

# Dementia – Inspiring Hope, Retaining Realism

*Henry Brodaty*





**Australian Government**

**NHMRC National Institute for Dementia Research**

**FIGHT  
SAVE ALZHEIMER'S  
AUSTRALIA**  
**FIGHTDEMENTIA.ORG.AU**



**Australian Government**

**National Health and  
Medical Research Council**

**N H M R C**

# Today's topics

- **Cause of AD**
- **It's important**
- **Diagnosis**
- **Prevention**
- **The silver bullet**
- **Quality of life**
- **Conclusions**

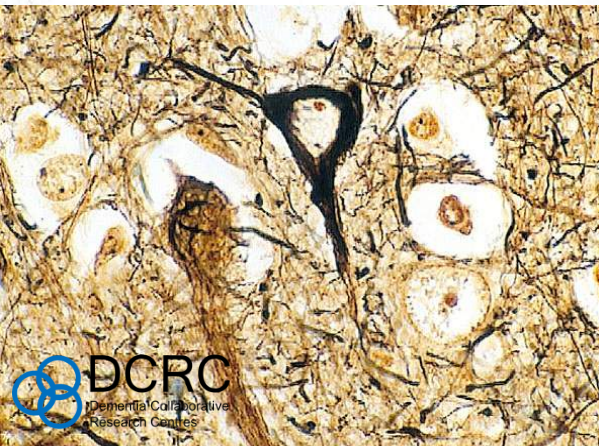
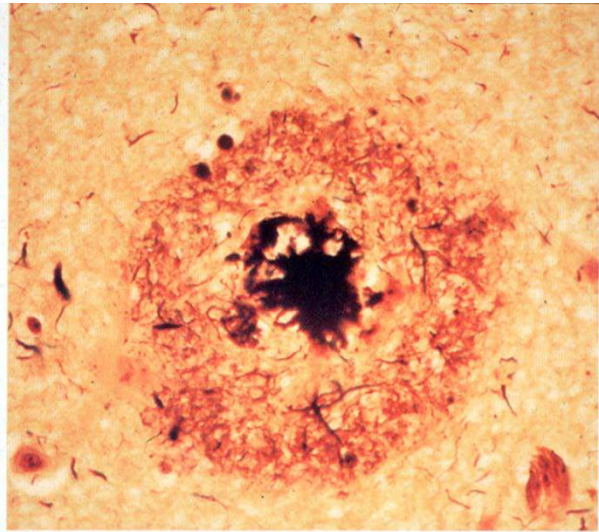
# Let's get our terms straight

- **Dementia/s – cognitive & functional decline**
  - **Alzheimer's disease (AD)**
  - **The other (non-Alzheimer's) dementias**
    - **Vascular dementia**
    - **Lewy body dementia**
    - **Fronto-temporal dementia**
    - **100 others**
- **Mild Cognitive Impairment – phase before dementia**



# Cause: Brain in AD

- Brain atrophy, loss of nerve synapses and branches
- Breakdown of APP releasing  $A\beta$  protein  $\rightarrow$  clumps  $\rightarrow$  toxic to brain  $\rightarrow$  plaques
- Phosphorylated tau  $\rightarrow$  paired helical filaments  $\rightarrow$  NFTs
- Chemicals in brain  $\downarrow$  esp ACh



# The cause of AD??

- **Make excess A $\beta$  protein**
  - **Familial AD, mutations in APP, PSEN1 or 2**
  - **Onset in 40s, 50s.**
- **Decreased clearance of  $\beta$ - amyloid**
  - **Late onset AD, ApoE4**
- **Role of tau**
- **Many other pathways involved, eg...**

# Many other factors ...

- Support cells (astrocytes, glial cells) in brain
- Inflammation
- Insulin resistance in brain
- Progranulin

# Cause: realism

- For young onset autosomal dominant AD cause seems clear
- For late onset sporadic AD, we know risk factors and pathological paths but not cause



# Why is dementia important...globally?

- 47 million people → 131 m by 2050
  - 2/3 in developing countries
- ≈10m new cases per year, every 3.2 seconds
- Cost US\$818 billion, 1.09% of global GDP

# Why is dementia important in Australia?

- 413,000 in 2017 → 1.1 million by 2056 <sup>1</sup>
- 244 new cases of dementia each day in 2017
- Cost to community \$14 billion in 2017
  - 61% direct costs, 38% opportunity costs
  - → \$28b by 2056

<sup>1</sup> *The Economic Cost of Dementia in Australia 2016-2056, NATSEM 2017*

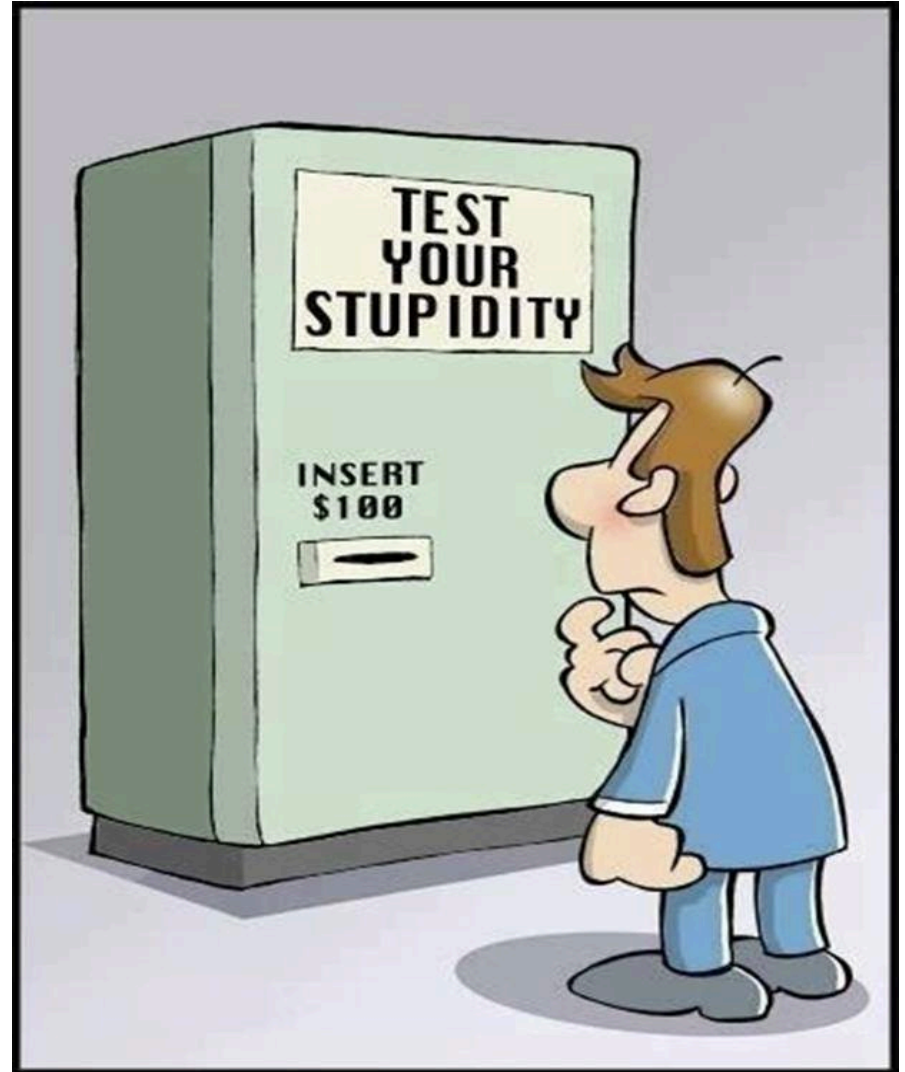
# Why is dementia important in Australia?

- If 5% fewer people aged 65+ were prevented from developing dementia, Australia would save \$5.7b from 2016-25 & \$120.4b by 2056 <sup>1</sup>
- 28,000 develop dementia when less than 65 years of age <sup>2</sup>

<sup>1</sup> *The Economic Cost of Dementia in Australia 2016-2056, NATSEM 2017;* <sup>2</sup> *Dementia in Australia, AIHW, 2012*

# Why is dementia important?

- Because we fear it





**Getting old isn't too bad ...  
except for a little forgetfulness**

# **Why is dementia important?**

- **Because we fear it**
- **Because we are getting older as a population**
- **Because we are living longer as individuals**
- **Because age is the major risk factor for dementia**
- **Because we have it OR we know someone who has it**
- **Because we see what dementia does**

# The hope

- **CURE? PREVENTION?**
- **Are numbers decreasing?**
- **Studies from Sweden, Denmark, Spain, Netherlands, USA show that the number of new cases per each age group has declined in the last 20 years**
- **Better education, health care, diet, lifestyle may be responsible**

# The realism

- **Prevalence, number of existing cases, is ↑**
  - **Ageing of population outweighs decline in new cases**
  - **People with dementia are living longer**
- **Obesity & diabetes epidemics may increase numbers of new cases**
- **Developing countries are ageing rapidly**



# Diagnosing Dementia



# Diagnosing Dementia: the gap



- 2-3 year gap from symptoms to diagnosis
- 50% of (mild) dementia undiagnosed by GPs
- *Timely Diagnosis* project<sup>1</sup>
  - Aim to reach 5000 GPs
  - Face-face or online

<sup>1</sup> DTA, AA, LaTrobe and DCRC

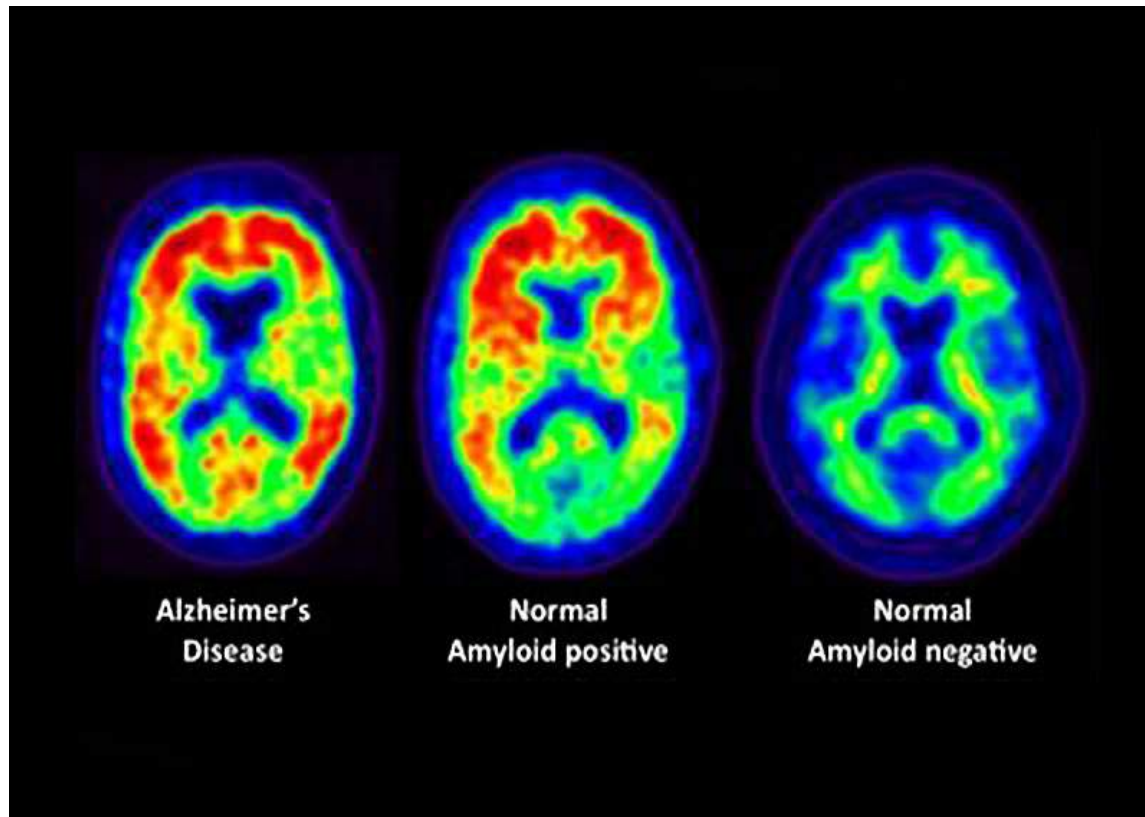
# Diagnosis: the revolution

**Tradition: History + Exam + Tests → Diagnosis**

**The revolution:**

- **Neuroimaging**
  - MRI scans
  - PET imaging, now of amyloid & tau protein
- **Cerebro-Spinal Fluid (Lumbar puncture)**
- **Genetics** - advances but not yet for most
- **Blood test** - advances but not yet

# PET amyloid imaging: normal vs AD



- 35% persons 60+ amyloid+
- Amyloid+ → ↑ risk clinical progression
- Will all amyloid+ develop AD?
- When??

Hotter colours = more amyloid

# **Lumbar puncture = Spinal tap**

## **Change in proteins in CSF**

- **Decrease in amyloid beta protein and increase in tau and phospho-tau proteins**
- **If all measures are normal in pt with mild memory disturbances almost excludes AD**

# Diagnosis of AD - realism

- Biggest challenge is in primary care
- No test 100% accurate yet
- No blood test sufficiently accurate to use yet
- The older the patient, the more likely the brain will have multiple pathologies AD, vascular changes,  $\alpha$ -synuclein, TDP43
- Predictive testing not accurate enough and not recommended
- And if there was a test.....???

**Would you be tested today to see  
if you would develop AD in...?**

**2 years?**

**5 years?**

**or 20 years?**

# Can we prevent dementia?

- Disease **elimination**
  - eg smallpox vaccination
  - best prospect is AD vaccine for those at risk
- Disease **postponement**<sup>1</sup>: delay AD onset by...
  - 2 years, ↓ prevalence by 20%
  - 5 years, ↓ prevalence by 50%

<sup>1</sup>Brookmeyer et al. (1998)



# Is early life the important target?

- **60-70% 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-indigenous<sup>1</sup>**

<sup>1</sup>Smith K et al, Neurology, 2008;71: 1470-1473



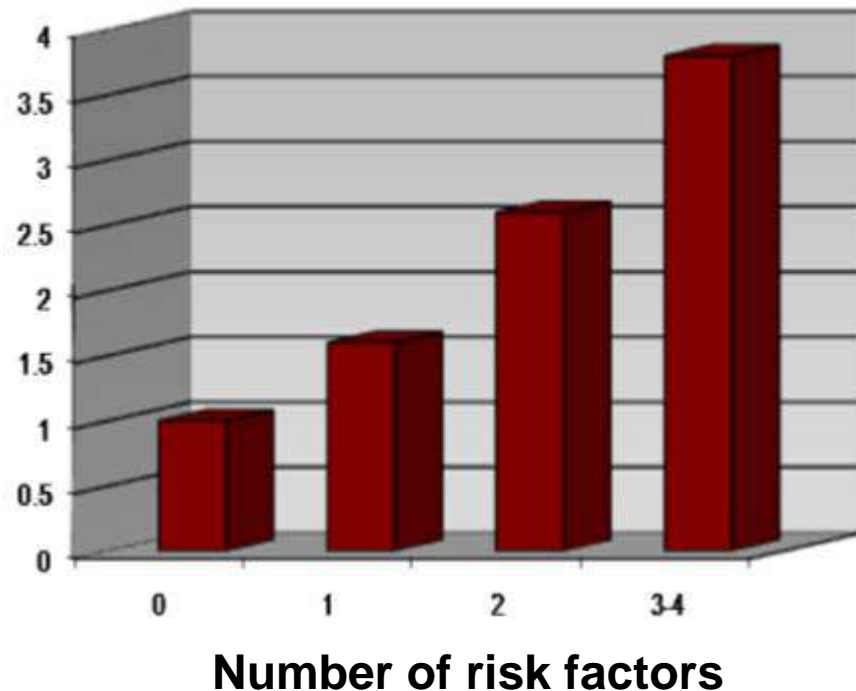
- Look after your heart
- Be physically active
- Mentally challenge your brain
- Follow a healthy diet
- Enjoy social activity

[yourbrainmatters.org.au](http://yourbrainmatters.org.au)

# Dosage effect

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

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



Luchsinger et al 2005

Slide adapted from Michael Valenzuela

**5p**  
CHEAPER THAN  
THE DAILY MAIL  
AND TEN TIMES  
AS FAST

# DAILY EXPRESS

THE WORLD'S GREATEST NEWSPAPER [express.co.uk](http://express.co.uk)



WEATHER: RAIN AND SNOW

WEDNESDAY APRIL 4, 2012 50p

**KATHERINE JENKINS**  
**HER TOUCHING**  
**STORY MAKES**  
**AMERICA CRY**

SEE PAGES 26&27



**Scandal of our benefits paid**  
**to migrants' children who**  
**have never set foot in the UK**

SEE PAGE SEVEN

**WIN A FORD TRIBUTE MOTORHOME WORTH OVER £35,500**

SEE PAGE 37  
premium rate  
phone line

# STATINS HALT ALZHEIMER'S

**40p a day pill**  
**used by millions**  
**tackles cruel**  
**brain disease**

By **Jo Wiley** Health Correspondent

**STATINS** used by millions of people in Britain to prevent heart illness could be the key to beating Alzheimer's, say researchers.

A daily dose of the pill costing as little as 40p may ward off the cruel brain disease.

Scientists found that Simvastatin - the statin most frequently prescribed in the UK and commonly given to elderly patients - improved blood flow in the brain while boosting learning and memory.

The breakthrough could have vital consequences for the long-term health of the nation. At least 850,000 people here have dementia, with more than half suffering from Alzheimer's. The figure is expected to soar by 1.7 million within the next 40 years as the population ages.

The new study brings hope of halting the illness through early intervention. More than six million people in this country take

TURN TO PAGE 2



The Arctic blast hit Britain yesterday, causing mayhem on the roads

**DAYS AFTER RECORD HIGH TEMPERATURES**  
**SNOW CHAOS SWEEPS BRITAIN (WE DID WARN YOU)**

SEE PAGE THREE



**UNSW**  
SYDNEY

# Statins to prevent AD

*Two reviews in 2016 conflict:*

- Good evidence that statins neither prevent nor increase risk of cognitive impairment or dementia<sup>1</sup>
- Statins linked to reduced AD risk – differences by sex, race & statin<sup>2</sup>



<sup>1</sup>McGuinness B et al, 2016; CD003160 (1) Cochrane Database of Systematic Reviews

<sup>2</sup>Zissimopoulos JM et al, 2016, JAMA Neurology



# Physical activity



# Can exercise protect against dementia?

- Preserve cognition and slow cognitive decline
- 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

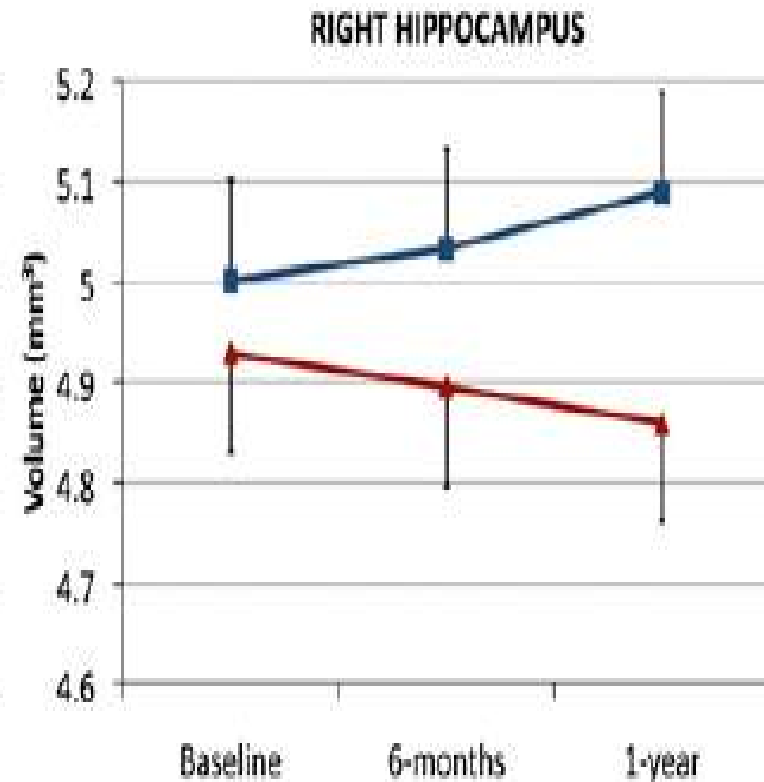
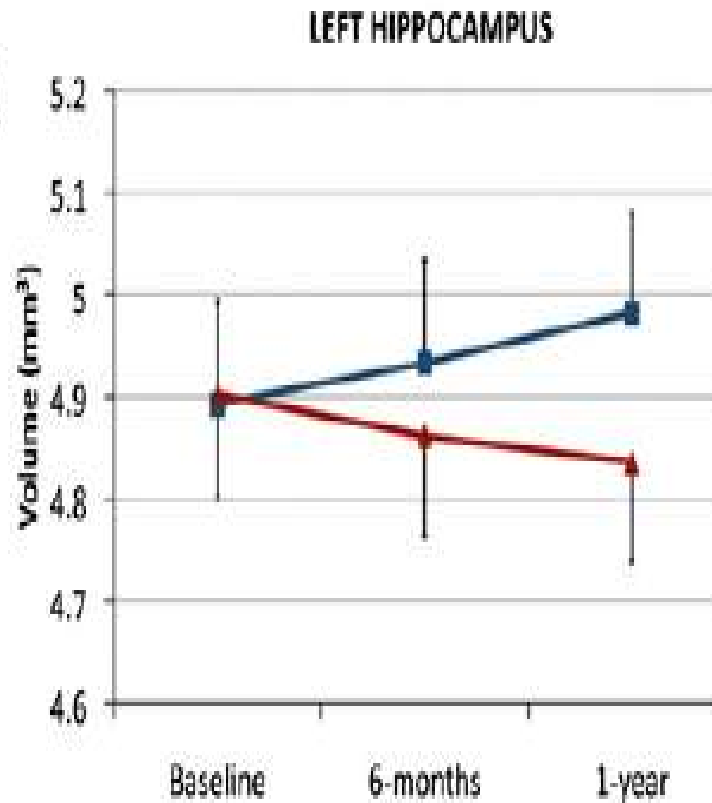
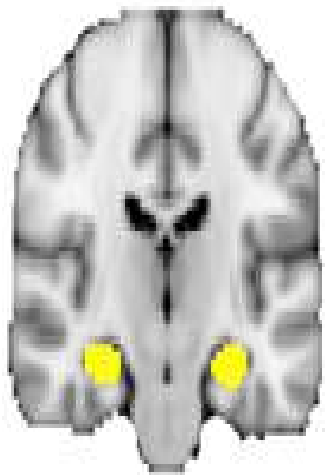
- **Physical activity benefits older adults to prevent dementia: Never too late to start**
- **Moderate intensity (brisk walking) 30 min 5d/week is minimum**
  - more is better, puffed and sweaty
- **Evidence for specific exercise:**
  - more than one type exercise may be better
  - resistance training may be better (SMART)

Denkinger et al. *Z Gerontol Geriat* 2012; 45:11–16 DOI 10.1007/s00391-011-0262-6  
Fiatarone Singh MA et al *JAMDA* 2014;15:873-80; Lautenschlager N, *JAMA* 2008



# The power of physical activity

## Hippocampus



Erickson et al., 2011

# The hope: physical activity...

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

[http://www.mednwh.unimelb.edu.au/research/health\\_promotion.htm](http://www.mednwh.unimelb.edu.au/research/health_promotion.htm)

# Mental Activity



# 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)<sup>1</sup>
- Dose - response relationship evident<sup>1</sup>
- Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence<sup>1</sup>
- Results held when covariates in source studies were controlled for<sup>2</sup>

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

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

# Cognitive training

- **Systematic review of RCTs with longitudinal follow-up (>3mths) in healthy elderly<sup>1</sup>**
  - 7 RCTs met inclusion criteria, low quality
  - Strong effect size for cognitive exercise intervention vs wait-and-see controls
  - Longer FU duration (>2yrs) → ES no lower
- **Review of cog. training or rehab in dementia<sup>2</sup>**
  - 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.

# Realism mental training

- Reverse causality
- Which mental activity
  - Crosswords?? Sudoku??
  - Musical instrument? New language?
  - Computer cognitive training, are benefits:
    - Sustained?
    - Generalise beyond computer?
      - ACTIVE Study 10 years later → benefits

NOW  
**10p**  
CHEAPER THAN  
THE DAILY MAIL AND  
THE DAILY MIRROR  
AND TEN TIMES BETTER

## YOUR HONOUR HITS OUT



Jailed John Hennigan

THE LADY JUDGE  
WHO SWORE  
BACK AT A VILE  
RACIST THUG

SEE PAGE 11



Judge Patricia Lynch

# DIET TO BEAT ALZHEIMER'S

**Med food good  
for the brain as  
well as the heart**

By Giles Sheidrick

A MEDITERRANEAN diet boosts brain power and slashes the risk of Alzheimer's, research shows.

Experts say eating like the Greeks with lashings of olive oil can protect against the onset of devastating mental decline.

The cure-all regime has long been considered a good way to shave off heart disease. Now scientists have said it is good for the brain too, whatever your age.

Fresh analysis suggests those who regularly eat plenty of fish, fruit, vegetables and nuts but consume little dairy or red meat have a much slower rate of memory loss.

Confirmation of the life-extending qualities of the sunshine way of life comes after researchers found links between diet and mental function.

Study author Roy Hardman, from Swinburne University of Technology in Melbourne, Australia, said: "There is encouraging evidence a

TURN TO PAGE 6



EXCLUSIVE

The Duke of Westminster, with the Queen, died on Tuesday  
SEE PAGE 7

**Dying wish of Britain's most generous aristocrat**



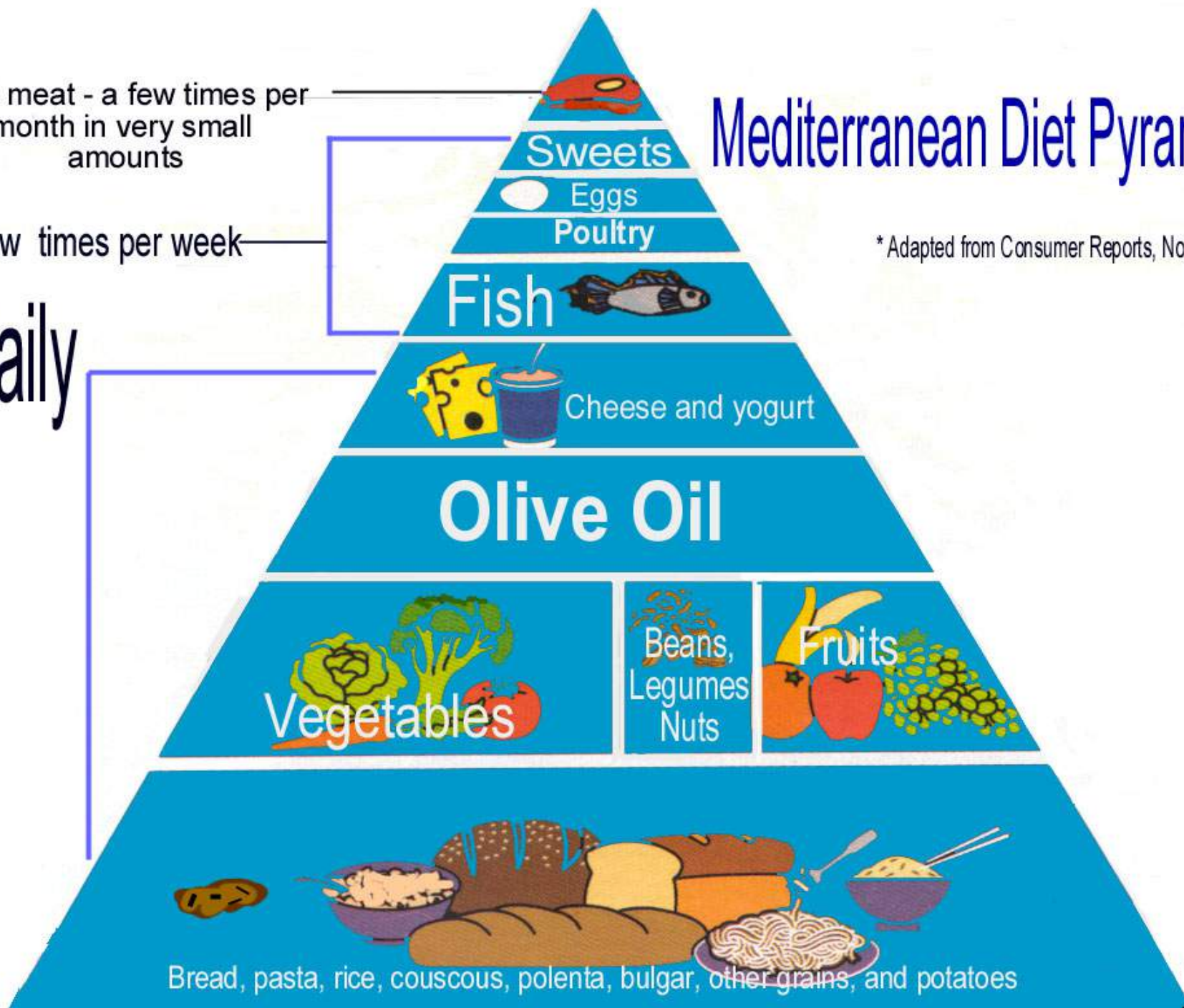
Red meat - a few times per month in very small amounts

A few times per week

Daily

# Mediterranean Diet Pyramid\*

\* Adapted from Consumer Reports, Nov'94





# Nutrition / Supplements



- Fish/Seafood/ $\omega$ 3 ?
- Folic acid & B Vits ?
- Vitamin D ?
- Caffeine ?
- Vitamin E ?
- Vitamin C x

***Food sources better than supplements***

# Smoking and AD



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

Anstey K. Am J Epidem 2008

# Alcohol

- **Some evidence benefit with moderate alcohol**
  - i.e. abstinent → higher risk, j-shaped curve
- **Not all studies confirm**
- **Interaction with ApoE4 – contradictory results?**
- **Heavy alcohol is risk factor**
- **Which alcohol – (red) wine?**
  - Evidence not strong
- **What is *moderate*?**

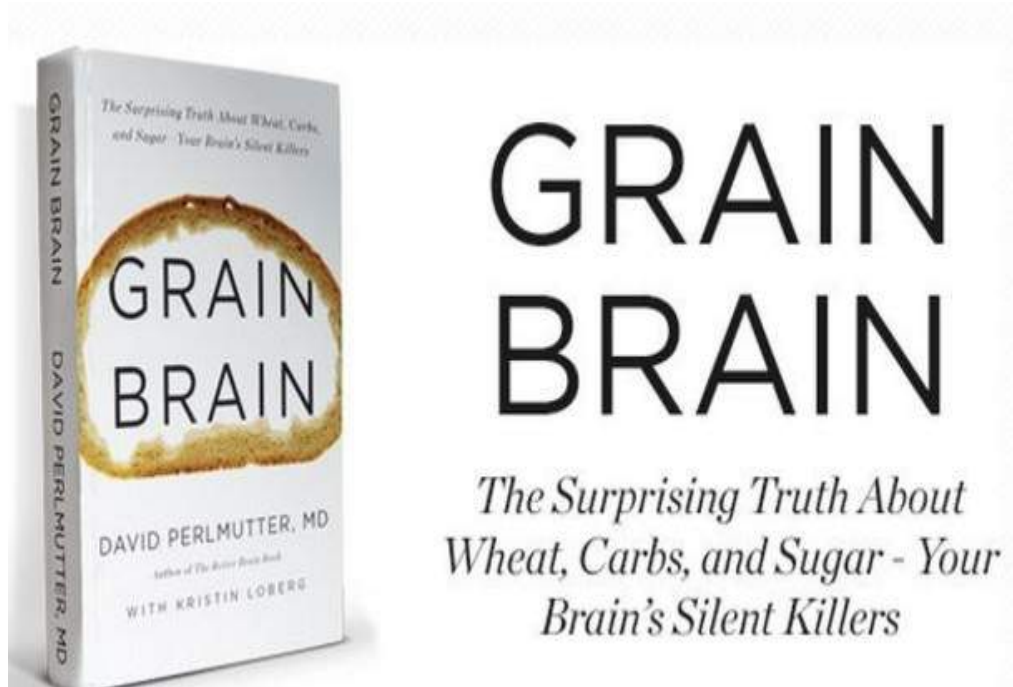
# Natural therapies

- **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**



# GRAIN BRAIN

*The Surprising Truth About  
Wheat, Carbs, and Sugar - Your  
Brain's Silent Killers*

**Many  
unproven  
claims**



[www.Alzheimers.net](http://www.Alzheimers.net)

# Diet: realism

- Mediterranean diet has best evidence
- Diet, exercise, vascular health, diabetes, obesity – all linked
- Obesity in mid-life is a risk factor; late life not
- Most claims are based on observational studies eg Okinawa diet
- RCTs for long periods impossible



# Other factors

- HRT – neither harmful nor beneficial close to menopause
- Hearing loss ↑ risk RR 1.55-2.32
- Less ‘socialisation’
  - increases risk of cognitive decline/ dementia
  - moderates effect of Alzheimer pathology on cognitive function
- Air pollution?





# 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<sup>u</sup> 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 and UK similar (20.3%, 95% 5.6–35.6)

Barnes & Yaffe, 2011; Norton et al, 2014



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

- **Diet**
- **Cognitive training**
- **Exercise – PMR and aerobic**
- **Manage metabolic and vascular risk factors**
- **Social activities**
- **Outcomes at 2 years:**
  - **improved test battery, executive function, processing speed, but not memory**

# Internet based prevention trials

- Healthy Aging Through Internet Counselling in the Elderly (HATICE) <http://www.hatice.eu/>
- *Maintain Your Brain*
  - NHMRC funded, 5 years, largest trial in world
  - 18,000 Australians 55-75 years old
  - Exercise, cognitive training, diet, depression
  - blood pressure, cholesterol, glucose
  - Tailored to individual risk factors

**[www.cheba.unsw.edu.au](http://www.cheba.unsw.edu.au)**



**Women who refuse to let their husbands see them naked** **Femail Magazine**  
STARTS PAGE 35



# ALZHEIMER'S REVOLUTION

**Breakthrough drug could stop dementia from ever developing**

By Fiona MacRae  
Science Editor

A REVOLUTIONARY drug to stop dementia will be trialled in Britain. Scientists say the breakthrough treatment has the potential to transform the fight against memory-robbing Alzheimer's. It works by tackling a rogue protein that plugs up the brain and develops cells. In preliminary tests the protein all but vanished in a year. Hospitals and clinics in London, Newcastle, Glasgow, Edinburgh and Dundee are looking for patients to take part in full-scale trials. The developers of aducanumab hope it could eventually be prescribed to healthy pensioners to halt dementia in much the same way that statins



**125,000 ops face axe in doctors' five day strikes**

By Sophie Borland  
Health Editor

JUNIOR doctors will stage the biggest strikes in NHS history over their new contract - despite being warned by their own officials that 'people will die' as a result. There will be a five-day walkout by junior doctors each month until the end of the year, meaning up to 125,000 operations will be cancelled, as well as about 100,000 patient appointments. Members of the doctors' union have voted for the strikes - which were revealed in yesterday's Mail - as they remain unhappy with changes to their terms for weekend work. All departments will be abandoned including A&E, intensive care and maternity, as well as cancer and consultant to fill in.

**Transfer deadline**  
Club by club: the dramatic right up to the...  
Inside story of who went where, and for how much  
First 20-year Q&A on the move

**The Daily Tel**

**Brexit deal will limit migration, May pledges**

PM draws red line on free movement whatever the impact on trade with EU

By Steven Ingham  
DEPUTY POLITICAL EDITOR

BRITAIN will restrict immigration from the European Union after David Cameron's pledge yesterday. Setting out his five "red lines" for the forthcoming EU negotiations, the Prime Minister told his Cabinet that immigration controls must not be weakened. European leaders have repeatedly insisted that Britain must accept the free movement of EU migrants in exchange for full membership of the single market. However, Mrs May's statement says that the UK will not accept any form of free movement of EU migrants that would mean that the UK would not be able to control its own borders. Mrs May said:

"Immigration gathered at Champs-Élysées, but official security measures, that Britain would partner a 'unique' model after it left the EU and would not adapt to 'all the self-sufficiency'." Her comments effectively rule out taking a similar approach to Norway, which allows access to the single market in exchange for accepting the free movement of EU migrants. A Downing Street spokesman said: "Several Cabinet members made it clear that we are leaving the EU but not leaving Europe, with a decision on whether the model we are working is now unique to the United Kingdom and not an off-the-shelf solution." "This means Britain remains on the doorstep of people who want to live in Britain, but also a positive outcome for those who wish to leave the UK and work elsewhere."



Challenging the notion of EU citizens coming to the UK is central to the Government's "pledge to reduce the level of net migration to 'near zero'." Last week it emerged that more than three million people from the EU are now living in the UK, as Poland and Slovakia join the queue to join the UK. The figures show that net migration was at its lowest level of 20,000 last year, more than three times Mrs May's target. Mrs May is considering plans to introduce a points system to limit the number of low-skilled workers from outside the UK. The Prime Minister also confirmed that she will "push" Britain's position on the issue.

**All-singing, all-dancing Oscar**



# Drug prevention trials

**Clinically normal but at high risk:**

- **A4 Study - Clinically normal, A $\beta$  positive**
- **DIAN – TU – Dominantly inherited AD**
- **Alzheimer Prevention Initiative (Colombia)**
  - **mainly antibody studies (vaccine)**

**Prevent MCI → AD:**

- **Tau therapeutics**
- **$\beta$ -secretase inhibitor**



# Drug trials for AD - the hope

**5p** **DAILY EXPRESS**  
THE WORLD'S GREATEST NEWSPAPER EXPRESS.CO.UK WEATHER: RAIN WEDNESDAY JULY 18, 2012 50p

**BURIED ALIVE: COUPLE FOUND DEAD IN CAR TEN DAYS AFTER LANDSLIDE**  
SEE PAGE 5

**BRITAIN'S ECONOMY BOOSTED AT LAST**  
SEE PAGE 2

**PILL TO BEAT ALZHEIMER'S**

**New treatment will stop disease for three years**  
By Giles Sheldrick

ALZHEIMER'S sufferers and their devastated families were last night given new hope after scientists hailed the "most exciting" breakthrough yet in the search for a cure.

A drug has been shown to stop the harrowing disease in its tracks for three years - whereas current treatments only slow down the symptoms.

Trials of the drug, known as immunoglobulin, have proved so successful it could be available at chemists in pill form within a decade.

**Excited**

The findings were revealed yesterday at the Alzheimer's Association International Conference in Vancouver, Canada. The world's largest gathering of dementia researchers was said to have been left stunned.

One leading scientist told the Daily Express: "This type of treatment is a new approach. Previously licensed drugs have only been able to slow the progression of symptoms whereas this drug harnesses the body's immune system to tackle the underlying cause of the disease. The reason that everyone is getting very excited about this is because it's the most

**KATE, WILLS AND HARRY'S PRINCELY SUM FOR CHARITY**  
TURN TO PAGE 4

THE DUCHESS OF CAMBRIDGE'S NAME HAS BEEN ADDED TO WILLIAM AND HARRY'S ROYAL FOUNDATION SEE PAGE 9

VICTIM: Rosemary Snell



Friday, July 25, 2014

**The rise of Power Hair**  
Do's and don'ts of fringe politics

**INSIDE TIMES?**  
Millions made in selfish The Taste



**Islamic hate books found in prisons despite ban**

By Sarah Lyall

Prisoners in British jails are still able to read books that glorify violence against Muslims, despite a ban on such material, a report by a senior government official has revealed.

The report, which was obtained by the BBC, says that the ban on such books is not being enforced in some prisons, and that some prisoners are still able to read books that glorify violence against Muslims.

The report also says that some prisoners are still able to read books that glorify violence against Muslims, despite a ban on such material.

## Scientists create the first drug to halt Alzheimer's

Brain deterioration stopped by twice-a-day pill

A "wonderful" discovery raises glimmers of hope

Scientists have created the first drug to halt Alzheimer's disease, a breakthrough that could revolutionize the treatment of the condition. The drug, which is taken twice a day, has been shown to stop the brain deterioration associated with the disease in a series of experiments.

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**IN THIS WEEK**  
Brazil's weak fiscal job  
Trump's book attack  
US ignores rule of law  
Women in City's plight

# The Daily

**Working in an office as bad as smoking**

By Sarah Lyall

Working in an office is as bad as smoking, according to a new study. The study found that working in an office is as bad as smoking, according to a new study. The study found that working in an office is as bad as smoking, according to a new study.

**Britain in business with I**

By Sarah Lyall

Britain is in business with I, according to a new study. The study found that Britain is in business with I, according to a new study. The study found that Britain is in business with I, according to a new study.

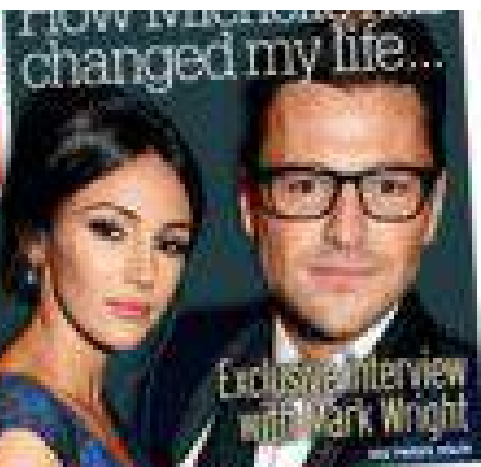
**US ignores rule of law**

By Sarah Lyall

US ignores rule of law, according to a new study. The study found that US ignores rule of law, according to a new study. The study found that US ignores rule of law, according to a new study.

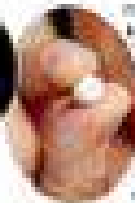


Send me a picture with your bikini off



## NEW HOPE FOR MILLIONS

# CANCER DRUG CAN STOP YOU GETTING ALZHEIMER'S



## POLICE: NAME FULL

Identities of suspected killer secret and, you guessed, it

By Andrew Adams

ALMOST half of justice bosses in Britain are refusing to identify dangerous suspects including his suspected killers - to protect their "human rights" to privacy. They say revealing their names could be dangerous, even if it means not naming them. The police are also worried that the public might be misled by the names of the suspects. The police are also worried that the public might be misled by the names of the suspects. The police are also worried that the public might be misled by the names of the suspects.



# Strategies

- **Anti-amyloid**
  - Enzyme inhibitors
  - Immunotherapies – active, passive
- **Anti- tau**
- **Neurotransmitter enhancers**
  - Cholinesterase inhibitors
  - Memantine
  - Serotonin receptor antagonists
- **Others: intranasal insulin, RAGE, NGF**

# Promote neuronal function

- **Mitochondrial dysfunction**
  - **Latrepirdine (Dimebon) - failed**
- **Nerve growth factors: Delivery to brain is a challenge:**
  - **Viral vectors**
  - **Nanotechnology**

# Other treatments

- Long acting intra nasal insulin
- Deep brain stimulation targeting limbic memory circuit in pts with mild AD
- 5-HT6 Receptor antagonist, idalopiridine
- Nutraceuticals – Axona, Souvenaid

# “Cures” for AD



**Dr Tobinick injecting Etanercept in spine**

# Realism: the graveyard of AD Cures

- Trimiprosate (Alzhemed)
- Flurbiprofen (tarenflurbil)
- Anti-inflammatory
- Rosiglitazone
- Statins
- Leuprolide
- Latrepirdine (Dimebon)
- Semagacestat ( $\gamma$ -secretase inhibitor )
- Bapineuzemab
- Verubecestat ( $\beta$ -secretase inhibitor )
- Celecoxib
- Intravenous Immunoglobulin

# Why failures despite Phase 1/2 trial success?

- Wrong time? Too late in disease process?
- Wrong target? Amyloid may not be the one
- Wrong patient? 30% of trial participants did not have AD as per amyloid PET Scans
- Wrong model? May need multiple drugs simultaneously eg TB, H. bacter, leukaemia

# Realism – drug treatments

- No silver bullets
- Billions invested with no return
- Pharma still interested but some not
- Most trials for AD
- World Dementia Council aim for cure by 2025 unlikely<sup>1</sup>



***‘The mainstay of treatments for AD is supportive care from family ..’<sup>2</sup>***

<sup>1</sup> Cummings J et al, 2016 Alz Research & Therapy

<sup>2</sup>Scheltens P et al, Lancet, 2016:388:505-17



# **Achieving quality of life....**

**...for person living with dementia and carer:**

- Reducing stigma**
- Building dementia friendly communities**
- Knowledgeable, skilled and empathic health professionals in primary, acute and residential care**
- Timely diagnosis & advice and quality care**
- Australian Clinical Practice Guidelines**

## Want information on the diagnosis, treatment and care for people with Dementia?

The Clinical Practice Guidelines  
and Principles of Care for People  
with Dementia, and the Consumer  
Companion Guide will be of help.



**Clinical:** [www.sydney.edu.au/medicine/cdpc/documents/  
resources/CDPC-Dementia-Recommendations\\_WEB.pdf](http://www.sydney.edu.au/medicine/cdpc/documents/resources/CDPC-Dementia-Recommendations_WEB.pdf)

**Consumer:** [www.sydney.edu.au/medicine/cdpc/documents/  
resources/consumer-companion-guide.pdf](http://www.sydney.edu.au/medicine/cdpc/documents/resources/consumer-companion-guide.pdf)

# **Improve quality of life by...**

- **Proactive guidance and care**
- **Optimal use of medications**
- **Improvements in community care**
- **Psychological & environmental strategies to manage behavioural & psychological symptoms**
- **Empowering affected persons and families**
- **Research on how to achieve all of these**

# Conclusions - HOPE

- HOPE - Research on dementias: AD *and* Vascular, Lewy body and fronto-temporal dementia
- Research can drive drug Rx *and* improvements in diagnosis and care
- Australia has leaders in areas of basic, diagnostic, carer, translational, residential care research
- World wide community collaborating



# Conclusions: REALISM

- **Funding for research is a major issue**
  - **Proportionately low vs**
    - **Other major diseases**
    - **Disease burden**
    - **Cost of health care**
- **Australian Dementia Registry would boost recruitment for prevention and treatment, improve standards of dementia diagnosis & care**

# Conclusions

- **Dementia research → hope**
- **Realistic expectations**
- **Prevent cognitive decline, delay onset of dementia**
- **Work towards drugs to delay or stop degenerative processes such as AD**

# Thank you

**Centre for Healthy Brain Ageing (CHeBA),  
UNSW Sydney**

**[www.cheba@unsw.edu.au](mailto:www.cheba@unsw.edu.au)**

**Dementia Collaborative Research Centre**

**[www.dementiaresearch.org.au](http://www.dementiaresearch.org.au)**