Aging Clinical and Experimental Research (2025) 37:250
https://doi.org/10.1007/s40520-025-03150-0

RESEARCH

Multimorbidity patterns and mortality in older adults: a two-cohort pooled analysis

Cecilia Damiano[1] · Simona Costanzo[2] · Benedetta Marcozzi[1] · Teresa Panzera[2] · Chiara Donfrancesco[1] · Augusto Di Castelnuovo[2] · Cinzia Lo Noce[1] · Sara Magnacca[2] · Federico Triolo[3] · Maria Beatrice Zazzara[4,5] · Luigi Palmieri[1] · Licia Iacoviello[2,6] · Graziano Onder[4,5] · Davide Liborio Vetrano[3,7] · for the BIO-SIGN Study Investigators

Received: 16 July 2025 / Revised: 28 July 2025 / Accepted: 29 July 2025

Abstract

Background Different multimorbidity patterns can affect health trajectories and influence survival.

Aims We investigated their association with mortality in two population-based cohorts of older adults.

Methods Two Italian cohorts of randomly selected individuals (60–79 years old) from general population: CUORE (baseline 2008–2012) and Moli-sani (baseline 2005–2010). Latent Class Analysis used to identify homogeneous groups of multimorbid individuals (≥2 diseases) with similar underlying disease patterns. Cox regression models used to assess the association of multimorbidity patterns and all-cause mortality (end of follow-up 12/31/2019). Results pooled in a random-effects meta-analysis.

Results Total samples of 3,695 individuals in CUORE (48% male, mean age 68.8 years [SD 5.6]) and 7,801 in Moli-sani (51% male, mean age 68.2 years [SD 5.4]). In both cohorts, six multimorbidity patterns were identified and named after their overexpressed diseases: *hypercholesterolemia; metabolic*, *depression and cancer; cardiometabolic and respiratory; gastrointestinal*, *genitourinary and depression; respiratory; unspecific* (i.e., no diseases overexpressed). Overall mortality rates were 1.66 per 100 person/years in CUORE and 1.85 per 100 person/years in Moli-sani. Compared to the multimorbidity-free group (<2 diseases), individuals displaying a *cardiometabolic and respiratory* pattern showed the highest mortality (pooled HR 2.62, 95% CI 2.15–3.10), followed by *unspecific* (pooled HR 1.45, 95% CI 1.21–1.68), *respiratory* (pooled HR 1.33, 95% CI 1.01–1.64) and *gastrointestinal*, *genitourinary and depression* (pooled HR 1.33, 95% CI 1.06–1.60).

Discussion Multimorbidity patterns in older adults are differentially associated to shorter survival.

Conclusions Their identification may help optimize clinical management by improving risk stratification, allowing for more targeted prevention and intervention strategies.

Keywords Survival · Personalized medicine · Chronic disease · Population-based study

Cecilia Damiano and Simona Costanzo contributed equally to the work and share the first authorship.

Graziano Onder and Davide Liborio Vetrano contributed equally to the work and share the last authorship.

✉ Cecilia Damiano
cecilia.damiano@iss.it

1 Department of Cardiovascular, Endocrine-Metabolic Diseases and Aging, Istituto Superiore di Sanità, Rome, Italy

2 Research Unit of Epidemiology and Prevention, IRCCS Neuromed, Pozzilli, Italy

3 Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden

4 Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

5 Department of Aging, Orthopaedics and Rheumatological Sciences, Università Cattolica del Sacro Cuore, Rome, Italy

6 Department of Medicine and Surgery, LUM University, Casamassima, Bari, Italy

7 Stockholm Gerontology Research Center, Stockholm, Sweden

Published online: 20 August 2025

Background and objectives

Multimorbidity is an unintended consequence of the modern achievements of biomedicine and public health. The effective treatment of previously lethal non-communicable diseases (e.g., heart disease, respiratory conditions, stroke, cancer) has turned them into conditions with a chronic course and progression, especially among older adults. As life expectancy rises, so does the prevalence of multimorbidity–defined as the coexistence of two or more chronic conditions within an individual [1]. Multimorbidity has become a key public health challenge, particularly in high-income countries, where it can be detected in up to 9 in 10 older individuals, and where healthcare systems are increasingly strained by the complex needs of an aging population [2]. The accumulation of chronic diseases over time is often accompanied by the onset of functional impairments—both cognitive and physical—that further contribute to disability, dependence, and increased mortality risk [2]. This translates into higher healthcare costs due to frequent hospitalizations, prolonged treatment regimens and the need of long-term care [1].

Chronic diseases do not occur randomly but tend to cluster in specific patterns within individuals. These multimorbidity patterns have been shown to influence the risk of various outcomes, including frailty, dementia, depression, disability, institutionalization, hospitalization, and mortality [3–9]. Understanding these patterns holds promise for improving risk stratification in older adults, allowing for more targeted prevention and intervention strategies. By identifying individuals at higher risk for adverse outcomes, healthcare providers may arguably tailor interventions to improve the aging process, delay the onset of disability and dependence, and ultimately increase health span.

Despite the growing body of literature on multimorbidity patterns, there remains a need for more rigorous and reliable methods to define and categorize these patterns in clinically meaningful ways [4]. Current research has yet to establish a universally accepted framework for identifying multimorbidity patterns that are stable and predictive across diverse populations. The heterogeneity of multimorbidity and its varied manifestations across different demographic groups further complicate the development of standardized approaches. Thus, it is essential to validate these patterns in various population-based cohorts to strengthen their clinical relevance and utility.

The present study aims to investigate the association between multimorbidity patterns and mortality in two Italian population-based cohorts of older adults. By exploring how specific clusters of chronic conditions relate to mortality risk, this research seeks to contribute to the growing understanding of multimorbidity as a critical determinant of health outcomes in aging populations. Furthermore, by analysing data from two cohort studies, we aimed to test a possible standardized analytical approach to defining multimorbidity patterns that could be applied across diverse populations. Besides, replication of the analyses across samples from different cohorts and geographic areas is critical for checking the robustness of the study results. The findings may provide valuable insights for developing more effective strategies to manage multimorbidity and improve the quality of life of older adults.

Research design and methods

Study design and population

This study is part of the project "Identification of Biomarker signatures of multimorbidity patterns for the development of an innovative and multidimensional tool to assess individual health risks" (BIO-SIGN), funded by the Italian Ministry of Health (grant number PNRR-MAD-2022-12376569; cup C52C22001120007). The project is based on the hypothesis that biological, clinical, environmental and behavioural factors interact in the definition of multimorbidity clusters and the determination of their severity and the effect of these factors on longitudinal outcomes can differ between multimorbidity patterns. Aim of the project is to assess the interaction of novel biomarkers, environmental, behavioural, clinical factors in the definition of specific multimorbidity patterns and in the determination of their severity.

We conducted this observational prospective analysis based on data from two Italian cohorts randomly selected from the resident population: the CUORE Project (from now on referred to as CUORE) and the Moli-sani study (from now on referred to as Moli-sani).

For CUORE, we considered the Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey 2008–2012 (OEC/HES 2008–2012) cohort, composed of participants aged between 35 and 79 years, randomly enrolled from the general population residing in all the regions of the national territory (N=8,696; 50% men). The aim of the Italian OEC/HES 2008–2012 was to provide a comprehensive picture of the adult population health by evaluating lifestyles and risk factors for major non-communicable diseases. Standardized procedures and methods were used for sample recruitment and measurements, as described in detail elsewhere [10]. The survey was conducted by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) and was implemented with the collaboration of the national scientific association of hospital cardiologists (ANMCO, Associazione Nazionale Medici Cardiologi Ospedalieri) and its foundation (Fondazione per il Tuo cuore– Heart Care Foundation). The survey was approved by the ethics committee of ISS and written informed consent was signed by all participants. The survey is included in the Italian National Statistical Program.

Moli-sani consists of a large, prospective cohort aged over 35 years that was randomly recruited from the general population of the Molise region in Southern Italy between 2005 and 2010 (N=24,325; 48% men). The main aim of Moli-sani was to investigate environmental and genetic determinants of major non-communicable diseases — such as cardiovascular disease (CVD), cancer, and neurodegenerative diseases — and mortality. The study complies with the Declaration of Helsinki and was approved by the Catholic University Ethical Committee in Rome, Italy. All participants provided written informed consent. Study design has been described previously [11, 12].

For the present study, we restricted the analyses to participants aged 60–79 years, as multimorbidity mostly impacts in older age. Figure 1 shows the flow-charts of sample selection in both cohorts.

Chronic diseases and covariates assessment

Similar approaches were used in the CUORE and Moli-sani studies to collect data on medical history, socio-demographic characteristics, and lifestyle information. Additionally, laboratory tests for both studies were conducted in the same center using standardized analytical methods and instruments [10]. Specific instrumental assessments were carried out, including blood pressure measurement, anthropometrics, and laboratory tests. A rigorous process of harmonization was carried out and any critical issues were identified and resolved, to ensure consistency and comparability between the two datasets and minimize the heterogeneity of the data, strengthening the robustness of the results.

In both cohorts, disease information was collected through extensive face to face questionnaires, based on self-reported information. Disease definition and operationalization was based on the methodology proposed by Calderón-Larrañaga and colleagues, and included self-reported information, use of specific drugs univocally linked to given diseases and laboratory tests [13]. For the present study, 42 chronic diseases were retrieved in both cohorts, and fitted into the above-mentioned categories (for details on the diagnostic criteria considered, see Supplementary Table 1 A and Supplementary Table 1B in the Supplement). Any critical issues due to the adoption of a different definition for given disease were resolved upon discussion, and the use of the same information source across the two cohorts was privileged to maximize comparability. In order to avoid statistical noise [4], diseases with a prevalence of less than 5% were aggregated into 4 homogeneous bigger categories, based on pathophysiological commonalities. Details of this aggregation can be found in Supplementary Table 2. Finally, a total of 33 chronic diseases were considered to identify the multimorbidity patterns (Table 1).

Baseline information on sex and age were derived from the registry offices. Through the administered questionnaires we derived information on educational level (none/primary school, secondary school or post graduate), marital status (partnered or unpartnered), area of residence (urban or rural environments defined considering the urbanization level descripted by the European Institute of Statistics [EUROSTAT] and obtained by the 'Atlante Statistico dei Comuni' provided by the Italian National Institute of Statistics [ISTAT] [14]), smoking habit (non-smoker or current/

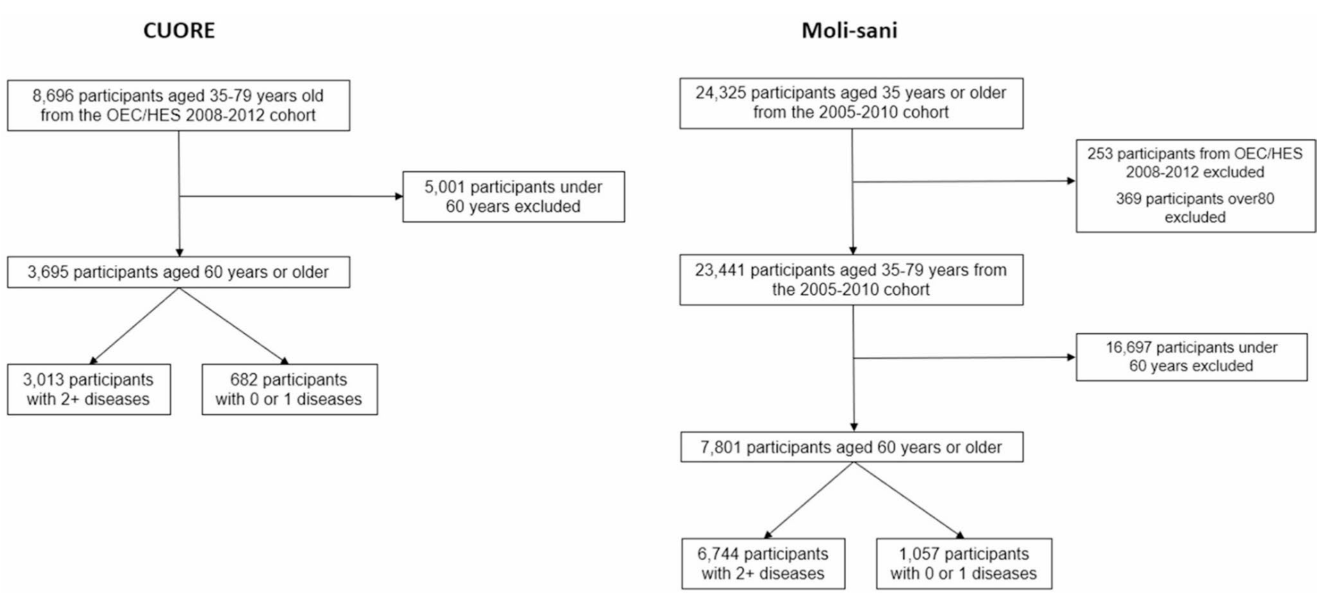

Fig. 1 Flow-charts of sample selection in CUORE and Moli-sani

Table 1 List of the 33 chronic diseases considered for the definition of Multimorbidity patterns by mean of latent class analysis

Allergy	Depression and other psychiatric behavioural disease[a]	Migraine facial pain syndrome
Anaemia	Diabetes	Obesity
Asthma	Epilepsy	Osteoporosis
Atrial fibrillation	Gastrointestinal disease[b]	Other cardiovascular disease
Bradycardias conduction disease	Genitourinary disease[c]	Other metabolic disease
Cardiac valve disease	Glaucoma	Other respiratory disease
Cerebrovascular disease	Heart failure	Parkinson-parkinsonism
Chronic infectious disease	Hypercholesterolemia	Peripheral neuropathy
Chronic kidney disease	Hypertension	Peripheral vascular disease
Chronic obstructive pulmonary disease (COPD)	Inflammatory/Autoimmune Disease[d]	Solid or haematological neoplasms
Dementia	Ischemic heart disease	Thyroid disease

Note. Diseases having a prevalence<5% that were aggregated into macro-categories: [a]Depression and other psychiatric behavioural disease: Depression and mood disorders, Other psychiatric and behavioural diseases; [b]Gastrointestinal disease=Colitis related disease, Esophagus stomach duoden disease, Chronic pancreatitis and gallbladder disease, Other digestive disease, Chronic liver disease; [c]Genitourinary disease: Prostate disease, Other genitourinary disease; [d]Inflammatory/Autoimmune Disease: Autoimmune disease, Inflammatory arthropathies, Inflammatory bowel diseases, Multiple sclerosis

former smoker), alcohol habit (non-drinker/former drinker, light-moderate drinker or heavy drinker), leisure time physical activity (reading/watching tv, walking/cycling, playing sports or competitive training).

Outcome definition

Death due to any cause was the outcome of interest and the end of follow-up was set to 12/31/2019. Follow-up was limited to this date to avoid recording deaths occurred during the SARS-CoV-2 pandemics. To retrieve the date of death of CUORE deceased participants, individual data on mortality owned by ISTAT were record linked on a yearly base to the CUORE dataset. For Moli-sani, deaths occurred during follow-up were ascertained through individual-level record linkage to the Molise regional register of deaths (ReNCaM: "Registro Nominativo delle Cause di Morte") and validated using Italian death certificates (ISTAT form).

Statistical analysis

Multimorbidity patterns definition

We applied Latent Class Analysis (LCA) to identify homogenous groups of individuals sharing similar multimorbidity patterns. LCA is an explanatory technique that, starting from a set of observed variables, identifies latent groups with similar characteristics. Specifically, LCA estimates for each subject the probability of being in each class and subsequently assigns them to the group for which they show the highest probability of belonging [15, 16]. The optimal number of latent classes, also referred to as multimorbidity patterns from here on, was defined using the Bayesian information criterion (BIC) and the adjusted BIC, which have proven to be reliable model selection criteria with categorical variables [17–19]. These two criteria were considered to compare data fitness of different numbers of classes in both samples, with lower values suggesting better fit of the model. To characterize the patterns, we used the observed/expected ratios (O/E ratios), which compare the frequency of a disease in a given class with respect to the one of the total study population. Moreover, we calculated disease exclusivity defined as the ratio between the number of disease cases in a class and the total number of individuals affected by that disease in the population. Diseases with both an exclusivity≥25% and an O/E ratio≥2 were considered over-expressed and subsequently used to name the patterns accordingly. The class models with the best fit to the data were assessed in terms of clinical plausibility based on expert judgement and evidence from the literature within each sample; the class solution that appeared to be most meaningful based on these criteria was used to classify participants in the other sample as well. LCA was performed using the statistical software R (version 4.2.0 and poLCA package from version 1.4.1).

Survival analysis

The incidence rates (IRs) of all-cause mortality were calculated both overall and by multimorbidity pattern (events per 100 person-years). To evaluate the risk of all-cause mortality among multimorbidity patterns, we used Cox proportional hazards regression models to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs), considering participants who had one or no disease– no multimorbidity– as the reference group. Models were adjusted for relevant confounders including age, sex, education, smoking habit, leisure-time physical activity, and alcohol habit. The covariates included in the models were chosen in light of their potential role as confounders in the association between multimorbidity patterns and all-cause mortality. Follow-up period consisted of the time from the enrolment to the date of death or end of follow-up, whichever occurred first. Participants with missing values for the covariates included in the models were retained in the analysis and possible missing values were treated as an additional category for the respective variable. Additional sensitivity analyses were performed excluding those having missing values for the covariates of interest. Statistical analyses were performed using R (version 4.2.0) and SAS (version 9.4). Finally, we used random-effects meta-analyses to estimate the pooled results for the associations between multimorbidity patterns and all-cause mortality in CUORE and Moli-sani; this analysis was performed using Stata (version 18.0).

Results

Characteristics of the samples

The analytical samples consisted of 3,695 participants from CUORE and 7,801 from Moli-sani. In the two cohorts, the proportion of participants with two or more diseases was of 81.5% and 86.5%, respectively. Descriptive characteristics across multimorbidity patterns are shown in Table 2 (for information on sample characteristics of the overall samples, see Supplementary Table 3). Mean age was 68.8 (SD 5.6) years in CUORE and 68.2 (SD 5.4) years in Moli-sani. The proportion of males in the two samples was comparable, being 48.2% and 51.2%, respectively. Participants mostly had a low education level (46.2% in CUORE, 54.3% in Moli-sani), lived in urban areas (82.0% and 66.4%), were partnered (73.4% and 81.7%) and non-smokers (53.4% and 52.1%). Mean body mass index (BMI; 28.5 kg/m^2 [SD 4.8] in CUORE and 29.1 kg/m^2 [SD 4.7] in Moli-sani) and mean number of diseases (approximately 3 diseases per participant) were similar, while the average number of drugs was 2.5 (SD 2.4) in CUORE and 1.8 (SD 1.7) in Moli-sani.

Multimorbidity patterns identification and their characteristics

The six-class solution derived from Moli-sani was found to be the most meaningful in terms of clinical plausibility and evidence from the literature (Supplementary Tables 4 and Supplementary Fig. 1). As such, we applied those weights of Moli-sani to CUORE for participants' classification. The identified multimorbidity patterns were named as follows: (1) *hypercholesterolemia pattern* (33.2% in CUORE, 26.4% in Moli-sani); (2) *metabolic*, *depression and cancer pattern* (12.7% and 10.9%); (3) *cardiometabolic and respiratory pattern* (5.2% and 6.3%); (4) *gastrointestinal*, *genitourinary and depression pattern* (6.3% and 8.5%); (5) *unspecific pattern* (i.e. no disease overexpressed, 18.1% in CUORE and 30.0% in Moli-sani); (6) *respiratory pattern* (6.1% and 4.4%). For the prevalence of single conditions within each multimorbidity pattern, see Supplementary Tables 5 A-B. Participants with no multimorbidity were 18.5% in CUORE and 13.5% in Moli-sani. When comparing study participants across multimorbidity patterns in both samples (Table 2), those in the *cardiometabolic and respiratory pattern* tended to be older and have higher number of diseases and drugs. The highest frequency of low level of education was observed in the *respiratory pattern*, while the *metabolic*, *depression and cancer pattern* showed the highest frequency of unpartnered people. The highest mean BMI was observed in the *unspecific pattern*, which also had a low mean number of diseases (the lowest, excluding those with no multimorbidity). Finally, as for smoking and alcohol habit, current/former smokers were most present in the *cardiometabolic and respiratory pattern*, while heavy drinkers were most present in the *hypercholesterolemia pattern* in Moli-sani and in the *metabolic*, *depression and cancer pattern* in CUORE.

Association with all-cause mortality

During the follow-up, a total of 544 deaths were recorded in CUORE (IR: 1.66 per 100 person-years; median follow-up: 9 years [IQR 8–10 years]), while 1,638 deaths occurred in Moli-sani (IR: 1.85 per 100 person-years; median follow-up: 12 years [IQR 11–13 years]). IRs varied across multimorbidity patterns (Table 3), with the *cardiometabolic and respiratory pattern* showing the highest (IR 4.56 in CUORE and 5.33 in Moli-sani) and the *metabolic*, *depression and cancer pattern* showing the lowest (IR 1.33 in CUORE and 1.22 in Moli-sani). The proportional hazards assumption of the Cox models was tested using both the Schoenfeld residual test and graphical assessment. The proportional hazards assumption was respected. Figure 2 shows results of the random-effects meta-analyses, combining findings from CUORE and Moli-sani using HR (95% CI) obtained from the multivariable Cox regression analyses. Across multimorbidity patterns, the risk of all-cause mortality for each cluster, compared to the multimorbidity-free group, was found to be very similar between the two cohorts. The meta-analyses identified four multimorbidity patterns associated with a higher risk of all-cause mortality: the *cardiometabolic and respiratory pattern* showed the highest mortality risk (pooled HR 2.62, 95% CI 2.15–3.10) followed by the *unspecific pattern* (pooled HR 1.45, 95% CI 1.21–1.68), the *respiratory pattern* (pooled HR 1.33, 95% CI 1.01–1.64), and the *gastrointestinal*, *genitourinary and depression pattern* (pooled HR 1.33, 95% CI 1.06–1.60).

Table 2 Participants' baseline characteristics across Multimorbidity patterns in CUORE and Moli-sani

	No multimorbidity		Hypercholesterolemia		Metabolic, depression, cancer		Cardiometabolic, respiratory		Gastrointestinal, genitourinary, depression		Unspecific		Respiratory	
Characteristics[a]	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani
Number of participants	682	1,057	1,225	2,063	471	852	191	488	234	660	667	2,339	225	342
Age, mean (SD), y	66.8 (5.4)	66.9 (5.2)	68.8 (5.4)	67.9 (5.3)	68.4 (5.6)	67.6 (5.3)	71.2 (5.5)	71.2 (5.3)	69.5 (5.6)	68.2 (5.4)	70 (5.5)	68.4 (5.4)	69.2 (5.4)	68.5 (5.6)
Age≥70, mean (SD), y	200 (29.3)	282 (26.7)	538 (43.9)	695 (33.7)	204 (43.3)	282 (33.1)	120 (62.8)	260 (53.3)	116 (49.6)	242 (36.7)	360 (53.9)	854 (36.5)	112 (49.8)	122 (35.7)
Sex, male	290 (42.5)	627 (59.3)	629 (51.4)	951 (46.1)	80 (17.0)	138 (16.2)	125 (65.5)	328 (67.2)	153 (65.4)	380 (57.6)	408 (61.2)	1,418 (60.6)	97 (43.1)	150 (43.9)
Number of diseases	0.8 (0.4)	0.8 (0.4)	3.2 (1.1)	3.4 (1.1)	3.4 (1.4)	3.9 (1.4)	6.0 (1.5)	6.1 (1.7)	3.4 (1.3)	3.9 (1.5)	2.8 (1.0)	3.0 (1.1)	4.3 (1.5)	4.7 (1.5)
Number of drugs	0.7 (1.0)	0.6 (0.9)	2.6 (2.2)	2.0 (1.8)	2.5 (2.2)	1.9 (1.5)	5.8 (3.1)	3.7 (2.0)	3.3 (2.1)	1.6 (1.4)	2.6 (2.04)	1.7 (1.5)	3.0 (2.4)	1.9 (1.4)
Education														
None, primary school	253 (37.8)	526 (49.9)	584 (48.5)	1,174 (57.1)	202 (43.4)	460 (54.0)	96 (53.3)	294 (60.9)	103 (45.2)	302 (45.8)	318 (48.3)	1,256 (53.8)	120 (54.8)	215 (62.9)
Secondary school	329 (49.2)	422 (40.0)	517 (42.9)	752 (36.5)	209 (45.0)	313 (36.7)	77 (42.8)	163 (33.7)	104 (45.6)	291 (44.2)	290 (44.1)	899 (38.5)	85 (38.8)	106 (31.0)
Post graduate	87 (13.0)	106 (10.1)	104 (8.6)	131 (6.4)	54 (11.6)	79 (9.3)	7 (3.9)	26 (5.4)	21 (9.2)	66 (10.0)	50 (7.6)	179 (7.7)	14 (6.4)	21 (6.1)
Residential area														
Rural	134 (19.6)	357 (33.8)	220 (18.0)	746 (36.2)	80 (17.0)	229 (26.9)	36 (18.9)	193 (39.5)	43 (18.4)	231 (35.0)	109 (16.3)	740 (31.6)	43 (19.1)	127 (37.1)
Urban	548 (80.4)	700 (66.2)	1,005 (82.0)	1,317 (63.8)	391 (83.0)	623 (73.1)	155 (81.1)	295 (60.5)	191 (81.6)	429 (65.0)	558 (83.7)	1,599 (68.4)	182 (80.9)	215 (62.9)
Marital status														
Partnered	523 (77.3)	909 (86.0)	917 (74.9)	1,677 (81.3)	304 (64.5)	627 (73.6)	135 (70.7)	381 (78.1)	176 (75.2)	562 (85.1)	489 (73.3)	1,950 (83.4)	162 (72.0)	268 (78.4)
Un-partnered	154 (22.7)	148 (14.0)	307 (25.1)	386 (18.7)	167 (35.5)	225 (26.4)	56 (29.3)	107 (21.9)	58 (24.8)	98 (14.9)	178 (26.7)	389 (16.6)	63 (28.0)	74 (21.6)
Leisure-time activity														
Reading, watching TV	161 (23.9)	207 (19.6)	424 (34.6)	654 (31.9)	189 (40.1)	350 (41.2)	82 (42.9)	196 (40.3)	69 (29.5)	201 (30.8)	243 (36.5)	695 (29.9)	103 (45.8)	114 (33.6)
Walking, cycling	439 (65.0)	783 (74.4)	686 (56.0)	1,275 (62.3)	239 (50.8)	444 (52.3)	104 (54.5)	261 (53.7)	147 (62.8)	397 (60.9)	378 (56.7)	1,485 (63.9)	99 (44.0)	204 (60.2)
Playing sports	69 (10.2)	59 (5.6)	106 (8.7)	115 (5.6)	43 (9.1)	54 6.4)	5 (2.6)	29 (6.0)	8 (7.7)	54 (8.3)	43 (6.5)	142 (6.1)	21 (9.3)	21 (6.2)
Competitive Training	6 (0.9)	4 (0.4)	8 (0.7)	3 (0.2)	0	1 (0.1)	0	0	0	0	2 (0.3)	3 (0.1)	2 (0.9)	0

Table 2 (continued)

	No multimorbidity		Hypercholesterolemia		Metabolic, depression, cancer		Cardiometabolic, respiratory		Gastrointestinal, genitourinary, depression		Unspecific		Respiratory	
Characteristics[a]	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani	CUORE	Moli-sani
Cigarette smoking habit														
Non smoker	336 (51.1)	506 (47.9)	641 (53.2)	1,145 (55.6)	301 (65.2)	571 (67.0)	76 (41.1)	198 (40.7)	112 (49.1)	308 (46.8)	348 (53.2)	1,144 (48.9)	116 (52.3)	192 (56.1)
Current/former smoker	322 (48.9)	550 (52.1)	565 (46.8)	916 (44.4)	161 (34.8)	281 (33.0)	109 (58.9)	289 (59.3)	116 (50.9)	350 (53.2)	306 (46.8)	1,194 (51.1)	106 (47.7)	150 (43.9)
Alcohol habit														
Non-drinker/Former drinker	263 (39.1)	226 (23.1)	486 (39.9)	476 (25.5)	245 (52.5)	286 (36.7)	78 (40.8)	121 (29.0)	94 (40.2)	177 (29.7)	294 (44.2)	540 (25.1)	112 (49.8)	109 (34.8)
Light-moderate drinker	127 (18.9)	279 (28.4)	309 (25.3)	543 (29.1)	42 (9.0)	245 (31.4)	68 (35.6)	140 (33.6)	89 (38.0)	197 (33.1)	207 (31.1)	681 (31.7)	50 (22.2)	75 (24.0)
Heavy drinker	283 (42.0)	475 (48.5)	424 (34.8)	847 (45.4)	180 (38.5)	249 (31.9)	45 (23.6)	156 (37.4)	51 (21.8)	222 (37.2)	164 (24.7)	930 (43.2)	63 (28.0)	129 (41.2)
BMI. Kg/m^2	25.8 (3.2)	26.3 (3.0)	29.1 (4.4)	29.5 (4.6)	27.4 (4.8)	28.6 (4.5)	29.8 (5.5)	29.9 (5.0)	26.9 (4.2)	27.1 (3.7)	30.6 (5.0)	30.4 (4.9)	29.6 (5.3)	30.0 (5.1)
SBP, mm Hg	133.5 (16.0)	143.2 (20.9)	147.3 (18.6)	156.0 (19.6)	137.6 (18.1)	148.2 (19.6)	139.9 (18.2)	153.2 (21.9)	131.2 (15.9)	141.6 (18.8)	147.2 (19.1)	156.2 (19.0)	139.8 (18.0)	151.8 (20.9)
DBP, mm Hg	80.1 (9.1)	80.2 (8.9)	83.6 (10.2)	83.3 (9.3)	80.0 (10.0)	80.8 (8.7)	77.9 (10.2)	80.2 (10.1)	77.6 (9.5)	79.1 (8.9)	83.0 (10.7)	84.4 (9.6)	79.9 (9.3)	83.0 (10.0)
Total cholesterol, mg/dL	204.3 (36.2)	204.1 (30.6)	216.4 (45.8)	234.7 (47.1)	216.6 (37.9)	227.1 (44.0)	176.7 (42.7)	190.0 (44.9)	203.5 (44.0)	212.3 (43.5)	188.7 (32.7)	194.5 (28.7)	206.0 (41.7)	223.5 (41.9)
HDL cholesterol, mg/dL	58.3 (15.3)	58.4 (15.4)	56.8 (14.5)	60.2 (15.2)	62.1 (16.2)	62.6 (15.2)	50.4 (15.3)	52.1 (13.8)	55.9 (15.0)	57.6 (14.5)	51.9 (13.5)	52.8 (12.9)	57.8 (13.4)	61.6 (17.6)
Glucose, mg/dL	93 (85–101)	95 (86–103)	99 (90–113)	103 (93–117)	91.5 (84–100)	96 (87–104)	113 (96–136)	110 (96–140)	91 (84–101)	96 (88–106)	101 (92–119)	102 (92–120)	97 (88–109)	100 (90–112)

Note. Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; SBP, systolic blood pressure. Missing data: **CUORE**: Education, 71; Marital status, 6; Job at the recruitment visit, 634; Cigarette smoking habit, 80; Leisure-time physical activity, 9; Alcohol habit, 21; BMI, 6; SBP and DBP, 4; Total cholesterol, 179; HDL cholesterol, 35; Glucose 180. **Moli-sani**: Education, 20; Job at the recruitment visit, 4; Cigarette smoking habit, 7; Leisure-time physical activity, 50; Alcohol habit, 698; BMI, 9; SBP and DBP, 7; Total cholesterol, 53; HDL cholesterol, 56; Glucose 53

[a] Unless otherwise indicated, data are expressed as number (percentage) for categorical variables, mean (SD) for continuous variables with normally distributed data and median (IQR) for skewed data

Table 3 All-cause death and incidence rates (IR) per 100 person/years in CUORE and Moli-sani. Results reported for the total sample and by Multimorbidity pattern (follow-up until 12/31/2019)

	Total sample	No multimorbidity	Hypercholesterolemia	Metabolic, Depression, Cancer	Cardiometabolic, Respiratory	Gastrointestinal, Genitourinary, Depression	Unspecific	Respiratory
CUORE								
N	3,695	682	1,225	471	191	234	667	225
Number of deaths (%)	544 (14.7)	58 (8.5)	165 (13.5)	57 (12.1)	68 (35.6)	42 (18.0)	122 (18.3)	32 (14.2)
Person-years	32,674	6,174	11,111	4,281	1,491	2,008	5,654	1,954
Incidence Rate (IR) per 100 person/years	1.66	0.94	1.49	1.33	4.56	2.09	2.16	1.64
(95% CI)	(1.53–1.81)	(0.71–1.21)	(1.27–1.73)	(1.01–1.73)	(3.54–5.78)	(1.51–2.83)	(1.79–2.58)	(1.12–2.31)
Moli-sani								
N	7,801	1,057	2,063	852	488	660	2,339	342
Number of deaths (%)	1,638 (21.0)	153 (14.5)	352 (17.1)	124 (14.6)	247 (50.6)	135 (20.5)	550 (23.5)	77 (22.5)
Person-years	88,490	12,282	23,829	10,196	4,634	7,337	26,317	3,894
Incidence Rate (IR) per 100 person/years	1.85	1.25	1.48	1.22	5.33	1.84	2.09	1.98
(95% CI)	(1.76–1.94)	(1.06–1.46)	(1.33–1.64)	(1.02–1.45)	(4.70–6.04)	(1.55–2.18)	(1.92–2.27)	(1.58–2.47)

Note. Abbreviations: CI, confidence interval

The sensitivity analysis, which excluded individuals with missing covariate data, showed no significant differences (Supplementary Table 6).

Discussion and implications

This study aimed at identifying and replicate multimorbidity patterns across two population-based cohorts, consisting of over 11,000 older adults from Italy, and quantify their association with mortality. Some main findings can be highlighted. First, by using LCA on two independent cohorts sharing similar data structure and disease assessment criteria, we were able to identify six clinically meaningful multimorbidity patterns, namely: *hypercholesterolemia; metabolic*, *depression and cancer; cardiometabolic and respiratory; gastrointestinal*, *genitourinary and depression; respiratory; unspecific*. Second, individuals part of the same multimorbidity patterns across the two cohorts showed similar sociodemographic and clinical characteristics, reinforcing the hypothesis that specific disease patterns are highly associated with given socio-demographic profiles. Finally, different multimorbidity patterns were differentially associated with mortality, suggesting they provide prognostic information that can be used to better tailor care pathways, therapeutic approaches and counselling of these individuals and their families. As regard of the unspecific pattern, where none of the assessed diseases resulted overexpressed, our interpretation is that it identifies individuals with a mix of diseases, not pointing at any specific underlying pathophysiological signature, still exerting a burden on survival that is higher than other patterns.

Multimorbidity is a common source of clinical complexity in older adults, which has a relevant impact on numerous negative health-related outcomes and increases healthcare resource consumption. As such, there is currently big interest in identifying replicable patterns of multimorbidity among the general population, which can be leveraged to personalize healthcare approaches to delay the onset of frailty and disability and prolong survival in older adults [2, 20, 21]. In general, looking at the literature on the topic of associative multimorbidity (i.e., multimorbidity patterns), a high number of different combinations of diseases have been reported. In a seminal review article from Prados-Torres et al. [22], 97 different disease patterns including two or more conditions were identified. Despite the methodological variability across studies, these authors identified relevant similarities for three recurrent disease patterns. The first including cardiometabolic diseases, the second including mental health problems, and the third characterized by musculoskeletal disorders. In a more recent review based on primary care findings, Beridze et al. [23] found that, despite

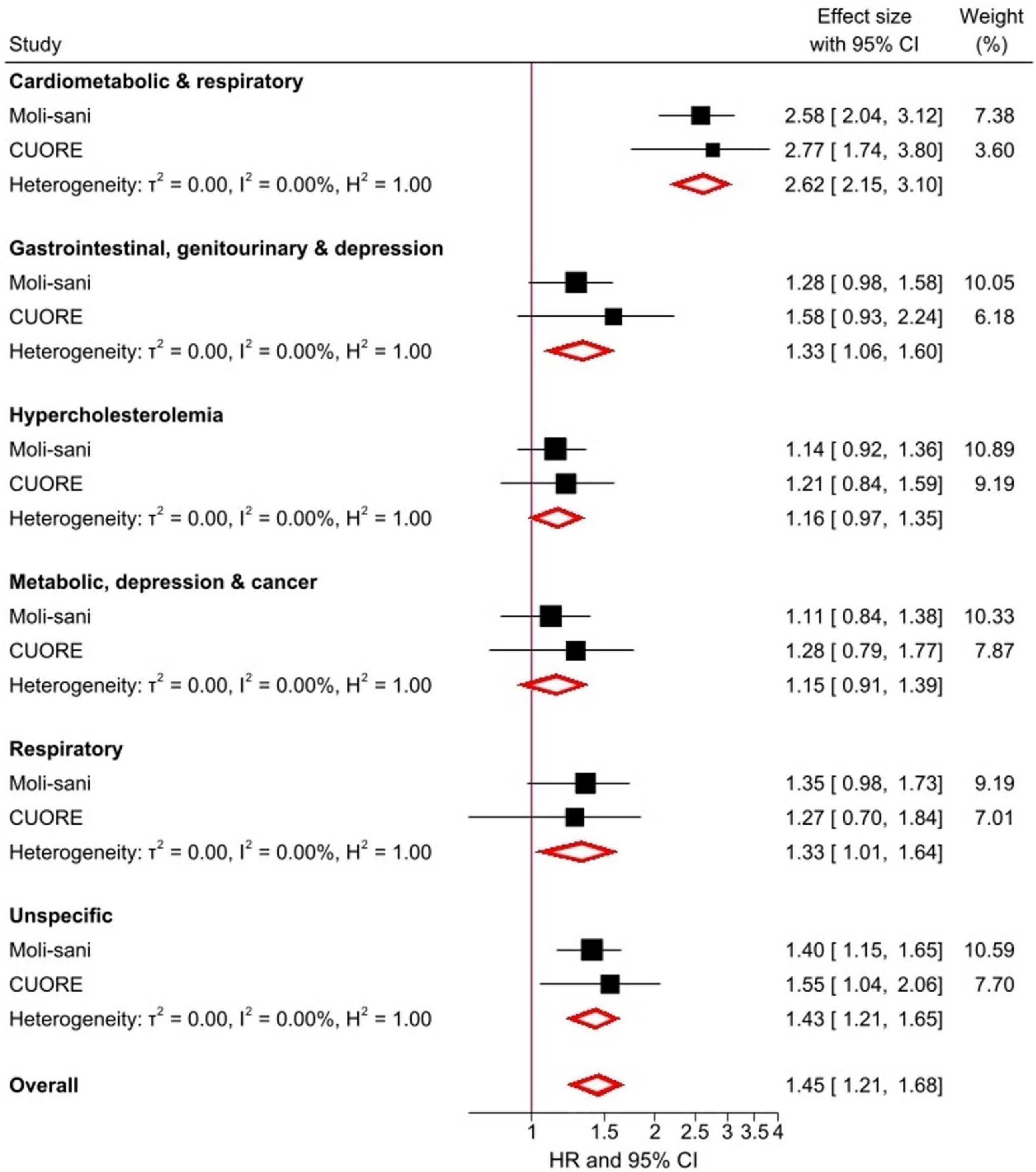

Fig. 2 Pooled hazard ratios (HR) of all-cause mortality in CUORE and Moli-sani (reference group: participants with no multimorbidity). *Note.* Abbreviations: CI, confidence interval. Model adjusted for age, sex, education, smoking habit, physical activity, alcohol habit

high heterogeneity in clustering methods and disease classifications, consistent patterns of multimorbidity emerged, namely: mental health and cardiovascular patterns, often combined with diseases affecting other organ systems (e.g., neurological, endocrine).

To the best of our knowledge, this is one of the first study that describes and replicates multimorbidity patterns, and their association with all-cause mortality, in two independent cohorts of community-dwelling older adults. The largely overlapping findings across the two cohorts provide robustness to the construct of disease pattern, suggesting that LCA is a promising method to classify older adults based on diagnostic characteristics. Previous studies have used LCA to identify multimorbidity profiles, although findings from these studies are hardly comparable with ours in terms of sample populations and disease ascertainment methods [24–26].

Several previous studies have identified patterns of multimorbidity in the general older population, including studies from our group. In consideration of the wide methodological heterogeneity that has characterized the literature on the topic, we report here the most relevant findings from previous studies that employed a methodology similar to ours, both in terms of operationalization of chronic diseases in 60 categories, and clustering methods. Marengoni et al. [27], in a study performed in almost 3000 Swedish individuals 60+participating in the SNAC-K study, identified six distinct patterns, namely: unspecific, respiratory and musculoskeletal diseases, eye diseases and cancer, cognitive and sensory impairment, heart diseases, and psychiatric and respiratory diseases. As compared with our study, while the same disease categories appear to characterize the five clusters, they were combined in a slightly different manner. The proper clinical examination and registry linkage carried out in the SNAC-K study may explain the different prevalence of relevant diseases (e.g., dementia, chronic kidney disease), which may translate in different disease clustering. Of note, also in the study from Marengoni et al., given sociodemographic and, in addition functional characteristics, clustered within individuals displaying different multimorbidity patterns. Interestingly, in a mortality analysis carried out in the same population by Vetrano et al., in line with the finding of the present study, the multimorbidity patterns overexpressing cardiovascular, neuropsychiatric and respiratory diseases presented the highest mortality rates [4]. In a Spanish study involving almost one million primary care patients, eight different patterns of multimorbidity were identified, based on electronic health records. Also in this case, an unspecific and prevalent pattern of multimorbidity was identified, along with more specific and complex patterns, encompassing among the most overexpressed diseases again, cardiovascular, respiratory, and neuropsychiatric diseases [28]. Consistently with our findings, Violán et al. also found a combination of psychiatric and genitourinary disorders clustering in the same individuals. They also found an overexpression of gastrointestinal disorders, as we did, but in four of the identified patterns, in combination with different other diseases. In the case of the study by Violán et al., a 100-fold larger population as compared with ours and the primary care nature of the diagnostic information, might explain the larger number of identified multimorbidity patterns and their different assortment.

The identification of clinically meaningful multimorbidity patterns may play a key role in the context of prevention and public health choices. Those at higher risk of experiencing major events such as unplanned hospitalizations and death, among other relevant outcomes, can benefit from prevention initiatives and targeted screening based on their clinical situation to identify those most in need of care, allowing for better source allocation. Recognizing that subjects belong to a certain profile of multimorbidity would allow to differentiate health actions, allowing to keep these people on-track for prevention, treatment or palliative care, according to their needs [2, 20, 21].

Strengths and limitations

Major strengths of the study are the prospective design, long follow-up, and use of two large datasets. Moreover, the use of standardized questionnaires to collect disease information and categorize it in homogeneous groups allowed for consistent exposure measures. For CUORE, it was possible to have a good national coverage, thanks to the random enrolment of study participants from all Italian regions distributed in the northern, central and southern areas of the country. Finally, this is one of the few studies to have identified clinically consistent multimorbidity profiles across two different Italian population-based cohorts.

Conversely, some study limitations should be taken in consideration. Given the observational design, possibility of residual confounding remains. Still, the main potential confounders according to the literature on this topic were considered. Second, information on certain diseases and covariates was self-reported, which may have led to misclassification of exposures. We also evaluated the multimorbidity patterns at the date of recruitment, hence possible newly diagnosed chronic diseases or medications' changes during the study period were not considered. Moreover, the use of a slightly modified disease categorization as proposed by Calderón-Larrañaga et al. might affect comparability of our and other results. At the same time, we have aggregated together rarer diseases, arguably with trivial effect on multimorbidity pattern identification. Finally, despite the national representativeness of the data, since it was derived from an individual country, caution is needed in the generalization of these findings to other populations.

Conclusion

In this study we identified and replicated six clinically meaningful multimorbidity patterns across two large population-based cohorts of older adults and quantify their prognosis in terms of mortality. Multimorbidity patterns characterized by an overexpression of cardiovascular, respiratory and gastrointestinal, as well as an unspecific pattern of multimorbidity, presented with higher mortality hazards as compared with older adults without multimorbidity. Understanding these patterns may help improve risk stratification in older adults, allowing for tailored prevention and intervention strategies. In particular, the replicability observed in the two cohorts supports the idea that this pattern identification process could also be applied in a clinical setting. For example, this could be used for risk stratification, with the aim of prognostication, and also in tailored healthcare, when the aims are preventive and therapeutic strategies. Finally, from a public health perspective, knowing the distribution of these patterns in the population could help measure healthcare needs and better target healthcare planning and investments.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40520-025-03150-0.

Acknowledgements CUORE: We are grateful to the OEC/HES 2008–2012 participants who enthusiastically joined the study and to the Associazione Nazionale Medici Cardiologi Ospedalieri/Health Care Foundation (ANMCO/HCF) for their collaboration, as well as all persons who supported the implementation of the survey (https://www.cuore.iss.it/eng/survey/hes). We are grateful to Dr. Eugenio Mattei of the ISS for collaborating in the preparation of the mortality database for the record linkage with the OEC/HES 2008-2012 database. We are grateful to Mrs. Tiziana Grisetti, Mrs. Claudia Meduri, and Mrs. Matilde Bocci for their essential support in the management of this study. Moli-sani Study: We are grateful to Moli-sani Study participants who enthusiastically joined the study, and to the Associazione Cuore Sano ETS (Campobasso, Italy) for its support to the communication research activities. The enrolment phase of the Moli-sani Study was supported by research grants from Pfizer Foundation (Rome, Italy), the Italian Ministry of University and Research (MIUR, Rome, Italy)–Programma Triennale di Ricerca, Decreto no.1588 and Instrumentation Laboratory, Milan, Italy. We are grateful to the Neuromed Biobanking Center for managing the baseline samples. BIO-SIGN Study Investigators: Graziano Onder, Rosella Liperoti, Maria Beatrice Zazzara, Enrico di Stasio, Camilla Cocchi, Anna Picca (IRCCS Fondazione Policlinico Universitario A. Gemelli, Rome, Italy); Luigi Palmieri, Chiara Donfrancesco, Cecilia Damiano, Benedetta Marcozzi, Cinzia Lo Noce, Teresa Dipol, (Istituto Superiore di Sanità, Rome, Italy); Simona Costanzo, Amalia De Curtis, Augusto Di Castelnuovo, Maria Benedetta Donati, Licia Iacoviello, Sara Magnacca, Teresa Panzera, Mariarosaria Persichillo (IRCCS Neuromed, Pozzilli, IS, Italy); Luca Soraci, Ersilia Paparazzo, Marco Fiorillo (IRCCS INRCA Istituto Nazionale di Ricovero e Cura per Anziani Cosenza, Italy), Giuseppe Pelliccioni, Tiziana Casoli, Leonardo Biscetti (IRCCS INRCA Istituto Nazionale di Ricovero e Cura per Anziani, Ancona, Italy); Davide Liborio Vetrano, Federico Triolo (Karolinska Institutet, Stockholm, Sweden).

Author contributions OG, DLV, CDa, SC, CDo and LP conceived and planned the study. CLN contributed to acquisition of data for CUORE; CDa, BM, CLN, CDo and LP contributed to the database preparation and statistical analyses for CUORE, SC, TP, SM, ADiC contributed to acquisition of data for Moli-sani. CDa and SC harmonized data of the two cohorts and performed the analyses. CDa, SC and DLV wrote the manuscript. All authors contributed to the data interpretation and critically revised the manuscript.

Data availability The data underlying this article will be shared on reasonable request to the corresponding author. The OEC/HES 2008-2012 data are stored in the Department of Cardiovascular, Endocrine-metabolic Diseases and Aging of the Istituto Superiore di Sanità-ISS, and access is restricted by the ethical approvals and the legislation of the European Union. The Moli-sani data are stored in an institutional repository (https://repository.neuromed.it), and access is restricted by the ethical approvals and the legislation of the European Union.

Declarations

Ethical approval For CUORE: “The survey was approved by the ISS ethics committee, and written informed consent was signed by all participants.” For Moli-sani: “The study complies with the Declaration of Helsinki and was approved by the Catholic University Ethical Committee in Rome, italy. All participants provided written informed consent”.

Competing interests Graziano Onder and Maria Beatrice Zazzara are members of the Editorial Board for Aging Clinical and Experimental Research. They have not taken part in the review or selection process of this article.

References

1. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B (2012) Epidemiology of Multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 380(9836):37–43. https://doi.org/10.1016/S0140-6736(12)60240-2
2. Vetrano DL, Calderón-Larrañaga A, Marengoni A et al (2018) An international perspective on chronic multimorbidity:

approaching the elephant in the room. Journals Gerontology: Ser A 73(10):1350–1356. https://doi.org/10.1093/gerona/glx178
3. Nguyen QD, Wu C, Odden MC, Kim DH (2019) Multimorbidity patterns, frailty, and survival in Community-Dwelling older adults. Journals Gerontology: Ser A 74(8):1265–1270. https://doi.org/10.1093/gerona/gly205
4. Vetrano DL, Roso-Llorach A, Fernández S et al (2020) Twelve-year clinical trajectories of Multimorbidity in a population of older adults. Nat Commun 11(1). https://doi.org/10.1038/s41467-020-16780-x
5. Tazzeo C, Rizzuto D, Calderón-Larrañaga A et al (2021) Multimorbidity patterns and risk of frailty in older community-dwelling adults: a population-based cohort study. Age Ageing 50(6):2183–2191. https://doi.org/10.1093/ageing/afab138
6. Akugizibwe R, Calderón-Larrañaga A, Roso-Llorach A et al (2020) Multimorbidity patterns and unplanned hospitalisation in a cohort of older adults. J Clin Med 9(12):4001. https://doi.org/10.3390/jcm9124001
7. Marengoni A, Tazzeo C, Calderón-Larrañaga A et al Multimorbidity patterns and 6-Year risk of institutionalization in older persons: the role of social formal and informal care. J Am Med Dir Assoc Published Online 2021:0–6. https://doi.org/10.1016/j.jamda.2020.12.040
8. Vetrano DL, Rizzuto D, Calderón-Larrañaga A et al (2018) Trajectories of functional decline in older adults with neuropsychiatric and cardiovascular multimorbidity: A Swedish cohort study. PLoS Med 15(3):1–15. https://doi.org/10.1371/journal.pmed.1002503
9. Triolo F, Vetrano DL, Sjöberg L et al (2024) Somatic disease burden and depression risk in late life: a community-based study. Epidemiol Psychiatr Sci 33:e6. https://doi.org/10.1017/S2045796024000064
10. Giampaoli S, Palmieri L, Donfrancesco C, Noce C, Lo, Pilotto L, Vanuzzo D (2015) Cardiovascular health in italy. Ten-year surveillance of cardiovascular diseases and risk factors: osservatorio epidemiologico cardiovascolare/health examination survey 1998–2012. Eur J Prev Cardiol 22(2suppl):9–37. https://doi.org/10.1177/2047487315589011
11. Iacoviello L, Bonanni A, Costanzo S et al (2007) The Moli-Sani project, a randomized, prospective cohort study in the molise region in italy; design, rationale and objectives. Italian J Public Health 4(2). https://doi.org/10.2427/5886
12. Di Castelnuovo A, Costanzo S, Persichillo M et al (2012) Distribution of short and lifetime risks for cardiovascular disease in Italians. Eur J Prev Cardiol 19(4):723–730. https://doi.org/10.1177/1741826711410820
13. Calderón-Larrañaga A, Vetrano DL, Onder G et al (2016) Assessing and Measuring Chronic Multimorbidity in the Older Population: A Proposal for Its Operationalization. *J Gerontol A Biol Sci Med Sci*. Published online December 21,:glw233. https://doi.org/10.1093/gerona/glw233
14. ISTAT: Istituto Nazionale di Statistica, Atlante statistico dei comuni. Edizione 2014. Accessed December 5 (2024) https://www.istat.it/it/archivio/113712
15. Linzer DA, Lewis JB (2011) PoLCA: an *R* package for polytomous variable latent class analysis. J Stat Softw 42(10). https://doi.org/10.18637/jss.v042.i10
16. Formann AK, Kohlmann T (1996) Latent class analysis in medical research. Stat Methods Med Res 5(2):179–211. https://doi.org/10.1177/096228029600500205
17. Schwarz G (1978) Estimating the dimension of a model. Annals Stat 6(2). https://doi.org/10.1214/aos/1176344136
18. Nylund KL, Asparouhov T, Muthén BO (2007) Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. Struct Equ Model 14(4):535–569. https://doi.org/10.1080/10705510701575396
19. Yang CC (2006) Evaluating latent class analysis models in qualitative phenotype identification. Comput Stat Data Anal 50(4):1090–1104. https://doi.org/10.1016/j.csda.2004.11.004
20. Skou ST, Mair FS, Fortin M et al (2022) Multimorbidity. Nat Rev Dis Primers 8(1):48. https://doi.org/10.1038/s41572-022-00376-4
21. Onder G, Vetrano DL, Palmer K et al (2022) Italian guidelines on management of persons with Multimorbidity and polypharmacy. Aging Clin Exp Res 34(5):989–996. https://doi.org/10.1007/s40520-022-02094-z
22. Prados-Torres A, Calderón-Larrañaga A, Hancco-Saavedra J, Poblador-Plou B, Van Den Akker M (2014) Multimorbidity patterns: A systematic review. J Clin Epidemiol 67(3):254–266. https://doi.org/10.1016/j.jclinepi.2013.09.021
23. Beridze G, Abbadi A, Ars J et al (2024) Patterns of Multimorbidity in primary care electronic health records: A systematic review. J Multimorbidity Comorbidity 14. https://doi.org/10.1177/26335565231223350
24. Olaya B, Moneta MV, Caballero FF et al (2017) Latent class analysis of Multimorbidity patterns and associated outcomes in Spanish older adults: a prospective cohort study. BMC Geriatr 17(1):186. https://doi.org/10.1186/s12877-017-0586-1
25. Gonsoulin ME, Durazo-Arvizu RA, Goldstein KM et al (2017) A health profile of Senior-Aged women veterans: A latent class analysis of condition clusters. Innov Aging 1(2). https://doi.org/10.1093/geroni/igx024
26. Gellert P, von Berenberg P, Zahn T, Neuwirth J, Kuhlmey A, Dräger D (2019) Multimorbidity profiles in German centenarians: A latent class analysis of health insurance data. J Aging Health 31(4):580–594. https://doi.org/10.1177/0898264317737894
27. Marengoni A, Roso-Llorach A, Vetrano DL et al (2020) Patterns of Multimorbidity in a population-based cohort of older people: sociodemographic, lifestyle, clinical, and functional differences. Journals Gerontol - Ser Biol Sci Med Sci 75(4):798–805. https://doi.org/10.1093/gerona/glz137
28. Violán C, Foguet-Boreu Q, Fernández-Bertolín S et al (2019) Soft clustering using real-world data for the identification of Multimorbidity patterns in an elderly population: cross-sectional study in a mediterranean population. BMJ Open 9(8):e029594. https://doi.org/10.1136/bmjopen-2019-029594