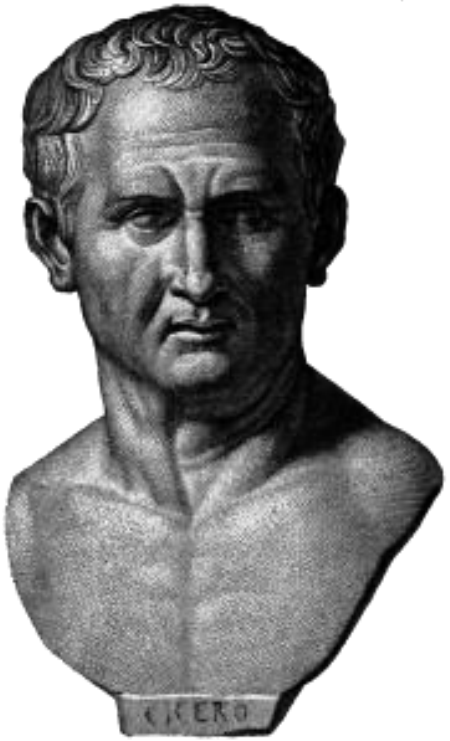
*60° Congresso della Società Italiana di Gerontologia e Geriatria*

# Palestra Cognitiva: Brain Training ed Attività Fisica

***Nicola Ferrara, MD***
***Dipartimento di Scienze Mediche Traslazionali***
***Università degli Studi di Napoli «Federico II»***
***Presidente della Società Italiana di Gerontologia e Geriatria***

# Much has been written over the ages about the benefits of physical activity…

**Marcus Tullius Cicero (106-65 BC):** "It is exercise alone that supports the spirits, and keeps the mind in vigor"



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**John Adams (1760-1829):** "Exercise invigorates, and enlivens all the faculties of body and of mind . . . It spreads a gladness and satisfaction over our minds and qualifies us for every sort of business, and every sort of pleasure"

"Le vecchie menti sono come i vecchi cavalli; le devi tenere in esercizio se vuoi che siano sempre pronte a lavorare."

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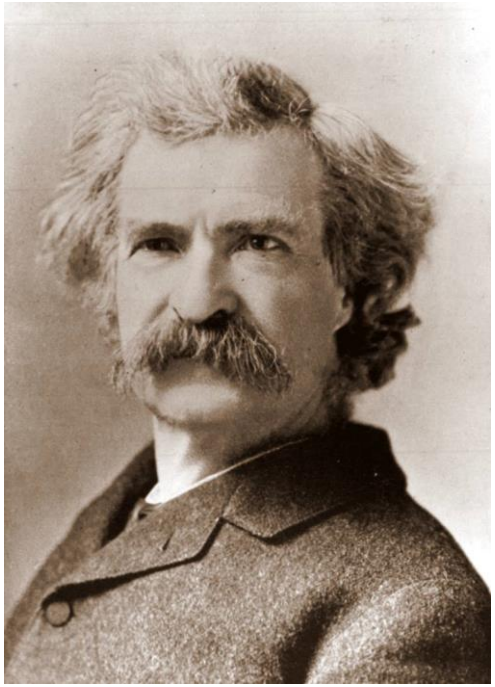
**Mark Twain (1835-1910):** "I take my only exercise acting as Pallbearer at the funerals of my friends who exercise regularly"

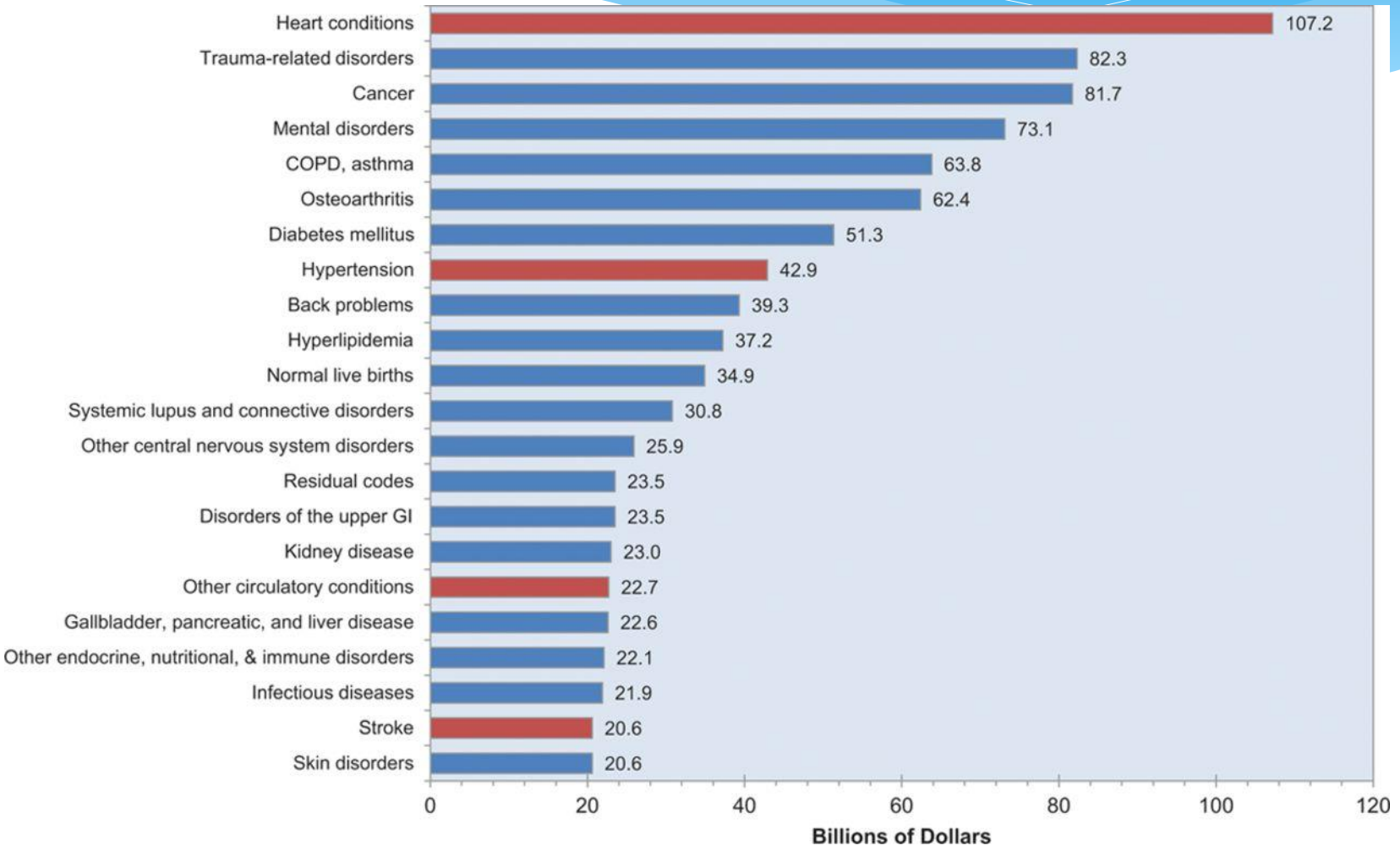


# Much has been written over the ages about the benefits of physical activity…

**Henry Ford (1863-1947):** "Exercise is bunk. If you are healthy, you don't need it, and if you are sick, you shouldn't take it"

# DIMENSIONE DEL PROBLEMA

# The 22 leading diagnoses for direct health expenditures, United States, 2010 (in billions of dollars).




**Alan S. Go et al. Circulation. 2014;129:e28-e292**

American Heart Association.

# Osservatorio Geriatrico Campano

**Table 2 Characteristics of the population selected to study the relationship between blood pressure and cognitive impairment (n = 1106) stratified by age**

| Variables | Age range (years) 65–74 (n = 717) | 75–84 (n = 312) | ⩾ 85 (n = 77) |
|---|---|---|---|
| Number of women (%) | 384 (53.5) | 174 (55.8) | 56 (72.4) |
| Educational level | 3.6 ± 1.4 | 3.1 ± 1.5* | 3.0 ± 1.6† |
| Percentage with MMSE < 24 | 19.2 | 24.5* | 34.4‡ |
| GDS score | 9.8 ± 6.3 | 12.2 ± 6.0* | 13.1 ± 6.4† |
| SBP (mmHg) | 143.8 ± 18.4 | 147.1 ± 19.3* | 148.3 ± 20.9† |
| DBP (mmHg) | 82.3 ± 9.1 | 81.5 ± 9.2 | 81.7 ± 8.8 |

Values of variables other than women and MMSE are expressed as means ± SD. MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure. *$P < 0.01$, 75–84 versus 65–74 years; †$P < 0.01$, ⩾ 85 versus 65–74 years; ‡$P < 0.01$, ⩾ 85 versus 75–84 years.

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| Diagnosis | Age (years) | | | | | | | | | |
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| **Men** | | | | | | | | | | |
| | | | | | | | | | | |
| AACD | 31 | 7.1 | 39 | 9.5 | 46 | 11.2 | 40 | 12.9 | 156 | 10.0 |
| AACD-3* | 72 | 16.6 | 75 | 18.3 | 83 | 20.1 | 57 | 18.4 | 287 | 18.3 |
| ND-N** | 89 | 20.5 | 62 | 15.2 | 72 | 17.5 | 41 | 13.3 | 264 | 16.9 |
| SCC-NI*** | 9 | 2.1 | 5 | 1.2 | 10 | 2.4 | 5 | 1.6 | 29 | 1.9 |
| | | | | | | | | | | |
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*Individuals with cognitive impairment without dementia fulfilling only 3 of the 5 AACD criteria.
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**Scafato E et al. Aging Clin Exp Res 2010**

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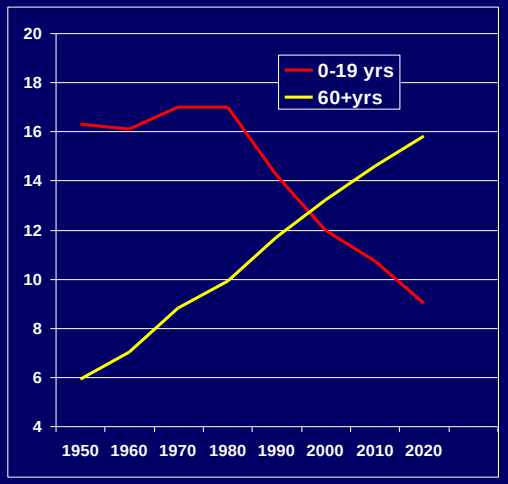
# Le previsioni epidemiologiche
# Età – Deficit Cognitivo

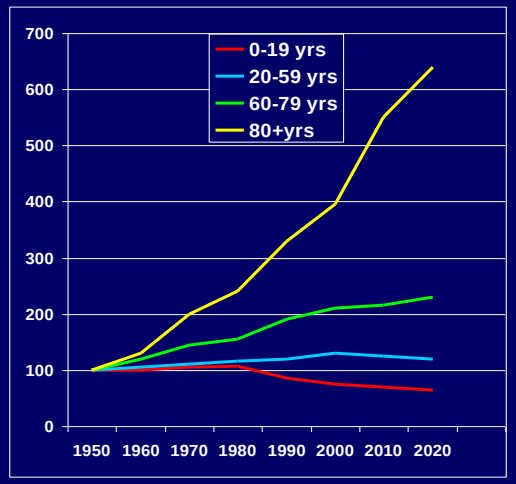
- Ad oggi si stima che 1 ultra-65 enne su 3 ha disturbi della sfera cognitiva.

- L’aumento della quota di ultra-85enni potrebbe modificare questo rapporto ad 1:2 visto l’aumento di questa fascia di popolazione.

## Young and Elderly Italian Population (milions) 1950-2020

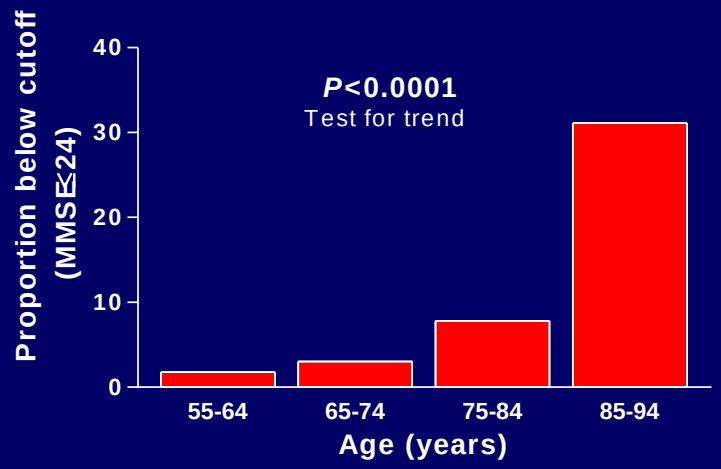



## Evolution of Italian Population by Age Class 1950-2020



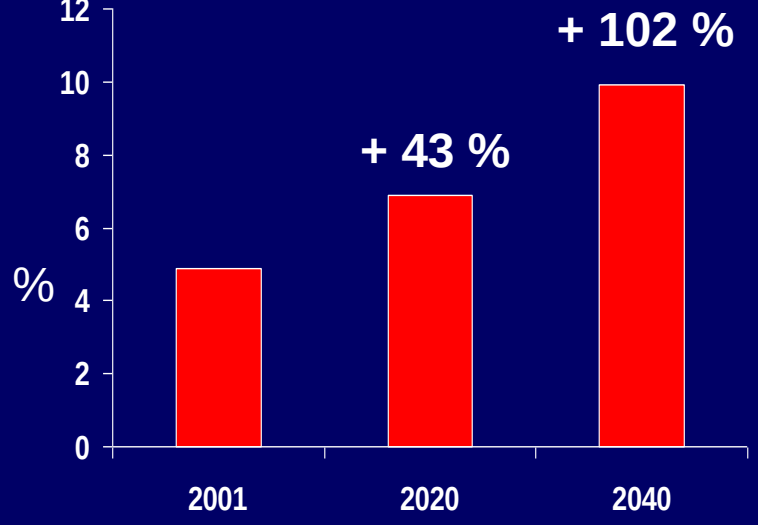

*modified by ONU, 1993*

## Characteristics of distribution of cognitive function among subjects aged 55 to 94 years according to age. THE ROTTERDAM STUDY



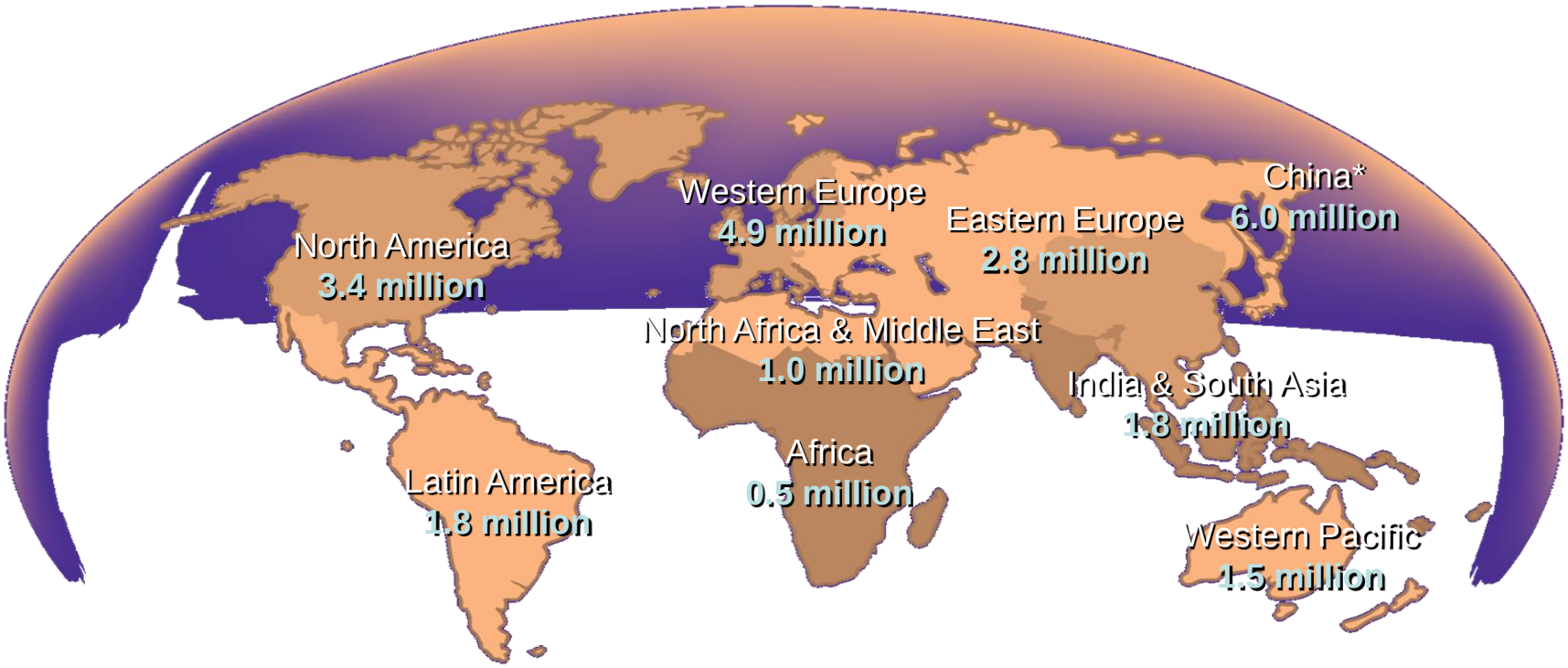

*Breteler MMB et al. BMJ 1994*

## Malattia di Alzheimer: modifica dei pattern epidemiologici nei paesi Europei 2000-2040

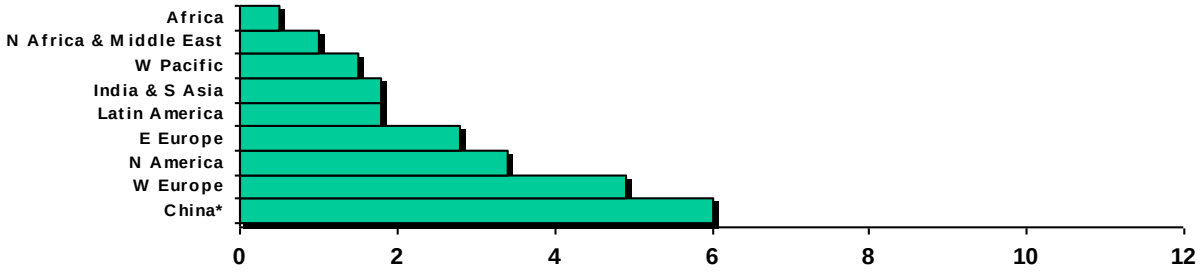



*Lancet 2005*

# Epidemiologia

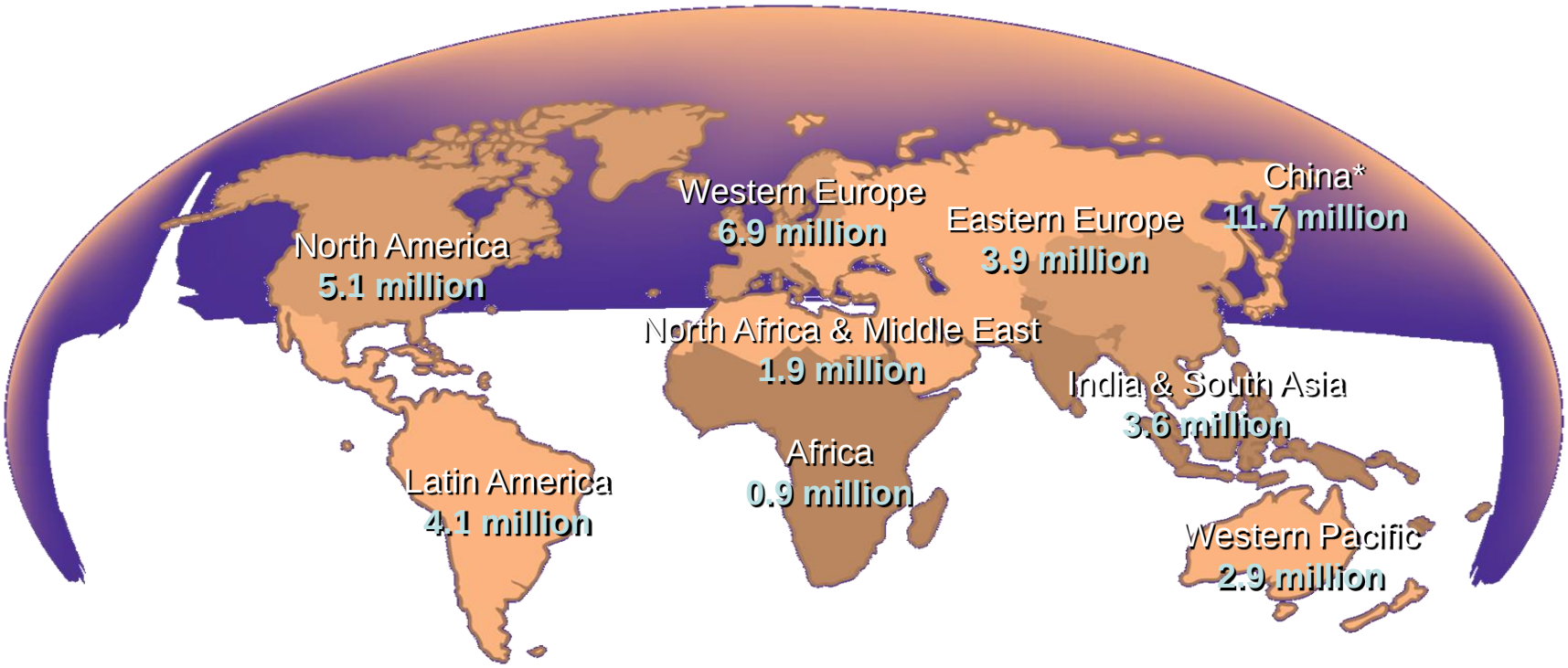



**2001** Total in all WHO regions: **24.3 million**

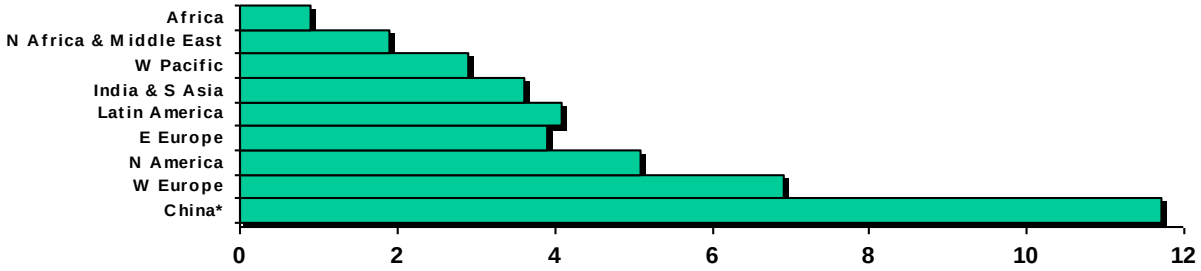



* & Developing Western Pacific Region. From Ferri et al, *Lancet* 2005;366:2112–2117.

# Epidemiologia




**2020** Predicted total in all WHO regions: **42.3 million**

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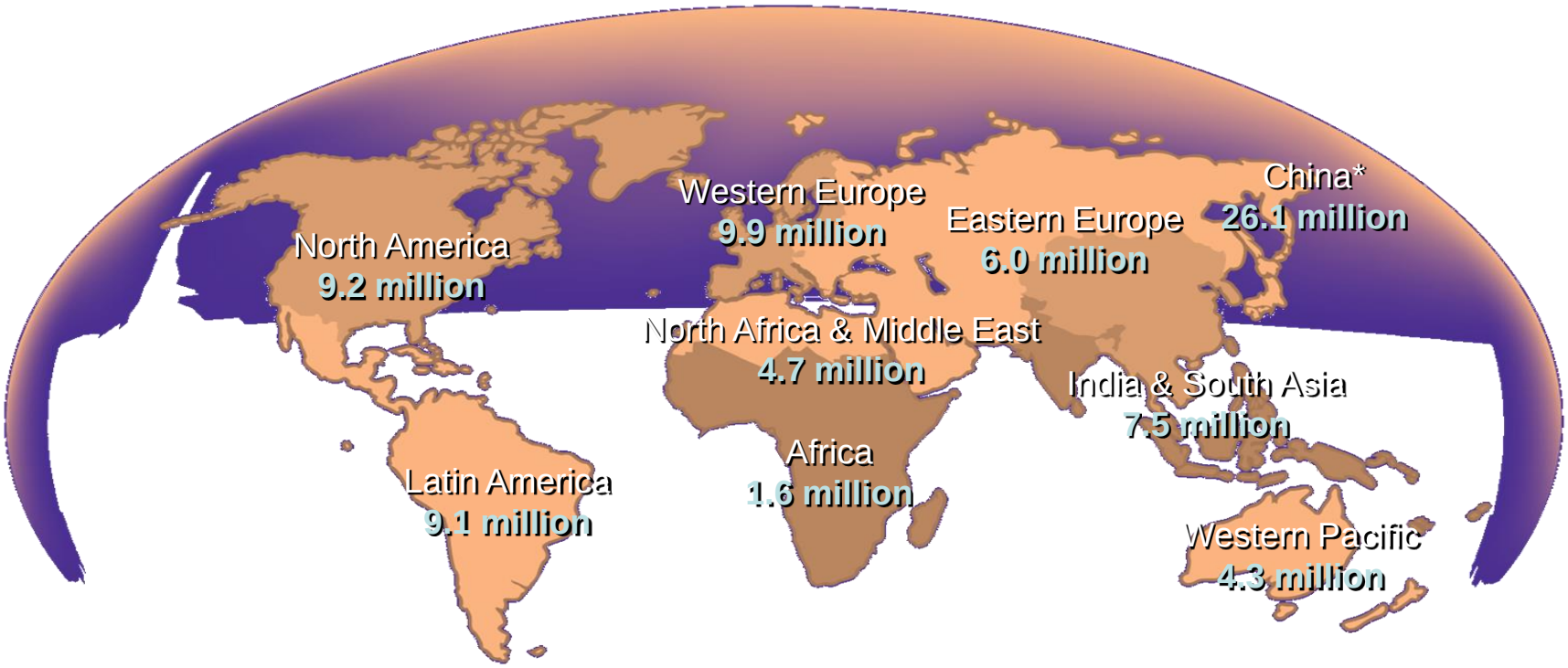
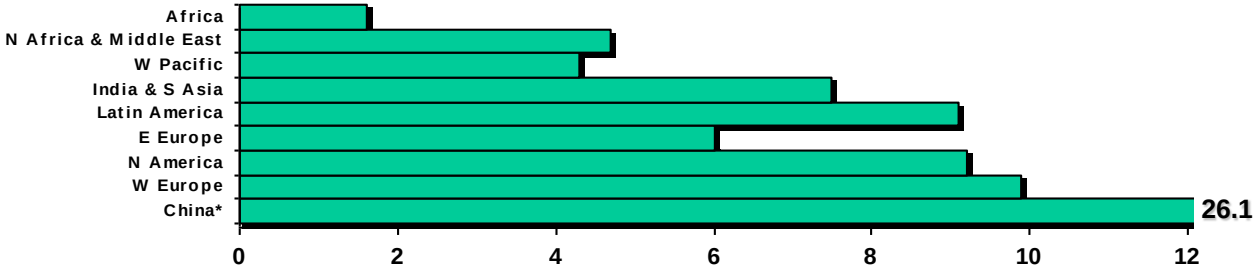



**2040** Predicted total in all WHO regions: **81.1 million**

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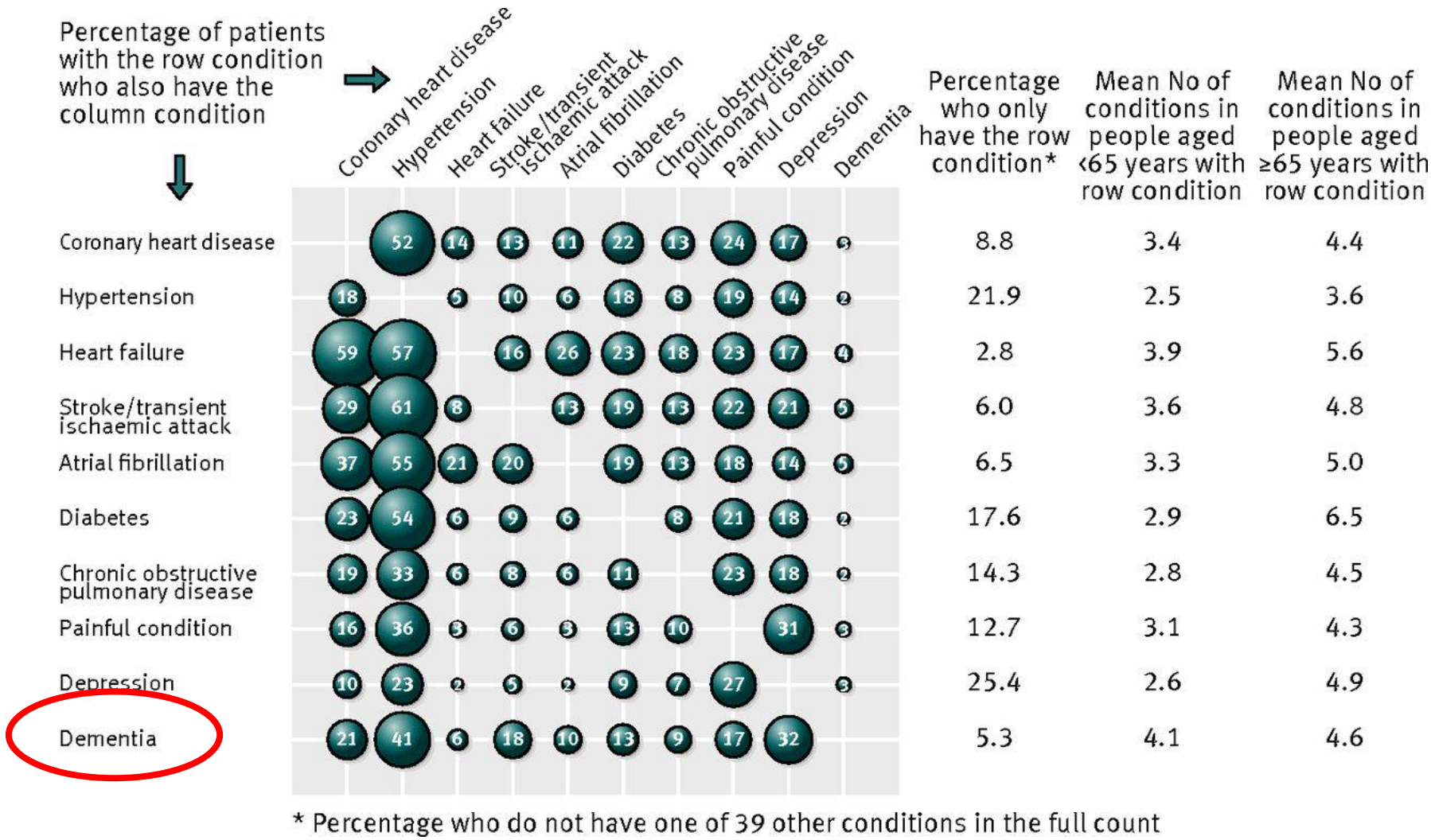
# Incidenza della demenza

| ILSA - CNR [Italian Longitudinal Study on Aging] | | | |
|---|---|---|---|
| **Età** | **Maschi** | **Femmine** | **Totale** |
| 65-69 | 4,1 | 3,8 | 4,0 |
| 70-74 | 5,8 | 9,9 | 7,7 |
| 75-79 | 13,7 | 21,6 | 17,4 |
| 80-84 | 32,1 | 27,3 | 29,9 |
| Totale | 10,3 | 13,3 | 11,9 |
| | | | (9,9-13,9) |

Questi dati di incidenza comportano una stima di circa **96.000 nuovi casi di demenza ogni anno** nella popolazione anziana italiana.

# Comorbidity of 10 common conditions

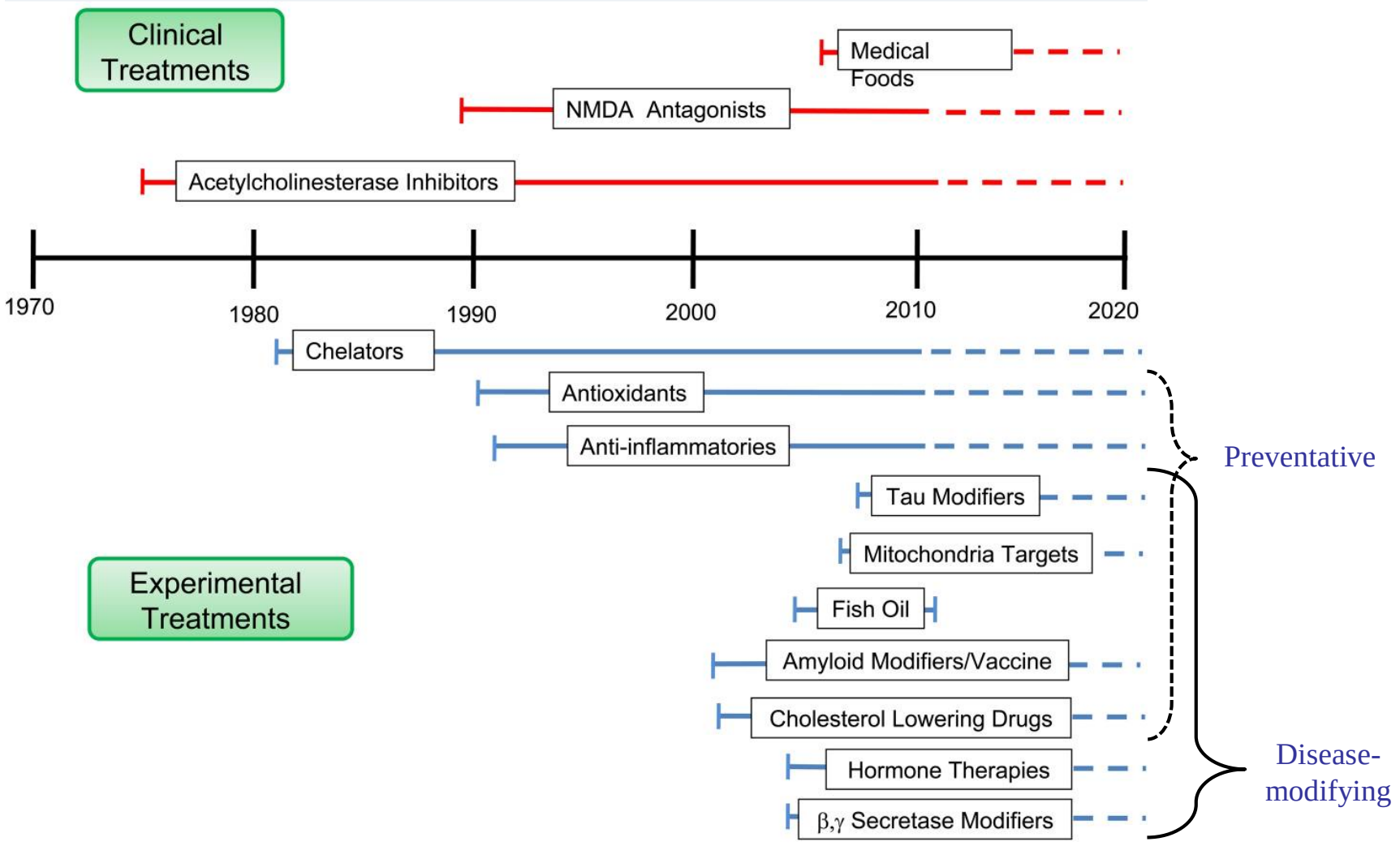



* Percentage who do not have one of 39 other conditions in the full count

Guthrie B et al. BMJ 2012;345:bmj.e6341

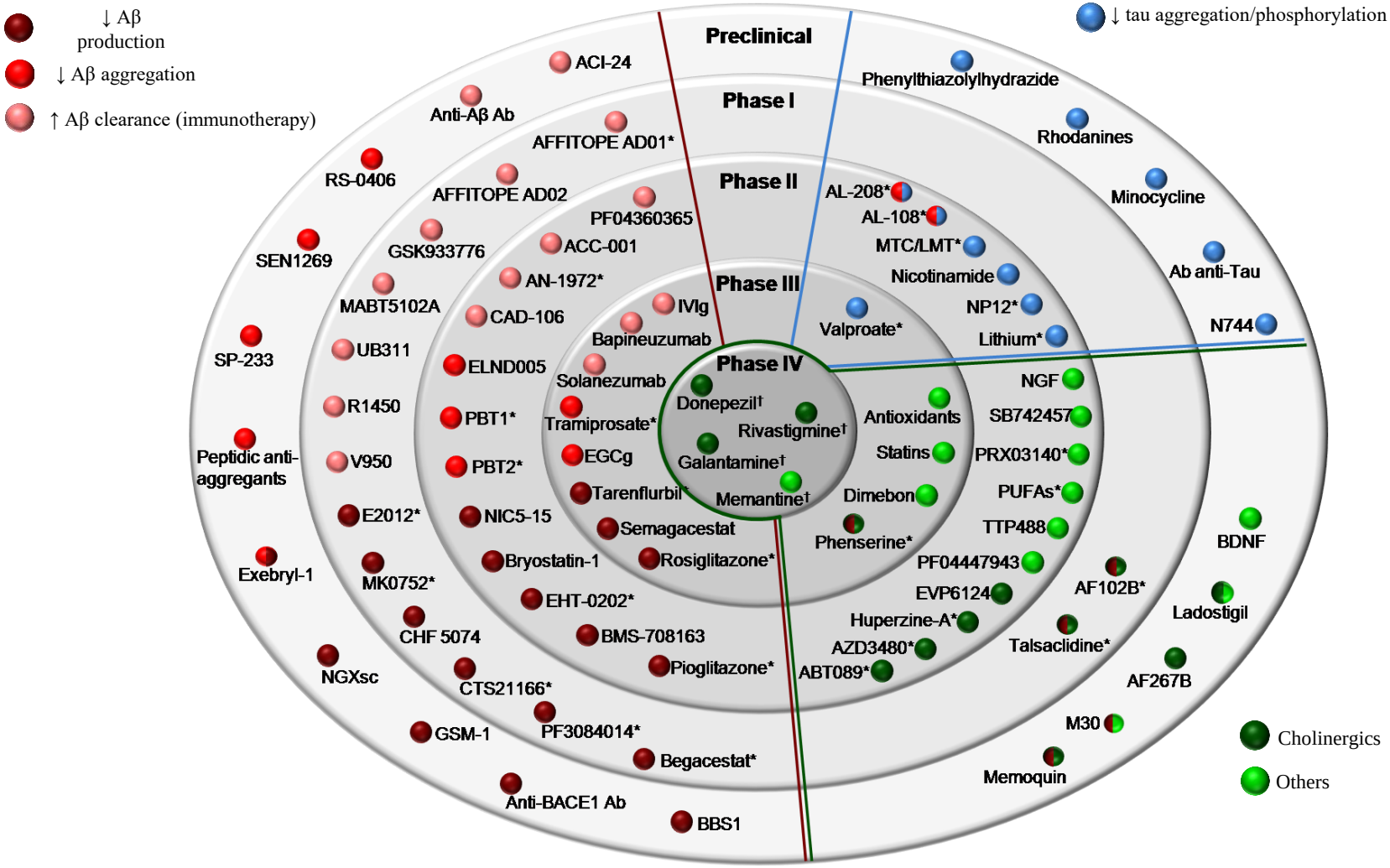
BMJ

# Pharmacological treatment of AD




Stone JG, Casadesus G, Gustaw-Rothenberg K, et al. Frontiers in Alzheimer's disease therapeutics. Ther Adv Chronic Dis 2011; 2 (1): 9-23

# Drug development in AD




Mangialasche F Lancet Neurol 2010; 9: 702-16

# The Diagnosis and Management of Mild Cognitive Impairment A Clinical Review

| Source | Patients: No. | Patients: Characteristics | Patients: Mean Age, y | Intervention | Trial Length | Primary Outcomes |
|---|---|---|---|---|---|---|
| **Pharmacologic Treatments**[a] | | | | | | |
| Salloway et al,[42] 2004 | 270 | Adults with MCI | 72 | Donepezil, 10 mg/d vs placebo | 24 wk | No significant differences between treatment groups in the 2 primary outcomes: New York University Paragraph Delayed Recall test and the ADCS-CGIC-MCI.[b] |
| Petersen et al, 2005[43] | 769 | Adults with amnestic MCI | 73 | Donepezil, 10 mg/d vs 2000 IU/d of vitamin E vs placebo | 3 y | Compared with placebo, there were no significant differences in the probability of progression to Alzheimer disease in the vitamin E group (HR, 1.02; 95% CI, 0.74-1.41; *P* = .91) or the donepezil group (HR, 0.80; 95% CI, 0.57-1.13; *P* = .42). |
| Doody et al,[44] 2009 | 821 | Adults with amnestic MCI | 70 | Donepezil, 10 mg/d vs placebo | 48 wk | The dual primary efficacy end point was not reached. At 48 weeks, there was a small, significant decrease in modified ADAS-cog[b] (−0.90 [SE, 0.37]) favoring donepezil (*P* = .01). Changes in CDR-SB scores[b] were minimal and not significantly different between treatment groups. |
| Koontz and Baskys,[45] 2005 | 19 | Men with MCI | 71 | Galantamine, 12 mg twice daily vs placebo | 16 wk | The primary outcome was the CANTAB.[b] At 16 weeks, only 1 of the 6 subtests of the CANTAB (stockings of Cambridge test)[b] differed significantly between galantamine and placebo groups (mean [SD], 8.3 [1.9] vs 7.0 [1.4]; *P* = .02). |

No medications have proven effective for MCI; treatments and interventions should be aimed at reducing cardiovascular risk factors and prevention of stroke. Aerobic exercise, mental activity, and social engagement may help decrease risk of cognitive decline.

*Langa KM JAMA 312: 2551-2561, 2014*

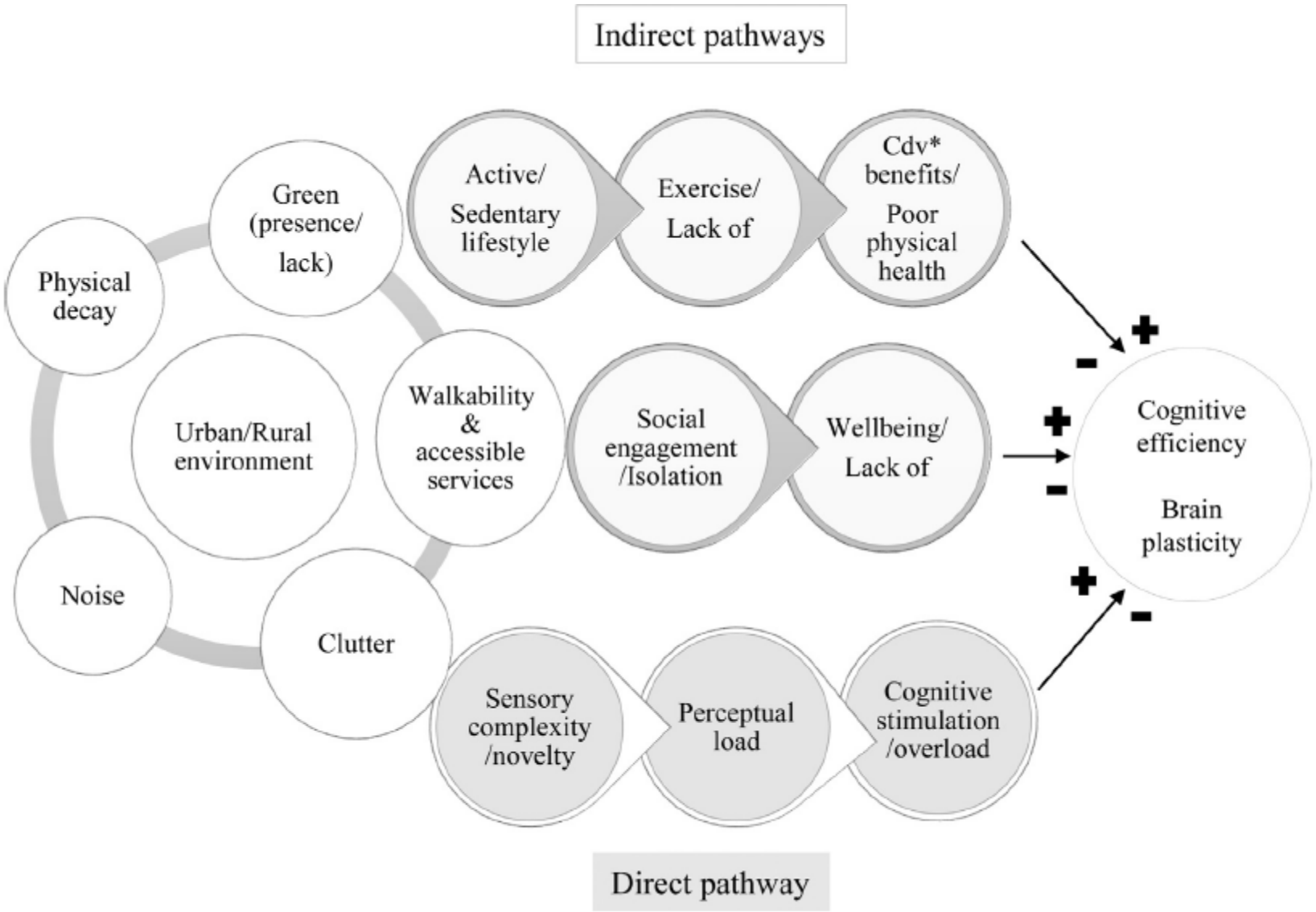
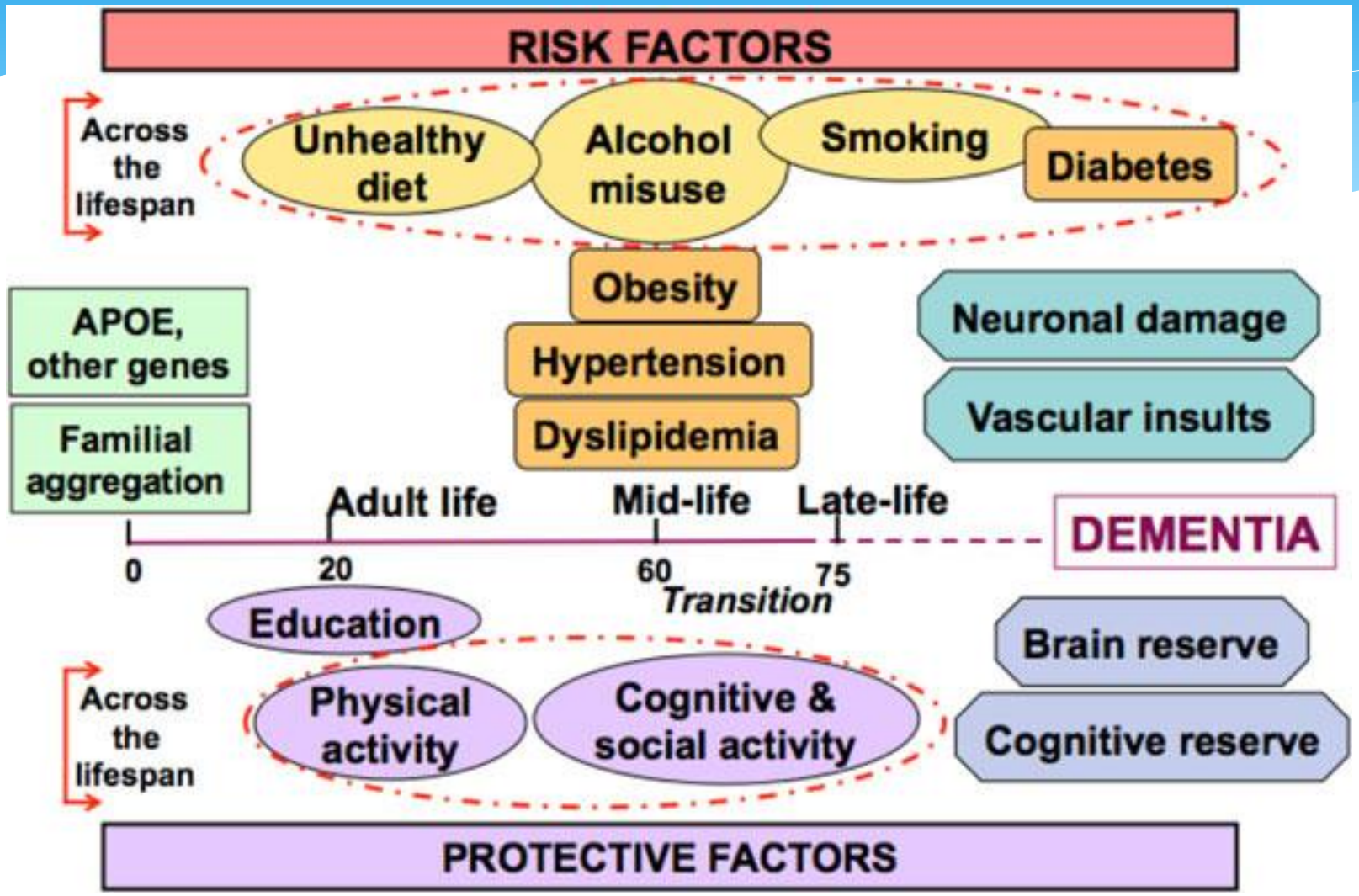



**Fig. 1.** Examples of direct and indirect associations between environment and cognition.

* Cardiovascular.

# Risk factors for dementia and Alzheimer's disease across the lifespan

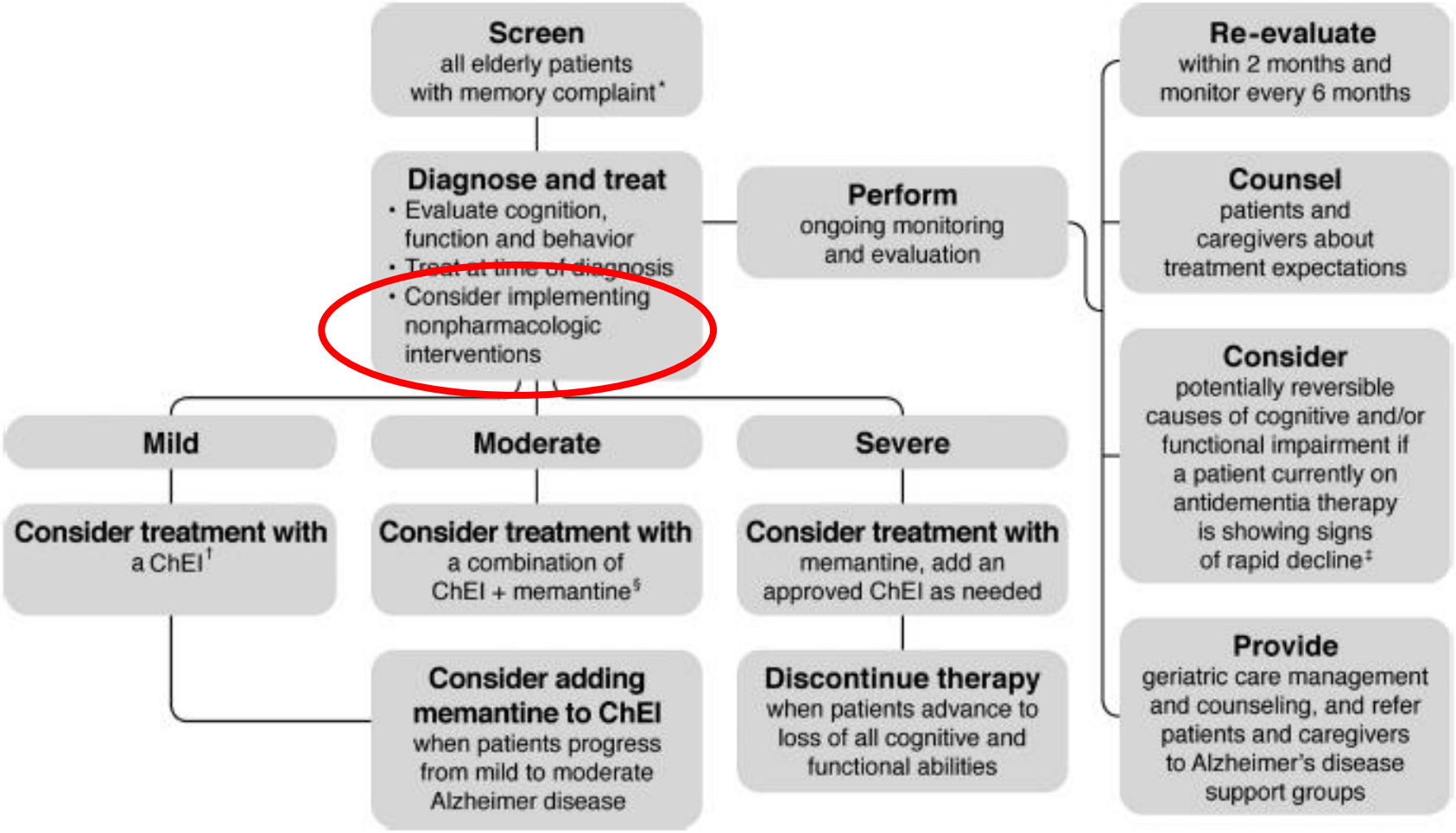



Sindi et al. F1000Prime Rep. 2015;7:50.

CLINICAL REVIEW

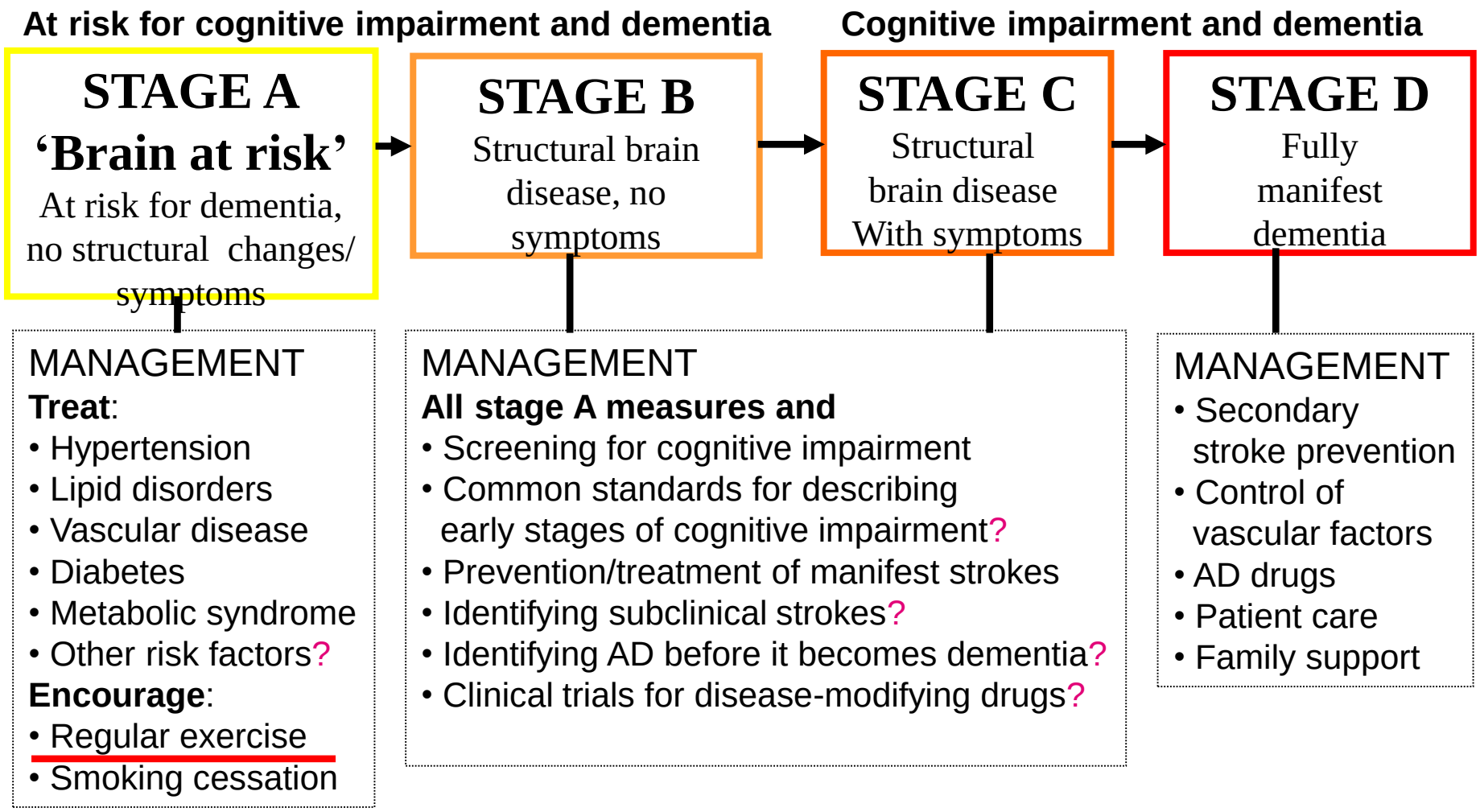
# Guidelines for the Management of Cognitive and Behavioral Problems in Dementia

*Carl H. Sadowsky, MD, and James E. Galvin, MD, MPH*




J Am Board Fam Med 2012; 25:350-366

# Therapeutic options for AD




*Kivipelto and Solomon, Neurology 2009*

# Brian Training and Cognitive Impairment

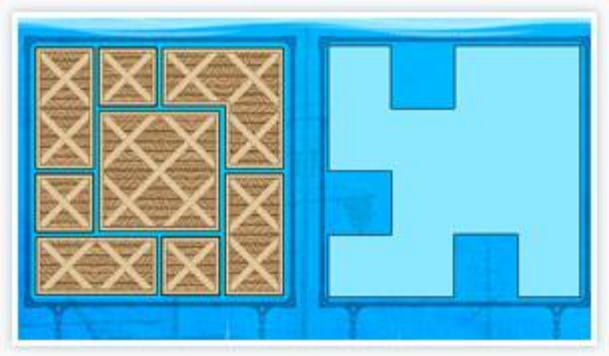
# Brain Test Britain

***the largest ever study into computer-based brain training***

# Brain Test Britain – partecipants

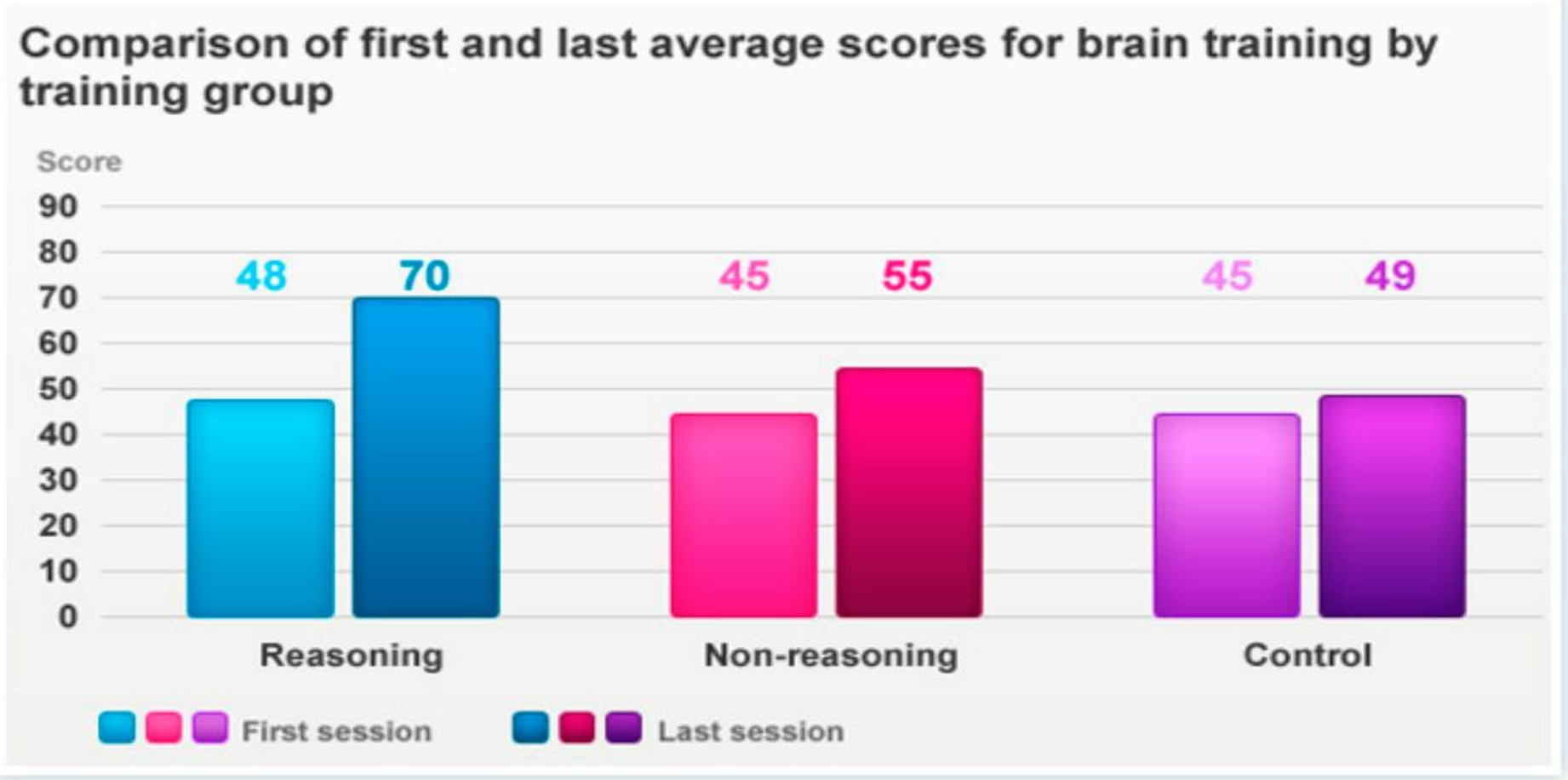
* **67,186 people (7 Sept to 25 November 2009)**
* **57.6% of Brain Test Britain participants were women**
* **Participants had generally reached a high level of education, The average age of people signing up to take part was 43**
* **Older trainers were more likely to complete more training sessions than younger trainers**

# Reasoning brain training

# Non-reasoning brain training


# Brain Test Britain is the largest ever study into computer-based brain training



Journal of Applied Gerontology
2015, Vol. 34(3) NP166–NP189

DOI: 10.1177/0733464812470747
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# Gaming for Health: A Systematic Review of the Physical and Cognitive Effects of Interactive Computer Games in Older Adults

## Abstract

This systematic review examined the physical and cognitive effects of physically based interactive computer games (ICGs) in older adults. Literature searching was carried out from January 2000 to June 2011. Eligible studies were trials involving older adults (>65 years) describing the effects of ICGs with a physical component (aerobic, strength, balance, flexibility) on physical or cognitive outcomes. Secondary outcomes included adverse effects, compliance, and enjoyment. Twelve trials met the inclusion criteria. ICG interventions varied in terms of software, game type, and nature of the computer interaction. Although there was preliminary evidence that ICG is a safe and effective exercise intervention for older adults, the dearth of high-quality evidence limits this finding. No major adverse effects were reported and two studies reported minor events. ICG could be improved further by tailoring interventions for older adults; in particular, they should aim to optimize participant safety, motivation, and enjoyment for this population.

Evid Rep Technol Assess (Full Rep). 2010;(193):1-727.

# Cognitive activities and risk of cognitive decline

| Study | Sample (n) | Followup | Exposure | Case definition | Confounding adjustment | Results |
|---|---|---|---|---|---|---|
| Yu et al., 2009[335] | Clinical cohort – HMO (626) | 14 years | Self-report on the socializing, educational, and cultural items on the Life Complexity Inventory<br><br>Proportion of time spent weekly in cognitive activities divided by time spent in all leisure activities | Longitudinal performance on:<br><br>Measures of verbal memory:<br>(a) Word fluency<br>(b) Immediate recall<br>(c) Delayed recall<br><br>Measures of inductive reasoning:<br>(a) PMA reasoning measure<br>(b) ADEPT Letter Series test<br>(c) Word series and<br>(d) Educational Testing Service number series | Age<br>Sex<br>Educational level<br>Income | Involvement in cognitive leisure activities was not associated with longitudinal performance on either the memory or inductive reasoning tasks. Specific results were not provided in the manuscript. |

Abbreviations: ADEPT = Adult Development and Enrichment Project; aMCI = amnestic mild cognitive impairment; CI = confidence interval; HMO = health maintenance organization; HR = hazard ratio; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; PMA = Primary Mental Abilities; SD = standard deviation; SE = standard error

# Recommendations for Future Trials Investigating the Effectiveness of Interactive Computer Games (ICGs)

| | |
|---|---|
| Selection/inclusion criteria | • Elderly adults with particular focus on participants aged > 80 years |
| Methodology | • Randomized controlled design (predetermined randomization schedule and allocation concealment)<br>• Blinded outcome assessment<br>• Minimize attrition bias through active tracking of dropouts/ intention to treat analysis |
| ICG intervention | • Game design or accessories developed to challenge a specific component of fitness, for example, strengthening or falls prevention<br>• User-friendly software tailored to elderly population<br>• Maximize enjoyment, engagement, and motivation during exercise by ensuring ICG themes correspond to the interests of the elderly population<br>• Maximize programmable game features, for example, incorporating baseline calibration to tailor game features to individuals' ability/fitness levels |
| Comparison group | • Nongame exercise<br>• Optimal exercise dose (duration intensity)<br>• Subgroup effects (gender, baseline physical, or cognitive ability)<br>• Active control group recognized as a necessity for cognitive intervention studies |
| Outcomes and follow-up | • Physical and cognitive-based outcomes<br>• Mechanistic and clinically relevant<br>• Active follow-up of predefined adverse events |

Bleakley et al J Appl Gerontolo 2015; 34(3)

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Bleakley et al J Appl Gerontolo 2015; 34(3)

# Physical Activity and Cognitive Impairment

**Physical activity level and future risk of mild cognitive impairment or dementia: a critically appraised topic.**

Objective measurement confirms that greater levels of physical activity are associated with decreased risk of a future diagnosis of MCI or AD. Further studies are needed to confirm the temporal association of exercise and future cognitive health and understand the relevant underlying biological mechanisms.

Schlosser Covell GE Neurologist 19: 89-91, 2015

Original Article

Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2010.02281.x

# Physical activity and risk of cognitive decline: a meta-analysis of prospective studies

F. Sofi[1,2,3], D. Valecchi[1], D. Bacci[1], R. Abbate[2], G. F. Gensini[1], A. Casini[3] & C. Macchi[1]

*From the [1]Don Carlo Gnocchi Foundation, Centro S. Maria agli Ulivi, Onlus IRCCS; [2]Department of Medical and Surgical Critical Care, Thrombosis Centre, University of Florence; and [3]Regional Agency of Nutrition, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy*

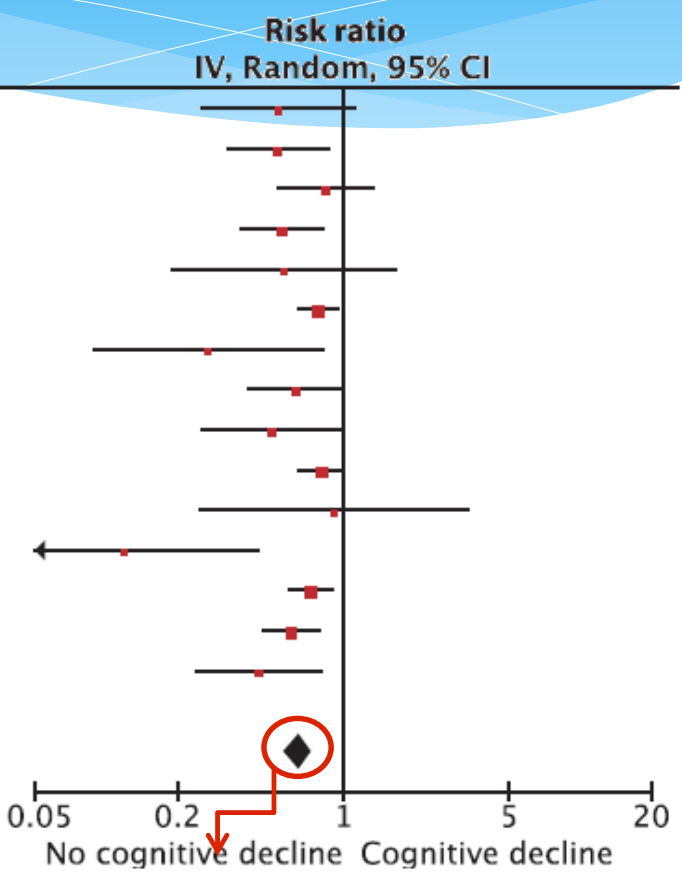
*J Intern Med* 2011; **269**: 107–117.

# Forest plot of studies investigating a low-to-moderate level of physical activity

| Study or Subgroup | Weight | Risk ratio IV, Random, 95% CI |
|---|---|---|
| Ho *et al.*, (M) | 3.0% | 0.53 [0.25, 1.12] |
| Ho *et al.*, (F) | 5.9% | 0.53 [0.32, 0.87] |
| Laurin *et al.*, (M) | 6.4% | 0.84 [0.53, 1.34] |
| Laurin *et al.*, (F) | 7.6% | 0.55 [0.36, 0.83] |
| Schuit *et al.*, | 1.5% | 0.56 [0.19, 1.66] |
| Yaffe *et al.*, | 16.0% | 0.78 [0.64, 0.96] |
| Pignatti *et al.*, | 1.4% | 0.27 [0.09, 0.82] |
| Lytle *et al.*, | 6.4% | 0.63 [0.40, 1.00] |
| Flicker *et al.*, | 3.4% | 0.50 [0.25, 1.00] |
| Singh–Manoux *et al.*, | 14.8% | 0.81 [0.65, 1.01] |
| Sumic *et al.*, (M) | 1.1% | 0.91 [0.25, 3.36] |
| Sumic *et al.*, (F) | 1.1% | 0.12 [0.03, 0.44] |
| Middleton *et al.*, | 15.2% | 0.73 [0.59, 0.91] |
| Niti *et al.*, | 12.1% | 0.60 [0.45, 0.80] |
| Etgen *et al.*, | 4.1% | 0.44 [0.24, 0.82] |
| **Total (95% CI)** | **100.0%** | **0.65 [0.57, 0.75]** |

Heterogeneity: Tau$^2$ = 0.02; $\chi^2$ = 20.93, df = 14 ($P$ = 0.10); $I^2$ = 33%

Test for overall effect: $Z$ = 6.17 ($P$ < 0.00001)




Sofi et al. J Intern Med 2011; 269: 107-117

# Association of physical activity and different components of healthy ageing over 8 years follow-up

| | Model 1 OR (95% CI) | Model 2 OR (95% CI) |
|---|---|---|
| Chronic disease | | |
| Inactive | 1.00 (ref) | 1.00 |
| Moderate physical activity | 0.70 (0.58 to 0.84) | 0.78 (0.64 to 0.95) |
| Vigorous physical activity | 0.61 (0.50 to 0.74) | 0.67 (0.54 to 0.84) |
| p-trend | <0.001 | 0.001 |
| Depressive symptoms (CES-D>3) | | |
| Inactive | 1.00 (ref) | 1.00 |
| Moderate physical activity | 0.51 (0.41 to 0.64) | 0.67 (0.53 to 0.85) |
| Vigorous physical activity | 0.36 (0.27 to 0.46) | 0.51 (0.39 to 0.67) |
| p-trend | <0.001 | 0.001 |
| Cognitive impairment | | |
| Inactive | 1.00 (ref) | 1.00 |
| Moderate physical activity | 0.71 (0.56 to 0.90) | 0.88 (0.69 to 1.13) |
| Vigorous physical activity | 0.49 (0.37 to 0.64) | 0.64 (0.48 to 0.85) |
| p-trend | <0.001 | 0.005 |
| ADL/IADL | | |
| Inactive | 1.00 (ref) | 1.00 |
| Moderate physical activity | 0.43 (0.35 to 0.52) | 0.57 (0.46 to 0.70) |
| Vigorous physical activity | 0.30 (0.24 to 0.37) | 0.41 (0.33 to 0.52) |
| p-trend | <0.001 | <0.001 |
| Impaired gait speed (<0.6 m/s) | | |
| Inactive | 1.00 (ref) | 1.00 |
| Moderate physical activity | 0.38 (0.30 to 0.49) | 0.54 (0.40 to 0.72) |
| Vigorous physical activity | 0.23 (0.17 to 0.32) | 0.41 (0.29 to 0.58) |
| p-trend | <0.001 | <0.001 |

Model 1; adjustment for age, sex.
Model 2; adjustment for age, sex and mutually for all components of healthy ageing model.
ADL, activities of daily living; CES-D, Centre of Epidemiological Studies Depression; IADL, instrumental activities of daily living.

Hamer M, et al. Br J Sports Med 2014;48:239–243

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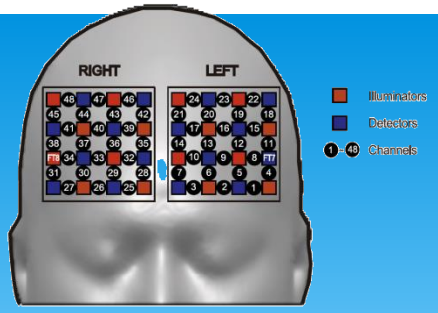
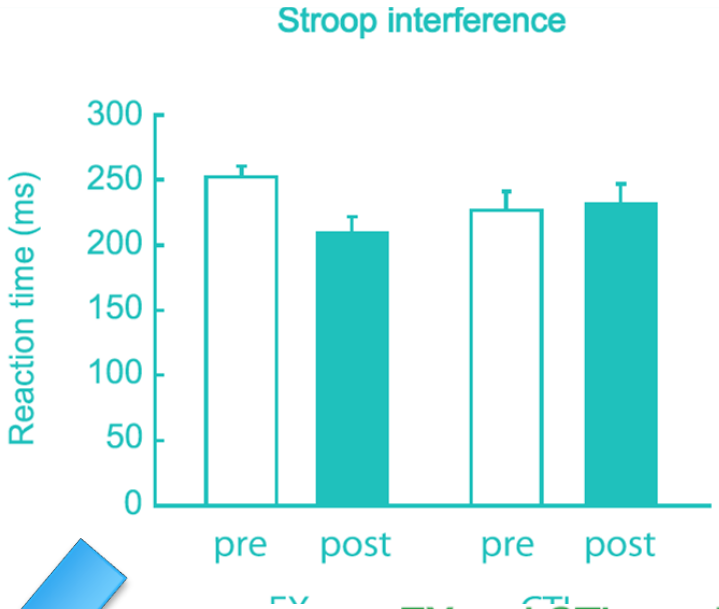
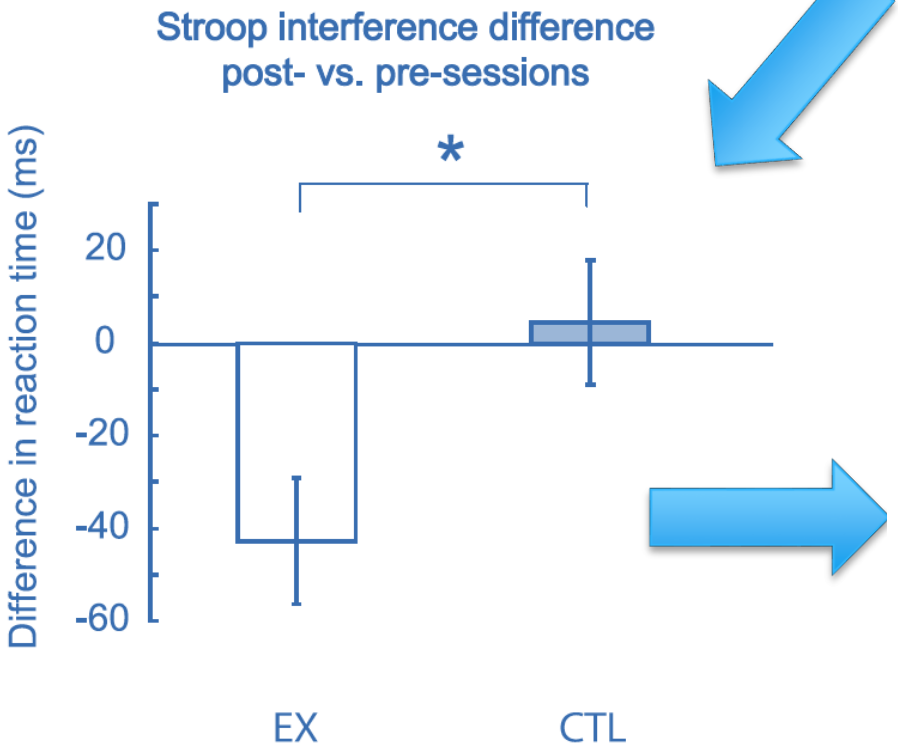
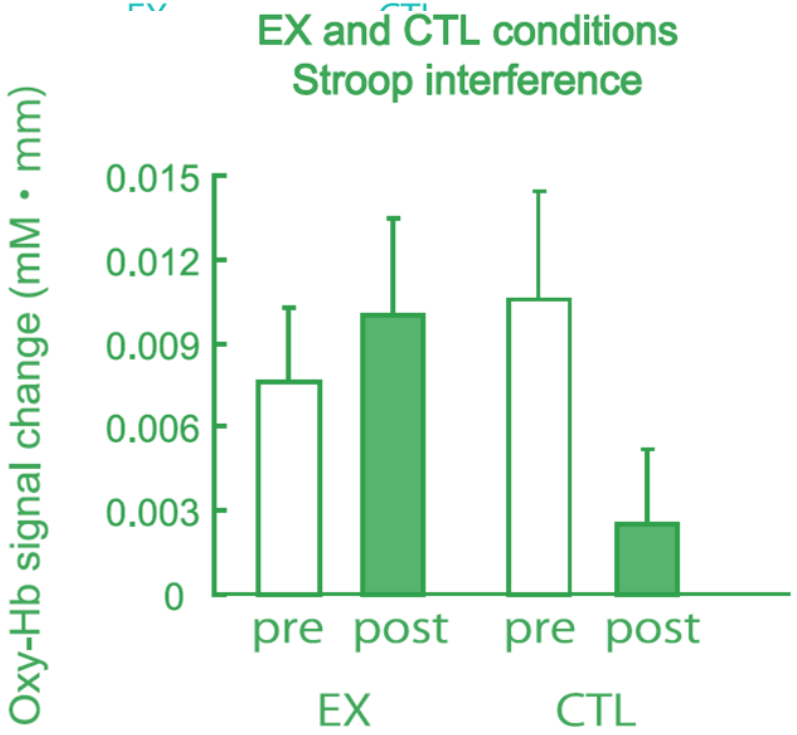
Hamer M, et al. Br J Sports Med 2014;48:239–243



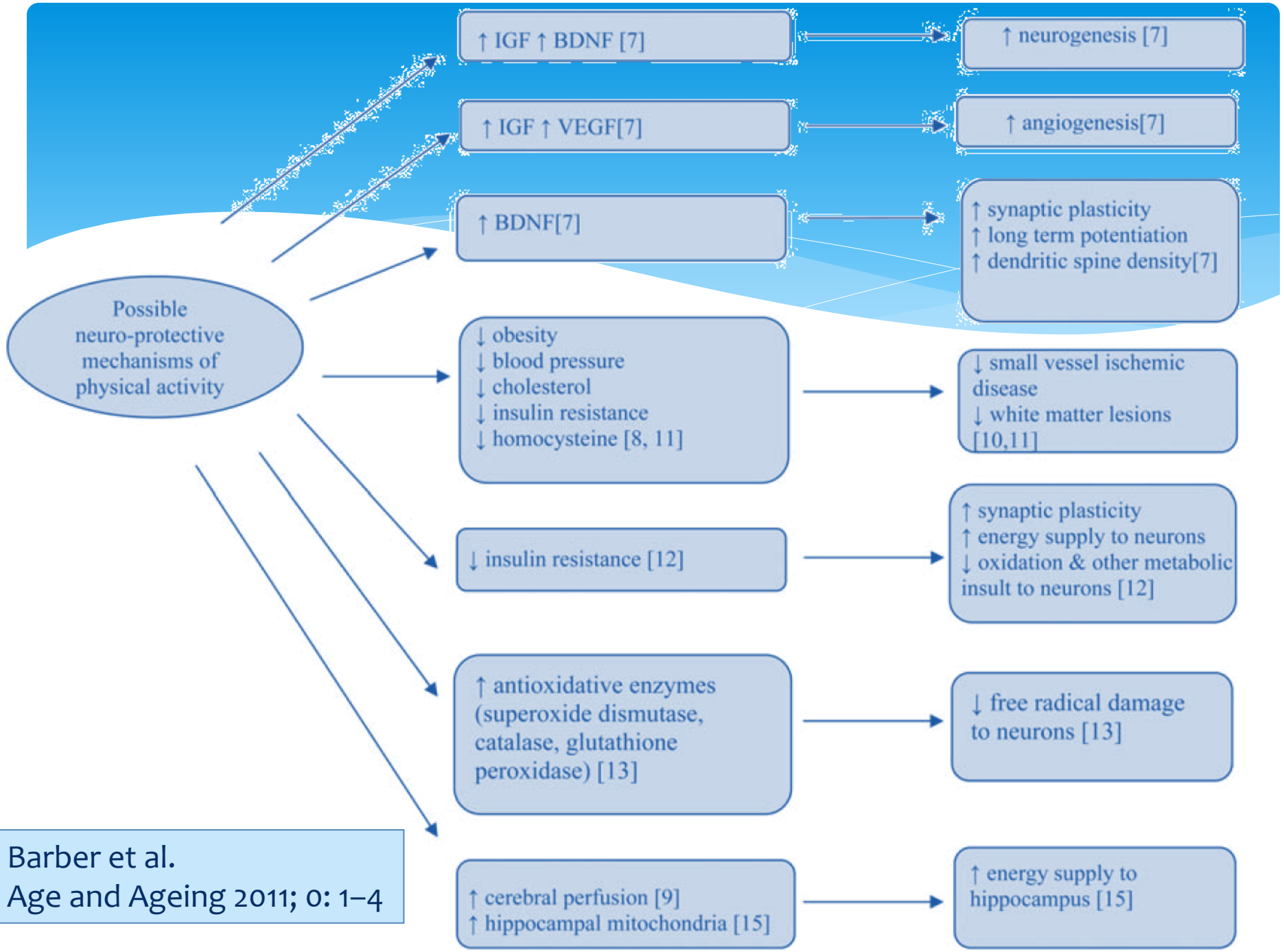

functional near-infrared spectroscopy probes



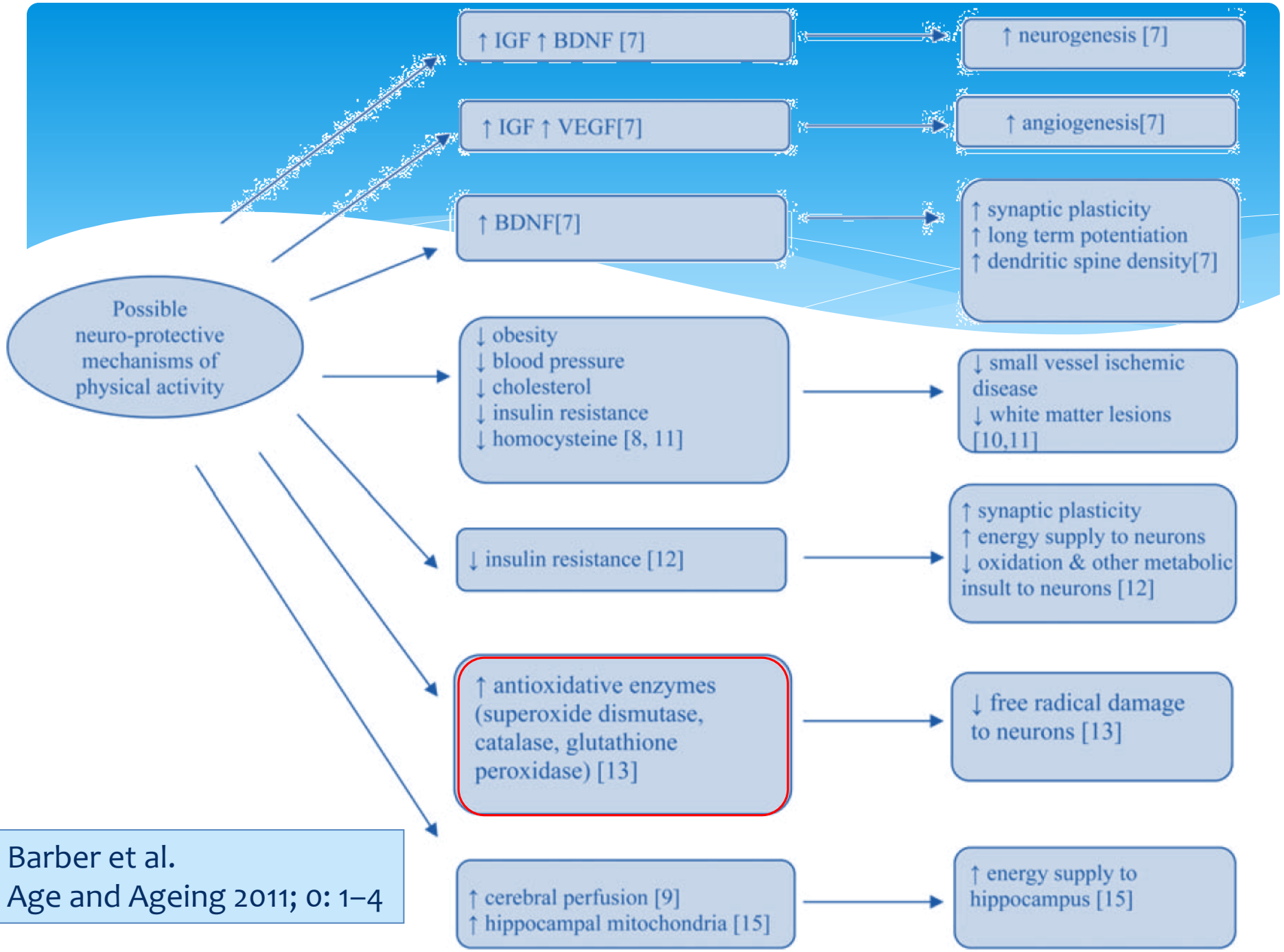




Hyodo et al. Neurobiology of Aging 2012;33:2621-32




Barber et al.
Age and Ageing 2011; 0: 1–4




Barber et al.
Age and Ageing 2011; 0: 1–4

Available online at www.sciencedirect.com
ScienceDirect
Experimental Gerontology 41 (2006) 764–770
Experimental Gerontology
www.elsevier.com/locate/expgero

# Exercise training affects age-induced changes in SOD and heat shock protein expression in rat heart

Barbara Rinaldi [a,*,1], Graziamaria Corbi [b,*,1], Silvia Boccuti [a], Walter Filippelli [c], Giuseppe Rengo [b], Dario Leosco [d], Francesco Rossi [a], Amelia Filippelli [a], Nicola Ferrara [b]

[a] *Department of Experimental Medicine and Excellence Center of Cardiovascular Disease, Second University of Naples, Naples 80138, Italy*
[b] *Department of Health Sciences, University of Molise and S. Maugeri Foundation, Scientific Institute of Telese Terme, Telese Terme 82037, Italy*
[c] *Faculty of Sport and Exercise Sciences, Parthenope University, Naples, Italy*
[d] *Department of Clinical Medicine and Cardiovascular and Immunological Sciences, University "Federico II", Naples, Italy*

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Available online 5 July 2006

REJUVENATION RESEARCH
Volume 10, Number 4, 2007

DOI: 10.1089/rej.2007.0576

# Exercise Training Promotes SIRT1 Activity in Aged Rats

Nicola Ferrara,[1,2*] Barbara Rinaldi,[3*] Graziamaria, Corbi,[1,2] Valeria Conti,[3] Paola Stiuso,[4] Silvia Boccuti,[3] Giuseppe Rengo,[2] Francesco Rossi,[3] and Amelia Filippelli [3]

REJUVENATION RESEARCH
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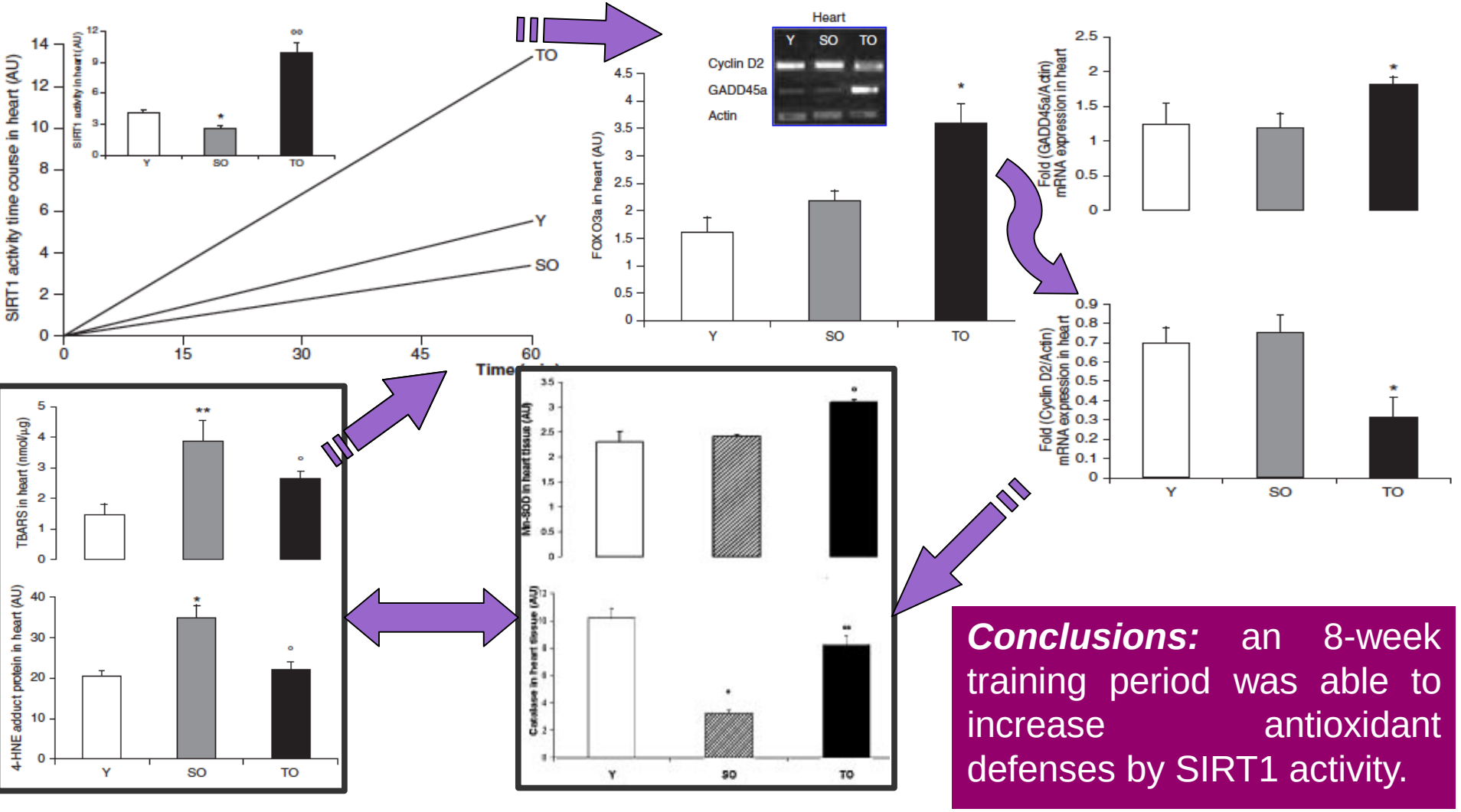



***Conclusions:*** an 8-week training period was able to increase antioxidant defenses by SIRT1 activity.

Rejuvenation Res. 2008 Feb;11(1):139-50.

## Exercise training promotes SIRT1 activity in aged rats.

Ferrara N, Rinaldi B, Corbi G, Conti V, Stiuso P, Boccuti S, Rengo G, Rossi F, Filippelli A.

Med Sci Sports Exerc. 2012 Jan;44(1):39-49. doi: 10.1249/MSS.0b013e318227f69c.

## Oxidative stress effects on endothelial cells treated with different athletes' sera.

Conti V, Corbi G, Russomanno G, Simeon V, Ferrara N, Filippelli W, Limongelli F, Canonico R, Grasso C, Stiuso P, Dicitore A, Filippelli A.

Med Sci Sports Exerc. 2013 Apr;45(4):644-53. doi: 10.1249/MSS.0b013e318279fb59.

## Aerobic training workload affects human endothelial cells redox homeostasis.

Conti V, Russomanno G, Corbi G, Guerra G, Grasso C, Filippelli W, Paribello V, Ferrara N, Filippelli A.

Aging Clin Exp Res. 2015 Aug;27(4):547-53. doi: 10.1007/s40520-015-0357-9. Epub 2015 Apr 3.

## Aging-related changes in oxidative stress response of human endothelial cells.

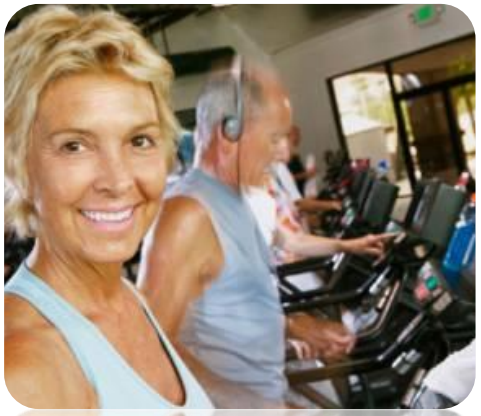
Conti V[1], Corbi G, Simeon V, Russomanno G, Manzo V, Ferrara N, Filippelli A.

# EXERCISE IN THE PREVENTION OF DEMENTIA (EPD)

- *>60 anni*
- *disturbo soggettivo della memoria*
- *>/=24  MMSE*

# STUDIO EPD

*GRUPPO SPERIMENTALE*

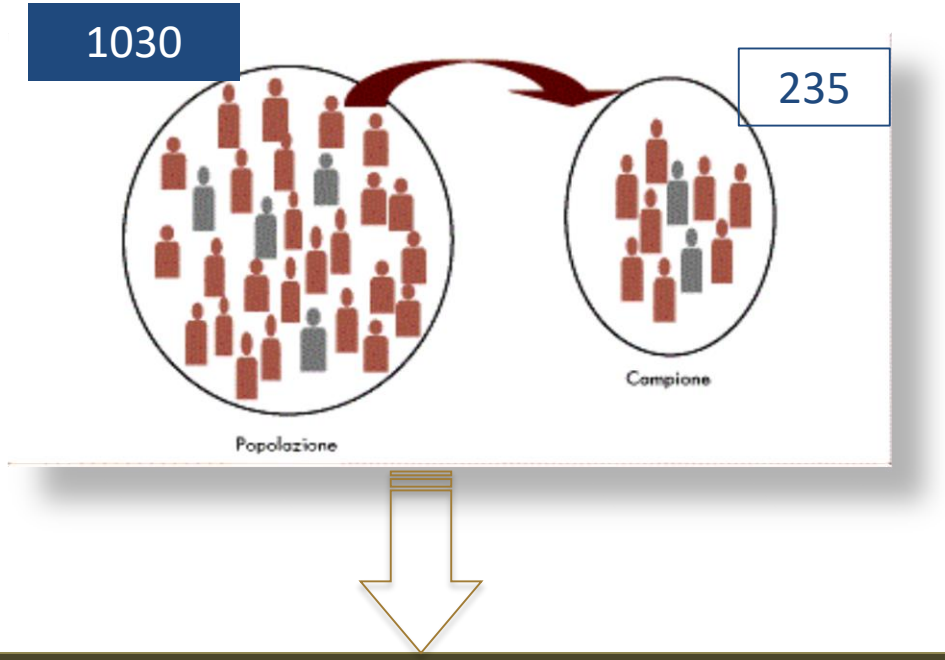


*GRUPPO CONTROLLO*

***FOLLOW UP A 6 – 12 – 24 MESI***

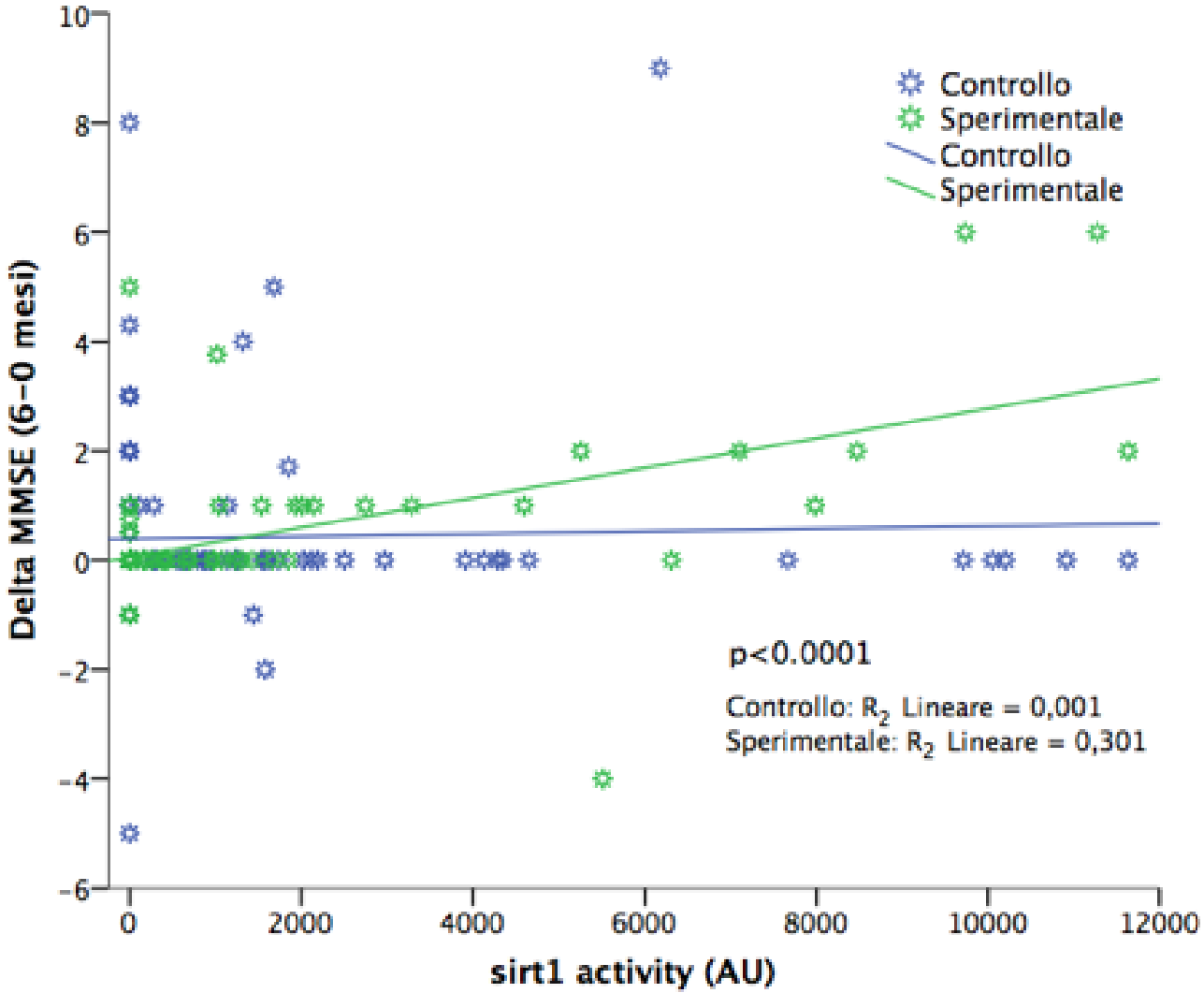
# STUDIO EP

## RECLUTAMENTO DEL CAMPIONE



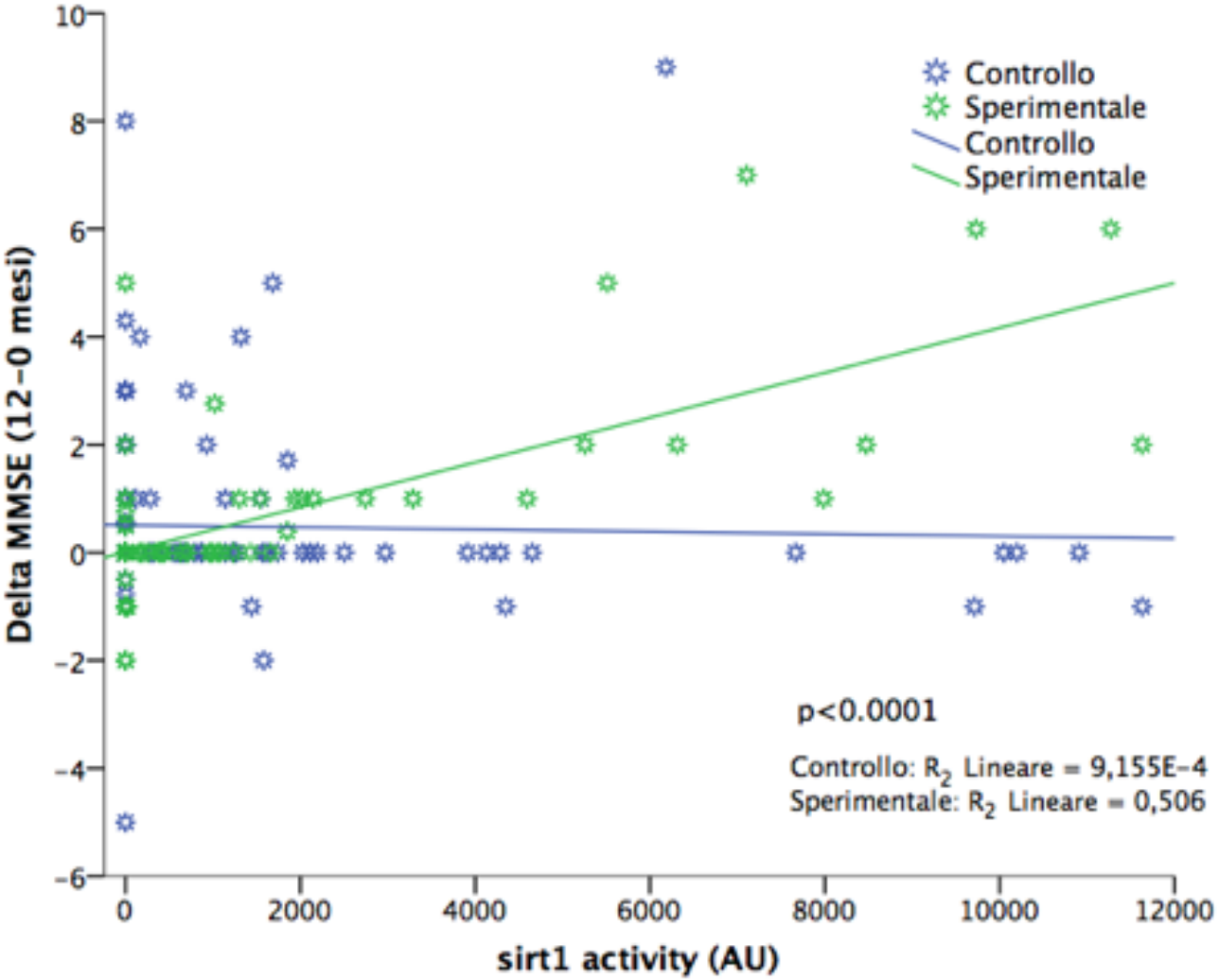

*Valutare se l'attività delle sirtuine condizionasse la risposta cognitiva all'esercizio*

# ANALISI DI REGRESSIONE LINEARE



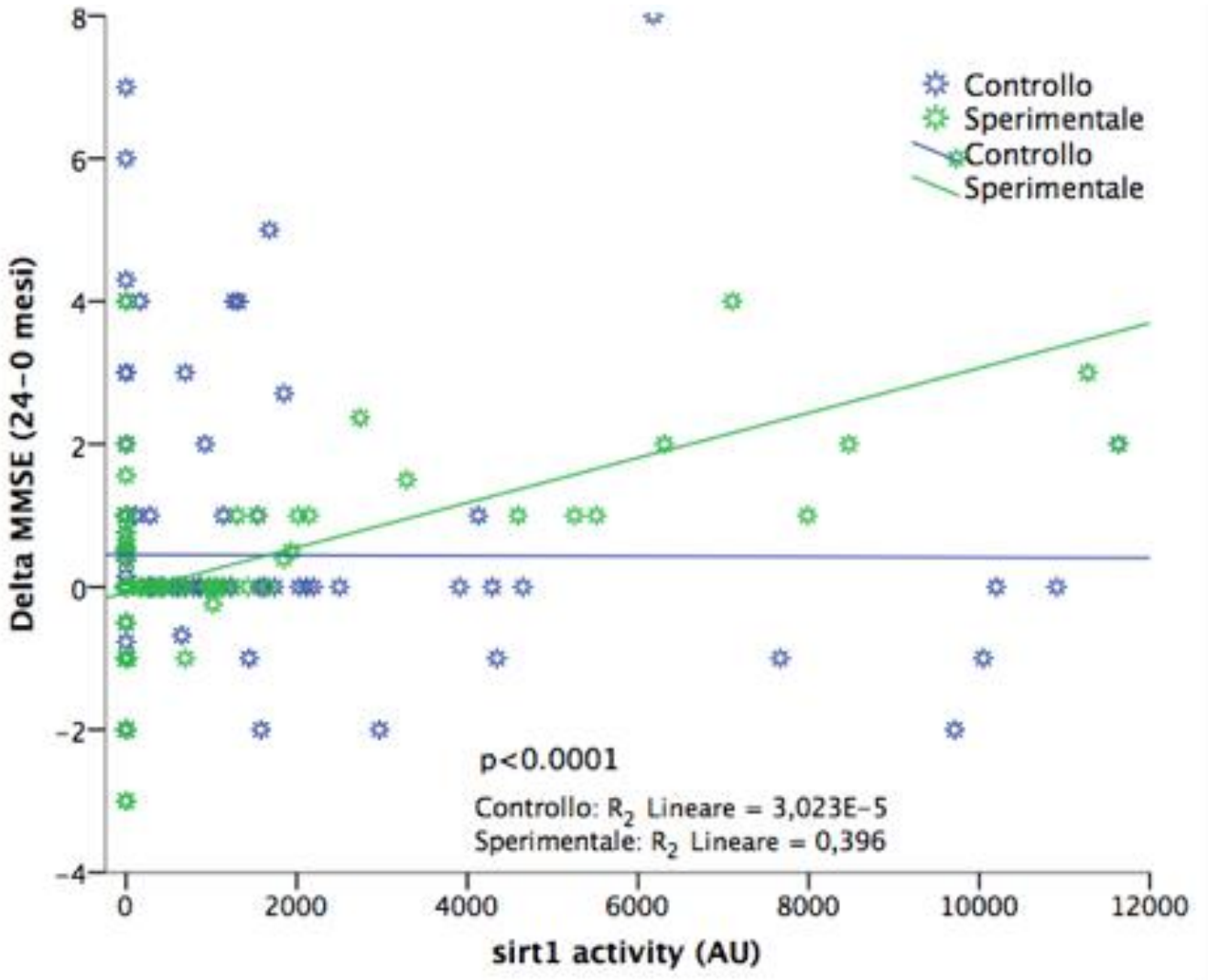

*Corbi et al. Unpublished data*

# ANALISI DI REGRESSIONE LINEARE




*Corbi et al. Unpublished data*

# ANALISI DI REGRESSIONE LINEARE




*Corbi et al. Unpublished data*

# Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)

*Ngandu T Lancet 385: 2255-63, 2015*

# A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

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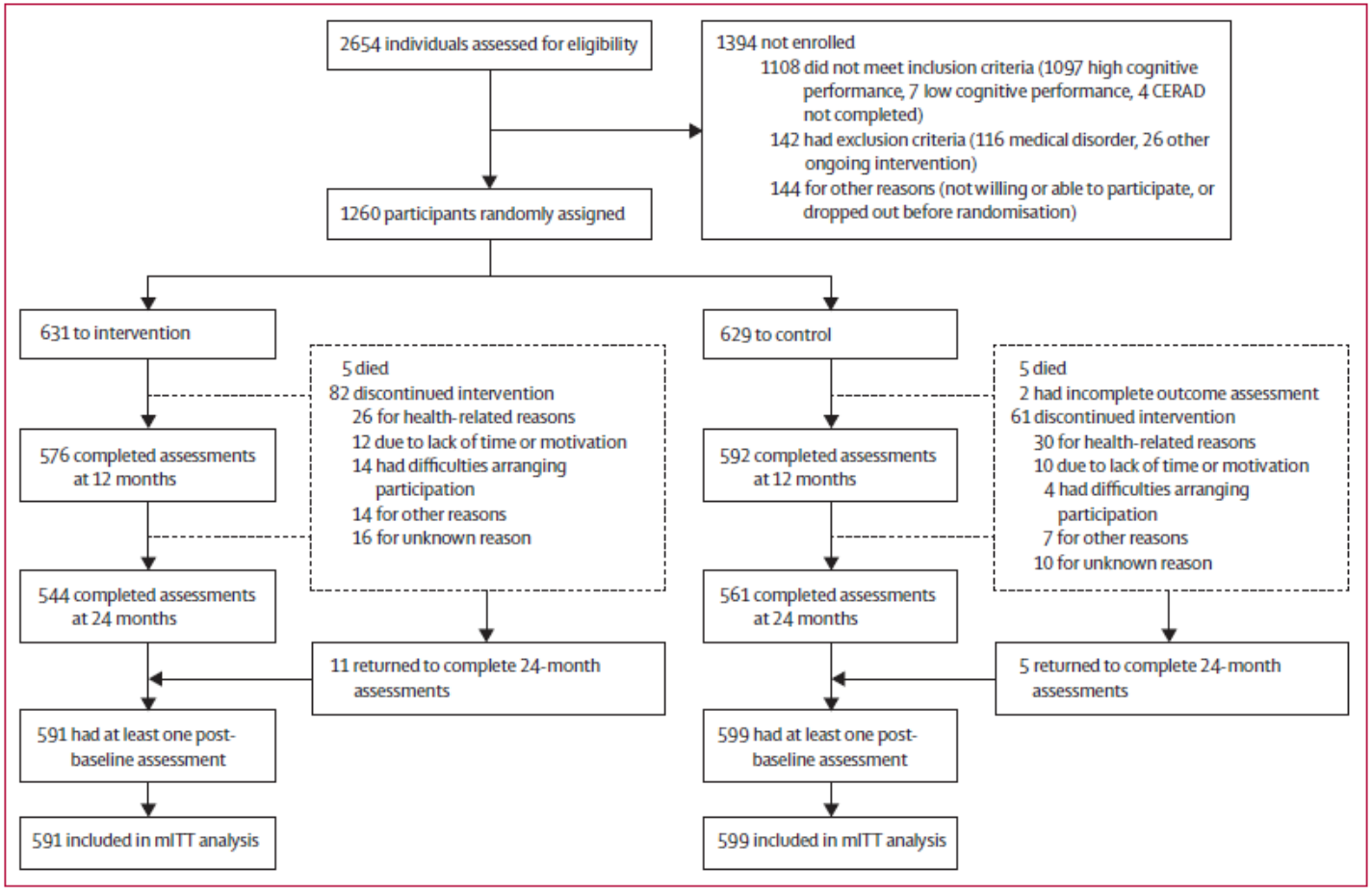
**diet, exercise, cognitive training, vascular risk monitoring**

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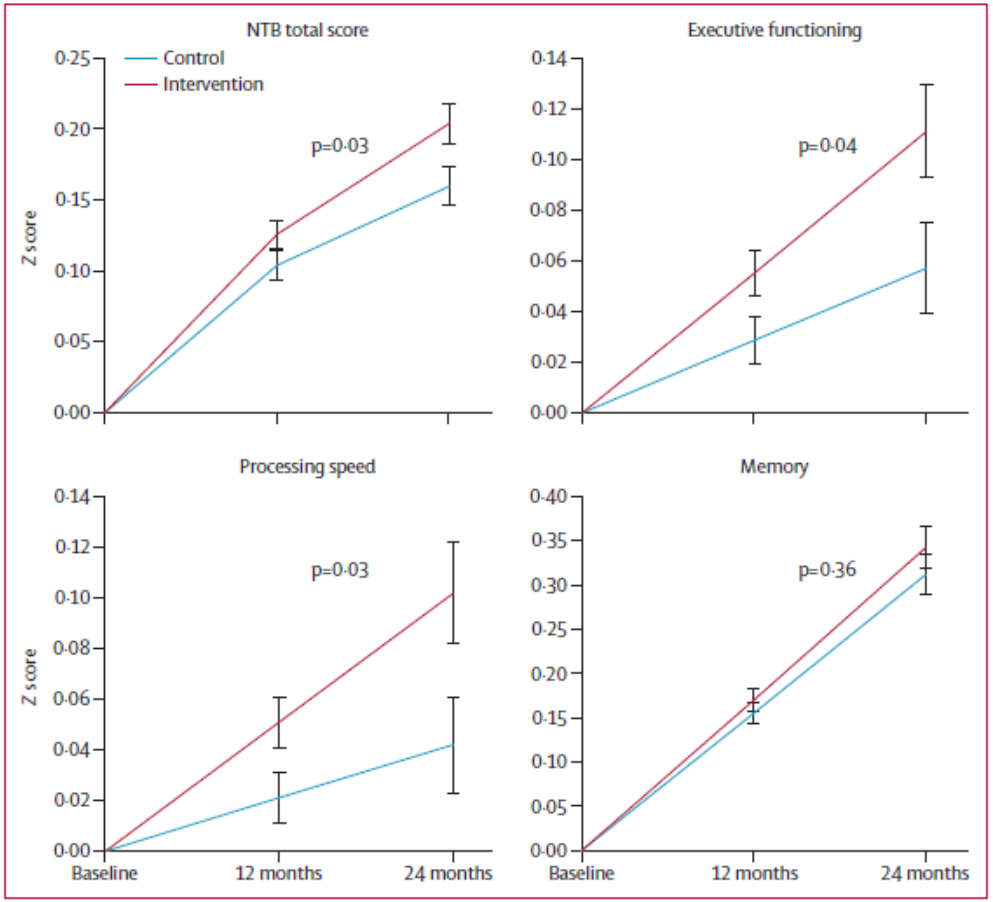
# A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial




…..a multidomain intervention could improve or maintain cognitive functioning in at-risk elderly people from the general population.

Ngandu T Lancet 385: 2255-63, 2015

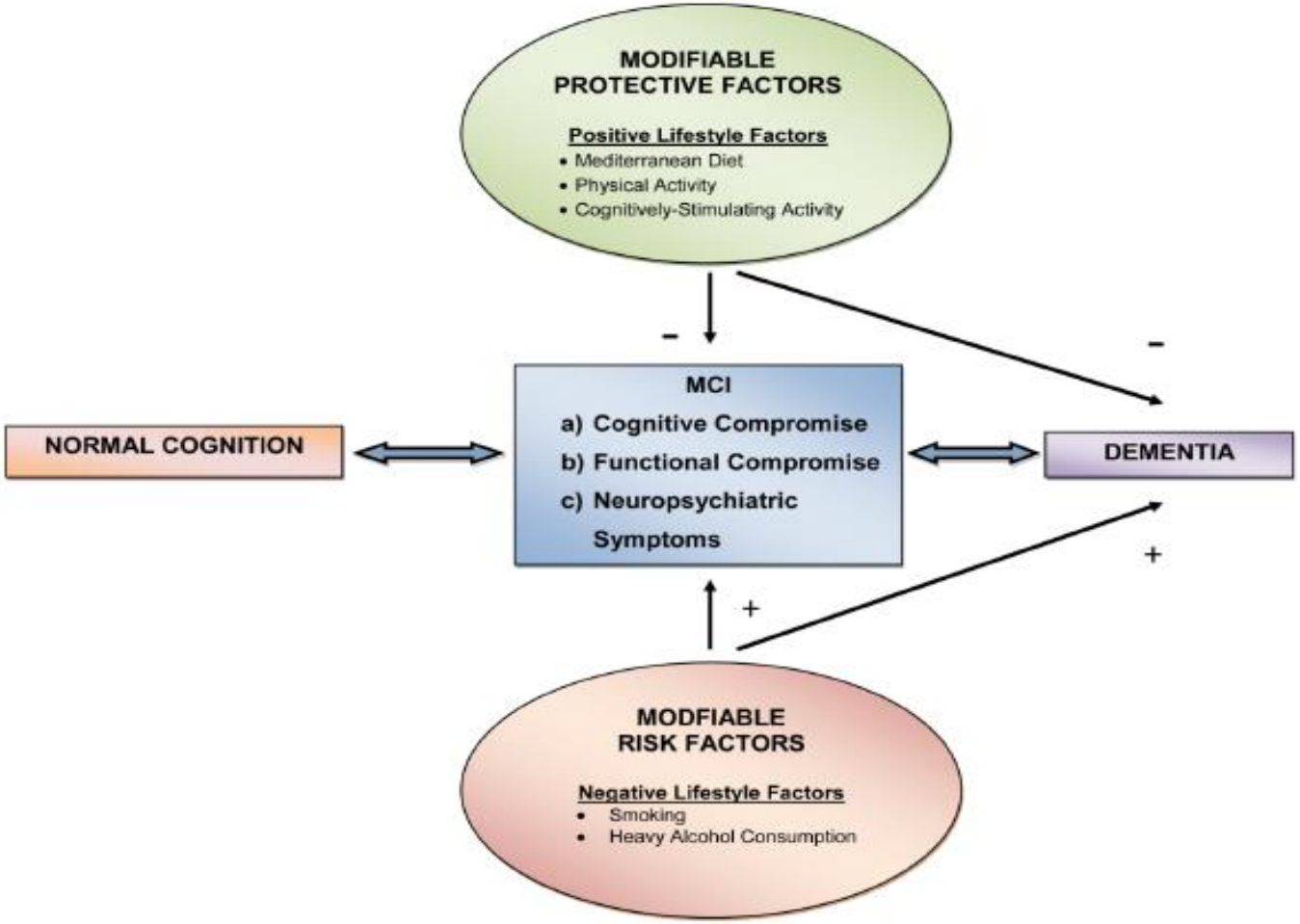
# Characteristics of selected RCTs for prevention of cognitive impairment, dementia and Alzheimer's disease based on multidomain interventions

| RCT | FINGER | MAPT | PreDIVA |
|---|---|---|---|
| Sample size | 1260 community dwellers, from previous population-based observational cohorts | 1680 community dwellers | 3533 community dwellers |
| Main inclusion criteria | CAIDE Dementia Risk Score >6 and cognition at mean level/slightly lower than expected for age (CERAD test battery) | Frail elderly people, subjective memory complaint, slow walking speed, limitation in IADL (MMSE≥24) | All elderly within GP practices, non demented (MMSE >23) |
| Age at enrolment | 60–77 yrs | ≥70 yrs | 70–78 yrs |
| Study design | Multi-center, randomized, parallel-group controlled trial | Multi-center, randomized, controlled trial | Multi-center, cluster-randomized, parallel group controlled trial |
| Intervention | Multi-domain: nutritional guidance, physical activity, cognitive training, increased social activity and intensive monitoring and management of metabolic and vascular risk factors | Multi-domain: vascular care, nutritional advice, exercise advice, cognitive training, and/or DHA 800 mg/day | Multi-domain: nurse-led vascular care including medical treatment of risk factors, nutritional advice, exercise advice |
| Duration | 2 yrs + 5 yrs extended follow-up | 3 yrs + 2 yrs extended follow-up | 6 yrs |
| Outcomes | Primary: change in cognitive function (neuropsychological test battery, Trail Making, Stroop), Secondary: dementia, cardiovascular events, depression, disability, quality of life, health resources utilisation, AD biomarkers change | Primary: change in cognitive function (Grober and Buschke memory test) Secondary: cognition (MMSE, CDR), functional status, depression, health resources utilisation, AD biomarkers change | Primary: dementia, disability Secondary: cognitive decline (MMSE, VAT), depression, cardiovascular events |
| Status | Intervention was completed in March 2014 | Intervention was completed in March 2014 | Ongoing, will be completed in 2015 |

CDR, clinical dementia rating scale; DHA, docosahexaenoic acid; FINGER, Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability; GP, general practitioner; IADL, instrumental activities of daily living; MAPT, Multidomain Alzheimer Prevention Study; PreDIVA, Prevention of Dementia by Intensive Vascular Care; VAT, visual association test.

Sindi et al. F1000Prime Rep. 2015;7:50.

# Efficacy of cognitive rehabilitation therapies for mild cognitive impairment (MCI) in older adults: Working toward a theoretical model and evidence-based interventions




Huckansa M Neuropsychol Rev. 23: 63-80, 2013

Int J Geriatr Psychiatry. 2010 Jan;25(1):30-6. doi: 10.1002/gps.2294.

# Education, occupation and retirement age effects on the age of onset of Alzheimer's disease.

Lupton MK[1], Stahl D, Archer N, Foy C, Poppe M, Lovestone S, Hollingworth P, Williams J, Owen MJ, Dowzell K, Abraham R, Sims R, Brayne C, Rubinsztein D, Gill M, Lawlor B, Lynch A, Powell JF.

Author information

## Abstract

**OBJECTIVE:** To determine the effects of early life education, mid life employment and later life retirement age on the age of onset (AOO) of Alzheimer's disease (AD).

**METHODS:** Multiple regression analyses were carried out using data for 1320 probable AD cases, of which 382 were males with employment and retirement age data, using informant based information on education and employment.

**RESULTS:** No relation was found between years of education, best qualification obtained, or employment variables in males and the AOO of AD. A significant effect of later retirement age in delaying the AOO of AD was seen in males.

**CONCLUSIONS:** In this study no effect of education or employment was seen, although this may be due to limited variance in the study population. The significant effect of retirement age may have several explanations, the most interesting of which would be the suggestion that active employment later in life allows an individual to prolong their cognitive assets above the threshold for dementia.

# LAVORARE FINO A TARDI ALLONTANA IL RISCHIO DI ALZHEIMER

## Ogni anno di lavoro in più ritarda di sei settimane l’inizio della vecchiaia

**Mantenere il cervello attivo lavorando fino a tardi e' un modo efficace per tenere lontano e ritardare l'Alzheimer**. A sostenerlo e' uno studio dell'istituto di psichiatrica del King's college di Londra, pubblicato sull'International Journal of Geriatric Psychiatry'. In particolare si stima che ogni anno in piu' di lavoro corrisponda a sei settimane di ritardo dell'inizio della vecchiaia. Alla conclusione i ricercatori vi sono giunti dopo aver analizzato i dati di 1.320 pazienti malati di demenza, di cui 382 uomini. Cosi' hanno scoperto che per gli uomini continuare a lavorare fino a tardi aiuta a mantenere il cervello abbastanza attivo e di ritardare la demenza, causata dalla perdita di cellule nel cervello. Secondo gli esperti un modo per accumulare il maggior numero possibile di connessioni cellulari e' quello di mantenersi mentalmente attivi nella vita. In questo senso una buona educazione intellettuale e scolastica puo' aiutare a mantenere la cosiddetta “riserva cognitiva” come anche la stimolazione intellettiva continuata in tarda eta'. Si e' visto infatti che le persone andate in pensionetardi hanno sviluppato l'Alzheimer successivamente rispetto a quelle che hanno lasciato il lavoro prima.