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Impact of multimorbidity and complex multimorbidity on mortality among older Australians aged 45 years and over: a large population-based record linkage study

Alamgir Kabir ,[1] An Tran,[1] Sameera Ansari,[2,3] Damian P Conway ,[4,5] Margo Barr[1]

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For numbered affiliations see end of article.

Correspondence to
Alamgir Kabir;
a.kabir@unsw.edu.au

ABSTRACT

Objectives Multimorbidity (MM, co-occurrence of two or more chronic conditions) and complex multimorbidity (CMM, three or more chronic conditions affecting three or more different body systems) are used in the assessment of complex healthcare needs and their impact on health outcomes. However, little is known about the impacts of MM and CMM on mortality in Australia.

Design Community-based prospective cohort study.

Setting New South Wales, Australia.

Participants People aged 45 years and over who completed the baseline survey of the 45 and Up Study.

Measures Baseline survey data from the 45 and Up Study were linked with deaths registry data. Deaths that occurred within 8 years from the baseline survey date were the study outcome. Eleven self-reported chronic conditions (cancer, heart disease, diabetes, stroke, Parkinson's disease, depression/anxiety, asthma, allergic rhinitis, hypertension, thrombosis and musculoskeletal conditions) from the baseline survey were included in the MM and CMM classifications. Cox proportional hazard models were used to estimate adjusted and unadjusted 8-year mortality hazard ratios (HRs).

Results Of 251 689 people (53% female and 54% aged ≥60 years) in the cohort, 111 084 (44.1%) were classified as having MM and 39 478 (15.7%) as having CMM. During the 8-year follow-up, there were 25 891 deaths. Cancer (34.7%) was the most prevalent chronic condition and the cardiovascular system (50.9%) was the body system most affected by a chronic condition. MM and CMM were associated with a 37% (adjusted HR 1.36, 95% CI 1.32 to 1.40) and a 22% (adjusted HR 1.22, 95% CI 1.18 to 1.25) increased risk of death, respectively. The relative impact of MM and CMM on mortality decreased as age increased.

Conclusion MM and CMM were common in older Australian adults; and MM was a better predictor of all-cause mortality risk than CMM. Higher mortality risk in those aged 45–59 years indicates tailored, person-centred integrated care interventions and better access to holistic healthcare are needed for this age group.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A large population-based prospective cohort study of people aged 45 years and over was used to evaluate the effect of multimorbidity (MM) and complex multimorbidity (CMM) on 8-year mortality.
⇒ Self-reported chronic health conditions were used to define MM and CMM.
⇒ Deaths registry data were probabilistically linked to the cohort data by the New South Wales Centre for Health Record Linkage for mortality ascertainment.
⇒ Though the study cohort has been shown to be generally representative of the population from which it is drawn, non-response at recruitment may mean the cohort varies slightly from the broader population.
⇒ Our analysis was restricted to the conditions listed in the 45 and Up Study baseline survey questionnaire; however, this included all of the most important chronic conditions.

INTRODUCTION

Multimorbidity (MM), the co-occurrence of two or more chronic health conditions in an individual, is often used in the assessment of complex healthcare needs and their impact on health outcomes.[1] As life expectancy increases over time due to advances in healthcare and living standards, the burden of chronic conditions is increasing globally.[2] Consequently, the proportion of national healthcare expenditure spent caring for people with MM has increased substantially. For example, managing MM accounts for 71% of total US healthcare spending.[3] While overall prevalence of MM is 33% globally,[4] prevalence among those aged 65 years or more is estimated to be 55%–98% in high-income countries.[5] In Australia, estimated prevalence of MM is 20% overall and 51% among those aged 65 years or more.[6]

MM is associated with increased risk of adverse mental and physical health outcomes[7 8] and poor quality of life overall.[9 10]

However, reported effects of MM on mortality in older adults are mixed: some studies reported MM was associated with greater risk of mortality,[11–16] while others reported no significant association.[17 18] A systematic review found an increased risk of mortality among those with MM, but noted the majority of studies were not population-based, had relatively small sample sizes and/or lacked internal validity.[14] Also, many studies reported the impact of MM on mortality among older adults overall without stratifying outcomes by age group. Though some Australian studies demonstrated an association between MM and mortality, these studies were not population-based and have limited generalisability.[19 20]

Some authors have proposed complex multimorbidity (CMM; co-occurrence of three or more chronic conditions affecting three or more different body systems) as an alternative and more specific metric to assess complexity of individual healthcare needs.[19 21] This metric provides lower prevalence estimates than MM and allows greater differentiation among older adults.[19] However, whether it enables more targeted patient care and health resource planning requires further investigation. To our knowledge, there have not been any published evaluations comparing the impact of MM and CMM on older adult mortality in Australia. Hence, we conducted a large population-based data linkage study to (1) compare the effect of MM and CMM on mortality among older adults aged 45 and above; and (2) assess whether any observed effect on mortality varies by age group.

METHODS

Study design and population

We conducted a prospective cohort study of people aged 45 years and over from New South Wales (NSW), Australia, enrolled in the Sax Institute's 45 and Up Study with 8-year follow-up from recruitment. People who completed the baseline survey questionnaire of the 45 and Up Study and who did not withdraw from the study were our study population. The 45 and Up Study is a large-scale population-based cohort study comprising 267 153 men and women aged 45 years and over. Details of the study have been described elsewhere.[22] In brief, potential study participants aged 45 years or older in NSW were randomly sampled from the Services Australia (formerly the Australian Government Department of Human Services) Medicare enrolment database, which provides near-complete coverage of the population and invited to participate between 2006 and 2009. However, people aged 80+ years from rural and remote areas were oversampled; about 18% of those invited participated, and participants included about 11% of the NSW population aged 45 years and over. Participants consented to self-completing the baseline questionnaire and to long-term follow-up with linkage of survey data to other administrative health records. Data collected via baseline survey included sociodemographic and lifestyle characteristics, and self-reported chronic conditions. We excluded people from the study population who had completed their baseline data before 20 February 2006 as the death records were only available from that date.

Data linkage and outcome ascertainment

All deaths between 20 February 2006 and 30 September 2018 recorded in the NSW Registry of Births, Deaths and Marriages were probabilistically linked to 45 and Up Study data by the NSW Centre for Health Record Linkage. Follow-up time for mortality was set at 8 years from baseline survey as baseline data collection was completed in December 2009 and the latest available deaths registry data were from September 2018. All-cause mortality occurring within 8 years of recruitment was our outcome of interest.

MM and CMM ascertainment

Self-reported chronic health conditions were ascertained from responses to two 45 and Up Study baseline survey questions: 'Has a doctor ever told you that you have (name of condition)?' and 'In the last month, have you been treated for (name of condition)?'. If the response was 'yes' for either question for a condition, we considered the person had the condition. These included cancer (all types), heart disease, diabetes, stroke, Parkinson's disease, depression, anxiety, asthma, allergic rhinitis, hypertension, thrombosis and musculoskeletal conditions. Accordingly, participants were classified as having MM (two or more chronic conditions at baseline) and/or CMM (three or more chronic conditions affecting three or more body systems at baseline, table 1).[23] To define CMM, we first classified the 11 chronic conditions into nine groups according to the body system: cardiovascular, musculoskeletal, neurological, psychological, respiratory, skin, endocrine/metabolic, female genital and male genital.[24] Conditions that occurred in different body parts (eg, cancer at different sites) were grouped into one condition for the MM measure but were classified into different body systems, depending on the sites.

Statistical analysis

Continuous variables were categorised and included one additional category for missing values if there were≥5% missing values. Psychological distress was measured using the Kessler Psychological Distress Scale (K10) and categorised as low or moderate (<22) and high (≥22).[25] Participant characteristics were compared for those with and without MM or CMM using χ^2 tests. We conducted a time-to-event analysis to measure impacts of MM and CMM on mortality. Follow-up time started at the date of baseline data collection and was censored at death or the date when participants completed the 8-year follow-up, whichever came first. We generated Kaplan-Meier survival curves for people with and without MM or CMM and used log-rank tests for comparison. Death rate was calculated using person-time at-risk as the denominator. Crude and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using univariate and

Table 1 Percentage of self-reported chronic conditions among older adults aged 45 years and over by condition and by body system

	n	Prevalence (95% CI)
Morbidity		
Cancer*	87 386	34.7 (34.5 to 34.9)
Heart disease†	32 690	13.0 (12.9 to 13.1)
Diabetes	22 575	9.0 (8.9 to 9.1)
Parkinson's disease	1566	0.6 (0.6 to 0.7)
Stroke	7893	3.1 (3.1 to 3.2)
Depression or anxiety	46 343	18.4 (18.3 to 18. 6)
Asthma‡	31 316	12.4 (12.3 to 12.6)
Allergic rhinitis‡	34 509	13.7 (13.6 to 13.9)
Hypertension	78 135	31.0 (30.9 to 31.2)
Thrombosis	13 834	5.5 (5.4 to 5.6)
Musculoskeletal conditions§	29 986	11.9 (11.8 to 12.0)
Multimorbidity (≥2 morbidities)	111 084	44.1 (43.9 to 44.3)
Body system morbidity: any conditions within these systems¶		
Cardiovascular	128 069	50.9 (50.7 to 51.1)
Musculoskeletal	35 272	14.0 (13.9 to 14.2)
Neurological	1566	0.6 (0.6 to 0.7)
Psychological	46 343	18.4 (18.3 to 18. 6)
Respiratory	55 279	22.0 (21.8 to 22.1)
Skin	13 811	5.5 (5.4 to 5.6)
Endocrine/metabolic	33 533	13.3 (13.2 to 13.5)
F genital**	7300	2.9 (2.8 to 3.0)
M genital††	23 850	9.5 (9.4 to 9.6)
Complex multimorbidity (≥3 body system)	39 478	15.7 (15.5 to 15.8)

*Cancer includes melanoma, breast cancer (F), prostate cancer (M) and other cancer.
†Heart disease includes heart attack, angina or other heart disease.
‡Asthma and allergic rhinitis were collected as aggregated for the first ~15% people, but they were separated for the remaining people.
§Musculoskeletal includes osteoarthritis, osteoporosis or low bone density.
¶Body system morbidities: cardiovascular includes heart disease, high blood pressure, blood clot (thrombosis), heart attack or angina and other heart disease; musculoskeletal includes osteoarthritis, osteoporosis or low bone density; neurological includes Parkinson's disease; psychological includes depression or anxiety; respiratory includes asthma or allergic rhinitis; skin includes melanoma; endocrine/metabolic includes diabetes and thyroid problems; F genital includes breast cancer; M genital includes prostate cancer or enlarged prostate.
**Denominator for this estimate was the total number of F participants.
††Denominator for this estimate was the total number of M participants.
F, female; M, male.

multiple Cox proportional hazard models. The potential confounders were selected based on the following steps: first, we selected those variables for the base model which were found to be associated with MM or CMM at p<0.20 using a χ^2 test; second, we applied the change-in-estimate strategy using the 'chest' package in R.[26 27] We then assessed potential effect modification for age groups, as there was a large variation in age at baseline, by adding an interaction term into the Cox proportional hazard model. If the interaction term was significant at p<0.05, we did a stratified analysis by age. We set 5% as the significance level for all statistical tests. We used R V.3.6.3 software (R Foundation, Vienna, Austria) for data analysis and SAS V.9.4 for data management.

Patient and public involvement

Patients or public were not involved in design, management or reporting of our study.

RESULTS

The analytical cohort comprised 251 689 people aged 45 years and over (figure 1). The percentage of the cohort assessed to have MM was 44.1% (95% CI 43.9% to 44.3%) with the most frequent chronic conditions being cancer (34.7%), followed by hypertension (31.0%) and depression or anxiety (18.4%) (table 1). The percentage of the cohort assessed to have complex MM was 15.7% (95% CI 15.5% to 15.8%), and the cardiovascular system was the

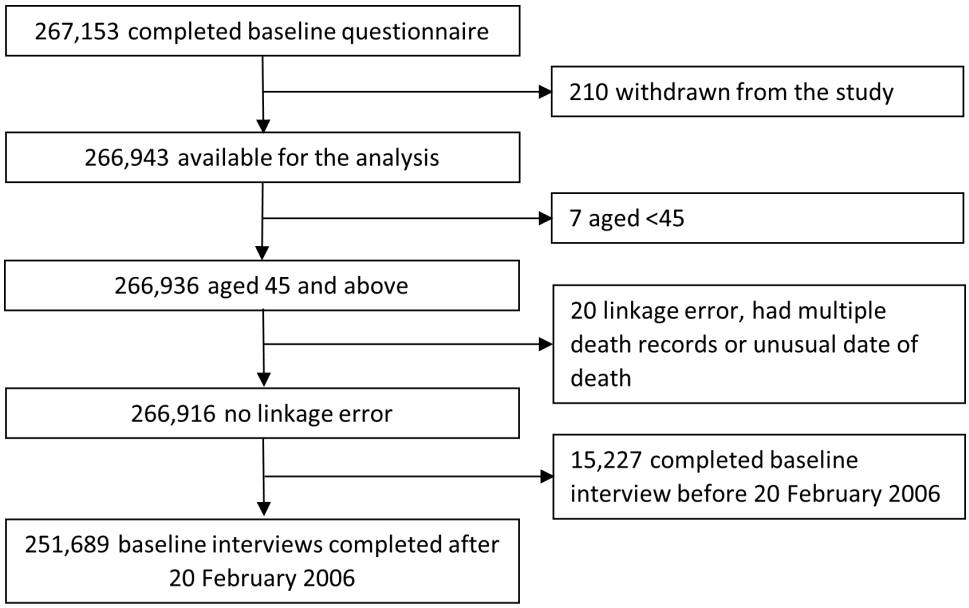

Figure 1 Assembly of the analytical cohort.

most prevalent body system (50.9%) followed by respiratory (22.0%) and psychological (18.4%).

Participants' baseline characteristics (see the online supplemental material for detailed descriptions) by morbidity status are presented in table 2. All baseline characteristics except current smoking status were significantly (p<0.001) different between people with and without MM, while all baseline characteristics were significantly different between people with and without CMM. The proportion of the cohort categorised as having MM and CMM increased with increasing age, but the proportion decreased with increasing household income. People not working, self-reporting fair/poor quality of life or having high levels of psychological distress had significantly higher proportions of MM and CMM than those not in these groups.

Survival probability for people with MM or CMM was significantly lower than for those without MM or CMM (p<0.001; figure 2). Mortality was 2.5 times higher among people with MM compared with those without (20.3 vs 8.3 deaths/1000 person-years, table 3). When adjusted for confounding, mortality was 36% (HR 1.36, 95% CI 1.32 to 1.40) higher among people with MM compared with those without. Absolute difference in deaths/1000 person-years between people with and without MM increased as age increased: 2.3 for 45–59 years, 6.0 for 60–74 years and 12.4 for 75 years and over, respectively. However, impact of MM on mortality decreased as age increased: adjusted HRs were 1.59 (95% CI 1.46 to 1.73) for 45–59 years, 1.49 (95% CI 1.41 to 1.57) for 60–74 years and 1.15 (95% CI 1.11 to 1.19) for 75 years and over.

Mortality was 2.2 times higher among people with CMM compared with those without (25.3 vs 11.4 deaths/1000 person-years, table 4). When adjusted for confounding, mortality was 22% (HR 1.22, 95% CI 1.18 to 1.25) higher among people with CMM compared with those without. Absolute difference in deaths/1000 person-years between people with and without CMM increased as age increased: 3.4 for 45–59 years, 6.3 for 60–74 years and 13.2 for 75 years and over, respectively. However, impact of CMM on mortality decreased as age increased: adjusted HRs were 1.49 (95% CI 1.33 to 1.67) for 45–59 years, 1.29 (95% CI 1.22 to 1.36) for 60–74 years and 1.08 (95% CI 1.04 to 1.12) for 75 years and over.

DISCUSSION

This is the first population-based analysis of the effect of CMM on mortality in Australia. MM and CMM were present in 44.1% and 15.7% of people within this cohort, respectively. During 8 years of follow-up, mortality in MM and CMM sub-groups was at least twice that of those without MM and CMM; 20.3 vs 8.3 deaths/1000 person-years, and 25.3 vs 11.4 deaths/1000 person-years, respectively. Adjusted risk of all-cause mortality was 36% higher for people with MM and 22% higher for people with CMM, compared with people not in either group. When adjusted risk of all-cause mortality due to MM and CMM was stratified by age, risk was highest in the youngest age group (45–59 years) and decreased towards the oldest age group (75 years or more). In our analysis, MM was found to have a greater impact on mortality than CMM, and both MM and CMM had the greatest impact on all-cause mortality in the youngest age group (45–59 years).

Our prevalence estimate for MM depends on self-reported survey data for 11 chronic conditions and is comparable with other Australian and international studies.[6 28 29] Prevalence of MM in the Australian 2017–2018 National Health Survey involving 10 self-reported chronic conditions was 47%, which is similar to our estimate.[6] However, 5 out of 10 conditions were different from those available in the 45 and Up Study baseline survey.

Table 2 Percentage of MM and CMM by characteristics for the study participants

	N*	MM		CMM	
		With MM n (%)	Without MM n (%)	With CMM n (%)	Without CMM n (%)
Age at baseline (years)					
45–59	116 085	37 374 (32.2)	78 711 (67.8)	10 718 (9.2)	105 367 (90.8)
60–74	93 060	46 770 (50.3)	46 290 (49.7)	17 587 (18.9)	75 473 (81.1)
75+	42 544	26 940 (63.3)	15 604 (36.7)	9229 (26.3)	31 371 (73.7)
Gender					
Male	117 059	52 750 (45.1)	64 309 (54.9)	17 463 (14.9)	99 596 (85.1)
Female	134 630	58 334 (43.3)	76 296 (56.7)	22 015 (16.4)	112 615 (83.6)
Highest education					
No school certificate or other qualification	29 344	15 328 (52.2)	14 016 (47.8)	6216 (21.2)	23 128 (78.8)
School, intermediate, higher school or leaving certificate	79 784	35 877 (45.0)	43 907 (55.0)	12 949 (16.2)	66 835 (83.8)
Trade, apprenticeship, certificate or diploma	80 141	35 328 (44.1)	44 813 (55.9)	12 291 (15.3)	67 850 (84.7)
University degree or higher	58 185	22 581 (38.8)	35 604 (61.2)	7246 (12.5)	50 939 (87.5)
Speaks language other than English at home					
No	227 541	102 934 (45.2)	124 607 (54.8)	36 354 (16.0)	191 187 (84.0)
Yes	24 145	8149 (33.8)	15 996 (66.2)	3124 (12.9)	21 021 (87.1)
Born in Australia					
No	61 166	22 623 (37.0)	38 543 (63.0)	8165 (13.3)	53 001 (86.7)
Yes	188 547	87 495 (46.4)	101 052 (53.6)	30 924 (16.4)	157 623 (83.6)
Household income					
<$20 000	49 296	28 472 (57.8)	20 824 (42.2)	12 260 (24.9)	37 036 (75.1)
$20 000–39 999	43 933	21 581 (49.1)	22 352 (50.9)	8030 (18.3)	35 903 (81.7)
$40 000–69 999	44 453	17 613 (39.6)	26 840 (60.4)	5534 (12.4)	38 919 (87.6)
$70 000 or more	59 794	20 084 (33.6)	39 710 (66.4)	5072 (8.5)	54 722 (91.5)
Won't disclose	54 213	23 334 (43.0)	30 879 (57.0)	8582 (15.8)	45 631 (84.2)
Work status					
Not working	124 277	69 118 (55.6)	55 159 (44.4)	28 029 (22.6)	96 248 (77.4)
Part time	47 577	17 175 (36.1)	30 402 (63.9)	5223 (11.0)	42 354 (89.0)
Full time	75 540	23 093 (30.6)	52 447 (69.4)	5600 (7.4)	69 940 (92.6)
Current partner (married/de facto)					
No	62 245	31 637 (50.8)	30 608 (49.2)	12 781 (20.5)	49 464 (79.5)
Yes	187 853	78 720 (41.9)	109 133 (58.1)	26 443 (14.1)	161 410 (85.9)
Current smoker					
No	233 130	103 890 (44.6)	129 240 (55.4)	36 883 (15.8)	196 247 (84.2)
Yes	18 552	7192 (38.8)	11 360 (61.2)	2595 (14.0)	15 957 (86.0)
Adequate physical activity†					
No	81 815	39 044 (47.7)	42 771 (52.3)	15 333 (18.7)	66 482 (81.3)
Yes	169 874	72 040 (42.4)	97 834 (57.6)	24 145 (14.2)	145 729 (85.8)
Alcohol consumption					
No	82 068	39 610 (48.3)	42 458 (51.7)	16 347 (19.9)	65 721 (80.1)
Yes	164 927	69 308 (42.0)	95 619 (58.0)	22 229 (13.5)	142 698 (86.5)
BMI¶ category					

Continued

Table 2 Continued

	N*	MM		CMM	
		With MM n (%)	Without MM n (%)	With CMM n (%)	Without CMM n (%)
Underweight	26 433	11 326 (42.8)	15 107 (57.2)	3972 (15.0)	22 461 (85.0)
Normal weight	79 040	30 429 (38.5)	48 611 (61.5)	9653 (12.2)	69 387 (87.8)
Overweight	91 879	40 234 (43.8)	51 645 (56.2)	13 684 (14.9)	78 195 (85.1)
Obese	54 337	29 095 (53.5)	25 242 (46.5)	12 169 (22.4)	42 168 (77.6)
Self-reported good quality of life‡					
No	25 379	17 190 (67.7)	8189 (32.3)	8912 (35.1)	16 467 (64.9)
Yes	212 841	89 079 (41.9)	123 762 (58.1)	28 731 (13.5)	184 110 (86.5)
Missing	13 469	4815 (35.7)	8654 (64.3)	1835 (13.6)	11 634 (86.4)
Psychological distress§					
Low or moderate	205 402	84 755 (41.3)	120 647 (58.7)	27 573 (13.4)	177 829 (86.6)
High (22 or more)	18 603	11 239 (60.4)	7364 (39.6)	5712 (30.7)	12 891 (69.3)
Missing	27 684	15 090 (54.5)	12 594 (45.5)	6193 (22.4)	21 491 (77.6)
Needing help with daily activity					
No	225 634	96 045 (42.6)	129 589 (57.4)	31 823 (14.1)	193 811 (85.9)
Yes	13 728	10 269 (74.8)	3459 (25.2)	5606 (40.8)	8122 (59.2)
Missing	12 327	4770 (38.7)	7557 (61.3)	2049 (16.6)	10 278 (83.4)

*Missing value: highest education (n=4235), speaks language other than English at home (n=3), born in Australia (n=1976), work status (n=4295), current partner (n=1591), current smoker (n=7), alcohol consumption (n=4694).
†Adequate physical activity was defined based on the amount of time spent on moderate and vigorous exercise in the week prior to the survey.
‡Self-reported good quality of life was defined if people reported their quality of life was good, very good or excellent in response to the self-rated quality of life question.
§Psychological distress was categorised based on the K10 score that ranges between 10 and 50.
¶Body mass index
CMM, complex multimorbidity; MM, multimorbidity.

Another Australian study estimated 37.4% prevalence for MM and 8.7% prevalence for CMM using the 45 and Up Study baseline survey data, but unlike our analysis, they did not include allergic rhinitis, thrombosis and musculoskeletal conditions and included only participants with consistent concession cardholder status in the Pharmaceutical Benefits Scheme (PBS) dataset (n=90 352).[28] A cross-sectional Scottish study reported MM prevalence ranging between 39% for people aged 55–66 years and 76% for people aged 75 years and over (which is similar to our estimates), while other studies have reported much higher prevalence among older adults.[5]

Several international studies have reported that MM and CMM are associated with a greater risk of mortality, but the effect size in most of the previous studies may not be directly comparable to our study because of the number and type of chronic conditions, different study designs, varying follow-up time and study population of different age groups.[14–16 30–32] Consistent with our study, a 2015 meta-analysis of 26 studies demonstrated greater mortality risk among older adults aged ≥65 years of age with MM compared with those without (HR 1.44, 95% CI 1.34 to 1.55).[14] More recently, the English Longitudinal Study of Ageing reported lower mortality risk associated with MM (HR 1.27, 95% CI 1.14 to 1.43) among 9171 people aged ≥50 years, which may be related to a relatively older population (90% were aged ≥60 years) who were at a greater risk of mortality.[30] However, other US and Scottish studies reported significantly greater effects of MM on mortality compared with our analysis.[15 16] The Scottish study involved younger people (≥18 years of age) and considered severe conditions to be those needing hospitalisation, while the US study had different classes of MM. Though several studies have evaluated the effect of MM on mortality, relatively few have evaluated the effect of CMM on mortality.[31 32] A Japanese population-based cohort study evaluating the effects of MM and CMM on mortality among adults aged 65 and over reported lower and similar effects for both MM and CMM compared with our study (HR 1.07, 95% CI 1.01 to 1.14 for MM and HR 1.07, 95% CI 0.99 to 1.16 for CMM). However, a Norwegian population-based cohort study found 22% higher mortality risk in those with CMM aged 60–69 years (relative risk (RR) 1.22, 95% CI 1.12 to 1.33).[32]

While all-cause mortality overall was higher in our study for the older age groups the relative effect sizes for mortality risk for both MM and CMM were higher in adults aged 45–59 years compared with the older age

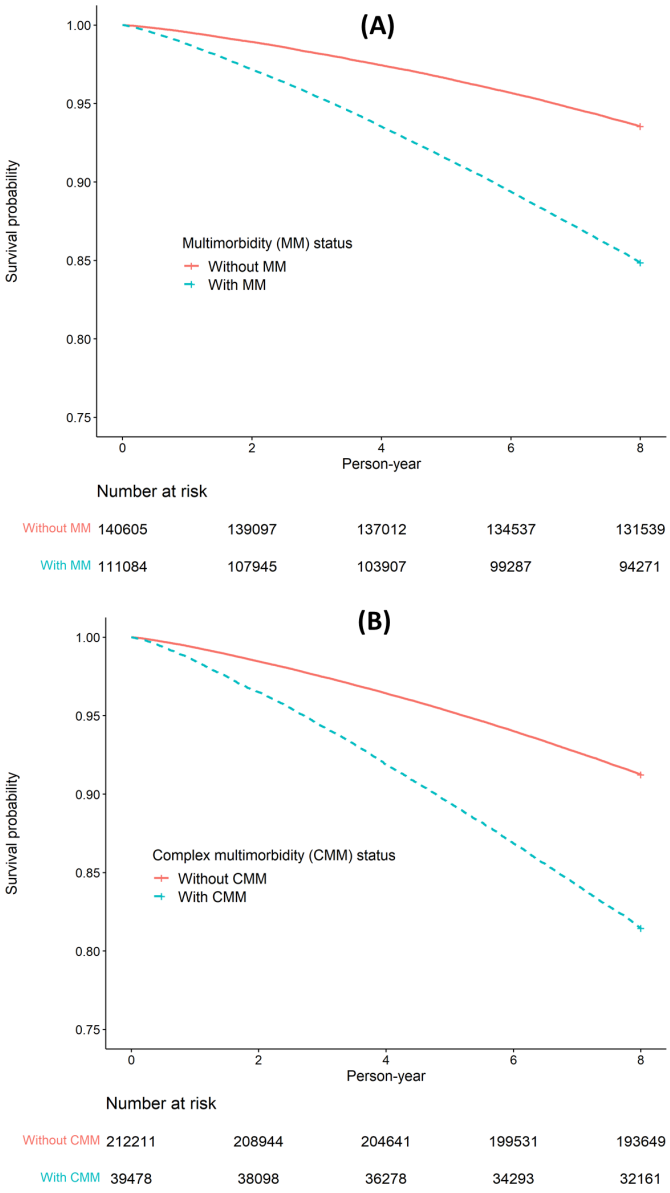

Figure 2 Kaplan-Meier curve: impact of MM and CMM on 8-year (from recruitment) mortality. CMM, complex multimorbidity; MM, multimorbidity.

groups. A study using the UK Biobank data (n=502 640) found similar results and concluded that this may be because most interventions to date have been directed at middle-aged populations.[33] They therefore highlighted the need for algorithms that could identify these younger people with MM to provide earlier, more targeted care. This phenomenon may also be explained, in part, because early-onset disease is often more aggressive and people are presenting later.[34 35] This again highlights the need for early diagnosis, treatment and targeted care.

Risk of all-cause mortality associated with MM was found to be higher than mortality risk associated with CMM. This was unexpected, given that CMM was proposed to be more specific in assessing the complexity of individual healthcare needs.[21] A possible reason for this finding is that our and other studies focused on prevalence of CMM and not the severity of illness.[23 36] For example, as Harrison *et al* identified, those with mild chronic conditions affecting three body systems could have less healthcare needs than someone diagnosed with one severe chronic condition.[21] Also, the most prevalent MM and CMM combinations may not necessarily be the most severe. Another potential explanation for this finding could relate to cancer conditions being split and allocated by affected body system for CMM categorisation, rather than kept as a group. This meant those with cancer and other chronic conditions affecting less than three body systems were excluded from being categorised with CMM.

The finding MM was a better predictor of all-cause mortality risk than CMM suggests individuals with MM should be prioritised for intervention in clinical practice. That all-cause mortality risk was highest in the youngest age group (45–59 years) suggests tailored innovative healthcare interventions and better access to integrated care are needed for this age group; for example, the delivery of a nurse-led self-management programme for COPD in the context of MM implemented in Australian general practice.[37] A holistic approach is required for healthcare management of MM, involving shared decision-making and care coordination across all levels of the health system; particularly cardiovascular, respiratory, and mental health conditions, which were the most prevalent domains in our study. Though CMM was not a better predictor of mortality than MM in our analysis, this finding needs further exploration and confirmation. As suggested in another Australian study, CMM could be used to 'examine the relationship between the number of diagnosed chronic conditions/body systems affected and overall severity of illness, complexity of care and health resource utilisation'.[21]

The major strength of this study was our use of a large community-dwelling cohort of older adults which was not restricted only to those engaged with health services, thus providing a more realistic denominator. Recruitment of individuals across the age spectrum to the 45 and Up Study at baseline enabled us to assess the impacts of MM and CMM on mortality across that age range. Also, to our knowledge, this is the first analysis to compare the effect of MM versus CMM on mortality.

Our study had several limitations. Though the 45 and Up Study cohort has been shown to be generally representative of the population from which it is drawn, non-response at baseline may mean the cohort varies slightly from the broader population. However, studies with relatively low response rates provide similar estimates to the studies with higher response rate.[38] There were some other important confounding variables, such as functional disability that we were unable to adjust for, and thus residual confounding is possible. Self-reported chronic conditions were considered without any clinical diagnosis, so misclassification might occur. We defined CMM based on participants' self-reported chronic conditions in the 45 and Up Study and used the International Classification of Primary Care 2nd edition for classification of

Table 3 Impact of MM on 8-year mortality (from recruitment)

	N	py	Deaths (n)	Death rate per 1000 py	Crude HR (95% CI)	Adjusted HR* (95% CI)
Overall						
With no MM	140 605	1 093 798	9071	8.3	1	1
With MM	111 084	828 231	16 820	20.3	2.47 (2.40 to 2.53)	1.36 (1.32 to 1.40)
Age 45–59†						
With no MM	78 711	625 463	1219	1.9	1	1
With MM	37 374	294 385	1241	4.2	2.16 (2.00 to 2.34)	1.59 (1.46 to 1.73)
Age 60–74						
With no MM	46 290	361 559	2625	7.3	1	1
With MM	46 770	357 454	4757	13.3	1.84 (1.75 to 1.93)	1.49 (1.41 to 1.57)
Age 75+						
With no MM	15 604	106 775	5227	49.0	1	1
With MM	26 940	176 392	10 822	61.4	1.27 (1.23 to 1.31)	1.15 (1.11 to 1.19)

*Adjusted for sex, current working status, needing help with daily activities and good quality of life.
†P interaction <0.05, age versus MM status.
MM, multimorbidity; py, person-year.

disease, so it was not possible to classify the 11 chronic conditions reported in our study according to the exact body system, as in the clinically coded and single disease-focussed International Classification of Diseases, 10th Revision.

For example, treatment of cancer can affect the whole body, taking into account the side effects of anticancer drugs and radiotherapy; therefore, lung cancer (though not reported separately in our study) would have the potential to affect the body in more ways than can be categorised as a respiratory disease. Another limitation was that we considered only those chronic conditions which were listed in the baseline survey, but some other important chronic conditions, such as dyslipidaemia, chronic kidney disease, blood disorders and rheumatic diseases, which also increase the risk of mortality, were not included in this study. As a result, the effect of MM or CMM might be underestimated due to non-differential misclassification bias. However, an Australian study exploring the concordance between the 45 and Up Study baseline survey and administrative healthcare datasets found that over 70% of individuals classified as having MM were identified from the baseline survey.[28] A systematic review has also found that self-report is a valid method for capturing MM.[39] There might have been some losses to follow-up in our study cohort due to overseas or interstate migration, but

Table 4 Impact of CMM on 8-year mortality (from recruitment)

	N	py	Deaths (n)	Death rate per 1000 py	Crude HR (95% CI)	Adjusted HR* (95% CI)
Overall						
With no CMM	212 211	1 632 781	18 571	11.4	1	1
With CMM	39 478	289 248	7320	25.3	2.24 (2.18 to 2.30)	1.22 (1.18 to 1.25)
Age 45–59†						
With no CMM	105 367	835 879	1973	2.4	1	1
With CMM	10 718	83 970	487	5.8	2.46 (2.23 to 2.72)	1.49 (1.33 to 1.67)
Age 60–74						
With no CMM	75 473	585 544	5328	9.1	1	1
With CMM	17 587	133 469	2054	15.4	1.70 (1.61 to 1.79)	1.29 (1.22 to 1.36)
Age 75+						
With no CMM	31 371	211 358	11 270	53.4	1	1
With CMM	11 173	71 809	4779	66.6	1.26 (1.22 to 1.31)	1.08 (1.04 to 1.12)

*Adjusted for sex, current working status, needing help with daily activities and good quality of life.
†P interaction <0.05, age versus CMM status.
CMM, complex multimorbidity; py, person-year.

the estimated migration rate in 2011 in the NSW population was ~3%, which had unlikely to have any impact.[40]

Further research exploring patterns of healthcare use, such as uptake of primary care chronic disease management plans, between those with MM and CMM would provide better understanding of our findings. Survey data could be combined with other data sources (PBS, Medicare Benefits Schedule, general practice clinic records and hospital administrative datasets) to assess whether our findings can be replicated when diverse data sources and a more extensive list of chronic conditions are used. Conducting research to explore how these associations may differ across health service regions in NSW, particularly between urban and rural settings, would also be beneficial. This would enable us to determine what works and does not work when managing those with MM across different settings.

CONCLUSION

MM and CMM were common in this large population-based cohort study of older adults in NSW, Australia. Mortality among people in MM and CMM subgroups was high, with MM being a better predictor of all-cause mortality risk than CMM. However, further research is required with additional data on chronic conditions to confirm that MM is a better predictor for mortality than CMM. All-cause mortality risk being highest in the youngest age group (45–59 years) is an important finding which indicates the need for tailored, person-centred integrated care interventions and better access to holistic healthcare for this age group.

Author affiliations
[1]Centre for Primary Health Care and Equity, University of New South Wales, Sydney, NSW, Australia
[2]School of Population Health, University of New South Wales, Sydney, NSW, Australia
[3]Faculty of Health Sciences and Medicine, Bond University, Robina, QLD, Australia
[4]The Kirby Institute, University of New South Wales, Sydney, NSW, Australia
[5]Population and Community Health Directorate, South Eastern Sydney Local Health District, Sydney, NSW, Australia

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ORCID iDs
Alamgir Kabir http://orcid.org/0000-0002-3762-8307
Damian P Conway http://orcid.org/0000-0003-3316-2199

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