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COHORT PROFILE

Cohort Profile: The 45 and Up Study

45 and Up Study Collaborators^{†*}

How did the study come about?

In common with virtually all industrialized countries and many less developed nations, Australia is facing rapid population ageing. Historical patterns of fertility and migration, along with changes in life expectancy, mean that the over 65 age group is likely to increase by around 50% in the next 15–20 years.¹ The further increase in the proportion of people in the very old age groups will result in the ‘ageing of the aged’. The challenges presented by the ageing of the population are far reaching. Discussions have tended to focus on its likely health and economic consequences; however, few aspects of society will remain unaffected by the issue.

There is an urgent need for reliable evidence to inform policy to support healthy ageing. The concept of healthy ageing encompasses traditional ideas relating to freedom from disease, as well as broader considerations including independence, quality of life, management of disability, participation in society and the workforce and productivity. A wide range of factors are likely to affect health in later life, including socioeconomic, environmental and cultural variables, cigarette smoking, alcohol consumption, diet, physical activity, reproductive and hormonal factors, infections, availability of healthcare and use of pharmaceutical agents, as well as individuals’ susceptibility to disease. A comprehensive investigation of the determinants of healthy ageing must incorporate assessment of disease risk, quality of life and other indices, in relation to a very wide range of possible exposures, and with consideration of how these exposures might interact with one another. Research needs to be of a sufficient scale to provide specific information on the major diseases and health problems experienced in later life. This is because reliable assessments of risk factor–disease relationships require a substantial degree of pathological homogeneity of outcome and appropriate consideration of confounding. At the same time, research needs to be able to assess the broad risks and benefits of particular exposures, to allow meaningful conclusions to be reached about suitable public health interventions. Finally, it needs to be large and

long term enough to track the impact of health interventions and policies at the population level.

Australia has some unique characteristics that will impact on healthy ageing and provide particular challenges in delivering health care. For example, it has: a relatively heterogeneous population with a large migrant community; an indigenous population with an average life expectancy 17 years less than for non-indigenous Australians; some remote and sparsely populated regions and a mixed health care system with responsibility shared between the national and state governments and delivery in both the public and private sectors. Excellent population-level databases relating to use of health services and medications, and registers of cancers and deaths, are available for statistical linkage with research data sets. There is therefore a need for research that addresses issues specific to the Australian population and makes use of the unique features of the Australian setting, giving the opportunity to provide insights of international relevance.

The 45 and Up Study was conceived as a long-term collaborative resource to investigate healthy ageing, in response to the gaps in existing knowledge and the needs of researchers.

Initial discussions among interested researchers resulted in the formation of a Scientific Steering Group in 2003 to oversee the development of the Study. The Study is auspiced by the Sax Institute, which also provided funding for its development. The Sax Institute is an independent organization with core funding from the state government of New South Wales, Australia’s most populous state. Its mission is to improve health through facilitating high-quality research and increasing the impact of this research on health policy and services; it has membership from public health and health service research centres and universities across New South Wales. Workshops, meetings and consultations with individual researchers were held to identify research priorities for the Study and researchers were invited to become 45 and Up Study Collaborators. There were 120 collaborators at the time of writing (see www.45andUp.org.au for details). The protocol for the Study was completed in late 2003, the Scientific Director was appointed in 2003, the Study materials, methods and governance framework were developed in 2004 and 2005 and recruitment of participants started early in 2006.

Following international peer review of the Study protocol, funding for the Study infrastructure was provided by Foundation Study Partners, The Cancer Council New South

[†] The Writing Committee is listed at the end of the report. For a list of the 45 and Up Study Collaborators please go to www.45andUp.org.au.

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Wales, the New South Wales Division of the National Heart Foundation of Australia and the New South Wales Department of Health. These were later joined by *beyondblue: the national depression initiative*, the New South Wales Department of Ageing, Disability and Home Care, with additional support from the Macquarie Bank Foundation, the Baxter Charitable Foundation, the Alma Hazel Eddy Trust and Freehills solicitors. Competitive funding for a range of research projects has been secured and researchers using Study data for their projects support the Study through contributions to cost recovery and Study sustainability.

What does it cover?

The 45 and Up Study is a large-scale Australian cohort study of individuals aged 45 and over aiming to provide researchers with timely and reliable information on a wide range of exposures and outcomes of public health importance for the ageing population. At the same time as addressing specific research questions, the Study is also designed as a framework for a range of future research activities. Priority areas for the Study are:

- (1) Social and economic determinants of healthy ageing, including income, education, ethnicity, work and retirement, social capital and rurality.
- (2) Health effects of obesity, overweight and physical activity.
- (3) Impact of environmental factors on healthy ageing.
- (4) Risk factors for, and the detection and management of, cancer, cardiovascular disease and mental health problems, including depression.
- (5) Use of health services in relation to ageing, including the determinants of use of residential aged care.
- (6) Health in people aged 80 years and over (the 'old old').

Who is in the sample?

The 45 and Up Study is in the process of recruiting 250 000 men and women aged 45 and over from the general population of the state of New South Wales, Australia (Figure 1). Individuals aged 45 and over and resident in New South Wales are randomly sampled from the Medicare Australia enrolment database. This is the database through which national healthcare is administered and includes all citizens and permanent residents of Australia, as well as some temporary residents and refugees. Eligible individuals are mailed an invitation to take part, an information leaflet, the study questionnaire and consent form and a reply paid envelope (available at www.45andUp.org.au). The data included in the baseline questionnaire are listed in Table 1. Participants join the study by completing the questionnaire and consent form and mailing them to the Study coordinating centre. Completed questionnaires are then scanned electronically and stored as images and data are double-entered.

The study over-samples, by a factor of two, individuals aged 80 years and over and people resident in rural areas; all residents of remote areas are sampled. People may also volunteer to join the study by calling the study helpline and requesting an invitation pack. When complete, the 45 and Up



Figure 1 Location of the 45 and Up Study: New South Wales, Australia

Study will include ~10.9% of the general population in the target age range.

Recruitment into the 45 and Up Study commenced in February 2006; since then 36 645 men and women have joined the study. By the end of 2007, 100 000 participants will have joined the study, with the full 250 000 recruited by the end of 2009. The current overall response rate to the mailed invitations to join the study is estimated to be 17.9% (95% CI 17.8–18.1), however, the exact response rate is difficult to specify as some people may not have received the invitation if their address details were incorrect in the Medicare Australia database. In addition to the 36 162 (98.7%) people joining the Study by invitation, 483 (1.3%) people have joined by contacting the helpline without receiving an invitation to take part.

The demographic characteristics of the first 36 645 members of the cohort are shown in Table 2. Overall, 52% of participants are females. Participants range in age from 45 to 101 years, with a mean age of 64.1 years (SD 11.7) for men and 61.3 years (SD 10.8) for women. They show considerable diversity in terms of location of residence (44% of men and 40% of women are resident in major cities, 54% of men and 57% of women are resident in regional areas and 2% of men and 3% of women are resident in remote areas), ethnicity (21% of all participants were born outside of Australia; 9% speak a language other than English in the home; 0.9% are of Aboriginal and/or Torres Strait Islander origin), level of education (14% of participants report having no educational qualifications; 22% report having a university degree) and income (32% of participants report a gross household income less than 30 000 Australian dollars per year; this is $\leq 60\%$ of the median gross household income in New South Wales²).

Based on self-reported height and weight, 4% of individuals have a body-mass index (BMI) of $<20 \text{ kgm}^{-2}$, 33% have a BMI from 20 to 24.9 kgm^{-2} and 56% have a BMI of 25 kgm^{-2} or over, meaning they are overweight or obese (Table 3). Overall, 8% of participants report they are current smokers and 65% report drinking alcohol at least weekly; 35% of participants report

Table 1 Data collected in the 45 and Up Study baseline questionnaire

Demographic and social characteristics	Personal health behaviours	General health-related data
Date of birth	Smoking	Disease and surgical history
Education	Alcohol	Family history of illness
Income	Physical activity	Medication
Marital status	Fruit and vegetable consumption	Functional capacity
Country of birth and ancestry	Other dietary information	Psychological distress
Retirement and work	Sleep habits	Cancer screening history
Social connectedness		Falls
		Oral health
		Skin pigmentation and response to sunlight
		Reproductive history
		Incontinence
		Prostate symptoms and sexual functioning (in men)

engaging in at least 30 minutes of vigorous physical activity at least weekly and 37% report no weekly vigorous physical activity.

A previous diagnosis of non-melanoma skin cancer was reported by 26% of participants, with a history of melanoma, heart disease and diabetes being reported by 6, 12 and 9% of participants, respectively (Table 4). Prostate cancer was reported by 6% of men and breast cancer by 5% of women. In terms of functional status, 5% of the cohort report needing help with day to day activities and 4% report that they are caring full time for a sick or disabled person.

Further details of the responses to the 45 and Up Study baseline questionnaire are available in the study preliminary data book, at www.saxinstitute.org.au.

What has been measured?

The data that will be collected for the 45 and Up Study include a baseline questionnaire, 5-yearly repeat questionnaires, linkage to routinely collected health data, biological samples and more intensive measures from sub-studies conducted within the cohort.

The baseline questionnaire for the study broadly includes: measures of health status and past medical and surgical history; known risk factors for major causes of morbidity and mortality; likely confounding factors; potential mediators of risk and some novel factors (Table 1). A pilot study conducted in July 2005 established the feasibility of the recruitment methods and allowed the refinement of a number of questions. Repeat questionnaires to all cohort members to update exposure data and health status are planned at 5-yearly intervals.

Questionnaire data from study participants are linked with routinely collected data from a range of population databases and registers. These include information on use of prescription medication, use of general practice services and updated address details, through Medicare Australia, and routine linkage to deaths, cancer registrations and hospitalizations, through the New South Wales Centre for Health Record Linkage (see www.cherel.org.au). Linkage is both retrospective and prospective, with the time period covered dependent on the properties of the specific data set. A range of additional data sets (e.g. use of community-based and residential aged care

services, screening records and transplant details) will become available for specific projects as the study progresses.

A number of more detailed sub-studies are already underway within the framework of the 45 and Up Study cohort, enhancing the information available on selected participants. For example, the first 100 000 participants will receive an additional questionnaire to provide more information on social, environmental and economic factors and health status.

It is planned that biological samples, including blood for genotyping and examination of a range of analytes, will be collected on as many participants as possible as the Study progresses and funding becomes available. Blood samples will be centrifuged and aliquotted, and stored long term in ultra low temperature freezers, with procedures in place for retrieval of samples for specific projects. The protocol for collection of samples is currently being developed and collection is planned to commence in 2008.

Following initial analyses of cross-sectional data, the main means of investigating relationships between exposure and outcome will be through cohort analyses and nested case-control studies. For conditions yielding at least 3500 incident cases or deaths during the first 10 years of follow-up (e.g. diabetes mellitus, myocardial infarction, stroke, colorectal cancer, prostate cancer, breast cancer and hip fracture), the study will be able to detect a minimum relative risk of 1.3 for exposures affecting 10–90% of controls and 1.4 for exposures affecting 5–95% of controls, with 95% power, 1% significance and four controls per case. With the same power, significance and ratio of cases to controls, for outcomes with 1000 or more events (e.g. ischaemic heart and cerebrovascular disease deaths and incident Parkinson's disease, non-Hodgkin's lymphoma and lung cancer) the study should be able to detect minimum relative risks of 1.4–1.5 for exposures affecting 20–80% and 1.6 for exposures affecting 10–90% of the population.

How is the Study optimizing use of the data?

The 45 and Up Study has sought to establish an approach that will make optimal use of the data. Data from the study are accessible to local researchers for approved research projects.

Table 2 Socio-demographic characteristics of the first 36 645 participants joining the 45 and Up Study

	Men N = 17 443 (%)	Women N = 19 202 (%)	Total N = 36 645 (%)
Age (years)			
45–49	12.4	16.0	14.3
50–59	29.9	36.2	33.2
60–69	26.2	25.8	26.0
70–79	18.5	14.9	16.6
80–89	11.9	6.5	9.1
≥90	1.0	0.6	0.8
Missing/invalid	0.0	0.0	0.0
Aboriginal or Torres Strait Islander origin			
Neither Aboriginal nor Torres Strait Islander	97.3	97.1	97.2
Aboriginal only	0.7	0.8	0.7
Torres Strait Islander only	0.1	0.1	0.1
Aboriginal and Torres Strait Islander	0.1	0.0	0.1
Missing/invalid	1.8	2.1	1.9
Language other than English spoken at home			
Yes	9.3	8.2	8.7
No	90.7	91.8	91.3
Missing/invalid	0.0	0.0	0.0
Marital status^a			
Single	7.3	6.4	6.8
Married	75.0	65.4	69.9
In a <i>de facto</i> relationship	5.4	5.1	5.3
Widowed	5.7	13.1	9.6
Divorced	6.2	9.6	8.0
Separated	3.1	3.2	3.1
Highest educational qualification			
No school certificate	12.9	14.5	13.7
School/intermediate certificate	16.2	28.8	22.8
Higher school certificate	10.0	9.8	9.9
Trade/apprenticeship	18.8	4.3	11.2
Certificate/diploma	18.9	21.9	20.5
University degree	23.2	20.6	21.9
Missing/invalid	0.0	0.0	0.0
Household annual pre-tax income^b			
<\$10 000	6.4	7.6	7.1
\$10 000–\$19 999	14.0	14.2	14.1
\$20 000–\$29 999	11.3	9.6	10.4
\$30 000–\$39 999	8.5	7.5	8.0
\$40 000–\$49 999	7.6	6.5	7.0
\$50 000–\$69 999	11.2	9.4	10.2
≥\$70 000	23.1	16.7	19.7
Prefer not to answer	13.7	22.1	18.1
Missing/invalid	4.3	6.4	5.4

^aMultiple responses permitted.^bIn Australian dollars.**Table 3** Lifestyle and social factors in the first 36 645 participants joining the 45 and Up Study

	Men N = 17 443 (%)	Women N = 19 202 (%)	Total N = 36 645 (%)
Tobacco smoking			
Current smoker	8.4	7.5	7.9
Former smoker	44.9	27.6	35.9
Never smoker	46.7	64.9	56.2
Missing/invalid	0.0	0.0	0.0
Alcoholic drinks per week			
0	23.3	40.2	32.2
1–4	18.7	22.7	20.8
5–7	14.5	14.5	14.5
8–14	18.7	14.0	16.3
≥15	22.9	5.9	14.0
Missing/invalid	1.9	2.7	2.3
Moderate or vigorous physical activity (minutes per week)			
None	11.4	10.9	11.2
1–30	6.6	6.2	6.4
30–60	6.6	5.7	6.1
60–90	9.1	9.1	9.1
90–120	5.8	5.7	5.7
≥120	55.7	57.0	56.4
Missing/invalid	4.8	5.3	5.1
Body mass index			
<20	2.3	5.5	4.0
20–22.4	8.3	14.4	11.5
22.5–24.9	20.1	21.3	20.7
25.0–29.9	43.6	30.4	36.7
≥30	20.2	21.8	21.0
Missing/invalid	5.4	6.6	6.0
Current work status^a			
Full time paid work	26.7	18.7	22.5
Part time paid work	6.1	18.6	12.7
Doing unpaid work	4.3	6.9	5.7
Self employed	16.6	9.2	12.7
Partially retired	7.0	4.5	5.7
Completely retired	41.7	37.5	39.5
Studying	0.9	2.0	1.5
Looking after home/family	3.1	18.3	11.1
Disabled/sick	4.9	3.6	4.2
Unemployed	2.3	2.1	2.2
Other	1.0	1.9	1.5
Times per week with family or friends			
None	13.0	8.0	10.4
1–3	48.5	46.1	47.3
4–6	22.9	28.9	26.0
≥7	11.9	13.7	12.8
Missing/invalid	3.8	3.2	3.5

^aMultiple responses permitted.

Table 4 Medical and surgical history and functional capacity of the first 36 645 participants joining the 45 and Up Study

	Men N = 17 443 (%)	Women N = 19 202 (%)	Total N = 36 645 (%)
History of^a			
Skin cancer (excluding melanoma)	29.5	23.2	26.2
Melanoma	6.9	4.2	5.5
Prostate cancer	6.3		
Breast cancer	0.0	5.4	2.8
Other cancer	6.6	6.6	6.6
Heart disease	16.4	8.2	12.1
High blood pressure ^b	35.9	33.0	34.4
Stroke	4.7	2.7	3.7
Diabetes	10.7	7.1	8.8
Thrombosis	3.9	5.8	4.9
Enlarged prostate	16.3		
Asthma or hayfever	14.1	20.9	17.7
Parkinson's disease	1.1	0.7	0.8
Past operations			
Removal of skin cancer	31.4	23.3	27.1
Vasectomy	22.7		
Part of prostate removed	6.6		
Whole of prostate removed	3.7		
Hysterectomy		29.2	
Bilateral oophorectomy		10.4	
Tubal ligation		28.0	
Repair of prolapsed bladder, womb or bowel		12.1	
Knee replacement	4.4	3.4	3.9
Hip replacement	3.8	2.9	3.3
Gallbladder removed	6.3	14.1	10.4
Coronary artery bypass surgery ^c	9.7	2.6	6.0
Current need for assistance			
Need help with daily tasks	5.3	5.3	5.3
Do not need help with daily tasks	94.7	94.7	94.7
Missing/invalid	0.0	0.0	0.0

^aself reported conditions.^bexcluding pregnancy related hypertension.^cincludes grafts, balloons and stents.

First, we have sought to encourage local researchers to use data from the Study by involving a large number of leading researchers, from across a range of institutions, in its management and design from the outset. A policy framework has been established for the Study that addresses issues including use of and access to the data, intellectual property, protecting the privacy and confidentiality of participants and charges for data use. We have convened a Community and Ethical Oversight Committee, which includes community leaders among its members. At the time of writing, 18 applications had been made to the Scientific Advisory Committee for access to Study data for research projects and funding applications. Six projects, spanning cancer risk factors, oral

health, health economics, functional capacity and psychological distress, are underway.

Second, to encourage use of the Study for research that will directly inform the planning and provision of services, we have convened a policy roundtable. This includes representation from major government and non-government agencies and private sector organizations that have responsibility for providing health and aged care services. The roundtable serves to generate ideas and opportunities for new policy-relevant research using the Study. It has been funded by the MBF Foundation (a non-profit charitable institution).

What are the main strengths and weaknesses?

When recruitment is complete, the 45 and Up Study will be the largest population-based cohort study in Australia and, to our knowledge, in the Southern Hemisphere. It is unique among large-scale cohorts internationally, in terms of the scope of its ongoing linkage, even for those participants who are otherwise lost to follow-up, with a large number of routinely collected databases and registers that provide virtually complete capture of use of a wide range of health services, as well as cancer registration and deaths. The combination of large numbers of participants with individual prospective information on exposures and additional linked exposure and follow-up information will provide a valuable resource for the investigation of many different causes of morbidity, mortality and of patterns of use of health and aged care services. The addition of biological samples to the study over time will further increase its usefulness. The study does not at present have the levels of funding required to collect biological samples on participants, so this is being introduced gradually, as funding is secured. A limitation of the study is the lack of large-scale clinical data on measures such as blood pressure, spirometry, anthropometry and cognition; it is intended that many of these will be gathered as part of sub-studies within the cohort.

The study population is relatively heterogeneous, with a good spread of responses across most variables. The oversampling of people 80 years and over (with no upper age limit to participation) and from rural areas will enable a particular focus on these groups. The Study will provide a good basis for the investigation of aetiological research questions, based on internal comparisons within the cohort. Although derived from the general population, the relatively low response rate means that the cohort is unlikely to be directly representative of the general population. Formal comparisons of the cohort with the general population will be conducted in due course. The questionnaire is currently only available in English, limiting the participation of people with insufficient literacy in English. Having said this, it is likely to be one of the most inclusive large-scale cohort studies conducted to date and the results from cohort studies based on internal comparisons remain generalizable even when the cohort is from a selected group.³⁻⁵ Additional strengths of the study include: the accessibility of data to collaborating researchers; its governance structure and community accountability and its partnerships with policy agencies.

Can I get hold of the data? Where can I find out more?

The Study is accessible to local and collaborating researchers for high quality policy-relevant research that is in the public interest. Details of the data access policy and procedures are available at www.saxinstitute.org.au.

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Conflict of interest: None declared.

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Appendix

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