Institution:
University of Cambridge

Unit of Assessment:
UoA2

Title of case study:
Dementia Research: The MRC Cognitive Functioning and Ageing Study (CFAS)

1. Summary of the impact (indicative maximum 100 words)

Research by Professor Carol Brayne, has led to increased understanding and awareness of dementia as a key public health issue of our time. Outcomes of her DH/MRC funded longitudinal Cognitive Function and Ageing Studies (CFAS) have contributed to national and international health policy on dementia as well as public debate.
Specifically, the CFAS study provided evidence that was used in the highly influential report "Dementia UK" which led to the development of the 2009 National Dementia Strategy. Results from CFAS have increased healthcare workers' understanding of the condition, such as the complexity of cognitive impairment and the relationship between illness and disability.

2. Underpinning research (indicative maximum 500 words)

Research setting: Since 1999, this multicentre longitudinal study has been led by Professor Brayne in the Department of Public Health and Primary Care (tenure since 1991).
Research group: Professor Brayne leads the CFAS research group with national and international collaborators. The support of the MRC Biostatistics Unit has been pivotal in providing rigorous statistical and innovative methodology to support the diverse outputs from CFAS (>220 peer reviewed publications to date).
Study rationale, and underpinning data and methods: Prior to CFAS, there was limited representative evidence on the incidence and prevalence of dementia in the UK population. In CFAS, survey methods have measured prevalence and incidence of dementia in the UK population, and have been applied to generate population representative findings for detailed neuropathology and molecular analyses. CFAS is a longitudinal study, with 18,000 subjects recruited at baseline in 1989/1991, and new generation studies (CFAS II) and CFAS Wales) which began in 2008 to test differences in prevalence across the two decades. CFAS I subjects have been surveyed at least three times since initial interview (in 1994, 1997 and 2001) and in CFAS II at two years, with continued follow up of those from CFAS I consenting to brain donation. To date, 47,000 interviews have taken place using standardised assessment for health, dementia, and measures of health and social care services utilisation. There are currently more than 560 brain donations from study participants.

Key findings and outcomes of the research include the following:

- **Dementia prevalence**. Before CFAS there were no population figures which could be confidently applied nationally and to specific geographical areas. CFAS showed that dementia is common, more prevalent than previously thought (overall prevalence of dementia in the 65+ population, 6.6%)**,** and increases as the population ages (prevalence in the 85-89 population, 25.3%). Differences were tested across six sites, enabling estimates to be made for different parts of the UK as well as for the institutional care population. (Section 3. Research ref 1 and 3)
- **Care utilisation and cost**. The study demonstrated the high cost of informal care in supporting people with dementia, which was much greater than previously estimated. The group was also able to predict future demand for long term care and likely associated costs. Modelling long term care needs and forecasting costs have been invaluable tools for policy makers. (Research ref 4)
- **Better understanding of neuropathology of dementia/demonstrating complexity of cognitive decline** (research refs 2 & 5). CFAS has been a major contributor (first brain donated in 1993) to a unique population representative brain resource, available to deepen our understanding of the neuropathological determinants of dementia. Insights from a unique sample of donated brains show no clear thresholds of Alzheimer-type and vascular pathology that predicted dementia status, challenging conventional dementia diagnostic criteria.
- **Features associated with a higher or lower risk of developing dementia.** CFAS demonstrated a relationship between demographic and lifestyle factors and risk of cognitive impairment, including age, stroke and Parkinson's disease, and the protective effect of higher education and of self-reported 'good' or 'excellent' health. (research ref 5 and 6)

3. References to the research (indicative maximum of six references)

1. Cognitive function and dementia in six areas of England and Wales: the distribution of MMSE and Prevalence of GMS organicity level in the MRC CFA Study. MRC CFAS. Psychological Medicine 28(2):319-335 (1998).
2. Pathological correlates of late-onset dementia in a multicentre, community-based population in England and Wales. Esiri M; Matthews FE; Brayne C; Ince PG; Neuropathology Group. MRC/CFAS. Lancet 357:169-175 (2001).
3. Dementia before death in ageing societies - The promise of prevention and the reality. Brayne C; Gao L; Dewey M; Matthews FE; MRC CFAS. PLoS Medicine 3(10):1922-1930 (2006).
4. Cognitive impairment in older people: future demand for long-term care services and the associated costs. Comas-Herrera A, Wittenberg R, Pickard L, and Knapp M. International Journal of Geriatric Psychiatry 22(10):1037-1045 (2007)
5. Age, neuropathology and dementia. Savva G, Wharton S, Ince P, Forser G, Matthews F, Brayne C. For the MRC CFAS. N Eng J Med 360(22):2302-2309 (2009)
6. Risk factors for incident dementia in England and Wales: The Medical Research Council Cognitive Function and Ageing Study. A population-based nested case–control study. Yip A; Brayne C; Matthews FE. Age and Ageing 35: 154-160 (2006);

Grants which supported CFAS:
CFAS I: MRC G9901400 (ended 2012) CFAS renewal grant £836,100 2005-2011
CFAS II: MRC G0601022 - £2,014,172 (2008-2013)
Subcontract to Cambridge University to provide the administrative support to Bangor University (CFAS Wales) : ESRC 2010-2015 RG60916 - £404,627.88
Sheffield (Neuropathology): RG57915 - £256,237.00 (the Cambridge part of the main grant) 01/02/2010 – 31/01/2014
In addition, the Brain Banking for MRC CFAS is supported in part by grants for the Newcastle and Cambridge NIHR Biomedical Research Centres.

4. Details of the impact (indicative maximum 750 words)

The impact of CFAS on policy, service and society can be seen widely, e.g. through citations in policy documents, clinical guidance and the quoting of findings in public discourse.

Epidemiology of dementia

1. CFAS provided the core prevalence estimates for dementia in the UK population in Dementia UK (2007), e.g. "*In terms both of sample size and scope the evidence base is dominated by the Medical Research Council Cognitive Function and Ageing Study" (*page 10, reference 1, section 5). These estimates remain those used nationally, though they may in time be modified by Professor Brayne's most recent work which includes a 20 year intergenerational comparison on prevalence in three CFAS areas holding methods steady (Matthews et al Lancet. 2013 Jul 17)
2. The Dementia UK report for the Alzheimer's Society was instrumental in bringing the weight of CFAS evidence into the 2009 National Dementia Strategy, e.g. "*Key data for the UK as a whole include the following: There are approximately 700,000 people with dementia; In just 30 years, the number of people with dementia is expected to double to 1.4 million; The national cost of dementia is about £17 billion per year*…", DoH (2009) Living well with Dementia: A National Dementia Strategy. p16. (Figures from research ref 1). See section 5, nos 1 and 2.
3. The UK End of Life Care Strategy 2008 used our institutional data which showed Dementia clearly to be a core business of care homes. See section 5, no 3.
4. Increased investment in dementia research. The 2012 announcement of a boost to funding for dementia research by the Secretary of State for Health and the Prime Minister's progress report on his 'dementia challenge' November 2012, quoted the Dementia UK 2007 projected prevalence figures, (research refs 1 and 3). See section 5 no 2.
5. Professional guidelines were influenced by baseline data on the ageing population over 65, e.g. *Good Practice Guidance for Commissioning Interventions* for people with dementia (DH 2011). (research refs 1, 3, 4) See section 5, no 11.
6. Research findings also now underpin practical tools for strategic planning and commissioning

services. The CFAS prevalence data is the driver of the 2012 *Dementia Prevalence Calculator* - a tool for General Practices and Commissioners to better understand local dementia prevalence in the community and care homes. (Research ref 1). See section 5, no 10.

7. Modelling of long term care and costs has made a significant contribution to the debate around the funding of long term care for the ageing population (research ref 4). The clear economic case made for better supporting dementia patients and carers was picked up by the Wanless social care review in 2006, (*"The MRC CFAS data provides a detailed breakdown of the level of demand that people with dementia living outside institutions present to the social care system"* p166. Section 5, no 4) which fed a debate that continued into the Dilnot Commission review (2011) and the 2012 White Paper on Social Care.

CFAS has also contributed additional knowledge (e.g. on risk factors, disease progression, disability and recovery, depression, and neuropathology), with the following impacts:

1. New knowledge identifying the complexity of cognitive decline and ageing (research refs 2 & 5) raised awareness of the need to better understand risk, cumulative risk, and vascular risk: *e.g. "mixed pathology was the most common finding at autopsy in the brains of older people" (MRC/CFAS)* (section 5, no 8) This knowledge had an important impact on the 'pharma' view, influencing prevention work and clinical trials that thereafter could no longer assume that any one drug suits all dementia sufferers, and contributing to a new MRC call for a Fresh Approach to Dementia.. (Section 5, no 8)
2. Professor Brayne's research has directly influenced a NICE guideline on dementia. (CG42: Supporting people with dementia and their carers' in health and social care) Estimates based on the improved understanding of neuropathology and dementia drove work for the 2009 NICE Final Appraisal Determination on donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease, which led to the amended guideline. (NICE technology appraisal guidance 217. See Section 5, no 9)
3. CFAS research outcomes are influencing policy beyond the UK, e.g. findings on dementia sub-types have been incorporated into WHO policy (Dementia: a public health priority. WHO and ADI, 2012. See section 5, #6, p19), and a 2012 Research Review forming the foundation for Ireland's developing National Dementia Strategy (see section 5, no 7, p42).
4. Public awareness and involvement in research has increased in a very real sense – in the numbers of 'CFAS brains' donated to its Bioresource, as well as dissemination efforts to increase awareness of brain banking. BBC News and The Culture Show covered an innovative exhibition in London, 2011: 'Mind Over Matter' was based on portraits and life stories of donors from the Cambridge longitudinal studies. The Science Museum's Dana centre held a parallel debate, with Professor Brayne presenting aspects of the neuropathological research, on the ethics and practice of brain donation for research. (section 5, no12).

5. Sources to corroborate the impact (indicative maximum of 10 references)

Policy

1. Dementia UK: the full report. A report to the Alzheimer's Society by Kings College London and the London School of Economics (2007). This report was instrumental in bringing the weight of CFAS evidence into the 2009 National Dementia Strategy, and consequently, current implementation of policies on dementia. http://alzheimers.org.uk/site/scripts/download_info.php?fileID=2
2. Living well with dementia: a National Dementia Strategy, DoH (2009). Quotes both Dementia UK (pp16, 34, 77, 94) and analysis on long term care costs which were grounded in CFAS data (p16).
3. The EOLC Strategy. Promoting high quality care for all adults at the end of life, DoH (2008).
4. Wanless D et al (2006) *Wanless social care review: securing good care for older people, taking a long-term view.* King's Fund, London. CFAS data used in modelling predictions of disability, death and need for long term care (p39, p165), prevalence of cognitive impairment and combined disability in care homes, and in anticipating the level of demand for social care and informal care (p166). This fed a debate on provision of and funding for long term care that continued into the Dilnot Commission review (2011) and the 2012 White Paper on Social Care.
5. Deaths from Alzheimer's disease, dementia and senility in England. National end of life Intelligence Network, (2010)

6. Dementia: a public health priority. WHO and ADI 2012. http://www.who.int/mental_health/publications/dementia_report_2012/en/
7. Creating Excellence in dementia care: A research review for Ireland's National Dementia Strategy, Cahill S, O'Shea O, Pierce M. (2012). http://www.dohc.ie/consultations/closed/dementiastrategy/
8. http://www.mrc.ac.uk/Fundingopportunities/Calls/dementia2013/MRC008995

Service

9. NICE Final appraisal determination 2009. Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended). (NICE technical report on the economic analyses resulting from further analyses by the MRC Biostatistics Unit. Also the mixed pathology findings (Research ref #2) were incorporated into NICE Clinical Guidance (CG42) Dementia: Full Guideline. http://guidance.nice.org.uk/CG42/NICEGuidance/pdf/English
10. The Dementia Prevalence Calculator 2012 (depends on CFAS data (Dementia UK 2007)): http://www.dementiapartnerships.org.uk/diagnosis/dementia-prevalence-calculator/ (N.B. No data on usage of the tool currently exists).
11. www.bbc.co.uk/news/health-15200246
12. www.danacentre.org.uk/events/2011/10/06/635