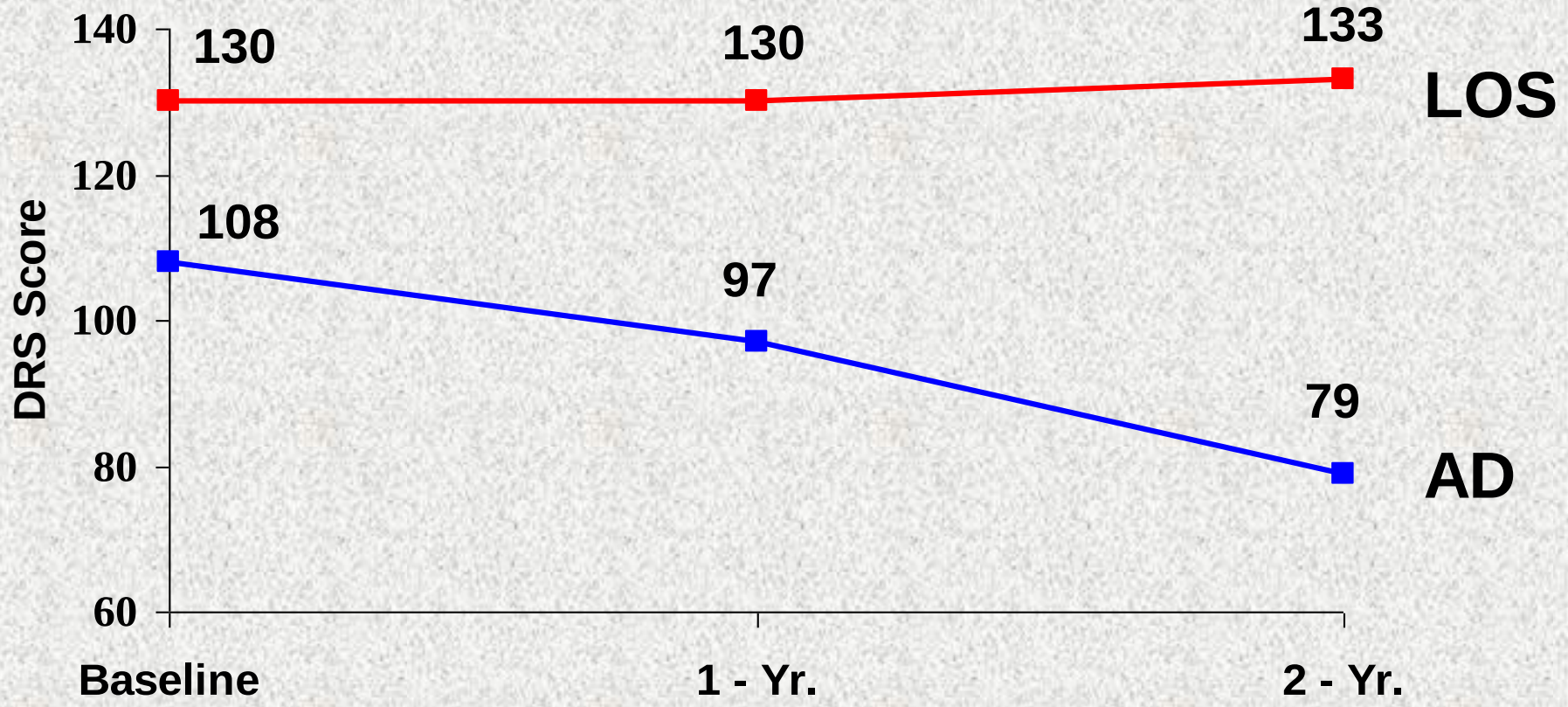
* p < .05; *** p < .0001(NC < MAOS, EOS)

Neuropsychological Deficit Scores



* p .05; *** p<.0001 (NC < MAOS < EOS)

MAOS (N=29) vs. AD (N=61)
Longitudinal DRS Scores



MAOS: Similarities with EOS

(II) Neuropsychological

(1) Overall pattern of cognitive impairment

(III) MRI

(1) Nonspecific MRI abnormalities

(IV) Course & Treatment

(1) Chronic Course

(2) Qualitative response to neuroleptics

(3) Increased mortality

(Jeste et al., Am J Psychiatry, 1995; Am J Geriatric Psychiatry, 1997)

MAOS: Differences from EOS

(II) Neuropsychological

(1) Less severe impairment in learning and in abstraction

(III) MRI

(1) Larger thalamus?

(IV) Course & Treatment

(1) Need for lower doses of neuroleptics

(Jeste et al., Am J Psychiatry, 1995; Am J Geriatric Psychiatry, 1997)

Very Late-Onset Schizophrenia-like Psychosis

- Heterogeneous group of disorders:
- Psychosis of dementia
- Psychosis secondary to general medical conditions or substance use
- Mood disorder with psychotic features
- Delusional disorder
- Psychosis NOS

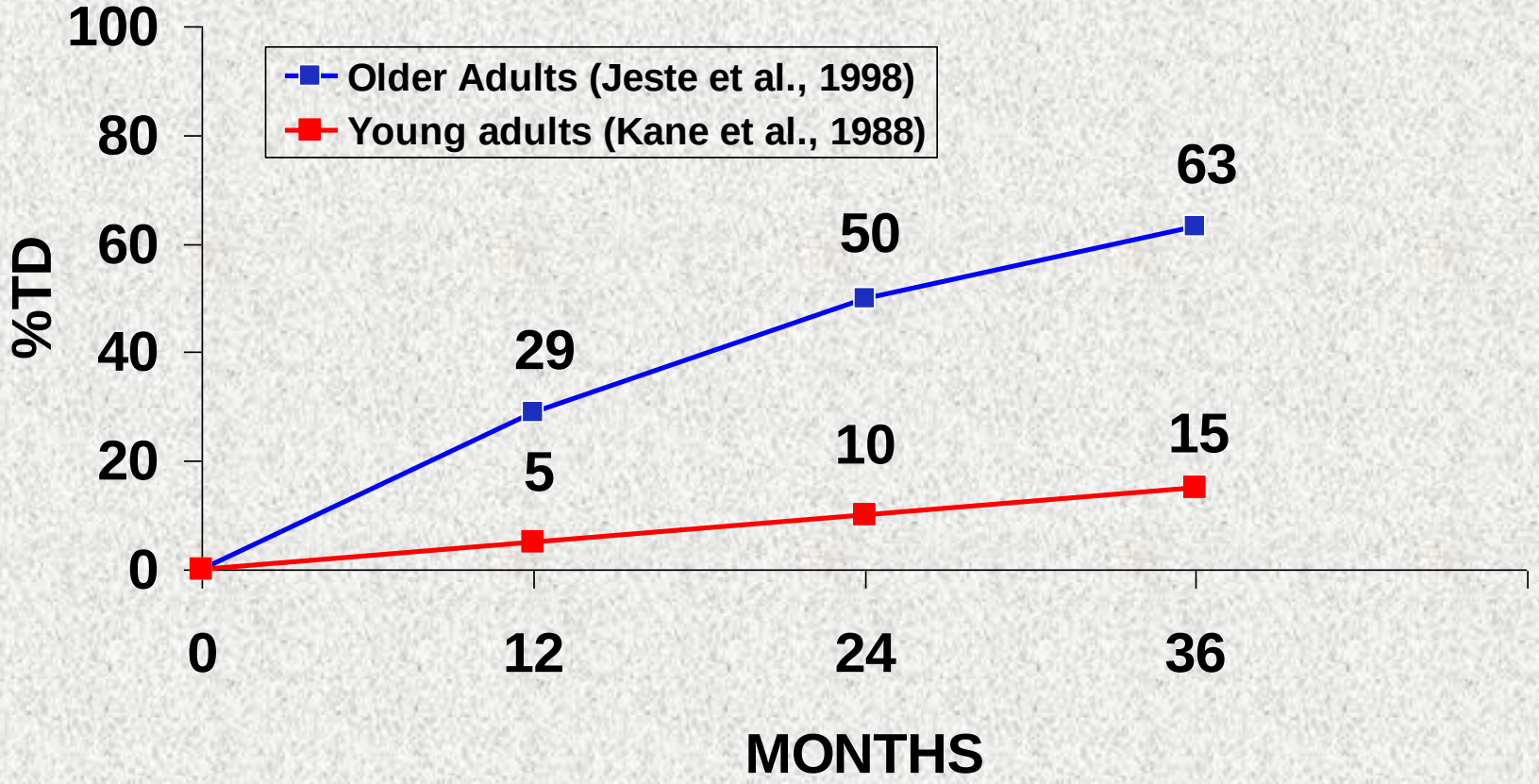
International Consensus Statement on Late-Onset Schizophrenia

In terms of epidemiology, symptomatology, and identified pathophysiology, LOS (onset after age 40) and very late-onset schizophrenia-like psychosis (onset after age 60) have face validity and clinical utility.

-Howard, Rabins, Seeman, Jeste, and International LOS Group (representatives from Australia, Brazil, Canada, Denmark, France, India, Japan, Spain, Switzerland, UK and USA)

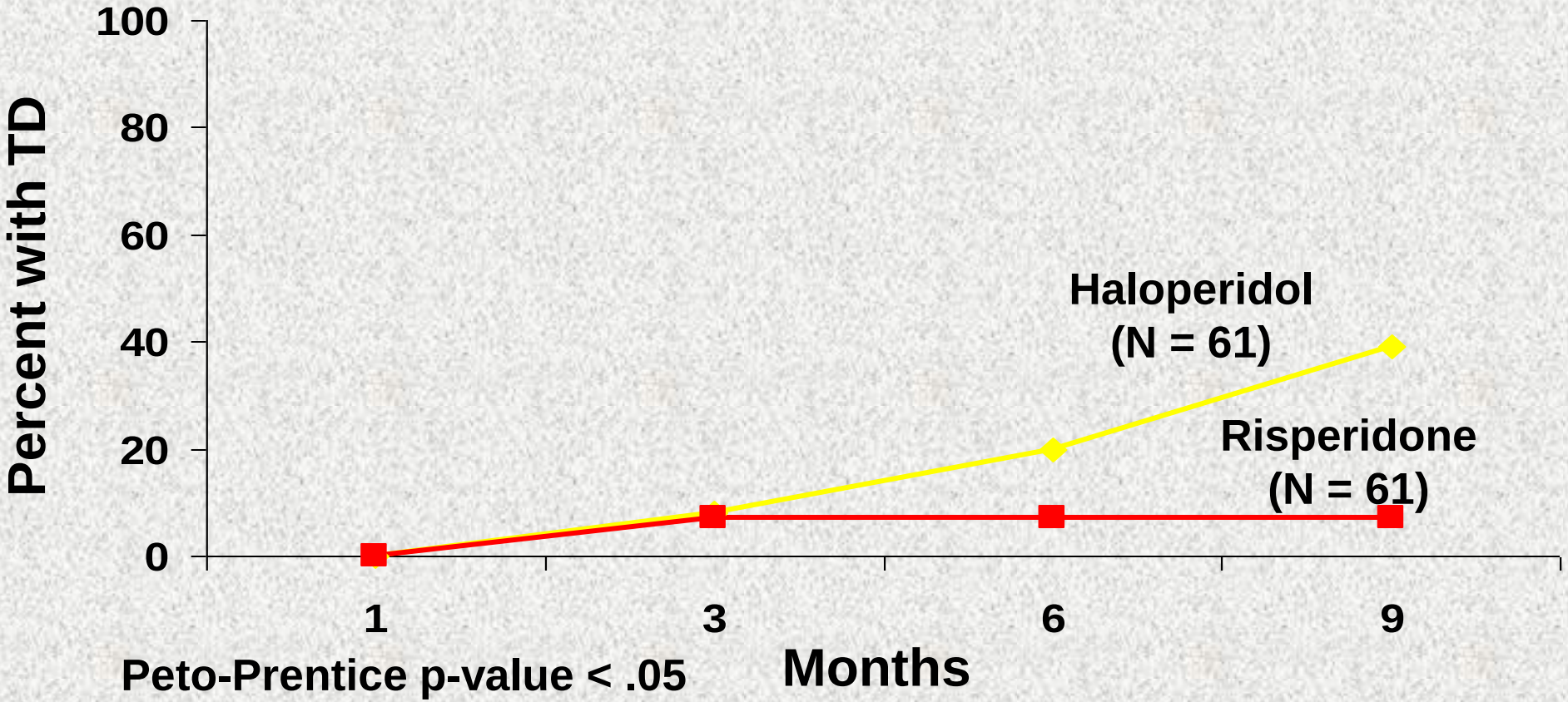
(American Journal of Psychiatry, 2000)

Cumulative Incidence of TD with Conventional Neuroleptics



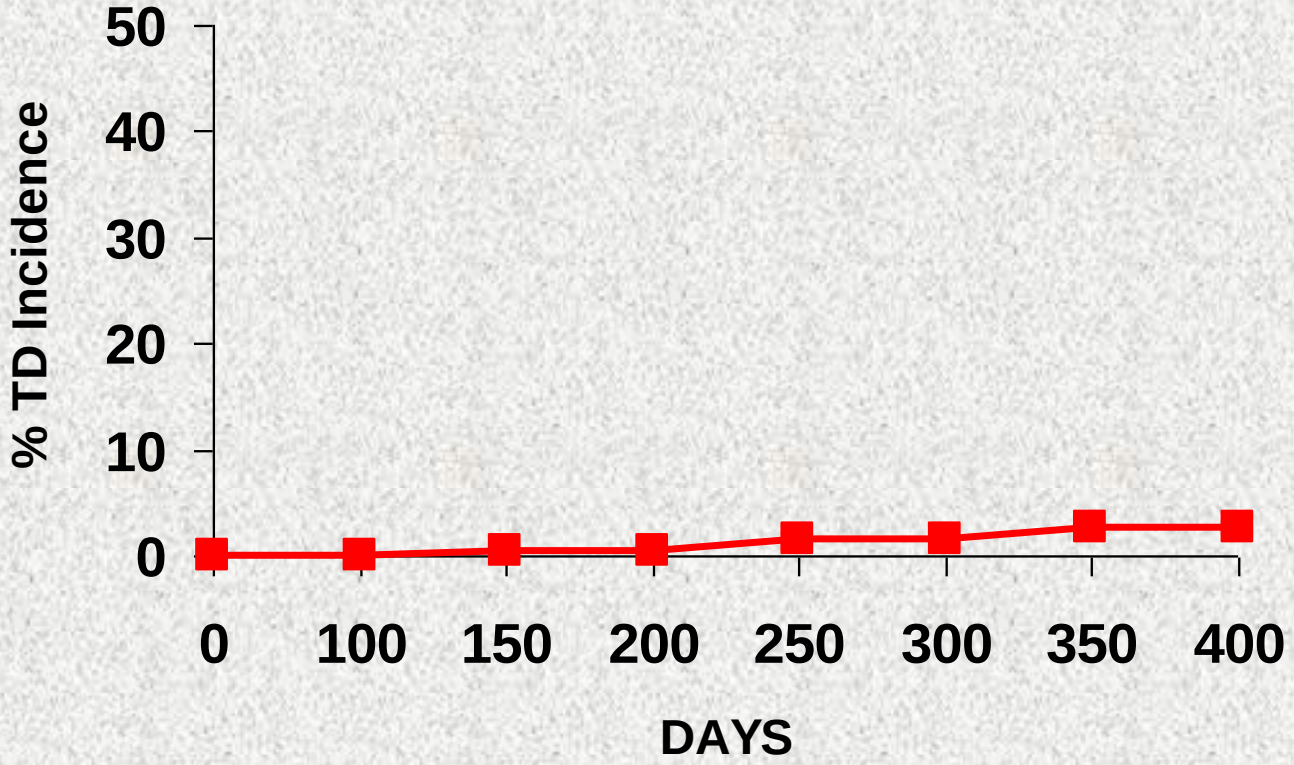
(Kane et al., J Clin Psychopharmacol, 1988) (Jeste et al., Am J Geriatric Psychiatry, 1998)

TD Incidence in Older Patients: Haloperidol versus Risperidone (1mg/d)



(Jeste, et al., JAGS, 1999)

Cumulative Incidence of Persistent TD With Quetiapine in Elderly Psychosis Patients (N=85): Open-Label Study



(Jeste et al., AAGP poster, 2000)

Atypical Antipsychotics: Possible Long-Term Side Effects

- Weight gain
- Type 2 diabetes mellitus
- Hyperprolactinemia
- Eye changes
- Cardiac conduction disorders

Recommended Dosages in Older Patients (mg/day)

Drug	Initial	Typical Range
Clozapine	6.25-12.5	50-150
Risperidone	0.25-0.5	1-3
Olanzapine	2.5-5	5-15
Quetiapine	12.5-25	75-200

Other Atypical Antipsychotics

- Ziprasidone
- Aripiprazole
- Iloperidone
- Zotepine
- Others

COGNITIVE BEHAVIORAL, SOCIAL SKILLS TRAINING (CBSST)

- Three modules, each with 4 weekly sessions
  - CBT – Thought challenging
  - SST – Symptom self-management
  - CBSST – Coping with persistent symptoms & medication adherence strategies
- Found useful for older patients with schizophrenia

(McQuaid et al., 2001; Granholm et al., 2002)

Treatment - Summary

- Atypical antipsychotics have a considerably lower risk of EPS and TD than conventional neuroleptics, but they must be used in low dosages
- Medications need to be supplemented by psychosocial therapies

Post Lecture Exam
Question 1

1. **True or False:** By the year 2030, it is estimated that the number of people over 65 years of age with psychiatric disorders in the USA will equal the number of people between ages 30 and 44 years of age with psychiatric disorders.

Question 2

2. The course of schizophrenia in late life is characterized by all of the following EXCEPT:

A. Relatively stable course

B. Persistence of negative symptoms

C. Improvement of positive symptoms

D. Severe cognitive deterioration

E. Relatively non-deteriorating course

Question 3

3. **MAOS (middle-age-onset schizophrenia) resembles EOS (early onset schizophrenia) in all but which of the following characteristics?**

A. Positive family history of schizophrenia is common.

B. Response to neuroleptics is often good.

C. Much lower rate of mortality is seen with MAOS.

D. Nonspecific MRI abnormalities are typical in both syndromes.

E. Chronic course is typical.

Question 4

4. **MAOS differs from EOS in all but which of the following characteristics?**

A. MAOS is less common among women.

B. Negative symptoms in MAOS tend to be less severe.

C. A greater percentage of patients with MAOS than EOS never have been married.

D. Lower dose of neuroleptics than in EOS may be effective in MAOS.

E. Learning and abstraction are less severely impaired in MAOS than in EOS.

Question 5

5. **Which of the following is NOT true of very late-onset schizophrenia-like psychosis?**

A. It is a heterogeneous group of disorders including medically-induced and other psychotic states.

B. It should not be treated with antipsychotic medications.

C. Patients with this disorder should receive appropriate psychotherapeutic help, e.g., with CBSST (cognitive behavioral social skills training)

D. Treatment with antipsychotic medication can produce TD.

E. Treatment with antipsychotic medication can result in increased weight gain, hyperprolactinemia, and changes in eye and/or heart functioning.

Question 6

6. Late-onset schizophrenia (LOS) differs from early-onset schizophrenia (EOS) in all of the following ways EXCEPT:

A. LOS is common in women.

B. LOS patients generally have less severe negative symptoms.

C. LOS is predominantly of the paranoid subtype.

D. LOS patients have a need for lower doses of antipsychotics.

Question 7

7. **Of the following statements regarding similarities between EOS and LOS, choose the one that is TRUE:**

A. Positive symptoms are less severe in LOS.

B. Both EOS and LOS have a chronic course.

C. LOS is not a true psychotic illness.

D. LOS patients have a better qualitative response to antipsychotics.

Question 8

8. **Which one of the following statements about controlled studies of typical antipsychotics in dementia is correct?**

A. Conventional antipsychotics are no better than placebo.

B. Improvement rates with conventional antipsychotics were more than double that of placebo.

C. Improvement rates with conventional antipsychotics were more than triple that of placebo.

D. No single conventional agent was better than others.

Question 9

9. Which of the following are adverse effects of conventional antipsychotics in the elderly?

A. Anticholinergic toxicity

B. Sedation and confusion

C. Extrapyramidal side effects

D. All of the above

Question 10

10. Which of the following is most commonly the appropriate dosage range of risperidone for the treatment of psychosis and agitation in dementia, considering both safety and efficacy?

A. 0.25 – 0.5 mg/day
B. 1 – 2 mg/day
C. 2 – 4 mg/day
D. 4 – 6 mg/day

Question 11

11. Which of the following are risk factors for tardive dyskinesia in older patients?

A. Baseline duration of antipsychotic use

B. History of alcohol abuse/dependence

C. Cumulative amount of antipsychotics used (especially high-potency conventional agents)

D. All of the above

E. Two of the above

Question 12

12. Which of the following is generally considered the most appropriate dosage range of olanzapine for the treatment of psychosis and agitation in dementia, considering both safety and efficacy?

A. 5 – 10 mg/day

B. 15 – 20 mg/day

C. 2.5 – 5.0 mg/day

D. 7.5 – 15 mg/day

Question 13

13. For which of the following medications have randomized controlled trials for agitation in dementia been conducted?

A. Valproate
B. Trazodone
C. Citalopram
D. Two of the above
E. All of the above

Question 14

14. Choose the one statement regarding tardive dyskinesia (TD) that is true:

A. Severity of TD is not associated with quality of well-being or everday functioning scores.

B. The cumulative annual incidence of TD in older patients treated with conventional agents is 5-10%.

C. In general, the risk of developing TD in older patients is reduced with the use of atypical antipsychotics compared to conventional agents.

D. TD risk is only slightly increased on older versus younger individuals.

Question 15

15. Read the following statements regarding the management of psychosis in the elderly and choose the correct statement(s):

I. Pharmacotherapy should be combined with supportive therapy and caregiver education.

II. Pharmacotherapy should always be the initial treatment of agitation in dementia.

III. Atypical antispsychotics are safer than conventional agents, but have their own limitations.

IV. Clear communication, consistent daily routines and a modified environment are all examples of nonpharmacologic management techniques for patients with dementia.

Please see next slide for choices

Question 15 (continued)

A. I only
B. II only
C. I, II, and III
D. I, III, and IV
E. I, II, III, and IV

Answers to Pre & Post Competency Exams

1. True
2. D
3. C
4. A
5. B
6. A
7. B
8. D
9. D
10. B
11. D
12. A
13. E
14. C
15. D