

# COGNITIVE DECLINE IN PATIENTS WITH DIABETES

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Diapositiva preparata da GIUSEPPE PAOLISSO e ceduta alla Società Italiana di Diabetologia.  
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# Inquadramento e strategie terapeutiche nel diabete dell'anziano

**Napoli 24 ottobre 2017**

Il Dr. Giuseppe Paolisso dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- MSD
- Novo Nordisk
- Novartis
- Lilly

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## PSYCHOLOGIC TESTS APPLIED TO DIABETIC PATIENTS

W. R. MILES, Ph.D.; H. F. ROOT, M.D.

*Arch Intern Med.* 1922;30(6):767-777.

Diabetes is well known to exert an important influence on the central nervous system. Kraus<sup>1</sup> recently summarized the more common neurologic lesions, and the psychoses occasionally associated with diabetes have been the subject of numerous studies.

The diabetic patient, on his own part, complains of loss of memory and of poor ability to concentrate the attention. So far as we are aware, there are no objective data which either substantiate or contradict this clinical picture in reference to attention and memory. We have undertaken to gain some light as to the extent of the impairment if such exists, comparing diabetic patients as a group with controls who are of about the same mental status.

# COGNITIVE FUNCTION IN PATIENTS WITH DIABETES MELLITUS

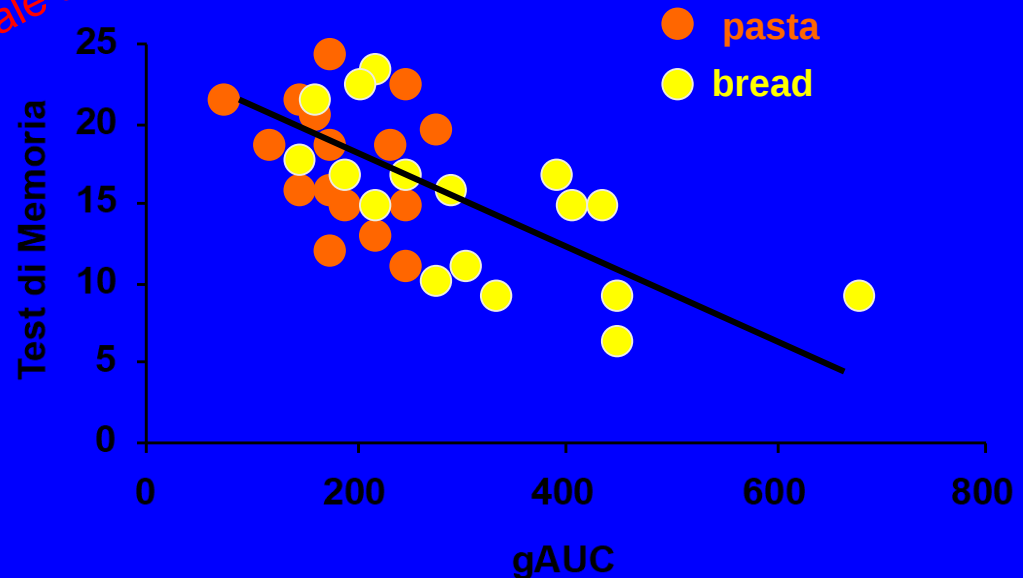
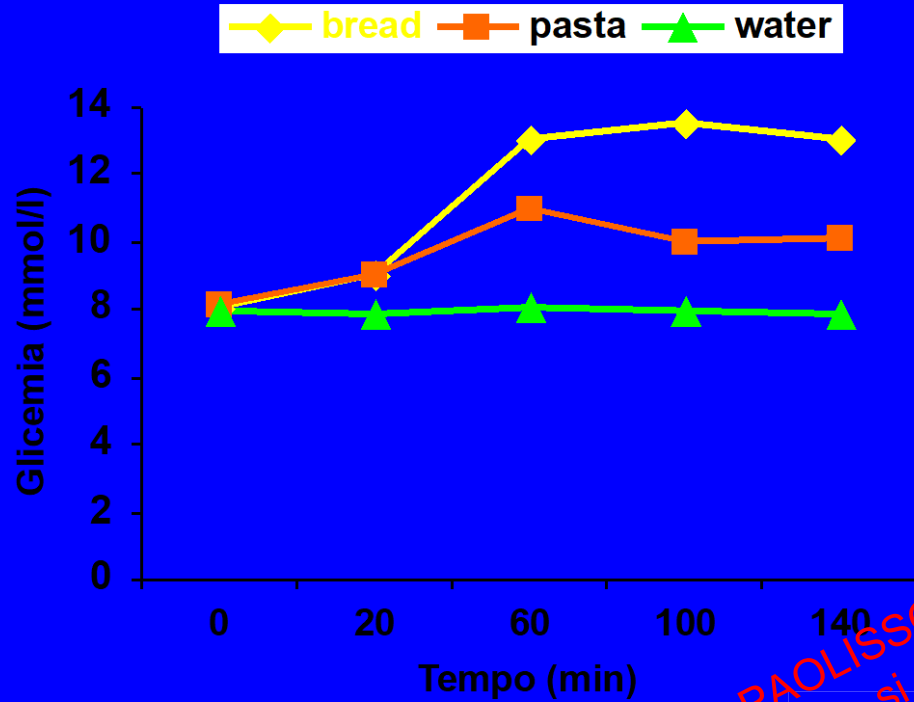
## Cognitive function in patients with diabetes mellitus: guidance for daily care

Paula S Koekkoek, L Jaap Kappelle, Esther van den Berg, Guy E H M Rutten, Geert Jan Biessels

Diabetes mellitus is associated with an increase in the risk of dementia and the proportion of patients who convert from mild cognitive impairment (MCI) to dementia. In addition to MCI and dementia, the stages of diabetes-associated cognitive dysfunction include subtle cognitive changes that are unlikely to affect activities of daily life or diabetes self-management. These diabetes-associated cognitive decrements have structural brain correlates detectable with brain MRI, but usually show little progression over time. Although cognitive decrements do not generally represent a pre-dementia stage in patients below the age of 60–65 years, in older individuals these subtle cognitive changes might represent the earliest stages of a dementia process. Acknowledgment of diabetes-associated cognitive decrements can help to improve understanding of patients' symptoms and guide management. Future challenges are to establish the importance of screening for cognitive impairment in people with diabetes, to identify those at increased risk of accelerated cognitive decline at an early stage, and to develop effective treatments.

|                                           | Type 1 diabetes                                                                                                                                                                                | Type 2 diabetes                                                                                                                                                                                                   |
|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pathophysiology                           | Autoimmune disorder with destruction of pancreatic cells leading to insulin deficiency                                                                                                         | Insensitivity to insulin and progressive $\beta$ -cell dysfunction                                                                                                                                                |
| Age of onset                              | Childhood or early adulthood                                                                                                                                                                   | Adulthood; prevalence increases with age                                                                                                                                                                          |
| Cognitive dysfunction                     | Subtle changes in all age groups, resulting in reduced intelligence, processing speed, and mental flexibility, usually with slow progression over time; link with dementia not established yet | Subtle changes in all age groups, resulting in reduced memory, processing speed, and executive function, usually slowly progressive over time; relative risk for mild cognitive impairment and dementia increased |
| MRI findings in patients without dementia | Reduced brain volume, as a result of altered brain development or atrophy; altered structural and functional connectivity                                                                      | Modest brain atrophy, increased burden of small vessel disease; disturbed structural and functional connectivity                                                                                                  |

# Post-prandial glucose and memory test



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# Blood Glucose, Diet-Based Glycemic Load and Cognitive Aging Among Dementia-Free Older Adults

*Journals of Gerontology: MEDICAL SCIENCES*

838 cognitively healthy adults  $\geq 50$  years (Mean age: 63 yrs)  
Follow up: 16 years

2015

Blood Glucose in Relation to Cognitive Performance and Change per Year of Age ( $n = 838$ )

| Blood glucose (contin)    | General Ability |      |       | Speed |      |       | Memory |      |       | Verbal |      |       | Spatial |      |       |
|---------------------------|-----------------|------|-------|-------|------|-------|--------|------|-------|--------|------|-------|---------|------|-------|
|                           | Est.            | SE   | p     | Est.  | SE   | p     | Est.   | SE   | p     | Est.   | SE   | p     | Est.    | SE   | P     |
| Model 1*                  |                 |      |       |       |      |       |        |      |       |        |      |       |         |      |       |
| Intercept                 | 51.50           | 0.35 | <.001 | 49.59 | 0.29 | <.001 | 51.48  | 0.34 | <.001 | 51.33  | 0.33 | <.001 | 50.32   | 0.32 | <.001 |
| Change                    | -3.45           | 0.18 | <.001 | -6.25 | 0.20 | <.001 | -2.93  | 0.23 | <.001 | -1.21  | 0.17 | <.001 | -4.26   | 0.19 | <.001 |
| Predictor                 | -0.70           | 0.38 | .060  | -1.03 | 0.31 | .001  | -0.82  | 0.35 | .020  | -0.42  | 0.35 | .220  | -0.59   | 0.35 | .100  |
| Change $\times$ predictor | -0.92           | 0.23 | <.001 | -0.80 | 0.20 | .002  | -0.30  | 0.31 | .330  | -0.64  | 0.22 | .004  | -0.73   | 0.25 | .004  |
| Model 2†                  |                 |      |       |       |      |       |        |      |       |        |      |       |         |      |       |
| Intercept                 | 51.69           | 0.35 | <.001 | 50.28 | 0.35 | <.001 | 51.50  | 0.40 | <.001 | 51.68  | 0.34 | <.001 | 50.89   | 0.37 | <.001 |
| Change                    | -2.64           | 0.40 | <.001 | -4.59 | 0.43 | <.001 | -1.17  | 0.52 | .024  | -0.94  | 0.36 | .009  | -2.97   | 0.46 | <.001 |
| Predictor                 | -0.15           | 0.34 | .354  | -0.82 | 0.30 | .006  | -0.33  | 0.33 | .326  | 0.00   | 0.31 | .993  | -0.41   | 0.33 | .219  |
| Change $\times$ predictor | -0.71           | 0.22 | .002  | -0.65 | 0.25 | .010  | -0.15  | 0.29 | .606  | -0.42  | 0.21 | .048  | -0.51   | 0.25 | .046  |
| Model 3‡                  |                 |      |       |       |      |       |        |      |       |        |      |       |         |      |       |
| Intercept                 | 51.72           | 0.35 | <.001 | 50.28 | 0.35 | <.001 | 51.48  | 0.40 | <.001 | 51.68  | 0.34 | <.001 | 50.84   | 0.37 | <.001 |
| Change                    | -2.56           | 0.40 | <.001 | -4.60 | 0.43 | <.001 | -1.13  | 0.52 | .040  | -0.92  | 0.36 | .010  | -3.04   | 0.45 | <.001 |
| Predictor                 | -0.15           | 0.36 | .670  | -0.82 | 0.32 | .010  | -0.26  | 0.34 | .440  | -0.03  | 0.33 | .930  | -0.39   | 0.35 | .260  |
| Change $\times$ predictor | -0.64           | 0.24 | .010  | -0.67 | 0.26 | .010  | -0.28  | 0.31 | .360  | -0.30  | 0.22 | .180  | -0.48   | 0.26 | .070  |

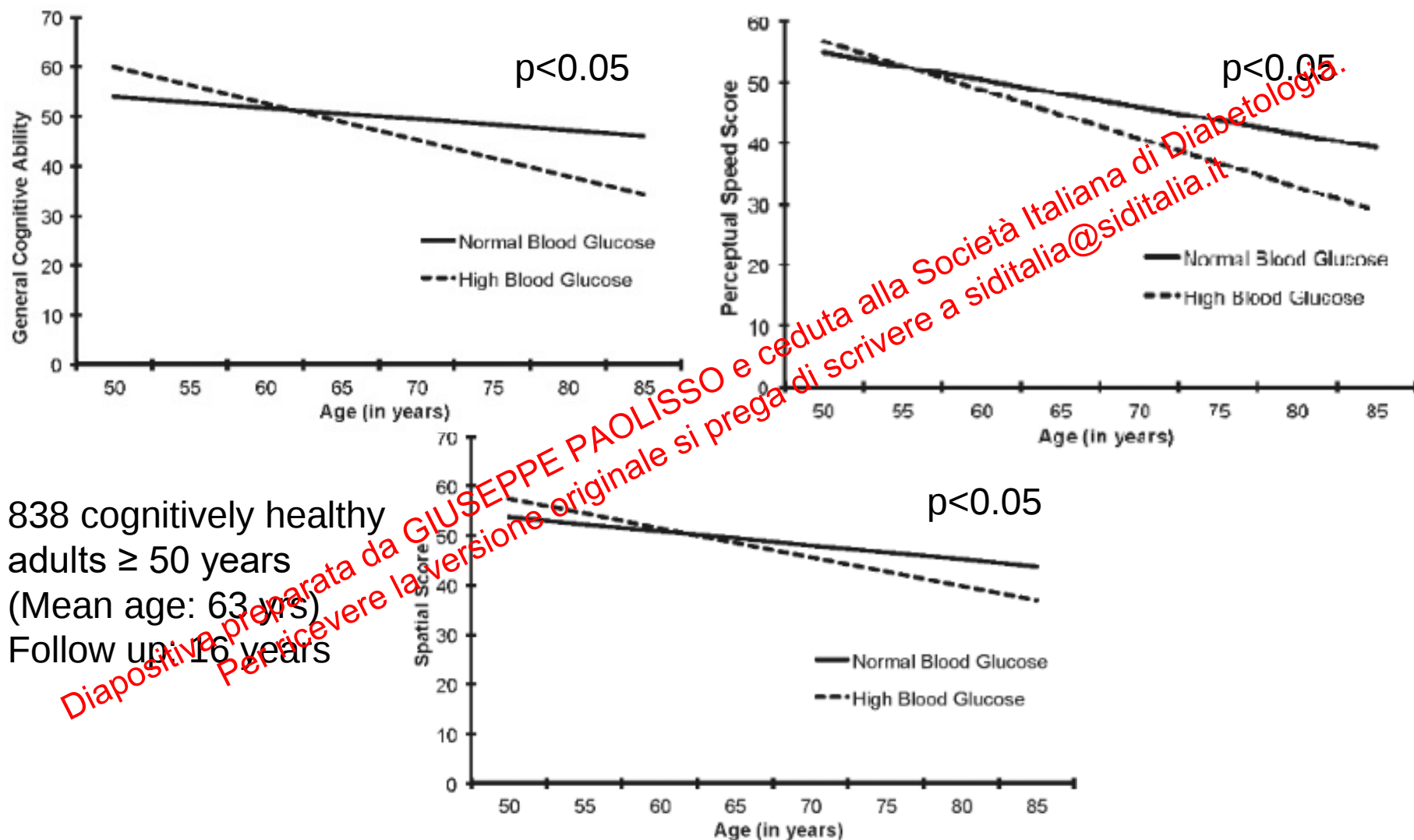
\*Unadjusted model.

†Results are adjusted for baseline age, gender, education, waist circumference, and depressive symptoms.

‡Results are adjusted for baseline age, gender, education, waist circumference, depressive symptoms, cardiovascular disease, and type II diabetes.

# Blood Glucose, Diet-Based Glycemic Load and Cognitive Aging Among Dementia-Free Older Adults

Journals of Gerontology: MEDICAL SCIENCES 2015



838 cognitively healthy  
adults  $\geq 50$  years  
(Mean age: 63 yrs)  
Follow up: 16 years

<sup>†</sup>Results are adjusted for baseline age, gender, education, waist circumference, depressive symptoms, cardiovascular disease, and type II diabetes.

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838 cognitively healthy adults  $\geq 50$  years (Mean age: 63 yrs)

Follow up: 16 years

## Diet-Based Glycemic Load in Relation to Cognitive Performance

|           | General Ability |      |       | Speed of Processing |      |       | Memory |      |       | Executive Function |      |       | P |
|-----------|-----------------|------|-------|---------------------|------|-------|--------|------|-------|--------------------|------|-------|---|
|           | Est.            | SE   | p     | Est.                | SE   | p     | Est.   | SE   | p     | Est.               | SE   | p     |   |
| Model 1*  |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Intercept | 50.01           | 0.30 |       | 49.62               | 0.38 | <.001 | 50.93  | 0.39 | <.001 | 50.26              | 0.42 | <.001 |   |
| Change    | -3.57           | 0.44 | <.001 | -4.11               | 0.22 | <.001 | -1.04  | 0.42 | .014  | -2.85              | 0.53 | <.001 |   |
| Predictor |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Change    |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Model 2†  |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Intercept | 50.01           | 0.30 |       | 49.62               | 0.38 | <.001 | 50.93  | 0.39 | <.001 | 50.26              | 0.42 | <.001 |   |
| Change    | -3.57           | 0.44 | <.001 | -4.11               | 0.22 | <.001 | -1.04  | 0.42 | .014  | -2.85              | 0.53 | <.001 |   |
| Predictor |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Change    |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Model 3‡  |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Intercept | 50.01           | 0.30 |       | 49.62               | 0.38 | <.001 | 50.93  | 0.39 | <.001 | 50.26              | 0.42 | <.001 |   |
| Change    | -3.57           | 0.44 | <.001 | -4.11               | 0.22 | <.001 | -1.04  | 0.42 | .014  | -2.85              | 0.53 | <.001 |   |
| Predictor |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Change    |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Model 4§  |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Intercept | 50.01           | 0.30 |       | 49.62               | 0.38 | <.001 | 50.93  | 0.39 | <.001 | 50.26              | 0.42 | <.001 |   |
| Change    | -3.57           | 0.44 | <.001 | -4.11               | 0.22 | <.001 | -1.04  | 0.42 | .014  | -2.85              | 0.53 | <.001 |   |
| Predictor |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |
| Change    |                 |      |       |                     |      |       |        |      |       |                    |      |       |   |

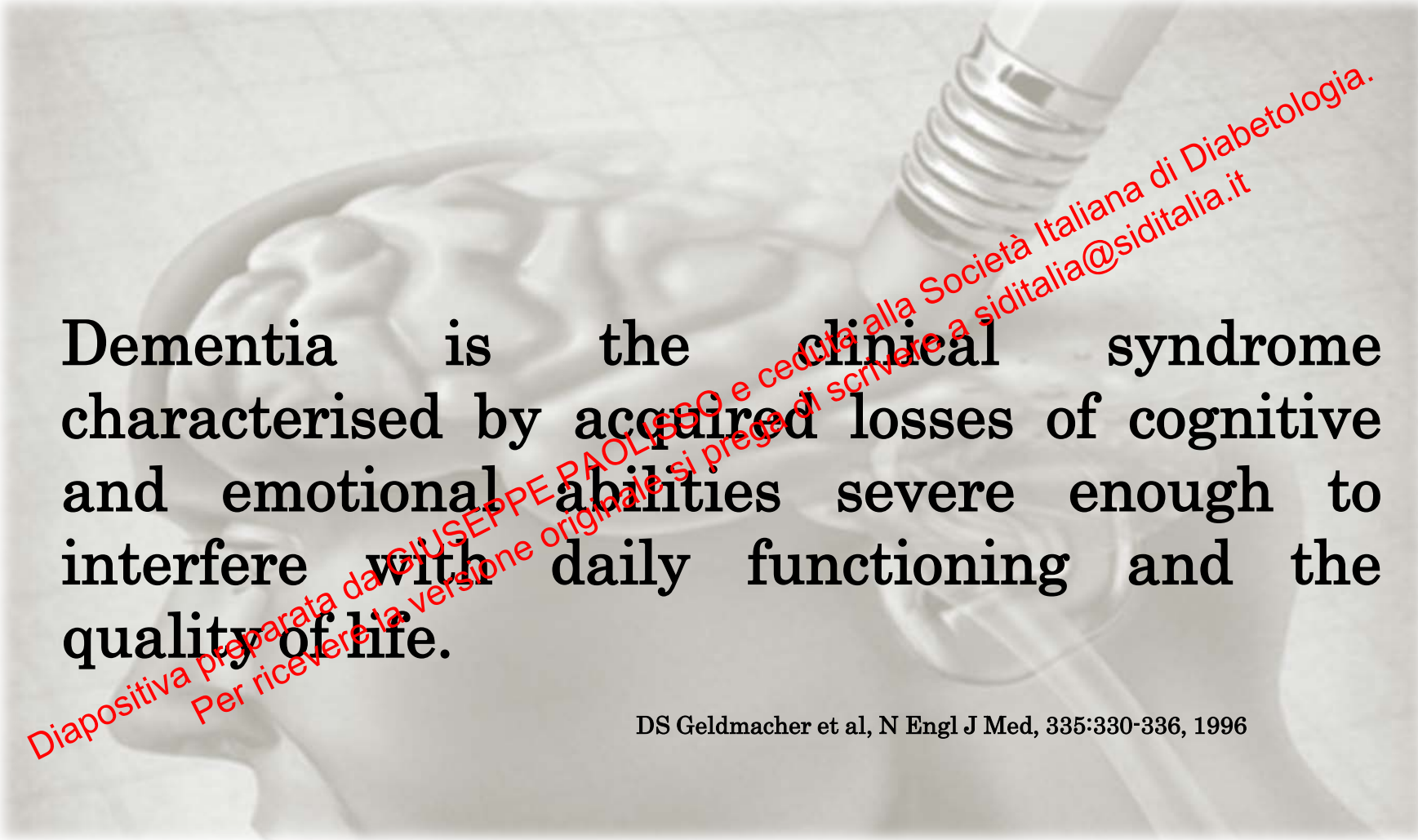
\*Unadjusted model.

†Results are adjusted for baseline age, gender, education, waist circumference, and depressive symptoms.

‡Results are adjusted for baseline age, gender, education, waist circumference, depressive symptoms, cardiovascular disease and type II diabetes.

**Diet based glycemic load over aging is a predictor of poorer cognitive performance**

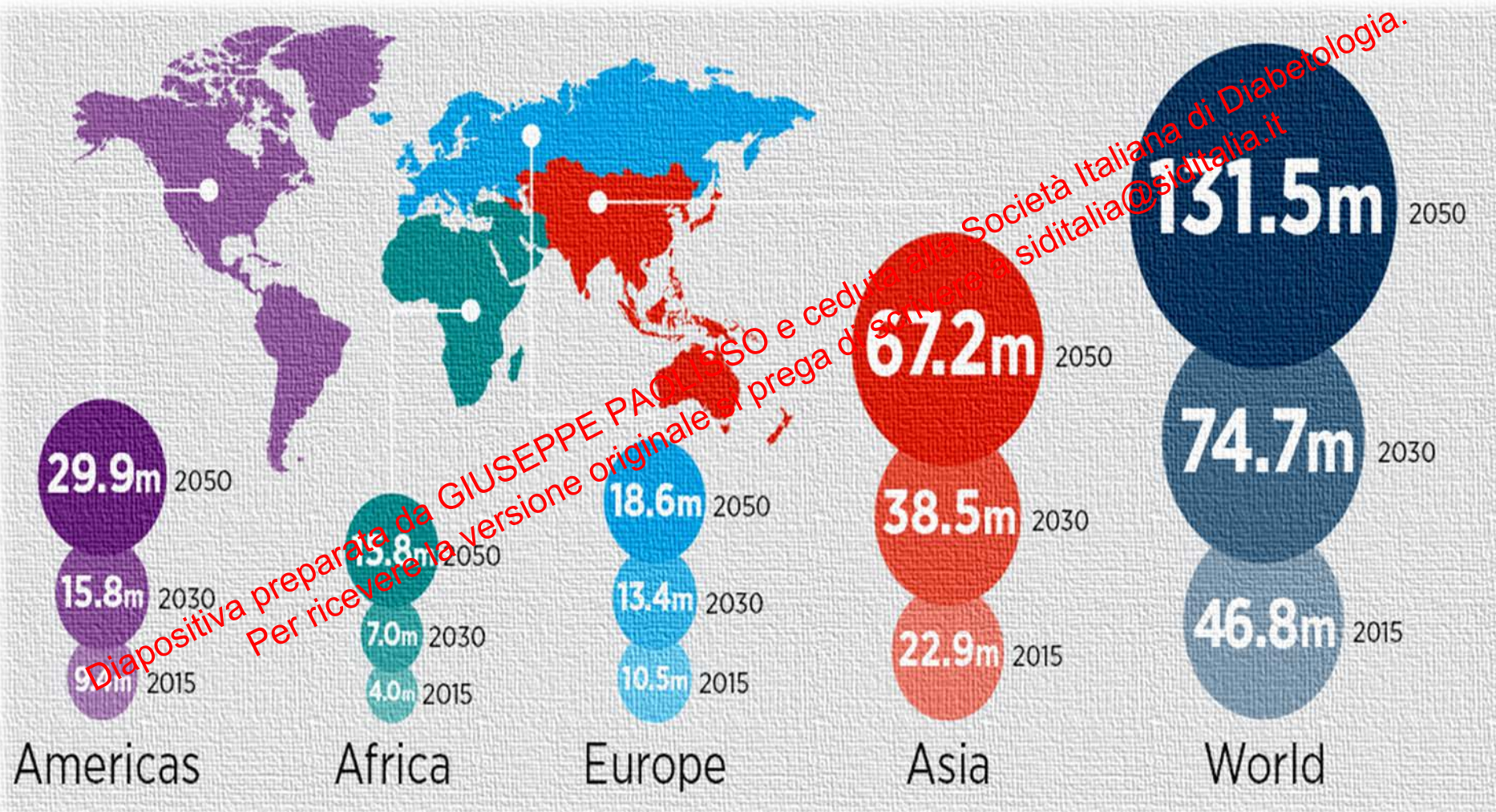
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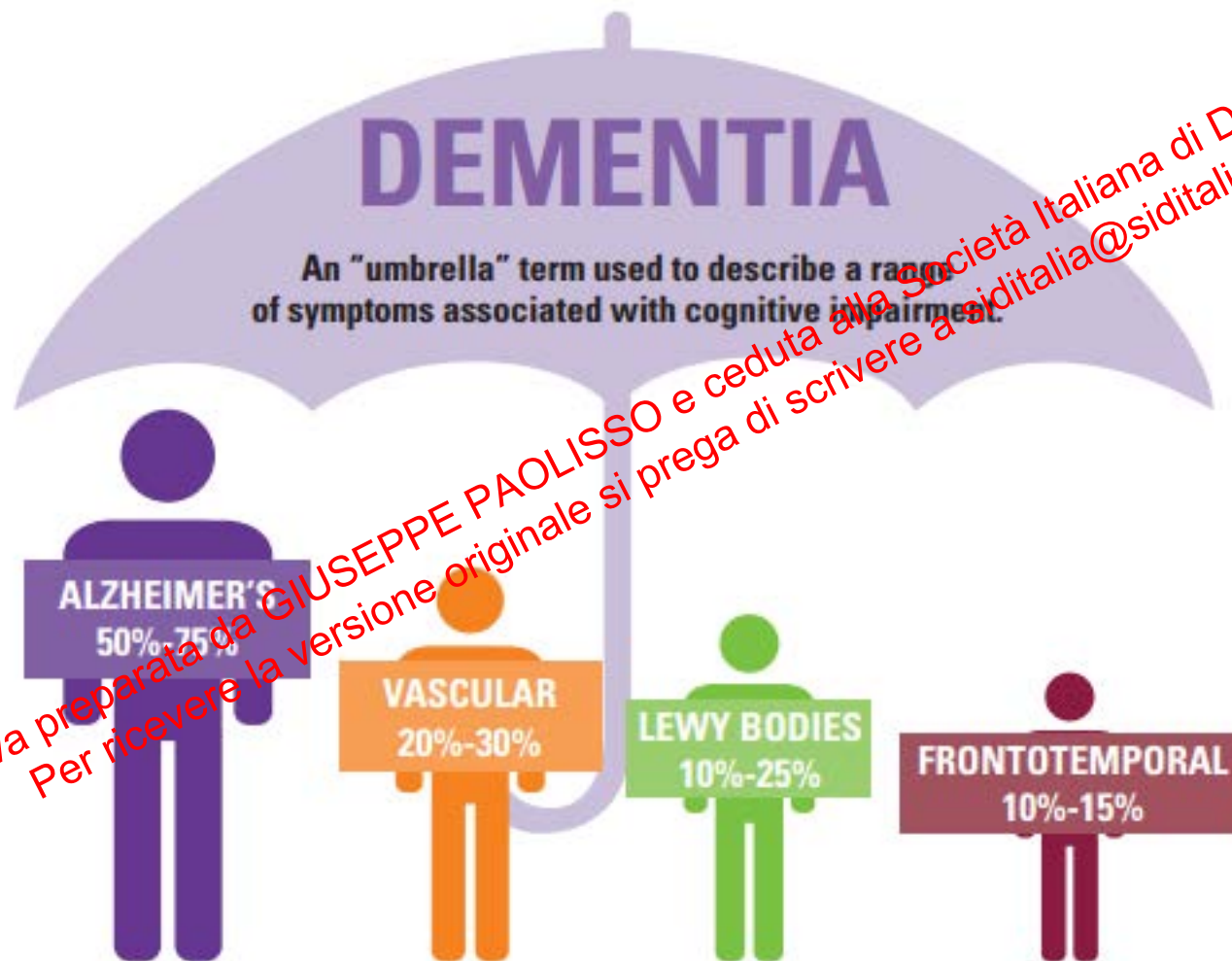
Dementia is the clinical syndrome characterised by acquired losses of cognitive and emotional abilities severe enough to interfere with daily functioning and the quality of life.

DS Geldmacher et al, N Engl J Med, 335:330-336, 1996

# PEOPLE LIVING WITH DEMENTIA AROUND THE WORLD



# COMMON FORMS OF DEMENTIA



An "umbrella" term used to describe a range of symptoms associated with cognitive impairment.

ALZHEIMER'S  
50%-75%

VASCULAR  
20%-30%

LEWY BODIES  
10%-25%

FRONTOTEMPORAL  
10%-15%

MIXED DEMENTIA = >1 NEUROPATHOLOGY - PREVALENCE UNKNOWN



alzheimer's association®

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# Major vs Mild Neurocognitive Disorders (DSM-V)

## Major Neurocognitive Disorder (Dementia)



- ❖ Significant cognitive decline
- ❖ Loss of independence

## Mild Neurocognitive Disorder (MCI)

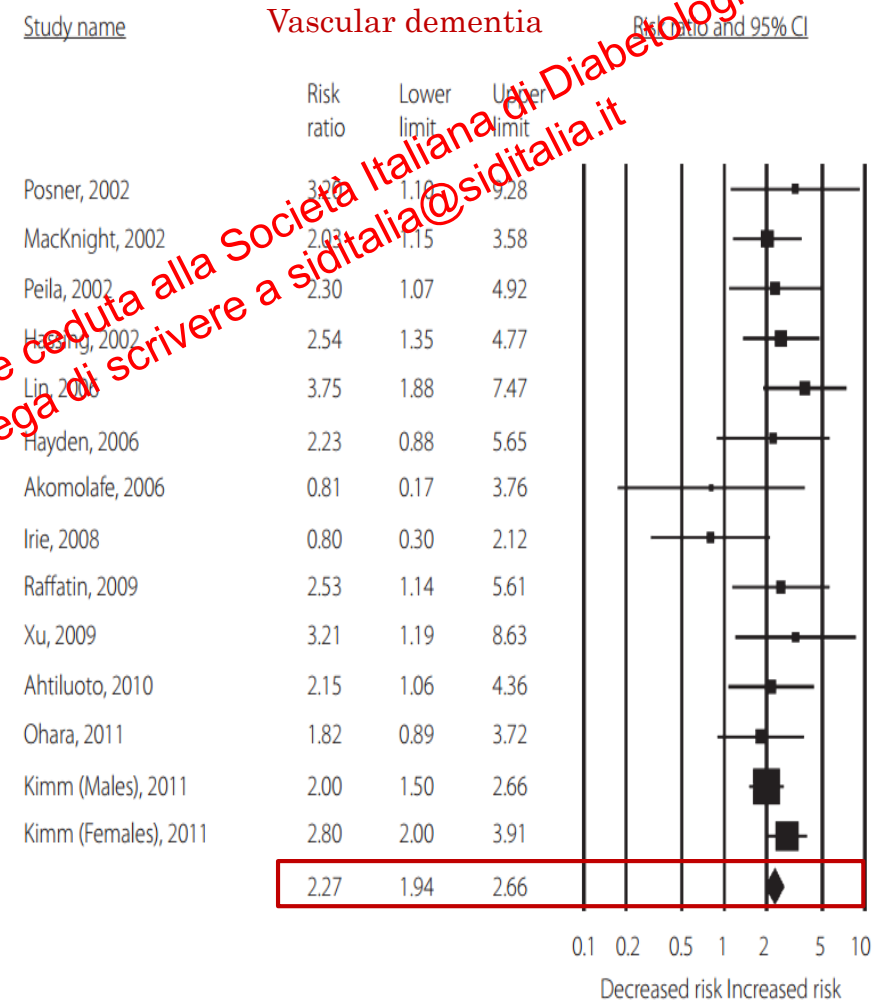
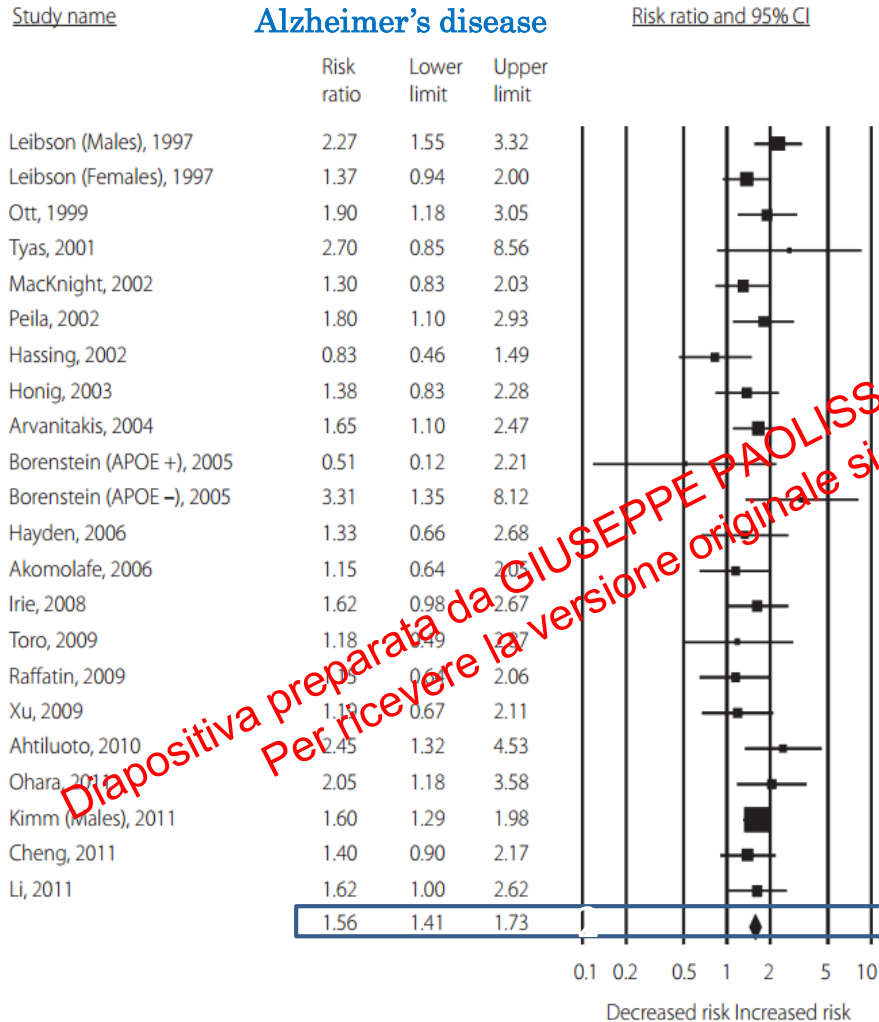


- ❖ Modest cognitive decline
- ❖ Preservation of independence

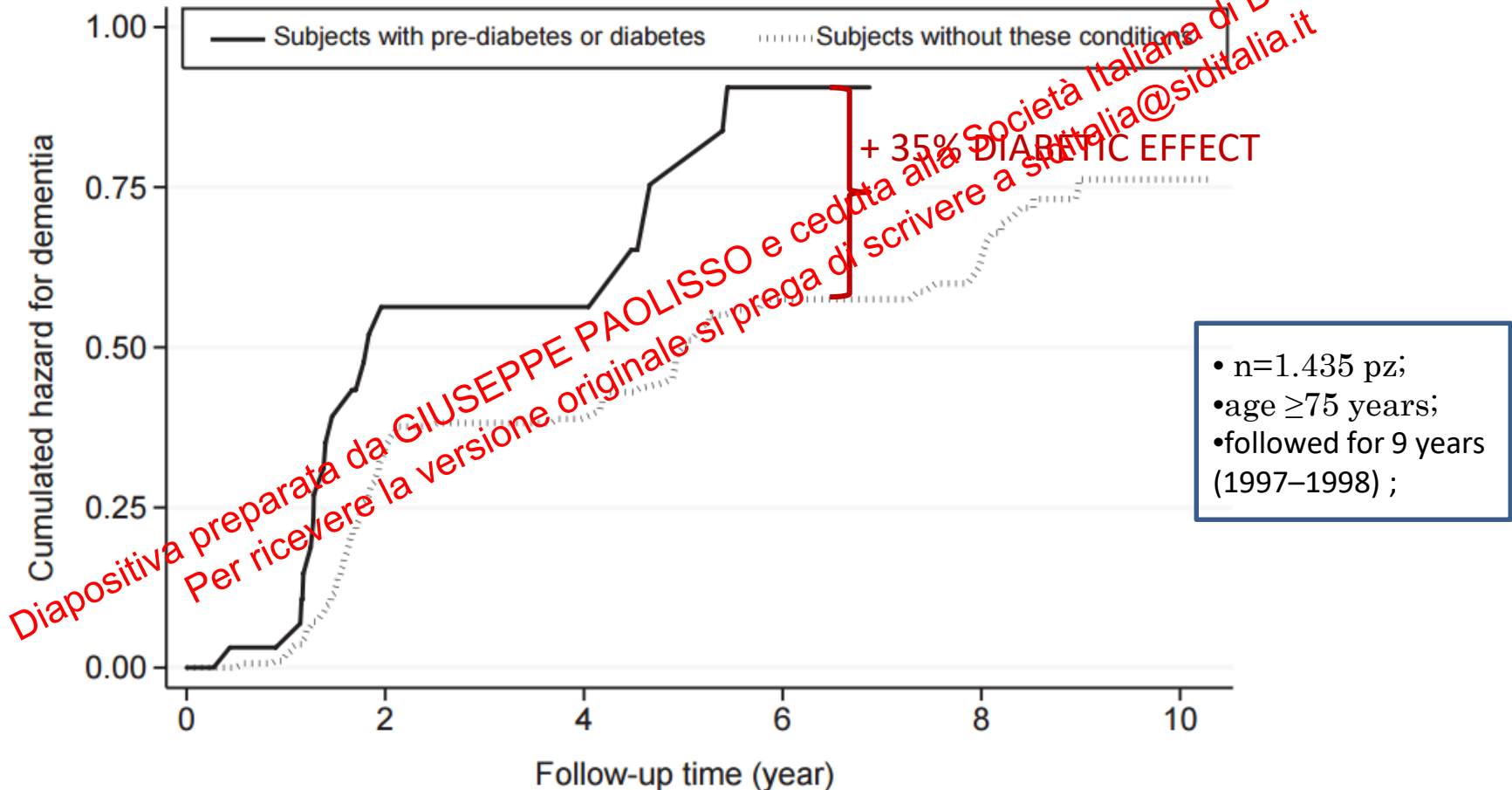
### Cognitive domains:

- ✓ Complex attention
- ✓ Executive function
- ✓ Learning and memory
- ✓ Language
- ✓ Perceptual motor
- ✓ Social cognition

# DIABETES AND RISK OF DEMENTIA: A META-ANALYSIS OF PROSPECTIVE OBSERVATIONAL STUDIES



# ACCELERATE PROGRESSION FROM MILD COGNITIVE IMPAIREMENT (MCI) TO DEMENTIA IN PEOPLE WITH DIABETES



Adjusted for age, sex, and education

# RELATIONSHIPS BETWEEN DAILY ACUTE GLUCOSE FLUCTUATIONS AND COGNITIVE PERFORMANCE AMONG AGED TYPE 2 DIABETICS

Linear multivariate analyses with MMSE and Composite score as dependent variable

|                   | MMSE  |      |       |        |      | Composite Score |       |       |        |      |
|-------------------|-------|------|-------|--------|------|-----------------|-------|-------|--------|------|
|                   | B     | SE   | Beta  | t      | p    | B               | SE    | Beta  | t      | p    |
| Age               | -.013 | .005 | -.140 | -2.73  | .008 | -.021           | .014  | -.122 | -1.52  | .131 |
| Gender            | .190  | .127 | .080  | 1.49   | .139 | .774            | .357  | .182  | 2.16   | .033 |
| BMI               | -.059 | .020 | -.160 | -2.96  | .004 | -.025           | .056  | -.038 | -.454  | .651 |
| WHR               | -1.23 | .789 | -.083 | -1.56  | .121 | -2.69           | 2.217 | -.102 | -1.216 | .227 |
| Drug intake       | -.056 | .122 | -.025 | -.463  | .644 | -.176           | .342  | -.041 | -.513  | .609 |
| Physical activity | .005  | .065 | .014  | .075   | .940 | .212            | .182  | .093  | 1.161  | .248 |
| MAGE              | -.037 | .004 | -.635 | -10.31 | .000 | -.050           | .010  | -.472 | -4.88  | .000 |
| PAS               | .065  | .003 | -.071 | -1.424 | .158 | -.004           | .010  | -.031 | -.394  | .695 |
| PAD               | .008  | .007 | -.058 | -1.168 | .246 | -.017           | .019  | -.067 | -.858  | .393 |
| HbA1c             | -.037 | .080 | -.027 | -.458  | .648 | -.084           | .225  | -.034 | -.372  | .711 |
| PP glucose        | -.006 | .002 | -.167 | -2.581 | .011 | -.028           | .009  | -.205 | -2.37  | .025 |
| Glucose           | -.003 | .003 | -.078 | -1.302 | .196 | .010            | .007  | .129  | 1.375  | .172 |

For MMSE : R2= 0.77

For Composite Score : R2= 0.44

# Risk of Incident Dementia Associated with Average Glucose Level over the Preceding 5 Years among Participants without Diabetes and Those with Diabetes.

| Average Glucose Level                | Hazard Ratio for Dementia (95% CI) |
|--------------------------------------|------------------------------------|
| <b>Participants without diabetes</b> |                                    |
| 95 mg/dl                             | 0.86 (0.77–0.97)                   |
| 100 mg/dl                            | 1.00                               |
| 105 mg/dl                            | 1.10 (1.03–1.17)                   |
| 110 mg/dl                            | 1.15 (1.05–1.27)                   |
| 115 mg/dl                            | 1.18 (1.04–1.33)                   |
| P value                              | 0.00                               |
| <b>Participants with diabetes</b>    |                                    |
| 150 mg/dl                            | 1.10 (0.92–1.30)                   |
| 160 mg/dl                            | 1.00                               |
| 170 mg/dl                            | 1.01 (0.92–1.12)                   |
| 180 mg/dl                            | 1.15 (0.98–1.34)                   |
| 190 mg/dl                            | 1.40 (1.12–1.76)                   |
| P value                              | 0.002                              |

Estimates were adjusted for more confounders

N= 35, glu

Higher dementia diabetes

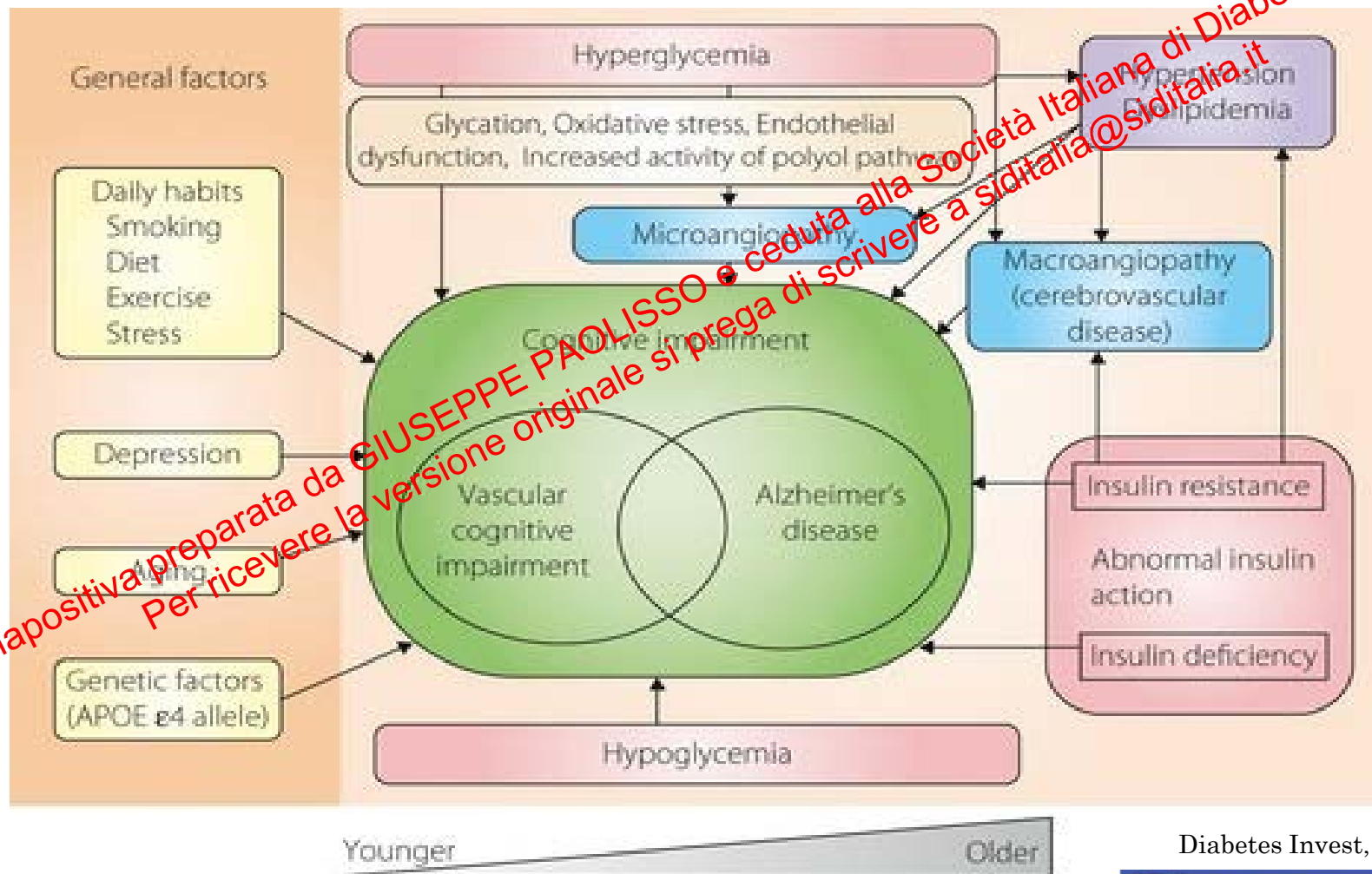
| Follow-up at 5 years                 |  | Hazard Ratio for Dementia (95% CI) |
|--------------------------------------|--|------------------------------------|
| <b>Average Glucose Level</b>         |  |                                    |
| <b>Participants without diabetes</b> |  |                                    |
| Preceding 5 yr                       |  |                                    |
| 95 mg/dl                             |  | 0.88 (0.77–1.00)                   |
| 100 mg/dl                            |  | 1.00                               |
| 105 mg/dl                            |  | 1.09 (1.01–1.17)                   |
| 110 mg/dl                            |  | 1.14 (1.01–1.27)                   |
| 115 mg/dl                            |  | 1.16 (1.00–1.35)                   |
| P value                              |  | 0.09                               |
| Between 5 and 8 yr earlier           |  |                                    |
| 95 mg/dl                             |  | 0.94 (0.81–1.08)                   |
| 100 mg/dl                            |  | 1.00                               |
| 105 mg/dl                            |  | 1.03 (0.95–1.10)                   |
| 110 mg/dl                            |  | 1.02 (0.91–1.15)                   |
| 115 mg/dl                            |  | 1.01 (0.85–1.20)                   |
| P value                              |  | 0.65                               |
| <b>Participants with diabetes</b>    |  |                                    |
| Preceding 5 yr                       |  |                                    |
| 150 mg/dl                            |  | 1.15 (0.94–1.42)                   |
| 160 mg/dl                            |  | 1.00                               |
| 170 mg/dl                            |  | 0.96 (0.85–1.10)                   |
| 180 mg/dl                            |  | 1.04 (0.84–1.28)                   |
| 190 mg/dl                            |  | 1.20 (0.89–1.62)                   |
| P value                              |  | 0.06                               |
| Between 5 and 8 yr earlier           |  |                                    |
| 150 mg/dl                            |  | 0.92 (0.79–1.07)                   |
| 160 mg/dl                            |  | 1.00                               |
| 170 mg/dl                            |  | 1.06 (0.96–1.18)                   |
| 180 mg/dl                            |  | 1.10 (0.91–1.34)                   |
| 190 mg/dl                            |  | 1.13 (0.85–1.50)                   |
| P value                              |  | 0.52                               |

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# POSSIBLE MECHANISTIC CONTRIBUTION TO COGNITIVE IMPAIRMENT SEEN IN DIABETES MELLITUS.



Diabetes Invest, 2012

Insulin has multiple functions in the brain that support neuronal function, including synaptogenesis, synaptic remodeling, and modulating neurotransmitter levels.

Craft S, et al. Journal of Alzheimer's disease : JAD. 2013



**Ageing**  
↓insulin, ↓insulin receptor, ↓insulin receptor signalling, ↓insulin degrading enzyme

*Insulin regulates synaptic plasticity and activity in the frontal cortex and hippocampus, brain regions generally associated with learning and memory.*

*Trends Neurosci 2000; 23 542-549.*

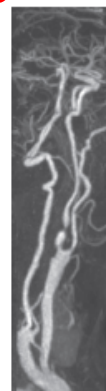
*Insulin stimulates the secretion of amyloid into the extracellular space where it can aggregate with other proteins to form senile plaques.*

*Lancet Neurol 2006*

(A) Hyperinsulinaemia: atherosclerosis

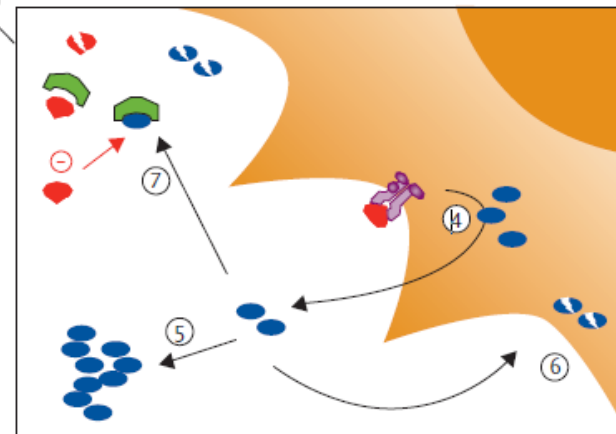
Insulin resistance syndrome

- Hypertension
- Dyslipidaemia
- Hyperglycaemia
- Hyperinsulinaemia
- Prothrombotic state
- Proinflammatory state



● Amyloid  $\beta$   
■ Insulin-degrading enzyme

(D) Insulin and amyloid metabolism



*Lancet Neurol 2006*

# INSULIN RESISTANCE AND EXECUTIVE DYSFUNCTION IN OLDER PERSONS

J Am Geriatr Soc 52:1713–1718, 2004.

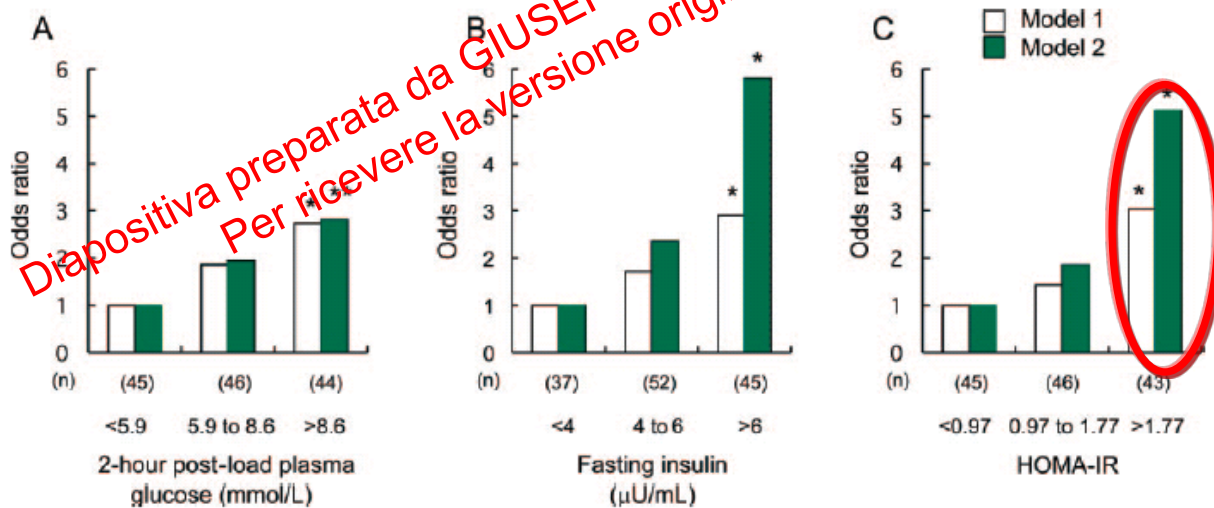
| Characteristic                                                 | Insulin Resistance Tertiles |                  |                  | P for trend |
|----------------------------------------------------------------|-----------------------------|------------------|------------------|-------------|
|                                                                | 1st<br>(n = 190)            | 2nd<br>(n = 192) | 3rd<br>(n = 196) |             |
| TMT-A, seconds, mean $\pm$ SD                                  | 76 $\pm$ 43                 | 84 $\pm$ 63      | 87 $\pm$ 73      | NS          |
| TMT-B, seconds, mean $\pm$ SD                                  | 167 $\pm$ 92                | 190 $\pm$ 108    | 207 $\pm$ 136    | .005        |
| DIFF B-A, seconds, mean $\pm$ SD                               | 92 $\pm$ 67                 | 106 $\pm$ 90     | 117 $\pm$ 92     | .011        |
| Sex, male/female                                               | 93/97                       | 81/111           | 95/101           |             |
| Insulin, mIU/L, mean $\pm$ SD                                  | 5.9 $\pm$ 1.7               | 15.1 $\pm$ 1.6   | 16.9 $\pm$ 5.9   | <.001       |
| Glucose, mg/dL, mean $\pm$ SD                                  | 85 $\pm$ 9                  | 88 $\pm$ 10      | 94 $\pm$ 12      | <.001       |
| Body mass index, kg/m <sup>2</sup> , mean $\pm$ SD             | 26.1 $\pm$ 3.8              | 26.5 $\pm$ 3.6   | 28.2 $\pm$ 4.2   | <.001       |
| Waist hip ratio, mean $\pm$ SD                                 | 0.90 $\pm$ 0.07             | 0.91 $\pm$ 0.1   | 0.91 $\pm$ 0.07  | NS          |
| High-density lipoprotein cholesterol, mg/dL, mean $\pm$ SD     | 59 $\pm$ 15                 | 57 $\pm$ 15      | 55 $\pm$ 14      | .017        |
| Triglycerides, mg/dL, mean $\pm$ SD                            | 115 $\pm$ 52                | 118 $\pm$ 48     | 140 $\pm$ 84     | <.001       |
| Total serum insulin-like growth factor-1, pg/mL, mean $\pm$ SD | 109 $\pm$ 50                | 124 $\pm$ 59     | 126 $\pm$ 58     | .005        |
| Physical activity score, mean $\pm$ SD                         | 3.6 $\pm$ 1.0               | 3.4 $\pm$ 0.8    | 3.3 $\pm$ 0.8    | .050        |
| Drug intake, yes/no                                            | 133/57                      | 137/55           | 132/64           |             |
| Arterial hypertension, yes/no                                  | 75/115                      | 84/108           | 81/115           |             |

## Multivariate Linear Regression Models with HOMA IR as an Independent Determinant After Adjusting for Multiple Confounders

| Model     | TMT-A  |       |         |                | TMT-B  |       |         |                | DIFF B-A |       |         |                |
|-----------|--------|-------|---------|----------------|--------|-------|---------|----------------|----------|-------|---------|----------------|
|           | Beta   | SE    | P-value | R <sup>2</sup> | Beta   | SE    | P-value | R <sup>2</sup> | Beta     | SE    | P-value | R <sup>2</sup> |
| 1*        |        |       |         |                |        |       |         |                |          |       |         |                |
| <65       | 7.741  | 2.195 | .001    | 0.281          | 16.590 | 5.130 | .001    | 0.347          | 8,849    | 3,994 | .028    | 0.270          |
| $\geq$ 65 | 11.607 | 4.460 | .009    | 0.185          | 28.471 | 7.628 | <.001   | 0.203          | 16,864   | 6,313 | .008    | 0.072          |
| 2†        |        |       |         |                |        |       |         |                |          |       |         |                |
| <65       | 9.824  | 2.659 | <.001   | 0.313          | 22.932 | 6.214 | <.001   | 0.382          | 13,107   | 4,822 | .007    | 0.308          |
| $\geq$ 65 | 10.872 | 4.784 | .023    | 0.225          | 28.495 | 7.896 | <.001   | 0.264          | 17,623   | 6,755 | .012    | 0.109          |

|                                         | OR for presence of NPs (CERAD score 1-3 vs 0) |         |                  |         | OR for presence of NFTs (Braak stage I-VI vs 0) |         |                  |         |
|-----------------------------------------|-----------------------------------------------|---------|------------------|---------|-------------------------------------------------|---------|------------------|---------|
|                                         | Model 1                                       |         | Model 2          |         | Model 1                                         |         | Model 2          |         |
|                                         | OR (95% CI)                                   | P Value | OR (95% CI)      | P Value | OR (95% CI)                                     | P Value | OR (95% CI)      | P Value |
| Fasting plasma glucose, mmol/L          | 1.33 (0.86-2.04)                              | 0.20    | 1.41 (0.88-2.26) | 0.15    | 1.31 (0.72-2.37)                                | 0.38    | 1.35 (0.74-2.47) | 0.33    |
| 2-hour post-load plasma glucose, mmol/L | 1.66 (1.04-2.63)                              | 0.03    | 1.71 (1.04-2.80) | 0.03    | 1.58 (0.85-2.93)                                | 0.15    | 1.67 (0.88-3.17) | 0.12    |
| Fasting insulin, $\mu$ U/mL             | 1.61 (1.04-2.48)                              | 0.03    | 2.03 (1.11-3.70) | 0.02    | 1.05 (0.62-1.79)                                | 0.85    | 1.06 (0.65-2.04) | 0.86    |
| HOMA-IR                                 | 1.67 (1.08-2.59)                              | 0.02    | 2.11 (1.18-3.79) | 0.01    | 1.14 (0.69-1.98)                                | 0.64    | 1.19 (0.62-2.30) | 0.60    |

Odds ratios and 95% confidence intervals for the presence vs absence of neuritic plaques and neurofibrillary tangles



Odds ratios for each tertile of glucose (A), insulin (B), and HOMA-IR (C) vs the lowest tertile for the presence of neuritic plaques

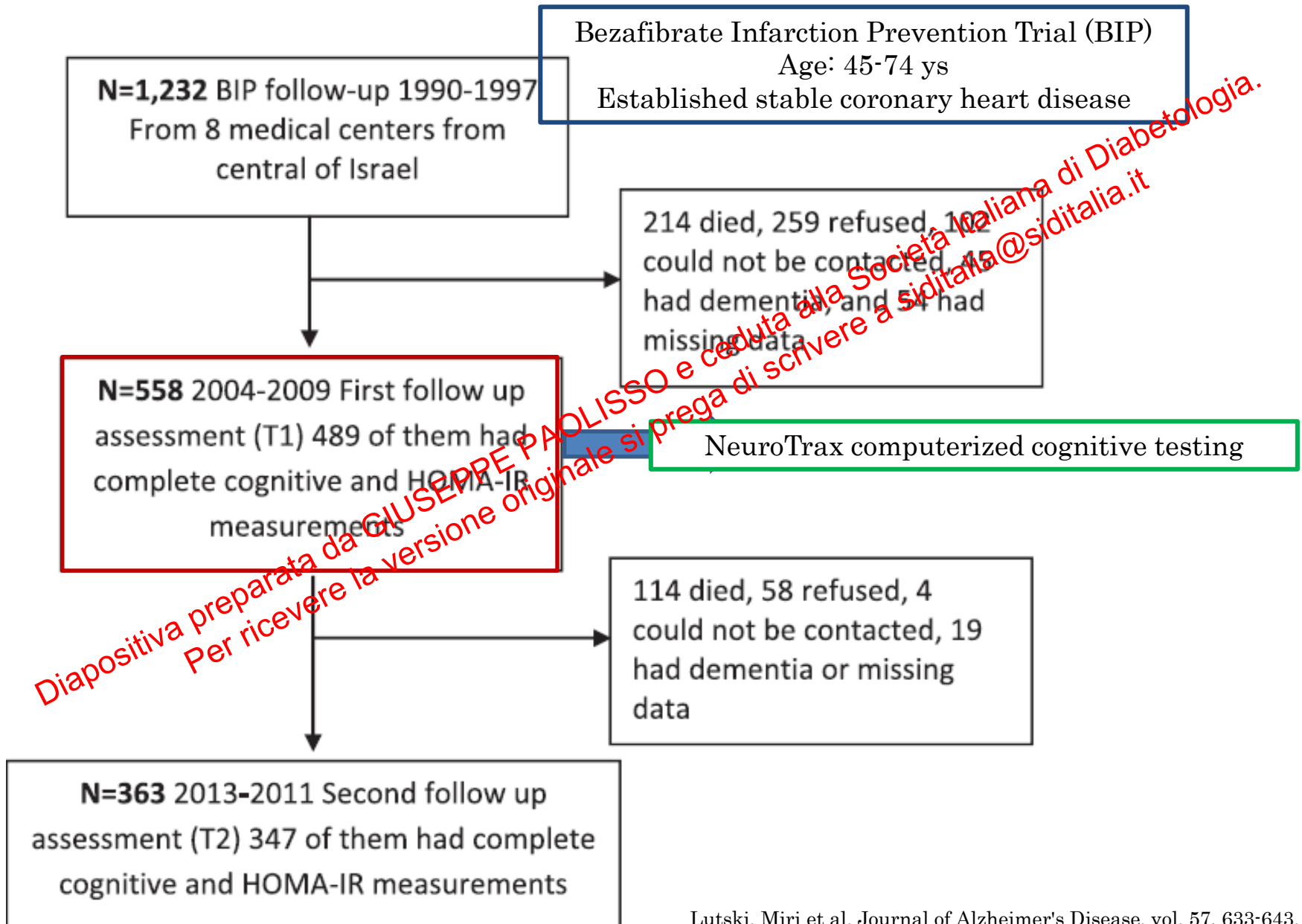
# Insulin Resistance and Future Cognitive Performance and Cognitive Decline in Elderly Patients with Cardiovascular Disease



Examine the associations between **INSULIN RESISTANCE** and cognitive performance and change in cognitive functions two decades later in individuals with cardiovascular disease with and without diabetes.

diapositiva preparata da GIUSEPPE PAOLISSO e ceduta alla Società Italiana di Diabetologia.  
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# STUDY FLOW CHART

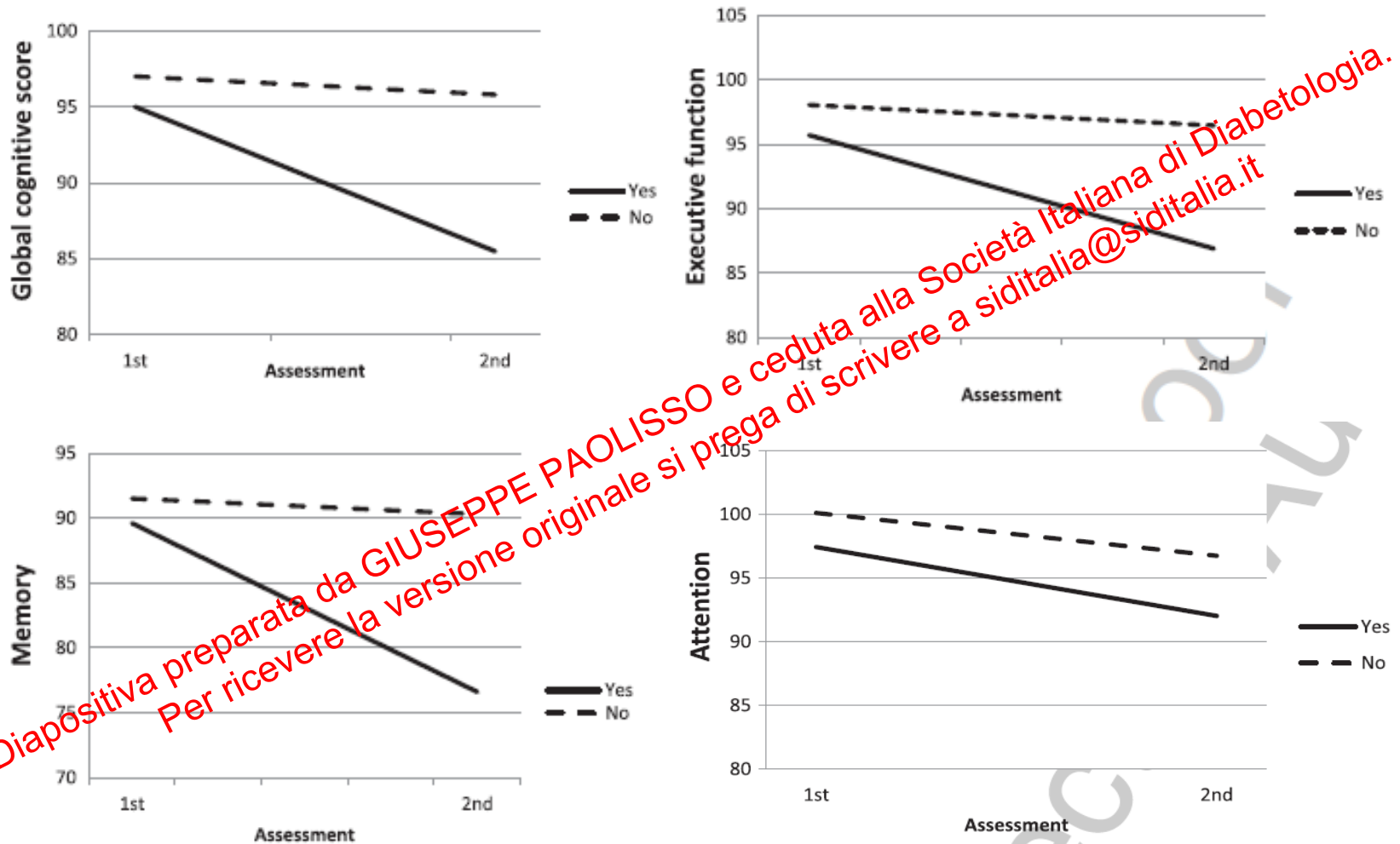


# BASELINE CHARACTERISTICS T1 ASSESSMENT ( $n = 489$ )

|                                         |              | HOMA >1.6mg/L<br>( $n = 122$ ) | HOMA $\leq$ 1.6mg/L<br>( $n = 367$ ) | <i>p</i> -value  |
|-----------------------------------------|--------------|--------------------------------|--------------------------------------|------------------|
| HOMA (mg/L)*                            |              | 2.1 [1.8–2.9]                  | 0.9 [0.6–1.2]                        | <b>&lt;0.001</b> |
| Age (years)                             |              | 57.8 $\pm$ 6.8                 | 57.7 $\pm$ 6.3                       | 0.6              |
| Males, <i>n</i> (%)                     |              | 323 (39)                       | 156 (93)                             | 0.6              |
| Smoking status, <i>n</i> (%)            | Current      | 18 (15)                        | 42 (11.4)                            | 0.7              |
|                                         | Past         | 71 (58.7)                      | 236 (64.3)                           |                  |
|                                         | Never        | 32 (26.4)                      | 89 (24.3)                            |                  |
| Place of birth, <i>n</i> (%)            | Middle East  | 20 (27.4)                      | 77 (20.8)                            | 0.7              |
|                                         | Europe       | 35 (47.9)                      | 109 (42.1)                           |                  |
|                                         | Israel       | 18 (24.7)                      | 56 (25.6)                            |                  |
| Education, <i>n</i> (%)                 | Elementary   | 26 (21.5)                      | 75 (20.5)                            | 0.9              |
|                                         | High school  | 60 (49.6)                      | 182 (49.7)                           |                  |
|                                         | Academic     | 35 (28.9)                      | 109 (29.8)                           |                  |
| Height tertiles, <i>n</i> (%)           | Bottom       | 43 (35.3)                      | 152 (41.4)                           | <b>0.032</b>     |
|                                         | Middle       | 47 (38.5)                      | 95 (25.9)                            |                  |
|                                         | Top          | 22 (26.2)                      | 120 (32.7)                           |                  |
| Physical activity                       | Yes          | 228 (62.1)                     | 66 (54.1)                            | 0.117            |
|                                         | No           | 139 (37.9)                     | 56 (45.9)                            |                  |
| Body mass index*                        |              | 27.4 [25.6–29.7]               | 25.6 [24.3–27.5]                     | <b>&lt;0.001</b> |
| Systolic BP (mmHg)                      |              | 133 $\pm$ 18                   | 129 $\pm$ 18                         | <b>0.03</b>      |
| Diastolic BP (mmHg)*                    |              | 80 [80, 90]                    | 80 [75.7, 90]                        | 0.6              |
| Total cholesterol (mg/dL)               |              | 212.8 $\pm$ 16.7               | 213.1 $\pm$ 17.4                     | 0.8              |
| LDL cholesterol (mg/dL)                 |              | 147 $\pm$ 16.0                 | 150 $\pm$ 16.0                       | 0.1              |
| HDL cholesterol (mg/dL)                 |              | 34.8 $\pm$ 5.8                 | 35.0 $\pm$ 5.2                       | 0.7              |
| Triglycerides (mg/dL)                   |              | 148.3 [117–188]                | 132.6 [102.1–177.4]                  | <b>0.02</b>      |
| C-reactive protein (mg/dL)*             |              | 2.9 [1.9–5.6]                  | 2.5 [1.5–4.5]                        | <b>0.05</b>      |
| Fibrinogen (mg/dL)*                     |              | 336 [295–392]                  | 331 [292–373]                        | 0.3              |
| Study arm = Bezafibrate, <i>n</i> (%)   | Yes          | 65 [40]                        | 188 (51)                             | 0.7              |
| Diabetes, <i>n</i> (%)                  | Yes          | 25 (20.5)                      | 24 (6.6)                             | <b>&lt;0.001</b> |
| Angina pectoris, <i>n</i> (%)           | Yes          | 63 (51.6)                      | 154 (39.5)                           | <b>0.019</b>     |
| Peripheral artery disease, <i>n</i> (%) |              | 4 (3.3)                        | 12 (3.3)                             | 0.9              |
| Myocardial infarction, <i>n</i> (%)     |              | 98 (80)                        | 285 (80)                             | 0.6              |
| Comorbidity score, <i>n</i> (%)         | Low          | 36 (29.5)                      | 68 (18.5)                            | <b>0.010</b>     |
|                                         | High         | 86 (70.5)                      | 299 (81.5)                           |                  |
| Late life evaluation (T1)               |              |                                |                                      |                  |
| Mean CVR*                               |              | 0.7 [0.45–0.93]                | 0.73 [0.48–1.10]                     | 0.2              |
| Mean CC-IMT                             |              | 0.99 $\pm$ 0.2                 | 0.96 $\pm$ 0.2                       | 0.08             |
| Bilateral plaques                       | Yes          | 65 (59.1)                      | 188 (54.7)                           | 0.4              |
| Depressive symptoms                     | GDS $\geq$ 5 | 23 (18.9)                      | 72 (19.6)                            | 0.8              |

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# COGNITIVE CHANGE IN DIFFERENT DOMAINS BY INSULIN RESISTANCE GROUPS



# INSULIN RESISTANCE AT BASELINE

|                    | Model 1          |          | Model 2          |          | Model 3          |          |
|--------------------|------------------|----------|------------------|----------|------------------|----------|
|                    | $\beta \pm SE$   | <i>p</i> | $\beta \pm SE$   | <i>p</i> | $\beta \pm SE$   | <i>p</i> |
| Composite score    | -2.50 $\pm$ 1.09 | 0.023    | -2.9 $\pm$ 1.13  | 0.010    | -3.66 $\pm$ 1.24 | 0.003    |
| Memory             | -3.22 $\pm$ 1.53 | 0.035    | -3.87 $\pm$ 1.63 | 0.018    | -5.22 $\pm$ 1.88 | 0.005    |
| Executive function | -3.12 $\pm$ 1.24 | 0.012    | -3.15 $\pm$ 1.31 | 0.016    | -4.03 $\pm$ 1.47 | 0.006    |
| Visual spatial     | -1.16 $\pm$ 1.66 | 0.487    | -1.87 $\pm$ 1.75 | 0.287    | -2.36 $\pm$ 1.94 | 0.224    |
| Attention*         | -2.08 $\pm$ 1.52 | 0.171    | -2.11 $\pm$ 1.59 | 0.186    | -2.5 $\pm$ 1.73  | 0.139    |

Model 1: adjusted for age, sex and education. Model 2: adjusted for age, sex, education, birthplace, hypertension, systolic blood pressure, body mass index, angina pectoris, comorbidity, depressive symptoms. Model 3: Model 2+ CVR, CC-IMT and bilateral plaques. \*transformed \*\*4; SE, standard error.

- Higher baseline HOMA-IR levels were associated with poorer executive function and memory performance 15 years later and with cognitive decline over a further period of 5 years. These observed relationships were independent of vascular risk factors, and remained similar after excluding those with a history of stroke, dementia or diabetes.

- None of the indices of cerebrovascular disease (CVR, CC-IMT, and carotid plaques) significantly mediated the associations between HOMA-IR and cognitive impairment or decline.

Our findings thus indicate a possible non-vascular component for the cognitive decline.

# CAN WE IDENTIFY THE DIABETIC PATIENTS AT RISK OF DEVELOPING COGNITIVE DISORDERS?

**Longer duration of DM2**

Spauwen PJ et al Diabetes care. 2013

**Severe hypoglycemic event**

Warren RE, et al Diabetes, obesity & metabolism. 2005

**Higher A1c levels**

Tuligenga RH, The Lancet Diabetes & Endocrinology. 2013

**RISK FACTORS FOR  
DEMENTIA AMONG PEOPLE  
WITH DIABETES MELLITUS**

**10-year dementia risk**

Exalto LG, The Lancet Diabetes & Endocrinology. 2013

**Depression**

Byers AL et al, Nature reviews Neurology. 2011

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# MIMICS COGNITIVE DECLINE IN DIABETIC PAZIENT

## DIFFERENTIAL DIAGNOSIS

LIVER DYSFUNCTION

HYPOTHYROIDISM

VITAMIN DEFICENCY  
(vit.B12)

DEPRESSION

RENAL DYSFUNCTION

ANAEMIA

When present, these disorders should be treated accordingly and cognitive function should be re-examined after the disorder has resolved.

In the **ACCORD-MIND** study, for example, depression in patients with type 2 diabetes was associated with increased cognitive decline in all cognitive domains compared with patients with type 2 diabetes without depression.

Sullivan MD et al. *JAMA Psychiatry* 2013;

# DIABETES SPECIFIC DEMENTIA RISK SCORE (DSDRS)

Baseline population characteristics of the development cohort by incident dementia status.

|                                      | No dementia<br>N=24788 | Dementia<br>N=5173 | p value |
|--------------------------------------|------------------------|--------------------|---------|
| <b>Sociodemographic</b>              |                        |                    |         |
| Age, y                               | 69.7 (±6.5)            | 74.2 ± (6.6)       | <0.0001 |
| Male                                 | 13611 (55%)            | 2566 (50%)         | <0.0001 |
| Race/ethnicity (n= 29665)            |                        |                    | <0.0001 |
| White                                | 15562 (63%)            | 3342 (65%)         |         |
| African American                     | 2730 (11%)             | 670 (13%)          |         |
| Hispanic                             | 2785 (11%)             | 508 (10%)          |         |
| Asian                                | 2807 (11%)             | 441 (9%)           |         |
| Native American                      | 550 (2%)               | 131 (3%)           |         |
| Other                                | 121 (0.5%)             | 18 (0.4%)          |         |
| Education (n= 27516)                 |                        |                    | <0.0001 |
| High school or less                  | 11417 (50%)            | 2665 (56%)         |         |
| College or more                      | 11363 (50%)            | 2071 (44%)         |         |
| Hospitalization in 1996-1997         | 5644 (23%)             | 1418 (27%)         | <0.0001 |
| KPNC membership duration, y          | 14.2 (±5)              | 15.0 ± (4.7)       | <0.0001 |
| <b>Diabetes specific</b>             |                        |                    |         |
| T2DM duration, y                     | 8.0 (IQR 9-11)         | 8.9 (IQR 11-14)    | <0.0001 |
| HbA1c, in %                          | 7.5 (±1.8)             | 7.7 (±1.8)         | 0.004   |
| Diabetes treatment type              |                        |                    | 0.002   |
| Nonpharmacological controlled        | 400 (2%)               | 939 (18%)          |         |
| Insulin only                         | 4823 (19%)             | 1082 (21%)         |         |
| Oral agents                          | 13400 (54%)            | 2847 (55%)         |         |
| Insulin and oral agents              | 1570 (6%)              | 305 (6%)           |         |
| Diabetic foot <sup>a</sup>           | 1061 (4%)              | 251 (5%)           | 0.07    |
| Acute metabolic event <sup>b</sup>   | 783 (3%)               | 250 (5%)           | <0.0001 |
| <b>Comorbid diseases</b>             |                        |                    |         |
| Depression <sup>b</sup>              | 5139 (21%)             | 1422 (27%)         | <0.0001 |
| Microvascular disease <sup>b</sup>   | 1749 (7%)              | 412 (8%)           | 0.02    |
| Cardiovascular disease <sup>a</sup>  | 6178 (25%)             | 1386 (27%)         | 0.005   |
| Cerebrovascular disease <sup>a</sup> | 1615 (7%)              | 534 (10%)          | <0.0001 |
| Head trauma <sup>a</sup>             | 89 (0.4%)              | 37 (0.7%)          | 0.003   |

The risk score was developed for patients with type 2 diabetes aged 60 years or older

**N=29.961**

- Clinics characteristics
- demographic characteristics

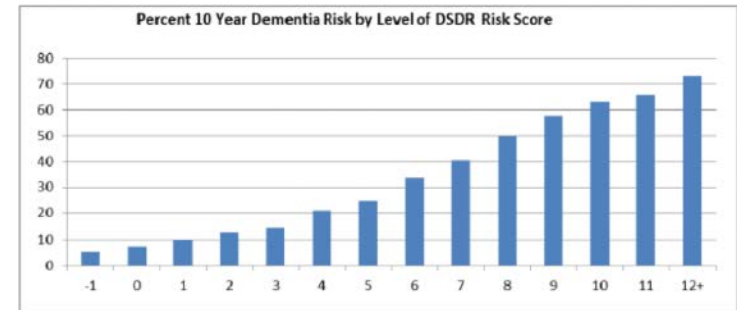
# DIABETES SPECIFIC DEMENTIA RISK SCORE (DSDRS)

| Points          |    | Points                  |   | Points                                         |    |
|-----------------|----|-------------------------|---|------------------------------------------------|----|
| 60-64 years     | 0  | Acute metabolic event   | 2 | Up to high-school education ( $\leq 12$ years) | 0  |
| 65-69 years     | 3  | Microvascular disease   | 1 | College or higher education ( $> 12$ years)    | -1 |
| 70-74 years     | 5  | Diabetic foot           | 1 |                                                |    |
| 75-79 years     | 7  | Cerebrovascular disease | 2 |                                                |    |
| 80-84 years     | 8  | Cardiovascular disease  | 1 |                                                |    |
| $\geq 85$ years | 10 | Depression              | 2 |                                                |    |

Add up points and look up predicted 10-year risk of dementia

| Predicted 10-year risk of dementia (%) |    |
|----------------------------------------|----|
| -1                                     | 5  |
| 0                                      | 7  |
| 1                                      | 10 |
| 2                                      | 13 |
| 3                                      | 15 |
| 4                                      | 21 |
| 5                                      | 25 |
| 6                                      | 34 |
| 7                                      | 40 |
| 8                                      | 50 |
| 9                                      | 58 |
| 10                                     | 63 |
| 11                                     | 66 |
| 12-19                                  | 73 |

- **SENSITIVITY** 77%
- **SPECIFICITY** 95%



# DIABETES CARE FOR OLDER ADULTS

## GENERAL RECOMMENDATIONS

### 1) SIMPLIFY DRUG REGIMENS AND INVOLVE CAREGIVERS IN ALL ASPECTS OF CARE.

#### Avoid hypoglycemia

- Screen for and manage by adjusting glycemic targets and pharmacologic interventions

#### Functional and cognitively intact older adults with long life expectancy

- Provide diabetes care with goals similar to those for younger adults

#### Glycemic goals may be relaxed based in selected individuals

- But avoid hyperglycemia leading to symptoms or risk of acute hyperglycemic complications

#### Individualize screening for diabetes complications

- Pay close attention to complications leading to functional impairment

#### Annual screening for cognitive impairment

- People who screen positive should receive diagnostic assessment as appropriate

**FRONT**

Anterior Cingulate  
(motivation)

**MOTOR**

**SENSORY**

**BACK**

**FRONTAL LOBE**  
(planning)

**CORTEX**

**PARIETAL LOBE**  
(movement)

Dorsolateral Prefrontal  
(executive & logical)

**OCCIPITAL LOBE**  
(vision)

Olfactory Bulb

**TEMPORAL LOBE**  
(language)

Lateral Orbitofrontal  
(appropriate social/  
emotional response)

Hypothalamus

**CEREBELLUM**  
(coordinate  
movement)

Amygdala  
(basic emotions)

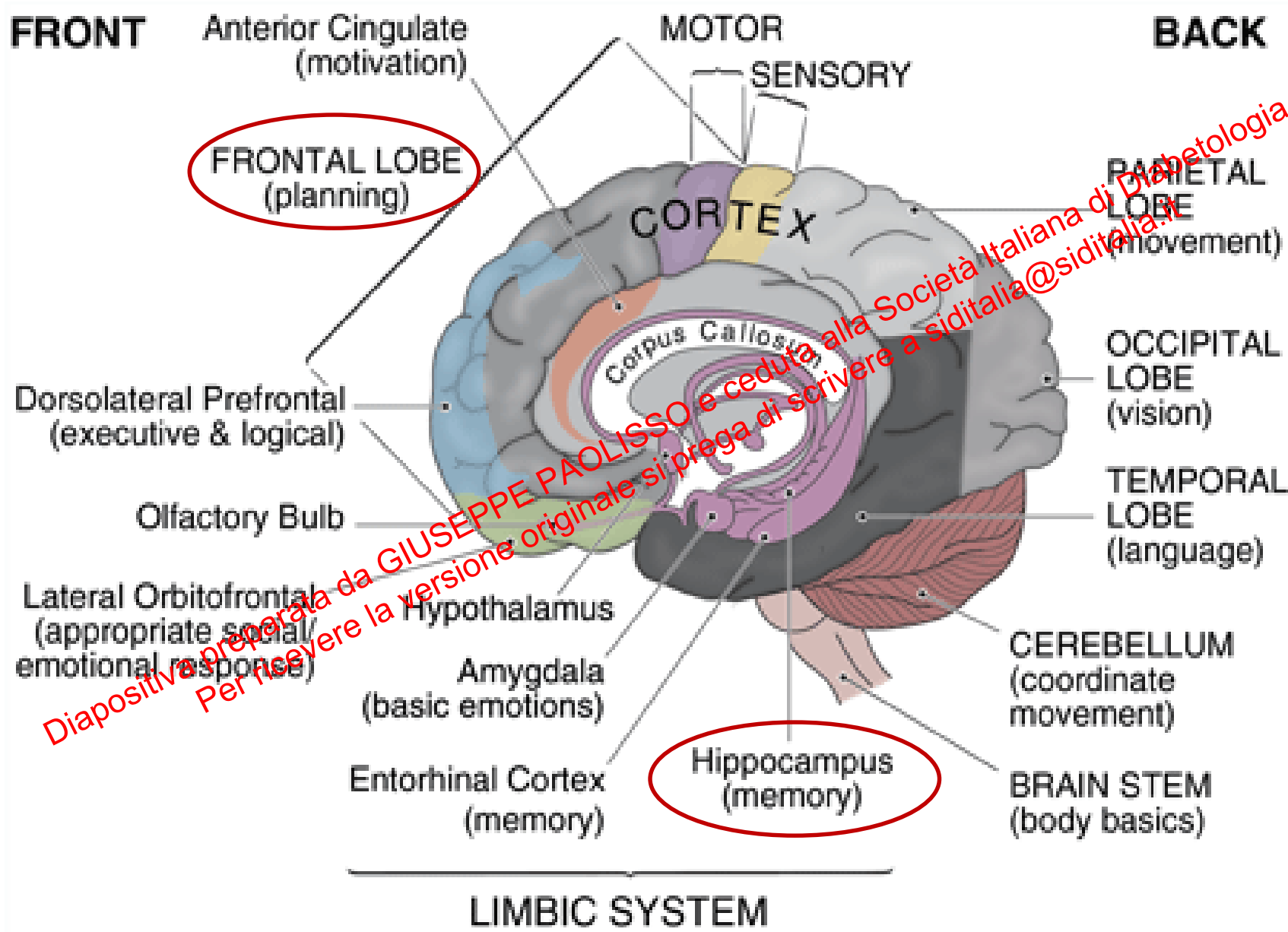
Entorhinal Cortex  
(memory)

**Hippocampus**  
(memory)

**BRAIN STEM**  
(body basics)

**LIMBIC SYSTEM**

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# NEUROPSYCHOLOGICAL TESTS

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“When MCI or dementia is suspected, the diagnostic assessment for people with diabetes is the same as for people without diabetes and should be done according to local guidelines.”

*Lancet Neurol* 2015; 14: 329–40

General screening test  
(multi-item)

Mini Mental State Examination (MMSE)

Montreal Cognitive Assessment (MoCA)

Addenbrooke's Cognitive Examination- Ace-R

Hachinski Ischaemic Scale

Specific cognitive tests

Trail Making Test Part A

Trail Making Test Part B

Semantic Verbal Fluency

Phonemic Verbal Fluency

Clock Drawing Test

Digit Span Forward

Digit Span Backward

Symbol Digit Test

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# MINI MENTAL STATE EXAMINATION (MMSE)

FOLSTEIN M.F. ET AL. 1975

## The Mini-Mental State Exam

Patient \_\_\_\_\_ Examiner \_\_\_\_\_ Date \_\_\_\_\_

Maximum Score

5 ( )

5 ( )

3 ( )

5 ( )

3 ( )

2 ( )

1 ( )

3 ( )

1 ( )

1 ( )

1 ( )

1 ( )

1 ( )

1 ( )

1 ( )

### Orientation

What is the (year) (season) (date) (day) (month)?

Where are we (state) (country) (town) (hospital) (floor)?

### Registration

Name 3 objects: 1 second to say each. Then ask the patient

all 3 after you have said them. Give 1 point for each correct answer.

Then repeat them until he/she learns all 3. Count trials and record.

Trials \_\_\_\_\_

### Attention and Calculation

Serial 7's. 1 point for each correct answer. Stop after 5 answers.

Alternatively spell "world" backward.

### Recall

Ask for the 3 objects repeated above. Give 1 point for each correct answer.

### Language

Name a pencil and watch.

Repeat the following "No's, ands, or buts"

Follow a 3-stage command:

"Take a paper in your hand, fold it in half, and put it on the floor."

Read and obey the following: CLOSE YOUR EYES

Write a sentence.

Copy the design shown.



Total Score

ASSESS level of consciousness along a continuum \_\_\_\_\_

Alert Drowsy Stupor Coma

"MINI-MENTAL STATE." A PRACTICAL METHOD FOR GRADING THE COGNITIVE STATE OF PATIENTS FOR THE CLINICIAN.  
*Journal of Psychiatric Research*, 12(3): 189-198, 1975. Used by permission.

✓ Mini-Mental State Examination: a normative study in Italian elderly population (Magni et al., 1996)

✓ The MMSE: normative study of an Italian random sample (Measso et al., 1993)

❖ 5-10 minutes

❖ Normal  $\geq 24$

| Decade età   | Anni scuola |       |       |       |
|--------------|-------------|-------|-------|-------|
|              | 0-4         | 5-7   | 8-12  | 13-17 |
| <b>65-69</b> | + 0.4       | - 1.1 | - 2.0 | - 2.8 |
| <b>70-74</b> | + 0.7       | - 0.7 | - 1.6 | - 2.3 |
| <b>75-79</b> | + 1.0       | - 0.3 | - 1.0 | - 1.7 |
| <b>80-84</b> | + 1.5       | + 0.4 | - 0.3 | - 0.9 |
| <b>85-89</b> | + 2.2       | + 1.4 | + 0.8 | + 0.3 |

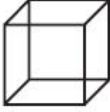
# MONTREAL COGNITIVE ASSESSMENT (MOCA)

Z.NASREDDINE MD VERSION, 2004

MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME: \_\_\_\_\_ Education: \_\_\_\_\_ Date of birth: \_\_\_\_\_  
Sex: \_\_\_\_\_ DATE: \_\_\_\_\_

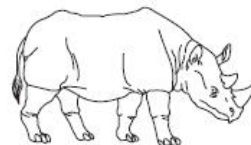
**VISUOSPATIAL / EXECUTIVE**

Copy cube  [ ]

Draw CLOCK (Ten past eleven) (3 points) [ ]

POINTS: [ ]/5

**NAMING**

 [ ]  [ ]  [ ]

[ ]/3

**MEMORY**

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

|           | FACE | VELVET | CHURCH | DAISY | RED | No points |
|-----------|------|--------|--------|-------|-----|-----------|
| 1st trial |      |        |        |       |     |           |
| 2nd trial |      |        |        |       |     |           |

**ATTENTION**

Read list of digits (1 digit/sec). Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

[ ]/2

Read list of letters. The subject must tap with his hand at each letter A. No points if  $\geq 2$  errors

[ ] FBACMNAAJKLBAFAKDEAAAJAMOFAB

[ ]/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt

[ ]/3

**LANGUAGE**

Repeat: I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

[ ]/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] \_\_\_\_\_ (N  $\geq 11$  words)

[ ]/1

**ABSTRACTION**

Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler

[ ]/2

**DELAYED RECALL**

|                                 | FACE | VELVET | CHURCH | DAISY | RED | Points for UNCUED recall only |
|---------------------------------|------|--------|--------|-------|-----|-------------------------------|
| Has to recall words WITH NO CUE | [ ]  | [ ]    | [ ]    | [ ]   | [ ] |                               |
| Category cue                    |      |        |        |       |     |                               |
| Multiple choice cue             |      |        |        |       |     |                               |

[ ]/5

**Optional**

**ORIENTATION**

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

[ ]/6

© Z.Nasreddine MD Version 7.1 [www.mocatest.org](http://www.mocatest.org) Normal  $\geq 26 / 30$  TOTAL [ ]/30

Add 1 point if  $\leq 12$  yr edu

❖ 5–10 minutes

❖ MOCA  $\geq 26$  Normal

❖ MOCA  $\leq 19$  Dementia

«The MOCA is better than other tools to detect Mild Cognitive Impairment in the elderly patients with 2 diabetes.»

Il MoCA is recommended by Consensus Conference del National Institute of Neurological Disorders and Stroke and Canadian Stroke Network Vascular Cognitive Impairment 2006.

# ADDENBROOKE'S COGNITIVE EXAMINATION- ACE-R

**ADDENBROOKE'S COGNITIVE EXAMINATION - ACE-R**  
Final Revised Version A (May 2004) - Australian Version

Name : \_\_\_\_\_ Date of testing: / /  
Date of birth: \_\_\_\_\_ Tester's name: \_\_\_\_\_  
Hospital no.: \_\_\_\_\_ Age at leaving full-time education: \_\_\_\_\_  
Occupation: \_\_\_\_\_  
Handedness: \_\_\_\_\_

**Addressograph**

**ORIENTATION**

➤ Ask: What is the Day Date Month Year Season (Score 0-5)

➤ Ask: Which Building Floor Town State Country (Score 0-5)

**REGISTRATION**

➤ Tell: 'I'm going to give you three words and I'd like you to repeat after me: lemon, key and ball'. After subject repeats, say 'Try to remember them because I'm going to ask you later'. Score only the first trial (repeat 3 times if necessary). Register number of trials (Score 0-3)

**ATTENTION & CONCENTRATION**

➤ Ask the subject: 'could you take 7 away from a 100? After the subject responds, ask him or her to take away another 7 to a total of 5 subtractions. If subject makes a mistake, carry on and check the subsequent answer (i.e. 93, 84, 77, 70, 63 -score 4) Stop after five subtractions (93, 84, 77, 70, 63) (Score 0-5)

➤ Ask: 'could you please spell **WORLD** for me? Then ask him/her to spell it backwards' (Score 0-2)

**MEMORY - Recall**

➤ Ask: 'Which 3 words did I ask you to repeat and remember?' (Score 0-3)

**MEMORY - Anterograde Memory**

➤ Tell: 'I'm going to give you a name, address and phone number to repeat after me. We'll be doing that 3 times, so you have a chance to learn. I'll be asking you later' (Score 0-7)

Score only the third trial

1<sup>st</sup> Trial 2<sup>nd</sup> Trial 3<sup>rd</sup> Trial

Harold Wilson \_\_\_\_\_  
72 Market Street \_\_\_\_\_  
Rochers plan \_\_\_\_\_  
Queensland \_\_\_\_\_

**MEMORY - Retrograde Memory**

➤ Name of current Prime Minister \_\_\_\_\_ (Score 0-4)  
➤ Name of the Premier of New South Wales \_\_\_\_\_  
➤ Name of the USA president \_\_\_\_\_  
➤ Name of the USA president who was assassinated in the 1950s \_\_\_\_\_

❖ Duration: 10- 15minutes

Table 1: Lower limit of normal (cut-off scores) for total ACE-R and sub-scores according to age (50-59, 60-69, 70-75), showing control mean minus two standard deviations.

| Age range | Education (years) | Total ACE-R score | Attention/Orientation | Memory | Fluency | Language | Visuospatial |
|-----------|-------------------|-------------------|-----------------------|--------|---------|----------|--------------|
| 50-59     | 12.7              | 86                | 17                    | 18     | 9       | 24       | 15           |
| 60-69     | 12.9              | 85                | 16                    | 17     | 8       | 21       | 14           |
| 70-75     | 12.1              | 84                | 16                    | 16     | 9       | 22       | 14           |

Table 2: Sensitivity, Specificity and Positive Predictive Values (PPV) at different prevalence rates of two cut-off total ACE-R scores. Values in parenthesis represent the respective Negative Predictive Values

| Dementia      |             | PPV at different prevalence rates |            |      |      |            |
|---------------|-------------|-----------------------------------|------------|------|------|------------|
| ACE-R cut-off | Sensitivity | Specificity                       | 5%         | 10%  | 20%  | 40%        |
| 88            | 0.94        | 0.89                              | 0.31 (1.0) | 0.48 | 0.68 | 0.85 (1.0) |
| 82            | 0.84        | 1.00                              | 1.0 (0.96) | 1.0  | 1.0  | 1.0 (0.90) |

The Addenbrooke's Cognitive Examination is a more comprehensive measure of cognitive function that incorporates the MMSE.

# Cognitive Tests to Detect Dementia: Systematic Review and Meta-analysis

| Screening Test                 | No. of Study Cohorts | Pooled (95% CI)  |                  | Pooled LR (95% CI) |                  |
|--------------------------------|----------------------|------------------|------------------|--------------------|------------------|
|                                |                      | Sensitivity      | Specificity      | Positive           | Negative         |
| MMSE <sup>7</sup>              | 108                  | 0.81 (0.78-0.84) | 0.89 (0.87-0.91) | 7.45 (6.25-8.88)   | 0.21 (0.18-0.25) |
| Very brief (≤5 min)            |                      |                  |                  |                    |                  |
| CDT                            |                      |                  |                  |                    |                  |
| Shulman et al <sup>29</sup>    | 9                    | 0.83 (0.75-0.89) | 0.84 (0.69-0.92) | 5.03 (2.61-9.64)   | 0.20 (0.14-0.29) |
| Sunderland et al <sup>28</sup> | 9                    | 0.76 (0.69-0.83) | 0.85 (0.76-0.91) | 5.09 (3.18-8.13)   | 0.28 (0.20-0.38) |
| Mini-Cog test <sup>10</sup>    | 9                    | 0.91 (0.89-0.96) | 0.86 (0.74-0.93) | 6.56 (3.25-13.24)  | 0.10 (0.04-0.25) |
| MIS <sup>30</sup>              | 6                    | 0.87 (0.68-0.86) | 0.91 (0.84-0.96) | 9.18 (4.81-17.55)  | 0.23 (0.15-0.36) |
| VF test <sup>33</sup>          | 7                    | 0.80 (0.73-0.86) | 0.82 (0.73-0.88) | 4.38 (2.82-6.79)   | 0.24 (0.17-0.35) |
| Brief (≤10 min)                |                      |                  |                  |                    |                  |
| AMT <sup>27</sup>              | 14                   | 0.88 (0.82-0.92) | 0.85 (0.81-0.89) | 5.94 (4.46-7.91)   | 0.15 (0.10-0.22) |
| GPCOG <sup>11</sup>            | 5                    | 0.92 (0.81-0.97) | 0.87 (0.83-0.90) | 6.79 (5.33-8.64)   | 0.10 (0.04-0.22) |
| MoCA <sup>31</sup>             | 20                   | 0.91 (0.84-0.95) | 0.81 (0.71-0.88) | 4.78 (3.10-7.39)   | 0.12 (0.07-0.20) |
| Detailed (≤20 min)             |                      |                  |                  |                    |                  |
| ACE-R <sup>9</sup>             | 13                   | 0.92 (0.90-0.94) | 0.89 (0.84-0.93) | 8.60 (5.62-13.16)  | 0.09 (0.06-0.11) |
| IQCODE                         |                      |                  |                  |                    |                  |
| Short form <sup>13</sup>       | 7                    | 0.89 (0.85-0.92) | 0.82 (0.63-0.93) | 4.91 (2.19-11.01)  | 0.14 (0.11-0.18) |
| Long form <sup>12</sup>        | 17                   | 0.84 (0.81-0.87) | 0.82 (0.75-0.87) | 4.73 (3.42-6.55)   | 0.19 (0.16-0.22) |
| 3MS <sup>32</sup>              | 9                    | 0.86 (0.83-0.89) | 0.85 (0.74-0.92) | 5.81 (3.20-10.55)  | 0.17 (0.13-0.21) |

# THE HACHINSKI ISCHAEMIC SCALE MAY BE USED TO ASSIST IN THE DIAGNOSIS OF VASCULAR DEMENTIA.

|                             |   |
|-----------------------------|---|
| Abrupt onset                | 2 |
| Stepwise deterioration      | 1 |
| Fluctuating course          | 2 |
| Nocturnal confusion         | 1 |
| Preservation of personality | 1 |
| Depression                  | 1 |
| Somatic complaints          | 1 |
| Emotional incontinence      | 1 |
| History of hypertension     | 1 |
| History of stroke           | 2 |
| Associated atherosclerosis  | 1 |
| Focal neurological symptoms | 2 |
| Focal neurological signs    | 2 |

❖ cut-off score  $\leq 4$  for Degenerative Dementia

❖  $\geq 7$  for Vascular Dementia

sensitivity 89% and specificity 89% (Moroney 1997)

It is not useful in determinations between mixed dementia and other dementia types.

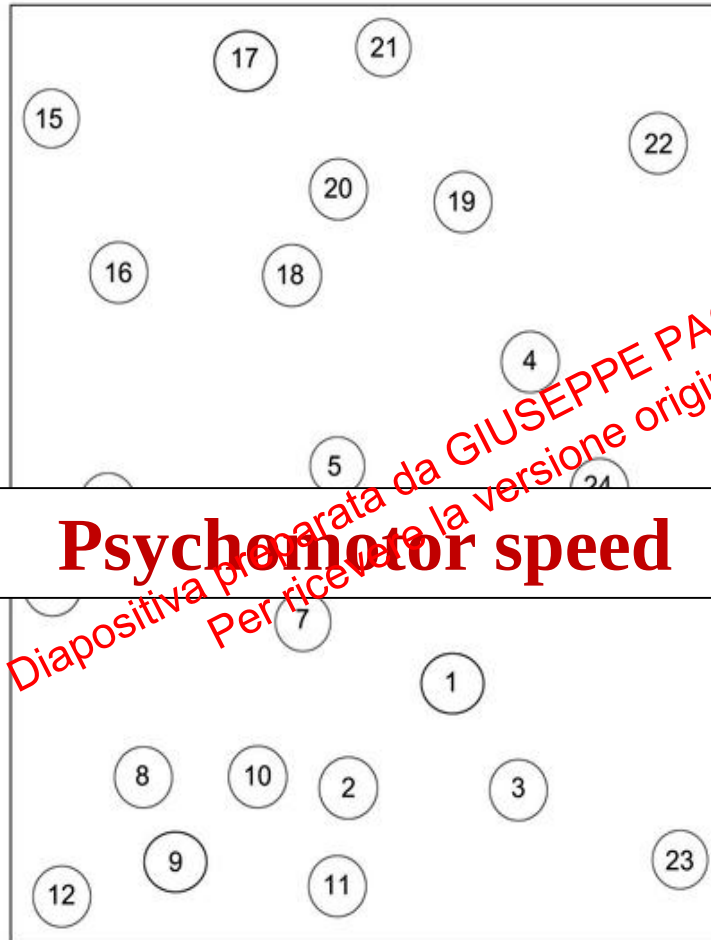
# NEUROPSYCHOLOGICAL TESTS EXPLORE COGNITIVE DOMAINS IN PEOPLE WITH DIABETES

|                    |                                                                                                                                                                                                                |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EXECUTIVE FUNCTION | <ul style="list-style-type: none"><li>▪ Trail Making Test Part A</li><li>▪ Trail Making Test Part B</li><li>▪ Semantic Verbal Fluency</li><li>▪ Phonemic Verbal Fluency</li><li>▪ Clock Drawing Test</li></ul> |
| ATTENTION          | <ul style="list-style-type: none"><li>▪ Digit Span Forward</li><li>▪ Digit Span Backward</li><li>▪ Trail Making Test Part A</li><li>▪ Symbol Digit Test</li></ul>                                              |
| WORKING MEMORY     | <ul style="list-style-type: none"><li>▪ Digit Span Forward</li><li>▪ Digit Span Backward</li><li>▪ Trail Making Test Part A</li></ul>                                                                          |
| EPISODIC MEMORY    | <ul style="list-style-type: none"><li>▪ Auditory Verbal Learning Test</li></ul>                                                                                                                                |

# TRAIL MAKING TASK

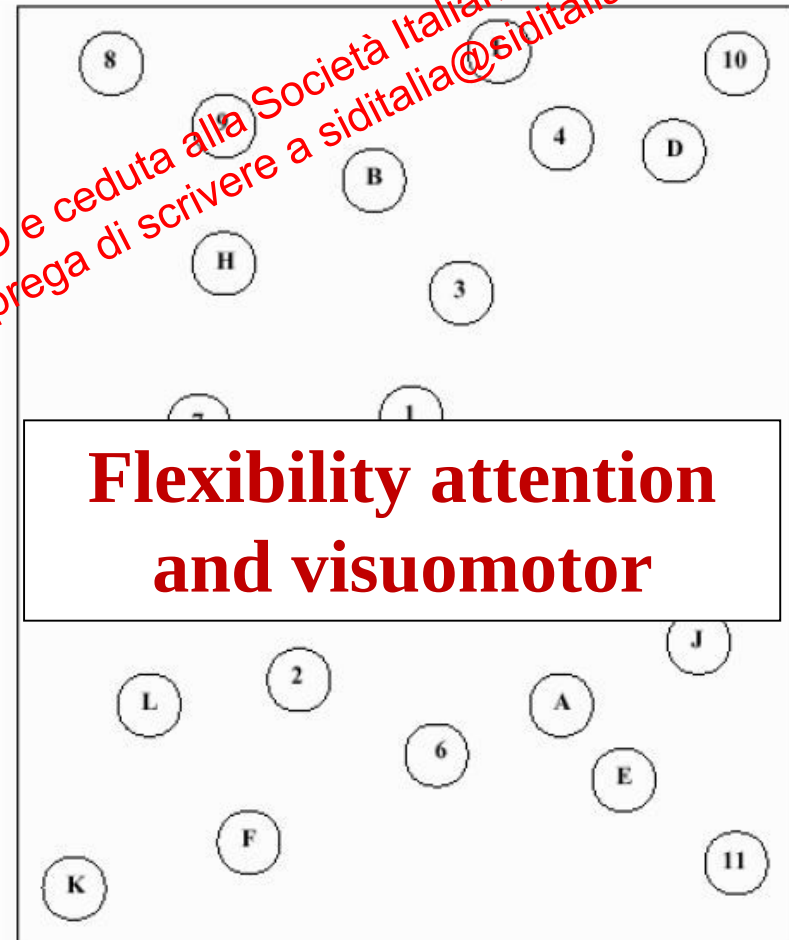
Influenced by: age, education , motor speed of the upper limbs and visual acuity

## TRAIL MAKING TEST - A



**Psychomotor speed**

## TRAIL MAKING TEST - B



**Flexibility attention  
and visuomotor**

Diapositiva preparata da GIUSEPPE PAOLISSO e ceduta alla Società Italiana di Diabetologia.  
Per ricevere la versione originale si prega di scrivere a [siditalia@siditalia.it](mailto:siditalia@siditalia.it)

# VERBAL FLEUNCY TEST

## ANIMAL NAMING

**Introduction:** "I'd like to ask a question to check your memory."

**Instruction:** "Tell me the names of as many animals as you can think of, as quickly as possible."

**Procedure:** Time for 60 seconds and record all responses.

If the person stops before 60 seconds, say "Any more animals?"

If the person says nothing for 15 seconds, say "A dog is an animal."

"Can you tell me more animals?"

- |           |           |
|-----------|-----------|
| 1. _____  | 12. _____ |
| 2. _____  | 13. _____ |
| 3. _____  | 14. _____ |
| 4. _____  | 15. _____ |
| 5. _____  | 16. _____ |
| 6. _____  | 17. _____ |
| 7. _____  | 18. _____ |
| 8. _____  | 19. _____ |
| 9. _____  | 20. _____ |
| 10. _____ | 21. _____ |
| 11. _____ | 22. _____ |

**Scoring:** Count the total number of animals (NOT including repetitions or non-animal words): \_\_\_\_\_

**Next step:** If the score is less than 14, further testing should be done.

| F | P | M |
|---|---|---|
|   |   |   |

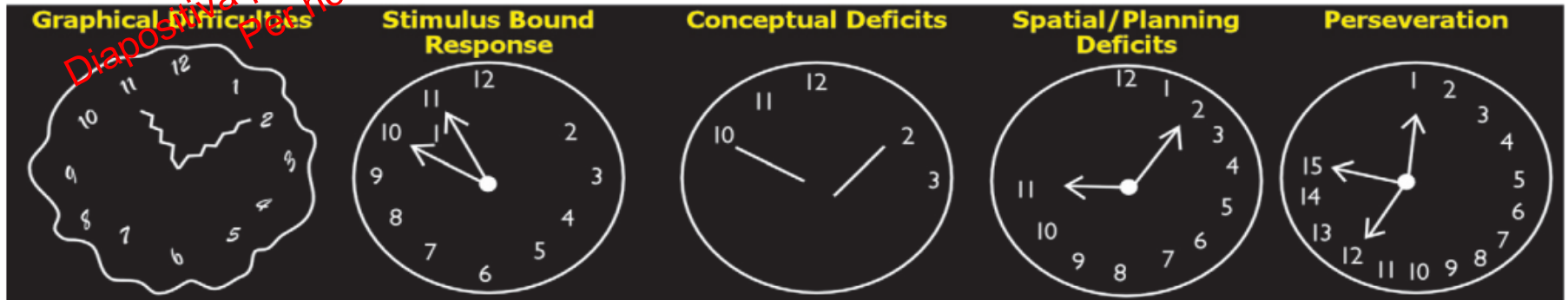
# CLOCK DRAWING TEST (CDT)

Clock Drawing Test. 3<sup>rd</sup> Edition. Oxford University Press 2006



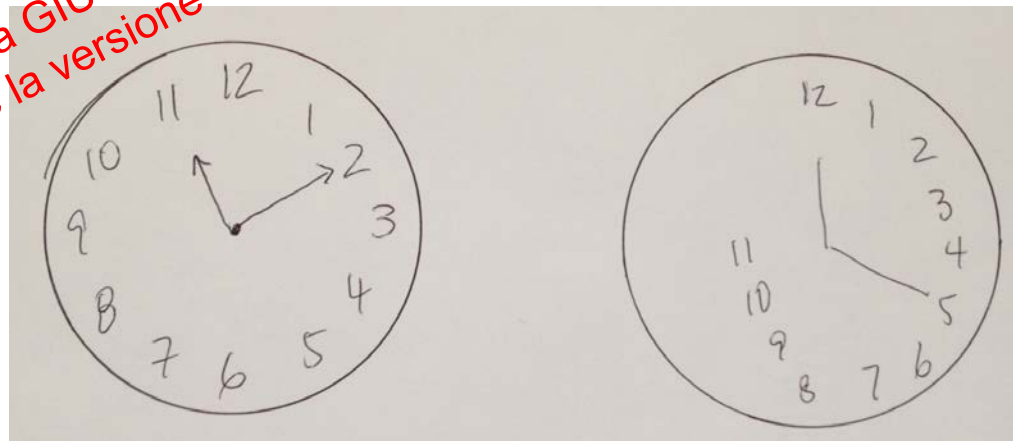
CDT was superior at identifying patients with cognitive dysfunction, compared with MMSE, a more widely used tool to evaluate cognitive dysfunction.

Diabetes Care. 2006 August ;



# IF CHOOSING TO USE INSULIN

- Clock drawing test can be used to predict who is likely to have problems with insulin therapy.
- “Write numbers on the blank clock face and draw hands on the clock to show 10 minutes past 11 o’clock”



# DIGIT SYMBOL SUBSTITUTION TEST

(J. Helmuth 1968)

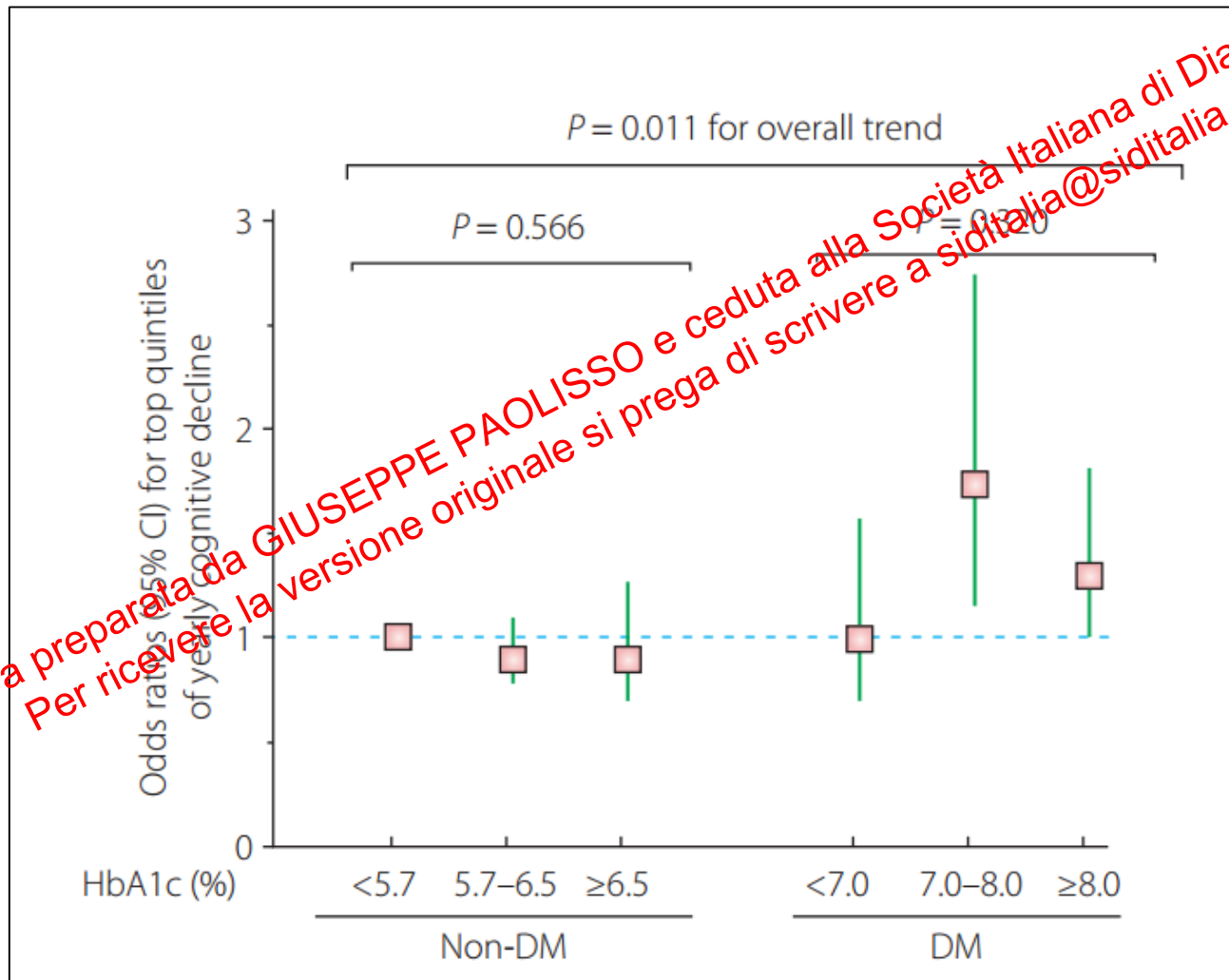
Digit symbol substitution test

|   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| ↔ | ↑ | ≡ |   | ≠ | □ | ○ | △ | ≡ |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | 9 | 2 | 9 | 4 | 9 | 4 | 9 | 1 | 8 | 9 | 1 | 7 | 2 | 3 | 6 | 4 | 8 | 3 | 1 | 7 | 8 | 2 | 5 |   |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 4 | 7 | 1 | 7 | 5 | 8 | 4 | 1 | 5 | 2 | 6 | 9 | 9 | 5 | 6 | 7 | 6 | 2 | 9 | 4 | 8 | 7 | 2 | 8 | 6 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 8 | 6 | 2 | 8 | 2 | 9 | 4 | 7 | 4 | 8 | 6 | 7 | 3 | 1 | 6 | 2 | 1 | 8 | 7 | 4 | 3 | 1 | 6 | 2 | 9 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 5 | 4 | 6 | 1 | 6 | 3 | 1 | 2 | 7 | 2 | 6 | 4 | 9 | 1 | 8 | 5 | 7 | 1 | 5 | 4 | 5 | 3 | 9 | 2 |   |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 3 | 9 | 7 | 1 | 7 | 1 | 3 | 5 | 7 | 6 | 1 | 6 | 5 | 9 | 1 | 3 | 1 | 3 | 9 | 8 | 9 | 7 | 3 | 4 | 3 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Diapositiva preparata da GIUSEPPE PAOLISSO e ceduta alla Società Italiana di Diabetologia.  
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# ASSOCIATION BETWEEN DIGIT SYMBOL SUBSTITUTION TEST (DSST) DECLINE AND GLYCOSYLATED HEMOGLOBIN A1C LEVELS



# GERIATRIC DEPRESSION SCALE

(Sheikh J.I., Yesavage J.A.,1986)

## Geriatric Depression Scale: Short Form

Choose the best answer for how you have felt over the past week:

1. Are you basically satisfied with your life? **YES** / NO
2. Have you dropped many of your activities and interests? **YES** / NO
3. Do you feel that your life is empty? **YES** / NO
4. Do you often get bored? **YES** / NO
5. Are you in good spirits most of the time? **YES** / NO
6. Are you afraid that something bad is going to happen to you? **YES** / NO
7. Do you feel happy most of the time? **YES** / NO
8. Do you often feel helpless? **YES** / NO
9. Do you prefer to stay at home, rather than going out and doing new things? **YES** / NO
10. Do you feel you have more problems with memory than most? **YES** / NO
11. Do you think it is wonderful to be alive now? **YES** / NO
12. Do you feel pretty worthless the way you are now? **YES** / NO
13. Do you feel full of energy? **YES** / NO
14. Do you feel that your situation is hopeless? **YES** / NO
15. Do you think that most people are better off than you are? **YES** / NO

Answers in **bold** indicate depression. Score 1 point for each bolded answer.

A score > 5 points is suggestive of depression.

A score ≥ 10 points is almost always indicative of depression.

A score > 5 points should warrant a follow-up comprehensive assessment.

Distribution of diabetic patients according to the severity of depression

|                     | Cases (n = 50) | Control (n = 30) | Significance  |
|---------------------|----------------|------------------|---------------|
| No depression       | 33 (66)        | 25 (83.3)        | $\chi^2=6.66$ |
| Mild depression     | 6 (12)         | 3 (10)           | $P=0.08$      |
| Moderate depression | 9 (18)         | 1 (3.3)          |               |
| Severe depression   | 4 (8)          | 1 (3.3)          |               |

Figures in parentheses are in percentage

Int J Diabetes Dev Ctries. 2009

Depression occurs more frequently in people with diabetes.

# FUNCTIONAL SCALES

## Katz Index of Independence in Activities of Daily Living

| Activities<br>Points (1 or 0)                                                                                                | Independence<br>(1 Point)                                                                                                                             | Dependence<br>(0 Points)                                                                                                                |
|------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                              | NO supervision, direction or personal assistance.                                                                                                     | WITH supervision, direction, personal assistance or total care.                                                                         |
| <b>BATHING</b><br>Points: _____                                                                                              | <b>(1 POINT)</b> Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity. | <b>(0 POINTS)</b> Need help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing |
| <b>DRESSING</b><br>Points: _____                                                                                             | <b>(1 POINT)</b> Get clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.      | <b>(0 POINTS)</b> Needs help with dressing self or needs to be completely dressed.                                                      |
| <b>TOILETING</b><br>Points: _____                                                                                            | <b>(1 POINT)</b> Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.                                                 | <b>(0 POINTS)</b> Needs help transferring to the toilet, cleaning self or uses bedpan or commode.                                       |
| <b>TRANSFERRING</b><br>Points: _____                                                                                         | <b>(1 POINT)</b> Moves in and out of bed or chair unassisted. Mechanical transfer aids are acceptable                                                 | <b>(0 POINTS)</b> Needs help in moving from bed to chair or requires a complete transfer.                                               |
| <b>CONTINENCE</b><br>Points: _____                                                                                           | <b>(1 POINT)</b> Exercises complete self control over urination and defecation.                                                                       | <b>(0 POINTS)</b> Is partially or totally incontinent of bowel or bladder                                                               |
| <b>FEEDING</b><br>Points: _____                                                                                              | <b>(1 POINT)</b> Gets food from plate into mouth without help. Preparation of food may be done by another person.                                     | <b>(0 POINTS)</b> Needs partial or total help with feeding or requires parenteral feeding.                                              |
| <b>TOTAL POINTS:</b> _____ <b>SCORING:</b> 6 = High ( <i>patient independent</i> ) 0 = Low ( <i>patient very dependent</i> ) |                                                                                                                                                       |                                                                                                                                         |

Source: *try this:* Best Practices in Nursing Care to Older Adults, The Hartford Institute for Geriatric Nursing, New York University, College of Nursing, [www.hartfordnig.org](http://www.hartfordnig.org).

## LAWTON - BRODY INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE (I.A.D.L.)

**Scoring:** For each category, circle the item description that most closely resembles the patient's highest functional level (either 0 or 1).

|                                                                                                               |   |                                                                                                                                         |   |
|---------------------------------------------------------------------------------------------------------------|---|-----------------------------------------------------------------------------------------------------------------------------------------|---|
| <b>A. Ability to Use Telephone</b>                                                                            |   | <b>E. Laundry</b>                                                                                                                       |   |
| 1. Operates telephone on own initiative-looks up and dials numbers, etc.                                      | 1 | 1. Does personal laundry completely                                                                                                     | 1 |
| 2. Dials a few well-known numbers                                                                             | 0 | 2. Launders small items-rinses stockings, etc.                                                                                          | 1 |
| 3. Answers telephone but does not dial                                                                        | 0 | 3. All laundry must be done by others                                                                                                   | 0 |
| 4. Does not use telephone at all                                                                              | 0 |                                                                                                                                         |   |
| <b>B. Shopping</b>                                                                                            |   | <b>F. Mode of Transportation</b>                                                                                                        |   |
| 1. Takes care of all shopping needs independently                                                             | 1 | 1. Travels independently on public transportation or drives own car                                                                     | 1 |
| 2. Shops independently for small purchases                                                                    | 0 | 2. Arranges own travel via taxi, but does not otherwise use public transportation                                                       | 1 |
| 3. Needs to be accompanied on any shopping trip                                                               | 0 | 3. Travels on public transportation when accompanied by another                                                                         | 1 |
| 4. Completely unable to shop                                                                                  | 0 | 4. Travel limited to taxi or automobile with assistance of another                                                                      | 0 |
|                                                                                                               |   | 5. Does not travel at all                                                                                                               | 0 |
| <b>C. Food Preparation</b>                                                                                    |   | <b>G. Responsibility for Own Medications</b>                                                                                            |   |
| 1. Plans, prepares and serves adequate meals independently                                                    | 1 | 1. Is responsible for taking medication in correct dosages at correct time                                                              | 1 |
| 2. Prepares adequate meals if supplied with ingredients                                                       | 0 | 2. Takes responsibility if medication is prepared in advance in separate dosage                                                         | 0 |
| 3. Heats, serves and prepares meals, or prepares meals, or prepares meals but does not maintain adequate diet | 0 | 3. Is not capable of dispensing own medication                                                                                          | 0 |
| 4. Needs to have meals prepared and served                                                                    | 0 |                                                                                                                                         |   |
| <b>D. Housekeeping</b>                                                                                        |   | <b>H. Ability to Handle Finances</b>                                                                                                    |   |
| 1. Maintains house alone or with occasional assistance (e.g. "heavy work domestic help")                      | 1 | 1. Manages financial matters independently (budgets, writes checks, pays rent, bills, goes to bank), collects and keeps track of income | 1 |
| 2. Performs light daily tasks such as dish washing, bed making                                                | 1 | 2. Manages day-to-day purchases, but needs help with banking, major purchases, etc.                                                     | 1 |
| 3. Performs light daily tasks but cannot maintain acceptable level of cleanliness                             | 1 | 3. Incapable of handling money                                                                                                          | 0 |
| 4. Needs help with all home maintenance tasks                                                                 | 1 |                                                                                                                                         |   |
| 5. Does not participate in any housekeeping tasks                                                             | 0 |                                                                                                                                         |   |
| <b>Score</b>                                                                                                  |   | <b>Score</b>                                                                                                                            |   |
|                                                                                                               |   | <b>Total score</b> _____                                                                                                                |   |

A summary score ranges from 0 (low function, dependent) to 8 (high function, independent) for women and 0 through 5 for men to avoid potential gender bias.

Source: *try this:* Best Practices in Nursing Care to Older Adults, The Hartford Institute for Geriatric Nursing, New York University, College of Nursing, [www.hartfordnig.org](http://www.hartfordnig.org).

# NEUROIMAGING STUDIES

- Structural MRI (magnetic resonance imaging) studies have consistently reported an association between T2D and cortical and subcortical cerebral atrophy among older adults.
- The association between T2D and cerebral infarcts in structural MRI studies is also relatively consistent across studies.

# Brain imaging in patients with Diabetes

Meta-analysis of 46 studies using MRI and/or CT

## 1. Cortical atrophy (10 studies);

**MRI findings in association with Type 2 diabetes**

113 DM2  
51 controls WMLs, cortical and subcortical atrophy are associated with cognitive decline

Cognitive dysfunction correlated to WML and brain atrophy. A1C was 6.9% (moderately well-controlled)

122 DM2  
56 controls WMLs, atrophy are associated with cognitive decline; pathology and other factors show interactions

Cognitive dysfunction correlated with WML, atrophy, hypertension, hyperinsulinemia, and "vascular events"; statin use was associated with improved WMLs and with improved cognition

92 DM2  
44 controls PVH, WMLs, lacunar infarcts, and cerebral atrophy observed; only PVH was associated with "motor slowing"

MRI findings less well associated with cognitive dysfunction in relation to HbA1C and duration of diabetes, which showed stronger correlation with cognitive dysfunction

40 DM1  
4 DM2 DM2 patients have more WMLs and cortical atrophy than controls; DM1 patients with much longer disease duration

DM2 patients had more cognitive dysfunction but also more of other metabolic aspects including more hypertension, lipid disorders, etc.

22 DM2  
56 controls WMLs, atrophy, which were not correlated with peripheral neuropathy within given patients

Authors conclude that CNS and PNS pathology of DM2 may be unrelated because of discrepancies within individuals

95 DM2 "White matter hyperintensities" in various areas correlated with declines in cognitive domains

Memory and "mental speed" deficits were associated most strongly with white matter hyperintensities in parietal lobe and thalamus

## 2. Lacunar infarcts (20 studies)

## 3. White matter lesions (27 studies)- some but not all studies show a positive correlation;

# Brain Atrophy in Type 2 Diabetes

Regional distribution and influence on cognition

## Associations between T2DM and MRI measures

| MRI measures                       | T2DM<br>(n = 350) | No T2DM<br>(n = 363) | Association of<br>T2DM with MRI measures <sup>1</sup> | P value for<br>regression |
|------------------------------------|-------------------|----------------------|-------------------------------------------------------|---------------------------|
| Gray matter<br>volume (mL)         | 579.9 (66.9)      | 583.4 (63.1)         | −13.1 (−18.7 to −7.6)                                 | <0.001                    |
| Right hippocampal<br>volume (mL)   | 2.32 (0.47)       | 2.77 (0.50)          | −0.47 (−0.54 to −0.40)                                | <0.001                    |
| Left hippocampal<br>volume (mL)    | 2.22 (0.44)       | 2.61 (0.48)          | −0.41 (−0.48 to −0.33)                                | <0.001                    |
| Total hippocampal<br>volume (mL)   | 4.54 (0.86)       | 5.38 (0.91)          | −0.88 (−1.01 to −0.75)                                | <0.001                    |
| White matter<br>volume (mL)        | 454.8 (62.1)      | 456.2 (55.5)         | −6.14 (−11.9 to −0.42)                                | 0.05                      |
| White matter lesion<br>volume (mL) | 6.04 (6.99)       | 7.40 (8.0)           | 0.59 (−0.54 to 1.71)                                  | 0.32                      |
| Infarct yes/no (%) <sup>a,b</sup>  | 75 (21)           | 58 (16)              | 0.62 (0.21 to 1.04)                                   | 0.001                     |
| Microbleed yes/no (%)              | 14 (4)            | 22 (6)               | −0.25 (−0.97 to 0.46)                                 | 0.41                      |

Data are mean (SD) and 95% CI. <sup>1</sup>Adjusted for age, sex, and total intracranial volume. <sup>a</sup>Not adjusted for total intracranial volume. <sup>b</sup>Not adjusted for stroke history.

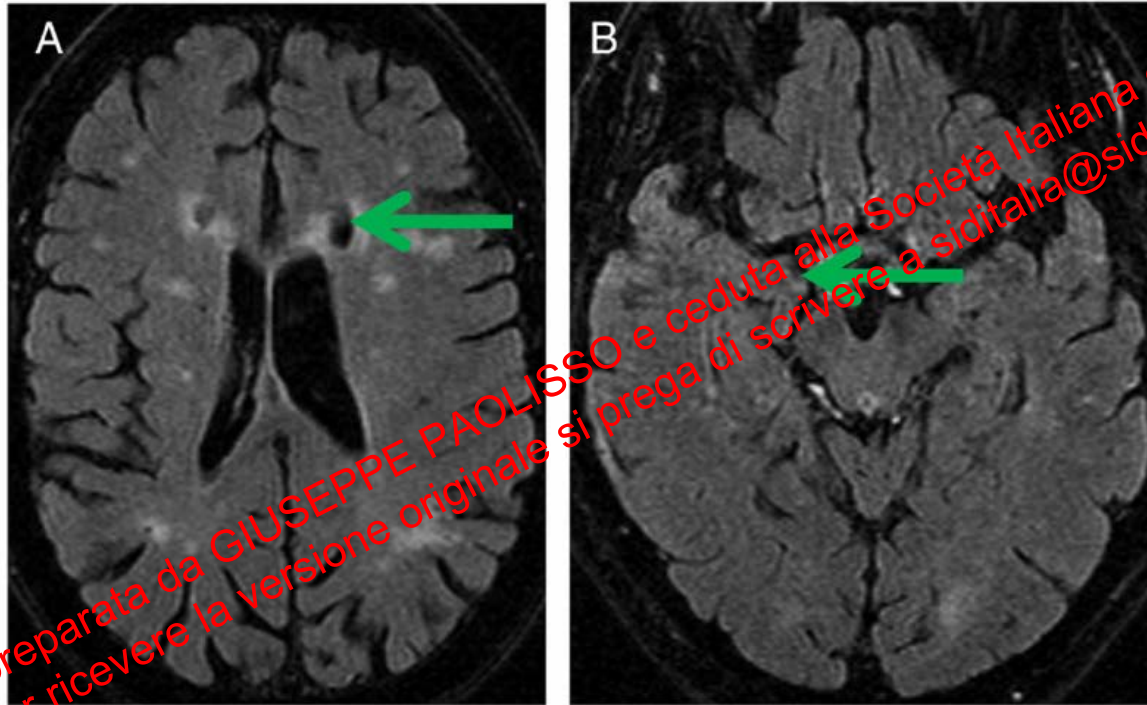
Cross-sectional study, participants ≥55 years of age with T2DM.

- Cortical atrophy in T2DM resembles patterns seen in preclinical Alzheimer disease.
- Neurodegeneration rather than cerebrovascular lesions may play a key role in T2DM-related cognitive impairment.

- Type 1 and type 2 diabetes are consistently have been associated with global brain atrophy in cross-sectional studies.
- Results showed an association between decreased brain volume and slowing of information processing speed, reduced attention and lower IQ subtest scores.

Diapositiva preparata da GIUSEPPE PAOLISSO e ceduta alla Società Italiana di Diabetologia  
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# Hippocampal atrophy – Lacunar frontatl cortex



- Hippocampal atrophy seems to be a more prominent feature of type 2 diabetes than of type 1.

# TAKE HOME MESSAGES

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The cognitive dysfunction in patients with diabetes is associated with poor glycaemic control—especially in the case of **impaired executive function**—with an increased frequency of hospital admissions and with an increased occurrence of severe hypoglycaemic episodes.

Therefore, diagnosis of cognitive impairment should be a reason for the diabetes care provider to reassess the patient's capacities for selfmanagement and treatment adherence, and to consider additional measures.

Lin CH,. *J Intern Med* 2013;

Munshi M. *Diabetes Care* 2006;

# GRAZIE PER L'ATTENZIONE

