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Maintain Your Brain

Never Stand Still

Medicine



What does it mean to be “old”?

At 65 years of age

- **In 1800, you were dead 27 yrs ago**
- **In 1900, you were dead 12 yrs ago**
- **In 2000, you had 12-15 yrs to go**
- **In 2100, you may be two-thirds through your life**

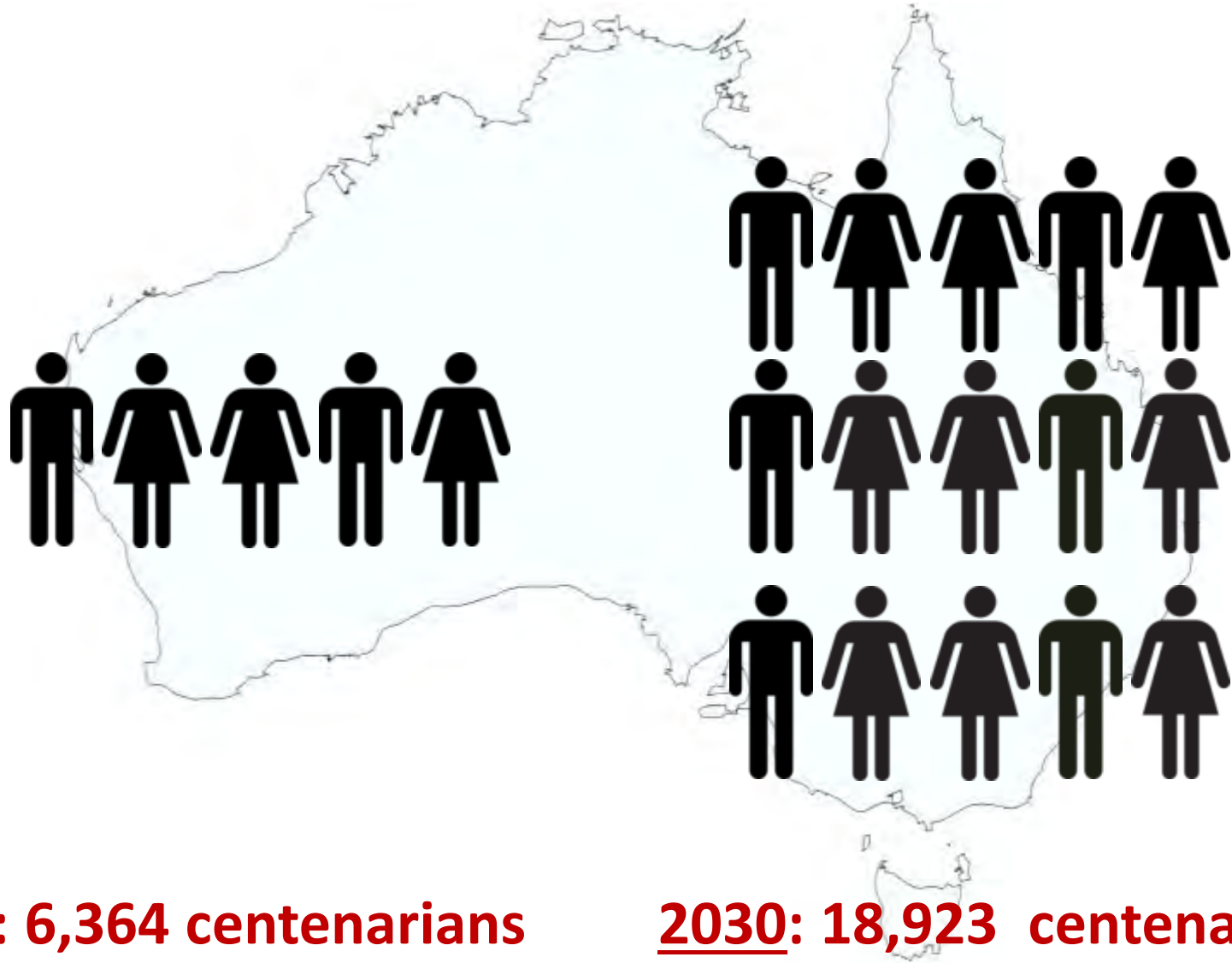


Ruthven, P. (2007): The challenge and opportunities for population ageing in the coming decades.

In 2030, Australia's population will be approx **28.48 million**



**There will be almost 3 times as many centenarians
as there are today**



2013: 6,364 centenarians

2030: 18,923 centenarians



**A girl born
today has a
40% chance of
reaching 100**

Adding years to life or adding life to years

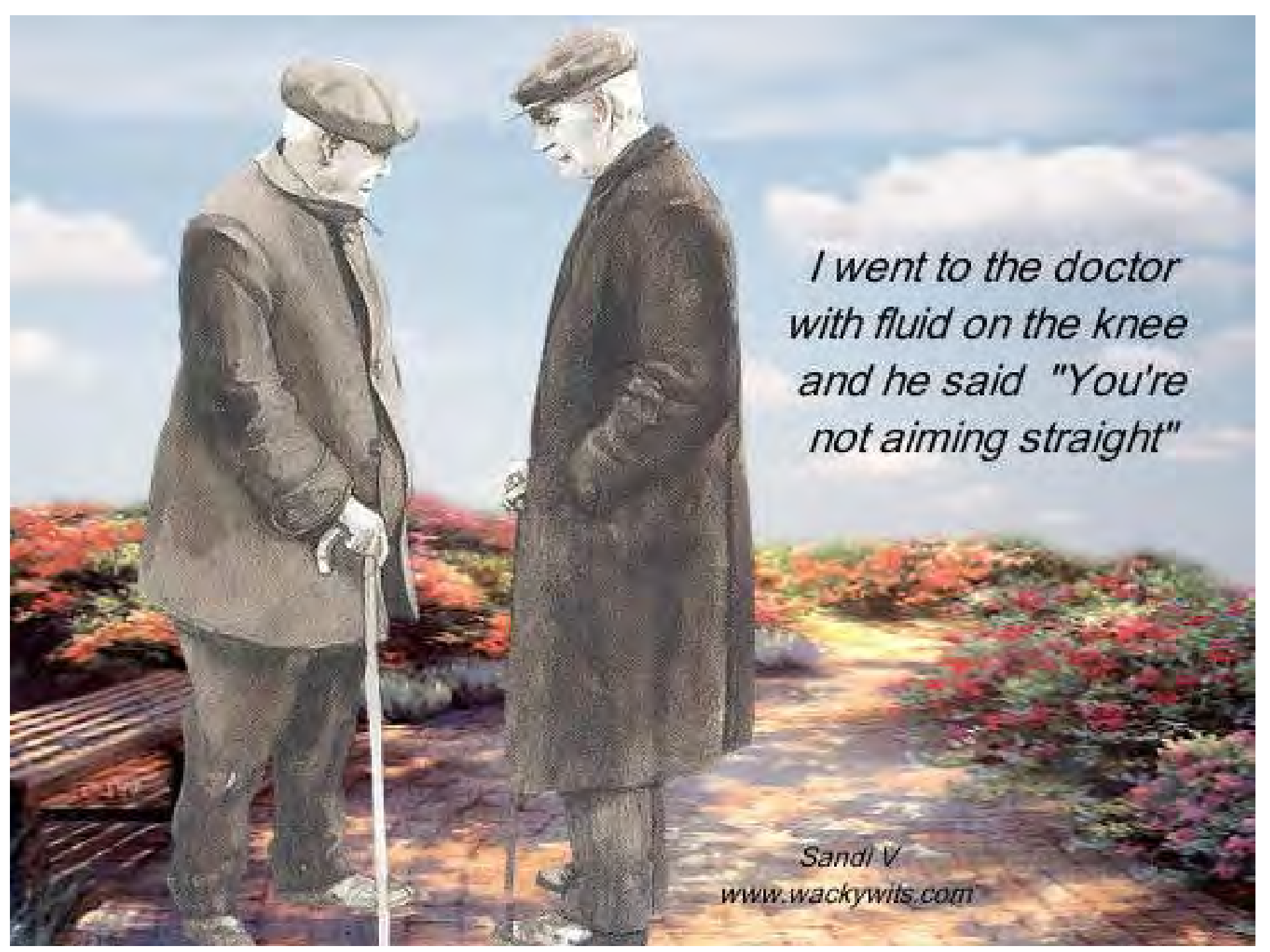


Successful ageing?



Successful ageing?



A painting of two elderly men standing in a field of red flowers under a cloudy sky. Both men are wearing brown coats and flat caps. The man on the left is leaning on a cane. The man on the right is also leaning on a cane. They are both looking down at their feet.

*I went to the doctor
with fluid on the knee
and he said "You're
not aiming straight"*

Sandi V.
www.wackywits.com

You've heard of the three ages of man?

- **Youth**
- **Age**
- **You are looking wonderful**

The secret of staying young is



- Live honestly
- Eat slowly, and
- Lie about your age

Getting Older

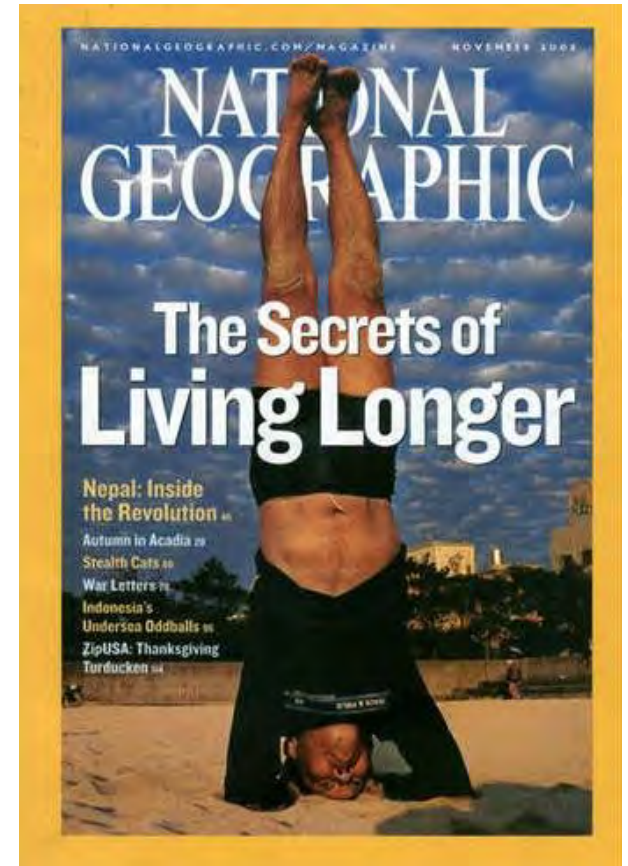


**I'm at an age when
my back goes out
more than I do**

Lifestyle

Seven protective factors

- Not being a smoker or stopping young
- Adaptive coping style
- Absence of alcohol abuse
- Healthy weight
- Stable marriage
- Some exercise
- Years of education



Vaillant, GE. & Mukamal, K. (2001). *American Journal of Psychiatry* 158, 839-847.



Centre for Healthy Brain Ageing

<https://cheba.unsw.edu.au/>

**Our vision is to achieve, through research,
healthier brain ageing and better clinical care
of age-related brain diseases**

Our brains

- The adult brain weighs about 1.3 kg
- Dementia shrinks it to ½ its usual size





**Who is
worried
about their
memory?**

NOW...
AM I GOING UPSTAIRS
FOR SOMETHING OR HAVE I
JUST COME DOWN?



Remember this shopping list

- **Milk**
- **Sausages**
- **Peas**
- **Flour**
- **Oranges**
- **Steak**
- **Cheese**
- **Apple**
- **Yoghurt**
- **Sugar**

HOLD ON...IF I'VE
GOT A SUPPOSITORY IN MY
EAR - WHERE THE HELL IS
MY HEARING-AID?





Can Alzheimer's disease (AD) and other dementias be prevented?

Can AD and other dementias be prevented?

Not yet butmay be delayed



**Can AD be prevented?
Not yet but ...
..may be delayed**

yourbrainmatters.org.au

- **Look after your heart**
- **Be physically active**
- **Mentally challenge your brain**
- **Follow a healthy diet**
- **Enjoy social activity**

Elimination vs Postponement

- **Disease elimination**
 - eg smallpox vaccination
 - best prospect is AD vaccine
- **Disease postponement¹: delay AD onset by...**
 - 2 years, ↓ prevalence by 20%
 - 5 years, ↓ prevalence by 50%

Brookmeyer et al. (1998)

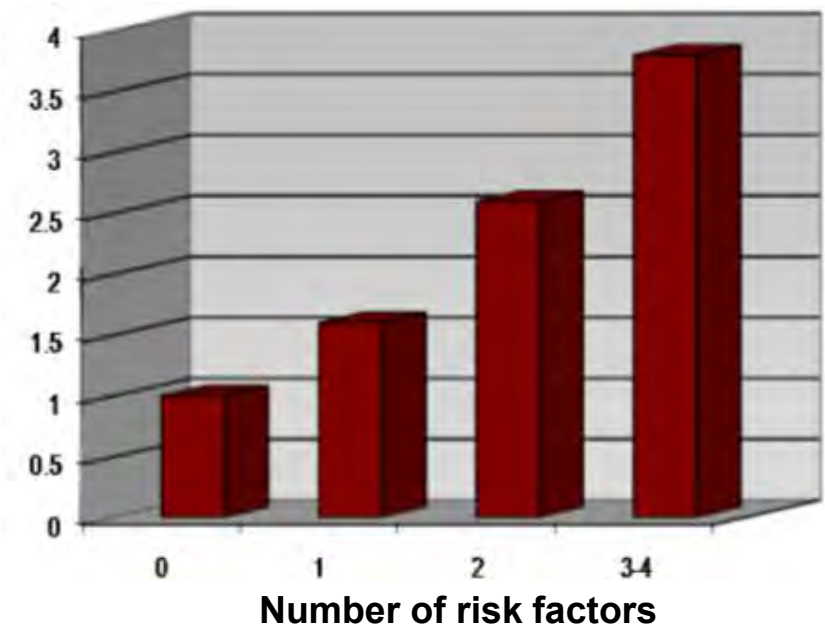
Dosage effect

**As CVD risk factors accumulate,
AD dementia risk increases**

If we count risk factors...

- *Hypertension*
- *Smoking*
- *Hypercholesterolemia*
- *Obesity*
- *Diabetes*
- *Physical inactivity*

Luchsinger et al 2005



Slide adapted from Michael Valenzuela

How much exercise do you do?

Each week

- Less than 1 hour
- 1 hour
- 2 hours
- 3 hours
- 4 hours
- 5 hours
- 6 or more hours

Each day

about 8.5 minutes

17 minutes

26 minutes

34 minutes

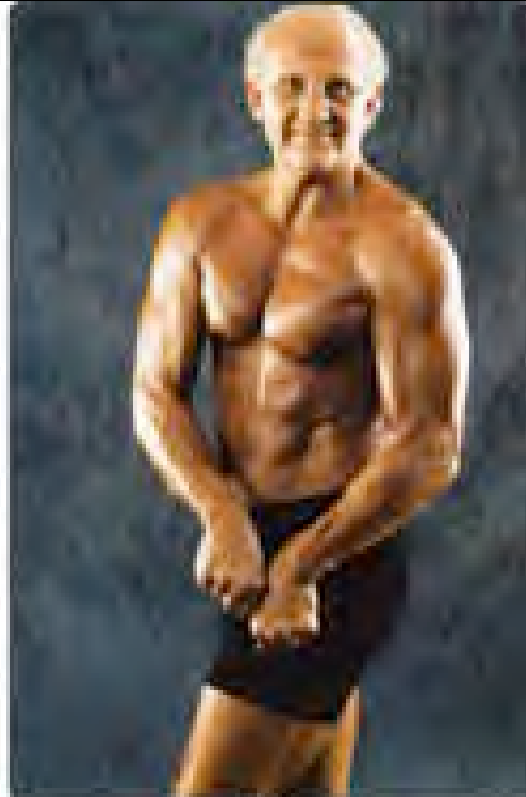
43 minutes

approaching 1 hr

Exercise addresses risk factors for cognitive decline and dementia



Before



After



6 Years Later

Dr. Jeffrey Life

Physical activity = protective

**AGE IS NO BARRIER. IT'S A LIMITATION
YOU PUT ON YOUR MIND.**



- Several studies show physical activity protective against cognitive decline, dementia, Alzheimer's, vascular dementia
- More is better – puffed, weights
- ≥ 3 x per week; >150 min/wk, e.g. Perth Study
- Check with your doctor

¹Jedrzejewski et al (2007). Alz Dem; 3:98-108; ² Lautenschlager et al (2008) JAMA; 300(9):1027-1037; ³Ravaglia et al (2007) Neurology; ⁴Larson et al (2006) Ann Intern Med; 144:73-81; ⁵Laurin et al, Arch Neurol 2001;58:498-504; ⁶Middelton et al, PLoS ONE 2008;3(9):e3124

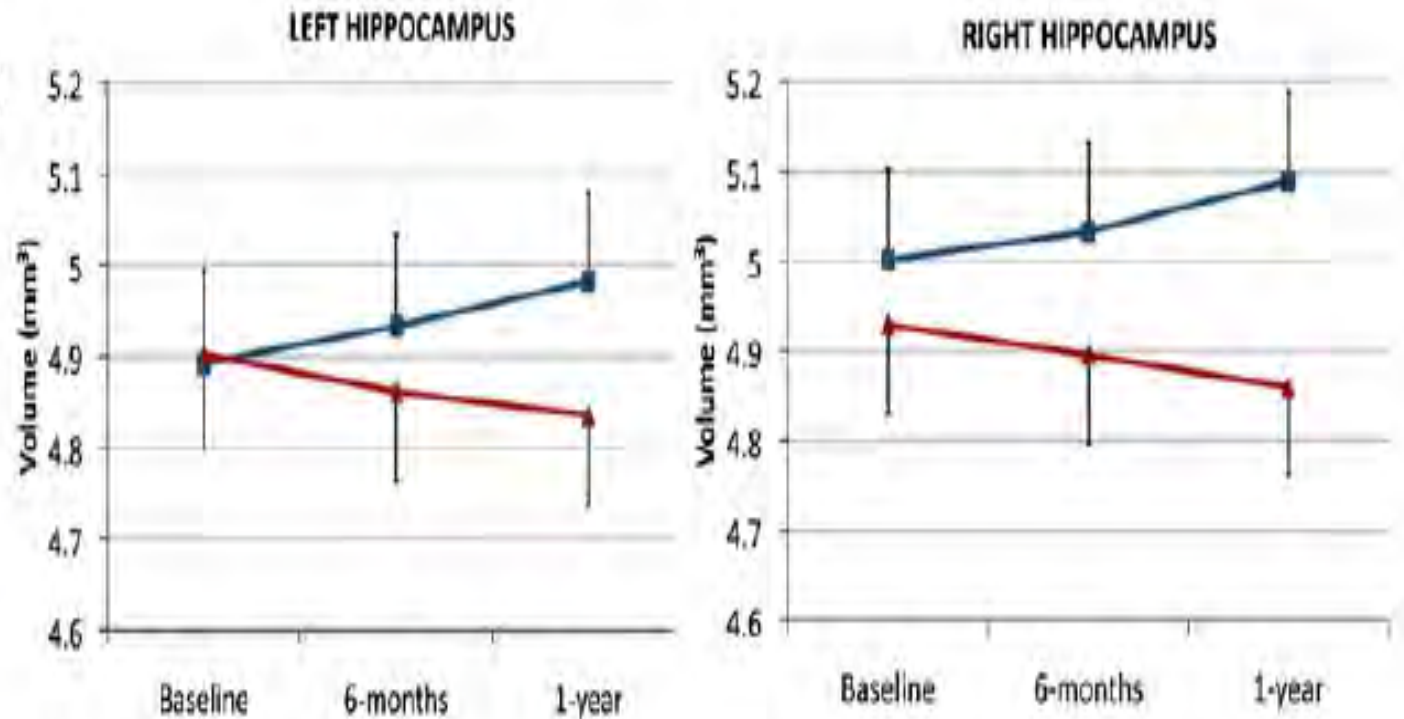
Can aerobic exercise protect against dementia?

- Preserve cognition and slow cognitive ↓
- Decreased incident dementia
- 8/11 RCTs in healthy older persons: cognitive & fitness improved
 - especially cognitive speed and attention
- Biomarkers ↑ e.g. brain volume
- Animal studies – growth factors↑, BDNF↑, neurogenesis↑, inflammation↓, AD path. ↓

Graff-Radford NR, *Alzheimer's Research and Therapy* 2011, 3:6

The power of physical activity

Hippocampus



Erickson et al., 2011

Physical activity benefits

- Improved fitness
- Improved physical health - ↓ heart disease, Hi BP, diabetes, some types of cancer, osteoporosis, sarcopenia
- Reduced morbidity & mortality
- Improved mental health
- Improved confidence, quality of life

http://www.mednwh.unimelb.edu.au/research/health_promotion.htm

Physical activity

- **Physical activity benefits older adults to prevent dementia: Never too late to start**
- **Moderate intensity (brisk walking) 30 min 5d/wk**
- **Evidence for specific exercise not clear; more than one type and more exercise may be better**
- **Resistance training better in SMART Trial²**
- **Combine with social and mental activity better?**

Denkinger et al. *Z Gerontol Geriatr* 2012; 45:11–16 DOI 10.1007/s00391-011-0262-6
Fiatarone Singh MA et al *JAMDA* 2014;15:873-80

***To get back my youth I would do anything
in the world, except take exercise, get up
early or be respectable.***



**Oscar Wilde
1854-1900**

Physical activity:

Recommendations for older adults

From National Ageing Research Institute

- **Think of movement as an opportunity, not an inconvenience**
- **Be active every day in as many ways as you can**
- **At least 30 minutes of moderate intensity physical activity on most, preferably all, days**
- **If you can, also enjoy some regular, vigorous activity for extra health and fitness**

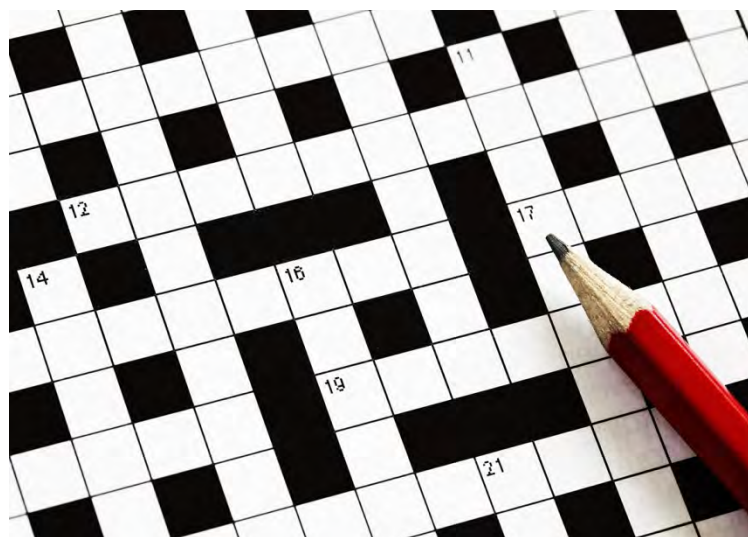
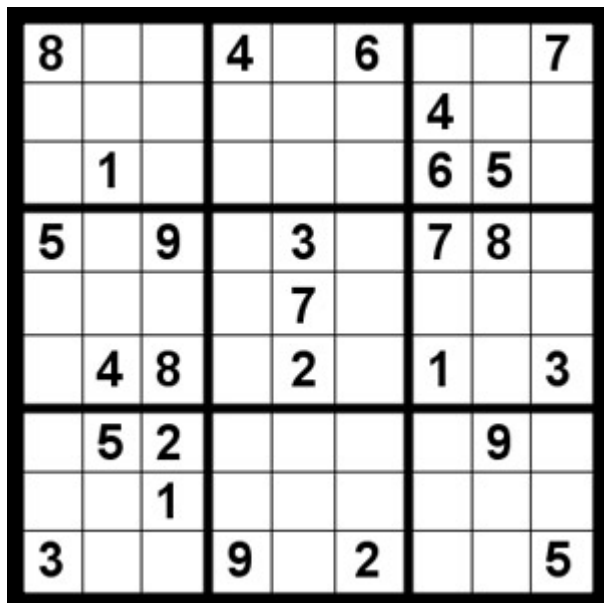
http://www.mednwh.unimelb.edu.au/research/health_promotion.htm



What about mental exercise?



- Education
- What mental exercise??
- At what age?



Computer cognitive training

- Lumosity
- Happy Neuron
- Posit Science
- Many others



Mental Activity & Dementia

- **Meta-analysis of 22 studies, 29,000 individuals**
- **↑ complex mental activity in late life = ↓ risk of dementia by half; OR = 0.54 (0.49-0.59) ¹**
- **Dose - response relationship evident¹**
- **Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence¹**
- **Results held when covariates in source studies were controlled for²**

¹Valenzuela MJ. Sachdev P. (2006). Psychol Med. 36(4): 441-454;

²Valenzuela MJ. Sachdev P. (2006) Psychol Med. 36(8): 1065-1073

Cognitive interventions healthy older adults & people with MCI

- **20 RCTs with healthy adults**
 - **Memory improvements in 17/20**
- **6 RCTs with MCI**
 - **Memory improvements in 4/6**
- **Unclear whether these improvements generalise to everyday activities**

Reijnders, J., et al., Ageing Res. Rev. (2012), doi 10.1016/j.arr.2012.07.003

Cognitive training

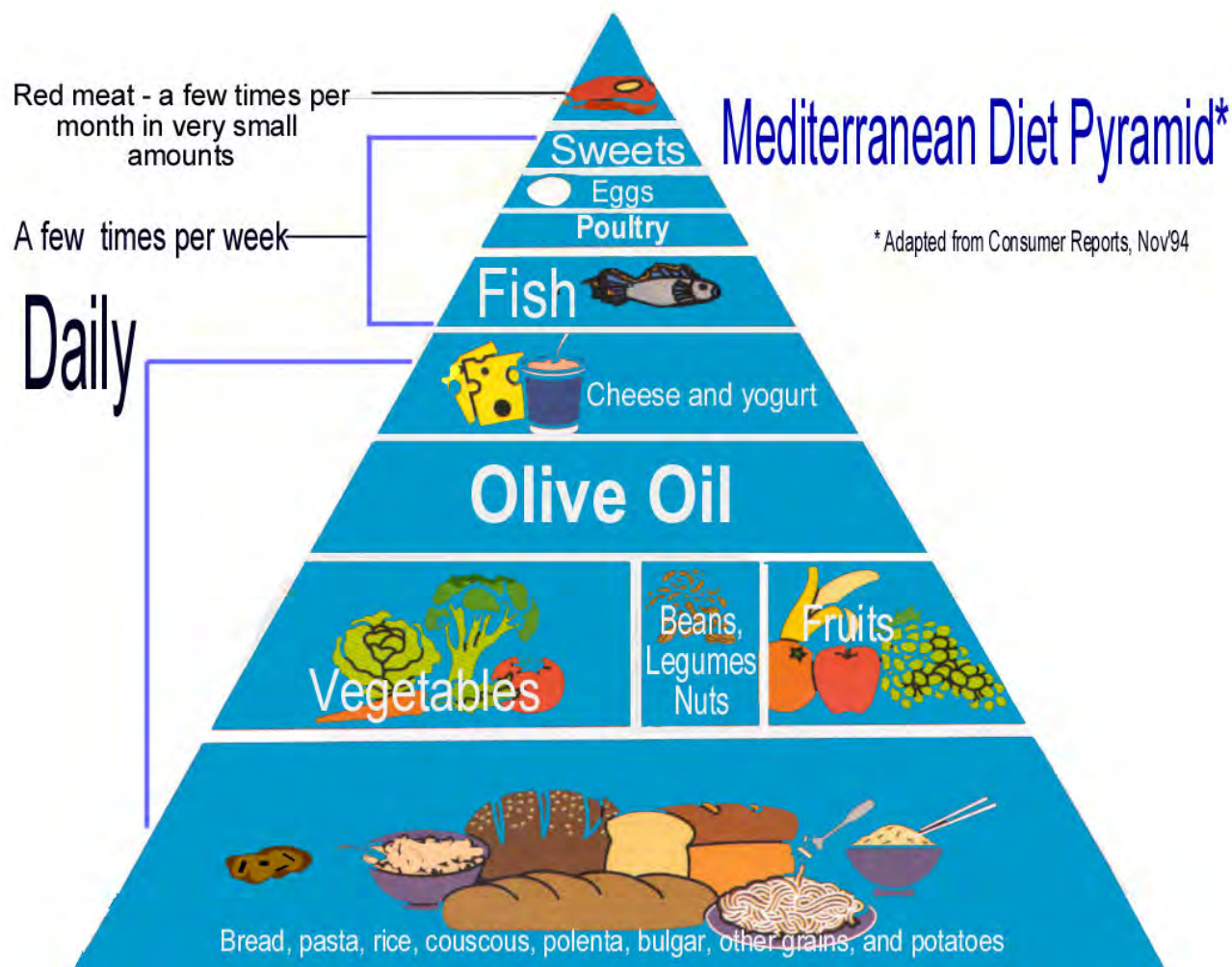
- **Systematic review of RCTs with longitudinal follow-up (> 3mths) in healthy elderly¹**
 - 7 RCTs met inclusion criteria, low quality
 - Strong effect size for cognitive exercise intervention vs wait-and-see controls
 - Longer follow-up (>2yrs) → effect no lower
- **Review of cog. training or rehab in dementia²**
 - 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)

Bahar-Fuchs, Clare, Woods – Cochrane Database Syst Rev. 2013 Jun 5;6:CD003260. doi:

10.1002/14651858.CD003260.pub2.

Eating for brain health



What is Mediterranean diet?



- Abundant plant foods
- Fresh fruit as typical daily dessert
- Olive oil as principal source of fat
- Dairy products (cheese and yogurt)
- Fish and poultry - low to moderate
- 0- 4 eggs week
- Red meat - low amounts
- Wine - low to moderate amounts
- Total fat = 25% to 35% of calories
- Saturated fat \leq 8% of calories

Socialising



© Alamy

Social ties linked to cognitive health

- **Marital status**
- **Frequency of contact with family, neighbours**
- **Volunteering**
- **6 yr Harvard study: the least socially integrated memory declined 2x more than the most**
- **At any age, 35-85, people with more social contacts did better on tests of memory and executive function**

Drugs to preserve memory



Do elixirs of youth exist?



Patriarchs

Enoch	365 yrs	Seth	912 yrs
Lamech	777 yrs	Adam	930 yrs
Mahalalel	895 yrs	Noah	950 yrs
Enosh	905 yrs	Jared	962 yrs
Kenan	910 yrs	Methuselah	969 yrs



Jeanne Calment

1875-1997

**10 oldest people on record
(according to modern
standards) have an age range
from 115 to 122 years**

Quest for eternal life

Ancient Greek myth

- Sorceress Medea injected King Aeson with a mixture of ram's blood, snake's skin, roots, herbs & other ingredients which gave him energy and youthful vitality



Quest for eternal life



- Pope Innocent VIII (1432-1492)
- Requested injection of blood of young men
- He died almost immediately

Quest for eternal life

19th century Dr. Charles Edouard Brown-Sequard claimed old men could be made young by the injections of mashed up dog testicles

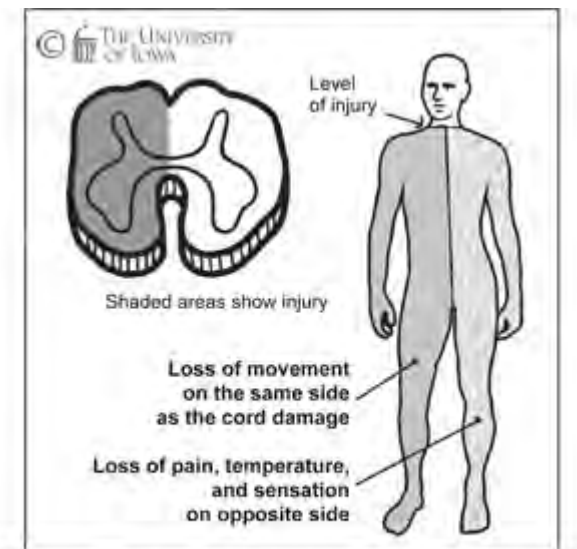
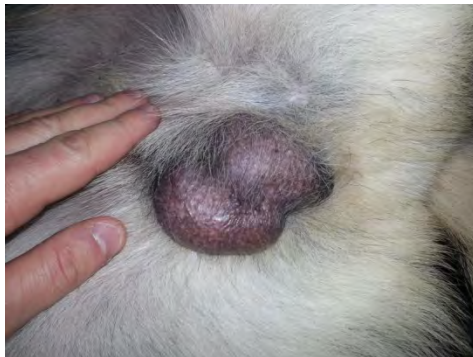


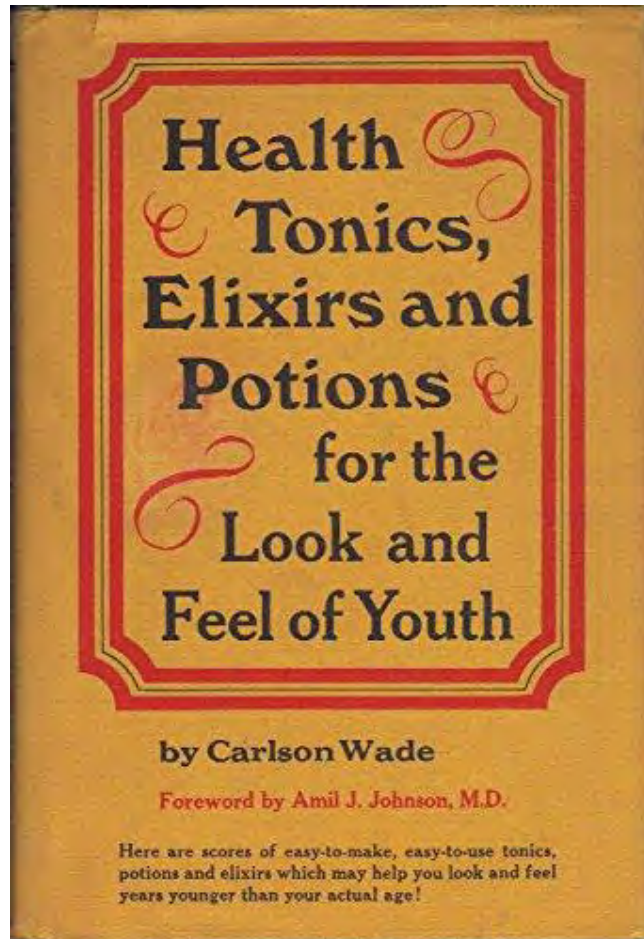
Figure 12. Brown-Séquard Syndrome

Quest for eternal life

20th century John Romulus Brinkley advocated transplanting goat testicles into men



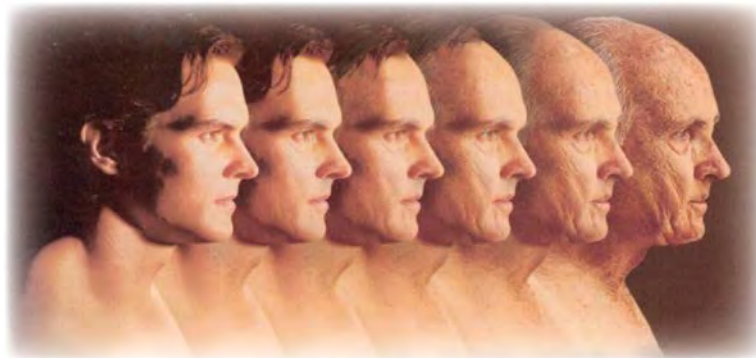
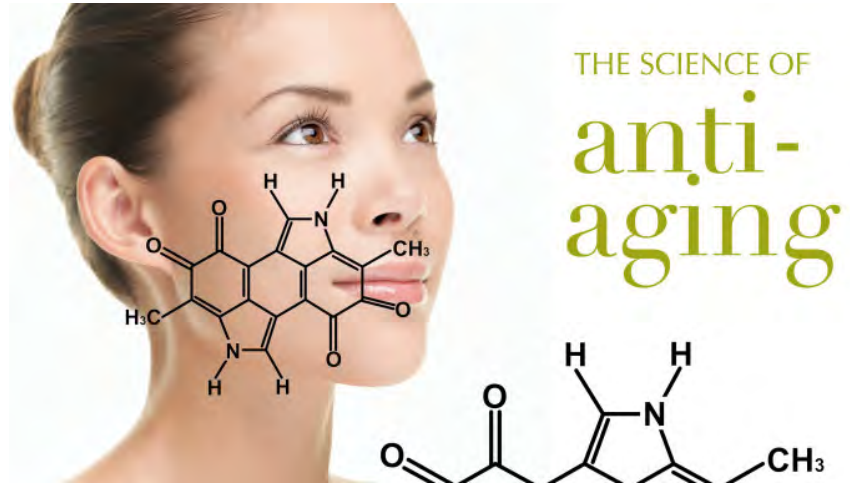
Goat testicles at Beijing market



GURU SHOTS™



High Vibration Life Elixirs.



Eternal life?

- *“What do the ancient purveyors of physical immortality all have in common?”*
- *They are all dead.”*
 - S. Jay Olshansky, (3/12/2004)



Natural therapies

- **Ginkgo biloba**
- **Turmeric, curcumin**
- **DHA, omega 3**
- **Fo-ti root**
- **Soy isoflavone**
- **Vitamin E, Selenium**
- **Folate, B6, B12**
- **Saffron**
- **Brahmi**
- **Huperzine A**

Ginkgo
leaves



Member of
ginger
family

A “cure” for ageing?

- Anti-ageing medicine
- Antioxidants, hormones
- Nutrition, Caloric restriction
- Resveratrol
- Exercise
- Telomerase
- Embryonic stem cells
- Replacing body parts
- Lifestyle modification





Environmental factors

- **30% of population attributable risk of AD cases from 7 environmental factors**
- **If 25% lower prevalence of these risk factors → 3 million fewer AD cases worldwide**
- **Highest estimated Pop^u Attributable Risk for AD**
 - **Global: low education (19·1%, 95% CI 12·3–25·6)**
 - **USA: physical inactivity (21·0%, 95% CI 5·8–36·6)**
 - **Europe, UK, US similar (20·3%, 95% CI 5·6–35·6)**

Barnes & Yaffe, 2011; Norton et al, 2014

How much AD can be attributed to environmental factors?

- 2% diabetes mellitus (type 2)
- 2% midlife obesity*
- 5% midlife hypertension
- 10% depression
- 13% physical inactivity*
- 14% smoking
- 19% cognitive inactivity/education#

Barnes & Yaffe, 2011

Is incidence of dementia/ cognitive impairment declining?

Is number of people with dementia ↓ ?

- **UK: Cohorts 1: c 1990 & 2: c. 2010**
 - Based on 1990 Cohort, estimated dementia prevalence in 2010 was 8.3%
 - Actual prevalence 6.5%
- **Sweden: Cohorts 1: c 1990 & 2: c. 2005**
 - Fewer new cases
- **Denmark: Cohorts 1 born 1905 (assessed at 93y) and 2, born 1915 (assessed at 95 yrs)**
 - 1915 performed better in cognitive measures

Matthews et al. *The Lancet*, 2013. [http://dx.doi.org/10.1016/S0140-6736\(13\)61570-6](http://dx.doi.org/10.1016/S0140-6736(13)61570-6).

Qiu et al. *Neurology* 2013;80:1888–1894

Christensen et al. *The Lancet* 2013. [http://dx.doi.org/10.1016/S0140-6736\(13\)60777-1](http://dx.doi.org/10.1016/S0140-6736(13)60777-1)

Implications of reduced prevalence

- **Environmental factors**
 - **Better education?**
 - **Better attention to lifestyle factors?**
 - **Cardiovascular?**
 - **Diet?**
 - **Perinatal and early childhood?**

SMART Trial

- **65yo+ with mild cognitive impairment**
 - Resistance training
 - Computer cognitive training
 - Both
 - Neither
- **Best results on cognition were with resistance training**
- **Too much not as good**

Fiatarone-Singh M, Valenzuela M et al JAMDA 2014

FINGER study

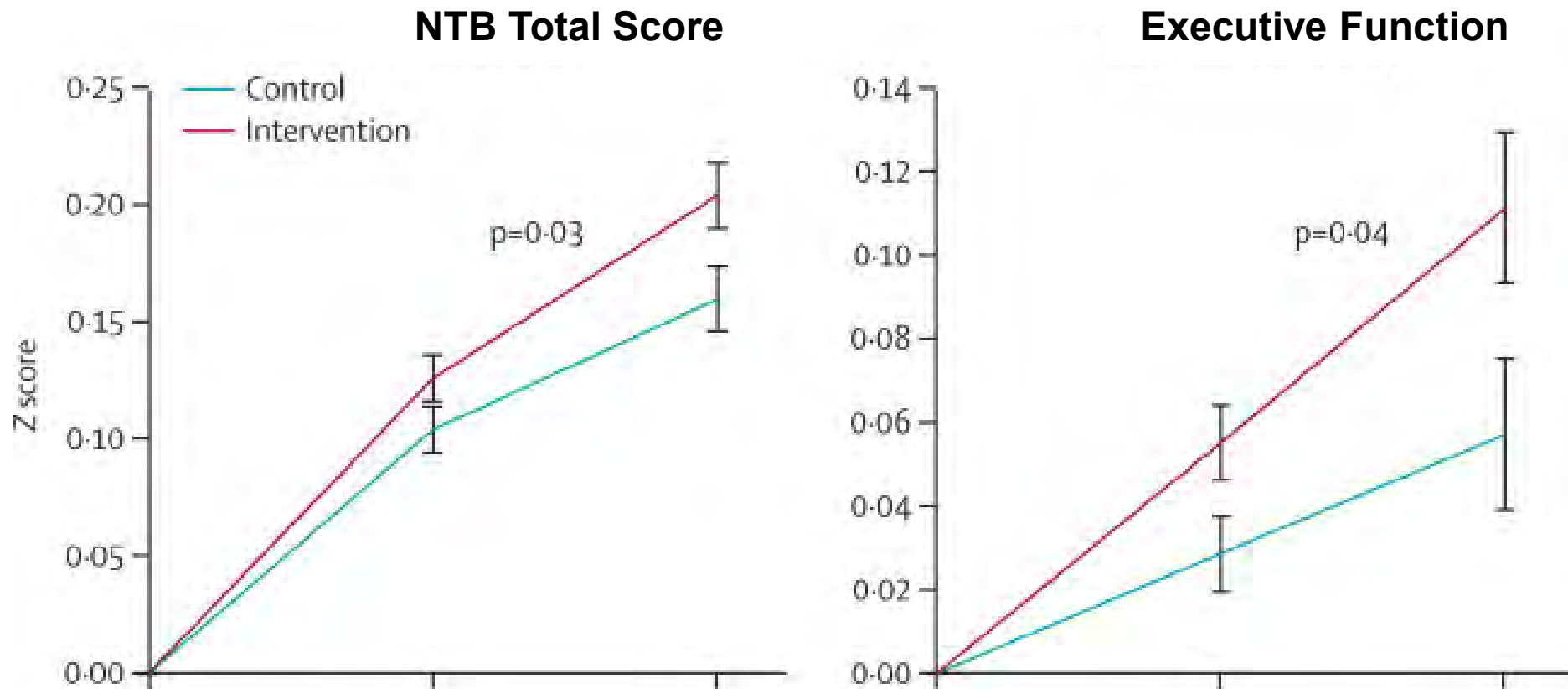
- **Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)**
- **First large, long term RCT of multi-domain interventions aimed at improving cognition**
- **Eligibility: 60-77 yrs, CAIDE dementia risk score ≥ 6 ; cognition at or slightly below mean for Finnish norms (eg, ≤ 26 MMSE)**

Ngandu et al. *The Lancet*. 2015;
[http://dx.doi.org/10.1016/S0140-6736\(15\)60461-5](http://dx.doi.org/10.1016/S0140-6736(15)60461-5)

Finger intervention

- **Diet**
- **Cognitive training**
- **Exercise – PMR and aerobic**
- **Manage metabolic and vascular risk factors**
- **Social activities**

Mean change in cognition over 2 years



Mediterranean Diet



Mediterranean Diet Pyramid



- **NHMRC funded Dementia Research Team Grant**
- **≈ \$6.5m over 5 years, team of 20 CIs and AIs**
- **Patron Ita Buttrose**
- **18,000 55-75 yos randomised to *information or active intervention* – internet based, GP liaison**
- **Tailored modules according to risk factor profile**
 - **Exercise, Diet, Cognitive Training, Depression**
 - **Weight, blood pressure, cholesterol**



MONTEFIORE

Centre for Healthy Brain Ageing

<https://cheba.unsw.edu.au/>

Our vision is to achieve, through research, healthier brain ageing and better clinical care of age-related brain diseases

Conclusions

- **About 30% of Alzheimer's is preventable**
- **Exercise is most important**
- **Mental stimulation, diet, health (BP, cholesterol, diabetes, obesity)**
- **No smoking**
- **Cannot prevent but can delay cognitive decline and dementia**



Fauja Singh, at 100 yrs old became the oldest person ever to complete a marathon (18/10/11)