

Dementia research: progress and challenges

University of Birmingham College of Medicine: Challenging Dementia
September 6th 2013

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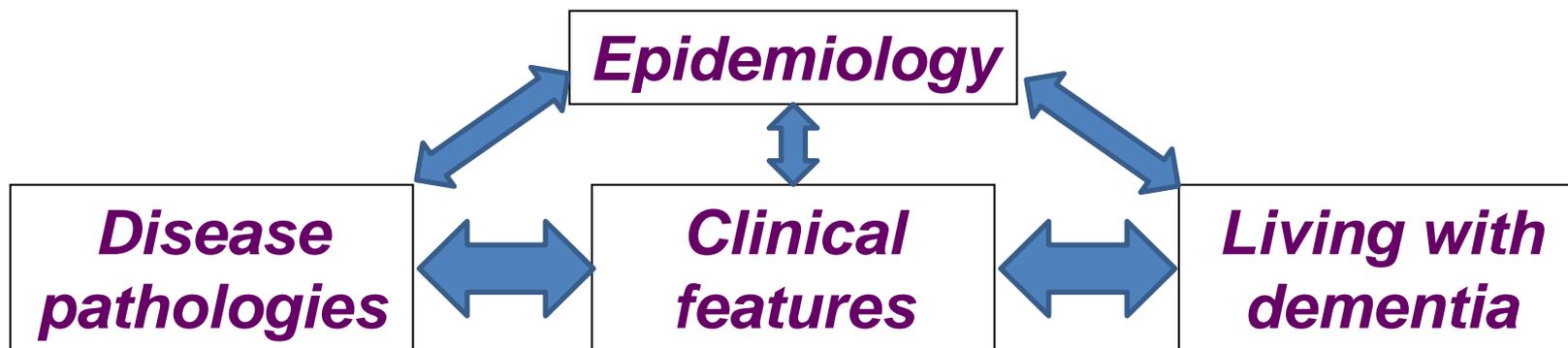
Alzheimer's Research UK

- Independent, dedicated biomedical research charity
- Remit covers causes, preventions, diagnoses and treatments of Alzheimer's disease and other dementias
- UK based; UK and international partnerships
- We have spent >£40million to fund >400 projects in the UK
- Our currently-active grants portfolio is ~130 projects worth £23m
- Leading UK charity funder and second largest charity funder of dementia research in the world

Outline

1. *Overview of dementia research and its importance*
2. *Progress and challenges – the science of dementia*
3. *Progress and challenges – doing and enabling research*

An overview of dementia research: *'cause, cure, care'*



Contexts: Social, economic, healthcare/service delivery

Best practices in care

Diagnoses

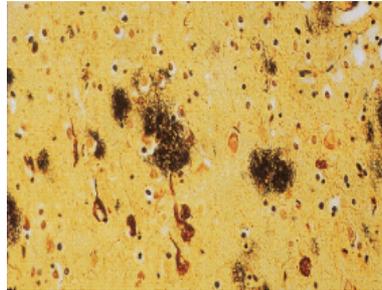
New treatments/preventions

100 years of biomedical Alzheimer's disease research

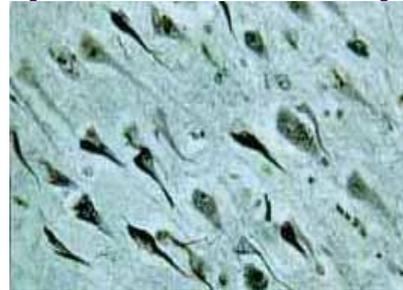
1906: Dr Alois Alzheimer describes the case of Auguste D:
Clinical symptoms and post-mortem pathology



**Plaques
(amyloid beta)**



**Tangles
(abnormal tau)**



1910-1960/70s

'Senile dementia' seen as a normal part of ageing

'Alzheimer's disease' seen as rare, 'non-senile' dementia

1970s

Levels of the neurotransmitter acetylcholine discovered to fall sharply in people with AD

1980s

Diagnostic criteria established for AD

Genetic links to familial early onset AD appear

Tau protein identified in tangles; amyloid beta plaques characterised

1990s

1st drugs approved: tacrine and donepezil (Archiept)

1st transgenic animal model of AD developed

First significant genetic risk factor found in late onset AD

2000 - 2013

New class of drug approved: memantine

Development of sophisticated neuroimaging

More genetic risk factors found for late onset AD

Many clinical trial failures; concerns about Pharma withdrawing

Pathologies and causes of dementia-causing diseases

- Alzheimer's, Parkinson's disease, Lewy Body Dementia, Prion disease, Frontotemporal dementias:
 - damage to and death of nerve cells in response to the build up of particular proteins
- Vascular dementia
 - damage to and death of nerve cells in response to reduced blood flow
- Mixed pathologies common; neuroinflammation
- Complex genetic and environmental causes
- Long pre-clinical phase is also likely to apply across these brain disorders
- ***We don't understand enough about these processes***
 - ***difficult to follow in people and to model expt'lly***

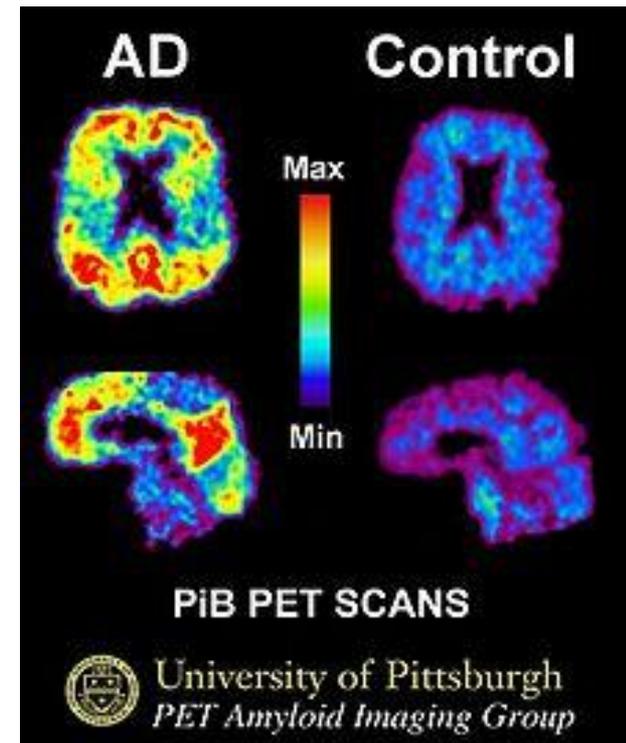
Clinical features

- ***‘Brain and mind’***
 - neurology, psychiatry, clinical psychology:
 - cognitive *and* behavioural & psychological symptoms of dementia
 - common co-morbidities: other chronic diseases of ageing, depression (can appear similar at early stages)
- ***More accurate and more sensitive tools are needed for:***
 - ‘timely’ and accurate diagnosis
 - prognosis
 - detection/stratification of pathologies
 - evaluating new treatments; surrogate end points in trials

Tools: *cognitive & behavioural/functional markers, biomarkers*

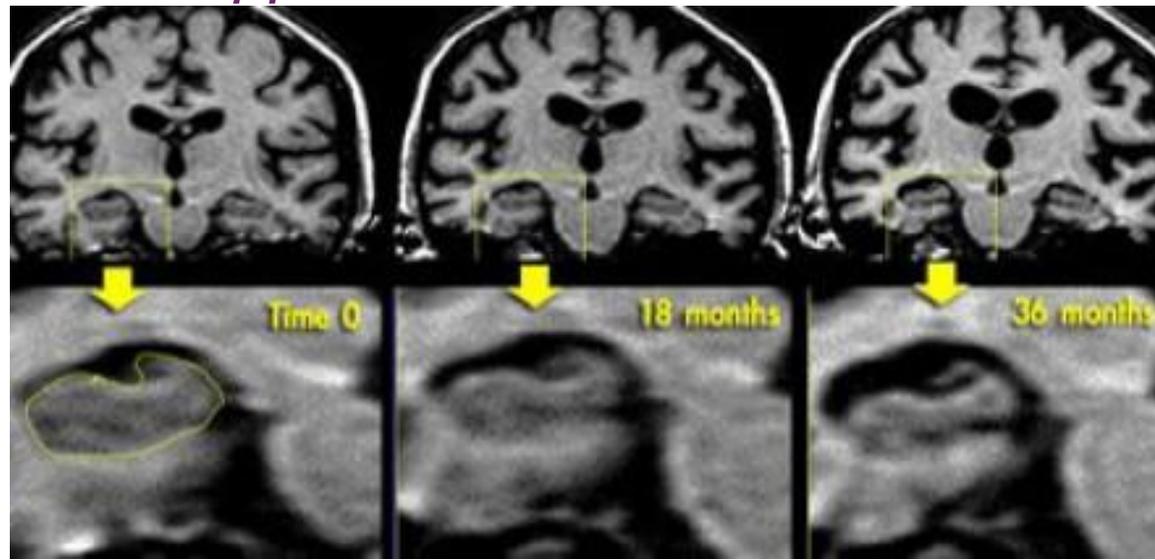
Biomarkers of direct pathology (AD only):

- **Cerebrospinal fluid:**
 - Tau, Phosphorylated Tau
 - Soluble amyloid beta
- ***Blood-based biomarkers?***
- **Positron Emission Tomography:**
 - Tau: PET ligands being developed
 - Amyloid beta: Pittsburgh Compound B, Florbetapir (18F)



Biomarkers and signatures of the functional and structural consequences of dementia pathologies

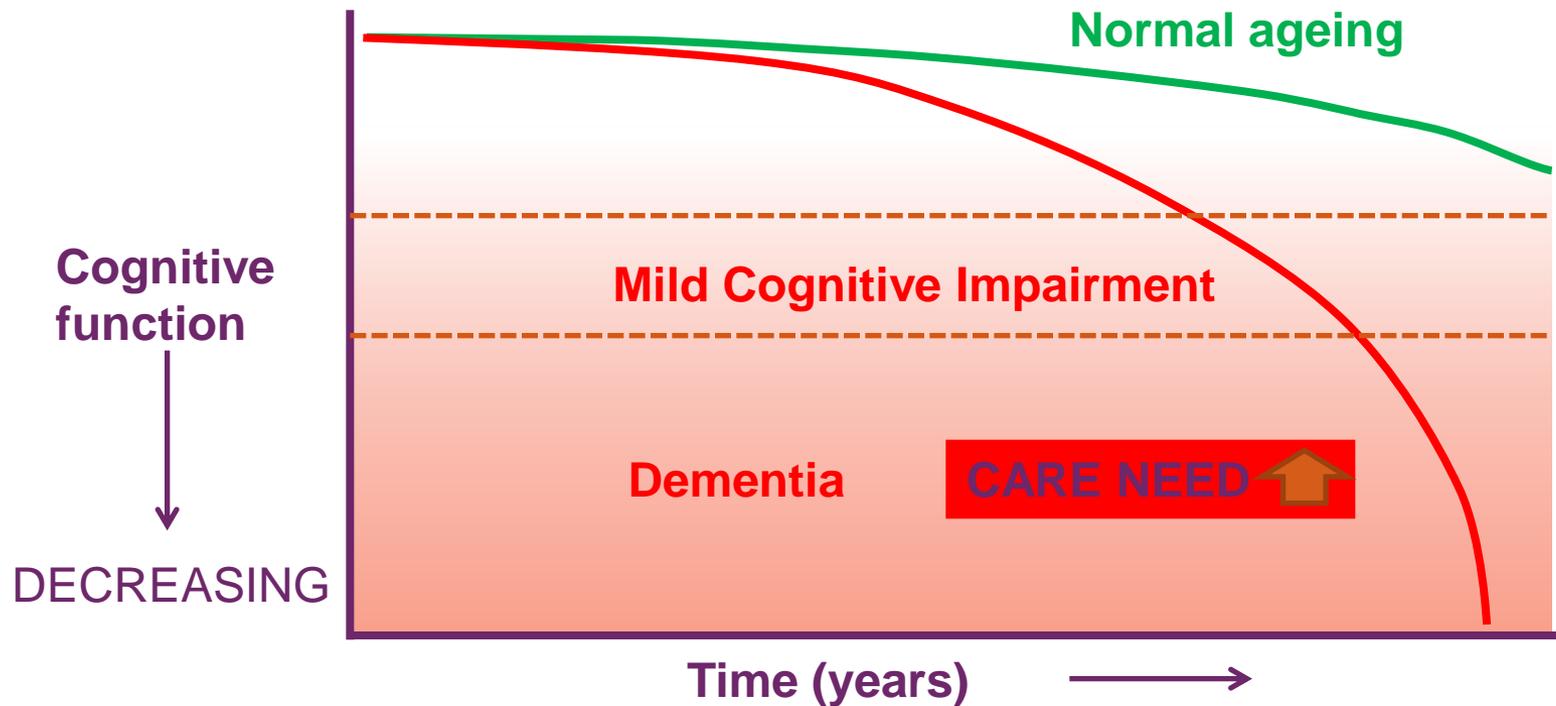
- Electrical activity, Network activity:
qEEG, functional MRI
- Metabolism:
Fludeoxyglucose (18F) PET
- Cerebrovascular integrity/function:
functional MRI, transcranial Doppler ultrasound
- Cell loss, atrophy:
volumetric MRI



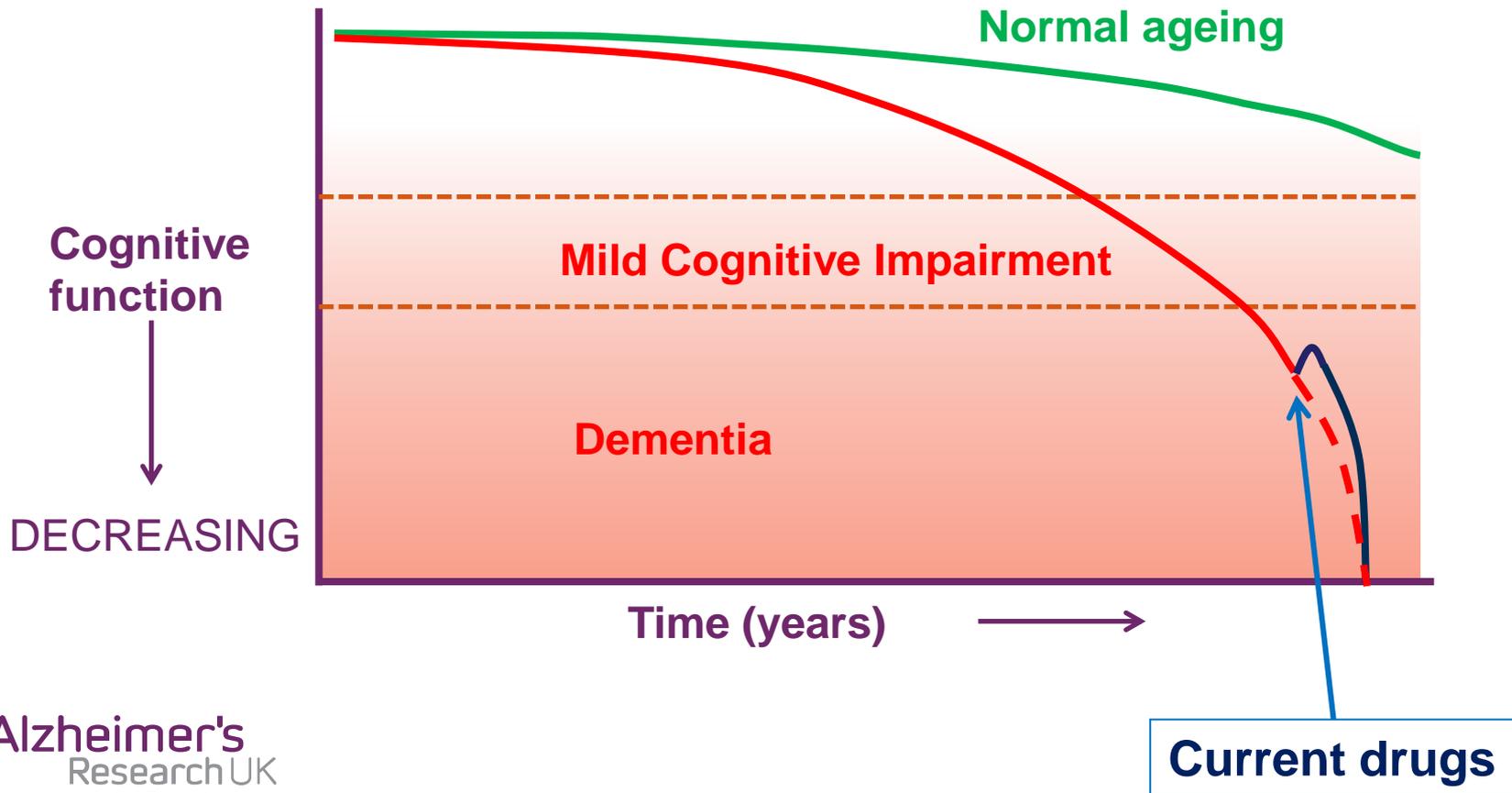
Treatments for Alzheimer's

- 4 licensed treatments help with cognitive symptoms for a limited time
- Room for improved cognitive enhancers
- Large research effort into developing 'disease modifying' treatments to:
 - delay the onset of dementia *and/or*
 - slow its progressive course
- Most 'disease modifying' AD drugs have been targeting amyloid – all have failed so far
- Concern about Pharma sector abandoning this area

A simplified model of cognitive decline in Alzheimer's disease

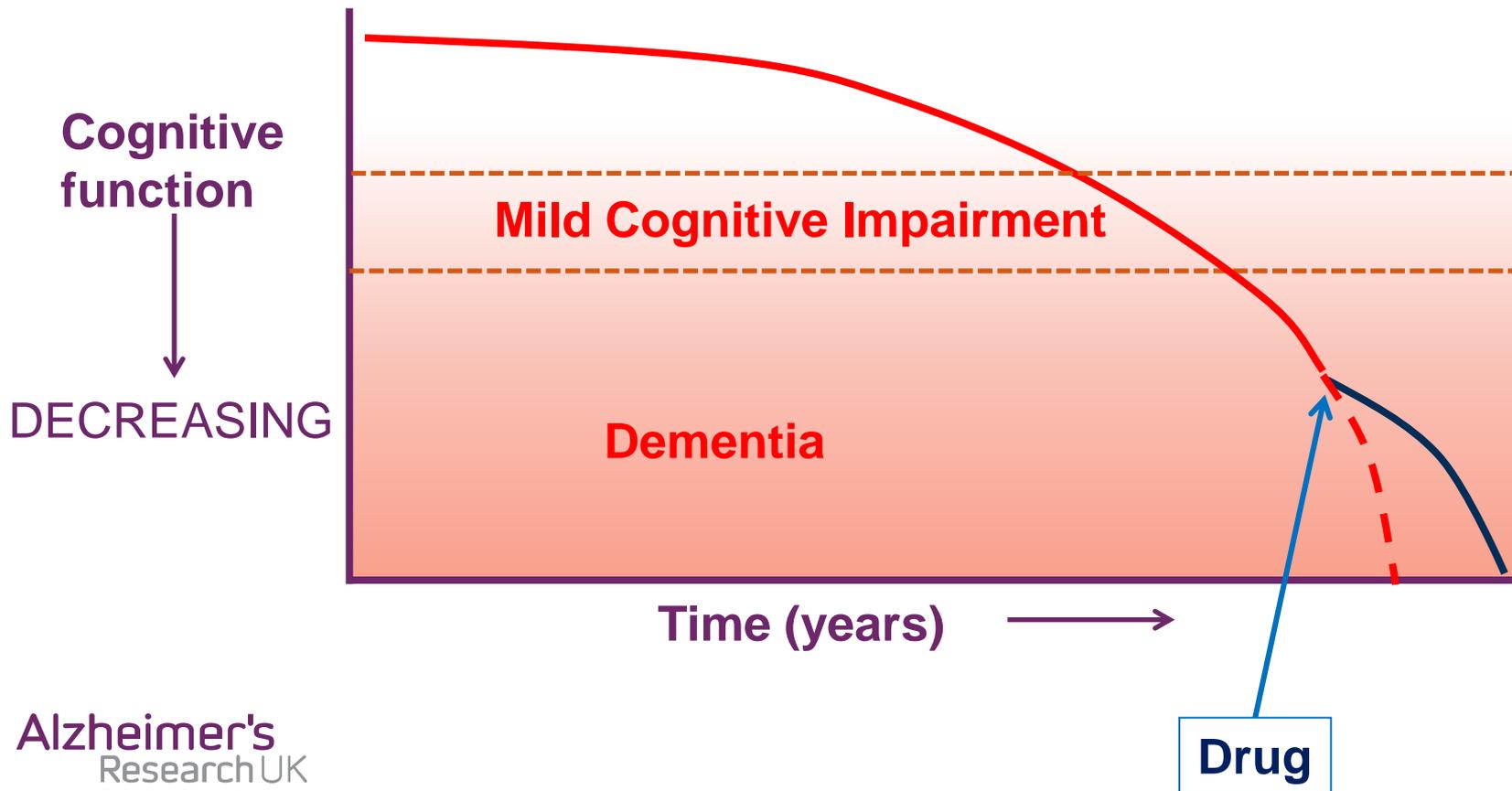


Current symptomatic treatments for AD

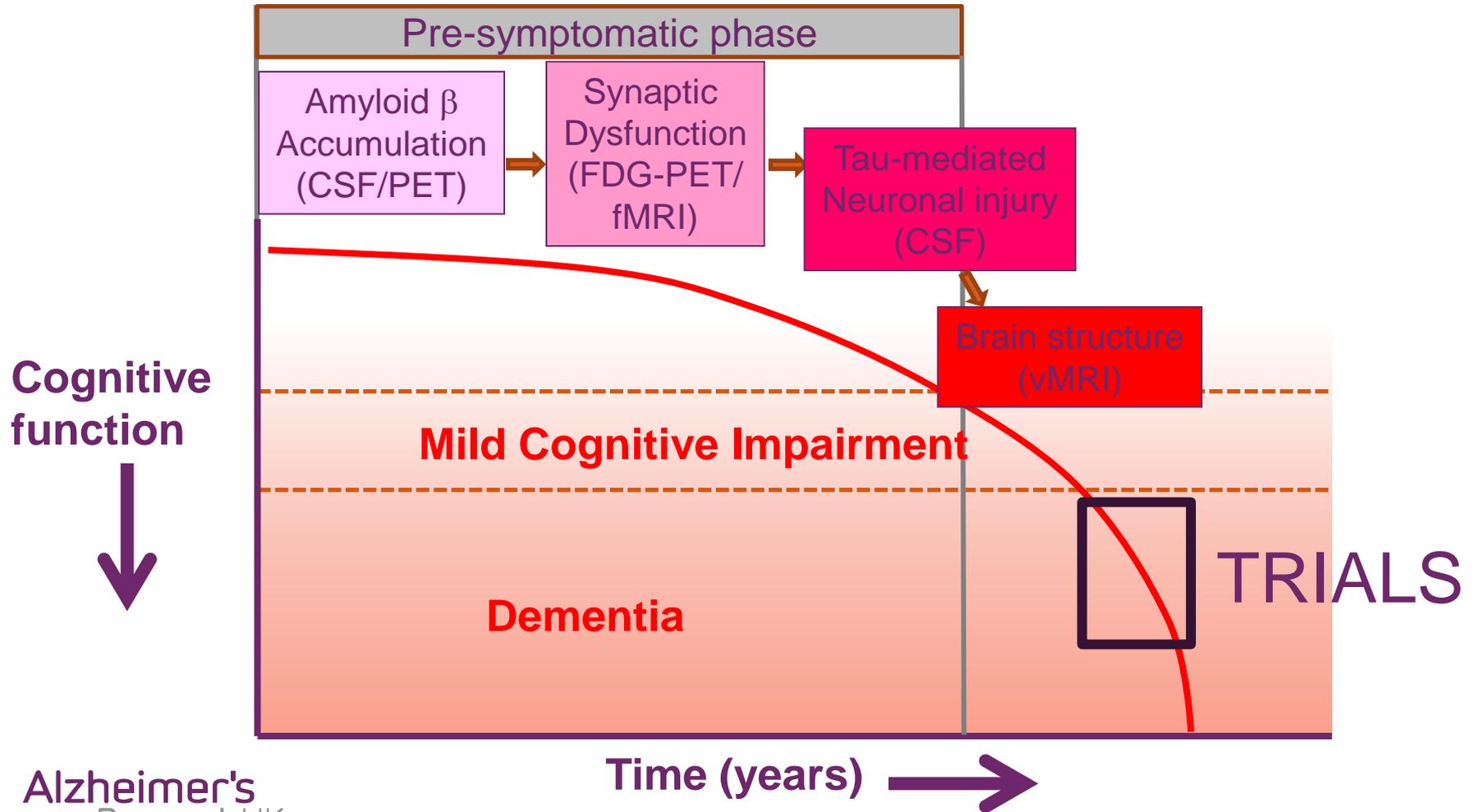


'Disease-modifying' drugs

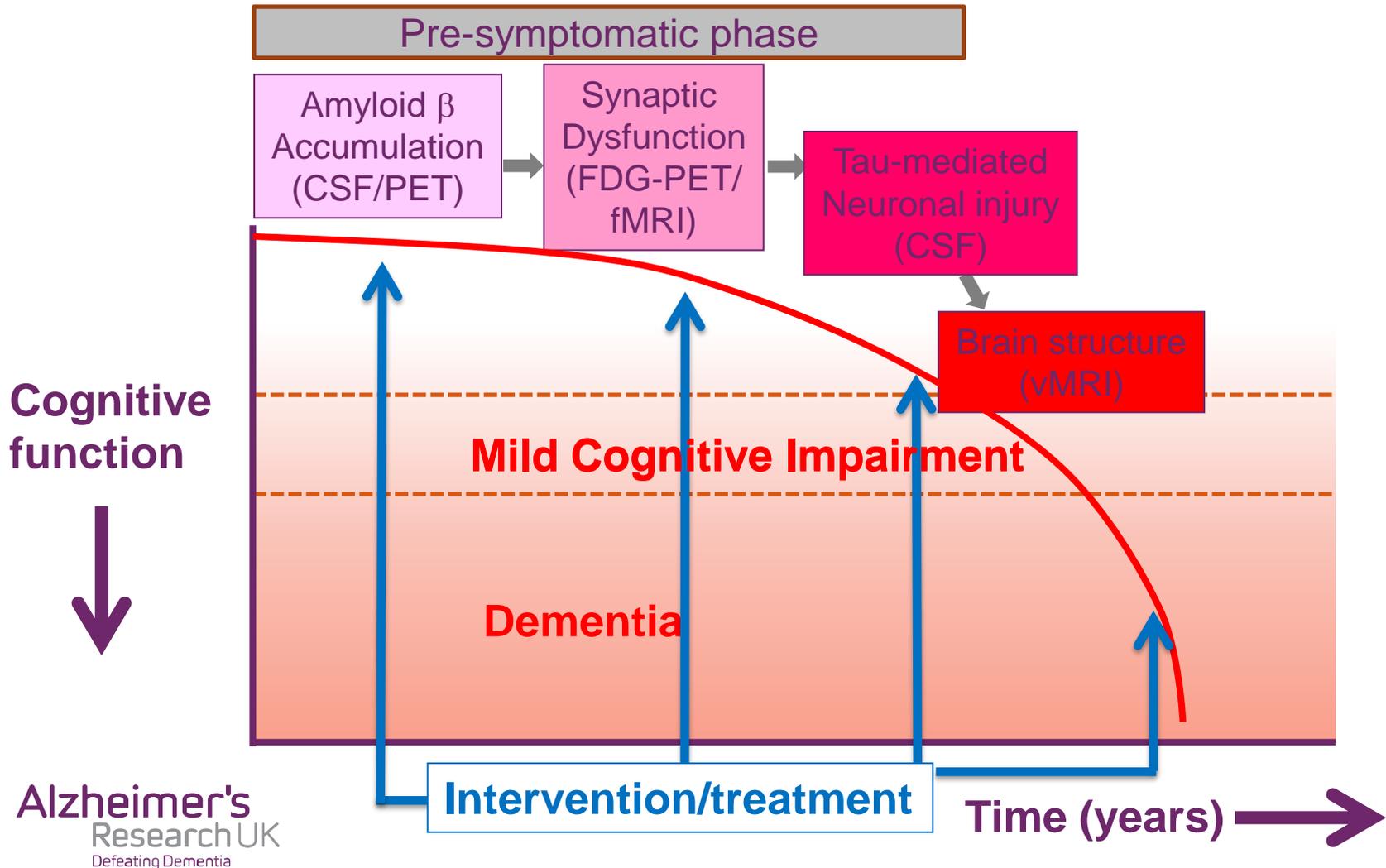
The previous six Phase 3 clinical studies in AD have sought this type of effect – but all have failed.



Trials of anti-amyloid drugs – wrong targets, wrong drugs, or tested too late?

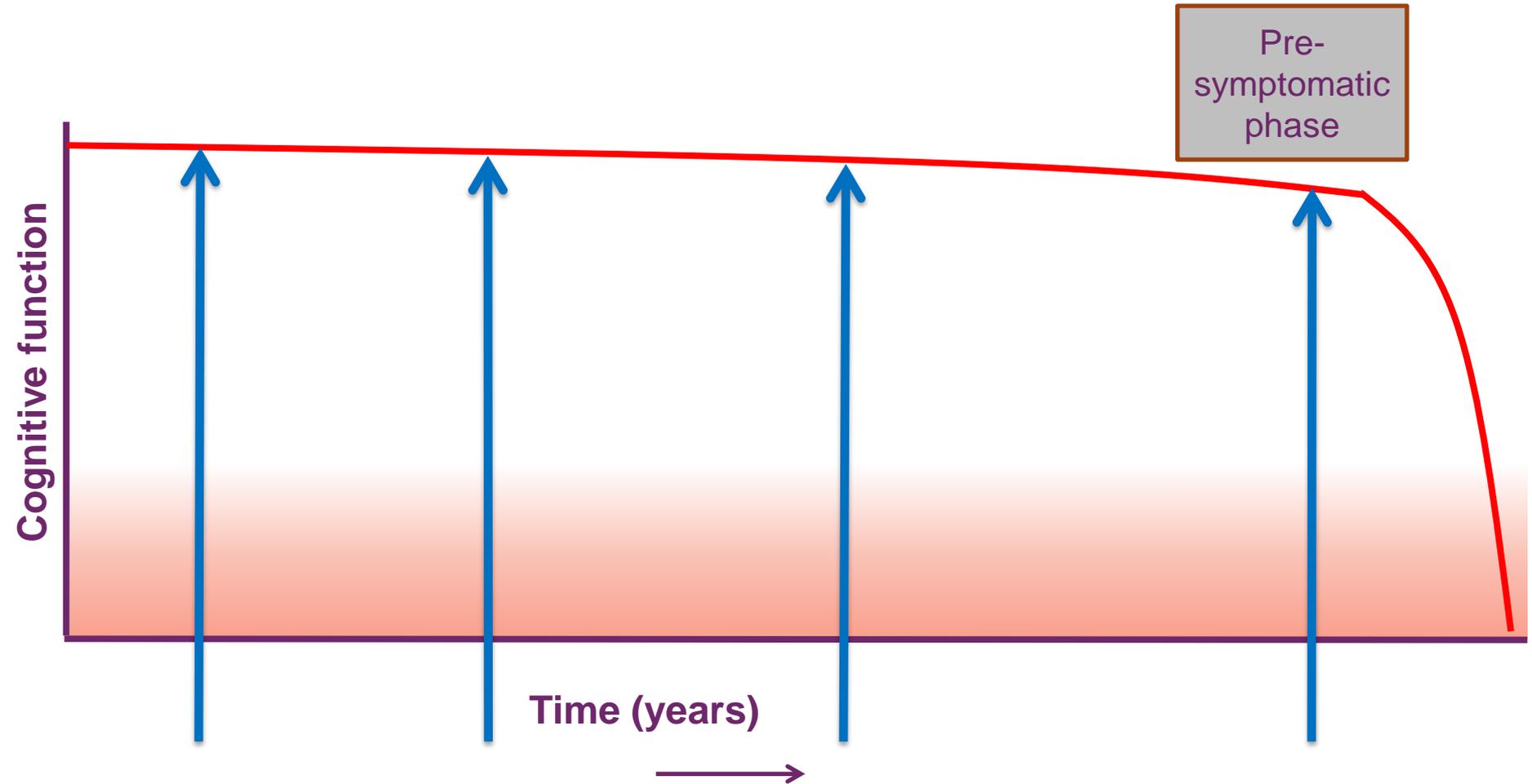


Prevention in pre-symptomatic phase – The best chance of success against amyloid? Other approaches needed...



A lifelong view of preventative risk reduction

Education, diet, exercise...



Living with dementia

Research is needed to inform care delivery and practice in care homes, hospitals, in the community:

- Ensuring that people with dementia are able to benefit from care and support services
- Management of pain or co-morbidities
- End of life care
- Effective ways of supporting carers

What is needed to ensure that dementia research can happen and deliver for patients in the short and long term?

- **People**
- **Resources, infrastructure:**
equipment, access to patients, samples, reagents, tools
- **Funding**

- **People** with ideas, knowledge of the field, methodologies
- Established researchers and ‘new blood’
- The UK and worldwide dementia research communities are small.
- For every dementia researcher in the UK, 8 work on cancer.
- Few research clinicians in dementia
 - a worry for the future in an area where UK has some world leaders.

*Why – dementia seen as difficult, poorly funded?
Changes in medical training?
Lack of opportunities, too few mentors?*

- Tackling dementia requires researchers from a wide variety of disciplines/backgrounds:

Medicine, biology, physics, chemistry.....

Academia and industry

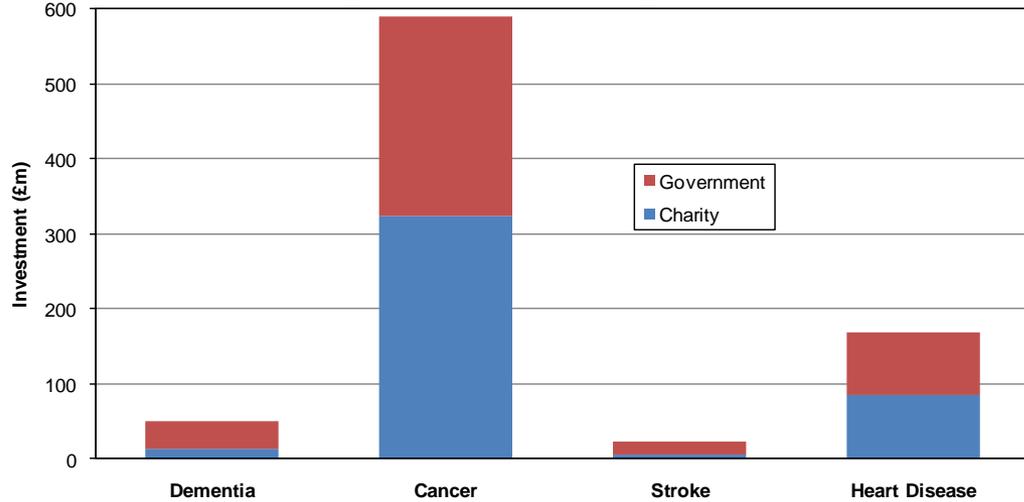
who need to interact and collaborate

- Research which seeks to address the direct requirements of patients and carers needs their direct input
- *How to achieve this?*

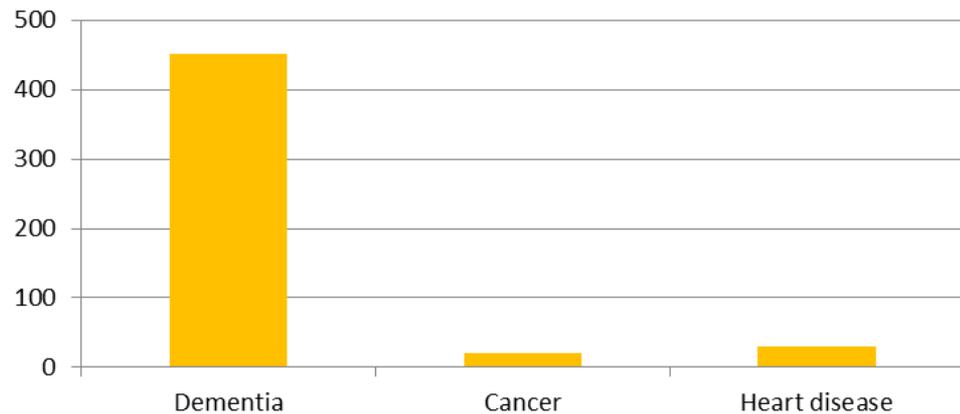
Networks of researchers, conferences, funding calls for multi-disciplinary approaches

Research into dementia has been underfunded in relation to the scale of the challenge it presents

UK research funding by disease (2007-8): government and charity

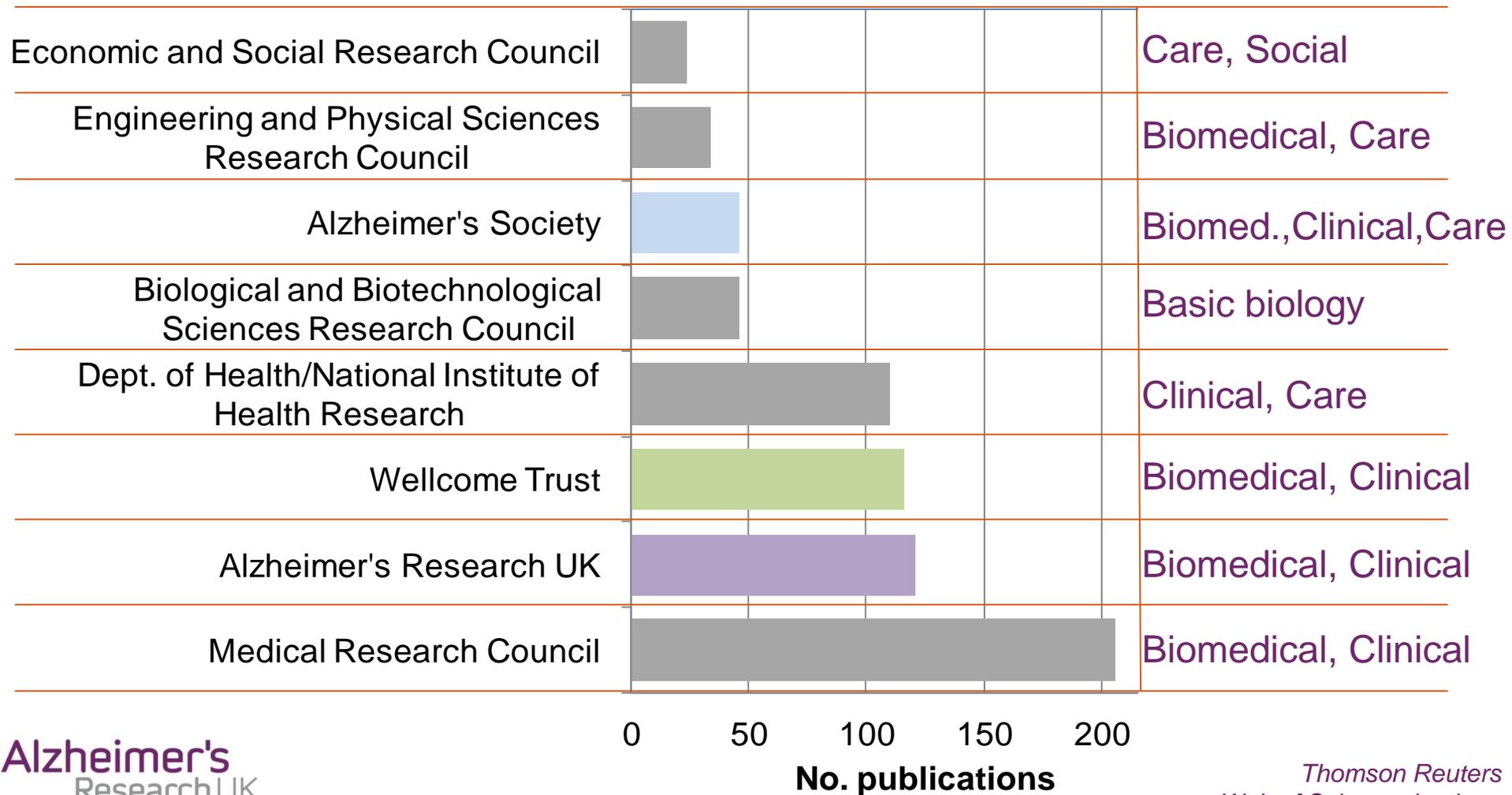


Disease cost/research spend ratio (2007-8)

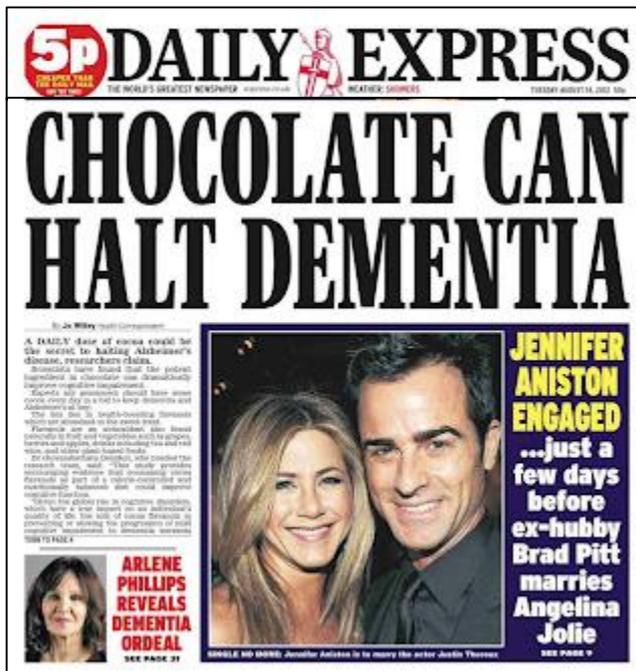


DEMENTIA 2010
The prevalence, economic cost and research funding of dementia compared with other major diseases

Funding avenues for UK dementia research: Charity and statutory funders, Publication analysis Sep 2011-Aug 2012



The profile of dementia research in the UK has never been higher



The Prime Minister's Challenge on Dementia (March 2012)



Prime Minister's challenge on dementia

Delivering major improvements in dementia care and research by 2015



3 components:

1. Driving improvements in health and care
2. Creating Dementia Friendly Communities

3. Better research:

- Overseen by 'Research Champions Group'
- Further pledges of funding for dementia research – doubling to £66m by 2015.
- Much investment in clinical research – projects, networks/infrastructure, cohorts

Some closing thoughts

- At all levels of healthcare provision, there is a vital need for a good understanding of:
 - dementia and the issues surrounding it
 - the particular needs of people with dementia and their carers

- The research effort against dementia needs:
 - Clinician scientists to be research leaders and to keep non-clinical researchers informed about the diseases they are working on
 - Non-research clinicians to be 'research-friendly'

Dementia research funders would like to hear from you!

Thank you