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COHORT PROFILE

Cohort Profile: The Cambridge City over-75s Cohort (CC75C)

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The Cambridge City over-75s Cohort (CC75C), one of the largest and longest-running population-based studies of the oldest old, is celebrating its 21st birthday. Its origins and subsequent evolution into one of the UK's key ageing cohort studies lie in the collaboration of many distinguished researchers, and its ongoing importance owes much to the invaluable contribution made by its many committed participants.

How did the study come about?

Sir Martin Roth is a key figure in the development of old age psychiatry as it is today, and he made a major contribution to research into dementia in the last half of the last century[1–4] (Figure 1). The field of dementia epidemiology developed naturally from his early work with hospital residents, which linked the study of their mental disorders to examination of their brains after death. In the 1980s questions were emerging about the best patterns of care for people with dementia, early detection and whether individuals would be best supported at home or within institutions. In this context Sir Martin Roth, Dr Peter Brook (old age psychiatry), Dr Bernard Reiss (general practice) and Dr Felicia Huppert (psychology) combined forces to seek funding from the Charles Wolfson Charitable Trust for a population-based dementia study. They recruited Dr Daniel O'Connor (old age psychiatry) and Dr Penelope Pollitt (anthropology) to implement their ideas. The design started as a mechanism to detect people in the earliest stages of dementia, not yet perceived by their families, who could then be followed and in whom different patterns of care might be investigated. At that time a multidisciplinary community resource team was being put together for different parts of Cambridge city, with teams defined by geographical areas. In one area the team was just starting up and usual care was available in the other area. Although a randomized controlled trial would have been desirable this was not held to be justified, and so the natural experiment was observed instead.

Thus, beginning in 1985, this original survey measured the prevalence of dementia,[5] including the mildest stages,[6] and then followed over the next 2 years the evolution of patterns of care,[7] recognition of the onset of dementia[8–11] and transitions to long-term care.[7]

The opportunity to follow on from this ground-breaking work was recognized by Professor Eugene Paykel who, along with Dr Huppert and Dr Carol Brayne, successfully raised Medical Research Council funding to carry out a study of new dementia incidence amongst those who had not been diagnosed with dementia by the original team.[12,13] When the original project ended the incidence study team became the stewards for the total data set, and they have continued to follow-up this population to the present day. Each phase had a new name—early publications refer to the Hughes Hall Project for Later Life, so called to reflect the support given by a college of Cambridge University, and the incidence survey was launched 2 years later as the Cambridge Project for Later Life, the name by which participants still know the study. However, the study as a whole, spanning over 20 years now, is known as the Cambridge City over-75s Cohort[14] (http://www.cc75c.group.cam.ac.uk).

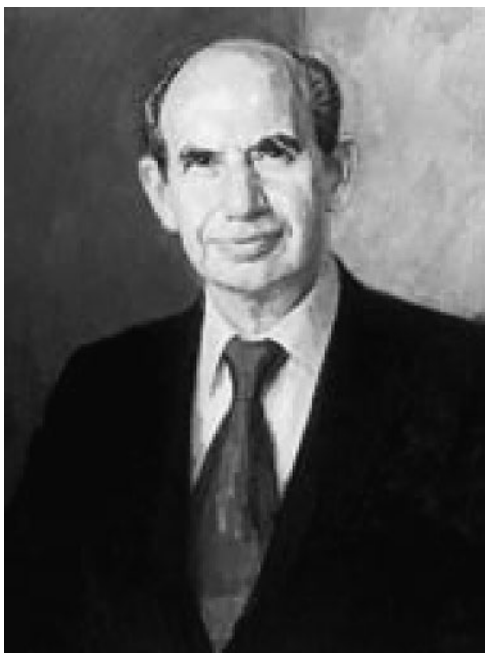

Figure 1 Sir Martin Roth

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Table 1 Demographic characteristics of the baseline sample population and of participants in the last survey completed

	Year 0 (Baseline sample) [$n = 2165$]		Year 17 (Survey 6 sample) [$n = 110$]	
Age				
Mean (SD)	81.3 (4.6)		94.4 (2.4)	
Median	80.4		93.8	
Inter-quartile range	77.6–84.0		92.7–95.8	
Range	75.0–106.3		91.6–105.8	
	n	(%)	*n*	(%)
Gender				
Women	1409	(65)	90	(82)
Men	756	(35)	20	(18)
Place of residence				
Living in the community				
house/flat/granny flat	1892	(87)	62	(56)
Supported living				
sheltered accommodation	182	(8)	19	(17)
Living in institutional care				
residential/nursing home/ long-stay hospital	91	(4)	29	(26)

Who is in the study sample?

The baseline study targeted all men and women aged 75 years or older, who were registered with a selection of geographically and socially representative practices in Cambridge, achieving a 95% response rate. From this original survey of 2609 people, 2165 individuals formed the baseline sample for the ongoing cohort study. This excluded one of the original general practices because of differential recruitment, and also a small group involved in a branch study. Survivors of this longitudinal cohort have been followed-up on at least five further occasions and sub-groups have been assessed more often.

Given the expected high attrition rates due to mortality, the study has paid close attention to the importance of keeping the sample representative by tracing survivors and using proxy informants where a frail participant might otherwise have been lost to follow-up. In the most recently completed survey, data were gathered on 84% of those still alive—110 people, 90% of them interviewed in person. At the time of going to press, more than 50 people, all aged 95 years or more, are alive and currently being surveyed again.

Table 1 describes the demographic characteristics of the baseline sample population (aged 75–106, 65% women, 4% living in care) alongside the participants who completed the last survey (aged 91–106, 82% women, 26% living in care). Figure 2a and b illustrate the shifting age range over the duration of the cohort study so far.

Key dimensions and measures

The study's core themes—cognition and function in older old age—cover multidisciplinary research interests as diverse

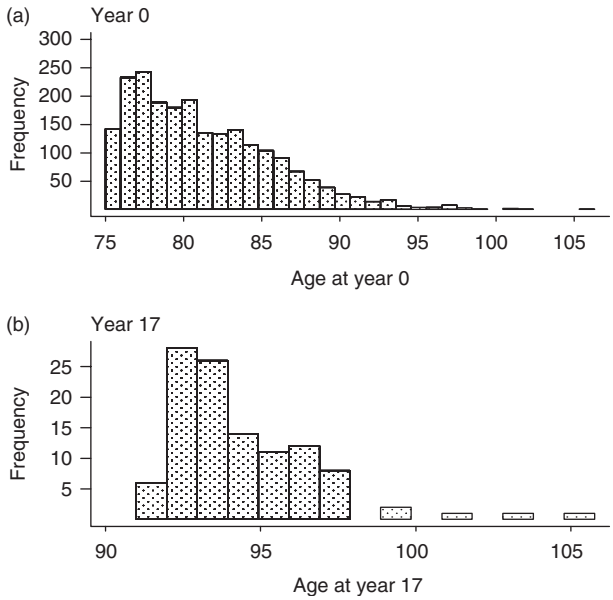

Figure 2 (a) Age distribution of the CC75C baseline sample (Survey 1 = Year 0). (b) Age distribution of the latest survivor sample (Survey 6 = Year 17)

as neuropsychology, genetics, palliative care and psychiatry with a range of investigations at various time-points including bone strength, falls, physical performance and brain pathology. Each survey has included a detailed cognitive assessment, including at least the Mini-Mental State Examination (MMSE),[15] usually its extended version and, in the majority of interviews, the Cambridge Cognitive Exam (CAMCOG).[16] After a series of intensive assessments with purposely selected sub-groups in the initial study stages, follow-up of the full cohort continued with interviews every few years. The flowchart in Figure 3 summarizes the main stages to date.

Interview data

The core data set comprises data collected from the six main surveys to date using the CC75C structured schedule administered by trained interviewers. This provides longitudinal data on socio-demographic variables (e.g. place of residence, household structure, marital status and social contact), activities of daily living, use of health and social service, health problems and medication. The interview schedule has undergone slight revisions over the years with the addition of new sections, such as questions on service use added in Survey 3, but maintaining continuity of core measures has remained a priority.

The CC75C study also holds other data resources collected at different periods in the study to examine specific topics of importance in ageing research.

CAMDEX assessments

After the baseline cognitive screening assessment, those who scored 23 or below in the MMSE, and a sample of those with MMSE scores 24 or 25, were assessed using the Cambridge Mental Disorders of the Elderly Examination (CAMDEX), a structured schedule specifically designed to

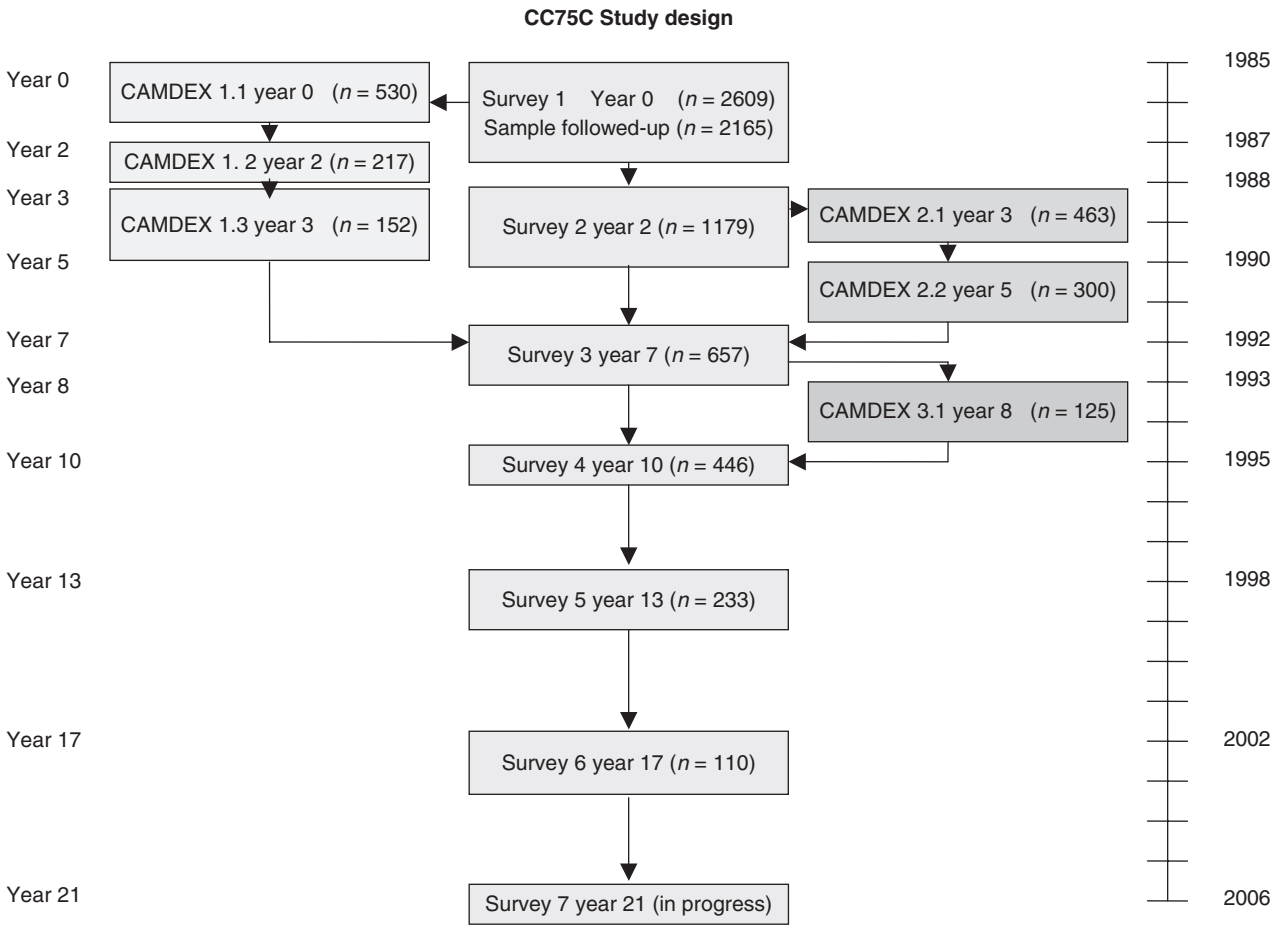

Figure 3 Flowchart illustrating the main phases in the CC75C study to date

detect mild dementia. The CAMDEX includes a mental state examination, a psychiatric history, detailed cognitive testing, and an interview with a proxy informant.

Biological resources

In the 3rd year of the study magnetic resonance imaging brain scans were taken of a sub-sample following Survey 2. During Survey 4 (Year 10) blood samples were gathered for genetic studies from all participants who consented. In Survey 6 (Year 17) new physical measurements were recorded for the first time: in addition to the usual CC75C questionnaire, the project nurse conducted functional assessments and scanned heel bones with quantitative ultrasound as part of this survey's focus on falls amongst over-90-year-olds.

Brain donation study

It was in Survey 2 that the brain donation programme began to identify study participants willing to donate brain tissue after their death. CC75C was the first study to approach individuals from a population sample, aiming to represent both the demented and non-demented, in order to examine the relationship of findings during life and the appearance of the brain after death in the whole population. The methods used to approach individuals have been used in many other studies, most particularly the MRC-Cognitive Function and Ageing Study.[17] This programme is still running, with 230 donations so far collected.

Other measures

In Survey 6 (Year 17) only, each participant was followed-up intensively for 12 months, tracking the consequences of falls in advanced old age—injuries, hospitalization and moves into long-term care.

For the current survey (Year 21) voice recordings have been introduced to capture in their own words the perspective of very old people and their relatives or other carers on important end-of-life issues, and qualitative research methods are adding a further element to the wealth of quantitative data from the study (Figure 4).

Proxy informant interviews

All study participants were interviewed in person at baseline, but interviews with proxy informants were used in subsequent surveys to minimize loss to follow-up that could under-represent the frailest elderly.

Table 2 Data collected at different study phases

	Survey						
Measure	1	2	3	4	5	6	7
Questionnaire data							
Socio-demographics	✓	✓	✓	✓	✓	✓	✓
Family structure and social support	✓	✓	✓	✓	✓	✓	✓
Affect and loneliness	–	–	✓	✓	✓	✓	✓
Anxiety and depression	✓	✓	✓	✓	✓	✓	✓
Personal activities of daily living	✓	✓	✓	✓	✓	✓	✓
Instrumental activities of daily living	✓	✓	✓	✓	✓	✓	✓
Leisure activities and social participation	✓	✓	✓	✓	✓	✓	✓
Physical activity including cycling	–	–	✓	✓	✓	✓	✓
Driving	–	–	–	✓	–	–	–
Self-rated health and reported diagnoses	✓	✓	✓	✓	✓	✓	✓
Falls	✓tf	✓tf	✓rf	✓rf	✓f	✓ff	✓ff
Medication	✓	✓	✓	✓	✓	✓	✓
Smoking and alcohol	–	–	✓	✓	✓	✓	–
Assessments							
Cognition –MMSE	✓	✓	✓	✓	✓	✓	✓
–CAMCOG (incl. MMSE)	✓cc x	✓cc½x	✓cc½	✓cc	✓cc	✓cc	✓cc
Hearing and eyesight	✓	✓	✓	✓	✓	✓	✓
Functional performance testing	–	–	–	–	–	✓	–
Physiological measures							
Blood and saliva samples	–	–	–	✓	–	–	–
Magnetic resonance image brain scans	–	✓	–	–	–	–	–
Quantitative ultrasound heel scans	–	–	–	–	–	✓	–

✓tf tendency to fall.
✓rf recent falls.
✓ff falls and fractures history.
✓cc x CAMCOG attempted with only participants selected for CAMDEX assessment groups.
✓cc½x CAMCOG attempted with only ~half participants interviewed plus CAMDEX groups.
✓cc CAMCOG attempted with all participants interviewed.

Retrospective informant interviews

Proxy informants are also interviewed, about study participants who have died, in order to provide information about their physical and mental health and their need for support services in the period leading up to death. These interviews concern those who became brain tissue donors when they died.

Table 2 summarizes the measures that were collected at particular stages of the study.

What has the study found?

A full list of papers arising from the study, with links to abstracts, can be found on the study website (http://www.cc75c.group.cam.ac.uk). The study is one of the first and largest prevalence studies of dementia and its sub-types to be conducted in the United Kingdom.[5] It has examined the evolution of the earliest stages of dementia[6,8] and optimal patterns of care,[7,18,19] The incidence study provided novel findings on the incidence of dementia in the oldest old,[13,14,20,21] the characterization of its sub-types[22] and also evidence of the continuous distributions of cognition and cognitive change in population samples.[23–26] The range and depth of neuro-psychology assessments used have provided detailed evaluation of clinically relevant measures.[16,27] The neuropathological findings demonstrated that there is much pathology in the non-demented, and that this only relates loosely to clinical status during life.[28–30] This is a finding which is now

Figure 4 Longevity and multiple generations are increasing—one of the CC75C participants who helped the study for 21 years with four succeeding generations of her family

well-replicated. Genetic studies have examined the role of a number of candidate genes and polymorphisms in relation to cognitive decline, dementia and particularly Alzheimer's disease.[31–37] Researchers from a variety of disciplines have reported such diverse findings as the prevalence of depression amongst the older old,[38–40] very old drivers,[41] disability and self-rated health[42] and patterns of service use by the physically and cognitively frail.[19,43,44] Current work is building on earlier survey findings concerning very old people's views on death.[45,46] There is ongoing analysis on bone strength, falls and their consequences in extreme old age.[47,48]

Main strengths

The cohort was based on a substantial proportion of those aged 75 and over in Cambridge city at the time it began and, with excellent response rates, is a highly representative sample. From the outset, it included people living in institutions as well as in the community, and the study continues to follow-up individuals who have moved into care, an increasing proportion of the sample over time. Whilst many of the older people involved have always shown a keen interest in helping research, recognition of all the participants' contribution by means of thank-you letters, newsletters, Christmas mailings and certificates have been important in encouraging their motivation to continue in the study. Proxy informant interviews continue to enhance the data collection, and acknowledging the role played by participants' family, friends and other carers is also important (Figure 4). The population has been followed-up to a very advanced age, and it is planned to follow-up individuals until the cohort has no living members. The collection of brains from respondents is ongoing and those individuals who die now contribute to the understanding of the survival elite into the oldest age groups. Besides being so representative, so long-running and including so many very old people, the study's other great strength is its wide range of measures.

Main weaknesses

This very breadth of perspective inevitably has some limitations as well—some measures are insufficiently detailed for certain research questions, and changes in a few measures have led to difficulties for particular longitudinal analyses. In common with much epidemiological work, there has never been secure core funding, thus the vagaries of grants awarded had contributed to irregular follow-up intervals with loss to follow-up in the earlier years of individuals who moved away, limited the scope of costly biological measures and in part contributed to some measurement changes as the focus of enquiry shifted.

Can I get hold of data?

The study welcomes external collaborators and there are mechanisms for submitting such research proposals to its management committee. The wealth of data—from interviews, assessments and the biological resources—have been archived and would-be collaborators are encouraged to discuss data requirements with the current study team.

Where can I find out more?

The study website (http://www.cc75c.group.cam.ac.uk) details these collaborative mechanisms, gives full contact information and list publications to date.

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Contributors

Core collaborators in order of joining the study: Sir Martin Roth (deceased), Bernard Reiss (deceased), Peter Brook (deceased), Felicia Huppert, Daniel O'Connor, Penny Pollitt, Eugene Paykel, Carol Brayne, Lynn Beardsall, Claude Wischik, Charles Harrington, Angela O'Sullivan, John Xuereb, Magnus McGee, David Rubinsztein, Tom Dening, Justin Chi, Elizabeta Mukaetova-Ladinska, Margaret Ely, Anne Ahmed, Rhian Gabe, Sarah Cullum, Rosemary Abbott, Jane Fleming, Fiona Matthews, Emily Zhao, Stephen Barclay, Morag Farquhar, Ann-Louise Kinmonth, Sophia Xie.

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