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RESEARCH ARTICLE

Comorbidity patterns in institutionalized older adults affected by dementia

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Abstract

Introduction: Dementia is common in nursing homes (NH) residents. Defining dementia comorbidities is instrumental to identify groups of persons with dementia that differ in terms of health trajectories and resources consumption. We performed a cross-sectional study to identify comorbidity patterns and their associated clinical, behavioral, and functional phenotypes in institutionalized older adults with dementia.

Methods: We analyzed data on 2563 Italian NH residents with dementia, collected between January 2014 and December 2018 using the multidimensional assessment instrument interRAI Long-Term Care Facility (LTCF). A standard principal component procedure was used to identify comorbidity patterns. Linear regression analyses were used to ascertain correlates of expression of the different patterns.

Results: Among NH residents with dementia, we identified three different comorbidity patterns: (1) heart diseases, (2) cardiovascular and respiratory diseases and sensory impairments, and (3) psychiatric diseases. Older age significantly related to increased expression of the first two patterns, while younger patients displayed increased expression of the third one. Recent hospital admissions were associated with increased expression of the heart diseases pattern ($\beta = 0.028$; 95% confidence interval [CI] 0.003 to 0.05). Depressive symptoms and delirium episodes increased the expression of the psychiatric diseases pattern ($\beta = 0.130$, 95% CI 0.10 to 0.17, and β 0.130, CI 0.10 to 0.17, respectively), while showed a lower expression of the heart diseases pattern.

Discussion: We identified different comorbidity patterns within NH residents with dementia that differ in term of clinical and functional profiles. The prompt recognition of health needs associated to a comorbidity pattern may help improve long-term prognosis and quality of life of these individuals.

KEYWORDS
care pathways, dementia comorbidities, nursing homes, older adults, personalized medicine

Highlights

- Defining dementia comorbidities patterns in institutionalized older adults is key.
- Institutionalized older adults with dementia express different care needs.
- Comorbidity patterns are instrumental to identify different patients' phenotypes.
- Phenotypes vary in terms of health trajectories and demand different care plans.
- Prompt recognition of phenotypes in nursing homes can positively impact on outcomes.

1 | INTRODUCTION

In the last decades, the proportion of older adults affected by dementia has significantly grown, especially in low- and middle-income countries.[1] The World Health Organization (WHO) has estimated that around the globe, more than 50 million people have dementia, with nearly 10 million new cases every year. The total number of people living with dementia is projected to reach 82 million by 2030 and 152 by 2050.[1]

Dementia is a common condition in nursing homes (NH), representing in most cases the trigger that leads to institutionalization. Especially in high-income countries, nearly half of people with dementia lives in NH and more than two-thirds of care home residents have dementia.[2] However, characteristics of patients with dementia and their care burden can vary largely, with behavioral and psychological symptoms of dementia and lack of independence in activities of daily life (ADL), representing the most frequent indications to receive continued care.[2,3] The identification of dementia comorbidities can support the recognition of subgroups of persons with dementia that differ in terms of prognosis and resources consumption. Implementing new strategies to recognize those individuals at higher risk of cognitive and functional decline, and consequent loss of independence, represents a public health priority to forecast different health trajectories.[4–6] A number of diseases, such as diabetes, atrial fibrillation, and depression, have been recognized as risk factors or frequent comorbidities of dementia.[6–8] The co-occurrence of two or more chronic diseases, a condition known as multimorbidity, is common among older adults[9] and is associated with poor quality of life, physical decline and frailty, cognitive dysfunction, and faster dementia progression,[10–12] and increases the risk of adverse outcome such as falls, hospitalizations, and deaths.[13–15] Among institutionalized older adults with dementia, the presence of one or more comorbidities other than dementia may be considered the norm, affecting virtually 100% of this population.[6,13] Co-occurrence of chronic conditions follows specific patterns, characterized by diseases that tend to systemically aggregate because of similar pathophysiological mechanisms or common risk factors, and different disease patterns may have a different impact on health outcomes.[16] A substantial body of evidence has focused on definition of disease patterns, their risk factors, and health consequences, but, to the best of our knowledge, no study has been carried out with the aim of identifying and addressing the potential impact of disease patterns on clinical and functional aspects of older adults with dementia living in NH.

Recognizing specific comorbidity patterns in this population could have a crucial role in understanding diseases trajectories, establishing health priorities, and creating interventions with the purpose of changing the natural history of this condition and improving overall health.[16,17] In this study, we aimed to identify different comorbidity patterns and their associated clinical, behavioral, and functional phenotypes in NH residents with dementia.

2 | METHODS

2.1 | Study population and data collection

We performed a cross-sectional retrospective study using a sample of 2563 NH residents with a diagnosis of dementia. Eligible age for NH in Italy is 65 years and older and criteria for reimbursement of the admission depend on income and level of disability and demand of care, for which the patient may receive an extra allowance. We included all data from NH residents in the Italian region of Umbria that were collected between January 2014 and December 2018. Evaluations of the residents were conducted using the multidimensional assessment instrument interRAI Long-Term Care Facility (LTCF), consisting of >250 data elements including sociodemographic variables, clinical information, cognition, and physical function. The interRAI LTCF instrument is currently used in several Italian regions and throughout the world for administrative and clinical purposes and enables the creation of databases that can be used to assess and compare characteristics of NH residents across countries and cultures with a demonstrated valid reliability.[18–20] Assessment is performed by a health professional trained to gather and verify information from as many sources as possible, including direct observations; direct interviews with the patient, family, friends, or formal service providers; medical and nursing clinical charts records; previous medical history; and other clinical documentation. The health professional assessor eventually registers the patient's

related medical and social information by filling in the interRAI LTCF check-box items list in which different health conditions and disease diagnoses are indexed. For the present study, we used all records with Alzheimer's disease (AD) or dementia other than AD to identify all residents with dementia. The validity of such diagnostic information has been verified using comparisons to administrative records, with recent work demonstrating high specificity and sensitivity (0.80 and 0.83, respectively) for the combined dementia measures.[21]

2.2 | Chronic diseases assessment

The presence of 55 diseases (Table S1 in supporting information) was evaluated considering the information available in the InterRAI LTCF data collection form, consistent with previously validated methodology.[22] Almost all of the InterRAI LTCF items were proven to meet high reliability standards.[20] Diseases were coded following the International Classification of Diseases 9th revision (ICD-9).[22,23] Final analysis focused on the 15 most common conditions (see Table S1).

2.3 | Other considered covariates

The demographic variable included age (70–79; 80–89; ≥90) and sex, number of comorbidities per person and number of drugs used per day (0–4; 5–9; ≥10), diagnosis of Alzheimer Disease (AD) (1: present; 0: absent), and a hospitalization in the previous 90 days prior the evaluation. Presence of weight loss was defined as the undesired loss of body weight ≥5% in the 30 days prior the evaluation or ≥10% within the previous 180 days. Bladder and bowel incontinence were defined using a binary variable (1: present; 0: absent). Tube feeding was defined by the presence (1) or absence (0) of parental or enteral feeding (both nasogastric tube and percutaneous endoscopic gastrostomy(PEG tube)). An episode of delirium was defined by the presence of at least one of the following three symptoms in the 3 days prior the interview: abnormal thought process, delusions, or hallucinations. Depressive symptoms were assessed through the Depression Rating Scale (DRS),[24] a reliable instrument for detecting depression among older adults; a score ≥3 diagnoses depression.[20,24] Cognitive level was evaluated through the Cognitive Performance Scale (CPS),[25] a scale ranging from 0 (intact) to 6 (very severe impairment) that combines information on memory impairment, level of consciousness, and executive function. As per previous studies,[20] cognitive impairment was categorized as moderate in case of a CPS score ranging from 2 to 4 and severe when the CPS score was equal to or above 5. Functional status was assessed using the Activities of Daily Living Hierarchy Scale (ADLH), a scale that ranges from 0 (no impairment) to 6 (total dependence) and groups activities according to the state of loss of independence in which they occur; early loss activities are assigned a lower score; hence, lower values mean less impairment or level of disability.[20,26,27] Potential health instability in long-term care populations was evaluated via the Changes in Health, End-Stage Disease, and Symptoms and Signs Scale (CHESS), a scale that ranges from zero to five, in which high CHESS levels have been independently associated with greater likelihood of an adverse event and greater risk of mortality in home care populations.[28]

RESEARCH IN CONTEXT

1. **Systematic Review**: After conducting a review of the literature using traditional sources (i.e., PubMed), we found a body of evidence that had focused on definition of disease patterns and consequence of different diseases on dementia. No studies identified and addressed the potential impact of comorbidity patterns on clinical and functional aspects in institutionalized older adults with dementia.
2. **Interpretation**: We identified three clinically relevant comorbidity patterns among institutionalized residents affected by dementia: heart diseases, cardiovascular and respiratory diseases, and sensory impairments and psychiatric diseases. These patterns differ in term of clinical, behavioral, and functional profiles and define different patients' phenotypes with potential diverse health priorities, care and assistance requirements, and prognosis.
3. **Future Directions**: Further studies are needed to elaborate standardized strategies and guidance to promptly assess and recognize care needs, establish health priorities, and implement personalized care plans and tailored interventions in institutionalized older adults affected by dementia.

2.4 | Statistical analyses

We used a standard principal component analysis (PCA) procedure to identify different comorbidity patterns. The aim of the PCA is to reduce the observed variables into a smaller set of composite variables, each indicating a possible different pattern of dementia comorbidity. Diseases absent in all subjects ($n = 3$) and those with a prevalence <2% ($n = 32$) were excluded from analysis. We then performed a first exploratory PCA on the 20 conditions. To reduce statistical noise, we excluded from the analysis those diseases that showed a proportion of unexplained variance equal to or >0.9 after the PCA ($n = 5$).[29] We then performed the PCA again, considering the final 15 diseases in the analysis. As the variables were all dichotomous, a correlation matrix with tetrachoric correlation was used in the procedure.[30] The optimal number of components was determined using the scree plot of the eigenvalues of the correlation matrix (Figure S1 in supporting information), looking at the distinct break of the curve (the "elbow" method). Only the components above the break were retained for analysis.[31] Component loadings, ranging from −1 to +1, were used to determine the relation between the original variables and the identified components, with a high component loading indicating a good representation of the disease by the

considered component. The threshold for significant loadings was set at 0.25. Components were then named in accordance with the diseases that most characterized them.

We finally performed three different linear regression analyses for each identified pattern, to ascertain correlates of expression of the different comorbidity patterns. The dependent variable was represented by the score indicating the magnitude of expression of the considered pattern per subjects. To avoid loss of information of potential nuances in the expression of each pattern, the outcome was analyzed as continuous. Analyses were adjusted for all potential covariates described in section 2.3. For all the tested hypotheses, two-sided *P*-values <.05 were considered statistically significant. All statistical analyses were performed using the software Stata version 16.0 (Stata Corporation).

3 | RESULTS

The 2563 participants (73% females) were observed for a mean follow-up period of 2.05 years (median value 1.5 years; maximum follow-up 5 years). Forty-eight percent of the study population was aged 80 to 89 years old with 32% aged 90 years and older; 1877 were women while 686 were men. The most prevalent chronic disease were ischemic heart disease (38.1%) and cerebrovascular diseases (21.7%) followed by neurotic stress-related disorders (29.2%) and depression (29.75%). Neurotic stress-related disorders comprise neurotic disorders, personality disorders, and other nonpsychotic mental disorders as enlisted by items 300 to 316 of the ICD-9 classification.[22,23] More than half of the sample used more than five drugs per day. Visual and hearing impairment were present in 33.0% and 30.5% of our sample, respectively. More than 80% of our sample reported moderate to severe cognitive impairment and presented bladder incontinence and almost 95% of the participants required around-the-clock assistance. Baseline characteristics of the sample are shown in Table 1.

Table 2 reports results of the PCA procedure aimed at identifying disease patterns and the diseases included in each pattern. The PCA procedure identified three different disease components: (1) heart diseases, (2) cardiovascular and respiratory diseases and sensory impairments, and (3) psychiatric diseases. The heart diseases pattern was characterized by individuals affected by ischemic heart disease, heart failure, arrhythmia, and atrial fibrillation; the cardiovascular and respiratory diseases and sensory impairments pattern was characterized by individuals affected by cerebrovascular diseases, ischemic heart disease, chronic obstructive pulmonary disease, and visual and hearing impairments; the psychiatric diseases pattern was characterized by individuals suffering from neurotic stress-related disorders, such as anxiety or phobic states, and depression. The schizophrenia component was not included the psychiatric diseases pattern because it presented a loading factor below the set threshold of 0.25. On the other hand, ischemic heart diseases were present in both the heart diseases and the cardiovascular and respiratory diseases and sensory impairments patterns because loading factors were above the set threshold.

Results from linear regression analyses aimed to ascertain correlates of expression of the disease patterns are shown in Table 3. A higher loading coefficient of the heart diseases pattern was positively associated with older age, recent hospitalization, polytherapy (indicating the consumption of 10 or more drugs per day), and a worsening level of health stability as measured by the CHESS scale, while it was negatively associated with female sex and depressive symptoms. The expression of the cardiovascular and respiratory diseases and sensory impairments pattern was also significantly associated with older age, but also to severe cognitive status, weight loss, and tube feeding, while displayed a significant inverse correlation with female sex, depressive symptoms, polytherapy, hospitalizations, and health instability as detected by the CHESS scale. A higher loading coefficient of the psychiatric diseases pattern showed a significant direct association to presence of delirium episodes and depressive symptoms, female sex, polytherapy, and moderate–high health instability as per CHESS scale, while displayed an inverse correlation to older age and cognitive impairment, weight loss, tube feeding, and bladder and bowel incontinence. Level of required assistance, as captured by the ADLH scale, did not significantly correlate with any of the components.

4 | DISCUSSION

In this study, we have identified three different patterns of comorbidity in institutionalized individuals with dementia and outlined possible associations with clinical, behavioral, and functional phenotypes in this population. The heart diseases and the cardiovascular and respiratory diseases and sensory impairments patterns were associated with older age and, respectively, with increased likelihood of recent hospitalization and cognitive impairment, while the psychiatric diseases pattern was displayed by younger patients and associated with increased episodes of delirium and depressive symptoms. To our knowledge, few studies have investigated comorbidity patterns in institutionalized older adults, and none of them was limited to individuals with dementia. Furthermore, few works have addressed the identification of dementia comorbidities. A recent study by Grande et al. showed that community-dwelling and institutionalized adults aged 60 years and older with neuropsychiatric and cardiovascular multimorbidity patterns had higher chances of experiencing dementia throughout 12 years, followed by those with sensory impairment and cancer, underlining how the timely identification and management of such patterns might have important clinical implications.[4] Another study, by Poblador-Plou et al., addressed comorbidities associated with dementia in older patients aged ≥65 years in primary care and underlined how different diseases were grouped around the index disease of dementia in a more sophisticated way other than just prevalence-based.[6] This is the first study addressing institutionalized older adults with dementia with the aim of investigating the presence of comorbidities that clustered into specific patterns and defined different patients' phenotypes. Some of the identified comorbidities may manifest a similar behavior in institutionalized patients without dementia, although, in the absence

TABLE 1 Sample characteristics at baseline

Characteristics	All ($n = 2563$)	Men ($n = 686$)	Women ($n = 1877$)
Age (years)			
<70	137 (5.6)	82 (11.9)	55 (2.9)
70–79	372 (14.5)	139 (20.3)	233 (12.4)
80–89	1233 (48.1)	349 (50.9)	884 (47.1)
≥90	821 (32)	116 (16.9)	705 (37.6)
Alzheimer's disease	634 (24.7)	125 (18.2)	509 (27.1)
Cerebrovascular disease	555 (21.7)	176 (25.7)	379 (20.2)
Ischemic heart disease	977 (38.1)	267 (38.9)	710 (37.8)
COPD	466 (18.2)	163 (23.8)	303 (16.1)
Heart failure	450 (17.6)	122 (17.8)	328 (17.5)
Neurotic stress-related disorders[a]	748 (29.2)	143 (20.9)	605 (32.2)
Depression	761 (29.7)	152 (22.2)	609 (32.4)
Schizophrenia	85 (3.3)	34 (5.0)	51 (2.7)
Arrythmia	105 (4.1)	30 (4.4)	75 (4.0)
Atrial fibrillation	103 (4.02)	30 (4.4)	73 (3.9)
Visual impairment	845 (33.0)	218 (31.8)	627 (33.4)
Hearing impairment	781 (30.5)	205 (29.9)	576 (30.7)
Hip fracture	134 (5.2)	29 (4.2)	105 (5.6)
Osteoarthritis	71 (2.8)	12 (1.8)	59 (3.1)
Other MSK diseases	100 (3.9)	27 (3.9)	73 (3.9)
Thyroid disease	67 (2.6)	7 (1.0)	60 (3.2)
Number of diseases, mean (SD)	2.4 (1.7)	2.3 (1.7)	2.5 (1.7)
Number of drugs			
0–4	1180 (46.0)	283 (41.2)	897 (47.8)
5–9	1153 (45.0)	343 (50.0)	810 (43.1)
10+	230 (9.0)	60 (8.8)	170 (9.1)
Weight loss	217 (8.5)	81 (11.8)	136 (7.3)
Hospitalization (past 90 days)	579 (22.6)	226 (32.9)	353 (18.8)
Bladder incontinence	2215 (86.4)	577 (84.1)	1638 (87.3)
Bowel incontinence	1927(75.2)	498 (72.6)	1429 (76.1)
Tube feeding	349 (13.6)	85 (12.4)	264 (14.1)
Delirium episode (past 3 days)[b]	833 (32.5)	218 (31.8)	615 (32.8)
CPS[c]			
Moderate impairment	863 (33.7)	251 (36.6)	612 (32.6)
Severe impairment	1426 (55.6)	354 (51.6)	1072 (57.1)
ADLH[d]			
Assistance required	1011 (39.5)	285 (41.6)	726 (38.7)
Dependence	1425 (55.6)	352 (51.3)	1073 (57.2)
DRS[e]			
2 or more depressive symptoms	1121 (43.7)	265 (38.6)	856 (45.6)

(Continues)

TABLE 1 (Continued)

Characteristics	All ($n = 2563$)	Men ($n = 686$)	Women ($n = 1877$)
CHESS[f]			
Minimal-low health instability	930 (36.3)	246 (35.9)	684 (36.4)
Moderate-high health instability	165 (6.4)	58 (8.4)	107 (5.7)

[a]Neurotic stress-related disorders comprised items 300–316 of ICD-9 codes (Neurotic disorders; Personality disorders; Sexual deviations and disorders; Alcohol dependence syndrome; Drug dependence; Nondependent abuse of drugs; Physiological malfunction arising from mental factors; Special symptoms or syndromes, not elsewhere classified; Acute reaction to stress; Adjustment reaction; Specific nonpsychotic mental disorders after organic brain damage; Depressive disorder, not elsewhere classified; Disturbance of conduct, not elsewhere classified; Disturbance of emotions specific to childhood and adolescence; Hyperkinetic syndrome of childhood; Specific delays in development; Psychic factors associated with diseases classified elsewhere).
[b]Delirium episode including abnormal thinking, delusions, or hallucinations.
[c]CPS, Cognitive Performance Scale (0 to 6).
[d]ADLH, Activities of Daily Living Hierarchy Scale (0 to 6).
[e]DRS, Depression Rating Scale (0 to 14).
[f]CHESS, Changes in Health, End-Stage Disease, and Symptoms and Signs Scale (0 to 5). Data expressed as number (percentages of participants).
Abbreviations: COPD, chronic obstructive pulmonary disease; ICD-9, International Classification of Diseases 9th revision; MSK, musculoskeletal; SD, standard deviation.

TABLE 2 Comorbidity components identified through principal component analysis (PCA)

Diseases	Heart diseases	Cardiovascular and respiratory diseases and sensory impairments	Psychiatric diseases
Cerebrovascular disease		0.28	
Ischemic heart disease	0.25	0.26	
COPD		0.29	
Heart failure	0.29		
Neurotic stress-related disorders			0.58
Depression			0.56
Schizophrenia	−0.39		
Arrythmia	0.52		
Atrial fibrillation	0.52		
Visual impairment		0.53	
Hearing impairment		0.48	
Hip fracture		−0.27	
Osteoarthritis			
Other MSK diseases			
Thyroid disease			

Note: Blanks are loadings < |0.25|.
Abbreviations: COPD, chronic obstructive pulmonary disease; MSK, musculoskeletal; SD, standard deviation.

of high-quality evidence and in light of the specific high care needs of the studied population, our results provide important insights useful to improve clinical management and define care priorities in a population requiring continuous care and around-the-clock assistance.

The heart disease pattern, characterized by ischemic heart disease, heart failure, arrhythmia, and atrial fibrillation, was associated to older age, recent hospitalization, polytherapy, and minimal–low health instability as captured by the CHESS scale. Cardiovascular patterns have been repeatedly described in several studies and associated with increased age, hospitalization, and geriatric syndromes.[4,14,32–34] While underlining the importance of interventions aimed at preventing and treating cardiovascular diseases, none of these studies addressed our population of NH residents with dementia. Institutionalized subjects with dementia expressing the heart diseases pattern could be more inclined to organs' decompensation due to higher difficulties in guaranteeing medication adherence or barriers in symptom communications with consequent delay in detecting signs of an acute condition, increasing the risk of a medical emergency or acute exacerbation of heart failure symptoms or atrial fibrillation[35–37] and re-hospitalization.[35–38] The association with health instability, as defined by the CHESS scale,

TABLE 3 Association between the identified comorbidity patterns and potential clinical and functional correlates

	Heart diseases		Cardiovascular and respiratory diseases and sensory impairments		Psychiatric diseases	
	β	95% CI	β	95% CI	β	95% CI
Female	**−.042**	**−0.07/−0.02**	**−.101**	**−0.13/−0.07**	**.119**	**0.09/0.15**
Age (years, ref. <70)						
70-79	**.078**	**0.03/0.13**	.026	−0.04/0.10	−.015	−0.09/0.06
80-89	**.105**	**0.06/0.15**	**.083**	**0.02/0.15**	**−.093**	**−0.16/−0.03**
≥90	**.119**	**0.07/0.17**	**.157**	**0.09/0.22**	**−.149**	**−0.22/−0.08**
Alzheimer's disease	.015	−0.01/0.04	.007	−0.03/0.04	−.0004	−0.04/0.04
Number of diseases	**.140**	**0.13/0.15**	**.206**	**0.20/0.22**	**.181**	**0.17/0.19**
Number of drugs (ref. 0-4)						
5-9	.017	−0.01/0.04	**−.039**	**−0.07/−0.01**	**.047**	**0.02/0.08**
10+	**.055**	**0.02/0.09**	**−.084**	**−0.13/−0.03**	**.071**	**0.02/0.13**
Hospitalization (past 90 days)	**.028**	**0.003/0.05**	**−.055**	**−0.09/−0.02**	−.008	−0.05/0.03
Weight loss	−014	−0.06/0.03	**.061**	**0.01/0.12**	**−.087**	**−0.15/−0.03**
Bladder incontinence	−.014	−0.05/0.02	−.021	−0.07/0.03	−.002	−0.06/0.06
Bowel incontinence	.017	−0.01/0.05	.030	−0.01/0.07	**−.060**	**−0.11/−0.0-1**
Tube feeding	.001	−0.03/0.03	**.095**	**0.05/0.14**	**−.083**	**−0.13/−0.03**
Delirium episode (past 3 days)[a]	**−.052**	**−0.07/−0.03**	−.004	−0.03/0.03	**.046**	**0.01/0.08**
CPS[b]						
Moderate	.004	−0.04/0.05	.037	−0.02/0.09	**−.094**	**−0.16/−0.0-3**
Severe	−.014	−0.06/0.03	**.131**	**0.07/0.19**	**−.193**	**−0.26/-0.13**
ADLH[c]						
Assistance required	.035	−0.02/0.09	.028	−0.04/0.10	.001	−0.07/0.08
Dependence	.029	−0.03/0.08	.052	−0.02/0.13	−.038	−0.12/0.04
DRS[d]						
2 or more depressive symptoms	**−.036**	**−0.06/−0.02**	**−.066**	**−0.09/−0.04**	**.134**	**0.10/0.17**
CHESS[e]						
Minimal–low health instability	**.024**	**0.001/0.05**	**−.033**	**−0.06/−0.003**	.024	−0.01/0.06
Moderate–high health instability	.037	−0.01/0.09	**−.082**	**−0.15/−0.02**	**.088**	**0.02/0.16**

Note: Significant beta coefficients and 95% confidence intervals (CI) are reported in bold.
[a]Delirium episode including abnormal thinking, delusions, or hallucinations.
[b]CPS, Cognitive Performance Scale (ref. Intact or minimal impairment).
[c]ADLH, Activities of Daily Living Hierarchy (ref. Total independence or supervision needed).
[d]DRS, Depression Rating Scale (ref. 0 or 1 depressive symptoms).
[e]CHESS, Changes in Health, End-Stage Disease, and Symptoms and Signs Scale (ref. No health instability).

and polytherapy, also outlines the importance of implementing in-site strategies to improve monitoring of health changes and avoid unnecessary adverse events.[39]

The cardiovascular and respiratory and sensory impairment pattern, characterized by cerebrovascular diseases, ischemic heart disease, chronic obstructive pulmonary disease, and visual and hearing impairment, showed a significant association to older age, severe cognitive status, weight loss, and tube feeding. The expression of this pattern in those affected by severe cognitive status enhances the relevance of the role of cerebrovascular diseases,[40] chronic obstructive pulmonary disease,[41] and hypoxia,[42] and visual and hearing loss[43,44] in worsening the cognitive performance. Furthermore, the association with weight loss and tube feeding, a possible direct consequence of the severity of the cognitive impairment[45] in individuals expressing this pattern, highlights the importance of promptly identifying residents displaying this phenotype to timily discuss an advanced care plan and enable a shared decision making with the patients and their caregivers concerning the potential indication of parental or enteral nutrition (via nasogastric or PEG tube) in institutionalized oldest old.[46]

The psychiatric diseases pattern showed a significant direct association to presence of delirium episodes and depressive symptoms,

female sex, polytherapy, and moderate–high health instability as per the CHESS scale, while displaying an inverse correlation to older age and cognitive impairment. In contradiction to other studies, hospitalization demonstrated a negative non-significant association with the expression of the psychiatric diseases pattern, possibly due to different characteristics of the study population[14] that, in the case of our study, lived in a more secure, medicalized, and controlled environment, able to guarantee in-site management of new symptoms. Nevertheless, the significant association with depressive symptoms and episodes of delirium is clinically meaningful to improve the rapid identification and early management of possible triggers of acute exacerbation of psychiatric symptoms.[47,48] Similarly, an early recognition of behavioral changes in these subjects may lead to appropriate therapeutical or environmental adjustments that could improve the psychological well-being of residents living with dementia. Interestingly, despite known associations with cognitive impairment and different psychiatric diseases, especially with depression,[49,50] cognitive status assessed via CPS inversely correlated with the expression of the psychiatric diseases pattern. This could relate to the fact that among NH residents, those displaying the psychiatric diseases pattern were on average younger and possibly at an early stage of dementia and could have been recently admitted to a residential setting due to reduced ability to self-care, progressive loss of independence in the ADL, or a worsening of the cognitive function.

Finally, conversely to other studies,[51] the independence in the ADL as captured by the ADLH scale did not significantly relate to the expression of any of the three patterns; this is probably due to the high level of required assistance upon admission, or even because the loss of independence represented the reason for the admission to the residential facility. In other words, the ADLH scale was probably not able to capture fine differences among NH residents, because of similar baseline characteristics of the subjects evaluated.

5 | STRENGTHS AND LIMITATIONS

This is the first study evaluating comorbidity patterns in NH residents affected by dementia using the interRAI instrument, a validated data collection tool. The identification of dementia comorbidities and their management in older institutionalized individuals is challenging for both researchers and clinicians because of the complex interplay between multiple chronic conditions and functional and cognitive status. We have analyzed this intricate interaction and described three different patterns of comorbidity. The identification of these phenotypes among older adults with dementia living in NH defines subgroups of individuals with similar medical, functional, and social needs and is instrumental to assess health trajectories and enforce scheduled reassessments of inpatients' assistance demands, facilitating the continuous remodeling of both pharmacological and non-pharmacological interventions to the patients' changing care needs. Several recommendations have been suggested for institutionalized individuals with dementia, such as medication revision and deprescribing,[52] and the identification of these health phenotypes represents an optimizing strategy to actualize those recommendations, especially important in a population prone to negative outcomes in case of incident health instabilities or unplanned hospitalization.[53] However, this study is not devoid of some limitations. The disease assessment was performed by trained assessors with a tool of demonstrated good reliability.[20] Although the assessors were able to consult medical history and clinical charts, the NH setting may have not allowed clinical confirmation of the diagnosis that might have led to possible misclassifications of some diseases or potential loss of information. Moreover, this study was carried out in the Italian region of Umbria, a setting with specific sociodemographic characteristics and guidance. Regional variability in the number of NH across Italy, with a north–south gradient,[54] may affect the generalizability of the results to a national and international scale. Also, regional income-related reimbursement criteria for access to long-term care facilities may change depending on regional policies and administrations, increasing the national variability and the potential resort to informal private home care assistance.[55,56]

6 | CONCLUSION AND IMPLICATIONS

We identified three clinically relevant comorbidity patterns among NH residents affected by dementia that differ in term of clinical and functional profiles: (1) heart diseases, (2) cardiovascular and respiratory diseases and sensory impairments, and (3) psychiatric diseases. Our study highlights the need for elaborating strategies to assess care needs and implement personalized care pathways for this population otherwise lacking standardized recommendations and guidelines,[57] leaving clinicians with the onerous burden of eliciting a best practice to evaluate effective treatable targets. Our study provides new evidence to support the implementation of a thorough personalized care plan, including advanced life plans, to ensure preventive intervention aimed at reducing and promptly treating adverse events like delirium or the exacerbation of a chronic condition that might worsen the health trajectories of NH patients with dementia. The prompt recognition of different health needs based on specific comorbidity profiles may ameliorate the prognosis of these individuals while improving cognitive and functional status, may help avoid unplanned hospitalization and increase overall quality of life of institutionalized older adults affected by dementia.

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CONFLICTS OF INTEREST

None of the authors has any conflict of interest to disclose.

AUTHOR CONTRIBUTION

Davide Liborio Vetrano and Graziano Onder designed and supervised the study. Davide Liborio Vetrano and Cecilia Damiano carried out data analysis. Maria Beatrice Zazzara contributed to literature search, the interpretation of results, and writing of the manuscript. Graziano Onder critically revised the analyses and the interpretation of the findings and contributed to writing of the manuscript. Angelo Carfì, Cecilia Damiano, Graziano Onder, Rosa Liperoti, and Davide Liborio Vetrano critically revised the manuscript. All the co-authors reviewed the manuscript and approved the final version.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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