

# **Improving the Methodology for Assessing Mild Cognitive Impairment Across the Lifespan**

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&

Red Sox Foundation and Massachusetts General Hospital Home Base Program

Presidential Address

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Two books, one is on the WAIS-IV/WMS-IV

# Standing on the Shoulders: Reitan, Mattarazzo, Golden, & Heaton

- Thanks for the Lift: Franzen, Larrabee, Millis, Rohling, Chelune, Crawford, Schretlen
- Primary Collaborators: Brooks, Holdnack, & Lange

# Broad Topics

- Defining and conceptualizing mild cognitive impairment
- Improving the scientific underpinnings of clinical judgment
- Using Multivariate Base Rates in Clinical Practice

- To challenge our assumptions and beliefs.
- To build the foundation for a change in our clinical practice.

# Prevalence of Low Scores in Healthy Children, Adolescents, Adults, and Older Adults?

- Most neuropsychologists don't know
- Higher the cut-off, greater the number of low scores
- More tests you give, the more likely you are to get low scores

# How Do You Define Impairment?

- Scores below the 16<sup>th</sup> percentile (1 SD)?
- Scores below the 10<sup>th</sup> percentile?
- 5<sup>th</sup> percentile?
- 2<sup>nd</sup> percentile (2 SDs)?



# Neuropsychological Assessment Battery (NAB)

- Takes approximately 3.5 hours to administer
- 24 tests
- 36 Primary Test Scores
- MANY additional test scores

# Impairment $< 1$ SD (16<sup>th</sup> percentile)

- What percentage of healthy adults have one or more low scores?

92%

- 3 or more? 66%

- 5 or more? 44%

# Impairment = 5<sup>th</sup> Percentile

- What percentage of healthy adults have one or more low scores?

70%

- 3 or more? 31%

- 5 or more? 16%

# Deficit Measurement & Confirmatory Bias

- Assume Something is Wrong
- Test Until You Find It
- Profile Sheets
- “Make Sense of the Data”
- HARKing
  - Hypothesizing After the Results are Known
- How many of you ran 100 t-tests for your dissertation?

# Challenges in Clinical Practice

- There is no well-accepted criteria for defining cognitive impairment.
- Two neuropsychologists analyzing the same battery of tests will often interpret them differently.
- The interpretation of neuropsychological tests relies heavily on clinical judgment. Clinical judgment is influenced greatly by “clinical experience.” Clinical experience is anecdotal evidence. Anecdotal evidence is one of the lowest forms of evidence.

- Until recently, we did not know the probabilities or our error rates.
  - If I say someone has an acquired deficit in memory, what is the probability that I am right?
    - What is the false positive rate for that conclusion?
  - If I say someone does not have a memory problem, what is the probability that I am right?
    - What is the false negative rate for that conclusion?

**IQ Score Distribution**

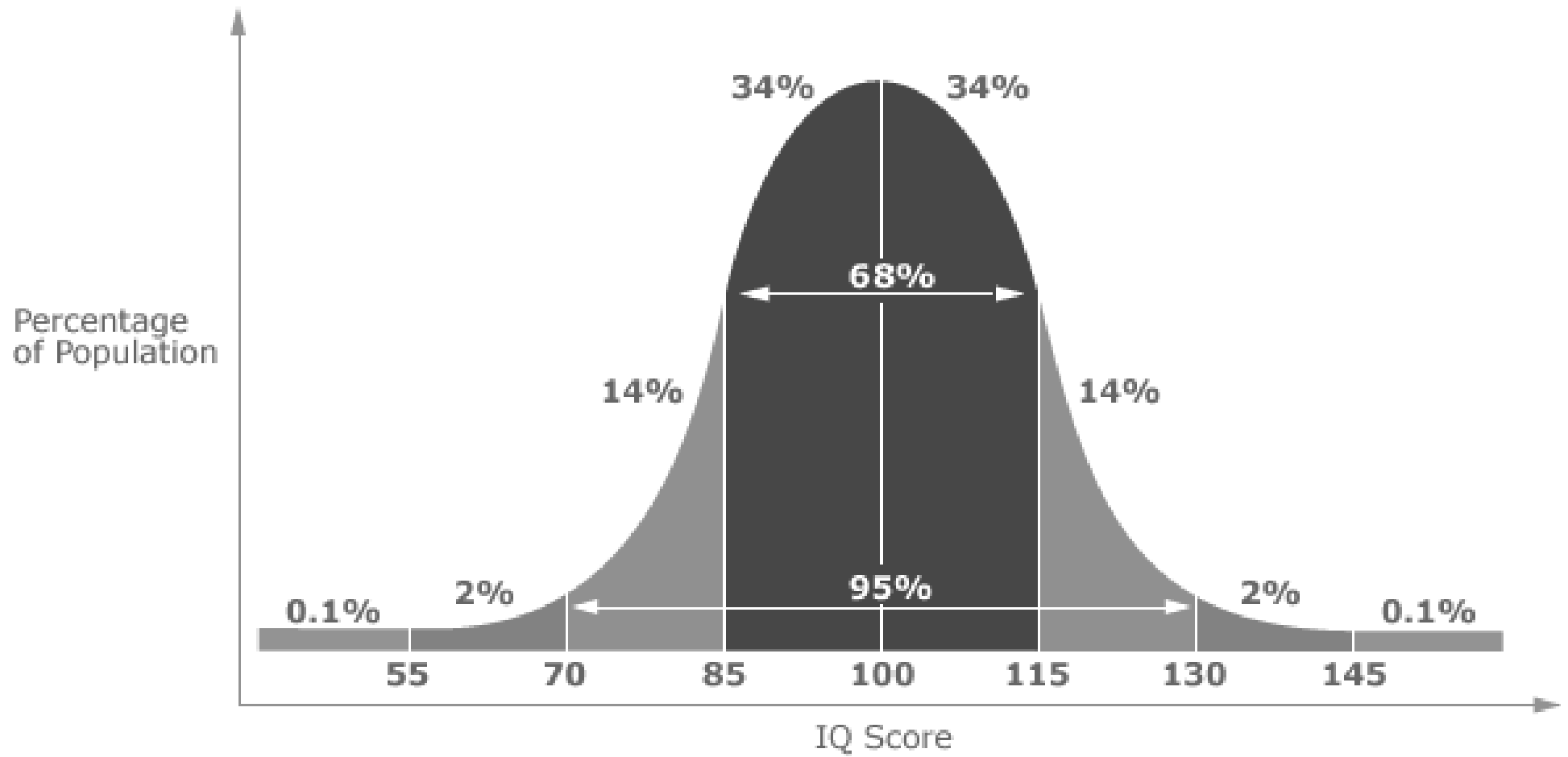
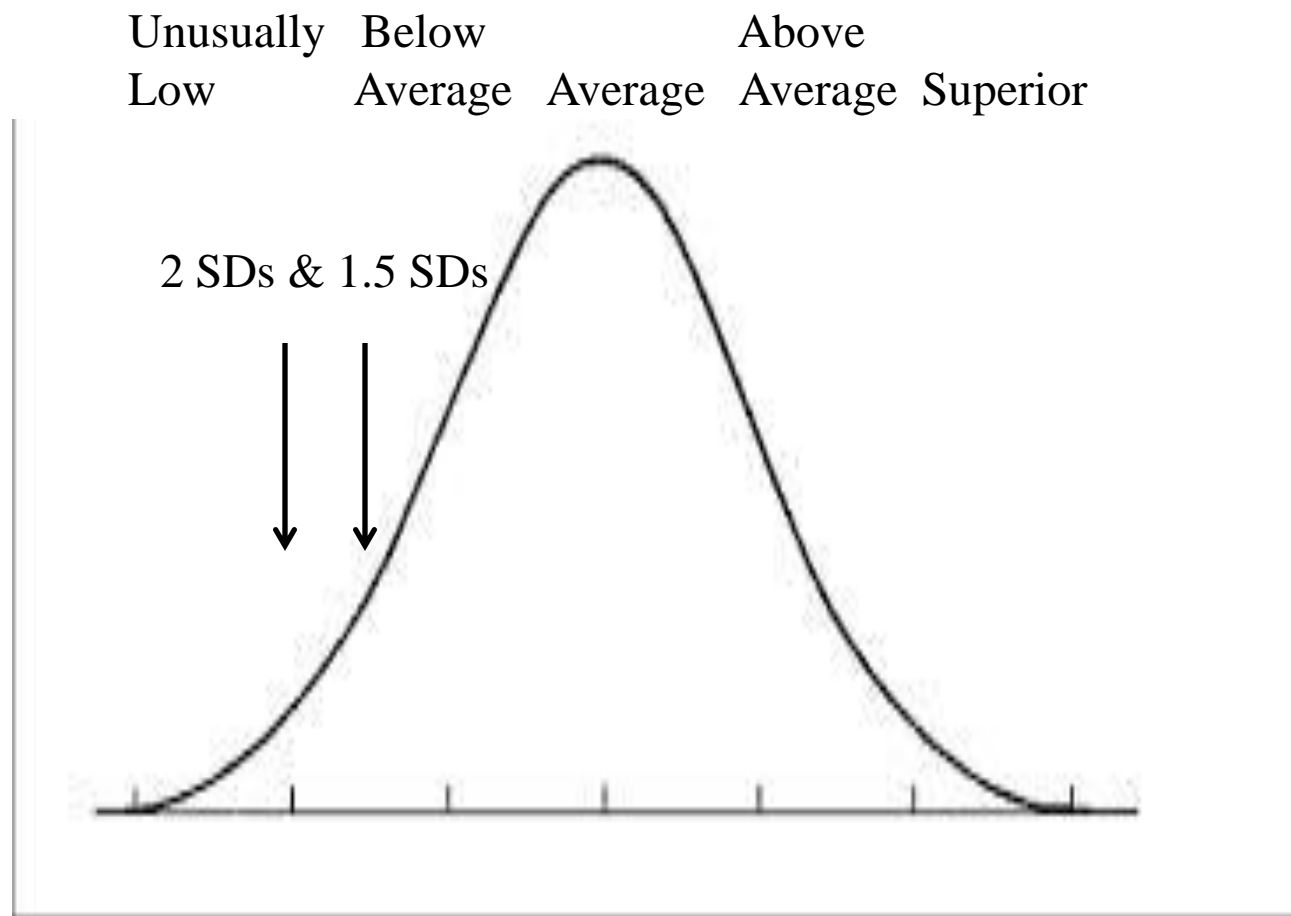


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Clinical Question: Does a pattern of performance occur at a specific point on the curve? (not a single test score)



# The Basics

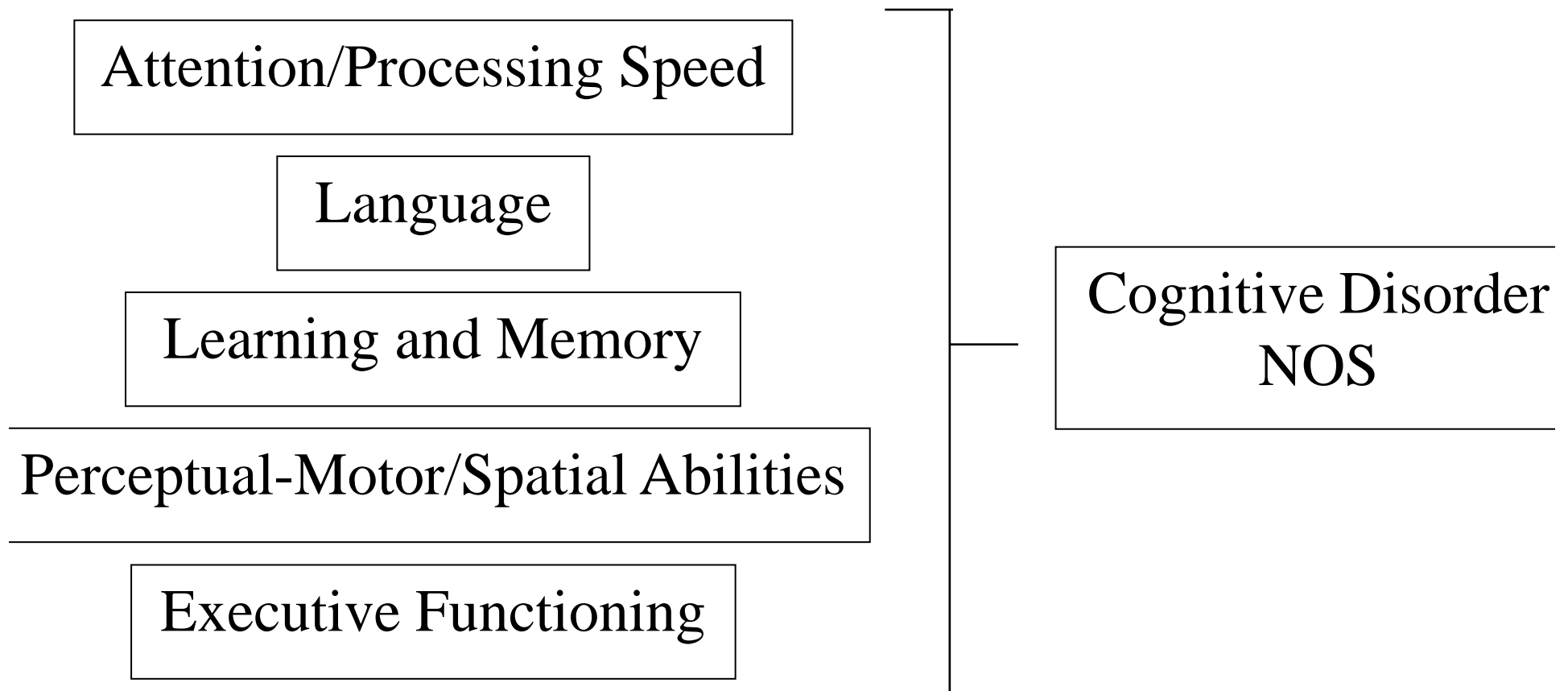
What is the definition of cognitive impairment?

- There is no universally agreed upon *definition* of cognitive impairment or methodology for establishing the severity of cognitive impairment.

# A Few Examples of Definitions

- Mild Cognitive Disorder (ICD-10)
- Cognitive Disorder Not Otherwise Specified (DSM-IV)
- Mild Neurocognitive Disorder (DSM-5)
- Major Neurocognitive Disorder (DSM-5)
- Dementia (ICD-10 and DSM-IV)

# DSM-IV Cognitive Disorder NOS: “Mild Neurocognitive Disorder”



# When Will We Have a Unified Definition of Cognitive Impairment?

- If we don't do it, our physician colleagues will do it for us.
- DSM-V
  - Major Neurocognitive Disorder
  - Minor Neurocognitive Disorder

# DSM-5

Mild Neurocognitive Disorder  
(aka, Mild Cognitive Impairment; MCI)

Major Neurocognitive Disorder (aka, Dementia)



# DSM-5

Impairment must be present in 1 or more cognitive domains.

For Major Neurocognitive Disorder, performance is typically 2 or more standard deviations below appropriate norms (3<sup>rd</sup> percentile or below).

For Mild Neurocognitive Disorder, performance typically lies in the 1–2 standard deviation range (between the 3<sup>rd</sup> and 16<sup>th</sup> percentiles).

# What does that mean?

- Based on what?
- Average cognitive domain scores?
- Individual tests?
- Based on how many scores in each domain?
- Test performance and clinical judgment?

# Neuropsychological Assessment Battery (NAB)

- Takes approximately 3.5 hours to administer
- 24 tests
- 36 Primary Test Scores
- Many additional test scores

# 5 NAB Domain Scores

(M=100; SD=15)

Attention (and processing speed; average of 11 scores)

Language (average of 5 scores)

Learning and Memory (average of 10 scores)

Spatial Skills (average of 6 scores)

Executive Functioning (average of 4 scores)

Percentage of Healthy Adults Meeting Testing  
Criteria for DSM-5 Mild Neurocognitive Disorder?

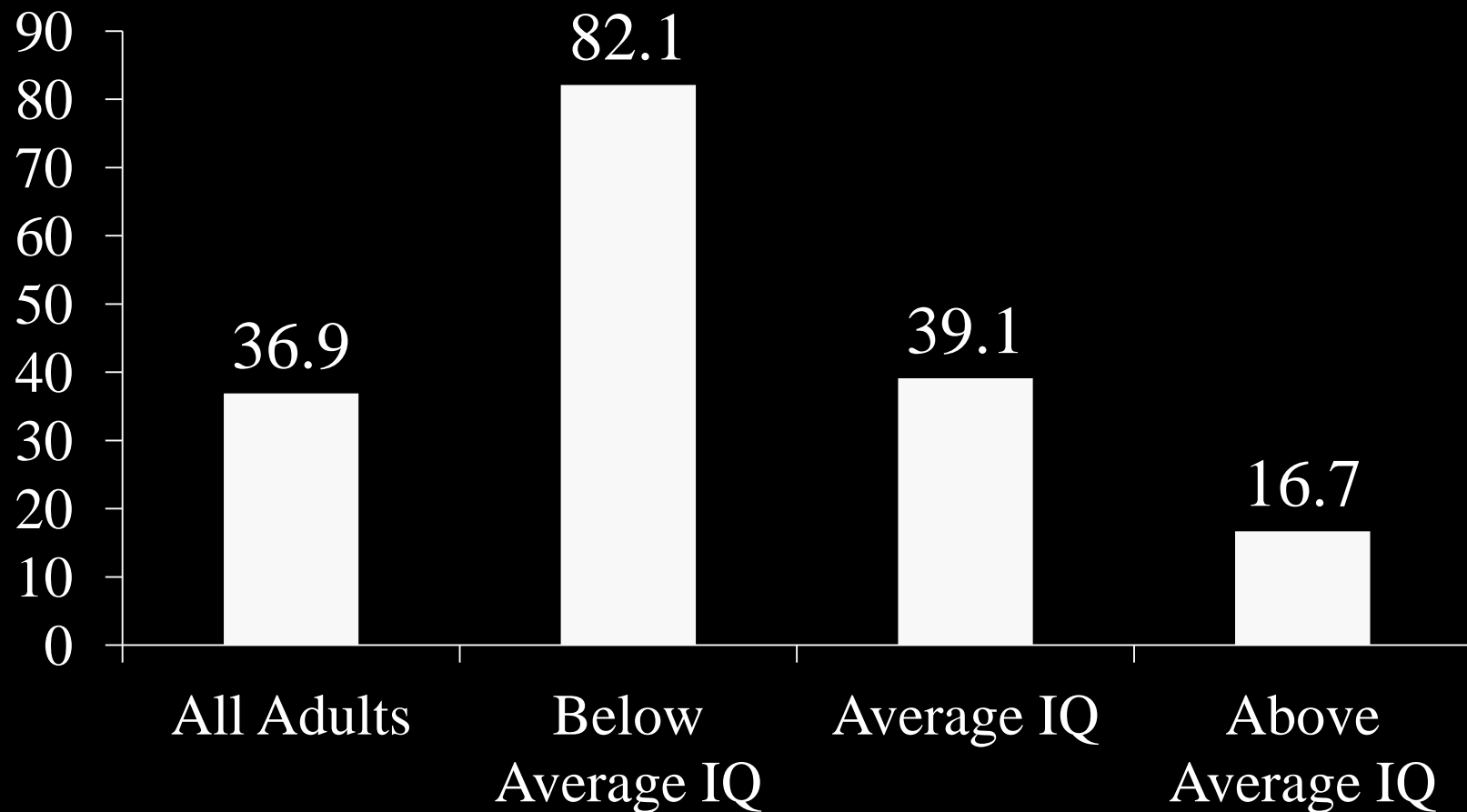
36.9%!

(based on 1 or more domain scores below 1 SD)

# Prevalence of Low Scores Varies by Estimated IQ

# Percentages of Healthy Adults Meeting Testing Criteria for DSM-5 Mild Neurocognitive Disorder! (considering 5 NAB Domain Scores; 1 or more $\leq 1SD$ )

(Source: Iverson et al., 2008)

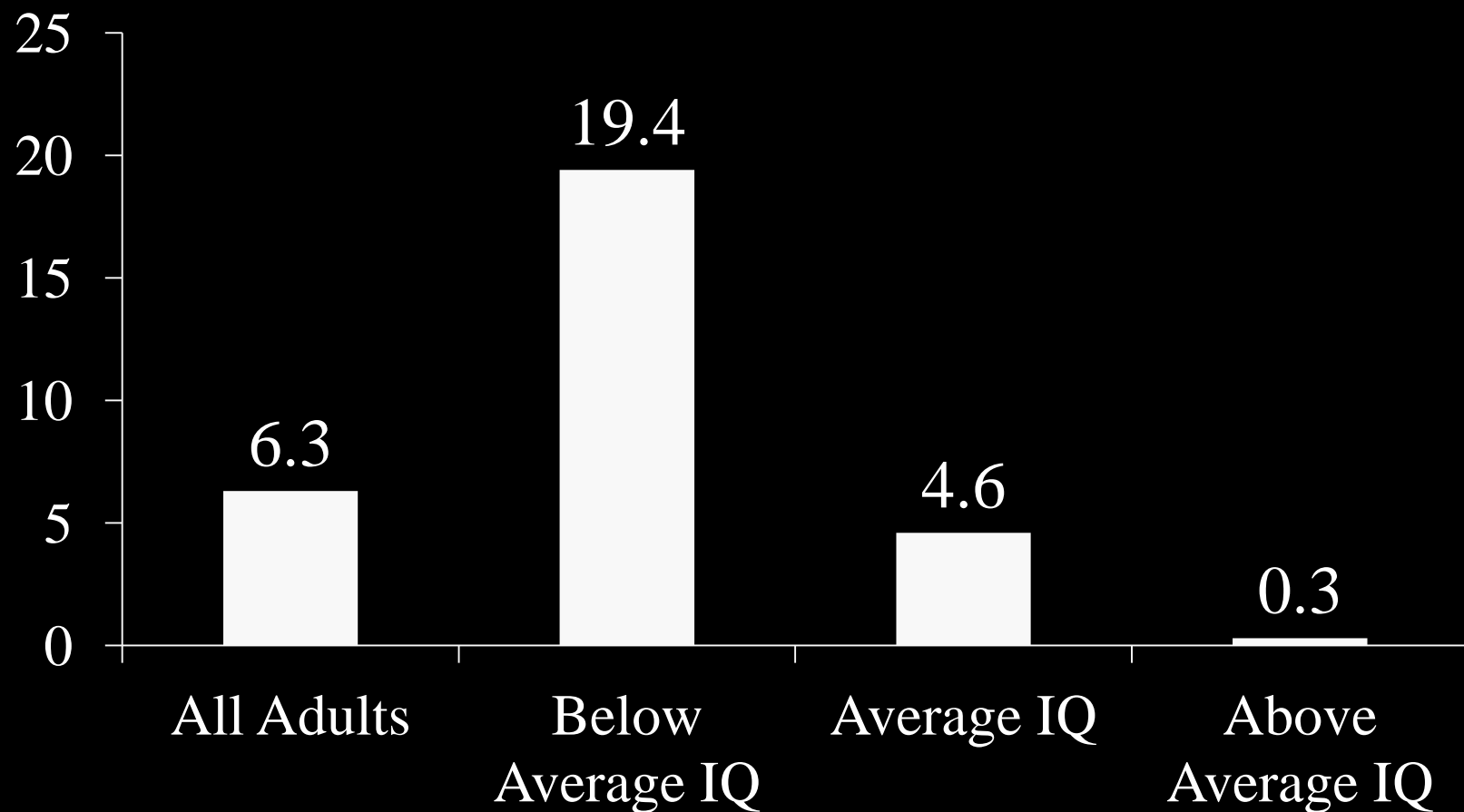


# What about DSM-5 Major Neurocognitive Disorder?



# Percentages of Healthy Adults Meeting Testing Criteria for DSM-5 Major Neurocognitive Disorder (considering 5 NAB Domain Scores; 1 or more $\leq 2SD$ )

(Source: Iverson et al., 2008)



# Wait, it gets worse

- What if a clinician or researcher defined impairment based on a single “abnormal” test score?

# Considering MCI / DSM-5 Mild Neurocognitive Disorder

- A selected battery of tests that takes approximately 2.5 hours to administer (derived from the NAB-which normally takes 3.5-4 hours to administer)
- Norms: Age, Education, and Sex adjusted
- Number of Tests: 18
- Number of Scores Considered: 23

If MCI is based on 1 score (out of 23)  
below 1 SD, how many healthy adults  
would have MCI?

81.2%

2 or more low scores?

63.4%

4 or more low scores?

35.8%!

If DSM-5 Major Neurocognitive Disorder is based  
on 1 score (out of 23) below 2 SD,  
how many healthy adults would have “Dementia”?

33.5%!

2 or more low scores?

13.2%

4 or more low scores?

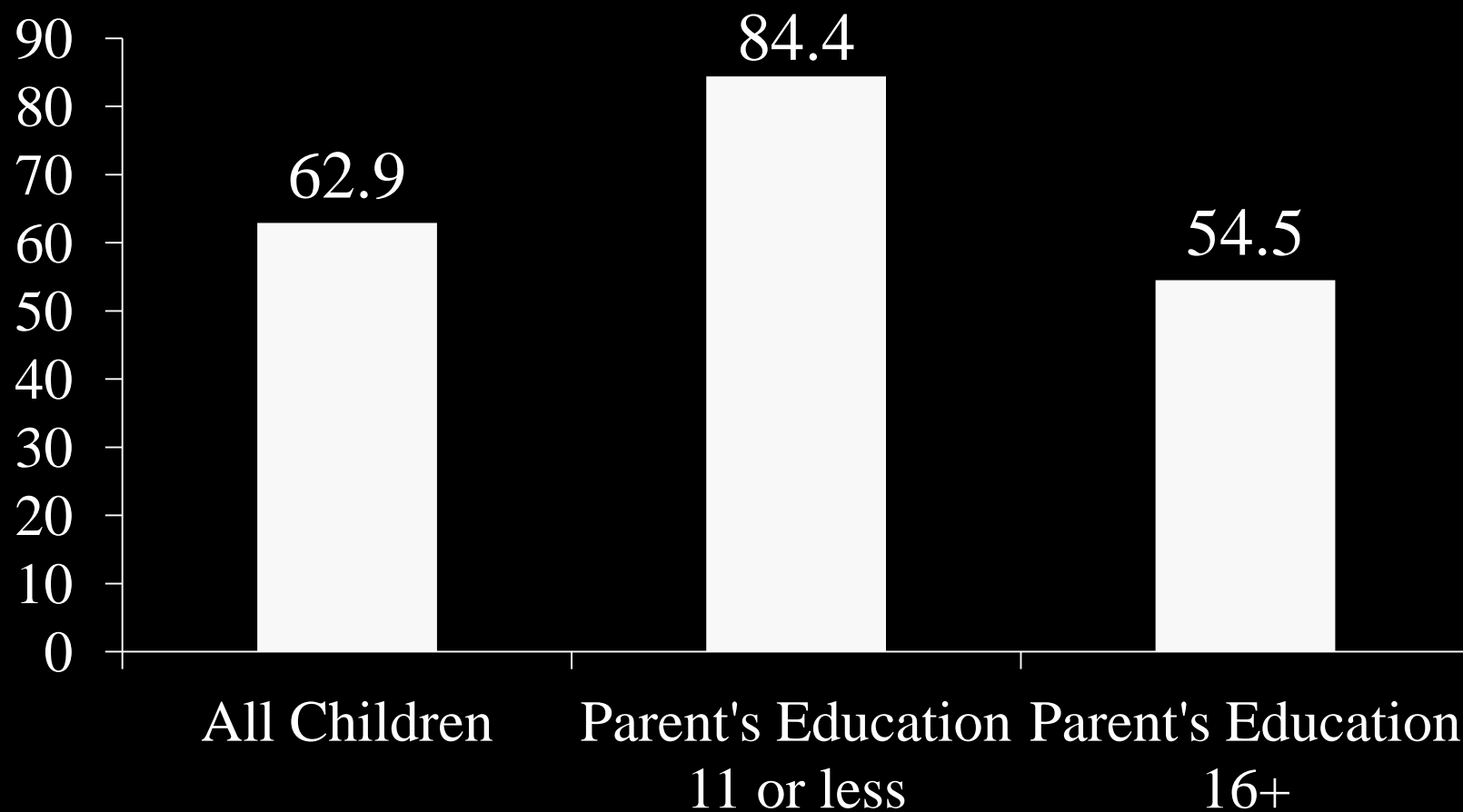
4%

# What about children?

# Percentage of Children with a Low Score on a 2-Hour NEPSY-II Battery

(age 7-16; considering 17 scores; 1 or more  $\leq 10^{\text{th}}$  percentile)

(Source: Brooks, Sherman, and Iverson, 2010)



If DSM-5 Major Neurocognitive Disorder in a child or adolescent is based on 1 score (out of 17 scores, on a 2-hour NEPSY-II battery) below 2 SD, how many healthy children would have the disorder?

14.7%

Parental education 11 or fewer years?

31.3%!

Brooks et al., 2010

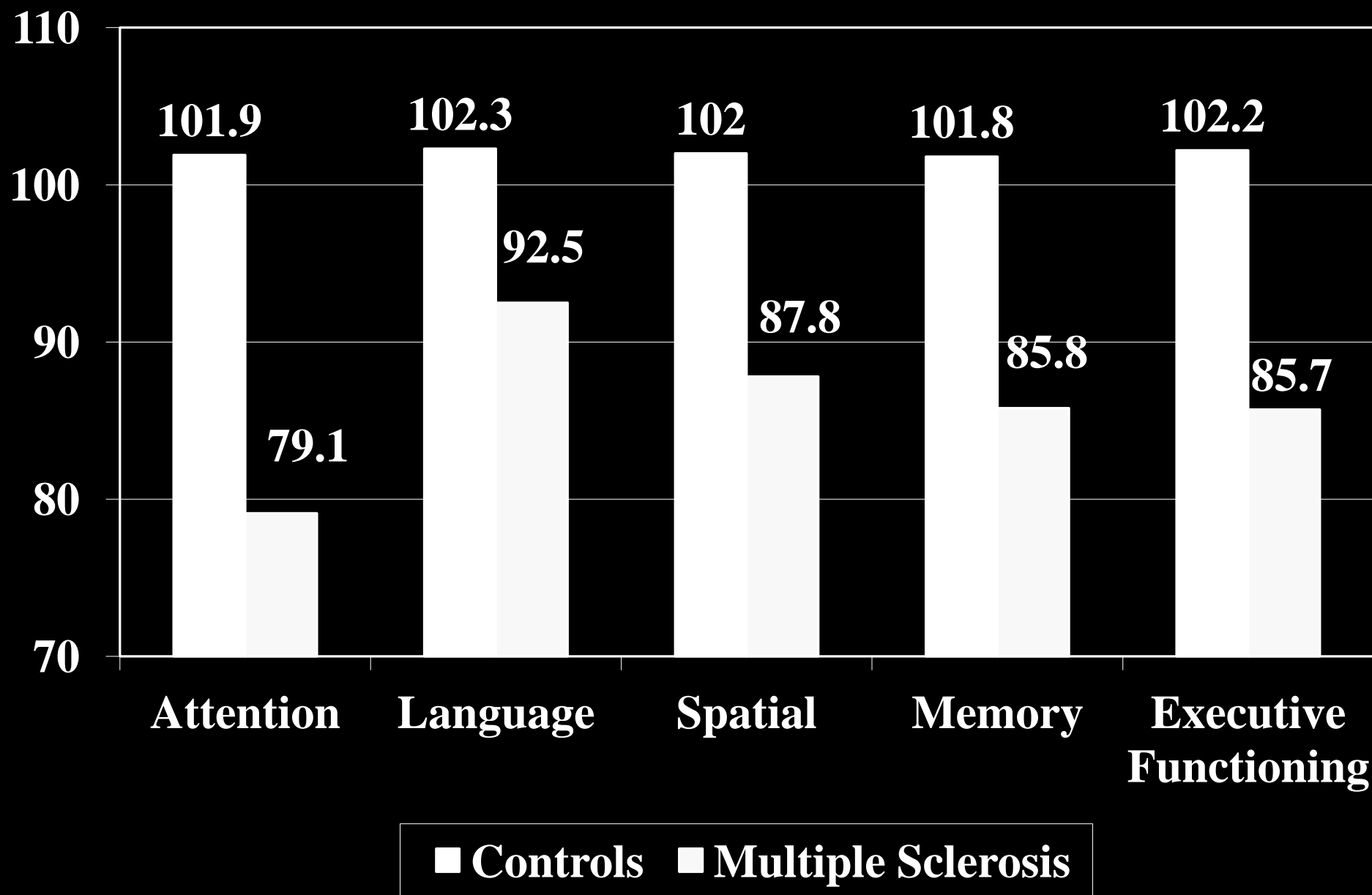




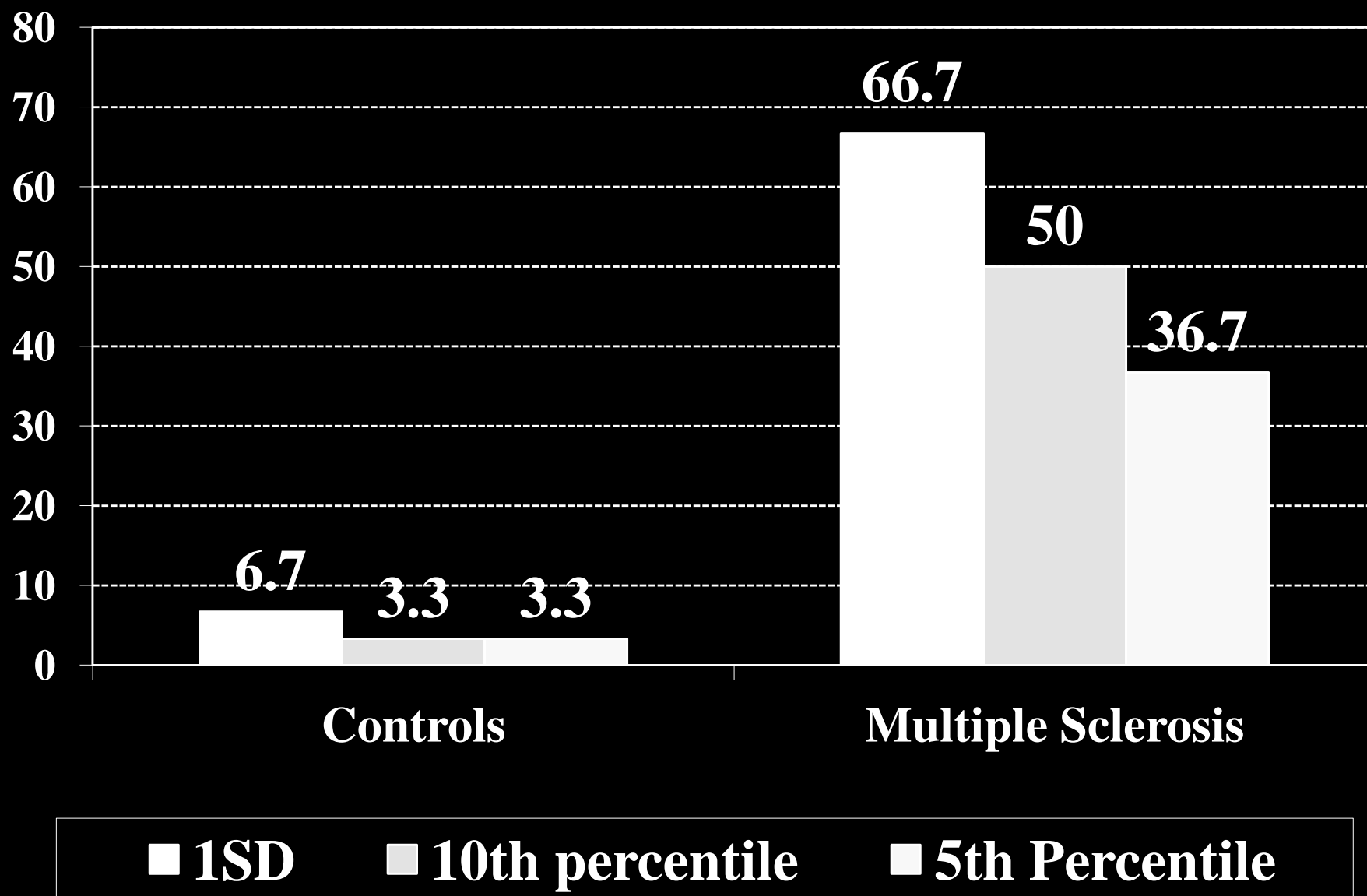
# Simple Application of Base Rates: Multiple Sclerosis

## **Participants**

- 30 patients with MS
- 30 healthy controls from the NAB standardization sample were individually matched on sex, age, education, and ethnicity
- Battery: Neuropsychological Assessment Battery (NAB): 5 Index Scores



# Percentage with 2 or More Low NAB Index Scores



# Back to Basics

Conceptualizing levels of cognitive impairment

# Levels of Cognitive Impairment

Mild Cognitive Diminishment

Mild Cognitive Impairment

Moderate Cognitive Impairment

Severe Cognitive Impairment

Profound Cognitive Impairment

# Mild Cognitive Diminishment

- This is not cognitive “impairment.”
- Instead, this represents a mild diminishment in cognitive functioning.
- It may or may not be identifiable using neuropsychological tests.
- It can, but does not always, have a mild adverse impact on a person’s social and/or occupational functioning.
- It may or may not be noticeable by others.

# Mild Cognitive Impairment

- Should be identifiable using neuropsychological tests.
- This impairment has a mild (sometimes moderate) adverse impact on a person's social and/or occupational functioning.

# Moderate Cognitive Impairment

- This level of cognitive impairment has a substantial impact on everyday functioning.
- This impairment should be noticeable to others in regards to the person's social and/or occupational functioning.



# Severe Cognitive Impairment

- The cognitive impairment has a substantial adverse impact on everyday functioning.
- This level of impairment would render the individual incapable of competitive employment.
- The person should not be driving a motor vehicle, and might have difficulty with activities of daily living.

# Profound Cognitive Impairment/ Severe Dementia

- The cognitive impairment would render the person in need of 24-hour supervision and assistance with daily activities, which he or she may receive at home, in a nursing home, or other institution.

Is all this really that important?

MCI / Prodromal Dementia

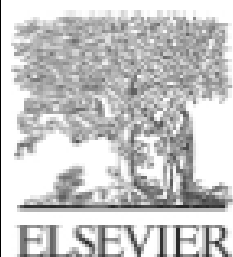
# Position Paper

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## © Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria

*Bruno Dubois\*, Howard H Feldman\*, Claudia Jacova, Steven T DeKosky, Pascale Barberger-Gateau, Jeffrey Cummings, André Delacourte, Douglas Galasko, Serge Gauthier, Gregory Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Yaakov Stern, Pieter J Visser, Philip Scheltens*

- Lancet Neurology, 2007



Alzheimer's & Dementia 7 (2011) 270–279

Alzheimer's  
&  
Dementia

# The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Marilyn S. Albert<sup>a,\*</sup>, Steven T. DeKosky<sup>b,c</sup>, Dennis Dickson<sup>d</sup>, Bruno Dubois<sup>e</sup>,  
Howard H. Feldman<sup>f</sup>, Nick C. Fox<sup>g</sup>, Anthony Gamst<sup>h</sup>, David M. Holtzman<sup>i,j</sup>, William J. Jagust<sup>k</sup>,  
Ronald C. Petersen<sup>l</sup>, Peter J. Snyder<sup>m,n</sup>, Maria C. Carrillo<sup>o</sup>, Bill Thies<sup>o</sup>, Creighton H. Phelps<sup>p</sup>

### *2.1.2. Impairment in one or more cognitive domains*

There should be evidence of lower performance in one or more cognitive domains that is greater than would be expected for the patient's age and educational background. If repeated assessments are available, then a decline in performance should be evident over time. This change can occur in a variety of cognitive domains, including memory, executive function, attention, language, and visuospatial skills. An impairment in episodic memory (i.e., the ability to learn and retain new information) is seen most commonly in MCI patients who subsequently progress to a diagnosis of AD dementia. (See the section on the cognitive characteristics later in the text for further details).

**\*Low scores in 1 or more Cognitive Domains**

**\*Low scores are 1 to 1.5 SDs below the mean**

### *2.2. Cognitive characteristics of MCI*

It is important to determine whether there is objective evidence of cognitive decline, and if so, the degree of this decline in the reports by the individual and/or an informant. Cognitive testing is optimal for objectively assessing the degree of cognitive impairment for an individual. Scores on cognitive tests for individuals with MCI are typically 1 to 1.5 standard deviations below the mean for their age and education matched peers on culturally appropriate normative data (i.e., for the impaired domain(s), when available). It is emphasized that these ranges are guidelines and not cutoff scores.

# MCI: Criteria for the Clinical and Cognitive Syndrome

- Concern regarding a change in cognitive functioning (patient or family)
- Impairment in one or more cognitive domains (1 to 1.5 SDs below the mean for age-education adjusted normative scores)
- Preservation of independence of functional abilities
- Not demented

# Potential Problem with Diagnostic Guidelines

- Greater than expected and poorly understood rates of:
  - False Positives
  - False Negatives



# Revert to Normal on Retesting

<u>Authors</u>	<u>Retest</u>	<u>Percentage</u>
Loewenstein et al., 2007	1 year	7.7%
Fischer et al., 2007	2.6 years	16.2%
Perri et al., 2007	2 years	17.2%
Fisk et al., 2003	5 years	31.2%
Alexopoulos et al., 2006	3.5 years	40%
Larrieu et al., 2002	2 years	41.4%
Kryscio et al., 2006	1.1 years	52.5%
Ganguli et al., 2004	4 years	55%

Were some misdiagnosed?

# Potential for misclassification of mild cognitive impairment: A study of memory scores on the Wechsler Memory Scale-III in healthy older adults

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BRIAN L. BROOKS,<sup>1</sup> GRANT L. IVERSON,<sup>1,2</sup> JAMES A. HOLDNACK,<sup>3</sup> AND  
HOWARD H. FELDMAN<sup>4</sup>

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<sup>2</sup>Department of Psychiatry, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia

<sup>3</sup>The Psychological Corporation, San Antonio, Texas

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(RECEIVED July 10, 2007; FINAL REVISION December 23, 2007; ACCEPTED January 1, 2008)

# WMS-III: “Accidental MCI”

- WMS-III Older Adults Study
- $N = 550$
- 8 Age-Corrected Scaled Scores
  - Logical Memory I & II
  - Verbal Paired Associates I & II
  - Faces I & II
  - Family Pictures I & II
- Base rates of low scores

Brooks, Iverson, Holdnack, & Feldman (2008)

## 5<sup>th</sup> Percentile Cut-Off (MCI)

- Total Sample = 26%

## WTAR-Demographics Predicted FSIQ

- Low Average = 43%
- High Average = 21%

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# **Minimizing Misdiagnosis: Psychometric Criteria for Possible or Probable Memory Impairment**

Brian L. Brooks<sup>a, b</sup> Grant L. Iverson<sup>b, c</sup> Howard H. Feldman<sup>c</sup> James A. Holdnack<sup>d</sup>

<sup>a</sup>Alberta Health Services and University of Calgary, Calgary, Alta., <sup>b</sup>British Columbia Mental Health & Addiction Services, Coquitlam, B.C., <sup>c</sup>University of British Columbia, Vancouver, B.C., Canada; <sup>d</sup>Pearson Assessment, San Antonio, Tex., USA

# 3 WMS-III Memory Subtests

- Logical Memory, Verbal Paired Associates, and Visual Reproduction
- 8 scores: Immediate, Delayed, Recognition
- 450 Healthy adults from the normative sample

# Criteria for MCI: $\leq 5^{\text{th}}$ Percentile

- Percentage of healthy older adults who met criteria:

30%

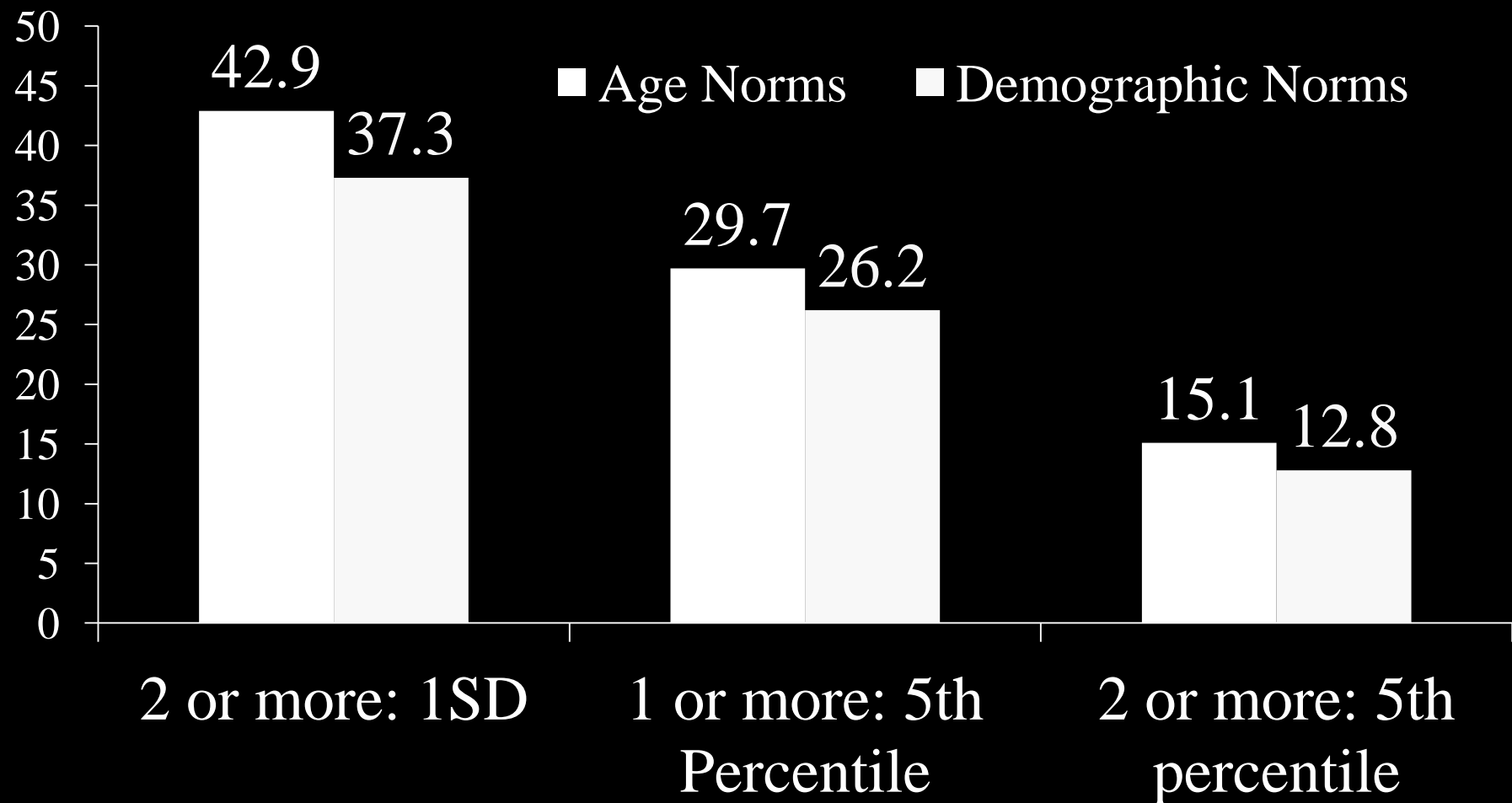
- However, having 3 or more scores at or below the  $5^{\text{th}}$  percentile occurred in only 5.1%



# Do Demographically-Adjusted Norms Correct the “Problem”?

Wechsler Memory Scale – Fourth Edition (WMS-IV)

**Prevalence (% of healthy adults) of low scores on the WMS-IV using age- and demographically-adjusted normative data: Cutoff  $< 1SD$  and  $\leq 5^{th}$  percentile.**



What if we stratify low scores by  
estimated premorbid  
intelligence?

Age versus Demographically-Adjusted Norms

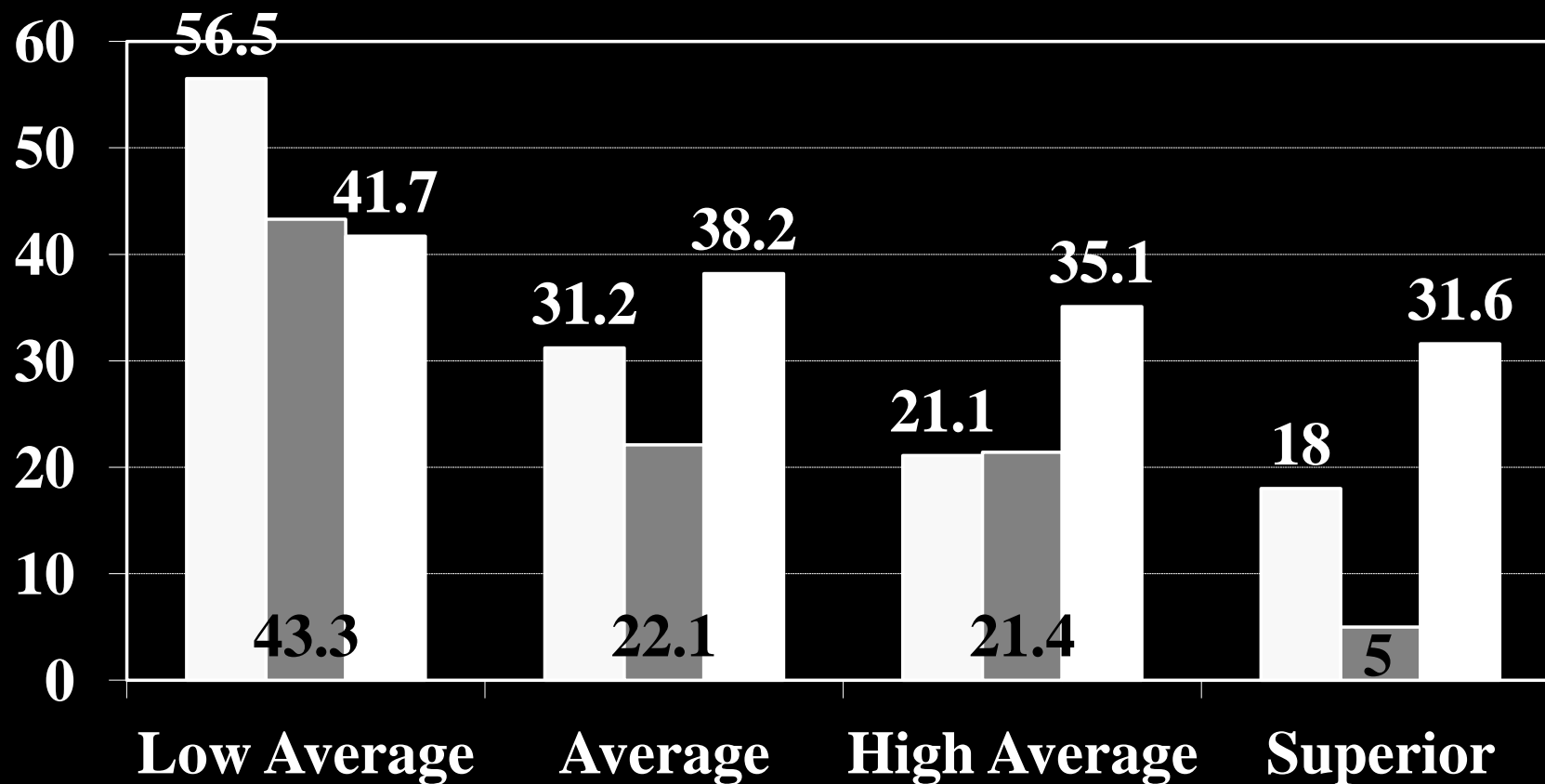
# Memory Batteries:

## Wechsler Memory Scale – Third Edition

### NAB Memory Module

- WMS-III: 4 tests, 8 scores (immediate and delayed)
- NAB: 4 tests, 10 scores (immediate and delayed)

## Percentage of healthy older adults with one or more low memory scores ( $\leq 5$ th percentile)



■ NAB Memory   ■ WMS-III Age   ■ WMS-III Demo

# Five psychometric principles for interpreting scores

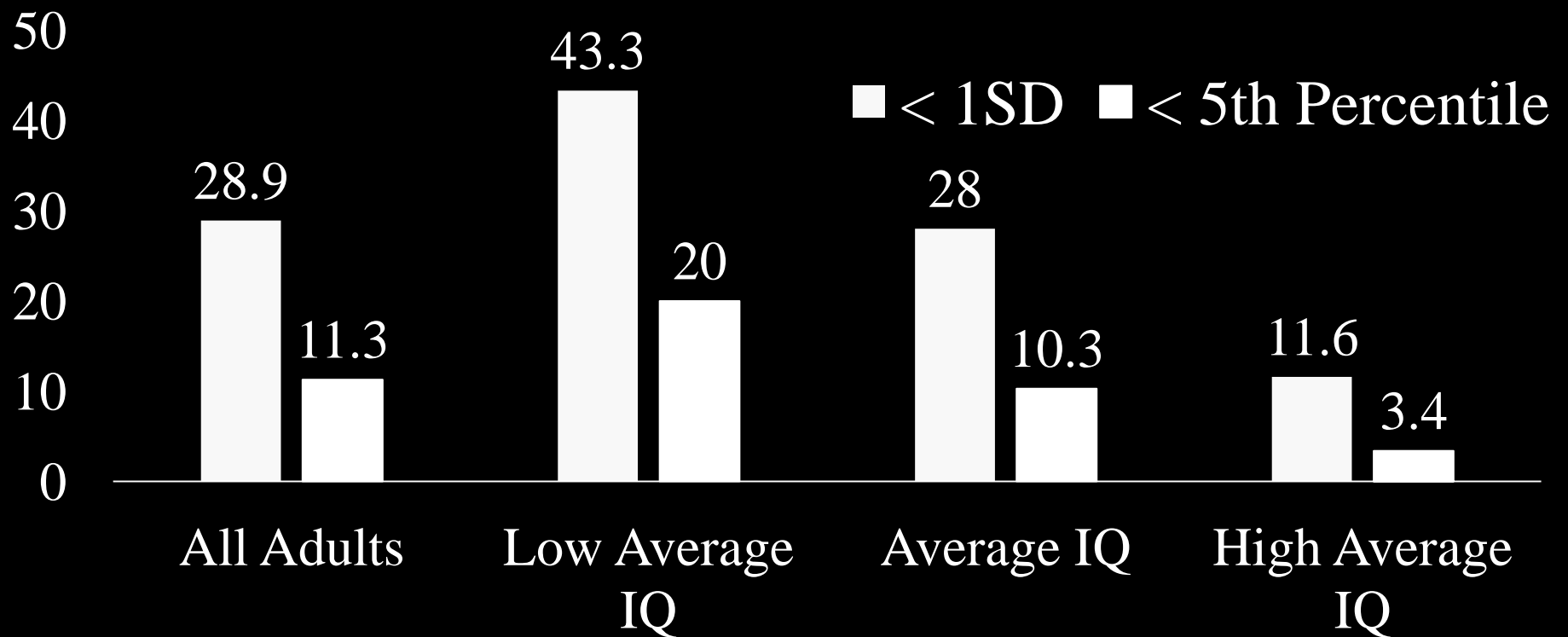
- Low scores are relatively common across all test batteries
- Low scores depend on where you set your cutoff score
- Low scores vary by number of tests administered
- Low scores vary by demographic characteristics of the examinee
- Low scores vary by level of intelligence.

# Intelligence

- The most sophisticated normative data is adjusted for sex, age, education, and ethnicity
- Good normative data is adjusted for sex, age, and education
- Many normative sets are adjusted for age only

Consider 4 WMS-IV Indexes: Auditory Memory,  
Visual Memory, Immediate Memory, Delayed  
Memory – 1 or more low scores

### ToPF-Demographics Estimated IQ Ranges





# Low Scores in Children by Years of Parental Education

(ages 7-16; 4 or more low scores out of 17,  
 $\leq 10^{\text{th}}$  Percentile, NEPSY-II)

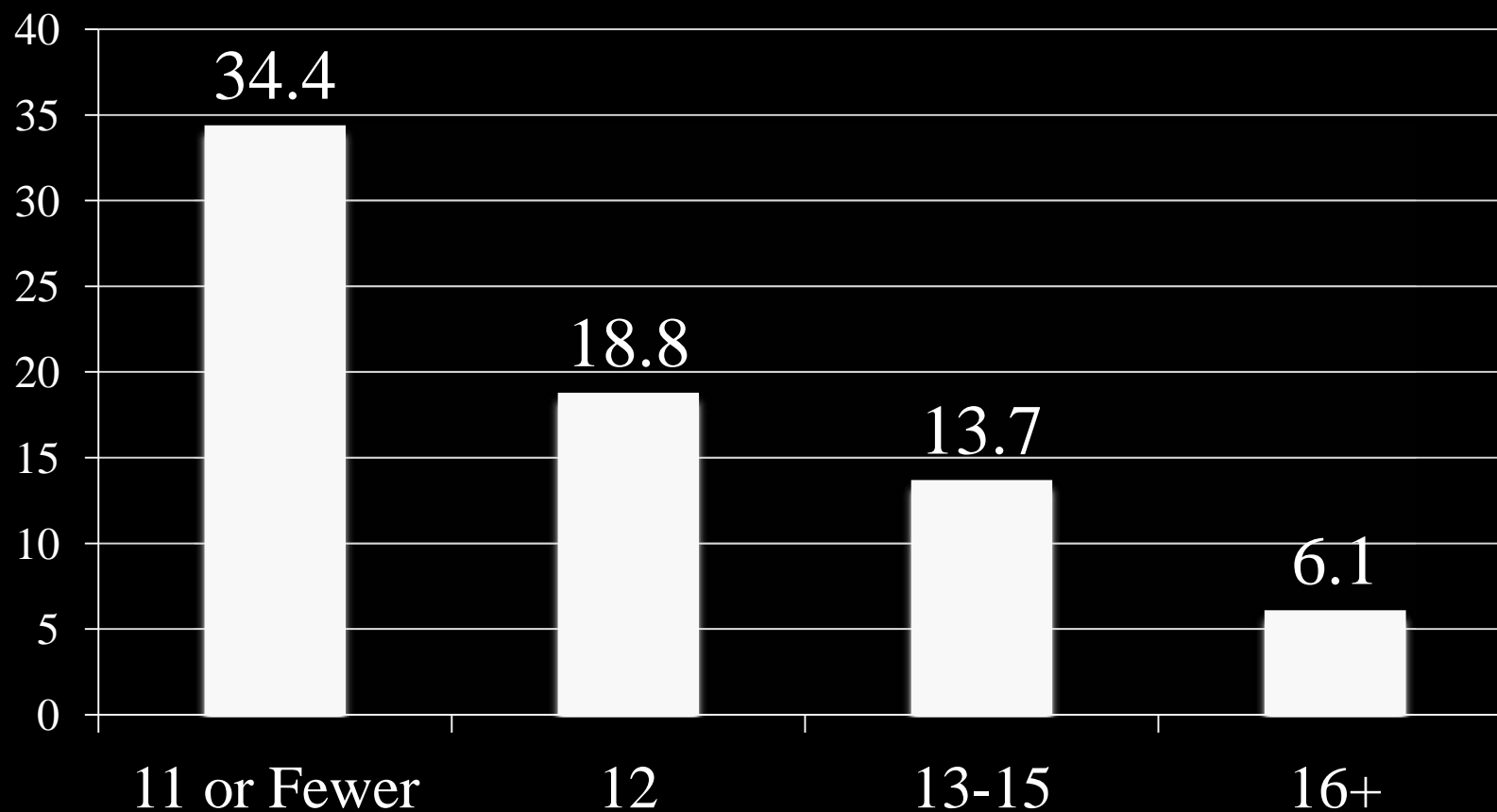
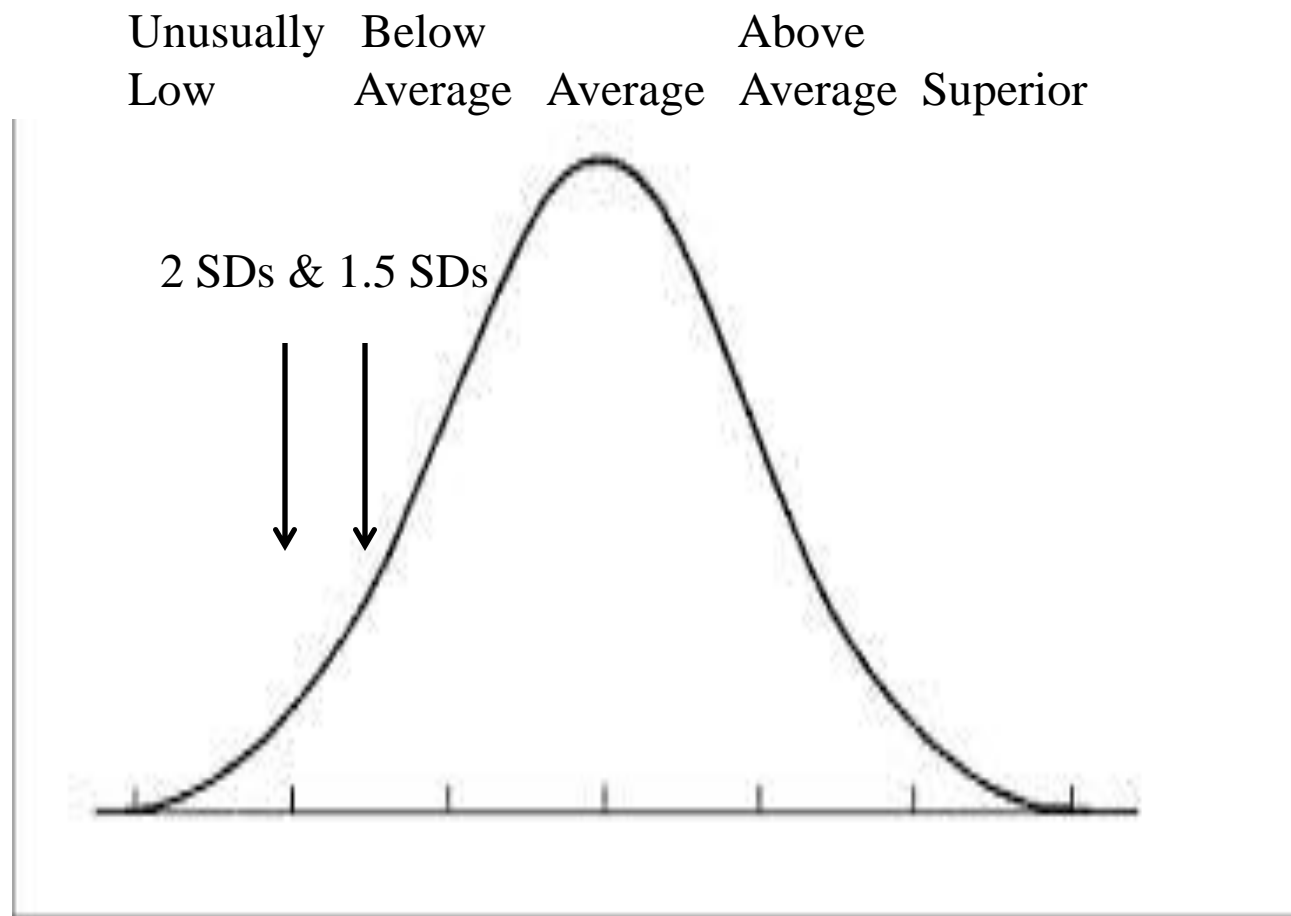


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Can multivariate base rates  
strengthen the foundation of  
clinical judgment?

Clinical Question: Does a pattern of performance occur at a specific point on the curve? (not a single test score)



# Published Base Rate Tables

## CHAPTER

# 2

## Understanding and Using Multivariate Base Rates with the WAIS–IV/WMS–IV

*Brian L. Brooks\*, Grant L. Iverson\*\* and  
James A. Holdnack\*\*\**

\*Alberta Children's Hospital and University of Calgary, Calgary, Alberta,  
Canada \*\*Harvard Medical School, Boston, Massachusetts, USA \*\*\*Pearson  
Assessment, San Antonio, Texas, USA

## WAIS-IV, WMS-IV, and ACS

### Advanced Clinical Interpretation

Edited by  
James A. Holdnack,  
Lisa Whipple Drozdick,  
Lawrence G. Weiss and Grant L. Iverson



# WAIS-IV/WMS-IV

Base rates of low scores

Battery: 20 Subtests

Domains: Processing Speed, Working Memory,  
Memory

# Impairment = 5<sup>th</sup> Percentile

- What percentage of healthy adults have one or more low subtest scores (out of 20)?

42.9%

- 3 or more? 17.3%

- 5 or more? 9.0%

- 7 or more? 5.2%

# Impairment < 1 SD (16<sup>th</sup> percentile)

- What percentage of healthy adults have one or more low subtest scores (out of 20)?

77.8%

- 3 or more? 51.6%
- 5 or more? 33.4%
- 9 or more? 14.4%



# Domain-Specific Base Rates

Refer to the online Appendix for Chapter 2  
(Multivariate Base Rates for WAIS-IV and WMS-IV)

# Processing Speed: WAIS-IV

(3 Test Scores: Coding, Symbol Search, Cancellation)

- Scaled Score = 7 or lower (Bell Curve Predicts: 16%)
  - 1 low score = 36.3%
  - 2 low scores = 17.4%
  - 3 low scores = 5.5%
- Scaled Score = 5 or lower (Bell Curve Predicts: 5%)
  - 1 low score = 12.8%
  - 2 low scores = 3.9%
  - 3 low scores = 0.7%

# Working Memory: WAIS-IV

(3 Tests: Digit Span, Arithmetic, Letter Number Sequencing)

## **Scaled Score = 7 or lower**

- 0 low scores = 68.2%
- 1 low score = 31.8%
- 2 low scores = 13.7%
- 3 low scores = 5.0%

- Bell Curve Predicts: 16%

## **Scaled Score = 5 or lower**

- 0 low scores = 90.2%
- 1 low score = 9.8%
- 2 low scores = 2.9%
- 3 low scores = 0.6%

- Bell Curve Predicts: 5%

# Considering 3 NAB Tests of Executive Functioning

(Mazes, Categories, and Word Generation)?

- How many healthy adults have 1 or more tests below 1SD (16<sup>th</sup> percentile)?

32.7%

- How many healthy adults have 1 or more tests below 2SD (2<sup>nd</sup> percentile)?

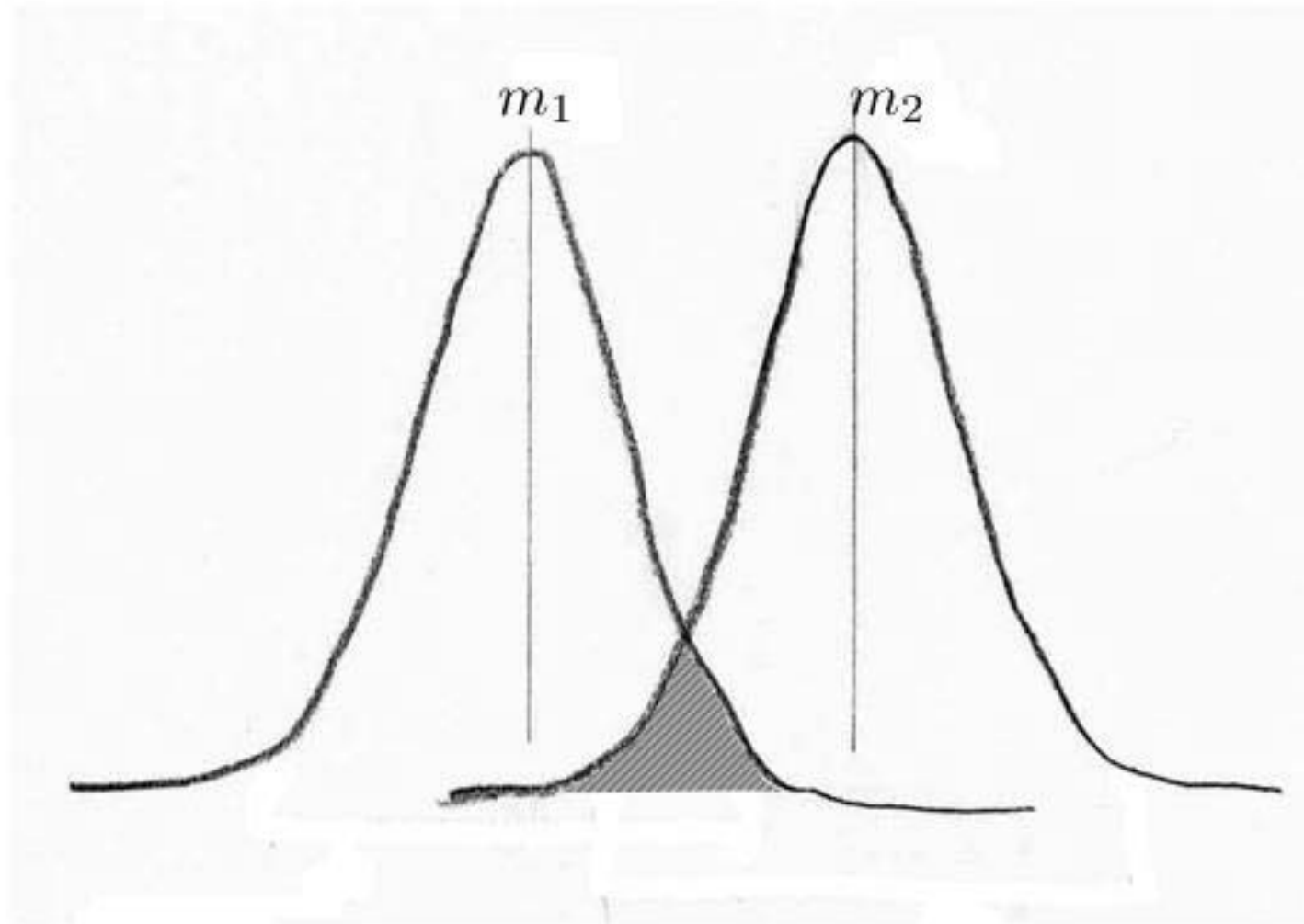
5.8%

Can we raise the bar for a low score?

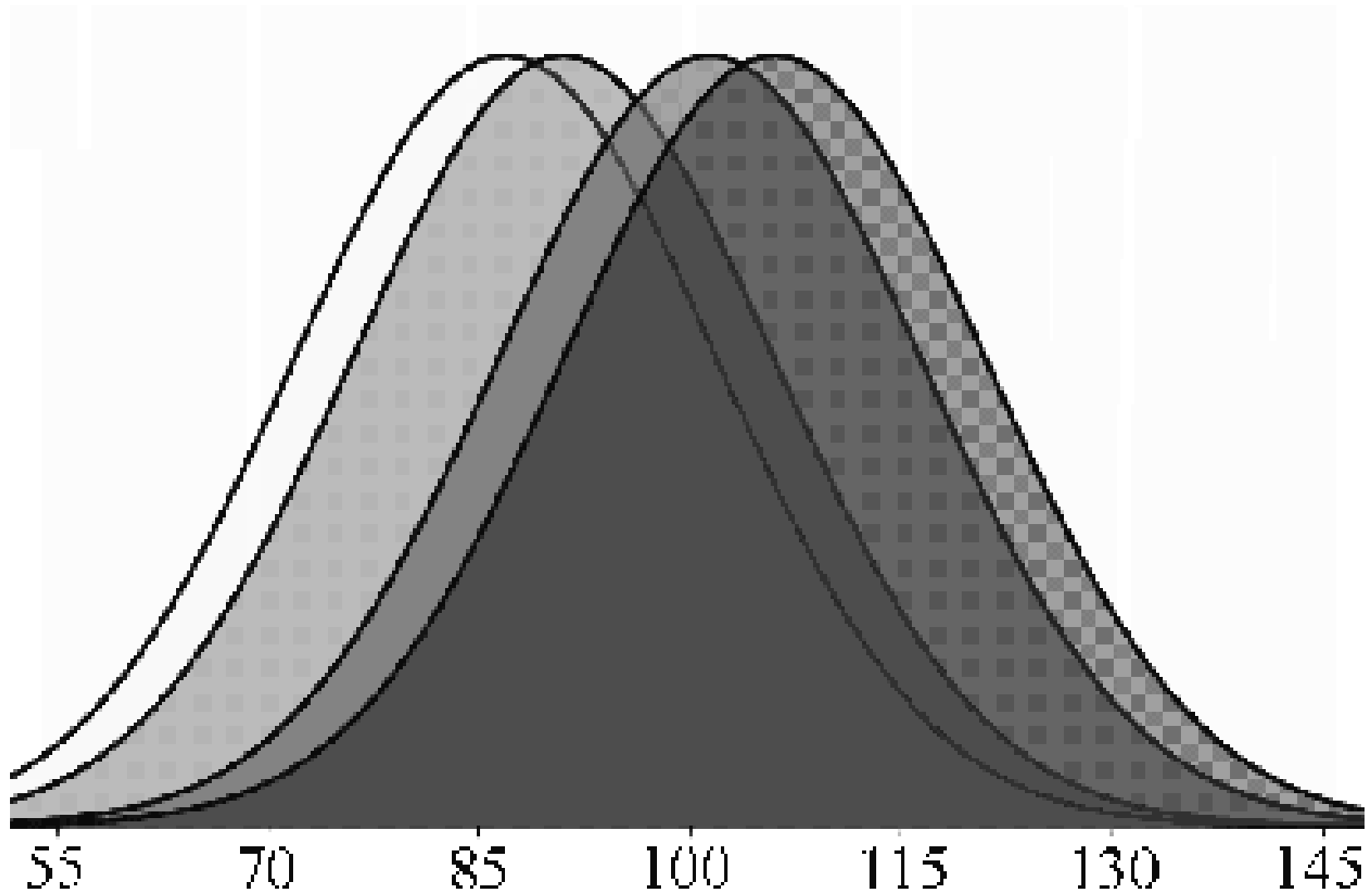
Heresy alert!

Heresy alert!

# Neuropsychologists' Dream of This (Normal vs. Clinical Groups)



# The Reality of Cognitive Assessment (Normal and Clinical Groups Overlap)



# Raising the bar for a low score



# Low Score = 25<sup>th</sup> Percentile

## WMS-IV: 4 Delayed Memory Subtests

- High Average Intelligence
  - 1 or more low scores = 37.4%
  - 3 or more low scores = 4.1%
- Average Intelligence
  - 1 or more low scores = 61.4%
  - 3 or more low scores = 15.4%

# Applying Domain-Specific Base Rates to a Patient with a Moderate TBI

# Moderate TBI

University Graduate: High Average IQ

- WAIS-IV Working Memory
  - Digit Span = 11
  - Arithmetic = 8
  - Letter Number Sequencing = 8
- Probability in Healthy Adults = 2.5%

# Moderate TBI

University Graduate: High Average IQ

- WAIS-IV Processing Speed
  - Coding = 8
  - Symbol Search = 10
  - Cancellation = 8

Probability in Healthy Adults = 12.7%

# Frontal Brain Tumor

(Average Premorbid IQ)

- 3 Executive Function Tests from the NAB
  - Mazes, Categories, and Word Generation
- Criteria for “Possible” Impairment (20% Base Rate)
  - 2 Scores  $\leq$  25<sup>th</sup> Percentile
  - 1 Score  $<$  10<sup>th</sup> Percentile
- Criteria for “Probable” Impairment (10% Base Rate)
  - 3 Scores  $\leq$  25<sup>th</sup> Percentile
  - 2 Scores  $<$  1 SD Percentile

# Child with ADHD and a Moderate TBI

- Children's Memory Scale
- 6 Index Scores: Learning, Verbal Immediate, Visual Immediate, Verbal Delayed, Verbal Delayed Recognition, and Visual Delayed
- 3 or More Scores  $< 1SD$ , Base Rate = 11.8%
- 2 or More Scores  $\leq 5^{\text{th}}$  Percentile, Base Rate = 8.6%

Brooks, Iverson, Sherman, and Holdnack, 2009

# Conclusions

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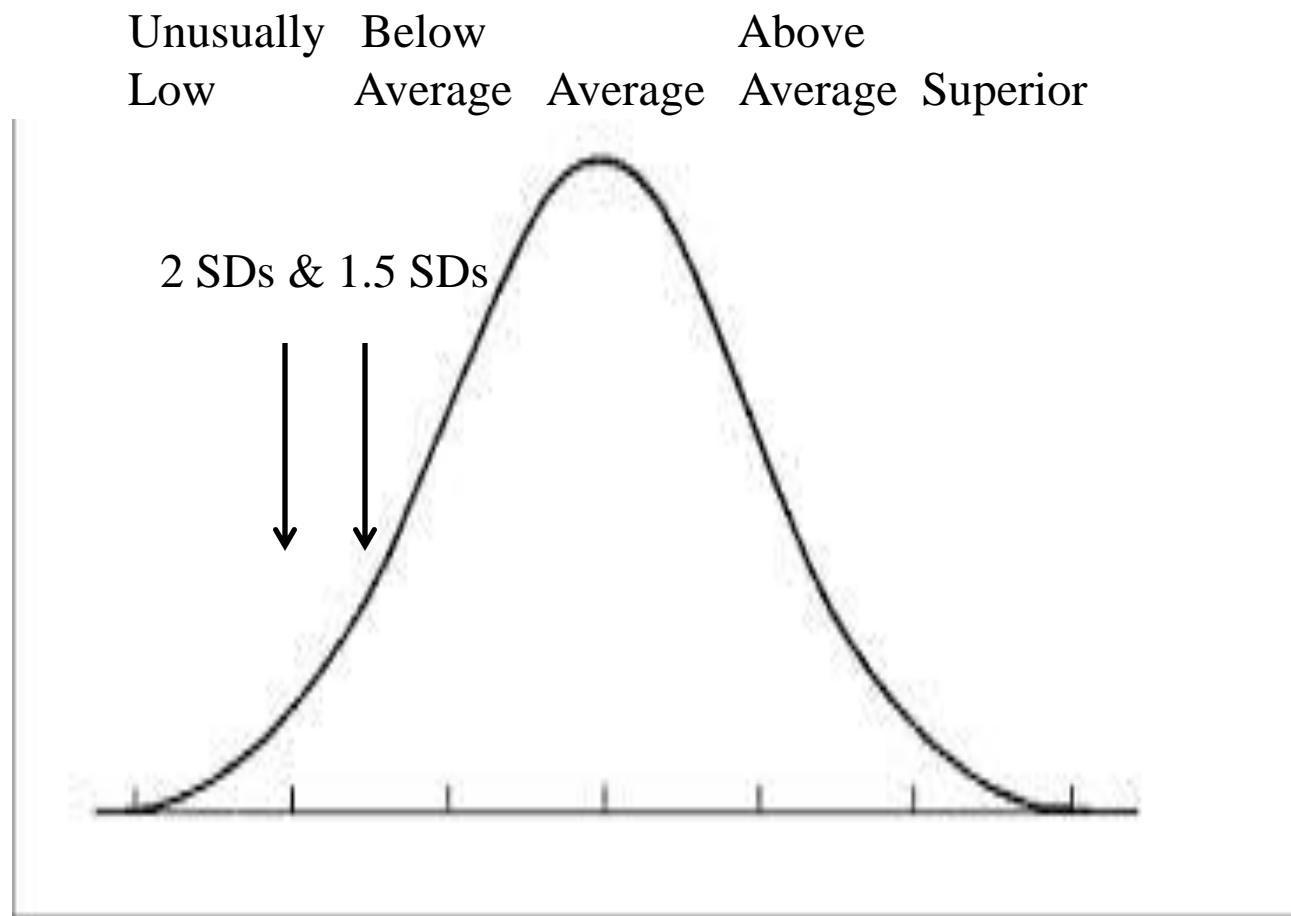
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- Low scores are relatively common across all test batteries
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- Low scores vary by demographic characteristics of the examinee
- Low scores vary by level of intelligence

# Base Rate Analyses Are Now Available For Many Batteries

- WAIS-III / WMS – III
- WMS-III
- WAIS-IV / WMS-IV
- WMS-IV
- WISC-IV
- Neuropsychological Assessment Battery (NAB)
- E-HRNB
- Children's Memory Scale
- NEPSY-II
- ImPACT®
- CNS-Vital Signs®
- ANAM TBI Mil

Clinical Question: Does a pattern of performance occur at a specific point on the curve? (not a single test score)



# Base Rates Help

Reduce False Positives in Low Functioning  
People

Reduce False Negatives (misses) in High  
Functioning People

Strengthen the Scientific Underpinnings of  
Clinical Judgment

Thank You

