Impact of smoking, diabetes and hypertension on survival time in the elderly: the Dubbo Study

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ABSTRACT

Objective: To study the impact of various risk factors on survival time in a cohort of elderly Australians.

Design, setting and participants: A longitudinal, prospective cohort study conducted in Dubbo, NSW. Participants were men and women aged 60 years or over living in the community, first assessed in 1988–1989 and followed for 15 years.

Main outcome measures: Mortality rates; risk factors; survival times.

Results: There were 668 deaths in 1233 men (54%) and 625 deaths in 1572 women (40%). Coronary heart disease was the major cause of death, rates being higher in men than women until age group 80+ years; stroke death rates were similar in both sexes; cancer and respiratory death rates were higher in men than women across all ages. In a proportional hazards model, the independent predictors of mortality were cigarette smoking, diabetes, very high blood pressure (BP), impaired peak expiratory flow (PEF), physical disability, and zero intake of alcohol. Over 15 years, the average reductions in survival time associated with various risk factors, in men and women respectively, were smoking, 22 and 15 months; diabetes, 18 and 18 months; very high BP, 16 and 9 months; impaired PEF, 14 and 17 months; physical disability, 16 and 12 months; zero alcohol intake, 9 and 5 months. Combinations of selected risk factors were associated with a multiplier effect.

Conclusion: The reduction in survival time in elderly citizens demonstrated in the presence of smoking, diabetes and hypertension highlights a potential benefit to healthy ageing to be gained from prevention and intervention.

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Risk factors for serious disease and mortality in elderly people have been documented in observational studies.[1-6] The individual contributions of cigarette smoking, diabetes and hypertension have been noted in the clinical sphere;[1-3] other factors, such as self-rated health, physical disability, marital status, social support and physical activity, have been noted in the sociodemographic sphere.[4-6]

The longitudinal Dubbo Study of elderly people commenced in 1988 with the broad aim of studying "healthy ageing" in a group of generally healthy senior citizens residing in the community.[7-9] Mortality data for this group are now available for a follow-up period of 15 years. Uniquely, this group was already advanced in age at baseline (mean entry age around 70 years) and represents a substantial proportion of the eligible population in a well defined community over a relatively long period. This report examines the impact of specific risk factors and combinations of risk factors on survival time over the first 15 years of the study.

METHODS

Participants and baseline examinations

The Dubbo Study is an ongoing prospective study of a cohort of elderly people first examined in 1988–1989.[7] All non-institutionalised residents of Dubbo, NSW, born before 1930 were eligible to participate.

Methods and measures have been described in detail elsewhere.[7-9] Briefly, the baseline examinations comprised demographic, psychosocial and standard cardiovascular risk assessments. The medical examination included anthropometry; blood pressure (BP) (mean of two readings, phase V diastolic, after 10 minutes' seated rest); resting electrocardiogram (ECG); peak expiratory flow (PEF) rate (best of two attempts, measured by a Wright peak flow-meter); and 12-hour fasting levels of blood plasma lipids, lipoproteins and glucose. A questionnaire explored measures of social support; depression status; education level; cognitive function; alcohol and tobacco use; medications; medical history; family history of coronary heart disease (CHD), myocardial infarction and chest pain; physical activity; self-rated health; and physical disability. The study population was broadly representative of the Australian population born before 1930 according to sex, age, employment, socioeconomic status, housing tenure, tobacco use, mean BP and other variables. However, a higher proportion of participants (90%) in our study were Australian-born compared with the proportion in the general population (73%).[7]

The definitions of many of the study variables are self-explanatory, but some require elaboration:

- *Prior CHD:* previous myocardial infarction and/or angina reported in the questionnaire and/or ECG changes;
- *Cigarette smoking:* reported as "never", "former" or "current";
- *Diabetes mellitus:* prior history and/or medication for diabetes and/or fasting plasma glucose level ≥ 7.8 mmol/L (a small, indeterminate group of participants had levels between 6.1 and 7.7 mmol/L);
- *PEF:* divided into sex-specific tertiles, tertile I indicating the greatest impairment;
- *Self-rated health:* reported as "very good to excellent", "good", or "fair to poor";

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- *Disability:* divided into three categories, based on a physical activities of daily living (ADL) scale ("no disability", "impairment in one ADL" or "impairment in more than one ADL");
- *Center for Epidemiologic Studies depression score:* divided into tertiles, tertile III indicating the greatest evidence of depression.[10]

Survival analysis

Deaths over 15 years (September 1988 – September 2003) were included in the analysis. Hospitalisation and death records were monitored continuously, with postal surveys conducted every 2 years to confirm vital status.

Records were coded according to the *International classification of diseases, 9th revision, clinical modification* (ICD-9-CM) and the *10th revision, Australian modification* (ICD-10-AM). The independent contribution of any factor to mortality was examined in a Cox proportional-hazards model. Point estimates and 95% CIs for the relative hazard of death were calculated from the regression coefficients and are presented as hazard ratios (HRs), a measure of relative risk. A large number of variables were entered in a single block and a final model was recalculated, retaining only variables of statistical significance ($P < 0.05$) and potential confounders.

Variables were treated as continuous (age and body mass index) or categorical (other variables). For categorical variables, the "nil", lowest or opposite category served as the reference group (eg, "not married", "never smoked", "no disability"). Interactions between age and sex and independent predictors of mortality were also explored in the final model.

The proportional-hazards model assumes constant relative hazard over the length of follow-up. A log-minus-log hazard plot demonstrating parallel curves over all categories for various predictors showed that this assumption was valid.

Survival curves were plotted using the same multivariate model. The difference between areas under respective survival curves gave a measure of the average effect of a given factor on survival at the mean of the covariates. Statistical analysis was conducted using SPSS software.[11]

Ethics approval

Our study was approved by institutional ethics committees at St Vincent's Hospital (Sydney), the University of New South Wales and the University of Western Sydney. All participants gave informed, written consent.

1 Sex- and age-specific mortality rates due to various causes over the first 15 years of the Dubbo Study

	Rate/100 (number of deaths)			
	60–69 years	70–79 years	80+ years	Rate/100 (age-standardised)*
Men	(*n* = 736)	(*n* = 410)	(*n* = 87)	
All causes	39 (285)	73 (301)	94 (82)	53
CHD	13 (93)	25 (103)	20 (17)	17
Stroke	3 (19)	7 (29)	11 (10)	5
Other CVD	3 (20)	4 (15)	10 (9)	4
Cancer	11 (80)	15 (63)	18 (16)	13
Respiratory disease	3 (21)	9 (36)	14 (12)	6
Other	7 (52)	13 (55)	21 (18)	10
Women	(*n* = 849)	(*n* = 549)	(*n* = 174)	
All causes	23 (194)	51 (277)	89 (154)	40
CHD	7 (61)	19 (104)	32 (56)	14
Stroke	2 (14)	5 (26)	13 (23)	4
Other CVD	2 (15)	6 (33)	10 (18)	4
Cancer	5 (44)	8 (42)	9 (15)	7
Respiratory disease	2 (18)	5 (29)	9 (16)	4
Other	5 (42)	8 (43)	15 (26)	7

* Based on new world standard population, calculated by direct method.[12] CHD = coronary heart disease; CVD = cardiovascular disease.

RESULTS

Of the population of elderly people eligible to join the study, 73% (1233 men and 1572 women) participated. Only 3% of subjects were lost to follow-up at the most recent postal survey.

Over the 15 years, there were 668 (54%) deaths in men and 625 (40%) deaths in women. Mortality rates, by age, sex and major cause, are summarised in Box 1. Total mortality rates and death rates from cancer and respiratory disease were higher in men than women across all age groups. CHD death rates were higher in men than women until the 80-plus age group, while stroke death rates were similar for both sexes.

The initial Cox model included many biological and psychosocial variables that did not approach statistical significance. They included prior stroke history, lipid and lipoprotein levels, urinary incontinence, education level, home ownership, depression score, social support, social activities, physical activity, and pet ownership.

Key baseline variables and the final Cox proportional hazards model for prediction of time to death are presented in Box 2. Variables showing the strongest independent contribution to mortality in both sexes were current cigarette smoking, diabetes, impaired PEF, physical disability, use of BP medication, and having very high blood pressure. Prior CHD was predictive of death in men, as was a poor self-rating of health in women. Several variables independently predicted a lower risk of mortality: alcohol intake (both sexes) and being married at study entry (men only). The interaction of significant predictors with age was significant only for male smokers (HR 2.19 [95% CI, 1.63–2.93] for age 60–74 years versus 1.08 [95% CI, 0.66–1.78] for age 75+ years) ($P < 0.002$).

The reduction in survival time over 15 years' follow-up was derived from survival curves in the Cox models and is presented in Box 3. Compared with those who had never smoked, 22 months of life were lost in male smokers and 15 months in female smokers. Men and women with diabetes both lost 18 months of life. There was substantial shortening of survival in both sexes associated with other factors such as hypertension, impaired PEF, physical disability and zero alcohol intake. Men (but not women) with prior CHD or who were not

2 Key descriptive data at study entry, and Cox-model hazard ratios for all-cause mortality over a 15-year period*

	Study entry data†		Hazard ratio (95% CI)	
	Men (*n* = 1233)	Women (*n* = 1572)	Men	Women
Age (years)	Mean, 68.6 (SD, 6.7)	Mean, 69.6 (SD, 7.3)	1.09 (1.07–1.10)	1.09 (1.08–1.11)
Married	79%	50%	0.75 (0.63–0.91)	0.75 (0.56–1.01)
Body mass index (kg/m^2)	26.2 (SD, 3.7)	25.9 (SD, 4.6)	1.00 (0.97–1.02)	0.98 (0.96–0.99)
Smoker:				
Former	48%	17%	1.34 (1.10–1.63)	1.25 (1.01–1.56)
Current	20%	11%	1.84 (1.44–2.35)	1.63 (1.24–2.15)
Alcohol intake (standard drinks):				
1–7/week	35%	37%	0.75 (0.61–0.92)	0.84 (0.70–1.00)
8–14/week	22%	13%	0.77 (0.61–0.97)	0.63 (0.47–0.85)
14–28/week	13%	3%	0.69 (0.52–0.91)	0.88 (0.51–1.53)
> 28/week	8%		0.75 (0.53–1.05)	No data
Taking BP medication	43%	52%	1.54 (1.30–1.82)	1.47 (1.22–1.77)
BP (systolic, diastolic):				
140–159 or 90–94	30%	31%	1.11 (0.91–1.35)	0.93 (0.75–1.15)
160–199 or 95–99	23%	24%	1.14 (0.93–1.40)	1.02 (0.81–1.27)
⩾200 or ⩾100	8%	7%	1.58 (1.18–2.12)	1.48 (1.10–2.00)
Diabetes mellitus	11%	8%	1.61 (1.28–2.03)	1.94 (1.49–2.53)
PEF (L/min):‡				
Tertile I	< 396	< 306	1.52 (1.23–1.89)	2.05 (1.60–2.64)
Tertile II	396–504	306–375	1.44 (1.17–1.79)	1.43 (1.11–1.85)
Prior CHD	25%	19%	1.36 (1.14–1.63)	1.02 (0.82–1.27)
Disability:				
Impairment in 1 ADL	25%	31%	1.29 (1.06–1.57)	1.31 (1.05–1.64)
Impairment in > 1 ADL	20%	25%	1.54 (1.26–1.89)	1.59 (1.25–2.03)
Self-rated health:				
Good	34%	31%	0.95 (0.77–1.16)	1.13 (0.92–1.38)
Fair–poor	22%	21%	1.05 (0.81–1.35)	1.29 (1.03–1.62)

ADL = activity of daily living. BP = blood pressure. CHD = coronary heart disease. PEF = peak expiratory flow. * Age and body mass index were entered as continuous variables, the remainder as categorical variables, with the "nil", lowest or opposite category as the reference value (eg, not married, never smoked, zero alcohol, no disability, excellent self-rated health, etc). † Expressed as proportion of participants, unless otherwise indicated. ‡ PEF tertile III (having cutoff point > 504 L/min in men and > 375 L/min in women) was the reference value for this variable.

married at study entry also experienced a reduction in survival.

When factors such as smoking and taking any alcohol were combined, the adverse impact on survival was somewhat lessened, in line with the opposite effects of smoking and alcohol on survival. The reduction in survival was exacerbated in people who smoked while having impaired respiratory function, in those with diabetes who were also taking BP medication, and in those having physical disability combined with impaired respiratory function.

DISCUSSION

The predominant cause of death in elderly Australian men and women is CHD, with lesser but important contributions from cancer, stroke and chronic respiratory disease. Our multivariate model identified key predictors of mortality based on data collected 15 years earlier. The unique feature of our study is its assessment of the impact of specific risk factors and combinations of risk factors on survival time over 15 years of follow-up in a group with a mean entry age of about 70 years. The burden of disease attributable to risk factors has been the subject of other Australian research;[13] however, these studies have been based on a cross-section of the population, and, for this and other reasons, direct comparisons with our study are not feasible.

The Dubbo Study has certain limitations. Although it involves a well defined population, to gain entry to the study Dubbo senior citizens needed to be non-institutionalised and able to attend baseline assessment. Most of the 27% of the target population who did not participate stated that they were "too old, too tired or too unwell".[7] In other words, we are studying the ageing process in a group of healthier "survivors" who have been willing and able to participate. On the other hand, we have succeeded in maintaining contact with 97% of the cohort.

Moreover, baseline observations were made at a single visit in 1988–89 and the Cox model assumes that the broad characteristics of the group will remain relatively unchanged over the time interval (eg, that people with diabetes will always behave as diabetics, or that those with an impairment in ADL will continue to be disabled). Although no treatments were offered by the study, interventions may have been offered by local medical officers or others. A variable such as marital status is quite likely to change over 15 years, so we are effectively measuring the effect of marital status *before* study entry. Furthermore, some of the associations found (or not found) between potential risk factors and mortality may have arisen through confounding by factors measured or unmeasured. Finally, some of the baseline data are based on self-reported behaviour and this may have introduced bias. Many of these variables have well-studied measurement effects.[4-6]

The demonstrated impact of smoking, diabetes, hypertension, impaired respiratory function and zero alcohol intake on mortality confirms the findings of previous studies.[1-3,14-17] But the duration of follow-up is a key factor. In an earlier report on the Dubbo Study, at 10 years' follow-up we calculated that any alcohol intake improved survival time by 8 months in men and 3 months in women.[18] By 15 years, this had extended to 9 and 5 months, respectively. While we have confirmed that this finding is robust, there must be a point at which alcohol or other factors no longer impinge on survival! In our study, alcohol has been shown to have a protective effect on mortality across all apparent levels of consumption, in contrast to the "U"-shaped relationship described by

3 Reduction in survival time (months) associated with various factors (recorded at study entry) over 15 years' follow-up*

	Men	Women
Single variables		
Not married	11	ns
Current smoker	22	15
Former smoker	10	5
Diabetes	18	18
Taking BP medication	16	8
BP 200 mmHg (systolic) or 100 mmHg (diastolic)	16	9
Zero alcohol intake	9	5
PEF tertile I	14	17
Prior CHD	12	ns
Impairment in > 1 ADL	16	12
Combined variables		
Current smoker and taking any alcohol	13	12
Current smoker and PEF tertile I	32	25
Diabetes and taking BP medication	25	20
PEF tertile I and impairment in > 1 ADL	19	26

ADL = activity of daily living. BP = blood pressure. CHD = coronary heart disease. ns = no significant difference in survival. PEF = peak expiratory flow. * Single variables were run in the same model as in Box 2, except that alcohol intake was converted to zero versus "any". Each category was compared with its "opposite" option (eg, non-smoker, no diabetes, any alcohol). Each combined category was run in a separate model containing all the single variables but excluding the main effects. The combined category was compared with the combined opposite or nil-disease option (eg, non-smoker and zero alcohol intake). Change in survival time was derived by subtracting areas under the respective survival curves in the Cox model.

others.[19] This contrast can not readily be explained, except to note that a "U"-shaped relationship has not been a general finding in the elderly, possibly because these cohorts contain an excess of "healthy survivors" who do not maintain very high intakes of alcohol.[17]

The lack of association between some potential risk factors and mortality deserves comment. Lipid and lipoprotein levels at baseline certainly predict heart attack in the Dubbo cohort,[20] yet many other factors contribute to CHD in old age and only about a third of deaths relate to CHD. Prior stroke at baseline failed to predict mortality; however, people with prior stroke comprised only 6% of the cohort, and they were clearly mild cases still living in the community. It is intriguing that prior CHD (found in 25% of men and 19% of women) showed significant prediction of mortality only in men. Most likely, this is not a real biological difference, but may be related to the heterogeneous criteria used to define prior CHD.

The Dubbo Study is an observational study. Where a risk factor for mortality has been identified, we can only hypothesise that intervention may be beneficial. Studies in Seventh-Day Adventists have shown that a lifestyle making appropriate choices in diet, exercise and cigarette smoking does indeed add years to life expectancy.[21] Other observational studies have confirmed this potential benefit.[22-24] Controlled intervention studies in hypertension[25] and diabetes[26,27] do suggest that a benefit can be realised. In our study, the reduction in survival among elderly Australians in the presence of cigarette smoking, diabetes and hypertension highlights the potential benefit from intervention. This may be capable of improving survival and hopefully improving quality of life, but further work is needed to assess this potential.

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