AGE (2014) 36:9732
DOI 10.1007/s11357-014-9732-2

Multiple, but not traditional risk factors predict mortality in older people: the concord health and ageing in men project

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Received: 30 August 2014 / Accepted: 5 November 2014 / Published online: 18 November 2014

Abstract This study aims to identify the common risk factors for mortality in community-dwelling older men. A prospective population-based study was conducted with a median of 6.7 years of follow-up. Participants included 1705 men aged ≥70 years at baseline (2005–2007) living in the community in Sydney, Australia. Demographic information, lifestyle factors, health status, self-reported history of diseases, physical performance measures, blood pressure, height and weight, disability (activities of daily living (ADL) and instrumental ADLs, instrumental ADLs (IADLs)), cognitive status, depressive symptoms and blood analyte measures were considered. Cox regression analyses were conducted to model predictors of mortality. During follow-up, 461 men (27 %) died. Using Cox proportional hazards model, significant predictors of mortality included in the final model ($p<0.05$) were older age, body mass index<20 kg m^2, high white cell count, anaemia, low albumin, current smoking, history of cancer, history of myocardial infarction, history of congestive heart failure, depressive symptoms and ADL and IADL disability and impaired chair stands. We found that overweight and obesity and/or being a lifelong non-drinker of alcohol were protective against mortality. Compared to men with less than or equal to one risk factor, the hazard ratio in men with three risk factors was 2.5; with four risk factors, it was 4.0; with five risk factors, it was 4.9; and for six or more risk factors, it

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was 11.4, respectively. We have identified common risk factors that predict mortality that may be useful in making clinical decisions among older people living in the community. Our findings suggest that, in primary care, screening and management of multiple risk factors are important to consider for extending survival, rather than simply considering individual risk factors in isolation. Some of the "traditional" risk factors for mortality in a younger population, including high blood pressure, hypercholesterolaemia, overweight and obesity and diabetes, were not independent predictors of mortality in this population of older men.

Keywords Mortality · Sociodemographic · Economic and lifestyle factors · Health conditions · Physical function · Disability

Introduction

Older community-dwelling people frequently have multimorbidities and varying functional abilities (Tinetti et al. 2012; Reuben 2009). It is very unlikely that any individual health or functional condition will be the sole predictor of mortality (Lubitz et al. 2003). It is therefore useful to determine which factors are the most important predictors of mortality.

There have been many studies of individual biomarkers as predictors of mortality in older people (Seeman et al. 2004; Crimmins et al. 2008). A number of prognostic indices for older adults living in the community have also been developed (Yourman et al. 2012); however, these indices are all based on subjects' responses to questionnaires and use of administrative datasets but do not include the wider range of information that can be easily collected in a clinical setting.

There are some studies, although limited, that have evaluated a comprehensive range of potential predictors of mortality in a sample of older people living in the community. The Cardiovascular Health Study (CHS) (Fried et al. 1998) included many detailed clinical measures that are not routinely measured in primary care practice. The Rotterdam study (Newson et al. 2010) examined variables predictive of survival to age 85 years, but did not include physical activity, detailed functional and a range of biochemical measures, or validated their predictive models. The aims of our study were to assess a comprehensive range of demographic and lifestyle variables, health and morbidity indicators and physiological markers as potential predictors of mortality in the large population-based sample of men aged 70 and over who participated in the Concord Health and Ageing in Men Project (CHAMP) study in Australia. We have examined a comprehensive set of potential predictors that can be easily measured in primary care practice, in order to identify the most common risk factors for mortality in community-dwelling older men.

Methods

Population

CHAMP is an epidemiological study of a wide range of health issues in Australian men aged 70 years and over (Cumming et al. 2008). Men were a particular focus of the CHAMP study as to date epidemiological studies of ageing have tended to focus on women. The selection of study subjects has been described in detail elsewhere (Cumming et al. 2008). Briefly, CHAMP involves men living in a defined urban geographical region (the Local Government Areas of Burwood, Canada Bay and Strathfield) near Concord Hospital in Sydney, Australia. The sampling frame was the New South Wales Electoral Roll, on which registration is compulsory in Australia. The only exclusion criterion was living in a residential aged care facility. Eligible men were sent a letter describing the study and, if they had a listed telephone number, were telephoned about 1 week later. Of the 2815 eligible men with whom contact was made, 1511 participated in the study (54 %). An additional 194 eligible men living in the study area heard about the study from friends or the local media and were recruited before receiving a letter, yielding a total cohort of 1705 subjects.

Data collection

Baseline data were collected between January 2005 and June 2007. Men completed a questionnaire at home before coming to the study clinic at Concord Hospital. The clinic visit consisted of physical performance measures, biological measures, medication inventory and neuropsychological testing. Data were collected by fully trained staff, and the same equipment was used for all measurements and assessments, which were carried out in a single clinic.

Measurements

Mortality

All men were phoned at four monthly intervals from the baseline clinic assessment, which enabled regular updating of survival data. Men who were not contactable by phone were sent letters at four monthly intervals. If men withdrew from the study but agreed to passive follow-up, the New South Wales Registry of Births, Deaths and Marriages was contacted to ascertain death status. Mortality follow-up ended on the date of death, date of withdrawal or 13 June 2013. Follow-up until the date of analysis was for a median of 6.7 years (range, 4.0 days–8.2 years) during which time there were 461 deaths and 61 men lost to follow-up.

Sociodemographic and economic measures

Sociodemographic variables included age and living arrangements (lives alone vs lives with others). Men were asked their country of birth, which enabled grouping into the categories of Australian-born, overseas-born from an English-speaking country and overseas-born from a non-English-speaking country. Income was categorised as reliant on a government pension only vs other sources of income.

Lifestyle factors

Smoking status (never smoker, ex-smoker and current smoker) was assessed. Participants were categorised into current non-drinkers, lifelong abstainers and ex-drinkers. For those who consumed at least 12 drinks in the past year, the frequency and quantity of alcohol consumption was assessed, enabling categorisation of drinkers as either safe drinkers (1–21 drinks per week) or harmful drinkers (>21 drinks per week) (Australian Institute of Health and Welfare (AIHW) 2011). Physical activity was measured using the Physical Activity Scale for the Elderly (PASE), a method that scores the level of physical activity in individuals aged 65 years or older (Washburn et al. 1993).

Anthropometric measurements

Height and weight were measured and body mass index (BMI) was calculated as kilogram per square metre and categorised as underweight (<20), normal weight (20–24.9), overweight (25.0–29.9) and obese (30.0 or over).

Blood pressure measurement

Blood pressure was measured by trained staff according to a standardised protocol using a sphygmomanometer. The mean of the two readings, taken on the right arm, with the participant in a standing and lying position were used in the analysis. The levels of blood pressure used to define hypertension were systolic blood pressure ≥140 mm Hg and diastolic ≥90 mm Hg (Heart Foundation of Australia (National Blood Pressure and Vascular Disease Advisory Committee) 2014). Men were also classified as hypertensive if they self-reported hypertension.

Health status

Data on medical conditions were obtained from the self-reported questionnaires in which participants reported whether a doctor or a health care provider had told them that they had any of the following diseases: diabetes, thyroid dysfunction, osteoporosis, Paget's disease, stroke, Parkinson's disease, epilepsy, hypertension, heart attack, angina, congestive heart failure, intermittent claudication, chronic obstructive lung disease, liver disease, cancer (excluding non-melanoma skin cancers), osteoarthritis and gout. For the purposes of this study, high comorbid burden was defined as the presence of four or more of these conditions. Data on self-rated general health were obtained and dichotomised into excellent/good versus fair/poor/very poor. Depressive symptoms were evaluated by the Geriatric Depression Scale (GDS), short form (Shiekh and Yesavage 1986). A total of five or more depressive symptoms were considered as indicative of possible depression. Participants also reported whether they had fallen in the past 12 months and were dichotomised into 0 or ≥1 falls.

All participants were screened for cognitive impairment using the Mini-mental State Examination (MMSE) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Folstein et al. 1975; Jorm 1994). Men who scored 26 or below on the Mini-mental State Examination or 3.6 or higher on the IQCODE were invited to have a detailed clinical assessment by a geriatrician. Using all the available information, a consensus meeting attended by two geriatricians, a neurologist and a neuropsychologist categorised

participants as having no cognitive impairment, mild cognitive impairment or dementia.

Frailty was defined as described previously in detail (Hirani et al. 2013) according to the frailty criteria used in the CHS (Fried et al. 2001). Subjects were considered frail if they had three or more of the following frailty components: weight loss, weakness/reduced muscular strength, slow walking speed, exhaustion and low activity level. All of the frailty components were objectively measured, except exhaustion, which was self-reported by participants in responses to a question from the Medical Outcomes Survey Short Form (SF12) (Ware et al. 1996).

Medications assessment

All participants brought prescription and non-prescription medications that they had used daily or almost daily to their baseline clinic appointment. Polypharmacy was defined as the use of five or more regular prescription medicines (Gnjidic et al. 2012).

Physical performance measures and disability

Muscle strength was assessed by hand grip strength using a Jamar dynamometer (Promedics, Blackburn, UK). Grip strength (kg) of the dominant hand (best of two trials) was used. Scores were dichotomised into two groups: the first quartile (the best hand grip scores), and the second category included the second to fourth quartile. Dynamic balance was assessed with a coordinated stability task (Lord et al. 2005). Scores were dichotomised at the highest (worst) quartile. Walking speed was measured in the clinic assessment on a 6-m course at usual pace (Fried et al. 2001; Orwoll et al. 2005). The mean value of two trials, adjusted for height, was used, and the speeds dichotomised into slow (based on the lowest quintile for walking speed in the CHS (Fried et al. 2001)) and normal/fast. Chair stands test-time to successfully complete five chair stands was assessed and time dichotomised at the slowest quartile. Participants who did not complete the tests due to physical inability were included in the worst quartile for the corresponding performance measure.

Physical disability was defined as needing help with one or more activities on the modified Katz activities of daily living (ADL) scale (Katz et al. 1970). Disability in instrumental ADLs (IADLs) was defined as needing help with one or more activities included in the OARS IADL scale (Fillenbaum and Smyer 1981).

Blood tests

All blood tests were performed at the Diagnostic Pathology Unit of Concord RG Hospital, which is a National Australian Testing Authority (NATA) accredited pathology service, using a MODULAR Analytics system (Roche Diagnostics, Castle Hill, Australia). Fasting blood samples for cholesterol and high-density lipoprotein (HDL) cholesterol analysis were performed on a Roche Cobas 8000 analyser using a standard automated enzymatic methodology. Fasting blood samples for glucose were taken into fluoride-oxalate (anticoagulant) tubes. Plasma glucose was measured using the Hexokinase method. For administrative reasons, unrelated to subject characteristics, there was a substantial amount of missing data for blood glucose (n=306).

Serum creatinine levels were used to estimate glomerular filtration rate (eGFR), using the following Modification of Diet in Renal Disease (MDRD) formulae for men (Levey et al. 2005): $eGFR = 175 \times (\text{Serum creatinine}/88.4)^{-1.154} \times \text{age}^{-0.203}$. eGFR was categorised into 90 mL/min/1.73 m^2 or more, 60–90 mL/min/1.73 m^2, 30–59 mL/min/1.73 m^2 and <30 mL/min/1.73 m^2 (Green and Ryan 2009). Alanine transaminase levels were categorised into lowest quartile 5–14.9 U/L, second quartile 15–17.9 U/L, third quartile 18–21.9 U/L and highest quartile ≥22 U/L (the referent category). Serum albumin was dichotomised into <40 g/L (1 SD below the mean), the reference category as ≥40 g/L. This cut-off has been used to define hypoalbuminemia in other studies (Takata et al. 2010; Sahyoun et al. 1996). Haemoglobin and white blood cell count (WBC) analysis was carried out at Concord RG Hospital. Haemoglobin was measured by absorption spectrophotometry and WBC by laser flow cytometry. The World Health Organization (WHO) criteria were used for haemoglobin levels (<13 g/dL) to define anaemia among older men (World Health Organization 1968; Isaks et al. 1999; Patel et al. 2009). In this study, WBC of 4–10,000 cells/μL was categorised as normal; <4000 cells/μL as low; and ≥10,000 cells/μL as high (Cheng et al. 2004).

Statistical analyses

Analysis was carried out using STATA v12 (Stata Corp., College Station, TX, USA). Descriptive characteristics

were expressed as means (SD) and percentages. Differences in characteristics among participants in the total sample, survivors and deceased were compared using the two-sided *t* test or chi-squared test. Cox proportional hazards model was used to predict time until mortality. Univariate Cox regressions were conducted to determine the unadjusted hazard ratios (HRs) for mortality with each of the study measures. We then repeated the Cox regression analysis with these variables, adjusting by age. Variables that had a $p<0.1$ in univariate analyses were then included in a Cox proportional hazards model. Backward stepwise elimination was used to eliminate non-significant variables to derive a final multivariate model. In the final model, the proportional hazards assumption was assessed through use of a time-dependent covariate and analysis of Schoenfeld residuals for each variable. In addition, subgroup analysis was conducted by age group (<80 years and aged over 80 years) to determine whether risk factors varied by age group. The mortality model was validated using the bootstrap method. The bootstrap is based on random resampling, with replacement, for 1000 iterations from the original sample to generate resamples of the data, which can be used as a basis for approximating the sampling distribution of model parameter estimates (Efron and Tibshirani 1993). The goodness of fit or discriminatory value of the multivariate model was assessed using the C statistic (Harrell 2001). We performed further post hoc analysis to investigate the relationship between the presence of multiple risk factors and mortality, which was based on final model of significant risk factors.

Ethics approval and informed consent

All participants gave written informed consent. The study was approved by the Sydney South West Area Health Service Human Research Ethics Committee, Concord Repatriation General Hospital, Sydney, Australia.

Results

Characteristics of participants

Table 1 shows the baseline characteristics of the men in the study. The mean age of the study population was 77 (range, 70–97) years). There were 461 deaths during the median follow-up period of 6.7 years (range, 4.0 days to 8.2 years) from January 2006 to June 2013. There were significant differences in most baseline measures between the men who died during follow-up and those who survived, apart from hypertension, diabetes (or fasting blood glucose level ≥7.0 mmol/L), cholesterol and HDL cholesterol (Table 1).

Univariate and age-adjusted analyses

A large number of factors were associated with increased mortality in univariate Cox regression models. Factors that were associated with a lower mortality rate were country of birth (non-English-speaking country) and high BMI (25–29.9 and ≥30 kg/m^2) (Table 2).

After adjustment for age, living alone, country of birth (non-English-speaking country) and reported history of stroke were no longer significant predictors of mortality, although the magnitude of hazard ratios declined in most cases, except for self-rated health and current smoking status, where the hazard ratios increased.

Multivariate analysis

The final multivariate model is shown in Table 3. Variables retained in the final model that increased risk of mortality were low BMI (kg/m^2), high white cell count, anaemia, low albumin, current smoking, history of cancer, history of MI, history of congestive heart failure, depressive symptoms, impaired chair stands, IADL and ADL disability. Overweight and obesity (20–29.9 and ≥30 kg/m^2) remained protective against mortality, and being a lifelong non-drinker of alcohol became significantly protective against mortality. The C statistic for the final model was 0.80, suggesting that the risk factors included in the model are very good predictors of mortality (Efron and Tibshirani 1993). The internal validation of the final model was estimated by the bootstrap procedure that showed a comparable C statistic of 0.79 with similar beta coefficients and standard errors to the original final model (Table 3).

Subgroup analysis by age group (<80 and ≥80 years) revealed only one difference. Underweight men (BMI< 20 kg/m^2) aged 80 years and above had a significantly increased risk of mortality (adjusted HR, 3.45 (95 % CI: 1.81, 6.56)) but underweight men aged below 80 years did not (adjusted HR, 1.06 (95 % CI: 0.32, 3.46 (data not shown).

Table 1 Characteristics of the study population according to survival status: demographic and lifestyle factors, health conditions, physical function and disability: the CHAMP study

Deaths up to 13 June 2013	Baseline characteristics (n=1705)	Survivors (n=1244) (% (n))	Deceased (n=461) (% (n))	p value
Socio-demographic and economic factors				
Mean age (SD)	77 (5.5)	76 (4.7)	80 (6.1)	<0.0001
Income	1683	1231	452	
Pension only	45.9 (773)	42.6 (524)	55.1 (249)	<0.0001
Living	1691	1373	318	
Lives alone	18.8 (318)	16.9 (208)	24.1 (110)	0.004
Country of birth	1705	1244	461	
Australian born	49.8 (849)	47.2 (587)	56.8 (262)	
Immigrant born in an English-speaking country	6.2 (105)	6.0 (74)	6.7(31)	
Immigrant born in a non-English-speaking country	44.1 (751)	46.9 (583)	36.4 (168)	0.004
Health risk factors				
Cigarette smoking status	1689	1233	453	
Never smoked	37.3 (629)	38.3 (472)	34.7 (157)	
Ex-smoker	56.7 (956)	56.4 (695)	57.6 (261)	
Current smoker	6.0 (101)	5.4 (66)	7.7 (35)	0.15
Physical activity (PASE score)	1686	1230	456	
Low (PASE<80)	25.1 (423)	19.9 (245)	39.0 (178)	<0.0001
BMI	1677	1229	448	
20–24.9 kg/m^2	22.5 (377)	20.1 (247)	29.0 (130)	
25–29.9 kg/m^2	48.6 (815)	49.7 (611)	45.5 (204)	
30 and over kg/m^2	27.3 (458)	29.2 (359)	22.1 (99)	
<20 kg/m^2	1.6 (27)	1.0 (12)	3.4 (15)	<0.0001
Alcohol consumption	1675	1222	453	
Safe drinker (1–21 drinks per week)	61.6 (1031)	62.6 (765)	58.7 (266)	
Harmful drinker (>21 drinks per week)	14.8 (247)	15.2 (186)	13.5 (61)	
Ex-drinker	14.9 (250)	12.7 (155)	21.0 (95)	
Lifelong non-drinker	8.8 (147)	9.5 (116)	6.8 (31)	<0.0001
Health conditions				
Self- rated general health	1682	1228	454	
Fair/poor/very poor	30.1 (506)	26.7 (328)	39.2 (178)	<0.0001
Doctor diagnosed conditions	1688	1232	456	
>4 conditions	26.1 (441)	21.8 (269)	37.7 (172)	<0.0001
Systolic blood pressure	1681	1233	448	
≥140 mm Hg	68.6 (1153)	69.8 (860)	65.4 (193)	0.09
Diastolic blood pressure	1681	1233	448	
≥90 mm Hg	16.6 (279)	16.2 (200)	17.6 (79)	0.50
Hypertension	1672	1220	452	
Yes	46.7 (780)	48.0 (586)	42.9 (194)	0.07
Diabetic	1689	1233	456	
Yes	18.2 (308)	17.5 (216)	20.2 (92)	0.22
Fasted blood glucose measurement ≥7.0 mmol/L	1336	970	366	
Yes	9.1(122)	9.7(94)	7.7(28)	0.25
Estimated glomerular filtration rate (eGFR)	1673	1234	439	

Table 1 (continued)

Deaths up to 13 June 2013	Baseline characteristics (n=1705)	Survivors (n=1244) (% (n))	Deceased (n=461) (% (n))	p value
GFR >90/min/1.73 m^2: normal kidney function	16.0 (268)	16.5 (203)	14.8 (65)	
GFR 60–90/min/1.73 m^2: stage 1–2 CKD	57.3 (959)	61.4 (757)	46.0 (202)	
GFR 30–59/min/1.73 m^2: stage 3 CKD	25.2 (422)	21.7 (268)	35.1 (154)	
GFR<30/min/1.73 m^2: stage 4–5 CKD	1.4 (24)	0.5 (6)	4.1 (18)	<0.0001
Myocardial infarction	1665	1217	448	
Yes	18.7 (311)	15.6 (190)	27.0 (190)	<0.0001
Angina	1661	1214	447	
Yes	17.6 (293)	15.7 (191)	22.8 (102)	0.001
Congestive heart failure(CHF)	1670	1220	450	
Yes	5.1 (85)	3.4 (42)	9.6 (43)	<0.0001
Stroke	1683	1229	454	
Yes	8.5 (143)	7.4 (91)	11.5 (52)	<0.0001
Cancer	1682	1228	454	
Yes	21.5 (361)	17.7 (217)	31.7 (144)	0.001
Depressive symptoms	1681	1228	454	
Yes	14.6 (246)	10.5 (129)	25.7 (117)	<0.0001
Cognitive status	1541	1133	408	
Normal	86.2 (1328)	89.1 (1009)	78.2 (319)	
Mild cognitive impairment	7.8 (120)	7.3 (83)	9.1 (37)	
Dementia	6.0 (93)	3.6 (41)	12.8 (52)	<0.0001
Physical function and performance				
Frail	1670	1225	445	
Yes	9.5 (158)	4.3 (53)	23.6 (105)	<0.0001
ADL disability	1702	1242	460	
Present	8.3 (141)	4.3 (53)	19.1 (88)	<0.0001
IADL disability	1676	1223	453	
Present	41.6 (697)	33.6 (411)	63.1 (286)	<0.0001
Dynamic balance	1645	1210	435	
Poor/not completed	29.1 (478)	24.1 (291)	43.0 (187)	<0.0001
Grip strength	1696	1239	457	
Poor/not completed	28.7 (486)	22.7 (281)	44.9 (205)	<0.0001
Walking speed	1668	1227	441	
Slow/not completed	14.5 (242)	8.8 (108)	30.4 (134)	<0.0001
Chair stands	1671	1228	443	
Lowest quartile and unable	27.7 (462)	20.6 (253)	47.2 (209)	<0.0001
History of falls	1683	1230	453	
Present	19.1 (322)	14.7 (181)	31.1 (141)	<0.0001
Medications				
Polypharmacy	1696	1240	456	
≥5 medications	37.7 (639)	32.5 (403)	51.8 (236)	<0.0001
Blood measures				
Cholesterol[b]	1673	1228	445	
≥5.2 mmol/L	17.3 (289)	18.4 (226)	14.6 (63)	0.05
HDL cholesterol[a]	1673	1228	445	

Table 1 (continued)

Deaths up to 13 June 2013	Baseline characteristics (n=1705)	Survivors (n=1244) (% (n))	Deceased (n=461) (% (n))	p value
<1.0 mmol/L	92.5 (1548)	92.2 (1132)	93.5 (416)	0.37
White cell count	1668	1226	442	
<4000 cells/μL	3.7 (62)	3.7 (45)	3.9 (17)	
4–10,000 cells/μL	92.6 (1544)	93.7 (1149)	89.4 (395)	
≥10,000 cells/μL	3.7 (62)	2.6 (32)	6.8 (30)	<0.0001
Haemoglobin(Hb)[b]	1666	1230	456	
Anaemia: <13.0 g/L	14.6 (243)	9.6 (118)	28.7 (125)	<0.0001
Alanine transaminase (ALT) (U/L)	1665	1223	442	
Highest quartile (≥22 U/L)	25.2 (419)	26.6 (325)	21.3 (94)	0.03
Second quartile (18–21.9 U/L)	25.2 (425)	28.3 (346)	17.9 (79)	<0.0001
Third quartile (15–17.9 U/L)	24.9 (415)	25.3 (309)	24.0 (106)	0.09
Lowest quartile (5–14.9 U/L)	24.6 (406)	19.9 (243)	36.8 (163)	<0.0001
Albumin	1673	1228	445	
<40 g/L	8.8 (147)	5.5 (67)	18.0 (80)	<0.0001

ADL activities of daily living, *IADL* instrumental activities of daily living

[a] Raised total cholesterol was defined as ≥5.5 mmol/l; low HDL cholesterol was defined as ≤1.0 mmol/l

[b] Anaemia; World Health Organisation criteria for anaemia: haemoglobin <13.0 g/dL for men

Table 4 shows the relationship between the presence of multiple risk factors and mortality. Around 10% of men had zero or one risk factor, and 17.6 % had at six or more risk factors. Compared to men with zero or one risk factor, the HR in men with three risk factors was 2.48 (p=0.003); with four risk factors, it was 4.03 (p<0.0001); with five risk factors, it was 4.87 (p<0.0001); and for six or more risk factors, it was 11.38 (p<0.0001).

Discussion

In this large prospective population-based study of men, we identified a set of simple routine measures that may be used to predict mortality. We found the following risk factors to be independent predictors of mortality: age, current smoking status, BMI<20 kg/m^2, history of cancer, myocardial infarction, congestive heart failure, depressive symptoms, ADL and IADL disability, impaired chair stands, increased WBC, low albumin levels and anaemia.

Our study is the first to identify multiple measures that are common risk factors for mortality. Our findings are comparable to the CHS for some risk factors but not for others (Fried et al. 1998). They also found that age, IADL, CHF and low albumin were strong predictors of mortality, but the CHS also included a range of measures such as detailed clinical investigations such as echocardiography, electrocardiography and carotid ultrasound that are not routinely used in primary care practice. The Rotterdam study (Newson et al. 2010) included a range of measures to predict survival up to the age of 85 years. They showed that the strongest predictors of survival were being female, having normal left ventricular functioning and unimpaired IADLs. In contrast to the Rotterdam study, we found that high WBC count and ADL disability were significant predictors of mortality. Compared to CHAMP, CHS had a shorter follow-up time of 5 years, whereas the Rotterdam study had a longer follow-up period of 14 years.

The findings in our study regarding the associations of individual and direct measures with mortality are consistent with prior reports. We found that smoking (Gellert et al. 2012; LaCroix et al. 1991), ADL and IADL disability (Stineman et al. 2012; Corti et al. 1994), presence of depressive symptoms (Cuijpers and Smit 2002), hypoalbuminemia (Fried et al. 1998), elevated WBC (Kim et al. 2013; Ruggiero et al. 2007) and anaemia (Penninx et al. 2006; Zakai et al. 2005) were significant predictors of mortality. The objective measures of physical function were predictors of mortality consistent with meta-analyses that have highlighted grip strength, chair stands, balance and walking speed as

Table 2 Unadjusted and age-adjusted hazard ratios (HRs) for mortality by demographic and lifestyle factors, health conditions, physical function and disability: the CHAMP study

	Hazard ratio (95 % CI, *p* value)	
	Model 1 unadjusted	Model 2 adjusted for age
Socio-demographic and economic factors		
Age (per unit increase)	1.12 (1.10,1.14) <0.0001	–
Income (pension only; Ref.: other income)	1.52 (1.26,1.83) <0.0001	1.33 (1.10,1.60) <0.0001
Living (lives alone; Ref.: lives with someone)	1.42 (1.15,1.76) <0.0001	1.07 (0.86,1.33) 0.54
Country of birth (Ref.: Australian born)		
Immigrant born in an English-speaking country	1.01 (0.69,1.46) 0.98	1.09 (0.75,1.59) 0.64
Immigrant born in a non-English-speaking country	0.70 (0.58,0.85) <0.0001	0.83 (0.69,1.01) 0.07
Health risk factors		
Cigarette-smoking status (Ref.: never smoked)		
Ex-smoker	1.12 (0.92,1.36) 0.27	1.16 (0.95,1.42) 0.14
Current smoker	1.50 (1.04,2.17) 0.03	1.90 (1.37,2.01) <0.0001
Physical activity (low PASE score <80; Ref.: high PASE≥80)	2.24 (1.86,2.71) <0.0001	1.71 (1.40,2.08) <0.0001
BMI (Ref.: 20–24.9 kg/m^2)		
25–29.9 kg/m^2	0.66 (0.53,0.83) <0.0001	0.75 (0.60,0.94) 0.01
30 and over kg/m^2	0.57 (0.44,0.74) <0.0001	0.75 (0.58,0.98) 0.04
<20 kg/m^2	2.12 (1.24,3.62) 0.01	1.85 (1.09,3.17) 0.02
Alcohol consumption (Ref.: safe drinker 1–21 drinks/week)		
Harmful drinker (>21 drinks per week)	0.94 (0.71,1.24) 0.67	1.13 (0.85,1.50) 0.39
Ex-drinker	1.61 (1.27,2.03) <0.0001	1.43 (1.13,1.80) 0.003
Lifelong non-drinker	0.81 (0.56,1.18) 0.28	0.76 (0.52,1.10) 0.14
Health conditions		
Self-rated general health (Fair/poor/very poor; Ref.: excellent/good)	1.67 (1.38,2.01) <0.0001	1.96 (1.62,2.37) <0.0001
Doctor diagnosed conditions (>4 conditions; Ref.: 0–4 conditions)	1.80 (1.44,2.26) <0.0001	1.56 (1.24,1.96) <0.0001
Systolic blood pressure (≥140 mm Hg)	0.83 (0.68,1.00) 0.05	0.84 (0.69,1.02) 0.07
Diastolic blood pressure (≥90 mm Hg)	1.00 (0.80,1.25) 0.98	1.17 (0.92,1.50) 0.20
Hypertension (yes; Ref.: no)	1.08 (0.83,1.40) 0.57	1.19 (0.92,1.55) 0.19
Diabetic (reporting diabetes; Ref.: not reporting diabetes)	1.17 (0.93,1.47) 0.18	1.13 (0.90,1.43) 0.28
Fasted blood glucose measurement (≥7.0 mmol/L; Ref.: <7.0 mmol/L)	0.82 (0.56,1.21) 0.32	0.80 (0.54,1.17) 0.25
Estimated glomerular filtration rate (eGFR) (Ref.: normal kidney function GFR>90/min/1.73 m^2)[a]		
GFR 60–90/min/1.73 m^2: stage 1–2 chronic kidney disease (CKD)	0.85 (0.64,1.12) 0.25	–
GFR 30–59/min/1.73 m^2: stage 3A and 3B CKD	1.62 (1.21,2.16) 0.001	–
GFR<30/min/1.73 m^2: stage 4 and 5 severe CKD	5.21 (3.09,8.79) <0.0001	–
Myocardial infarction (yes; Ref.: no)	1.81 (1.47,2.22) <0.0001	1.41 (1.18,1.80) <0.0001
Congestive heart failure (CHF) (yes; Ref.: no)	2.31 (1.69,3.17) <0.0001	1.95 (1.42,2.68) <0.0001
Angina (yes; Ref.: no)	1.49 (1.19,1.86) <0.0001	1.32 (1.06,1.65) 0.01
Stroke (yes; Ref.: no)	1.49 (1.12,1.99) <0.0001	1.30 (0.97,1.73) 0.08
Cancer (yes; Ref.: no)	1.92 (1.58,2.34) <0.0001	1.67 (1.37,2.04) <0.0001
Depressive symptoms (yes; Ref.: <5 depressive symptoms)	2.47 (2.00,3.05) <0.0001	2.21 (1.79,2.73) <0.0001
Cognitive status (Ref.: normal)		
Mild cognitive impairment	1.35 (0.96,1.89) 0.09	1.19 (0.85,1.67) 0.32
Dementia	2.97 (2.21,3.98) <0.0001	1.73 (1.27,2.35) <0.0001
Physical function and performance		

Table 2 (continued)

	Hazard ratio (95 % CI, *p* value)	
	Model 1 unadjusted	Model 2 adjusted for age
Frail (yes; Ref.: no)	4.42 (3.55,5.51) <0.0001	2.86 (2.26,3.63) <0.0001
ADL (yes; Ref.: no)	3.67 (2.91,4.63) <0.0001	2.63 (2.07,3.34) <0.0001
IADL (yes; Ref.: no)	2.81 (2.32,3.40) <0.0001	2.07 (1.69,2.52) <0.0001
Dynamic balance (Ref.: good)		
Poor/not completed	2.10 (1.74,2.54) <0.0001	1.61 (1.31,1.95) <0.0001
Grip strength (poor; Ref.: good)	2.39 (1.99,2.87) <0.0001	1.65 (1.35,2.01) <0.0001
Walking speed (slow; Ref.: normal/fast)	3.34 (2.72,4.09) <0.0001	2.29 (1.85,2.84) <0.0001
Chair stands (lowest quartile and unable; Ref.: 1st to third quartile)	2.81 (2.33,3.38) <0.0001	1.94 (1.59,2.37) <0.0001
History of falls (≥1 fall; Ref.: no falls in past 12 months)	2.20 (1.80,2.68) <0.0001	1.66 (1.35,2.03) <0.0001
Medications		
Polypharmacy (≥5 medications; Ref.: <5 medications)	1.98 (1.64,2.38) <0.0001	1.67 (1.38,2.01) <0.0001
Blood measures		
Cholesterol (≥5.2 mmol/L; Ref.: <5.2 mmol/L)[b]	0.80 (0.64,1.01) 0.06	0.87 (0.69,1.09) 0.22
HDL cholesterol (<1.0 mmol/L; Ref.: ≥1.0 mmol/L)[b]	1.19 (0.82,1.73) 0.37	1.11 (0.76,1.62) 0.59
White cell count (Ref.: 4–10,000 cells/μL)		
≥10,000 cells/μL	2.28 (1.57,3.30) <0.0001	2.68 (1.84,3.88) <0.0001
<4000 cells/μL	1.16 (0.71,1.88) 0.56	1.28 (0.79,2.08) 0.32
Haemoglobin[c] (anaemia <13 g/dL; Ref.: ≥13.0 g/dL)	2.99 (2.43,3.68) <0.0001	2.15 (1.73,2.67) <0.0001
Alanine transaminase (ALT) (highest quartile ≥22 U/L)		
Second quartile (18–21.9 U/L)	0.80 (0.59,1.08) 0.15	0.73 (0.54,0.99) 0.04
Third quartile (15–17.9 U/L)	1.15 (0.87,1.52) 0.33	0.86 (0.65,1.15) 0.31
Lowest quartile (5–14.9 U/L)	2.02 (1.57,2.61) <0.0001	1.30 (1.00,1.70) 0.05
Albumin (low albumin<40 g/L; Ref.: ≥40 g/L)	2.91 (2.29,3.72) <0.0001	2.32 (1.82, 2.96) <0.0001

ADL activities of daily living, *IADL* instrumental activities of daily living; *model 1* unadjusted, *model 2* adjusted for age

[a] Not adjusted for age; the Modification of Diet in Renal Disease formulae taking age into account: $eGFR = 175 \times (\text{serum creatinine}/88.4)^{-1.154} \times \text{age}^{-0.203}$

[b] Raised total cholesterol was defined as ≥5.5 mmol/L; low HDL cholesterol was defined as ≤1.0 mmol/L

[c] Anaemia; World Health Organisation criteria for anaemia: haemoglobin <13.0 g/dL for men

important predictors of mortality in older adults (Cooper et al. 2010). However, in multivariate analyses, only impaired chair stands remained significantly associated with mortality in our study. It is possible that adjusting for related variables on the same causal pathway reduces their association as a result of competition. This may also be the explanation for why physical activity, frailty and history of falls were not in the final model.

Our findings showed that men who were overweight and obese had lower mortality rates, consistent with research on the protective effect of high BMI with ageing (Janssen et al. 2005) with the view that extra body weight, including lean tissue mass and fat mass, may provide protection against nutritional and energy deficiencies, metabolic stresses, the development of wasting and frailty and loss of muscle and bone density caused by chronic diseases (Janssen 2007). Our findings are in contrast to a recent meta-analysis that showed increased risk of mortality for older adults with a BMI above 33 kg/m^2 (Winter et al. 2014). These differences could possibly due to the inclusion of both men and women in the meta-analysis, and due to inclusion of a younger population aged 65 and over, whereas our sample include men with mean age of 77 years.

Surprisingly, in contrast to another study (Holahan et al. 2010), our study showed that lifelong abstinence of alcohol consumption was protective of mortality. In many studies, abstainers may include former drinkers

Table 3 Fully adjusted hazard ratios (HRs) for mortality according to age, lifestyle factors, health conditions, physical function and disability: the CHAMP study

N=1508	Hazard ratio (95 % CI, *p* value) Model 3 adjusted for all covariates[a]	Validation estimates[b] hazard ratio (95 % CI, *p* value)
Age	1.07 (1.05,1.09) <0.0001	1.07 (1.05,1.09) <0.0001
Health risk factors		
Cigarette smoking status (Ref.: never smoked)		
Ex-smoker	0.98 (0.87,1.23) 0.87	1.01 (0.80,1.27) 0.92
Current smoker	1.75 (1.15,2.67) 0.001	1.75 (1.15,2.67) 0.01
BMI (Ref.: 20–24.9 kg/m^2)		
25–29.9 kg/m^2	0.70 (0.55,0.90) 0.005	0.69 (0.54,0.89) 0.004
30 and over kg/m^2	0.62 (0.46,0.83) 0.001	0.61 (0.45,0.82) 0.001
<20 kg/m^2	1.98 (1.09,3.60) 0.02	2.10 (1.17,3.79) 0.01
Alcohol consumption (Ref.: safe drinker 1–21 drinks/week)		
Harmful drinker (>21 drinks per week)	1.26 (0.94,1.70) 0.12	1.25 (0.92,1.71) 0.16
Ex-drinker	1.15 (0.88,1.52) 0.31	1.16 (0.89,1.54) 0.28
Lifelong non-drinker	0.57 (0.38,0.87) 0.009	0.59 (0.39,0.89) 0.01
Health conditions		
Myocardial infarction (yes; Ref.: no)	1.33 (1.04,1.70) 0.02	1.32 (1.04,1.69) 0.02
Congestive heart failure (CHF) (yes; Ref.: no)	1.70 (1.19,2.43) 0.004	1.63 (1.14,2.32) 0.01
Cancer (yes; Ref.: no)	1.76 (1.42,2.19) <0.0001	1.76 (1.42,2.18) <0.0001
Depressive symptoms (yes; Ref.: no depression symptoms)	1.53 (1.18,2.00) 0.001	1.54 (1.19,2.00) 0.001
Physical function and performance		
ADL (yes; Ref.: no)	1.79 (1.30,2.47) <0.0001	1.76 (1.28,2.43) 0.001
IADL (yes; Ref.: no)	1.37 (1.08,1.75) 0.01	1.41 (1.11,1.79) 0.01
Chair stands (lowest quartile and unable; Ref.: 1st to third quartile)	1.44 (1.12,1.84) 0.004	1.45 (1.13,1.85) 0.003
Blood measures		
White cell count (Ref.: 4–10,000 cells/μL)		
≥10,000 cells/μL	1.84 (1.20,2.81) 0.005	1.82 (1.19,2.77) 0.01
<4000 cells/μL	0.70 (0.40,1.25) 0.23	0.76 (0.44,1.34) 0.34
Albumin Haemoglobin[c] (Ref ≥ 13.0 g/dL)(low albumin<40 g/L; Ref.:≥40 g/L)	1.50 (1.12,2.00) 0.006	1.50 (1.13,2.00) 0.006
Anaemia	1.96 (1.54,2.49) *p*<0.0001	1.95 (1.53,2.48) *p*<0.0001

[a] Internal validation using the bootstrap method

[b] Model 3—adjusted for all covariates in the model: age, smoking status, BMI, alcohol consumption, myocardial infarction, congestive heart failure, cancer, depressive symptoms, IADL disability, ADL disability, chair stands, white blood cell count, haemoglobin albumin

[c] Anaemia; World Health Organisation criteria for anaemia: haemoglobin <13.0 g/dL for men

who have ceased drinking due to existing health problems and may therefore differ to drinkers in terms of sociodemographic and social–behavioural factors associated with mortality (Holahan et al. 2010). In our study, there were no differences in abstainers by sociodemographic factors in our study, and abstainers only included lifelong non-drinkers not ex-drinkers. In our study, ex-drinkers had an increased mortality risk compared to moderate drinkers, consistent with other studies (Holahan et al. 2010). In contrast to a systematic review (Reid et al. 2002), heavy alcohol consumption was not a significant risk factor for mortality in our study. These conflicting findings may be due to lack of standardisation in the classification of moderate and heavy drinking, cultural differences in drinking habits and measurement error in self-reports of alcohol consumption.

Table 4 Hazard ratios (HRs) for mortality by number of risk factors: the CHAMP study

	N	Prevalence (%)	No. of deaths (% of deaths by number of risk factors)	Hazard ratio (95 % CI, *p* value)
No. of risk factors[a]				
0/1 (Ref.)	166	9.9	13(7.8)	–
2	320	19.2	30 (9.4)	1.17 (0.61,2.24) 0.64
3	382	22.9	72 (18.9)	2.48 (1.38,4.48) 0.003
4	306	18.3	89 (29.1)	4.03 (2.25,7.22) <0.0001
5	202	12.1	68 (33.7)	4.87 (2.69,8.81) <0.0001
≥6	294	17.6	178 (60.5)	11.38 (6.48,19.9) <0.0001

[a] Risk factors—age 75 and over, current smoking status, BMI<20 kg/m^2 , high white cell count(>≥10,000 cells/μL), anaemia (<13.0 g/dL), low albumin (<40 g/L), history of cancer, history of MI, history of congestive heart failure, depressive symptoms, impaired chair stands, IADL and ADL disability

Several variables were significant predictors of mortality in univariate and age-adjusted analyses but did not remain significant in fully adjusted analysis. Dementia became a significant predictor of mortality when ADL disability was removed from the final model. It is likely that in our community-dwelling men, those who had dementia did not yet have advanced dementia. However, we were unable to investigate this in our sample. The implications of our findings are that maintenance of functional dependence is important for survival, and both dementia and functional dependence are related in this context.

Poor renal function (GFR<30/min/1.73 m^2) did not remain in the final model; it became non-significant despite the HR remaining high at 1.60. This loss in significance may have been due to under powering with there being too few men (n=24) with the poorest renal function after full adjustment.

Further analysis showed an overall C statistic of 0.80 of the final model, indicating that it has strong predictive value for mortality. Moreover, bootstrap analyses with a C statistic of 0.79 in the validated model confirmed good internal validity. The results of our analyses suggest that the model should perform well in other similarly defined populations. The predictive ability of our model is comparable to other studies of older people living in the community (Lee et al. 2006; Schonberg et al. 2009).

Ageing results in an accumulation of deficits, i.e. multiple risk factors that are more important than individual risk factors. Considering complexity, multiple problems and the cumulative effect of deficits over time is critical to the care of older adults. The findings of our study suggest that, in clinical practice, the management of multiple risk factors is important for extending survival in older men, rather than simply considering individual risk factors in isolation. Our study has important implications for clinical practice and the development of future strategies for health promotion in older people. Our findings suggest that the screening and management of common multiple risk factors in combination with management of other comorbidities may contribute to increased survival rates.

There are potentially clinically significant interactions that may be interesting to examine for example the impact of pre-existing health conditions on the association between disability and mortality, i.e. investigating interactions of cancer, heart conditions on the association between disability and mortality. It would also be interesting to study interactions of behaviour patterns such as alcohol consumption and smoking with disease and mortality.

Some of the "traditional" risk factors for mortality in a younger population, including high blood pressure, hypercholesterolaemia, overweight and obesity and diabetes, were not independent predictors of mortality in this population of older men. These common risk factors for cardiovascular diseases were not associated with mortality. This may be partly explained by the effect of adjusting for the "end stage" of cardiovascular diseases, i.e. myocardial infarction and heart failure. Our findings for cholesterol are similar to the CHS (Fried et al. 1998), but not for hypertension and diabetes.

Strengths and limitations

The major strength of the CHAMP study is that it includes a representative sample from the community and data on a comprehensive range of important risk factors. The age distribution of the men in the CHAMP study is similar to that of the target population

(Cumming et al. 2008), and the prevalence of self-reported disease in CHAMP participants is very similar to that found in a recent Australian national telephone survey of men's health (Holden et al. 2005).

However, our study has some limitations. The CHAMP study had a baseline participation rate of about 50 %; it is an acceptable response rate for a longitudinal study in men of this age and uncommon for studies of this nature involving a clinic visit including the Massachusetts Male Ageing Study (Feldman et al. 2001) and the Australian Longitudinal Study of Ageing (Andrews et al. 1989). Missing data for blood glucose was due to an administrative error (blood glucose), and as it was considered as missing at random (Little and Rubin 2002), it should not have caused any bias. We do not have clinical data for the men who refused to participate in the study so we are unable to provide a direct comparison between participants and non-participants. However, the demographic data show that the age distribution of participants was similar to that of men in the target population (Cumming et al. 2008). Men who participated in CHAMP are considered to be a healthier group since there are able to attend the clinic at Concord hospital so may be more likely to participate in the study. Our study was limited to community living men, as institutionalised men were not invited, and it is likely that the frailest men in the community may not have participated. Our study was among men, so we could not look at gender differences in mortality risk.

Conclusion

We have identified common risk factors that predict mortality; many of them can be easily assessed in primary medical practice or may be useful in making clinical decisions for further assessments. Our findings suggest that, in primary care, screening and management of multiple risk factors is important to consider for extending survival, rather than simply considering individual risk factors in isolation. Our study highlights that some of the "traditional" risk factors for mortality in younger populations, such as high blood pressure, hypercholesterolaemia, overweight and obesity and diabetes, seem less important among older men.

Acknowledgements The CHAMP study is funded by the National Health and Medical Research Council (project grant number 301916) and the Ageing and Alzheimer's Institute. We thank all the staff working on CHAMP and the participants in the project. The lead author is funded by the ARC Centre of Excellence in Population Ageing Research (CEPAR).

Funding The views expressed are those of the authors, not of the funders. Data analysis and interpretation were carried out by the authors independently of the funding sources based on the available data. The corresponding author had full access to the survey data and had final responsibility for the decision to submit for publication.

Conflicts of interest The authors do not have any conflict of interest to declare.

Authors' contributions VH and RC designed and developed the study. VH conducted the data analyses and wrote the initial versions of the manuscript. RC edited the manuscript. All authors contributed to interpretation of the results, revised subsequent drafts, reviewed and approved the final version of the manuscript. RC and VH had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Sponsor's role The funding body played no role in the formulation of the design, methods, subject recruitment, data collection, analysis or preparation of this paper.

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