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## ORIGINAL ARTICLE

## EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

# Multimorbidity patterns, all-cause mortality and healthy aging in older English adults: Results from the English Longitudinal Study of Aging

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**Aim:** This study aimed to investigate the relationships between multimorbidity, healthy aging and mortality.

**Methods:** Using data from 9171 individuals aged  $\geq 50$  years at wave 2 and mortality data at wave 5 of the English Longitudinal Study of Aging, a multiple linear regression model and a Cox proportional hazards model were used to investigate how multimorbidity patterns (identified as cardiorespiratory/arthritis/cataracts, metabolic and relatively healthy) were associated with a composite index of healthy aging (derived from 41 intrinsic capacity and functional ability items) and with mortality.

**Results:** A total of 60% of the sample with multimorbidity had a moderate or high level of healthy aging. Both the cardiorespiratory/arthritis/cataracts group ( $n = 1826$ ) and the metabolic group ( $n = 844$ ) were negatively associated with healthy aging. The expected healthy aging index score decreased by 5.81 points (95% CI  $-6.69, -4.92$ ) for the first group, and by 2.39 points (95% CI  $-3.54, -1.24$ ) for the latter group. Only the cardiorespiratory/arthritis/cataracts group was positively associated with mortality. The risk of death for this group was 1.27-fold (95% CI: 1.14, 1.43) than the relatively healthy group. The relationship between multimorbidity patterns and mortality did not differ when considering levels of healthy aging.

**Conclusions:** Although it is not impossible for people with multimorbidity to age healthily, those with the most complex combination of diseases are at higher risk of death and have lower levels of healthy aging. *Geriatr Gerontol Int* 2020; ••: ••–••.

**Keywords:** chronic diseases, epidemiology, healthy aging, mortality, multimorbidity.

## Introduction

With advancements in healthcare and medicine, people worldwide are living longer.<sup>1</sup> By 2050, one in six people in the world will be aged  $>65$  years.<sup>2</sup> As age is a well-known risk factor of multiple

conditions, the growing aging phenomenon presents several challenges to population health globally.<sup>3</sup> The declines and losses in intrinsic capacity (e.g. physical and mental health functioning) associated with aging frequently manifest themselves in the form of multimorbidity (defined as two or more co-existing chronic

conditions).<sup>1</sup> One-third of the global population are living with multimorbidity,<sup>4</sup> and this is projected to rise by 2035.<sup>5</sup> Multimorbidity has been linked to adverse health outcomes, such as frailty,<sup>6</sup> disability<sup>7</sup> and mortality.<sup>8</sup> This exacerbates the burdens of disease management and healthcare costs.<sup>9</sup>

Nevertheless, aging is not synonymous with ill health. Health in older age goes beyond intrinsic capacity and includes functional ability, as well as the interaction between intrinsic capacity and the environment.<sup>1</sup> Healthy aging, thus, emerges as an attempt to conceptualise the health-related dimension of quality of life in older age.<sup>10</sup> This is described by the World Health Organization as “the process of developing and maintaining the functional ability that enables well-being in older age”.<sup>1</sup> A wide range of indices have recently been developed to measure this concept.<sup>11</sup> Commonly, these indices take the form of a continuous scale, capturing the whole spectrum of the aging process (where the higher the score, the healthier a person is deemed to be).<sup>11</sup>

Although multimorbidity is often perceived as a prognostic factor of unhealthy aging and mortality, there are people that cope well with multiple health conditions and therefore achieve satisfactory healthy aging.<sup>1</sup> Indeed, multimorbidity is not always associated with declined functional status, mortality or poorer quality of life.<sup>12</sup> It

was found that the impact of multimorbidity on healthy aging and mortality was determined not only by the number of co-existing conditions, but also by particular combinations of diseases and how they interact.<sup>1</sup> Evidence showed that certain conditions tend to cluster together more frequently than expected.<sup>13</sup> This is partly attributable to changes in immune functions associated with aging.<sup>1</sup> Further research also showed that some disease clusters were strongly associated with mortality and declined functioning in older individuals.<sup>14</sup> However, this association depended on the patterning of diseases (e.g. number, type).<sup>15</sup> The risk of death, for instance, was found to be higher in some clusters of diseases (e.g. heart failure, chronic renal failure or chronic obstructive pulmonary disease)<sup>16</sup> and lower in others (e.g. psychiatric, psychosomatic and pain-related disorders).<sup>17</sup> Furthermore, the association between multimorbidity and mortality was reported to become non-significant when disability or functional status were adjusted for.<sup>18</sup>

In the present study, we aimed to explore the interrelationship between multimorbidity with mortality and healthy aging. Our objectives were: (i) to assess how multimorbidity patterns were associated with (a) healthy aging and (b) mortality; and (ii) to evaluate whether healthy aging affected the relationship between multimorbidity patterns and mortality risk.

**Table 1** Sample characteristics

	Cardiorespiratory/arthritis/cataracts, <i>n</i> = 1826 (19.9%)	Metabolic, <i>n</i> = 844 (9.2%)	Relatively healthy, <i>n</i> = 6501 (70.9%)	Total, <i>n</i> = 9171
<b>Mortality status, <i>n</i> (%)</b>				
Dead	659 (36.1)	141 (16.7)	768 (11.8)	1568 (17.1)
Alive	1167 (63.9)	703 (83.3)	5733 (88.2)	7603 (82.9)
<b>Sex, <i>n</i> (%)</b>				
Male	779 (42.7)	495 (58.6)	2810 (43.2)	4084 (44.5)
Female	1047 (57.3)	349 (41.4)	3691 (56.8)	5087 (55.5)
<b>Age, <i>n</i> (%)</b>				
50–59 years	192 (10.5)	239 (28.3)	2494 (38.4)	2925 (31.9)
60–69 years	472 (25.8)	297 (35.2)	2151 (33.1)	2920 (31.8)
70–79 years	649 (35.5)	250 (29.6)	1304 (20.1)	2203 (24.0)
≥80 years	513 (28.1)	58 (6.8)	552 (8.5)	1123 (12.2)
<b>Education, <i>n</i> (%)</b>				
Higher	312 (17.1)	168 (19.9)	1756 (27.0)	2236 (24.4)
Intermediate	571 (31.3)	298 (35.3)	2546 (39.2)	3415 (37.2)
No qualification	943 (51.6)	378 (44.8)	2185 (33.6)	3506 (38.2)
<b>Quintile of net financial wealth, <i>n</i> (%)</b>				
Quintile 1 (lowest)	418 (22.9)	208 (24.6)	1082 (16.6)	1708 (18.6)
Quintile 2	444 (24.3)	158 (18.7)	998 (15.4)	1600 (17.4)
Quintile 3	374 (20.5)	161 (19.1)	1191 (18.3)	1726 (18.8)
Quintile 4	304 (16.6)	167 (19.8)	1316 (20.2)	1787 (19.5)
Quintile 5 (highest)	237 (13.0)	130 (15.4)	1473 (22.7)	1840 (20.1)
<b>Smoking status, <i>n</i> (%)</b>				
Smoker	1232 (67.5)	604 (71.6)	3895 (59.9)	5731 (62.5)
Non-smoker	544 (29.8)	235 (27.8)	2497 (38.4)	3276 (35.7)
<b>Drinking, <i>n</i> (%)</b>				
Regularly	384 (21.0)	200 (23.7)	2232 (34.3)	2816 (30.7)
Occasionally	624 (34.2)	346 (41.0)	2558 (39.3)	3528 (38.5)
Rarely/never	442 (24.2)	185 (21.9)	950 (14.6)	1577 (17.2)
<b>Physical exercise, <i>n</i> (%)</b>				
Sedentary	953 (52.2)	340 (40.3)	1514 (23.3)	2807 (30.6)
Moderate	675 (37.0)	399 (47.3)	3478 (53.5)	4552 (49.6)
High	144 (7.9)	103 (12.2)	1435 (22.1)	1682 (18.3)
<b>Healthy aging, mean (SD)</b>				
HAI score	41.7 (8.4)	47.2 (9.0)	51.8 (18.6)	49.4 (16.8)

Kruskal-Willis rank tests and *t*-tests *P*-values < 0.001. HAI, healthy aging index.

## Methods

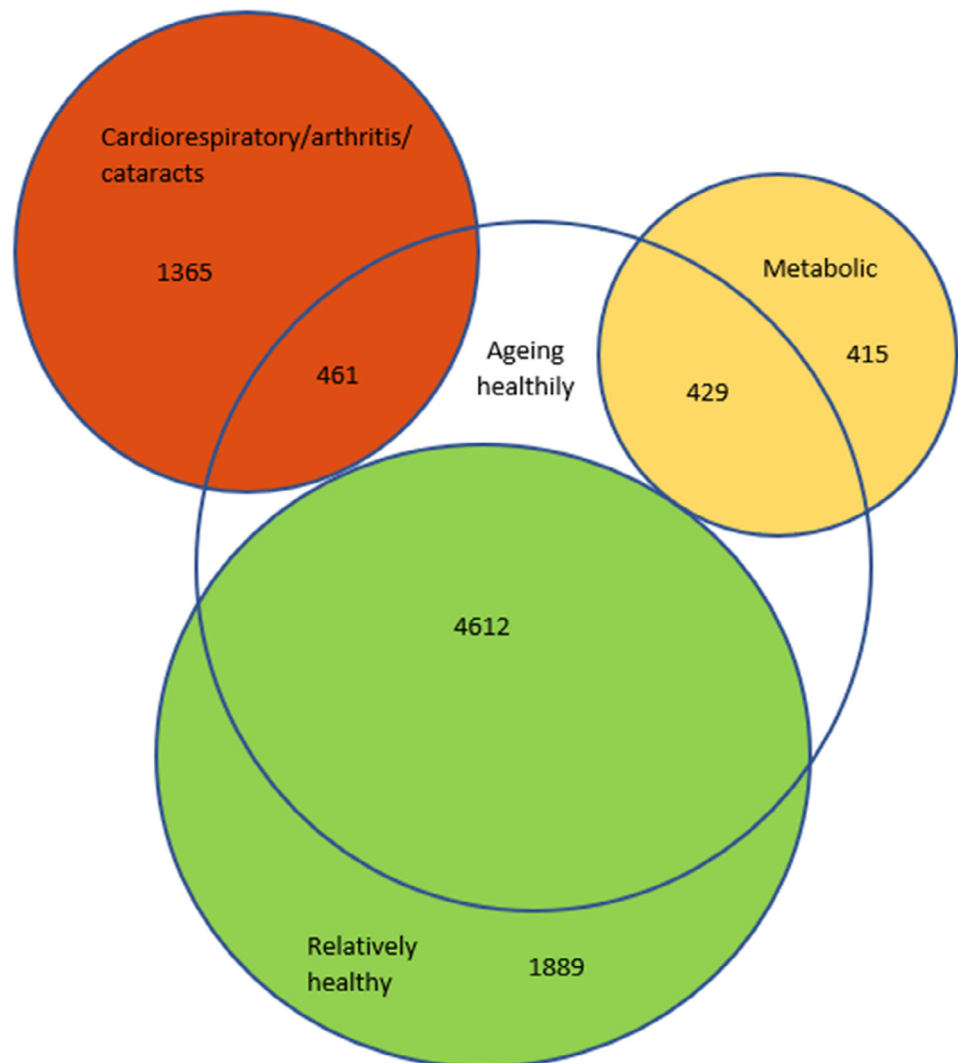
### Data and sample

The present study used data from wave 2 and mortality data at wave 5 of the English Longitudinal Study of Aging (ELSA), a panel study of a representative sample of men and women aged  $\geq 50$  years living in England.<sup>19</sup> The ELSA cohort profile has been described in detail elsewhere.<sup>19</sup> Briefly, the study commenced in 2002, and has been followed up every 2 years.<sup>19</sup> At wave 2 (2004/2005), the sample consisted of 9171 individuals (55.5% women) with an average age of 66.4 years (SD 10.3 years). Wave 2 was chosen as the baseline of the present study, as it included data from nurse visits, thus allowing for more conditions (e.g. chronic obstructive pulmonary disease, obesity, anemia, blood clotting disorders and dyslipidemia) to be considered. The mortality status of participants at wave 2 was assessed at wave 5 (2010/2011), when 10-year mortality data were gathered.

### Multimorbidity patterns

At wave 2, the presence or absence of a disease was assessed by the question “Has a doctor ever told you that you have/have had

any of the following diseases?”. Additional information obtained from objective measures during nurse visits were also included. To avoid potential bias caused by spurious association, we excluded diseases with prevalence  $< 1\%$ .<sup>17</sup> The total number of diseases included in our analysis was 26. These were hypertension, angina, heart murmur, myocardial infarction, heart arrhythmia, diabetes, stroke, asthma, chronic lung disease, chronic obstructive pulmonary disease, arthritis, osteoporosis, cancer, diabetic eye disease, cataracts, glaucoma, macular degeneration, dementia, obesity, anemia and iron deficiency, blood clotting disorder, psychiatric disorder, hyperlipidemia, hypertriglyceridemia, hypoalbuminemia, and high triglyceride/high density lipoprotein ratio. Each disease was coded as a dichotomous variable, where presence = 1 and absence = 0. Based on these 26 diseases, three patterns of multimorbidity were identified, using the latent class analysis method.<sup>20</sup> These included: (i) a relatively healthy group (71% of the sample) with the lowest prevalence in most diseases; (ii) a metabolic group (9% of the sample) with the highest prevalence in diabetes, hypertriglyceridemia, hypoalbuminemia and high triglyceride/HDL ratio; and (iii) a cardiorespiratory/arthritis/cataracts group (20% of the sample) with the highest prevalence in myocardial infarction, arrhythmia, chronic obstructive pulmonary disease, arthritis and cataracts.<sup>20</sup>



**Figure 1** Individuals with a high level of healthy aging by multimorbidity patterns. A high level of healthy aging observed in all three patterns of multimorbidity.

## Outcome variables

### Healthy aging

Healthy aging was measured using a healthy aging index (HAI) score developed by the Aging Trajectories of Health: Longitudinal Opportunities and Synergies (ATHLOS) project.<sup>21</sup> The HAI score was generated based on the ATHLOS harmonized dataset, which consisted of 16 general population longitudinal studies.<sup>21</sup> Item response theory modeling was used to comprise 41 items, covering various aspects of health and aging, such as mobility, sensory skills, cognition, vitality, psychological symptoms, activities of daily living and instrumental activities of daily living,<sup>22</sup> and estimated latent trait scores using the baseline data of all individuals aged  $\geq 18$  years. To provide straightforward interpretation of the results, the estimated latent trait scores were rescaled to a range from 0 (least healthy) to 100 (most healthy).<sup>22</sup> This healthy aging metric was computed across waves at an individual level for all participants in the 16 studies. The score at ELSA wave 2 was used for analyses. We determined levels of healthy aging by quintiles of the HAI score. Participants at ELSA wave 2 were categorized into five groups: Q1 ("very low level" of healthy aging), Q2 ("low level"), Q3 ("moderate level"), Q4 ("high level") and Q5 ("very high level").<sup>23</sup>

### Mortality

Information about vital status at wave 5 was collected from a number of sources e.g. interviews during fieldwork, communication

**Table 2** Cross-sectional association between multimorbidity patterns and healthy aging

	Unadjusted model ( <i>n</i> = 9171) coefficient (95% CI)	Adjusted for covariates ( <i>n</i> = 9171) coefficient (95% CI)
Multimorbidity patterns (Ref: relatively healthy)		
Cardiorespiratory/ arthritis/cataracts	-10.1 (-11.0, -9.3)	-5.8 (-6.7, -4.9)
Metabolic	-4.6 (-5.7, -3.4)	-2.4 (-3.5, -1.2)
Age		-0.1 (-0.2, -0.1)
Sex (Ref: female)		
Male		0.6 (-0.1, 1.2)
Education (Ref: degree level)		
Intermediate		-1.7 (-2.6, -0.9)
No qualification		-2.7 (-3.6, -1.7)
Net financial wealth (Ref: quintile 5 [richest])		
Quintile 1 (poorest)		-3.4 (-4.8, -2.1)
Quintile 2		-2.4 (-3.6, -1.1)
Quintile 3		-1.7 (-3.2, -0.3)
Quintile 4		-1.3 (-2.5, 0.1)
Smoking (Ref: non-smoker)		
Smoker		-1.5 (-2.1, -0.8)
Drinking (Ref: rarely/never)		
Regularly		1.9 (0.9, 2.9)
Occasionally		2.1 (1.2, 3.1)
Physical activity (Ref: High)		
Sedentary/low		-8.4 (-9.4, -7.4)
Moderate		-2.8 (-3.6, -1.9)

Adjusted and unadjusted linear regression models investigating the cross-sectional association between multimorbidity patterns and healthy aging. Results shown were derived from 10 imputed samples. Diagnostic tests for complete case models: mean variance inflation factor = 1.16, tolerance ranged between 0.82 and 0.91. No collinearity detected. 95% CI, 95% confidence interval; Ref, reference category.

from relatives and the National Health Service Central Register.<sup>20</sup> Respondents who did not consent to linking their data to the National Health Service Central Register (2.5% of the sample) participated in ELSA wave 5, and thus were determined as alive at this wave.

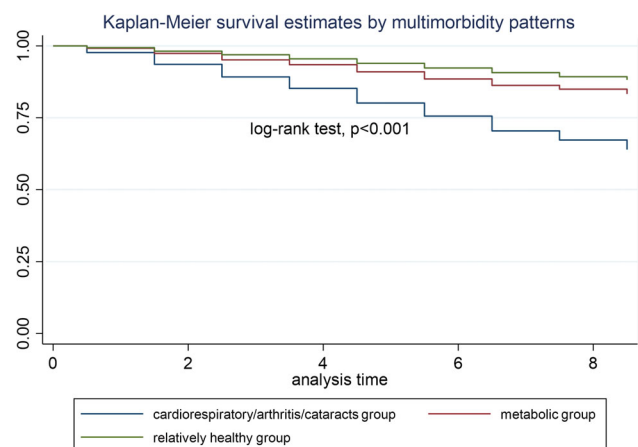
## Independent variables

The disease group variable, which represented multimorbidity patterns, was a key variable in our analyses. Drawing on evidence from recent research, we controlled for sex, age, education (higher, intermediate, no qualification), wealth (measured in quintiles with quintile 1 [Q1] being the lowest wealth and quintile 5 [Q5] the highest), smoking (ever/never smoke), drinking (regularly, occasionally, rarely/never) and physical activity (high, moderate, low/sedentary).<sup>24</sup>

## Statistical analysis

We visualized the relationship between multimorbidity patterns and healthy aging by plotting a Venn diagram to show the proportion of people who had multimorbidity, yet still had a high level of healthy aging (i.e. belonging to Q3–Q5 of the HAI quintiles). We then used a cross-sectional linear regression model with the HAI score at wave 2 as the outcome, and the disease group variable as a key predictor to examine how multimorbidity patterns were associated with healthy aging. Sociodemographic and lifestyle risk factors at wave 2 were also adjusted for.

To explore the association between multimorbidity patterns and mortality, a Cox proportional hazards regression model was used. The Cox proportional hazards regression model is a method for analyzing the time to the occurrence of an event (in this case death) based on longitudinal cohort data.<sup>25</sup> In the present study, participants were followed up from the time of the interview with a nurse during ELSA wave 2 (start date) until the earliest of year of death, dropout year or year of the wave 5 interview (end date). The time to death was calculated as the difference between the year of death and the year of baseline interview. Mortality risk, expressed as hazard ratios, was compared between different groups of individuals based on their patterns of multimorbidity. We used the relatively healthy group as the reference, as it was the lowest risk and largest sized group. The model was run initially



**Figure 2** Kaplan–Meier survival estimates by multimorbidity patterns. Risk of death was highest in the cardiorespiratory/ arthritis/cataracts group, and lowest in the relatively healthy group. *P*-value <0.001 for log-rank test.



with only the disease group variable as the predictor, and then extended to include sociodemographic and lifestyle risk factors. Next, we included the HAI quintiles in the model to investigate how multimorbidity patterns and healthy aging together might affect mortality, adjusting for covariates. Finally, we added an interaction term between disease groups and the HAI quintiles to test whether the mortality risk in each group of diseases differed by their levels of healthy aging.

Multiple imputation (10 datasets) using chained equations was applied to missing data, assuming missing-at-random. A sensitivity analysis was carried out to compare results between complete case analysis and multiple imputation. Both the multiple linear regression and the Cox proportional hazards models, as well as multiple imputation using chained equations, were carried out using Stata 15 (StataCorp, College Station, TX, USA).<sup>26</sup>

## Results

### Sample characteristics

Table 1 shows that from 9171 individuals at baseline, 1568 people (51% men) had died by wave 5. Of these 1568 deceased individuals, 36.1% belonged to the cardiorespiratory/arthritis/cataracts group, 16.7% belonged to the metabolic group and 11.8% belonged to the relatively healthy group. The cardiorespiratory/arthritis/cataracts group had the highest proportion of older (i.e. aged  $\geq 70$  years) and physically inactive people (63.6% and

52.2%, respectively) with the lowest HAI score (mean 41.7, SD 8.4). The metabolic group had the highest proportion of smokers (71.6%) and people with limited wealth (24.6%). The relatively healthy group had the highest percentage of regular drinkers (34.3%).

### Multimorbidity patterns and healthy aging

A total of 25.2% of the cardiorespiratory/arthritis/cataracts group had a high level of healthy aging. These proportions were 50.8% for the metabolic group and 70.9% for the relatively healthy group (Fig. 1)

Results from Table 2 show that multimorbidity patterns were negatively associated with healthy aging. In the unadjusted model, compared with the relatively healthy group, the cardiorespiratory/arthritis/cataracts group had a lower HAI score by 10.11 points (95% CI  $-10.96$ ,  $-9.26$ ), whereas the difference was 4.56 points (95% CI  $-5.73$ ,  $-3.38$ ) in the metabolic group. When socio-demographic and lifestyle covariates were adjusted for, the expected HAI score decreased by 5.81 points (95% CI  $-6.69$ ,  $-4.92$ ) for the cardiorespiratory/arthritis/cataracts group and 2.39 points (95% CI  $-3.54$ ,  $-1.24$ ) for the metabolic group.

### Multimorbidity patterns and mortality

Figure 2 shows that the probability of being alive at wave 5 was lowest for the cardiorespiratory/arthritis/cataracts group. The risk

**Table 3** All-cause mortality as a function of multimorbidity and healthy aging

	Unadjusted model HRs (95% CI)(n = 9171)	Adjusted model (without HAI quintiles) HRs (95% CI)(n = 9171)	Adjusted model (with HAI quintiles) HRs (95% CI)(n = 9171)
Multimorbidity patterns (Ref: relatively healthy)			
Cardiorespiratory/arthritis/cataracts	3.5 (3.2–3.9)	1.5 (1.3–1.7)	1.3 (1.1–1.4)
Metabolic	1.5 (1.2–1.7)	1.1 (0.9–1.3)	1.0 (0.8–1.2)
Age		1.1 (1.1–1.1)	1.1 (1.0–1.1)
Sex (Ref: female)			
Male		2.2 (1.7–2.7)	2.2 (1.8–2.8)
Education (Ref: degree level)			
Intermediate		1.0 (0.8–1.1)	0.9 (0.8–1.1)
No qualification		1.1 (0.9–1.2)	1.0 (0.9–1.2)
Net financial wealth (Ref: quintile 5 – richest)			
Quintile 1 (poorest)		1.4 (1.1–1.6)	1.2 (1.0–1.5)
Quintile 2		1.2 (1.0–1.4)	1.1 (0.9–1.3)
Quintile 3		1.2 (1.0–1.5)	1.2 (1.0–1.4)
Quintile 4		1.0 (0.8–1.2)	1.0 (0.8–1.2)
Smoking (Ref: non-smoker)			
Smoker		1.4 (1.2–1.6)	1.3 (1.2–1.5)
Drinking (Ref: rarely/never)			
Regularly		0.9 (0.7–1.0)	0.9 (0.8–1.0)
Occasionally		0.8 (0.7–0.9)	0.8 (0.7–0.9)
Physical activity (Ref: High)			
Sedentary/low		5.8 (3.3–10.4)	4.5 (2.5–8.0)
Moderate		2.4 (1.3–4.3)	2.2 (1.2–4.0)
HAI quintiles (Ref: quintile 5 – highest level of healthy aging)			
Quintile 1			2.6 (2.1–3.4)
Quintile 2			1.9 (1.5–2.5)
Quintile 3			1.6 (1.3–2.1)
Quintile 4			1.2 (0.9–1.5)

Unadjusted and adjusted Cox proportional hazards regression models investigating mortality risk (hazard ratios [HRs], with 95% confidence interval [CI]) over a 10-year period among older adults in different groups of multimorbidity and healthy aging. Results shown were derived from 10 imputed samples. HAI, healthy aging index; Ref, reference category.

of death for the metabolic group was similar to that of the relatively healthy group for the first 2.5 years. After this period, it declined, but was still higher than the cardiorespiratory/arthritis/cataracts group.

Results from the Cox regression showed that in the unadjusted model, mortality risk was 3.49-fold higher (95% CI 3.15–3.87) among the cardiorespiratory/arthritis/cataracts group, and 1.45-fold higher (95% CI 1.21–1.74) among the metabolic group, compared with the relatively healthy group. When sociodemographic and lifestyle covariates were added to the model, the hazard ratio of the metabolic group became non-significant, and the risk of death among the cardiorespiratory/arthritis/cataracts group was reduced, but still higher by 1.50-fold (95% CI 1.34–1.68) than the reference group (Table 3).

### ***Effect of multimorbidity patterns and healthy aging on mortality***

The hazard ratio for the cardiorespiratory/arthritis/cataracts group decreased to 1.27 (95% CI 1.14, 1.43) when adjusted for the HAI quintiles. The mortality risk among people with the lowest level of healthy aging was 2.64-fold higher (95% CI 2.05–3.40) than those in the highest HAI quintile. The interaction between disease groups and HAI quintiles was non-significant, meaning mortality in each disease group did not differ by the level of healthy aging. The interaction term was therefore dropped. Table 3 shows results from the full model. Sensitivity analysis showed that the results in Tables 2 and 3 were comparable with those obtained from complete case analysis (Table S1).

## **Discussion**

In the present study, we described the association of multimorbidity patterns with healthy aging and mortality. We also examined whether the effect of multimorbidity patterns on healthy aging influenced mortality. The present findings showed that both the cardiorespiratory/arthritis/cataracts and metabolic groups were negatively associated with healthy aging, but only the former was positively associated with mortality. In both of our multiple linear regression and Cox proportional hazard models, the cardiorespiratory/arthritis/cataracts group was the group with the strongest magnitude of association with healthy aging and the highest mortality risk. This could probably be because this group consisted of older people (>60% were aged  $\geq 70$  years) who already had low HAI score at baseline. Furthermore, it was the most complex multimorbidity pattern, both in terms of treatment and self-management. This hypothesis seemed to be supported by findings in other studies, where a similar trend (i.e. higher mortality and poorer health status were associated with complex multimorbidity) was observed.<sup>27</sup>

That being said, we also found that in our sample, a large proportion of participants with multimorbidity actually had a high level of healthy aging. In fact, even within the most complex multimorbidity group, 25% of the people were still considered to age relatively healthily. This finding supports the claim that people with multimorbidity are a heterogeneous group, in terms of the number and type of diseases that they experience, as well as their healthy aging capital (preservation of intrinsic capacity, functional ability and wellbeing).<sup>3</sup>

Although we found that the lower the level of healthy aging, the higher the risk of death, healthy aging had no modulatory influence on the association between multimorbidity patterns and mortality. This was evident by the non-significant interaction between multimorbidity patterns and healthy aging quintiles. Instead, it seemed healthy aging had a mediating effect on the multimorbidity

patterns–mortality relationship. This mediating effect appeared to be partial for the cardiorespiratory/arthritis/cataracts group (illustrated by a decreased hazard ratio when adjusted for HAI quintiles), and complete for the metabolic group (hazard ratio became non-significant). This supported our hypothesis that healthy aging lies on the causal pathway between multimorbidity patterns and mortality.

The present study was carried out on a national representative sample of people aged  $\geq 50$  years, and included a wide range of diseases and sociodemographic covariates. The HAI score was constructed using a harmonized dataset from different longitudinal cohorts, allowing for comparisons across age groups. It has been tested on multiple datasets, and showed high validity and reliability.<sup>11</sup> The HAI was a distinctive approach to conceptualize and measure healthy aging. It was different from other methods that also attempted to assess health status in the geriatric population, such as the frailty phenotype<sup>28</sup> and the frailty index.<sup>29</sup> Unlike the frailty phenotype, the HAI did not focus solely on biological and physiological declines in health functioning (e.g. unintentional weight loss, self-reported exhaustion and weakness).<sup>28</sup> The HAI measured healthy aging as a latent construct and accounted for measurement errors, allowing for different patterns in participants' responses to observed items. The item response theory method used to create the HAI score was also more sophisticated and had more statistical power than other approaches used in indices for frailty/deficit accumulation, where age-related abnormalities and impairments were simply summed up. It did not include a disease component, which was one of the items embedded in the frailty index; thus, was a more appropriate measure to use alongside multimorbidity, as the issues with collinearity were eliminated.<sup>29</sup>

However, the HAI score did not include the affective dimension of healthy aging, such as emotional well-being and stability. The cross-sectional design of the present study did not allow causality inference, and although the relationship between multimorbidity and healthy aging is believed to be bidirectional, in the present study we hypothesized that multimorbidity preceded healthy aging.<sup>30</sup> We did not assess the patterns of multimorbidity longitudinally. Patterns of multimorbidity might not be stable over time. For instance, individuals from the relatively healthy group might develop conditions that place them in either the metabolic group or the cardiorespiratory/arthritis/cataracts group. Equally, those from the metabolic group could move into cardiorespiratory/arthritis/cataracts group and vice versa. This might influence the risk of mortality. Additionally, our sample included only individuals aged  $\geq 50$  years; thus, the findings presented here could not be generalized to younger age groups. Finally, there might be residual confounding that had not been accounted for in the present study, which might affect the findings. The present results, therefore, should be interpreted with these caveats in mind.

To conclude, we have shown that multimorbidity patterns were associated with healthy aging. Complex multimorbidity, such as the cardiorespiratory/arthritis/cataracts group, was also associated with mortality. Although there were people who achieved a high level of healthy aging while living with multimorbidity, healthy aging had no modification effect on the association of multimorbidity patterns and mortality. By identifying which group of diseases had the highest risk of death and lowest HAI score, we could offer insights into burdens of diseases and provide a starting point for further research to explore possible solutions to these problems.

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## Disclosure statement

The authors declare no conflict of interest.

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## Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's website:

### Appendix S1 Supporting information

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