

Dementia - a new era?

Dr Antoinette O'Connor

MB BCh BAO, Clinical Education (PDip), MRCPI,
PhD



**Tallaght
University
Hospital**

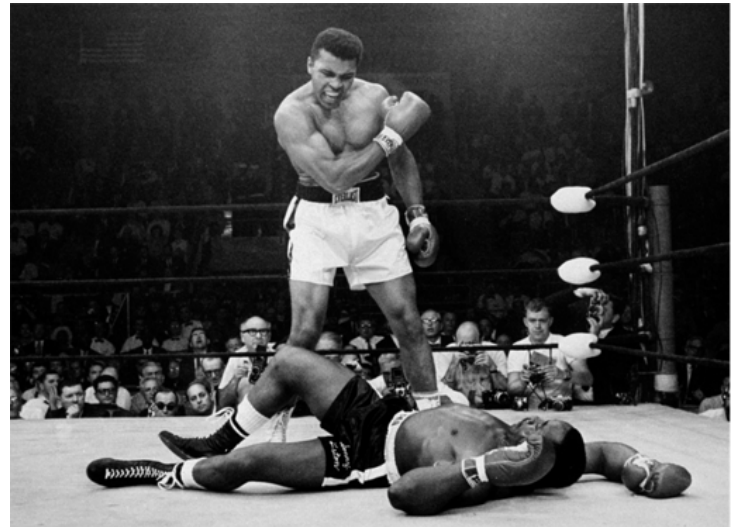
Ospidéal
Ollscoile
Thamhlachta

An Academic Partner of Trinity College Dublin

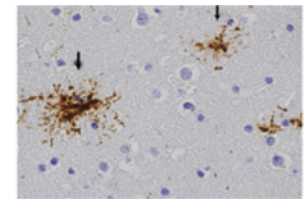
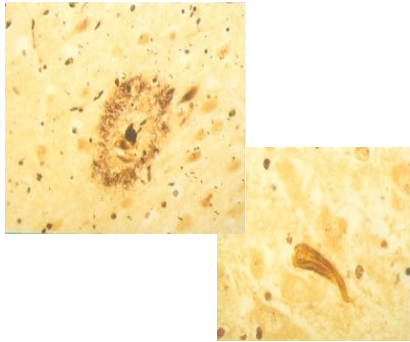
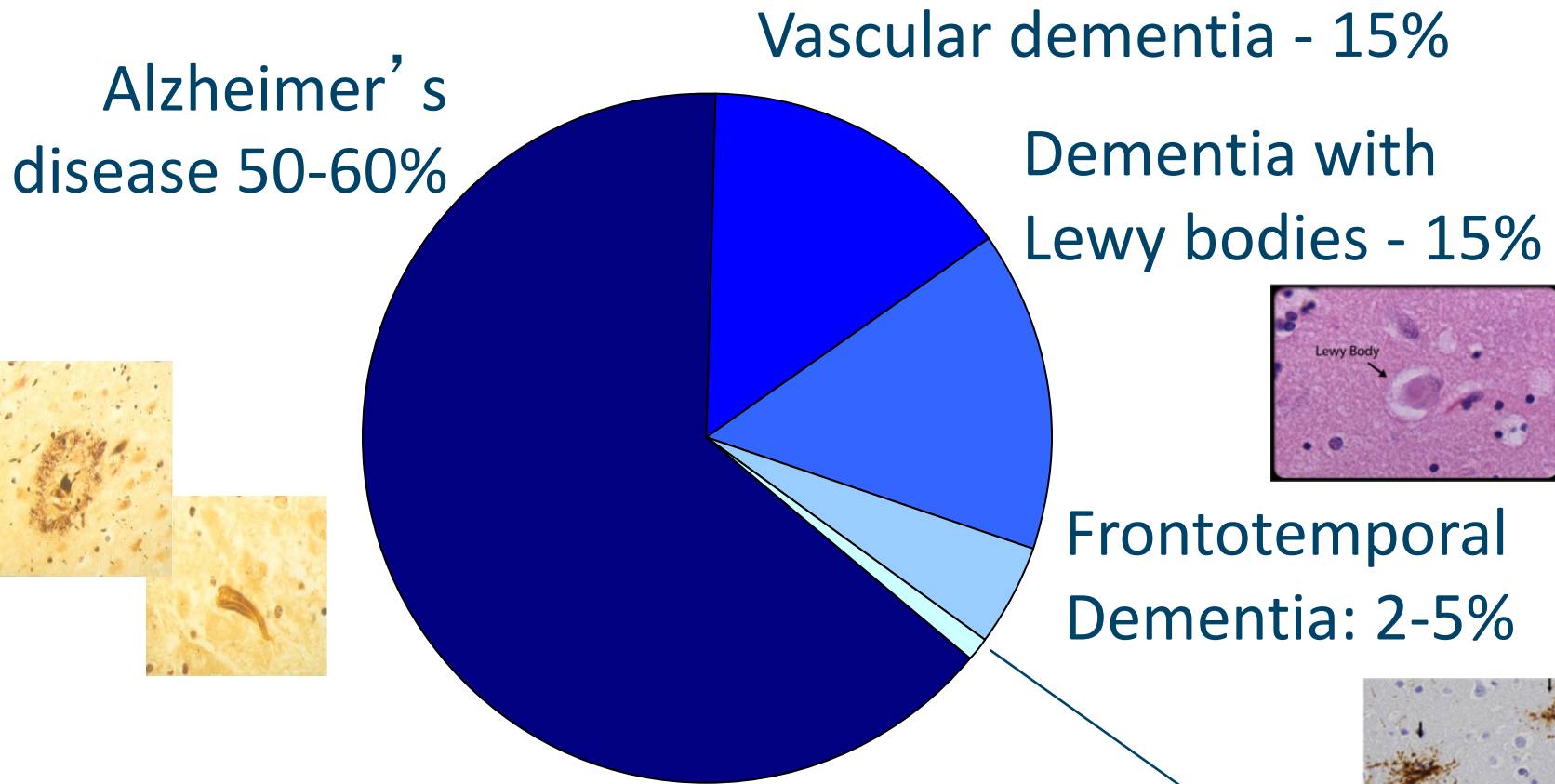
- What is dementia?
- What causes dementia?
- Risk reduction
- Importance of timely diagnosis
- Hope for the future – advances in treatments and diagnostic methods

What is dementia?

- Not just ageing
- Not a single disease
- No-one is immune



Alzheimer's is the most common cause



HIV, Head injury, Prion diseases/CJD, Corticobasal degeneration, PSP, Huntington's, alcohol-related dementia, tumours, infections, vitamin & hormone deficiencies, ...

Other
~2%

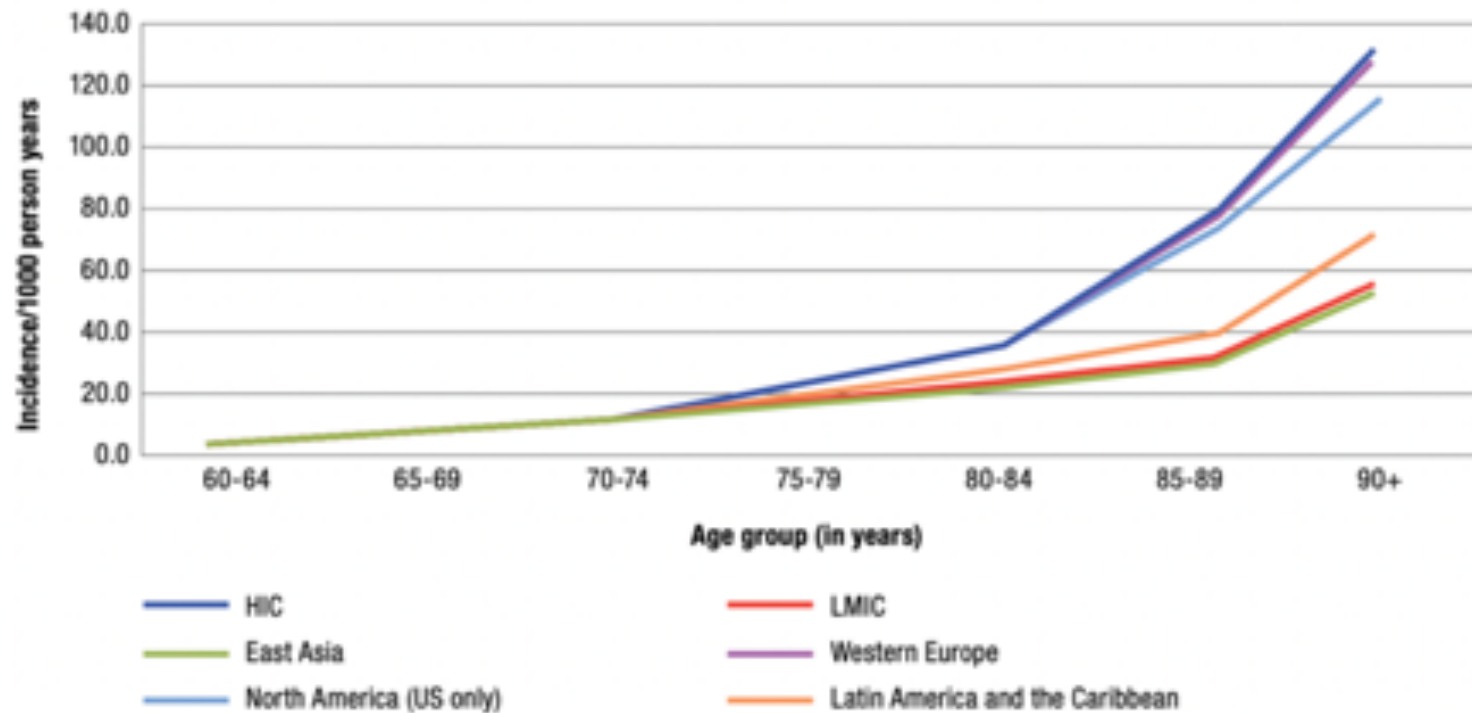


Figure 1-1 Estimated age-specific annual incidence of dementia for world regions, reproduced from the World Alzheimer's Report 2015³. Abbreviations: HIC = high income countries; LMIC = low and middle income countries

4-15% of all AD cases develop symptoms before the age of 65.

Not always memory led

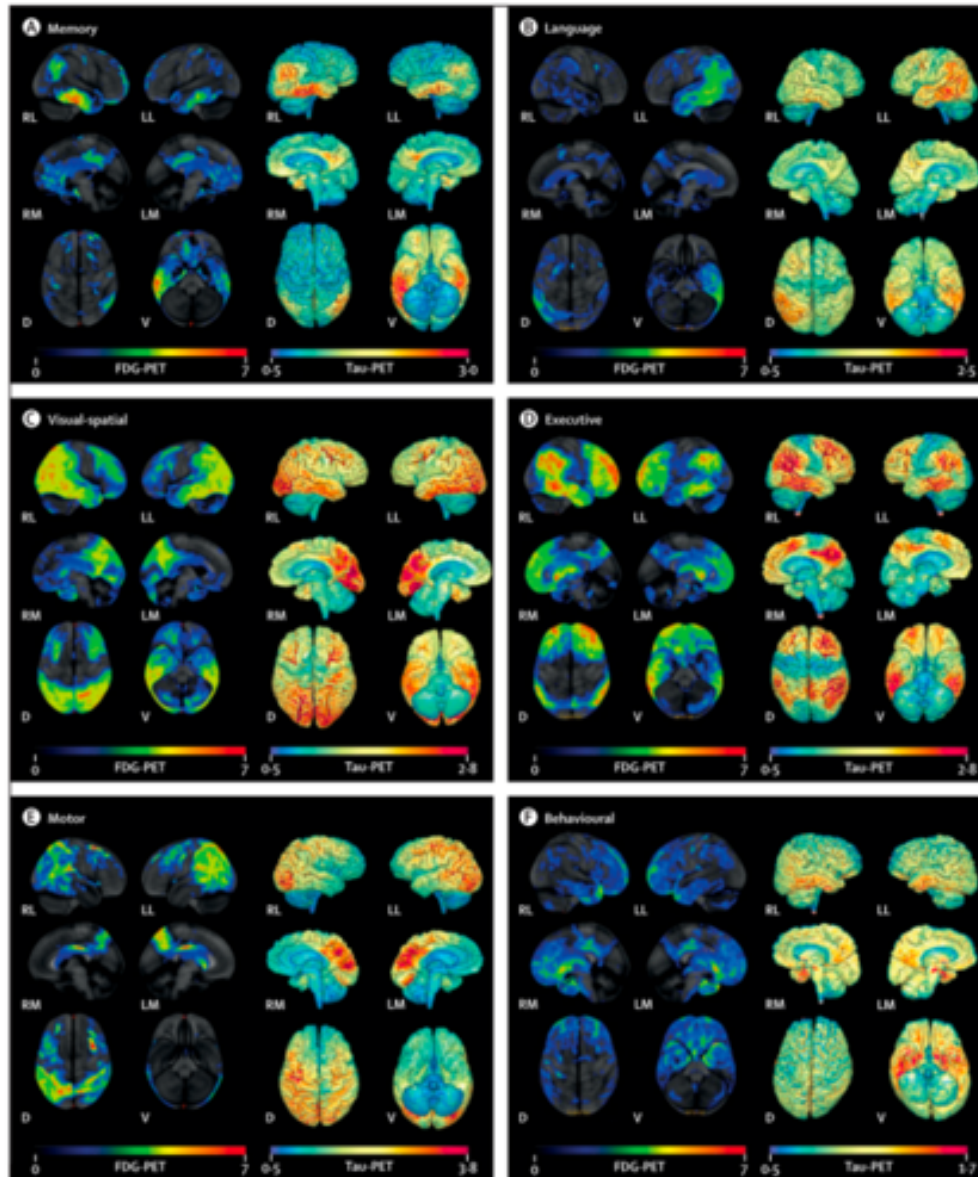


Figure 4. PET scans of the brain showing functional connectivity.

Lewy Body Disease

Table 1 Revised^{1,2} criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuosperceptual ability may be especially prominent and occur early.

Core clinical features (*The first 3 typically occur early and may persist throughout the course.*)

Fluctuating cognition with pronounced variations in attention and alertness.

Recurrent visual hallucinations that are typically well formed and detailed.

REM sleep behavior disorder, *which may precede cognitive decline.*

One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.



Frontotemporal dementia

Interview

Terry Jones: 'I've got dementia. My frontal lobe has absconded'

Robin McKie

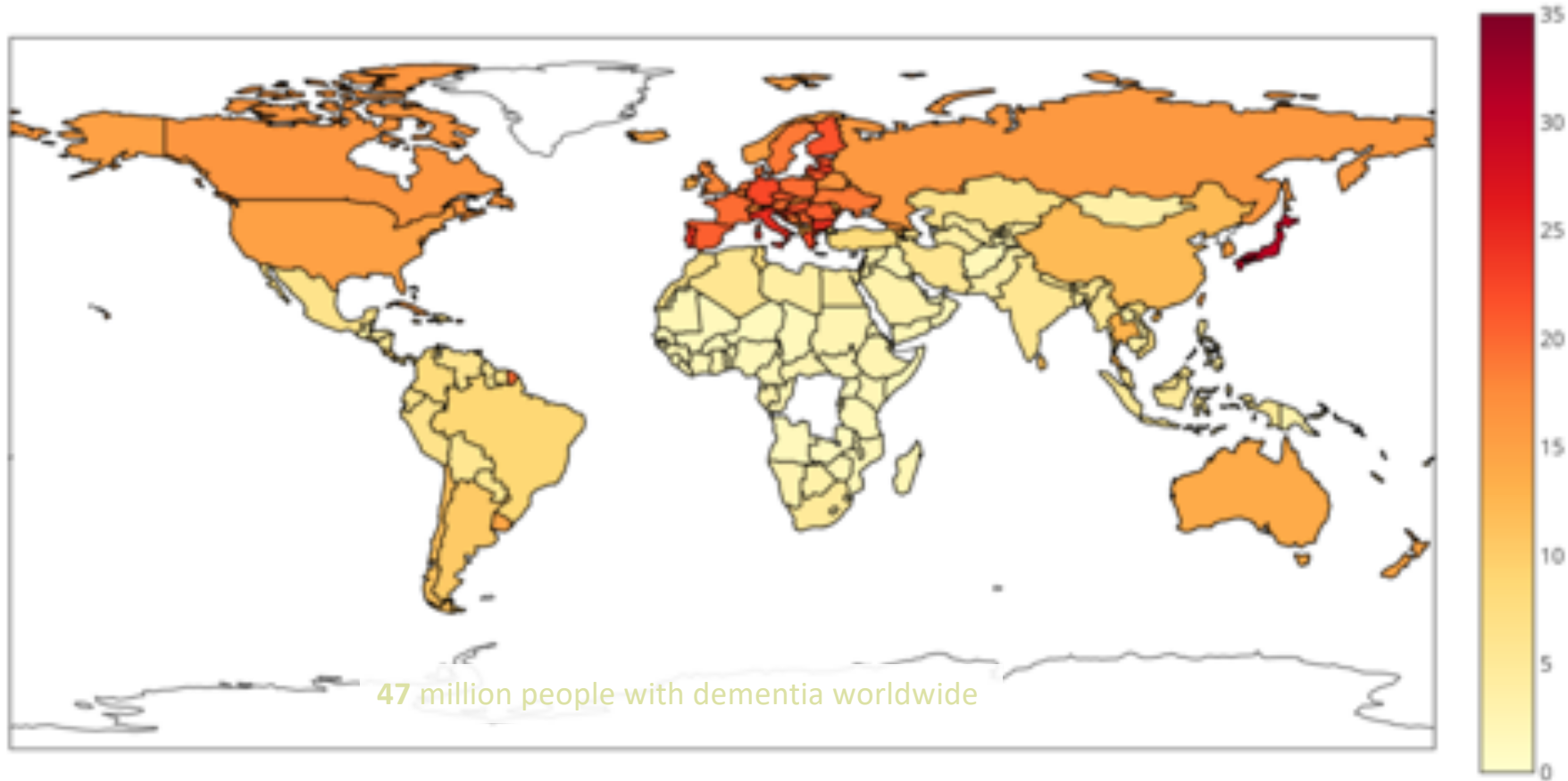
The Monty Python star talks about learning to live with his illness



Old friends Michael Palin and Terry Jones, right, at Jones's home in London this month.
Photograph: Robin McKie/The Observer

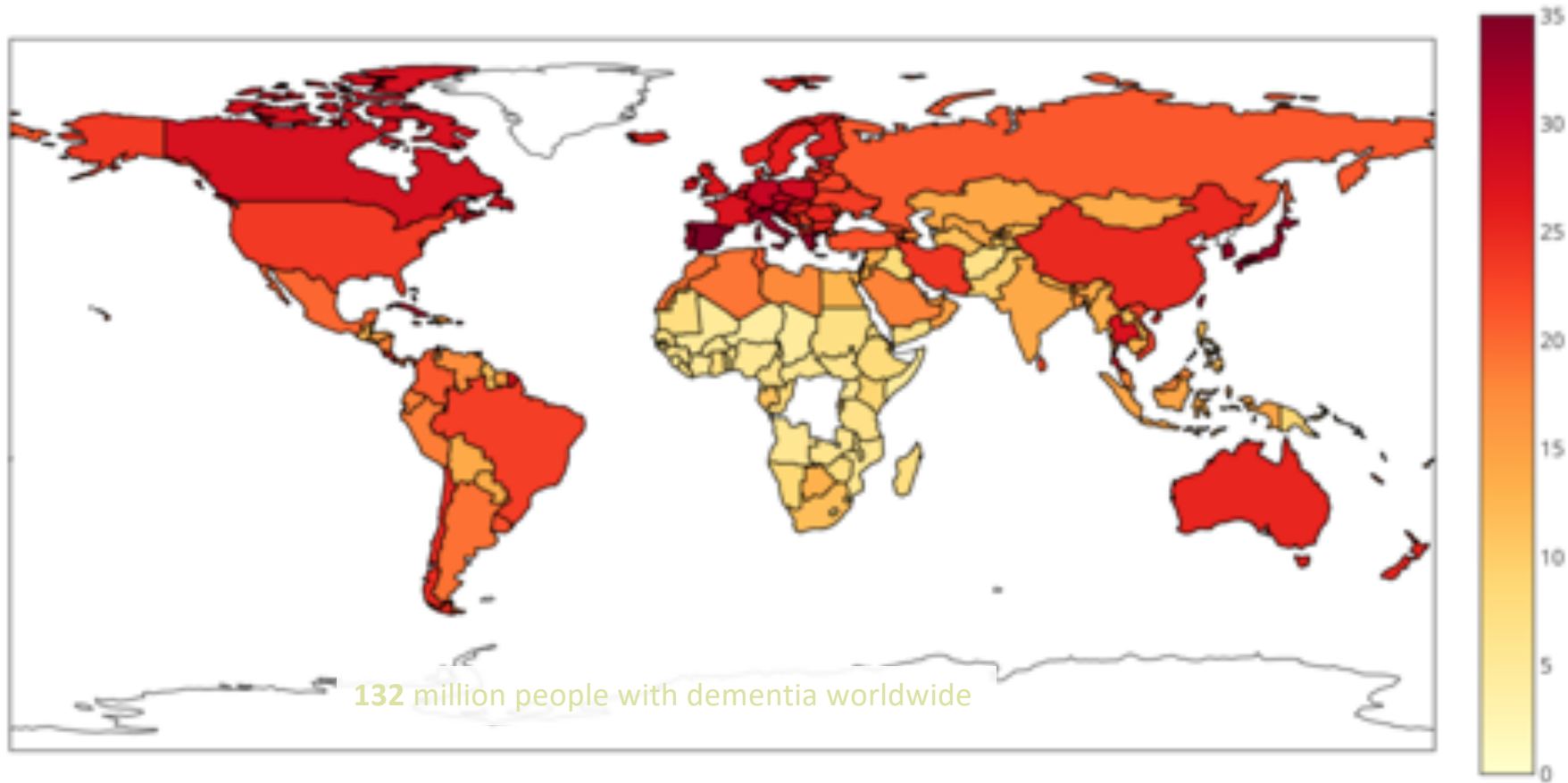


Percentage of population aged over 65
2015



Data: United Nations World Population Prospects 2017

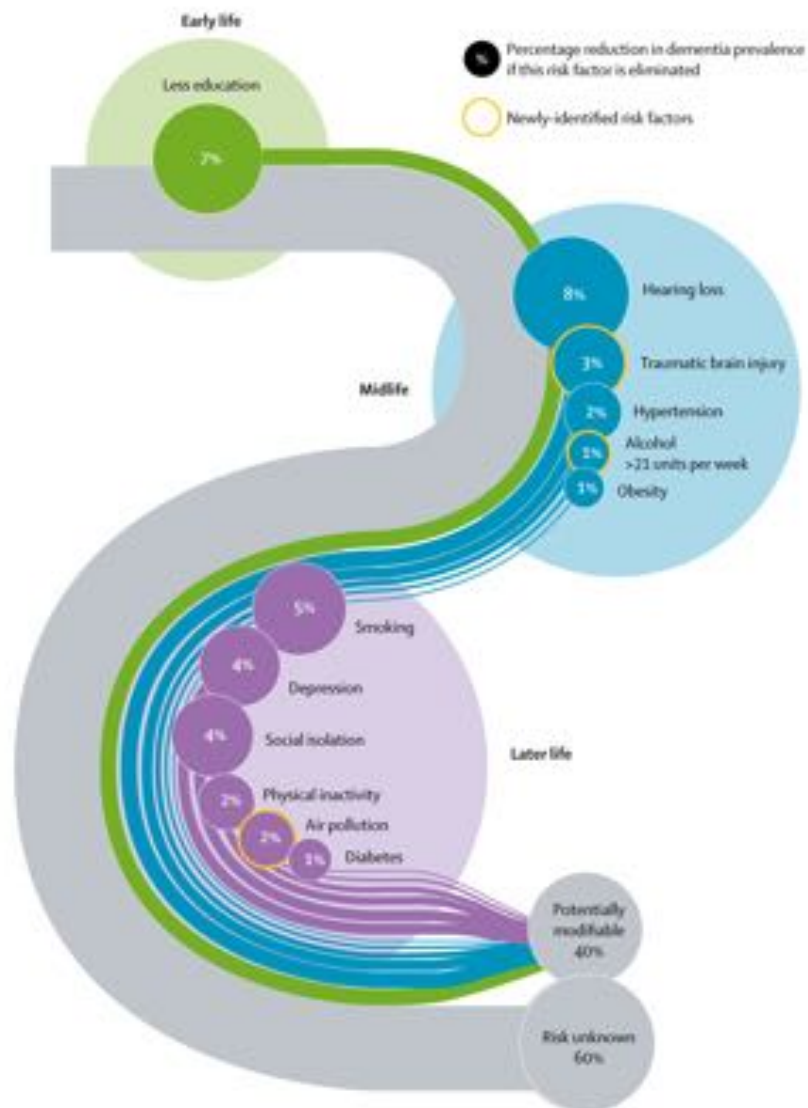
Percentage of population aged over 65
2050



Data: United Nations World Population Prospects 2017

Risk factors for dementia

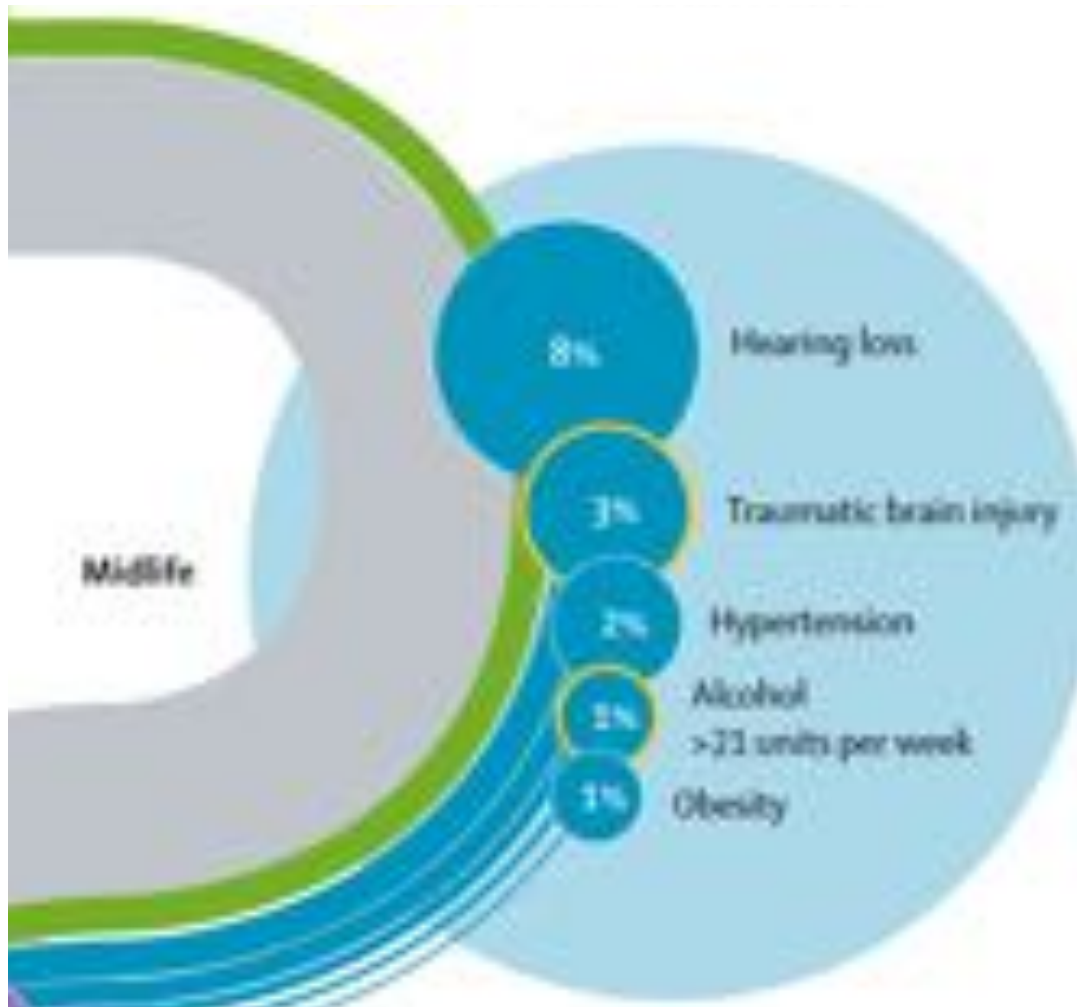
An update to the Lancet Commission on Dementia prevention, intervention, and care presents a life-course model showing that 12 potentially modifiable risk factors account for around 40% of worldwide dementias



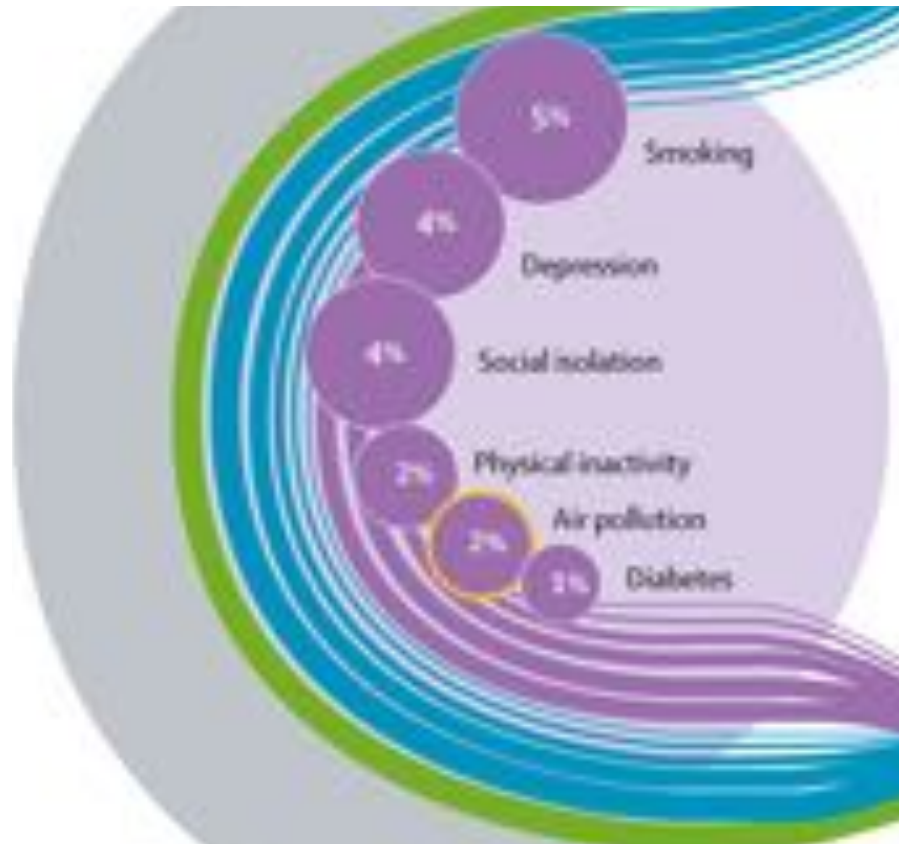
Early life

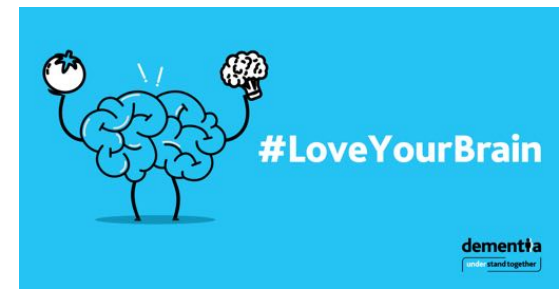


Midlife



Later life

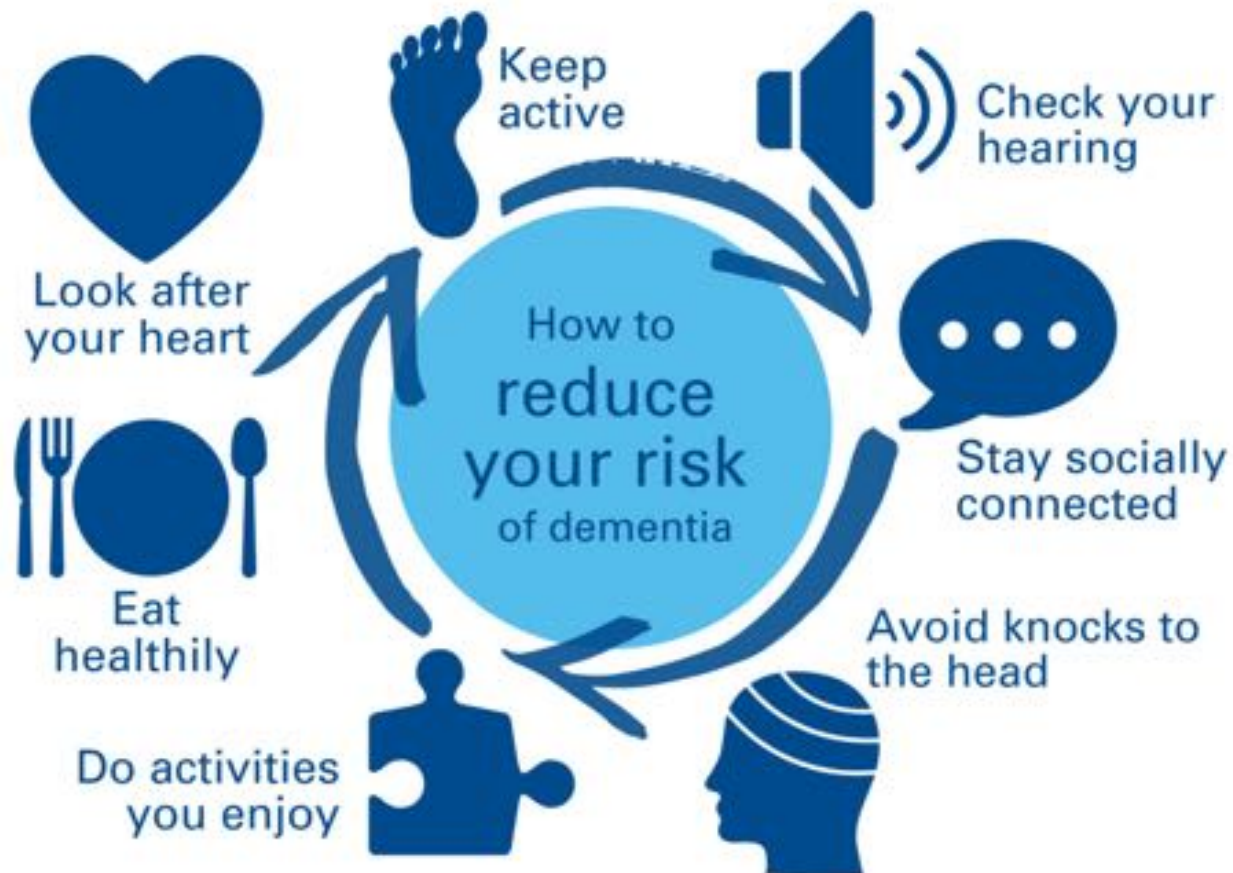




Some of the risk factors overlap with known risks for heart disease and stroke, like hypertension and diabetes.

Some also increase the risk of cancer, such as smoking. Thus, reducing these risks has wide health benefits.

Some risks are more specific to dementia, like hearing loss and brain trauma, but still very worthwhile as part of an overall approach to reducing individual risk.



Source: The Lancet Commission



Tallaght
University
Hospital

1. **Under pressure:** Healthy adults above 40 years of age should have their blood pressure (BP) checked annually to see if it is within the healthy range. There are many ways to decrease blood pressure such as exercising, losing weight, reducing salt intake, limiting alcohol, and taking medication if prescribed.
2. **Listen up:** Reduce hearing loss by protecting ears from excessive noise exposure. If experiencing hearing problems, you should get your hearing tested. It's also important to wear a hearing aid if prescribed one.
3. **Breathe carefully:** Reduce exposure to air pollution and to second-hand tobacco smoke.
4. **Use your head:** Prevent head injury, including concussion, which can occur in certain sports, or due to falls. In addition to national policies for safe sports, each individual can take precautions such as always wearing the correct protective headwear for sports, cycling, work, etc.

5. Drink in moderation: If you drink alcohol, stay within the low-risk weekly guidelines, i.e. less than 17 standard drinks for men or 11 standard drinks for women. For more information on low-risk drinking guidelines, visit www.askaboutalcohol.ie, or call the HSE Alcohol Helpline on 1800 459 459.

6. Up in smoke: Quitting smoking may reduce your risk of developing dementia as well as your risk of developing cancers and heart disease. Stop smoking for 28 days and you're five times more likely to stop for good. For more information, visit www.quit.ie or call the QUITline on 1800 201 203

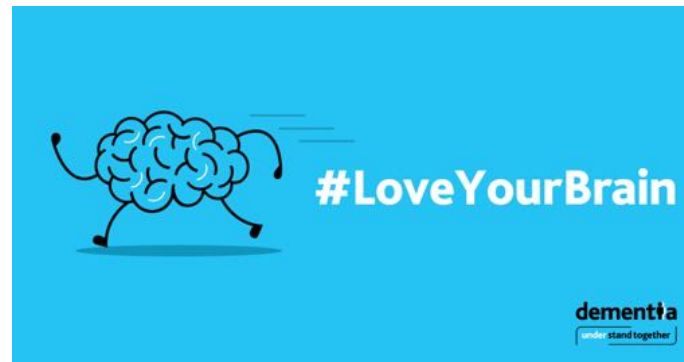
7. Adopt a healthy weight: Achieving or maintaining a healthy weight during your lifetime, but particularly in mid-life, is also important – being more active and following a healthy diet can help this.

8. Be a good sport: Physical activity is very important for brain health. Sustained exercise in mid-life, and possibly in later life, protects from dementia. Every adult should aim to include 150 minutes of physical activity, such as brisk walking, in their week.

9. **Eat well:** Eating a wide variety of nourishing foods provides the energy and nutrients you need to keep your brain healthy. A balanced diet that is rich in vegetables, fruit, wholegrains, and fish, and that is low in salt and sugar, is a good starting point.
10. **Mind your mind:** Depression might be a risk for dementia, although dementia itself can also cause depression. Visit www.yourmentalhealth.ie for ways to look after your mental health.
11. **Early to bed:** Addressing other possible risk factors, like sleep, through lifestyle interventions, will improve general health and may reduce your risk.
12. **Brain box:** Keep your brain active.

Key take home messages on brain health:

- 1) Dementia risk factor modification needs to start in middle-aged people, not in older age.
- 2) We may not always be able to prevent dementia, but delaying the age of onset in Ireland by 5 years would halve the prevalence of dementia.





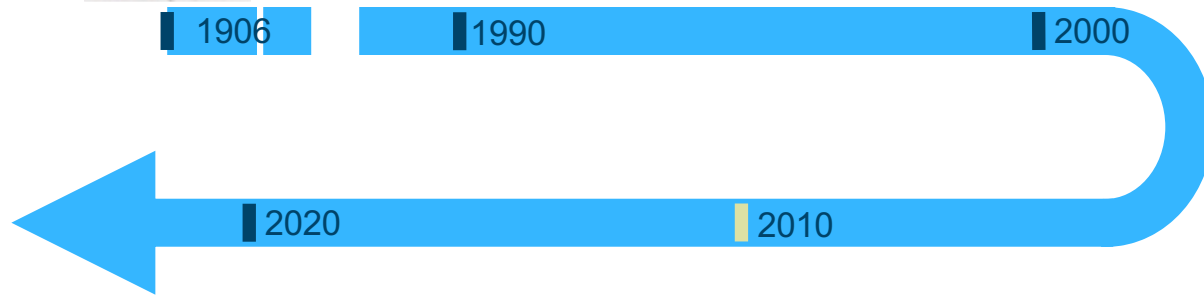
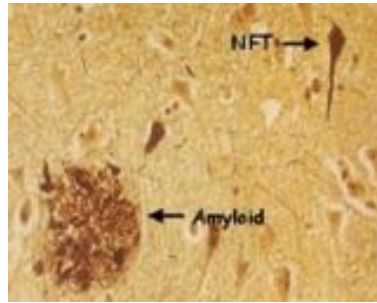
Impact on families and society

- Impacts whole families – and society
 - $\frac{1}{4}$ of hospital beds
 - $\frac{3}{4}$ of those in residential care
 - $\frac{1}{2}$ of us will care for someone ...
- We need to improve diagnosis, care and support ... and find ways to prevent it

Why “detect” dementia early

- Timely diagnosis -
 - When patient or family seeks help
 - To protect from harm
 - Appropriate investigation and treatment
 - Research and trials
 - Support, benefits, advice
 - Allows involvement in decisions when most able to do so
 - Reduces anxiety and depression

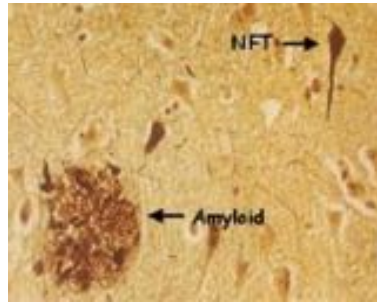
Detecting Alzheimer's disease



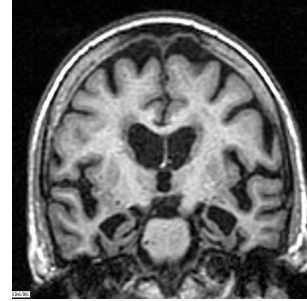
Detecting Alzheimer's disease



1906



1990



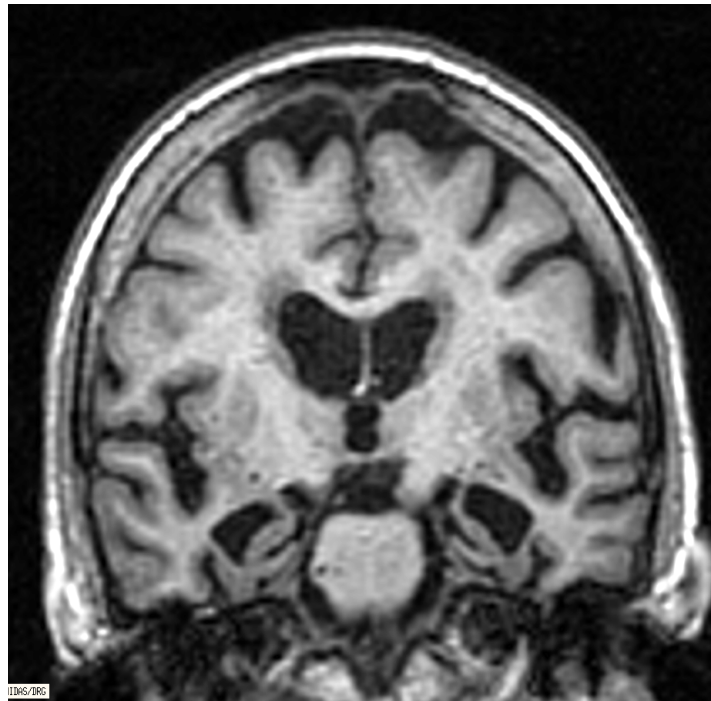
2000

2020

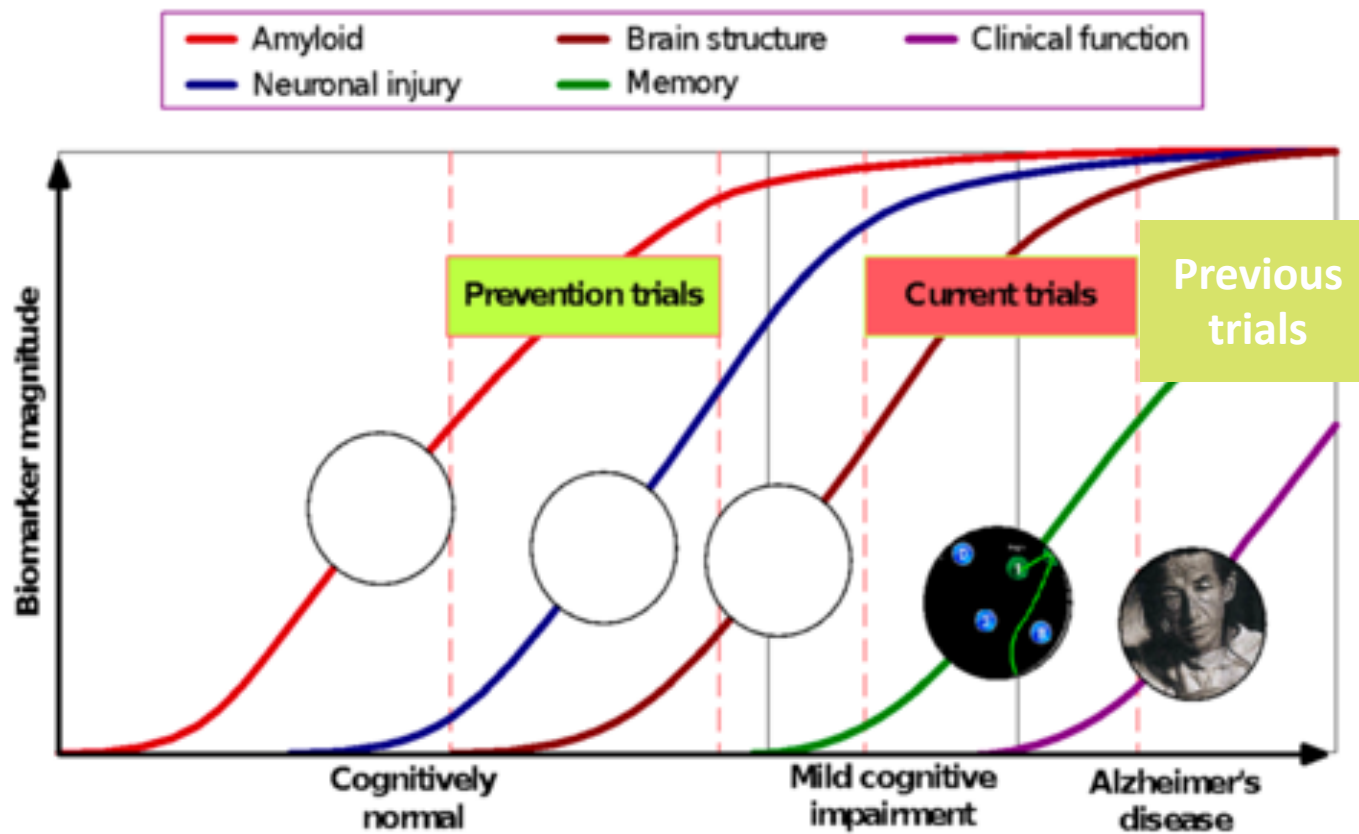
2010

Benefits of earlier intervention

Fewer neurons lost = more to save



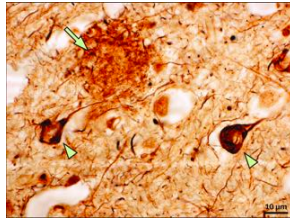
In moderately severe AD the hippocampus can be down by 30 - 40%



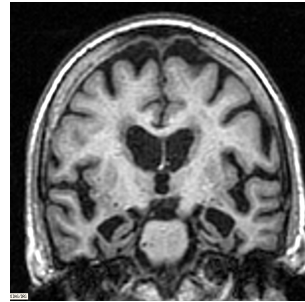
Detecting Alzheimer's disease



1906



1990

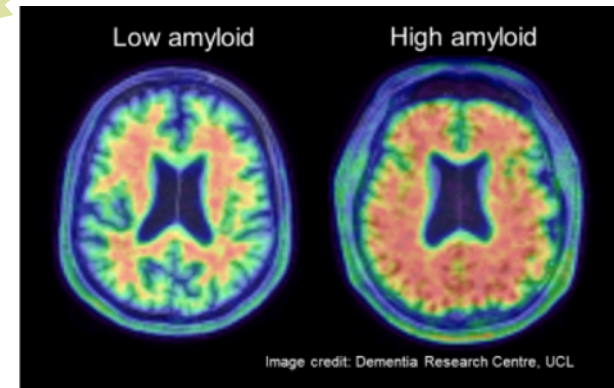


2000



2020

2010



11 THINGS WE'D REALLY LIKE TO KNOW

Will We Ever Cure Alzheimer's?

🕒 This article is more than 2 years old

Dismay as Alzheimer's drug fails in clinical trials

HEALTH AND SCIENCE

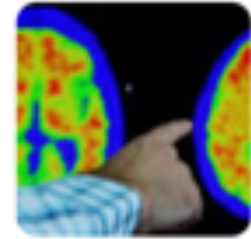
Failed Alzheimer's trial leaves families and patients heartbroken. Medical community reels

PUBLISHED SAT, MAR 23 2019 • 12:24 PM EDT | UPDATED SAT, MAR 23 2019 • 3:38 PM EDT

New Alzheimer's drugs bring hope of slowing disease for UK patients

The first of these medicines – lecanemab – was recently approved in the US and Japan, where treatments using it have already been launched. A...

18 Dec 2023



THE IRISH TIMES

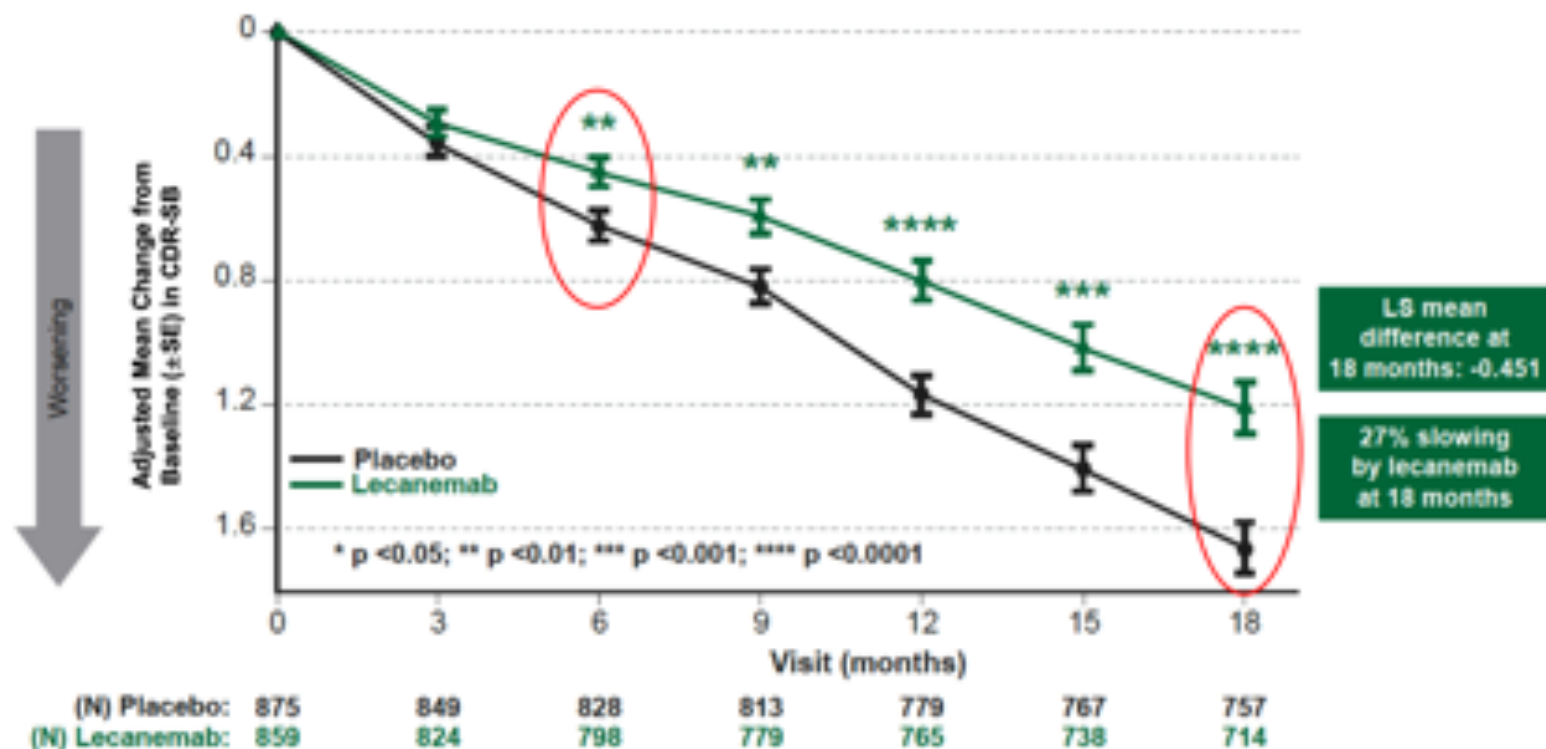
New drug found to slow Alzheimer's hailed as 'turning point'



Tallaght
University
Hospital

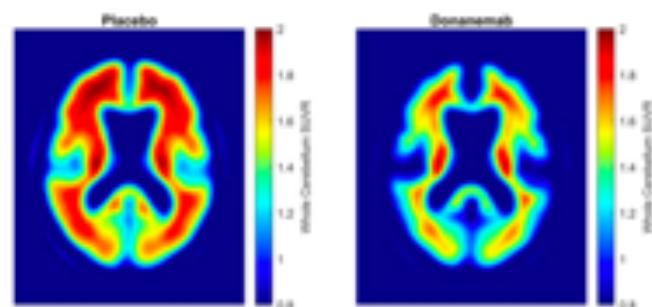
Clarity AD Primary Endpoint: CDR-SB

Lecanemab Significantly Slowed Disease Progression on CDR-SB by 27% at 18 Months and at All Time Points Beginning at 6 Months

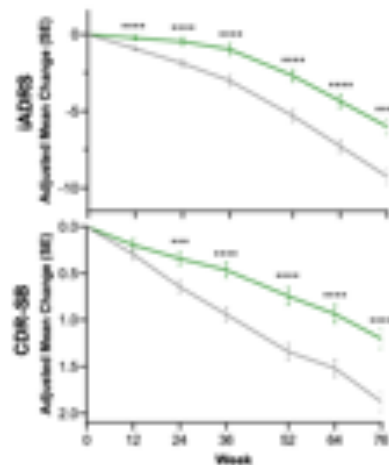


Note: Based on modified intention-to-treat analysis population. Adjusted mean change from baseline, SE and p-value are derived using mixed model repeat measures (MMRM) with treatment group, visit, treatment group by visit interaction, clinical subgroup, use of Alzheimer's disease symptomatic medication at baseline, ApoE4 carrier status, region, baseline value by visit interaction as fixed effects, and baseline value as covariate. CDR-SB, Clinical Dementia Rating - sum of boxes; LS, least squares; SE, standard error.

Summary of TRAILBLAZER-ALZ 2 key results



- Donanemab treatment reduced amyloid plaque by **87 Centiloids** in 76 weeks.
- 69%** of participants cleared amyloid and switched from donanemab to placebo by 76 weeks.

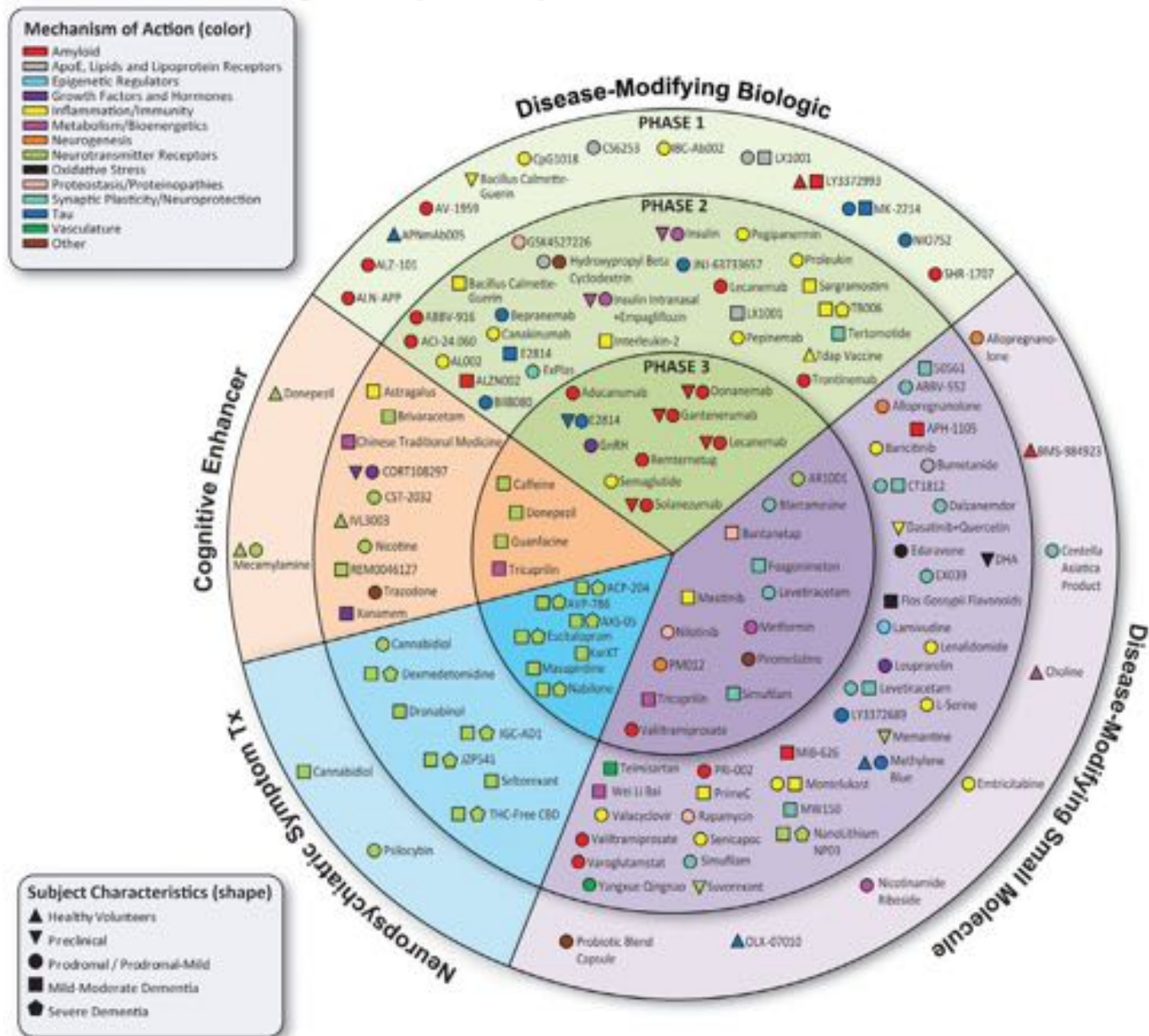


- Donanemab slowed progression on the iADRS by **35%** and on CDR-SB by **36%** at 76 weeks in the low-medium tau population.

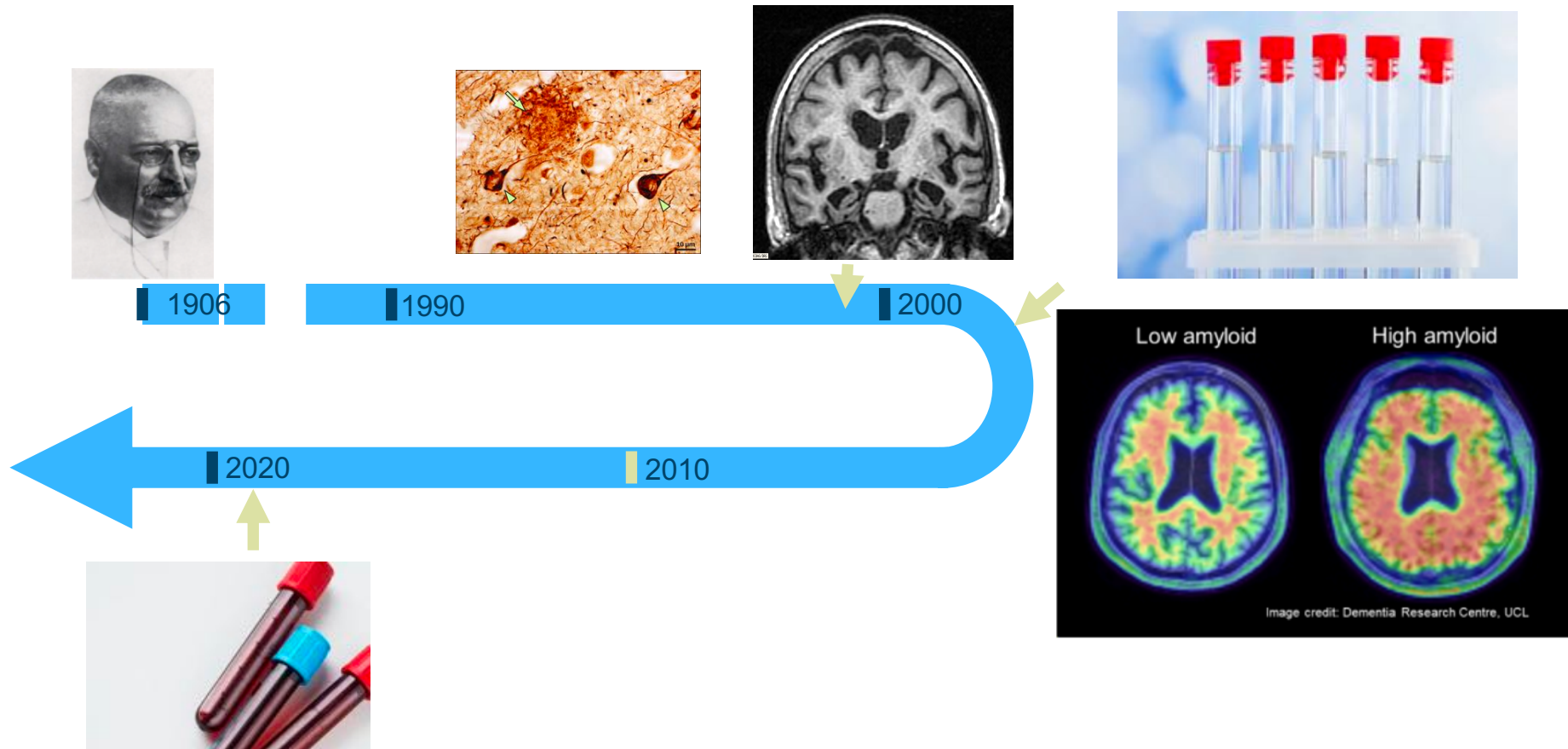


- ARIA-E was the most common side-effect, (**24%** of donanemab-treated participants).
- Three** deaths from ARIA-related complications occurred.

2024 Alzheimer's Drug Development Pipeline



Detecting Alzheimer's disease



The New York Times

A Blood Test for Alzheimer's? It's Coming, Scientists Report



Structural Change



Clinical Outcomes



Cognitive Change

Dr. John Hardy.

11th. April '86

Dear Sir,

I was very interested to read
of your research in the Alzheimers
Disease Society News and think my
family could be of use. Actually I



Thank you