



Healthy Cognitive Ageing Hunter's Hill (11.04.18)

Henry Brodaty

Never Stand Still

Medicine





**My grandpa started
walking five kilometres a
day when he was 65**

Now he's 97 years old



My grandpa started
walking five miles a day
when he was 60

Now he's 97 years old

**And we have no idea
where he is**

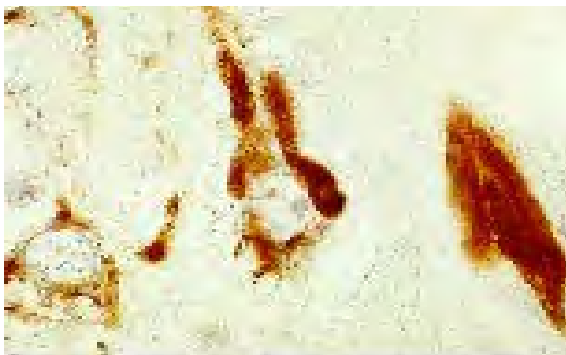
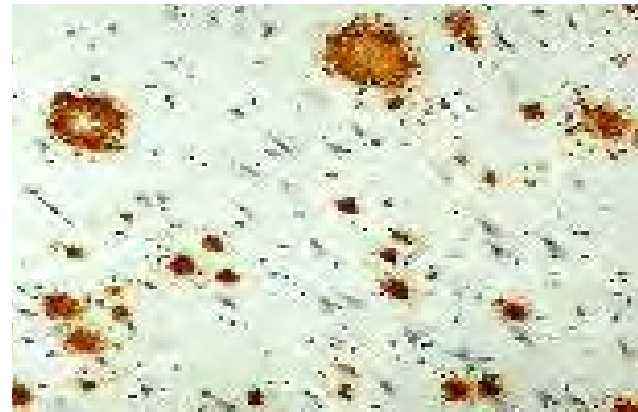
HOLD ON...IF I'VE
GOT A SUPPOSITORY IN MY
EAR - WHERE THE HELL IS
MY HEARING-AID?



Dementia: quick facts

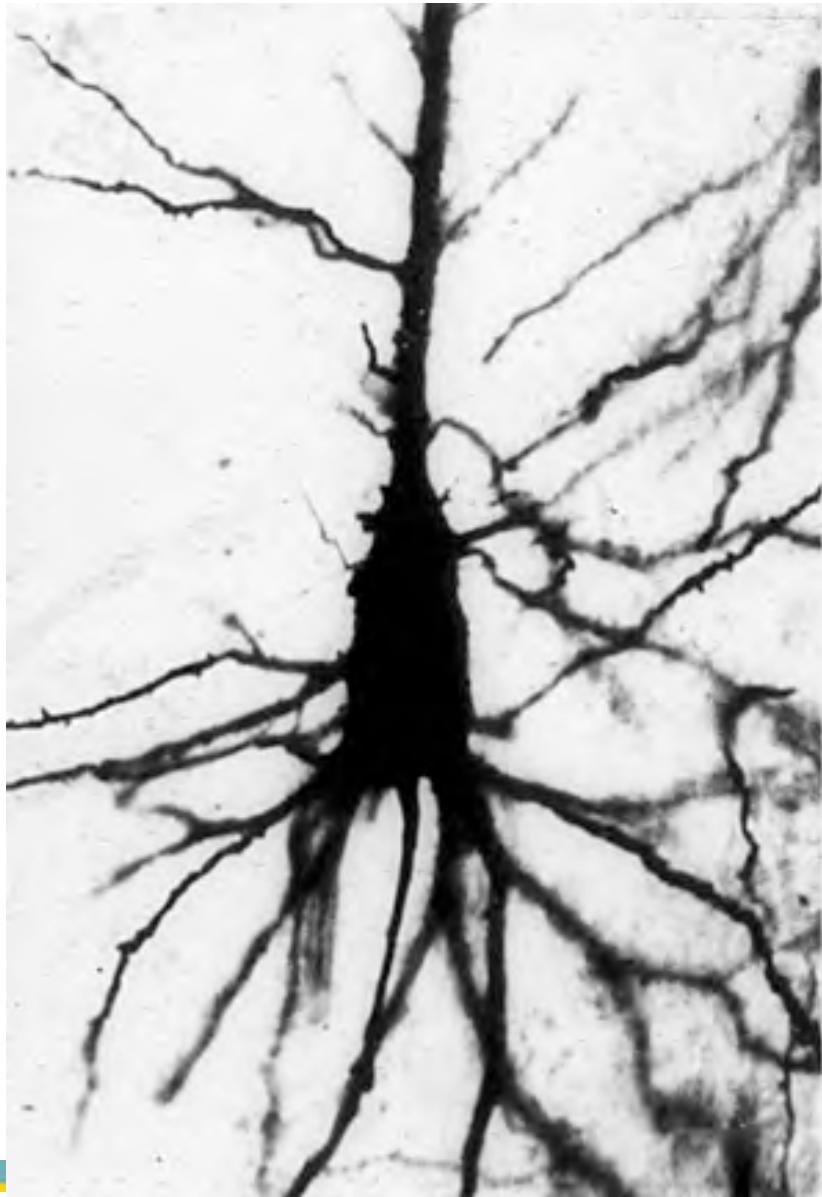
- **Umbrella term, >100 causes**
 - **Alzheimer's 50% of dementias**
 - **Vascular 15-20%**
 - **Mixed 15-20%**
 - **Lewy body; Fronto-temporal dementia**
- **Global: 46.8m worldwide → 136m by 2050**
- **Australia: 425,000 → 1.1m by 2056**
- **Costs: Global USD818b; 1.09% GDP**
 - **Australia AU\$14b+ (2/3 direct costs); ≈1% GDP**

AD: a progressive CNS disorder with a characteristic pathology

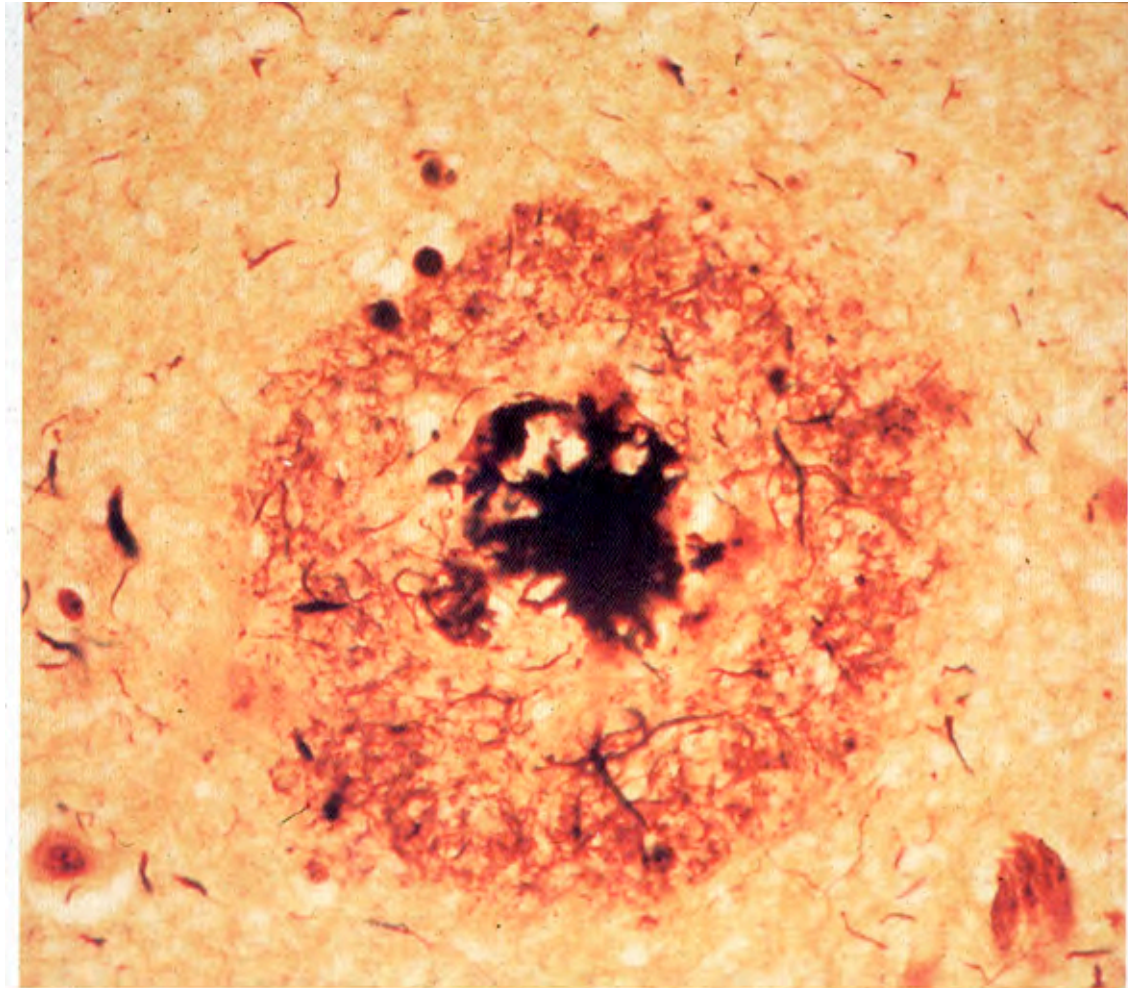


Katzman, 1986

Cummings and Khachaturian, 1996

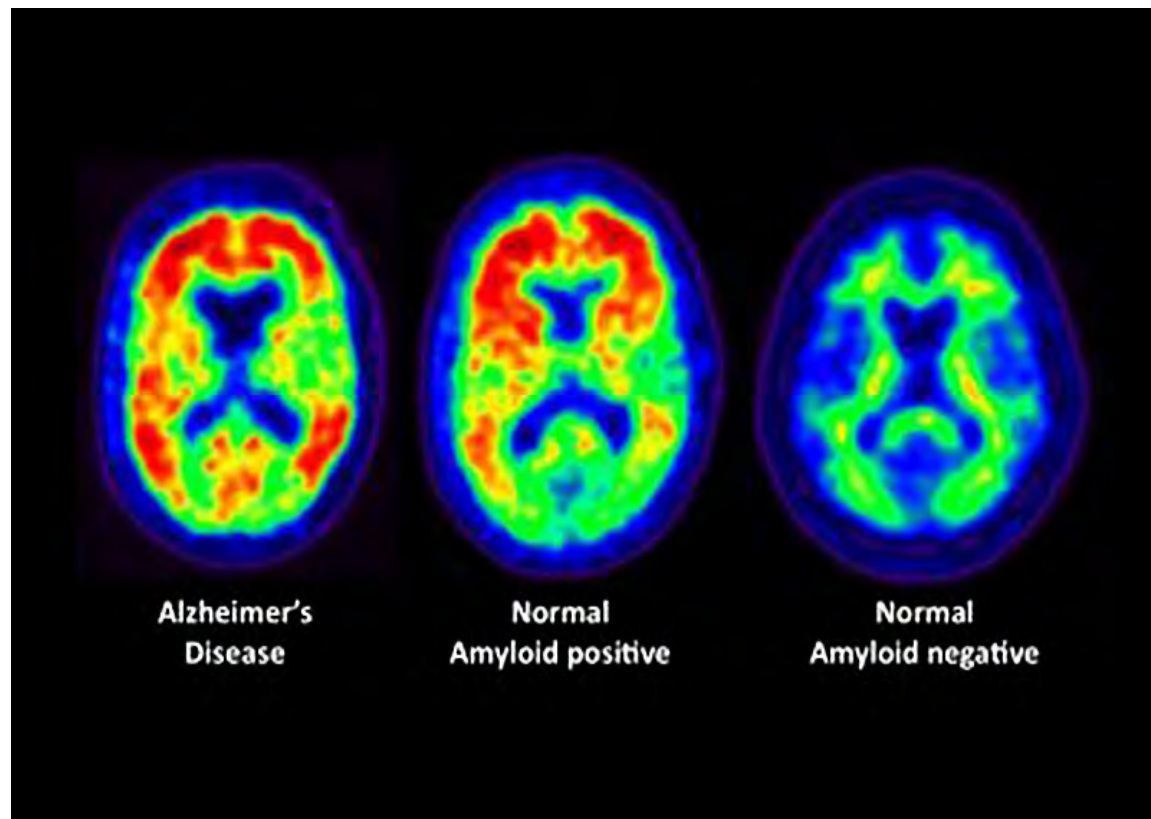


Amyloid plaque



PLAQUE OF AMYLOID BETA-PROTEIN in the brain of an Alzheimer patient is visible as a black globular mass in this stained image. The plaque is surrounded by a halo of abnormal neurites (axons and dendrites) and degenerating neural cell bodies that appear darker than the normal neurons.

PET amyloid imaging: normal vs AD



Hotter colours = more amyloid

- 1 in 3 persons over 60 have amyloid+
- Amyloid+ → ↑ risk clinical progression
- Will all amyloid+ develop AD?
- When??

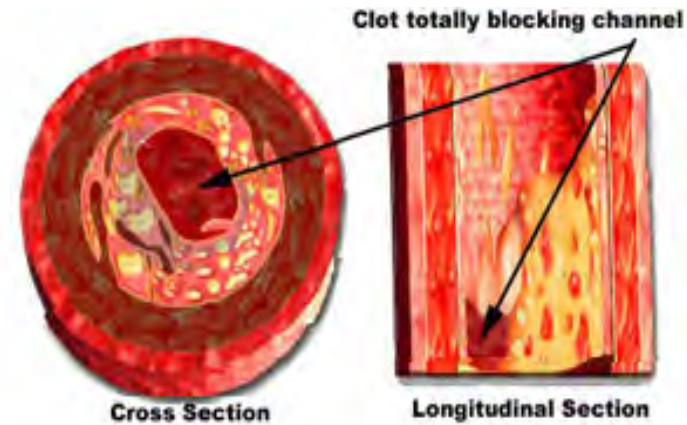
Vascular dementia types

- **Single strategic stroke**
- **Multiple small strokes**
- **Thickening of walls of arterioles**
- **Haemorrhage**

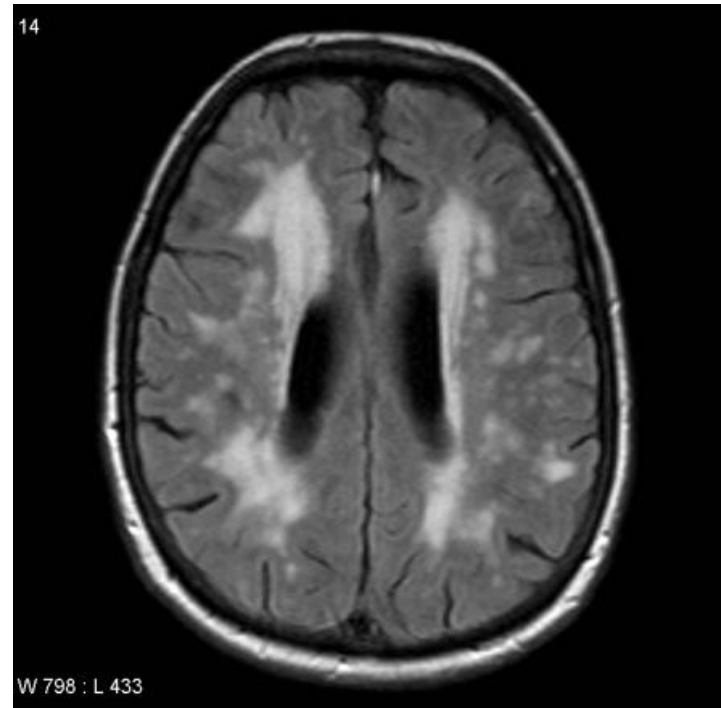
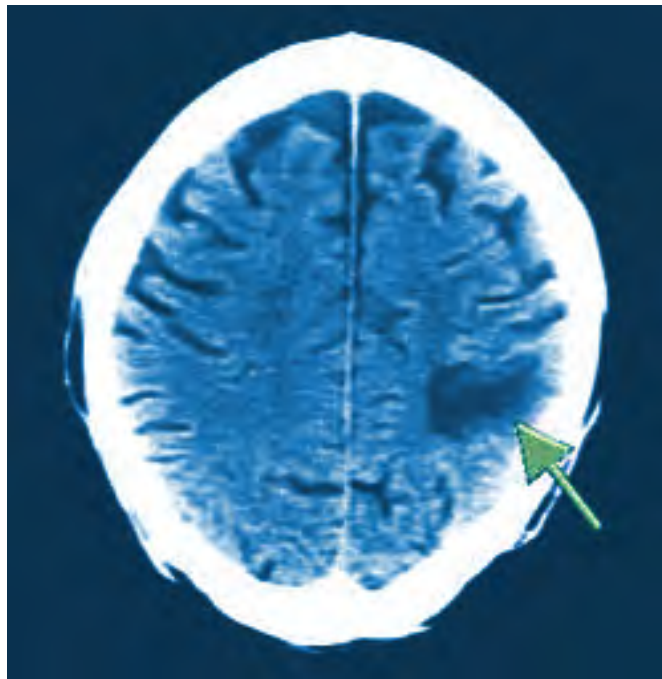
Plumbing



Arteries



Strokes on brain scan



**Can we prevent
dementia?**

**Can we prevent
Alzheimer's disease?**

**Can we prevent any other type of
dementia?**

Can we prevent dementia?

- The adult brain weighs about 1.3 kg
- Dementia shrinks it to 1/2 its usual size

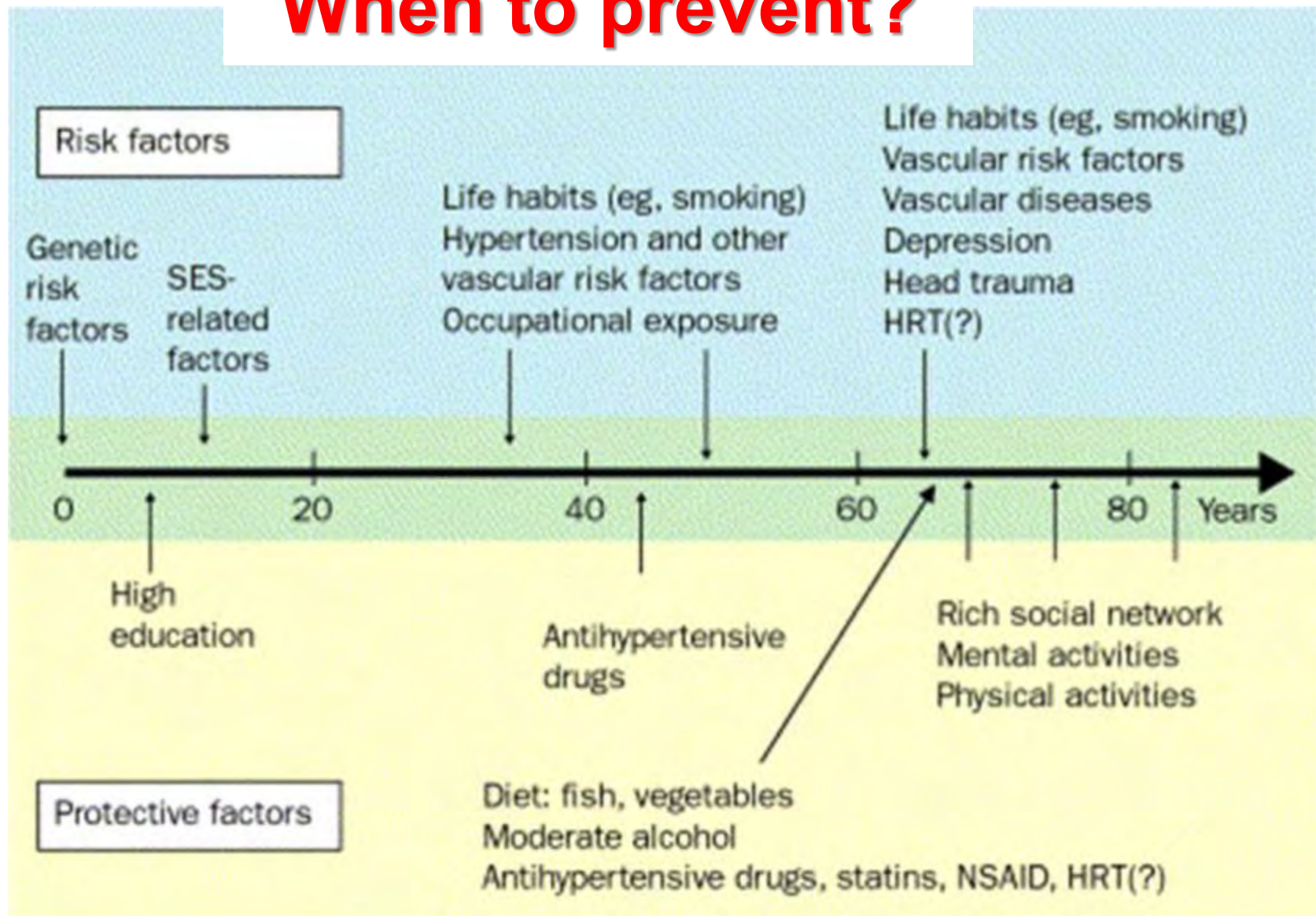


Elimination vs Postponement

- **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%

¹Brookmeyer et al. (1998)

When to prevent?



Is early life the most important target?

- **70% of world dementia in developing countries**
 - Low foetal birth weight
 - Poor or no education
 - Poor socio-economic environment
- **12.4% West Australia's Kimberley Aboriginal people have dementia = 5.2x non-indigenous¹**

Smith K et al, Neurology, 2008;71: 1470-1473



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

yourbrainmatters.org.au

Blood Pressure (BP) and Dementia

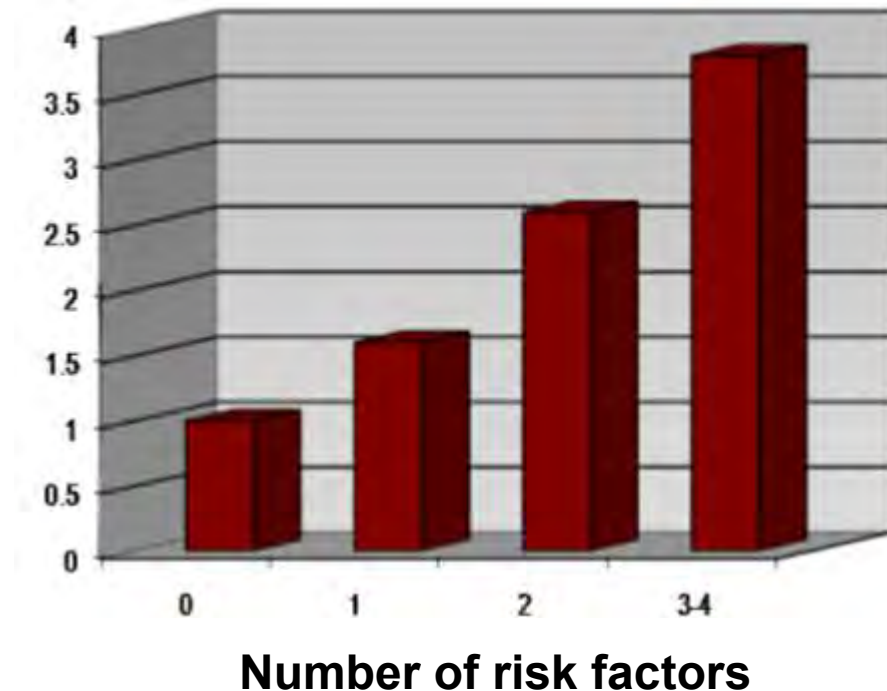
- Mid-life hypertension associated with late-life dementia
- BP ↓ before dementia onset
- Hypertension Rx may → risk ↓
- Each year of Rx → dementia risk ↓
- 5 RCTs conflicting results
- Can harm if lower BP too much in older old



Dosage effect

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

- If we count risk factors...
 - *Hypertension*
 - *Smoking*
 - *Hypercholesterolemia*
 - *Obesity*
 - *Diabetes*
 - *Physical inactivity*



Statins to prevent AD



Mixed evidence

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

¹Jedrziwski 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

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

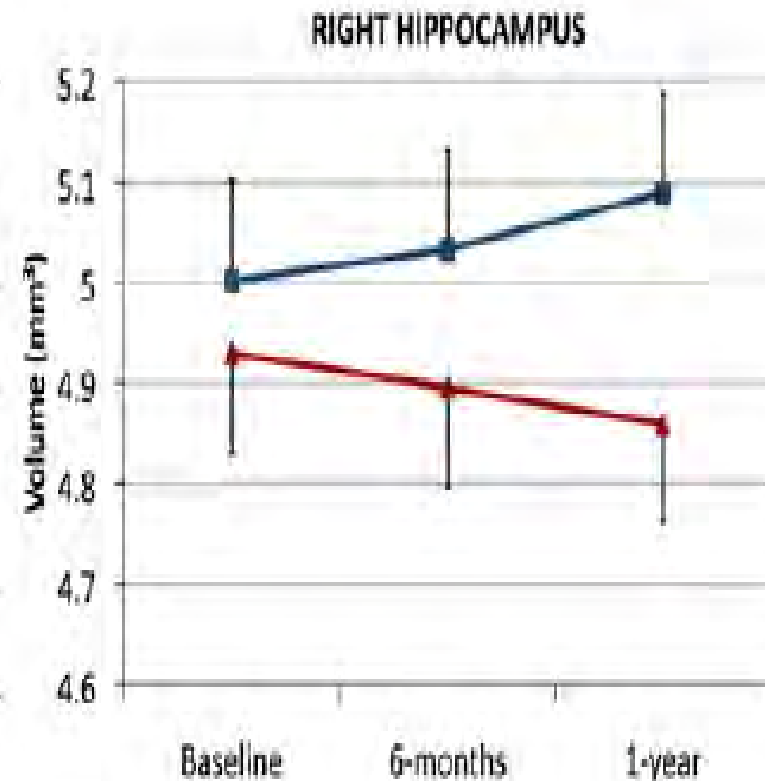
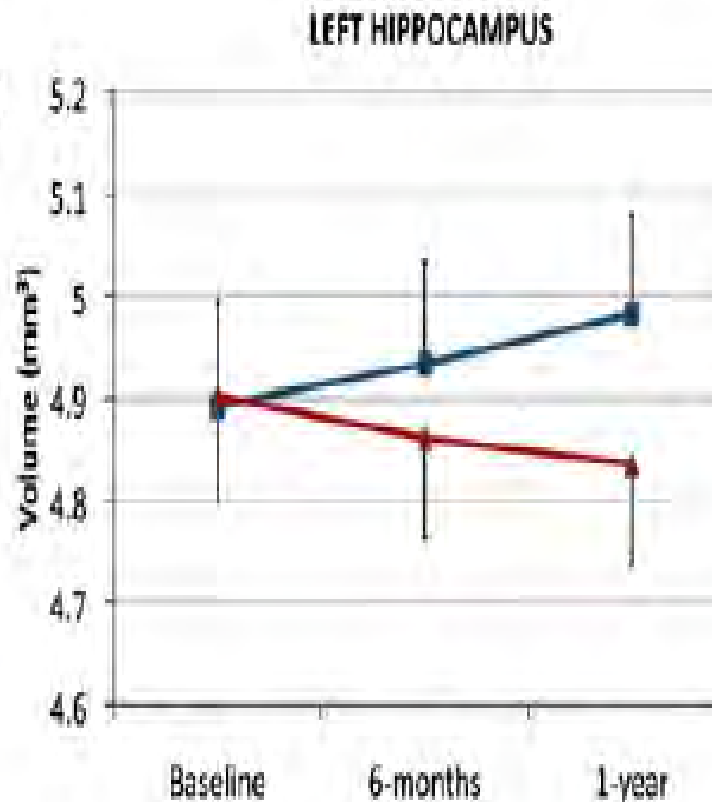
Physical activity

- **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

The power of physical activity

Hippocampus



Erickson et al., 2011

Cognitive training

- **Sudoku, crossword puzzles, reading, bridge??**
- **New language, musical instrument ?**
- **Computer cognitive training**



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 Randomised Controlled Trials with follow-up (more than 3mths) in healthy elderly¹**
 - 7 RCTs met inclusion criteria, low quality
 - Strong effect size for cognitive exercise intervention versus wait-and-see controls
 - Longer follow-up effect remained
- **Review of cog. training or rehabⁿ 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.



Mind your diet

- Mediterranean diet
- Antioxidants

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



Meditⁿ Diet



Nutrition / Supplements



- Alcohol ? moderate
- Fish/Seafood/ ω 3 ?
- Vitamin D ?
- Caffeine ?
- Vitamin E ?
- Vitamin C x

Food sources better than supplements

B Vits and homocysteine

- **OPTIMA: Folic acid 0.8mg + Vit B12 0.5mg + B6 20mg ^{1,2}**
 - Reduce brain atrophy and improve cognition
 - Principally in people with high homocysteine
- **Two systematic reviews and one trial did not find homocysteine lowering treatments beneficial ^{3,4,5}**

1. Smith AD et al, PLoS ONE, 2010;
2. Douaud et al. PNAS 2013;110:9523-9528
3. Ford AH, Almeida OP Systematic review 19 RCTs *J Alz Dis.* 2012;29:133-49 doi: 10.3233/JAD-2012-111739
4. Clarke R et al Am J Clin Nutr 2014;100:657–66 Effect of homocysteine lowering treatment on cognitive function: a systematic review and meta-analysis of randomized controlled trials. – 11 large trials, 22,000 individuals
5. van der Zwaluw 2yr RCT, B vits in 2919 Ps w Hcy↑ *Neurology*;2014;83:1–9

Centenarian Hotspots Blue Zones

**Loma Linda,
CALIFORNIA**

**Sardinia,
ITALY**

**Okinawa,
JAPAN**

**Nicoya,
COSTA RICA**

**Ikaria,
GREECE**

Okinawa: Reasons for Longevity

- **A lean diet with fewer calories:**
 - **Vegetables**
 - **Tofu**
 - **Miso soup**
 - **A little fish or meat**
- **Confucian-inspired adage:**
 - **"hara hachi bu" = until your stomach is 80% full**

Power 9 Principles of the Blue Zones

1. Moderate, regular physical activity
2. Life purpose
3. Stress reduction
4. Moderate calories intake
5. Plant-based diet
6. Moderate alcohol, esp wine
7. Engage in family life
8. Engage spiritually/ religion
9. Engage in social life

1. Move Naturally

Right Outlook

2. Know your purpose
3. Down shift

Eat Wisely

4. 80% rule
5. Plant slant
6. Wine@5

Belong

7. Family first
8. Belong
9. Right tribe

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Buettner D,

Research Centres

Nutrition / Supplements



- Fish✓ ω3 ?
- Vitamin D ?
- Caffeine ?
- Vitamin E ?
- Vitamin C x

Food sources better than supplements

Vit D, NSAIDs, fish, curcumin

- **Vit D – low levels of Vit D are common and associated with development of dementia**
 - **No evidence that taking Vit D lowers risk**
- **Anti-inflammatories – mixed epidem. evidence**
- **Fish oil – some evidence, natural source ie fish (epidemiological)**
- **Curcumin – some evidence (laboratory)**

Smoking and AD



- **Current smoking**
 - increase risk for AD
- **Previous smoking**
 - Risk not significantly increased

Anstey K. Am J Epidemiol 2008

Alcohol

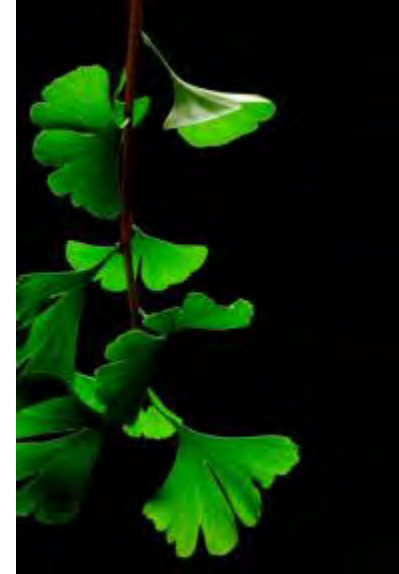
- **Some evidence benefit with moderate alcohol**
 - i.e. abstinent → higher risk, j-shaped curve
- **Not all studies confirm**
- **Heavy alcohol is risk factor**
- **Which alcohol – (red) wine?**
 - Evidence not strong
- **What is *moderate*?**



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**

Unproven but popular

- Ketogenic diet
- Grain Brain
- Coconut oil
- Many others??

Promising?

- Resveratrol
- Next generation anti-ageing compounds



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



- **Prevention trial, NHMRC funded, 5 years**
 - Internet based, largest trial in world
 - 18,000 Australians 55-75 years old
 - Exercise, cognitive training, diet, blood pressure, cholesterol, glucose, depression
 - Tailored to individual risk factors

www.cheba.unsw.edu.au

HEALTHY AGEING FORUM

10am – 1pm Wed 31 October 2018

The Juniors
558A Anzac Pde
Kingsford
Free to attend and
enjoy morning tea
You must book
Phone: 9382 3753



Email: ACPforum@health.nsw.gov.au

Thank you

- **Eat half**
- **Exercise double**
- **Love without limit**

**Centre for Healthy Brain
Ageing (CHeBA)**

www.cheba@unsw.edu.au

**Dementia Collaborative
Research Centre**

www.dementiaresearch.org.au