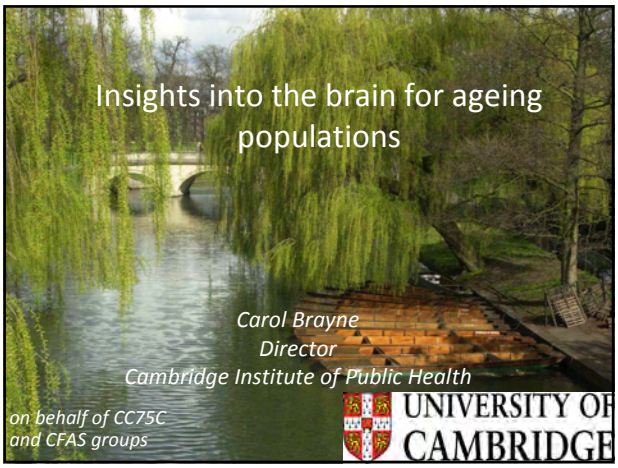


Reflection on recent attention, particularly G8 summit

- Remarkable momentum achieved
- Gradual build up over last decade
- Awareness of ageing populations and results from studies set in motion in 80s and 90s
- More data on dementia
- Highly effective lobbying to increase awareness
- Charities and Business sectors influential with government and Clinician led activities
- How does this sit with the evidence?

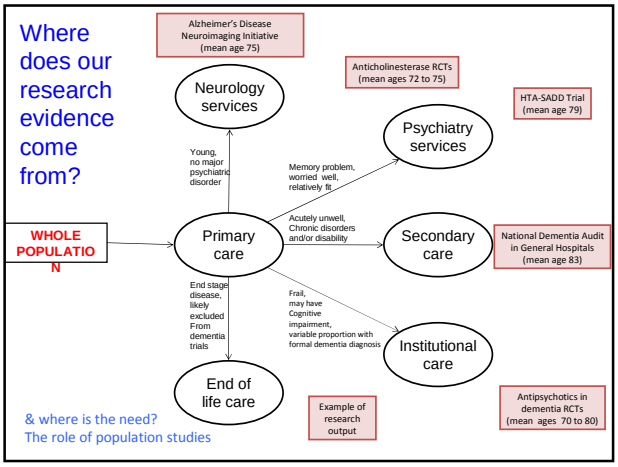
First, define public health

- Organised efforts of society for the improvement of the health of the public
- Science and Art
- Public Health and Dementia requires advancement of knowledge of dementia and associated conditions in the whole population
- Why is this important?

The role of population based studies

- Investigate performance and correlates of diagnostic criteria from neutral standpoint without filters
- Identify populations of relevance
- Test new (and old) concepts – MCI, preclinical dementia
- Over time see what is true change and what is relabelling of old concepts
- Provide basic, current knowledge for policy development and service configuration

Where does our research evidence come from?



& where is the need?
The role of population studies

Need to define dementia ..not disease but syndrome

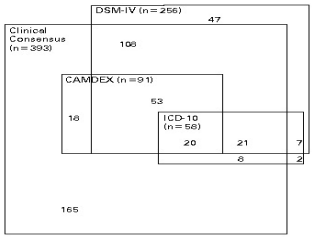
Each component of its diagnostic criteria is complex

•dementia syndrome is deterioration in thinking abilities, once impacting on ability to function day to day in presence of clear consciousness

•Multiple re-defining of criteria for syndrome and subtypes over years – highly unstable with different international systems/cultures

Performance of diagnostic criteria

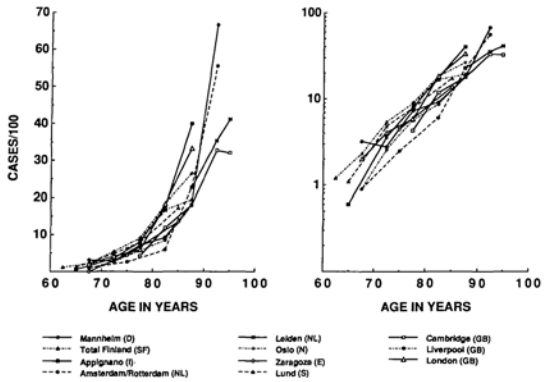
- Not surprising that different criteria identify different groups of people particularly at milder end of spectrum



N Engl J Med. 1997 337, 1667-74. **The effect of different diagnostic criteria on the prevalence of dementia.** Erkinjuntti T, Ostbye T, Steenhuis R, Hachinski V.

Generating relevant evidence

- Need to be able to use components of syndrome and measure in populations
- Routine data sources traditionally poor for these conditions
- Most epidemiological knowledge comes from population derived or representative cohort studies
- Cambridge based/run studies since last century focused on brain ageing
- True populations aged 65 and over followed over time with detailed repeat interviews

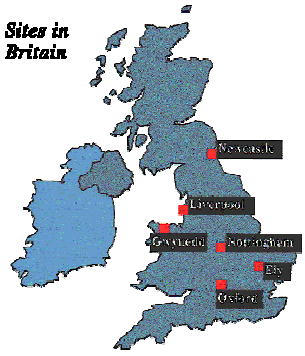


Ref: Hofman A, Rocca WA, Brayne C, Breteler MMB, Clarke M, Cooper B, Copeland JRM, Dartigues JF, Da Silva Droux A, Hagnell O, Heeren TJ, Engedal K, Jonker C, Lindesay J, Lobo A, Mann AH, Molsa PK, Morgan K, O'Connor DW, Sulkava R, Kay DW &Amaducci L. The Prevalence of Dementia in Europe: a collaborative study of 1980-1990 findings. Int J of Epidemiol 1991, 20(3), 736-48.

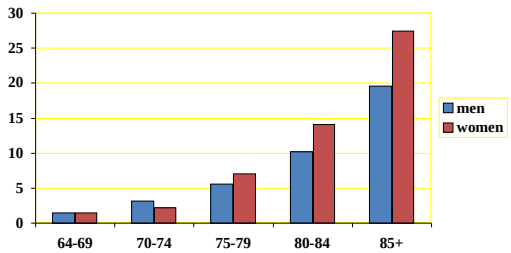
MRC CFAS – brief introduction

- 13,004 individuals (5 identical centres)
- 5, 300 individuals (1 non identical centre)
- Aged 65 and above in 1991, equal weight
- Rural and urban sites
- Population sampling including institutions
- ~ 80% response rate at each stage
- Followed up at regular intervals
- Detailed interviews to capture data relevant to differential diagnosis of mental health disorders in later life (GMS and CAMDEX)
- Brain donation

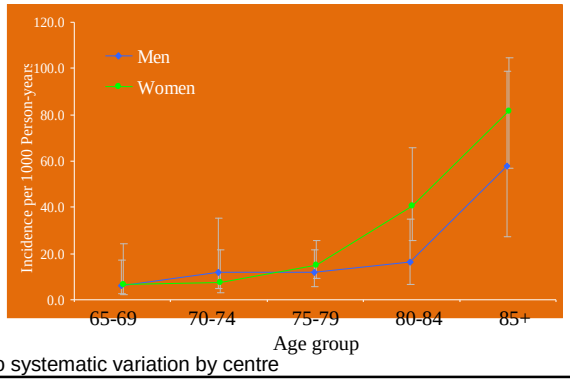
Cognitive Function and Ageing Studies



Prevalence (%) of dementia MRC CFA Study

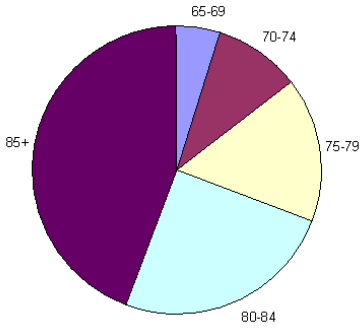


MRC CFAS dementia incidence – ~ 20 years ago



no systematic variation by centre

Dementia distribution for people over 65 years old in 2010



Source: Population size come from ONS Statistics.
Prevalence of Dementia come from Dementia UK full report 2007.

Survival with dementia in CFAS

- Median age at onset 84 years
- Median age at death 89 (90w,87m)
- Survival 4.6 years women, 4.1 years men

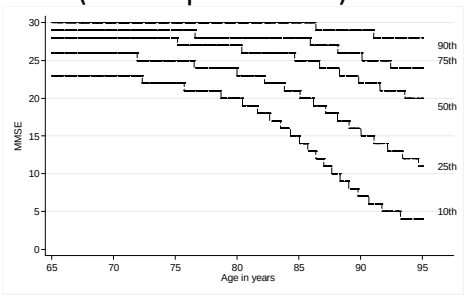
Data uses of these descriptive results

- Government policy documents on dementia
- Dementia UK estimates, Alz Soc and then ARUK
- Numbers currently in use officially still based on these figures generated in early 90s
- Huge impact nationally and internationally
- National strategies across the world and also WHO
- Most recently G8

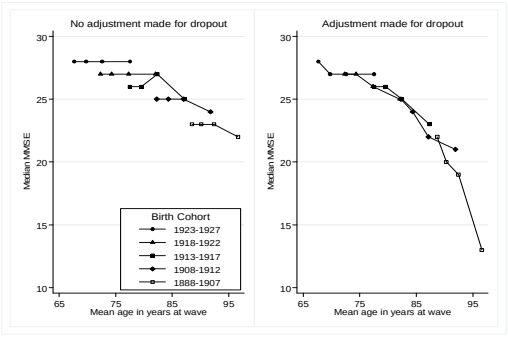
Major messages from 30 years of population based research

- Cognitive decline is 'normal' in that most people do have some deterioration in later life
- By the 10th decade it is very unusual to have the same cognitive performance on cognitive tests as in earlier decades
- Dementia and severe cognitive impairment is 'usual' in statistical sense before death once over age of 90

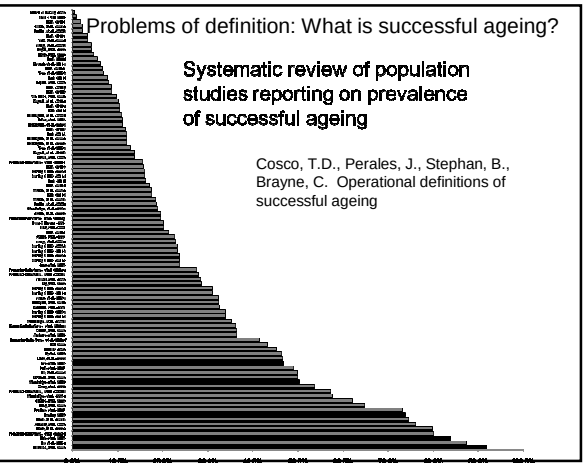
Population profiles for cognition (MMSE percentiles)



MMSE change with age - averages



Problems of definition: What is successful ageing?



Systematic review of population studies reporting on prevalence of successful ageing

Cosco, T.D., Perales, J., Stephan, B., Brayne, C. Operational definitions of successful ageing

Defining MCI

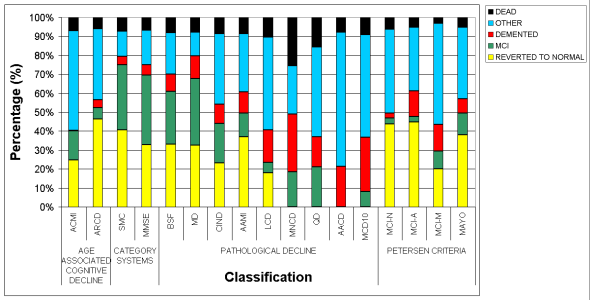
- Various definitions
- Differences in focus and diagnostic criteria
- Definitions can be broadly divided into four groups

System	Description
(1) Classifications Associated With Age Related Cognitive Change	
ACMI	Age Consistent Memory Impairment
ARCD	Age Related Cognitive Decline
(2) Category System	
MMSE Grouping	Mini Mental State Examination Cut-offs
SMC	Subjective Memory Complaint
(3) Classifications Associated With Pathological Decline	
MNCD	Mild Neurocognitive Disorder (DSM-IV)
CIND	Cognitive Impairment No Dementia
BSF	Benign Senescent Forgetfulness
AAMI	Age Associated Memory Impairment
LCD	Limited Cognitive Disturbance
QD	Questionable Dementia
AACD	Age Associated Cognitive Decline
MCD	Mild Cognitive Disorder [ICD-10]
(4) Mayo Clinic Criteria	
N-MCI	Non-Amnestic MCI
A-MCI	Amnestic MCI
M-MCI	Multiple-domain MCI

Systematic review search strategy: 1950-January 2006

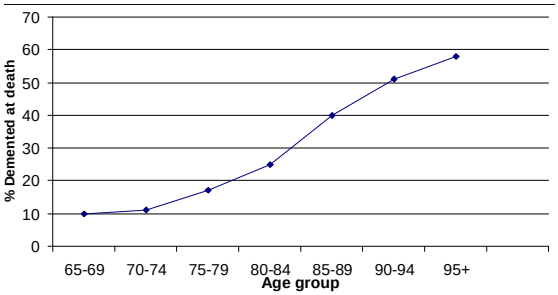
Two-year Outcomes from MCI

- The majority of MCI cases revert to normal or develop an impairment outside the MCI range at 2-years follow-up



Reference Matthews, Stephan et al 2008, JAGS

Understanding the whole picture: prevalence of dementia and/or severe cognitive impairment in year preceding death (MRC CFAS)



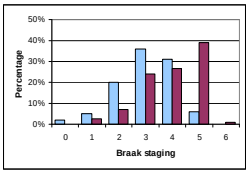
PLoS Medicine Matthews et al 2005

Major messages from 30 years of population based research

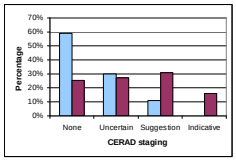
- Dementia diagnoses in the oldest age groups is not 'pure' but mixed
- Large numbers of people in the older age groups die without dementia but with the neuropathology associated with Alzheimer's disease
- 'Usual' dementia in the oldest age groups (i.e. those at greatest risk) is associated with many additional pathobiologies
- Education and lifecourse considerations seem to protect from the expression of dementia in the presence of pathology

Plaques and Tangles (i.e. Alz Disease neuropathology) in people dying at older age in whom we know state in period before death

TANGLE measure
(Braak staging)



PLAQUE measure
(CERAD staging)



Distributions of Braak staging and CERAD staging in CC75C (population sample 75+) without clinical dementia (blue) and with clinical dementia (red)

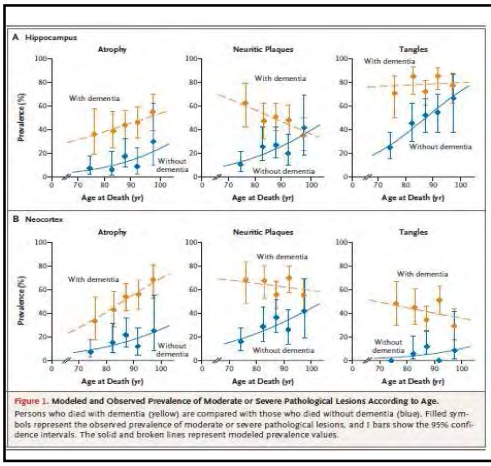
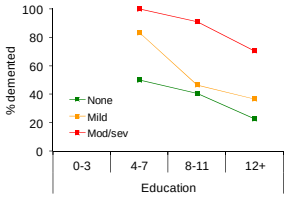


Figure 1. Modeled and Observed Prevalence of Moderate or Severe Pathological Lesions According to Age.
Persons who died with dementia (yellow) are compared with those who died without dementia (blue). Filled symbols represent the observed prevalence of moderate or severe pathological lesions, and I bars show the 95% confidence intervals. The solid and broken lines represent modeled prevalence values.

Age-Effect on Relationship Of Pathology to Dementia

NEJM 2009; 360:2302-2309

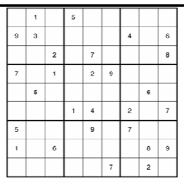
How close is relationship of clinical phenotype to neuropathology measured at death – role of compensation?



Cortical tangles: expression of dementia lower for higher education at same level of neuropathology in brain post mortem (apart from atrophy) ECliPsE: CC75C, CFAS & Vantaa

Major messages from 30 years of population based research

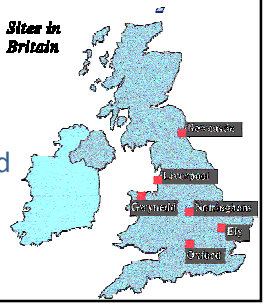
- New studies suggest current population at lower age specific risk of dementia
- CFAS II study set up to test for differences …



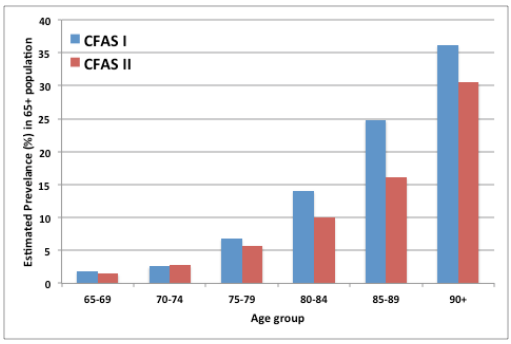
Sodukos, blueberries and a bit of exercise – is dementia prevention really going to be that easy?

Testing change over time: CFAS I and II

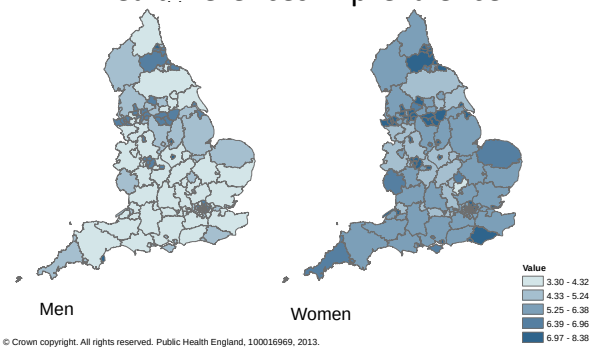
- Building on MRC CFAS (6 sites)
- Three areas taken forward for new study
  - Cambridgeshire
  - Newcastle
  - Nottingham
- CFAS II Repeat
- Health profiles changed
- Ageing of population



Prevalence (%) two decades ago and now



Area differences in prevalence



Research summary

- Dementia is most common in the oldest age groups, average age at onset 83 years
- The neuropathology associated with dementia is almost universal if we die older than 80
- Dementia does appear to be changing in that age specific prevalence is lower in the most recent study in UK than 20 years ago
- Estimated numbers therefore remain stable, not a huge increase
- Education & Deprivation, which may reflect both health and compensatory advantage, potentially important
- Efforts to influence health relevant to the brain in earlier life worthwhile
- Dementia is not inevitable before death, but very common and either dementia or severe cognitive impairment are usual in the oldest age groups
- Different aims for different components of dementia – preventable elements, early high risk onset, 'usual' dementia in oldest age groups and nearing end of life

How does this fit with G8, December 2013? Interaction of policy and evidence…

The countries agreed to:

•set an ambition to identify a cure, or a disease-modifying therapy, for dementia by 2025

•significantly increase the amount spent on dementia research

•increase the number of people involved in clinical trials and studies on dementia

•establish a new global envoy for dementia innovation, following in the footsteps of global envoys on HIV and Aids and on Climate Change (Dennis Gillings)

•develop an international action plan for research

•share information and data from dementia research studies across the G8 countries to work together and get the best return on investment in research

•encourage open access to all publicly-funded dementia research to make data and results available for further research as quickly as possible.

Carol Brayne, Antony Arthur, Linda Barnes, John Bond, Carol Jagger, Louise Robinson on behalf of the CFAS studies collaboration

Acknowledgements

- CFAS (I and II), CC75C and ECliPSE research teams (iph.cam.ac.uk for study websites)
- Participants and families
- Health service and primary care staff in all fieldwork sites
- Funders include: MRC, NIHR bodies: CLAHRC-CP, SPHR, BRC, & Charities: Alz Soc, ARUK, PDS; Cure PD; Patrick Bertoud Trust; Rosetrees Trust; Raymond and Beverley Sackler Trust; Wellcome Trust
- Cambridge activities include major focus on dementia and whole populations through variety of major initiatives (SPHR, CLAHRC, BRC and BRU)

With thanks to you and to current MRC CFAS and CC75C collaborative groups and funders (mainly MRC)

- Cambridge Institute of Public Health (Barnes, Cosco, Fleming, Gao, Matthews, Muniz, Zhao)
- Bangor (Woods)
- East Anglia (Savva)
- Exeter (Melzer)
- Gwynedd and Liverpool (McCracken)
- Herriott Watt (McDonald)
- IoP (Dewey)
- Newcastle (Jagger, McKeith, Bond, Robinson, Stephan)
- Nottingham (Dening, Lowe)
- Oxford (Evans, Esiri, Wilcock, Clarke)
- Kings College, London (Parry), LSE (Comas Herrera, Wittenberg)
- Sheffield and wider neuropath groups elsewhere (Ince, Forster, Wharton)