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Identifying comorbidity patterns of mental health disorders in community-dwelling older adults: a cluster analysis

Joshua Tobin[1*], Michaela Black[2], James Ng[1], Debbie Rankin[2], Jonathan Wallace[7], Catherine Hughes[3], Leane Hoey[3], Adrian Moore[4], Jinling Wang[2], Geraldine Horigan[3], Paul Carlin[5], Helene McNulty[3], Anne M. Molloy[6] and Mimi Zhang[1]

Abstract

As global life expectancy increases, understanding mental health patterns and their associated risk factors in older adults becomes increasingly critical. Using data from the cross-sectional Trinity Ulster Department of Agriculture study (TUDA, 2008-2012; $n = 5186$; mean age 74.0 years) and a subset of participants followed-up longitudinally (TUDA 5+, 2014-2018; $n = 953$), we perform a multi-view co-clustering analysis to identify distinct mental health profiles and their relationships with potential risk factors. The TUDA multi-view dataset consists of five views: (1) mental health, measured with Center for Epidemiologic Studies Depression Scale [CES-D] and Hospital Anxiety and Depression Scale [HADS], (2) cognitive and neuropsychological function, (3) illness diagnoses and medical prescription history, (4) lifestyle and nutritional attainment, and (5) physical well-being. That is, each participant is described by five distinct sets of features. The mental health view serves as the target feature set, while the other four views are analyzed as potential contributors to mental health risks. Under the multi-view co-clustering framework, for each view data, the participants (rows) are partitioned into different row-clusters, and the features (columns) are partitioned into different column-clusters. Each row-cluster is most effectively explained by the features in one or two column-clusters. Notably, the row-clusterings across views are dependent. By analyzing the associations between row clusters in the mental health view and those in each of the other four views, we can identify which risk factors co-occur and contribute to an increased risk of poor mental health. We identify five distinct row-clusters in the mental-health view data, characterized by varying levels of depression and anxiety: Group 1, mild depressive symptoms and no symptoms of anxiety; Group 2, acute depression and anxiety; Group 3, less severe but persistent depression and anxiety symptoms; Group 4, symptoms of anxiety with no depressive symptoms; and Group 5, no symptoms of either depression or anxiety. Cross-view association analysis revealed the following key insights: Participants in Group 3 exhibit lower neuropsychological function, are older, more likely to live alone, come from more deprived regions, and have reduced physical independence. Contrasting Group 3, participants in Group 2 show better neuropsychological function, greater physical independence, and higher socioeconomic status. Participants in Group 5 report fewer medical diagnoses and prescriptions, more affluent backgrounds, less solitary living, and stronger physical independence. A significant portion of this group aligns with cognitive health row-clusters 1 and 3, suggesting a strong link between cognitive and mental health in older age. Participants with only depressive (Group 1) or anxiety

*Correspondence:
Joshua Tobin
tobinjo@tcd.ie
Full list of author information is available at the end of the article

symptoms (Group 4) exhibit notable differences. Those with anxiety symptoms are associated with healthier clusters across other views. The co-clustering methodology also categorizes the questions in the CES-D and HADS scales into meaningful clusters, providing valuable insights into the underlying dimensions of mental health assessment. In the CES-D scale, the questions are divided into four clusters: those related to loneliness and energy, those addressing feelings of insecurity, worthlessness, and fear, those concerning concentration and effort, and those focused on sleep disturbances. Similarly, the HADS questions are grouped into clusters that reflect themes such as a strong sense of impending doom, nervousness or unease, and feelings of tension or restlessness. By organizing the questions from both scales into these smaller groups, the methodology highlights distinct symptom patterns and their varying severity among participants. This approach could be leveraged to develop abridged versions of the assessment scales, enabling faster and more efficient triage in clinical practice.

Introduction

The global population of individuals aged 65 years or older is projected to reach 994 million by 2030 and 1.6 billion by 2050 [1]. As life expectancy increases and fertility falls globally, promoting healthier aging becomes a critical global health priority [2]. A crucial aspect of formulating successful health policies for older people involves gaining a better understanding of the mental health challenges they encounter as they age [3]. Previous studies seeking to comprehend the prevalence of mental health issues and their causes among older individuals have yielded inconsistent findings [4]. This inconsistency can, in part, be attributed to the diverse range of issues considered relevant to the mental health of older individuals. While existing literature primarily considers anxiety and depression disorders in isolation, recent works are increasingly considering the comorbidity patterns of such disorders [3, 5, 6]. Additionally, key predictors of mental health problems have been investigated independently, with studies separately exploring the relationships between mental health and risk factors, including social isolation and cognitive function [5], polypharmacy [7], nutrition [8], and physical ability [9]. Such studies may fail to adequately consider the interactive relationships among these risk factors and the various facets of mental health.

Several studies have explored the prevalence and risks associated with mental health disorders in older adults. Depression diagnoses among older individuals are deemed particularly perilous, linked to an increased risk of suicide and a more challenging prognosis for survivors compared to younger age groups [10]. Moreover, depression stands out as the most common mental disorder in older adults, often remaining under-recognized and insufficiently treated in this population [11, 12]. Estimates of the prevalence of the two most common mental health disorders, anxiety, and depression, exhibit considerable variability. In community-dwelling adults, anxiety prevalence estimates range from 1.2% to 15%, while in clinical settings, the prevalence spans from 1% to 28% [13]. For depression, recent meta-analyses suggest point prevalence ranging from 4.6% to 9.3% [14], whereas separate studies propose point prevalence in community-dwelling adults ranging between 1% and 4% [15]. The disparity in these estimates is attributed to assessment challenges [16] and the high prevalence of sub-threshold symptoms (15%–52.3% for anxiety symptoms; 4.5%–37.4% for depressive symptoms). Moreover, while the prevalence of comorbid anxiety disorders in depression is much higher than predicted by chance, there is not broad consensus in the literature regarding the rates of comorbid anxiety and depression disorders. Estimated comorbidity rates are seen to vary when samples are taken from clinical or community settings. Large variations between the rates of anxiety symptoms and diagnosable disorders are also observed [16–18].

Risk factors associated with mental health disorders in older adults

The association between mental health disorders and cognitive function in older adults has been a subject of exploration in various studies. A crucial discovery establishes a link between late-life depression and an elevated likelihood of developing dementia, highlighting the relationship between depression and other cognitive risk factors [19]. Additionally, cognitive deficits associated with depression diagnoses are shown to persist even after depressive symptoms enter remission. The cognitive profile of older adults with depression indicates poor learning and recall functions, while cued recall and recognition in memory testing remain intact. Verbal fluency and executive function tend to decline, but visuospatial skills and orientation remain unaffected [20, 21]. Typically, older adults with depression diagnoses demonstrate intact temporal explicit memory systems, allowing for the encoding and consolidation of memories, but exhibit poor executive function, leading to inefficient learning of stimuli [22].

Older adults with other illness diagnoses, encompassing issues with organ systems and chronic diseases such

as low vision, pulmonary disease, and diabetes, have been found to exhibit poorer mental health [23]. The relationship appears to be reciprocal, as adults diagnosed with depression between the ages of 50 and 62 are more likely to develop diabetes, heart problems, and arthritis in older age [24]. Polypharmacy is also recognized as a significant factor in the mental health of older individuals, with multi-drug therapy associated with deterioration in both physical and psychological health over extended periods [25].

Broader socio-demographic and lifestyle factors have also been considered in several studies for their association with mental health. Clinical advice suggests that depressed adults should increase their physical activity and exercise, improve their level of nutritional attainment, and aim to increase social engagement [26]. Cross-sectional and longitudinal studies have shown that widowed, divorced, or separated adults, and those living in more deprived areas are at a greater risk of developing mental health disorders [27]. Heavy smoking is also identified as a major risk factor for poor mental health, although its magnitude as an independent effect is unclear [28, 29]. Nutritional vulnerability can exacerbate symptoms of depression, and a two-way relationship exists between the manifestation of depressive symptoms and poor eating [30]. Older adults with depression also exhibit lower attainment of omega-3 fatty acids, phospholipids, cholesterol, niacin, folate, vitamin B6, and vitamin B12 [31], and such nutritional risk further impacts their quality of life [32].

Lastly, numerous in-depth studies have contributed to our understanding of the intricate relationship between physical ability and mental health in older individuals. This connection is reciprocal, wherein the level of physical health in the early stages of aging contributes to individuals' mental health as they age. Simultaneously, the quality of a person's mental health influences their physical health over time [33, 34]. Physical activity plays a pivotal role in mitigating the risk of developing mental health disorders with aging. Anxiety and depression are more prevalent among individuals with physical inactivity, those who are homebound, and those experiencing severe physical disabilities [28, 29, 35, 36].

Objectives of the present study

The uncertainty associated with estimates of the point prevalence of mental health disorders in the population is related to the challenges associated with a binary diagnosis and variation in assessment methods. As such, a richer understanding of the different profiles of mental health exhibited by older adults would be worthwhile. Furthermore, since the risk factors associated with poor mental health are wide-ranging and diverse, knowledge of which risk factors coexist and contribute to an increased risk of poor mental health would also be valuable in the targeting of appropriate interventions.

The data provided by the TUDA study is well-suited for this aim. The TUDA study was designed to provide a better understanding of risk-factors for age-related diseases, with a particular focus on the prevention of cardiovascular disease, osteoporosis and mental health. To achieve this aim, detailed information on numerous risk factors including socio-demographics, clinical, nutritional and lifestyle was collected in both the original cross-sectional investigation and in the follow-up study. The TUDA study recruited community-dwelling older adults as opposed to those living in nursing/residential care as the aim of the study was to better understand risk-factors for age-related diseases and how improving nutrition can provide solutions to prevent their development. To achieve this aim, older adults ranging from healthy to those exhibiting early predictors of common diseases of aging (e.g. early memory loss, hypertension) were recruited from the community. The TUDA dataset is a unique resource for aging research as participants were recruited from the island of Ireland using standardized protocols for participant sampling, assessment and data recording and centralized laboratory analysis.

The objective of our study is to describe the profiles of mental health exhibited in a population of community-dwelling adults aged 60+, and in particular, to examine the prevalence and patterns of diverse sets of risk factors that co-occur for each profile. The prevalence of coexisting risk factors has been examined in a limited number of studies [27, 37]. However, studies providing clusters or profiles of mental health in older adults and studies investigating the clustering behavior of the risk factors for poor mental health are lacking. Although we accept that other factors which were not measured as part of the TUDA study may also contribute to poor mental health, the richness of the dataset on disease risk factors allowed for a comprehensive exploration in relation to mental health using novel data-driven techniques in the current study.

We investigate the relationships between the mental health profiles revealed by this analysis and four sets of features: (1) cognitive health; (2) illness diagnoses and medications; (3) lifestyle and nutrition; and (4) physical health. Finally, we investigate the longitudinal relationships present in the data, aiming to understand if characteristics associated with the mental health profiles uncovered are immutable and if the membership of each cluster is fixed across time.

Mental health assessment and risk factors

The current study uses the Trinity Ulster Department of Agriculture (TUDA) study dataset, a large observational study examining socio-demographic, health, nutritional, and genetic factors concerning aging in community-dwelling older adults. TUDA participants were recruited from geriatric medicine day hospital/outpatient clinics in St James's Hospital Dublin, Ireland, and from general practice in the Western and Northern Health and Social Care Trust catchment areas in Northern Ireland. The participants included healthy older adults along with those exhibiting early predictors of common diseases of aging (e.g. early memory loss). Any potential participants with an existing clinical diagnosis of dementia were excluded from the study. Further details on the TUDA dataset are available in other studies, including investigations of risk factors for cognitive dysfunction [38–41] and depression and anxiety disorders [42]. The TUDA dataset includes 5,186 participants who completed a comprehensive 90-minute cognitive and health assessment between 2008 and 2012. During this time, detailed demographic and lifestyle information, along with medical and medication histories, were meticulously recorded. As part of the TUDA 5+ study, around 20% of TUDA participants underwent a repeat cognitive and health assessment between 2014 and 2018. An interval of 5+ years was chosen firstly from a practical point of view as recruitment and sampling of the initial cohort lasted for 4 years. Secondly, as the primary outcome of the longitudinal analysis was cognitive health, the interval ensured that sufficient time had elapsed to detect a change in cognitive function whilst at the same time increasing the chances of re-sampling participants as they ranged in age from 60–102 years.

The study generates five distinct feature sets, with the first set capturing the mental health of the sample, and the remaining four sets encompassing various risk factor covariates that shed light on different aspects of participants' lives. These four sets focus on (1) cognitive and neuropsychological health, (2) illness diagnoses and prescribed medications, (3) lifestyle patterns and nutritional biomarker levels, and (4) physical health. This allows longitudinal relationships of the mental health function of older adults to be assessed. Detailed information about the features within each set and the data format of each feature is provided in the appendices.

Mental health assessment

The mental health of the sample participants was assessed using two questionnaires, the Centre for Epidemiological Studies Depression (CES-D) scale [43] and the Hospital Anxiety and Depression Scale (HADS) scale [44].

CES-D is a 20-item scale which captures how often participants felt certain ways during the past week, including being bothered by things, and feeling lonely, fearful, and depressed. The CES-D scale is a four-point ordinal scale, with responses ranging from 0 (never or rarely) to 3 (most of the time). The responses to all of the questions are coded so that higher values are indicative of increased likelihood of depression. In a clinical setting, CES-D scores greater than 15 indicate probable depression.

HADS is a 7-item questionnaire on a four-point scale. HADS captures feelings of tension, worry, and panic. Scores greater than 10 on the HADS scale indicate probable anxiety.

Experts in clinical gerontology involved in designing the study chose to use the CES-D to assess depression rather than the depression related items included in HADS in line with their clinical practice as CES-D includes more items covering depression criteria.

In total, there are 27 features in this set.

Covariate set 1: cognitive health

Detailed global and domain-specific cognitive functions were assessed for each participant. The Mini-Mental State Examination (MMSE) was used first, as a general cognitive screen [45]. It involves 11 questions capturing a high probability of cognitive impairment or dementia. Consistent with normative data for the MMSE in a representative Irish population, those with a score of < 25 are considered to have established impairment or dementia [41].

To assess neuropsychological performance in more detail, the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) was used [46]. We here consider the total scores from domain-specific scores from immediate memory, visual-spatial, language, attention, and delayed memory, yielding 12 total numeric scales. A score of less than 80 is indicative of cognitive dysfunction.

We also include 6 questions from the Frontal Assessment Battery (FAB) [47], a popular and fast way of assessing frontal lobe function. The FAB is a brief battery of six neuropsychological tasks designed to assess frontal lobe function. These include similarities, lexical fluency, motor series tests, conflicting instructions, Go/No-Go tests of inhibitory control, and prehension behavior. A cut-off score of 12 on the FAB has a sensitivity of 77 and a specificity of 87 in differentiating between frontal dysexecutive-type dementias and dementia of Alzheimer's type.

In total, there are 29 features in this set.

Covariate set 2: illness & medication

The medical and medication history of participants was also obtained. History of hypertension, diabetes, hyperlipidaemia, ischaemic heart disease, angina, heart attack, atrial fibrillation, stroke, TIA, peripheral artery disease, carotid endarterectomy, bypass operation, osteoporosis, epilepsy, GI disease, rheumatoid arthritis, atrophic gastritis, and other serious diseases (as suggested by participants) was collected via self-report.

Furthermore, a list of current medications and information about the duration of use was collected and coded using the Anatomic Therapeutic Classification (ATC) system. We only consider medications taken daily and continuously for at least six months at the time of assessment. To account for differences in available medication across sample regions, the medications are collected into categories: statins medications, lipid medications, anxiety medications, antidepressant medications, antipsychotic medications, dementia medications, and vitamin D supplements.

In total, there are 26 features in this set.

Covariate set 3: lifestyle & nutrition

Geo-referenced using address-based information, participants were linked to official socioeconomic indicators of deprivation within the United Kingdom and the Republic of Ireland in [48]. Each participant was assigned an individual deprivation score related to the smallest administrative area in which they lived, on a five-point scale. Additionally, marital status and living arrangements (whether participants lived alone or with others) were included. Smoking and drinking status were also included.

A non-fasting blood sample (50mL) was collected from each participant using aseptic venipuncture. Blood samples were kept chilled following venepuncture and centrifuged within 3 hours of collection at local hospital laboratories. Serum was aliquoted and stored at −80deg C until later analysis. Of interest in this study is the level of the following hospital-measured biomarkers: C-reactive protein (CRP), white cell count (WCC), haemoglobin (Hb), mean corpuscular volume (MCV), platelet count (PLT), Hematocrit (HCT), albumin, gamma FT, urea, creatinine, aklaine phosphatase (AlkPhos), glomerular filtration rate (GFR), sodium (Na), potassium (K), calcium (Ca), phosphate (Po3), parathyroid hormone (PTH), cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, glucose, and glycated haemoglobin (HbA1c) whose levels were compared with ranges obtained from standard laboratory blood specimen request/result forms. We also consider the levels of the following nutritional biomarkers: serum folate, red blood cell folate, plasma pyridoxal-5-phosphate (vitamin B6), EGRac (riboflavin), serum total vitamin B12, serum holotranscobalamin, serum methylmalonic acid, serum total homocysteine, and serum 25(OH)D (vitamin D) whose levels are compared with ranges obtained from the literature. The comparison ranges, and their sources if applicable, are available in the appendices.

In total, there are 37 features in this set.

Covariate set 4: physical health

To capture differences in physical health among sample participants, their age and sex (coded as Male/Female binary) were recorded. Body Mass Index (BMI) was calculated from weight and height and recorded using electronic scales and a wall-mounted stadiometer. Frailty was captured in the study using, firstly the Timed-Up-and-Go (TUG) Test [49] and, secondly, using the Lawton instrumental activities of daily living (IADL) scale [50]. The TUG test asked participants to stand from a seated position (seat height approximately 46cm), walk 3m at their usual pace, turn around, walk back to the chair, and sit down. No physical assistance was given, and the time taken from command "Go" to completion of the task was measured using a stopwatch. The IADL scale, a 10-item questionnaire, asks participants about their ability to complete representative activities. The responses are measured on a three-point scale, ranging from 0 (completely unable to complete the task) to 2 (able to complete the task without help). Another scale used to assess the ability of sample participants to live independently is the Physical Self-Maintenance Scale (PSMS) [50]. This scale, again a three-point scale, records participants' competence in toileting, feeding, dressing, grooming, motion, and bathing. Information was also captured on the frequency of falls, dizziness, and fainting via self-report, and participants were asked if they limit their household and outdoor activities due to physical incapacity.

In total, there are 29 features in this set.

Missing data analysis

The TUDA team made extensive efforts to collect complete data and biological samples from all participants, achieving this for the vast majority. Missing data were minimal, with a maximum of 9 missing values (0.2%) for any feature in the mental health view. A small proportion of participants (n=225, 4.3%) were unable to complete certain components of the cognitive assessment tools due to functional or literacy difficulties. Additionally, over 99% of participants provided blood samples for laboratory analysis. The co-clustering method employed in this study is capable of handling missing values. As such, no observations were excluded from the study.

Co-clustering with the multi-view latent block model

Co-clustering is an advanced clustering technique for analyzing complex datasets with many instances and features. Unlike traditional clustering, which groups only instances, co-clustering simultaneously groups both instances and features. For example, in a data matrix where rows correspond to individuals and columns represent features, co-clustering groups the rows into row-clusters and the columns into column-clusters. That is, co-clustering partitions the data matrix into distinct blocks, where each block corresponds to the intersection of a row-cluster and a column-cluster. Each column-cluster can be viewed as a meta-feature, and each row-cluster is typically relevant with only a few meta-features. This means that co-clustering identifies the most relevant features for explaining each row-cluster, making it a highly effective method for dimension reduction. By revealing these relationships, co-clustering provides a clearer understanding of how instances and features interact, helping to uncover patterns and insights in complex data. This approach has provided new insights for genomics and quality of life datasets in past research [51, 52]. An illustrative example of co-clustering is shown in Fig. 1.

Multi-view latent block model

The mental health assessments, combined with four distinct sets of features, provide several perspectives on the participants, allowing phenomena of interest to be explored from multiple angles. To effectively analyze this integrative data, a co-clustering method that can handle multi-view data is required. The Multi-View Latent Block Model (MVLBM), a recently developed co-clustering technique, is particularly suited for this purpose. MVLBM is designed to handle an arbitrary number of views (i.e., multiple sets of features) and is thus applicable to datasets with varying complexities. In this study, it takes as input the five views and partitions participants and features into distinct groups for each view, while accounting for dependencies in row-cluster memberships across views. By analyzing the associations between the mental health row-clusters and the row-clusters from the other four views, MVLBM reveals the clustering behavior of risk factors and pinpointing patterns of co-occurring conditions [52]. It characterizes each block cluster using a parametric distribution, rendering the block interpretable through its distribution parameters. To determine the optimal number of row and column clusters for the MVLBM, one effective approach is to use the integrated classification likelihood (ICL) criterion. This method is supported by strong theoretical foundations and has been validated through practical applications [53]. The procedure for clustering the data using the MVLBM is shown in Fig. 2.

The TUDA dataset encompasses features of continuous, ordinal, and binary nature. Given that the MVLBM is a model-based co-clustering method, it necessitates the specification of a probability distribution for each data type. As suggested by [52], we employ a normal distribution, characterized by the mean (μ) and standard deviation (σ), to model continuous data. For ordinal data, the Binary Ordinal Search (BOS) distribution is employed, consisting of two parameters: μ representing the mode of the ordinal data, and β representing precision. When $\beta = 0$, all categories are equally likely; conversely, when $\beta = 1$, the data consistently reflects the mode μ. Binary

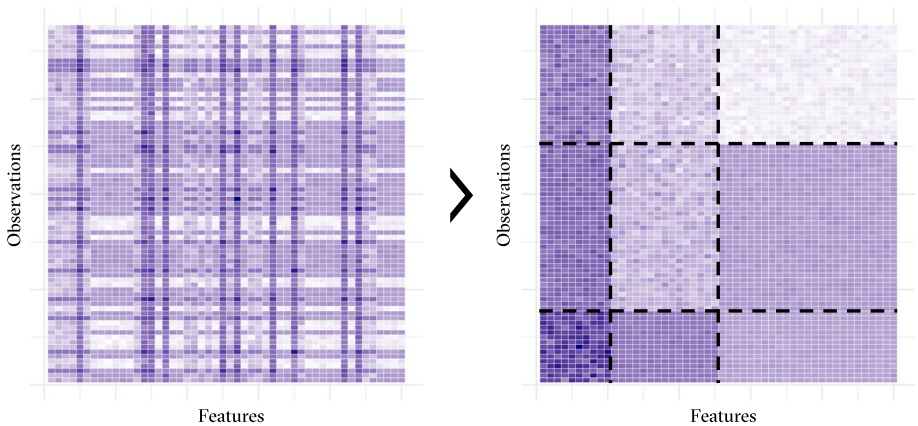


Fig. 1 Co-clustering (also known as bi-clustering) is a data analysis technique that simultaneously groups rows (i.e., observations) and columns (i.e., features) of a data matrix into clusters, uncovering block structures. This toy example demonstrates a convenient permutation of rows and columns, revealing a checkerboard pattern where each block-cluster corresponds to a subset of rows and columns with similar values. The method identifies specific column clusters that are most relevant to each row cluster. For instance, in this example, the second column cluster is most predictive of the third row cluster, while the third column cluster is most predictive of the first row cluster

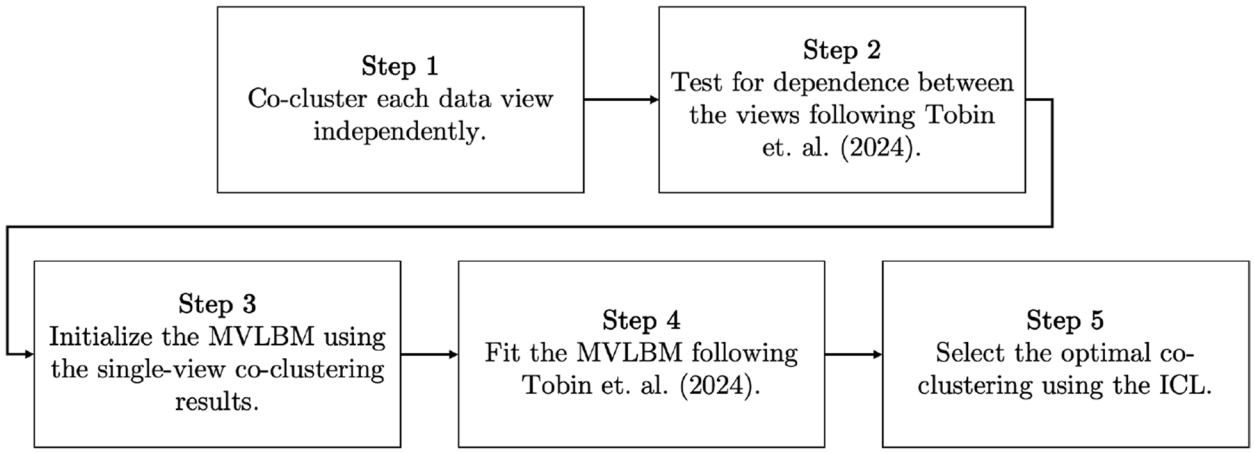


Fig. 2 Clustering procedure of the MVLBM method described in [52]. **Step 1**: The Latent Block Model (LBM) is applied independently to each view of the dataset, clustering rows (observations) and columns (features) into distinct groups specific to each view. **Step 2**: Perform hypothesis testing to assess the independence of row clusters across different views. If dependency is detected between views, they are incorporated into the multi-view analysis. Pairwise tests are performed, with adjustments for multiple comparisons applied when analyzing more than two views. **Step 3**: Use the co-clustering results from the single-view LBMs as the initialization for the multi-view analysis. The initial clustering assignments inform the joint row-cluster membership structure and the column-cluster parameters for each view. **Step 4**: Employ the stochastic Expectation-Maximization algorithm combined with Gibbs sampling for parameter estimation. This approach accounts for the dependency structure among views. The MVLBM algorithm iteratively updates (1) row and column cluster assignments, (2) cluster parameters within each view, and (3) the joint row-cluster membership matrix, which captures dependencies across views. **Step 5**: The iterative process terminates when the Integrated Completed Likelihood (ICL) criterion fails to increase between iterations. This ensures that the best-fitting model is identified

data are modeled using the standard binomial distribution, parameterized by the probability p.

Implementation procedures

The MVLBM is implemented in Python, running on Python version 3.11.4. We estimate the MVLBM following the procedure outlined in [52] (see Fig. 2). We report the number of row- and column-clusters recovered for each view, along with the p-values from hypothesis tests assessing associations between the views. We present a typology of mental health profiles within the population and link these profiles to the four risk-factor views considered. Finally, for each feature view, we analyze the clustering behavior of the risk factors, their relationship to participant clusters within the view, and their connection to the previously described mental health profiles.

Statistical analyses were conducted in RStudio using R version 4.3.2. Graphical visualizations utilized the matplotlib package in Python and the ggplot2 package in R. Differences among mental health profiles were statistically validated employing multivariate non-parametric Wilks' Lambda statistics, as developed by [54] and implemented in the npmv package in R. The difference between the mental health profiles were evaluated using the Kruskal-Wallace test for interval or non-normally distributed variables, while categorical variables underwent the Chi-squared test. Given the number of comparisons, and considering an α level of 0.05, a Benjamini-Hochberg correction was used to adjust the significance level such that the false discovery rate is retained at 0.05 [55].

Ethics

Ethical approval for the TUDA study was granted by the Research Ethics Committee in St James's Hospital, the Adelaide and Meath Hospital, Dublin, Ireland, and the Office for Research Ethics Committees Northern Ireland (ref: 08/NIR03/113) with corresponding research governance approval from the Northern and Western Health and Social Care Trusts in Northern Ireland.

Results

Baseline characteristics of the TUDA study participants are presented in Table 3. The clustering results for the TUDA dataset are obtained by applying the MVLBM, following the procedure described in Fig. 2. The p-values resulting from tests of associations between the row-clusters obtained by applying the single-view LBM to each of the five views (Step 1–2). A p-value smaller than the significance level of 0.05 indicates rejection of the null hypothesis, suggesting dependence between the row-clusters. The corresponding p-values for the test of no association between the row-clusterings for the TUDA feature views were all below 0.001. We observe statistically significant pairwise relationships between the clusters of participants in the five views. The MVLBM is then applied to the dataset with five views, and the optimal

model-specifically, the number of row- and column-clusters for each view-is determined using the ICL criteria (Steps 3–5). An iterative process is used to assess models of different sizes and the optimal model is selected when the ICL criteria fails to improve. The process is described in detail in Appendix C. Table 1 presents the number of row- and column-clusters for each view in the optimal model. The resulting detailed parameter estimates for each block-cluster and data view in the optimal model are provided in Appendix D.

The rest of this section is structured as follows. We first present the co-clustering results for the mental health view, which is of primary importance. The co-clustering results for the cognitive, illness, lifestyle and physical views section are subsequently detailed. The relationships between the mental health view and the remaining views, as revealed by the co-clustering analysis, are explored. Finally, the mental health profiles in a follow-up cohort are analyzed.

Co-clustering results for the mental health view

The co-clustering results for the mental health data view is depicted in Fig. 3. In all figures below, clusters are interpreted from left to right and top to bottom. The frequency distribution of responses for each of the block-clusters is shown in Fig. 4.

The MVLBM method identifies five row-clusters, hereafter referred to as mental health groups (MHGs). Figures 3 and 4 illustrate that mental health Group 2 ($n = 315$) consistently exhibits higher or equal responses to questions in both the CES-D and HADS scales compared to the other groups. This trend is supported by the detailed parameter estimates provided in the appendices, indicating that Group 2 experiences more intense levels of depression and anxiety than the other groups.

Mental health Group 3 ($n = 1088$) demonstrates response patterns similar to Group 2 but with reduced severity. The lower modal scores in the fourth column-cluster of the CES-D scale (1 for Group 3 and 3 for Group 2) and the fourth column-cluster of the HADS scale (0 for Group 3 and 2 for Group 2) suggest a less severe manifestation of symptoms. However, this group still experiences depression more intensely than Groups 4 and 5, and anxiety more intensely than Groups 1 and 5.

Being the smallest group with $n = 152$, mental health Group 1 exhibits the fewest symptoms of anxiety on the HADS scale. However, members of this group still experience symptoms of depression, particularly physical ones such as difficulty concentrating, a sense of effort in daily tasks, and restless sleep.

Mental health Group 4 ($n = 602$) exhibits the opposite patterns of disease to Group 1. Here, scores for the CES-D scale are uniformly low, while scores for the anxiety scale are high. This group records the most severe symptoms for the third and fourth column-clusters of the HADS variable group.

Mental health Group 5 ($n = 3029$) recorded the fewest symptoms of all. They exhibit almost zero symptoms for the questions contained in CES-D column-clusters 1, 2, and 3 and rarely record non-zero responses for the anxiety symptoms contained in HADS column-cluster 1, 2, and 4. It can be said that this group has the best mental health of the groups returned by the co-clustering.

The differences in responses to the CES-D scale across the five mental health groups are statistically confirmed. A a multivariate non-parametric analysis of variance tests the null hypothesis of equality between the mental health

Table 1 The number of row- and column-clusters selected as optimal using the ICL criterion from the multi-view co-clustering of the TUDA data is summarized

View	Number of Row Clusters	Number of Column Clusters					
Mental	5	CES-D	HADS				
		4	4				
Cognitive	3	RBANS	MMSE	FAB			
		3	6	2			
Illness	2	Diagnoses	Medications				
		3	3				
Lifestyle	2	Deprivation	Living Status	Smoke/Drink	Nutrition		
		1	2	1	4		
Physical	2	Female	Age	TUG	BMI	IADL	PSMS
		1	1	1	1	3	3

Column-clusters are grouped to reflect the original scales used in the study. For instance, within the cognitive view, participants were partitioned into three row-clusters. The RBANS-related features were divided into three column-clusters, the MMSE-related features into six column-clusters, and the FAB-related features into two column-clusters

Fig. 3 Co-clustering results on the set of mental health features. Each small colored box represents a single participant (row) and their corresponding response in either CES-D or HADS (column). Participants were grouped into five row-clusters. The CES-D-related features were organized into four column-clusters, and the HADS-related features into another four column-clusters. Darker colors indicate a higher frequency of symptoms. The results reveal that participants in Group 2 (from top to bottom) consistently exhibit higher or equal responses to questions on both the CES-D and HADS scales compared to the other groups

groups. This test uses the Wilks' Lambda test statistic and considers the sum of responses within each CES-D column-cluster as a variable, with mental health group as the common factor. The overall differences across the mental health groups on the CES-D scale clusters were highly significant ($\lambda = 386.28, df = 16, p < 0.001$). The pairwise comparisons for each of the mental health groups indicate that each group is significantly different from all of the others, controlling for maximum overall type I error at 0.05. Finally, the pairwise comparison of the column-cluster variables shows that each is significantly different from the others, again controlling for maximum overall type I error at 0.05.

The analysis is reiterated for the HADS column-clusters, and once more, statistical confirmation of differences in responses across the mental health groups was achieved through a multivariate non-parametric analysis of variance, again using the Wilks' Lambda test statistic. The overall differences among the mental health groups along the HADS scale were highly significant ($\lambda = 237.97, df = 16, p < 0.001$). In pairwise comparisons for each mental health group, it was observed that each group significantly differed from all others, maintaining control over the maximum overall type I error at 0.05. Similarly, in pairwise comparisons for the column-cluster variables, it was observed that each group significantly differed from mall others, again maintaining control over the maximum overall type I error at 0.05.

The questions contained in each of the column-clusters for the mental health data are outlined in Table 2.

Specifically, four clusters are identified for the CES-D scale questions. Upon closer examination of the questions within each cluster, it is evident that: The first cluster encompasses questions related to loneliness and energy. The second cluster captures inquiries concerning insecurity, worthlessness, and fear. The third cluster addresses issues related to concentration and effort. The fourth cluster pertains to questions addressing problems with sleeping. Examining the block clusters in Fig. 3, we see that questions from the first and third column clusters are useful for differentiating between participants with and without depressive symptoms. For the third column-cluster, mental health Groups 1, 2, and 3 have higher modal values than Group 4 and 5. Furthermore, the precision parameters for the first column-cluster are higher for Groups 4 and 5, indicating the data is concentrated and symptoms are rarely observed. The feelings captured by questions present in the second column

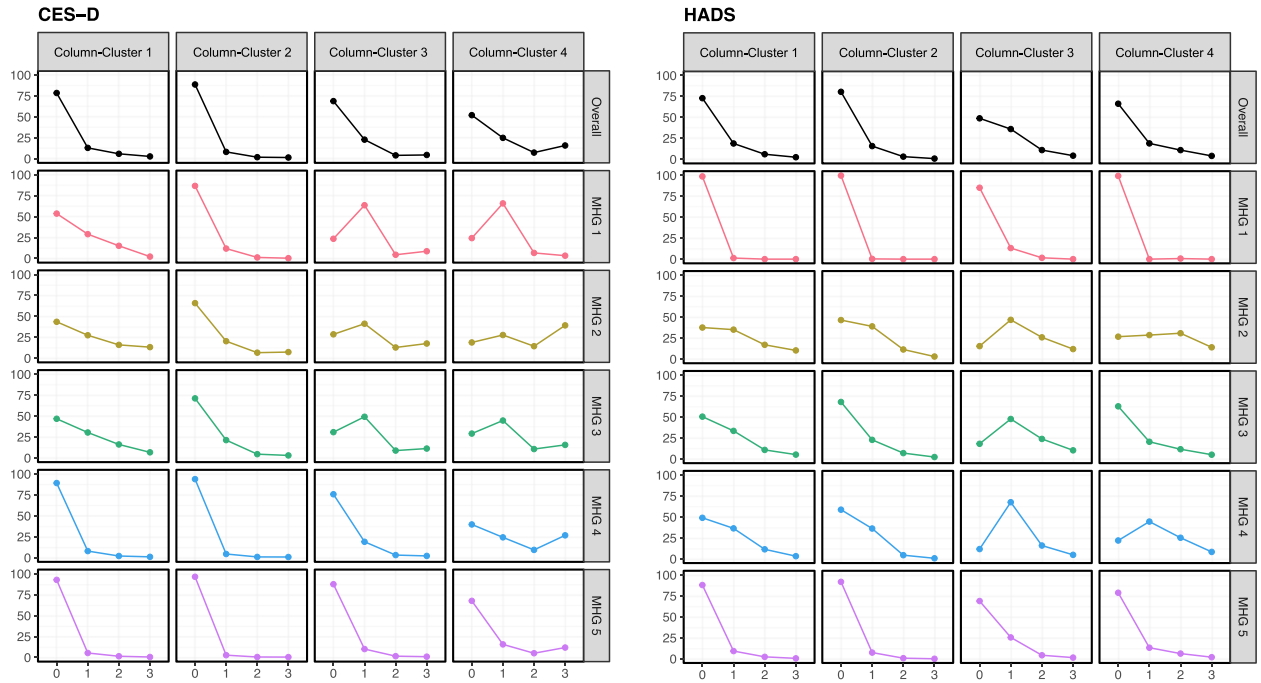


Fig. 4 The x-axis represents the four-point scale (0: 'rarely or none of the time'; 1: 'some or a little of the time'; 2: 'occasionally or a moderate amount of time'; 3: 'most or all of the time'). The y-axis indicates the percentage frequency of responses for each scale point. The curves in the top row depict the average frequency distribution of responses across all participants for each column cluster. In contrast, the curves in rows 2 to 6 show the average frequency distribution for participants within each mental health group, highlighting differences in symptom severity and response patterns across groups

Table 2 The questions (namely, features) from the CES-D scale were divided into four column-clusters: the first and second clusters each contain eight questions, the third contains three questions, and the fourth contains one question

	CES-D			
	Col C1	Col C2	Col C3	Col C4
n	8	8	3	1
	Bothered by things	Poor appetite	Felt sad	Restless sleeping
	Felt depressed	Felt the blues	Everything is an effort	
	Hopeful about future	Worse than others	Trouble concentrating	
	Happy	Felt life a failure		
	Talk less than usual	Felt fearful		
	Felt lonely	People are unfriendly		
	Enjoyed life	Crying spells		
	Couldn't get going	People dislike me		
	HADS			
	Col C1	Col C2	Col C3	Col C4
n	2	2	2	1
	Feel something awful coming	Butterflies in stomach	Tense and wound up	Restless on the move
	Unable to sit at ease	Sudden feeling of panic	Worrying thoughts	

Similarly, the HADS scale questions were grouped into four column-clusters: the first three clusters each contain two questions, while the fourth contains one question

cluster related to insecurity, worthlessness, and fear are exhibited more rarely and thus can differentiate those who experience depressive symptoms more acutely. The MVLBM method has separated the questions in the CES-D scale into groups with varying severity. Lastly, we note the idiosyncratic response pattern of column-cluster

4, namely experiencing restless sleeping. Respondents record severe symptoms for this question without exhibiting any other symptoms.

Four column-clusters are also identified for the HADS scale. Again, the MVLBM method separates the questions by the frequency of non-zero responses. Questions related to tension and worry are in column-cluster three and are esomewhat prevalent across all participant groups. Questions related to feeling frightened of something awful happening and inability to sit at ease are experienced more rarely and thus are placed in the first cluster. Mental health Groups 2, 3, and 4 are most likely to exhibit non-zero responses to the HADS scale questions. Questions in the third column-cluster provide a useful way of differentiating between groups with no anxiety and possible anxiety. Similar to the CES-D scale, we can assess participants with the most acute symptoms of anxiety through non-zero responses to questions in column-cluster 2. These feelings are typically felt only by the sample participants with the highest scores on the HADS scale. Regularly experiencing sudden feelings of panic and butterflies in your stomach are the rarest symptoms and separate participants who experience anxiety most acutely.

By placing the questions from the CES-D and HADS scales into a small number of groups, the column clusters offer a concise method for categorizing sample participants. The question represent the varying severity of symptoms experienced by the participants and could be used to produce abridged assessment scales for faster triage in clinical practice.

Co-clustering results for the cognitive, illness, lifestyle and physical views

We next explain the row-clusters for the data views containing the four sets of risk factors. We present graphical summaries of each of the views in Fig. 5. It is important to note that the rows (representing participants) differ across the data views. The features in each of the views are also clustered. Features with similar response patterns in the sample are grouped together. The feature clusters in each of the views are detailed in Appendix E.

The cognitive health data view reveals three distinct row-clusters. The second row-cluster ($n = 1234$) stands out with the lowest neuropsychological function among the clusters, characterized by challenges in fluency, recall scores, and conceptualization. In contrast, the third row-cluster ($n = 2259$) demonstrates the highest cognitive function, showcasing little to no issues in tasks like copying figures, naming pictures, and repeating phrases. The first row-cluster ($n = 1693$) falls between clusters two and three in terms of cognitive function.

The illness and medicine view consists of two row-clusters, primarily differentiated by the prevalence of anti-anxiety, anti-depressive, and anti-psychotic medication. The first row-cluster ($n = 1905$) is 2.7 times more likely to regularly take anti-anxiety and anti-depressive medication (27% vs. 10%) and eight times more likely to take anti-psychotic medication (8% vs. 1%) compared to the second row-cluster ($n = 3281$).

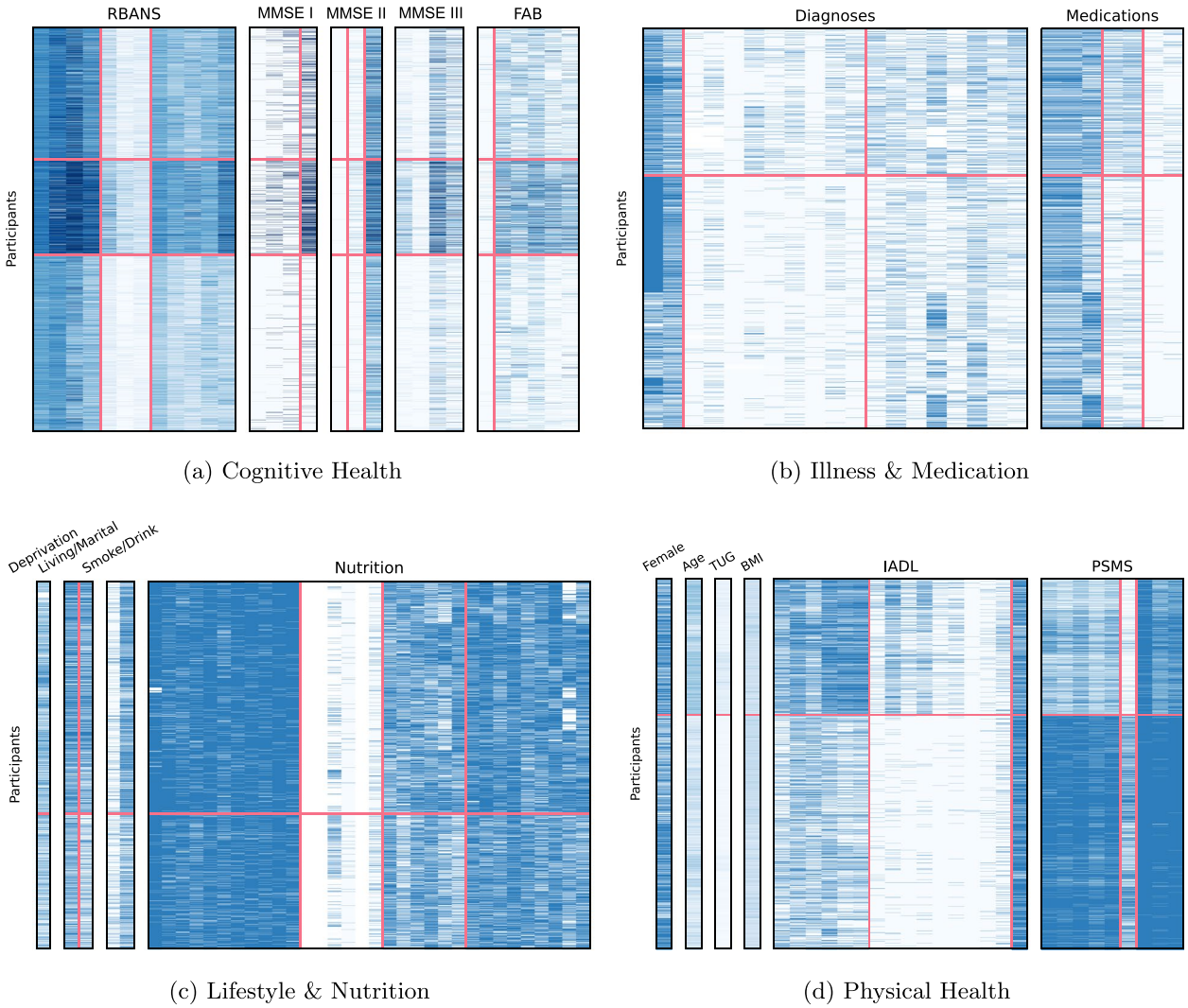
The lifestyle and nutrition view also presents two row-clusters. Participants in the first row-cluster ($n = 3281$) reside in less deprived areas than those in the second row-cluster ($n = 1905$). Notably, regions with the least deprivation are most common in the first row-cluster, while regions with the highest deprivation are predominant in the second row-cluster. Additionally, the first row-cluster is nearly twice as likely to be married as the second row-cluster (63% vs. 35%), and individuals in the first cluster are 26% more likely to live with someone else (72% vs. 57%).

The clustering analysis identifies two row-clusters for physical health features, distinguished by age. The first row-cluster ($n = 1905$) is nine years older than the second cluster ($n = 3281$) (79.7 years vs. 70.7 years). The first row-cluster exhibits significantly poorer performance on the TUG test (21.4s vs. 9.9s), indicating greater frailty. Furthermore, it records higher occurrences of falls and dizziness, lower ability to eat and bathe independently, and less independence in daily household tasks.

Relationships between mental health and the four sets of covariates

The MVLBM approach offers a significant advantage by constructing the row-clusters for each data view simultaneously, facilitating a comprehensive understanding of the relationships among the row-clusters in different views. Given our primary interest in the mental health profiles of the participants, we focus on pairwise comparisons between the mental health view and each of the four covariate views. The contingency tables, depicting the row-clusters identified in the mental health view and each covariate view, are presented in Fig. 6.

Figure 6 shows that the two mental health profiles with the worst symptoms of anxiety and depression, Groups 2 and 3, exhibit different patterns in the other views. The participants in mental health Group 3 are members of cognitive health clusters 1 and 2, illness and medicine cluster 1, lifestyle and nutrition cluster 2, and physical health cluster 1. These cluster memberships indicate that those in mental health Group 3 have lower neuropsychological functions, are from more deprived regions, are more likely to live alone, are older, and are less physically independent. This echoes many of the risk factors uncovered in the existing literature and suggests an interactive



(a) Cognitive Health

(b) Illness & Medication

(c) Lifestyle & Nutrition

(d) Physical Health

Fig. 5 Co-clustering results for the other four data views: cognitive, illness, lifestyle and physical. The participants with similar response patterns are clusters together in the rows. Similarly, the features to which the participants responded similarly are grouped together in the columns. Top Left: Darker colors indicate poorer cognitive performance. The three MMSE groups represent the different feature types in the MMSE instrument. Top Right: Blue cells indicate the presence of the diagnosis or prescription of medications. Bottom Left: Darker cells indicate more affluent areas, that the participant lives with someone, is married, currently smokes, currently drinks, and has normal levels of the given nutritional biomarker. Bottom Right: Darker cells indicate the participant is female, is older, has a longer TUG score, has a higher BMI, and is less able to self-maintain

as well as independent effect of combinations of risk factors. By contrast, mental health Group 2, the smaller group, exhibits the very opposite patterns for prominent risk factors: the participants in mental health Group 2 are members of cognitive health cluster 3, illness and medicine cluster 2, lifestyle and nutrition cluster 1, and physical health cluster 2. This group indicates that prominent risk factors for mental health disorders in older adults do not account for the full picture, and that exogenous mental health disorders persist in the population.

Likewise, the mental health Groups 1 and 4 also exhibit opposite patterns: participants in Groups 1 and 4 never belong to the same row-cluster in any of the other four views. Comparing Groups 1 and 4, which exhibit solely depressive and anxiety symptoms respectively, we note that those with solely anxiety symptoms belong to healthier clusters in the other views.

Examining mental health Group 5, the group without anxiety and depressive symptoms, we note the majority of them also belong to illness and medicine row-cluster 2, lifestyle and nutrition row-cluster 1, and physical health row-cluster 2. These are the groups with fewer medical diagnoses and prescriptions, more affluent backgrounds, less solitary lives, younger, and more independent.

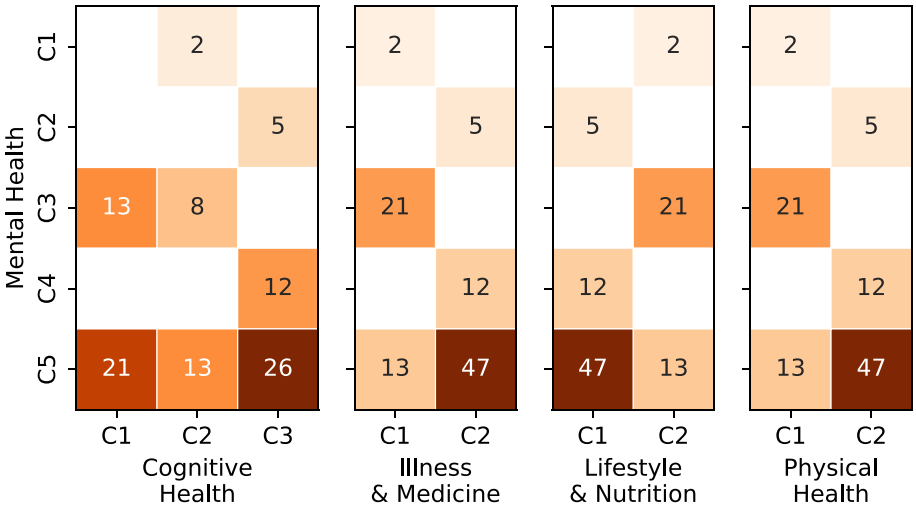


Fig. 6 The row-clustering in each view gives a partition of the participants. We here present contingency tables for the row-clusters found in the mental health data view and the row-clusters found in the four risk-factor views. The values inside the table are percentages. For example, when examining the cognitive health view, 12% of the participants fall into both Group 4 in the mental health view and the third row-cluster in the cognitive health view. Notably, Group 4 does not intersect with the other two row-clusters in the cognitive health view, suggesting that the features in the third row-cluster of the cognitive health view may be potential risk factors for participants in Group 4

Moreover, a significant portion of this group belongs to cognitive health row-clusters 1 and 3, indicating that strong cognitive and mental health are related in older age.

Table 3 displays the demographic characteristics, mental health outcomes, cognitive health outcomes, medical diagnoses, lifestyle factors, nutritional biomarker levels, and physical well-being outcomes for the five mental health groups.

- **Demographics**: Age variations were not significant among groups, but substantial differences emerged in gender and deprivation ($p < 0.001$).
- **Mental Health**: Concerning diagnostic scales for depression and anxiety, no group has a median level above the threshold levels, 15 for CES-D and 10 for HADS. Nevertheless, the difference in mean ranks among the mental health groups is highly significant for both scales ($p < 0.001$). The severity of symptoms endured by Groups 2 and 3 is clear in this analysis, as is the uncoupling of depressive and anxiety-based symptoms for Groups 1 and 4. Furthermore, we note that Groups 2 and 3 are most likely to be clinically diagnosed with either depression or anxiety.
- **Cognitive Health**: Concerning cognitive resources, again the differences between the groups are highly statistically significant for all scales, MMSE, RBANS, and FAB ($p < 0.001$). We see that mental health Group 1 has by far the lowest cognitive performance. Groups 2 and 4 have the highest neuropsychological function, with Group 5 exhibiting larger variance than the other groups.
- **Lifestyle & Nutrition**: The lifestyle differences between the groups are also highly pronounced. The groups most likely to live alone and least likely to be married, Groups 1 and 3, both exhibit high depression scores. Furthermore, they are the least likely groups to consume alcohol. These groups also perform among the poorest when considering having nutritional and vitamin biomarkers at normal levels. The differences are particularly acute for B-vitamins (including Folate, red blood cell folate, vitamin B6, and riboflavin) and liver function variables (this includes albumin, gamma GT, urea, creatinine, and alkaline phosphatase) ($p < 0.001$).
- **Physical Health**: Finally, we consider the physical health of the participants in each mental health group. While there are no significant differences in BMI levels across the groups ($p = 0.683$), there are significant differences between the TUG test and the PSMS and IADL scales. Again, Groups 1 and 3 appear to have the lowest physical health, exhibiting slow TUG times ($p < 0.001$) and the lowest median IADL and PSMS scores ($p < 0.001$).

Mental health profiles in a follow-up cohort

A subset of patients ($n = 953$) participated in a follow-up study, responding to the same CES-D and HADS scale questions. Our focus here is twofold: (1)

Table 3 Baseline characteristics of the participants in each mental health group

	Overall	Group 1	Group 2	Group 3	Group 4	Group 5	*p*
Number (%)	5186 (100.0)	152 (2.9)	315 (6.1)	1088 (20.9)	602 (11.6)	3029 (58.4)	
Demographics							
Female, *n* (%)	3487 (67.2)	95 (62.5)	218 (69.2)	806 (74.1)	422 (70.1)	1946 (64.2)	< 0.001[a]
Mean Age (std.dev.)	74.0 (8.3)	83.1 (6.3)	68.4 (5.7)	78.2 (7.8)	69.3 (6.0)	73.6 (8.0)	0.326[b]
Median Deprivation (IQR)	2 (3)	4 (3)	3 (3)	4 (3)	3 (2)	3 (2)	< 0.001[b]
Mental Health							
Median CES-D, (IQR)	3 (9)	10 (5)	15 (10)	12 (10)	4 (5)	1 (4)	< 0.001[b]
Probable Depression, *n* (%)	555 (10.7)	13 (8.6)	154 (49.5)	381 (35.2)	0 (0.0)	7 (0.2)	< 0.001[a]
Median HADS, (IQR)	2 (5)	0 (1)	7 (5)	4 (6)	5 (3)	1 (2)	< 0.001[b]
Probable Anxiety, *n* (%)	347 (6.7)	0 (0.0)	85 (27.0)	167 (25.4)	56 (9.3)	39 (1.3)	< 0.001[a]
Comorbid, *n* (%)	143 (2.7)	0 (0.0)	54 (17.4)	89 (8.2)	0 (0.0)	0 (0.0)	< 0.001[a]
Cognitive Health							
Median MMSE, (IQR)	28 (3)	24 (4)	28 (1)	27 (3)	29 (1)	28 (3)	< 0.001[b]
Mean RBANS, (IQR)	85.4 (16.9)	64.3 (9.0)	93.8 (11.8)	75.1 (14.2)	96.9 (10.4)	86.6 (16.9)	< 0.001[b]
Median FAB, (IQR)	16 (3)	13 (4)	17 (3)	15 (5)	17 (2)	16 (3)	< 0.001[b]
Diagnoses							
Hypertension, *n* (%)	3711 (71.6)	105 (69.5)	228 (72.8)	756 (70.5)	457 (76.2)	2165 (72.1)	0.149[a]
Hyperlipidaemia, *n* (%)	2755 (53.1)	66 (43.4)	193 (62.9)	561 (52.5)	331 (56.3)	1604 (54.4)	0.001[a]
Diabetes, *n* (%)	660 (12.7)	28 (18.5)	38 (12.2)	163 (15.1)	52 (8.7)	379 (12.5)	0.001[a]
Osteoporosis, *n* (%)	1376 (26.5)	37 (33.9)	63 (20.5)	325 (35.5)	146 (24.5)	805 (28.4)	< 0.001[a]
Angina, *n* (%)	700 (13.5)	15 (9.9)	57 (18.3)	213 (19.6)	81 (13.5)	334 (11.0)	< 0.001[a]
Lifestyle							
Drinking, *n* (%)	2975 (57.3)	65 (42.8)	215 (68.3)	488 (44.9)	399 (66.3)	1808 (59.7)	< 0.001[a]
Smoking, *n* (%)	623 (12.0)	14 (9.2)	37 (11.8)	157 (14.4)	82 (13.6)	333 (11.0)	0.022[a]
Married, *n* (%)	2709 (52.2)	41 (27.0)	176 (55.9)	404 (37.1)	408 (67.9)	1680 (55.5)	< 0.001[a]
Living Alone, *n* (%)	1754 (33.8)	79 (51.9)	108 (34.2)	466 (42.8)	147 (24.5)	951 (31.4)	< 0.001[a]
Nutrition							
B-Vitamins - All Normal, *n* (%)	2943 (56.7)	71 (50.0)	182 (60.7)	519 (50.4)	364 (64.1)	1807 (63.9)	< 0.001[a]
Liver - All Normal, *n* (%)	1578 (30.4)	22 (14.6)	123 (40.2)	213 (20.0)	268 (45.5)	952 (32.4)	< 0.001[a]
Electrolytes - All Normal, *n* (%)	4606 (88.8)	135 (88.8)	287 (92.0)	922 (85.3)	552 (92.5)	2710 (90.8)	< 0.001[a]
Bone - All Normal, *n* (%)	3141 (60.5)	72 (47.4)	202 (64.7)	587 (54.3)	408 (68.8)	1872 (63.0)	< 0.001[a]
Lipid - All Normal, *n* (%)	1937 (37.3)	71 (48.3)	95 (31.0)	440 (41.3)	198 (33.7)	1133 (38.7)	< 0.001[a]
tHcy Normal, *n* (%)	3587 (69.1)	78 (52.0)	256 (81.3)	608 (55.9)	489 (81.4)	2156 (71.4)	< 0.001[a]
Vitamin D, *n* (%)	2856 (55.0)	75 (49.3)	167 (53.0)	524 (48.2)	370 (61.8)	1720 (57.0)	< 0.001[a]
Physical Health							
Mean TUG, (std.dev.)	14.0 (9.2)	25.0 (10.9)	9.9 (3.6)	21.0 (10.4)	9.2 (3.3)	12.4 (8.0)	< 0.001[b]
Mean BMI (std.dev.)	27.9 (5.4)	26.8 (5.0)	28.7 (5.6)	27.9 (6.3)	27.8 (4.9)	27.9 (5.1)	0.683[b]
Median IADL, (IQR)	26 (7)	18 (7)	27 (2)	21 (7)	27 (2)	27 (4)	< 0.001[b]
Median PSMS, (IQR)	24 (2)	23 (4)	24 (1)	23 (4)	24 (0)	24 (1)	< 0.001[b]

Significant group differences are noted, providing insights into the variation of mental health profiles in the population. Statistical differences among the clusters were evaluated using the Kruskal-Wallis test (b) for continuous variables and the Chi-square test (a) for categorical variables

[a]Chi-Square test

[b]Kruskal-Wallis test

examining the evolution of row-cluster parameters and (2) understanding changes in row-cluster memberships between the two studies. This analysis aims to ascertain whether (1) symptomatic profiles revealed by co-clustering persist and (2) membership in specific groups remains stable. The follow-up study cohort, being younger and with a lower burden of risk factors than the overall baseline cohort, is reflected in the mental health group distribution presented in Table 4. For

example, 95 participants in the follow-up cohort are from the mental health Group 2.

We apply co-clustering to the CES-D and HADS data for the follow-up cohort as before. The results of the co-clustering are visualized in Fig. 7, the parameters for the block-clusters are given in Table 5, and the mental health scales for each row-cluster are described in Table 6. It is noted that only one patient from mental health Group 1 in the original study participated in the follow-up study. The co-clustering method detects four clusters of mental health patterns in the follow-up cohort. The second row-cluster ($n = 36$) experiences the highest symptoms of both anxiety and depression (Table 6). Notably, 100.0% of the members in this group are diagnosed with probable depression, and 58.3% of the group members show indications of probable anxiety. We link this row-cluster to mental health Group 2 in the original cohort. The first row-cluster ($n = 256$) experiences anxiety and depression symptoms, with a median CES-D score of 10 and a median HADS score of 5. These symptoms are less acute than the second row-cluster, yet are persistent. We thus connect this cluster to mental health Group 3. The third row-cluster ($n = 53$) of the follow-up cohort experiences the second lowest median CES-D scores. The is coupled with persistent symptoms of anxiety, the second highest among the clusters found. We thus draw a connection between this group and mental health Group 4. Finally, the largest group uncovered in the follow-up cohort displays few to no symptoms of either anxiety or depression ($n = 608$), as also observed for mental health Group 5 in the original cohort. The concurrence between the row-clusters from the original and follow-up cohorts evidence that they are distinct and permanent phenotypes observable cross-sectionally and longitudinally.

Table 4 Distribution of the participants in the follow-up cohort w.r.t. the five mental health groups in the original cohort

Group	*n* (%)
1	1 (0.1)
2	95 (10.0)
3	43 (4.5)
4	187 (19.6)
5	627 (65.8)

The evolution of row-cluster membership across the period is depicted visually in Fig. 8 and presented as a contingency table in Table 7. The broad concurrence between the clusters is evident. Notably, changes in membership for those in mental health Group 4 in the original study are noteworthy. In the original study, this group exhibited symptoms of anxiety without symptoms of depression. In the follow-up study, 75 members

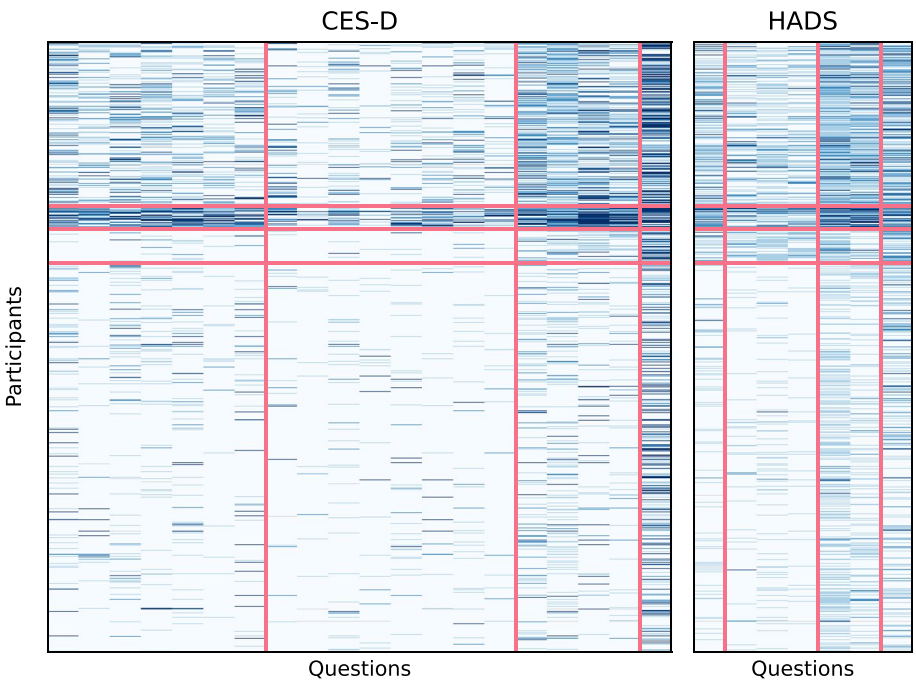


Fig. 7 Participants in the follow-up cohort are partitioned into four row-clusters. Darker colors indicate a higher frequency of symptoms. Participants in the second row-cluster exhibit the most severe symptoms of both anxiety and depression, while participants in the fourth row-cluster show little to no symptoms of either condition

Table 5 Estimated parameter values of the parametric model for each block cluster

		CES-D (μ, β)			
		Col C1	Col C2	Col C3	Col C4
	n	8	8	3	1
Row C1	256	(0, 0.66)	(0, 0.79)	(0, 0.34)	(3, 0.12)
Row C2	36	(3, 0.01)	(0, 0.44)	(3, 0.34)	(3, 0.45)
Row C3	53	(0, 0.89)	(0, 0.90)	(0, 0.66)	(0, 0.22)
Row C4	608	(0, 0.90)	(0, 0.91)	(0, 0.88)	(0, 0.55)
		HADS (μ, β)			
		Col C1	Col C2	Col C3	Col C4
	n	2	2	2	1
Row C1	256	(0, 0.45)	(0, 0.56)	(1, 0.55)	(0, 0.23)
Row C2	36	(1, 0.34)	(0, 0.23)	(3, 0.33)	(2, 0.12)
Row C3	53	(0, 0.67)	(0, 0.67)	(0, 0.46)	(0, 0.34)
Row C4	608	(0, 0.89)	(0, 0.90)	(0, 0.67)	(0, 0.67)

Given the ordinal nature of the data, each block is modeled using a Binary Ordinal Search (BOS) distribution, characterized by a position parameter μ and a precision parameter $\beta \in [0, 1]$. Higher values of μ indicate a greater frequency of symptoms. A β value closer to 1 suggests that the data are more tightly concentrated around the position parameter μ

(40%) of this group have transitioned to row-cluster C1, indicating the development of symptoms of depression alongside symptoms of anxiety. In contrast, 81 group members (43%) have moved to the no-symptoms cluster C4. Similarly, in mental health Group 2 - another group characterized by anxiety symptoms in the original study - 51 members (54%) have shifted to row-cluster C1 in the follow-up study. This may reflect decreased severity of symptoms or be influenced by differences in the distributional parameters of the block-clusters uncovered by the co-clustering. For the other mental health groups (Group 3 and Group 5), most participants remained in their corresponding clusters in the follow-up study. For example, the majority of participants in Group 3 continued in row-cluster C1, indicating consistency in their symptom profile.

Discussion

In this large sample of patients recruited from primary care, we aimed to describe and characterize the patterns of mental health in older adults, identifying groups of individuals who are similar to each other but different from those in other groups. Among the numerous techniques for clustering observations, we chose the MVLBM co-clustering method because it naturally handles data of varying types (continuous, ordinal, binary), provides insightful clustering of the features in the dataset, is capable of describing the relationships between row-clusters in different views, and yields parametric summaries of the detected block clusters in the form of distribution parameters for easy interpretation. Our study unveils the presence of a cluster structure in mental health within this dataset. The MVLBM reveals a five-row-cluster model that effectively captures the intricate interplay among depression and anxiety indicators. In summary, we provide the following profile descriptions based on the row clusters uncovered by the MVLBM algorithm: Group 1, physical symptoms of depression without anxiety symptoms; Group 2, severe symptoms of anxiety and depression; Group 3, symptoms of depression and anxiety are present but less acute than Group 2; Group 4, symptoms of anxiety without co-occurring symptoms of depression; and Group 5, who exhibit no major signs of either depression or anxiety. These groups reflect various phenotypes of mental health in older adults. A summary of the groups and key risk factors is provided in Table 8.

Overall, the prevalence of depression and anxiety symptoms that meet the threshold for clinical diagnoses (CES-D scale ≥ 15, HADS scale ≥ 10) aligns closely with findings from previous studies. We record that 10.7% ($n = 287$) of the sample participants meet the threshold for clinical depression, and 6.7% ($n = 347$) meet

Table 6 Mental health profiles of the four row-clusters in the follow-up cohort

	Overall	**Row-Cluster 1**	**Row-Cluster 2**	**Row-Cluster 3**	**Row-Cluster 4**	***p***
Number (%)	953 (100.0)	256 (26.9)	36 (3.8)	53 (5.6)	608 (63.8)	
Mental Health						
Median CES-D, (IQR)	4 (7)	10 (7)	28.5 (8)	4 (4)	2 (4)	< 0.001[b]
Probable Depression, *n* (%)	83 (1.6)	46 (18.1)	36 (100.0)	0 (0.0)	1(0.2)	< 0.001[a]
Median HADS, (IQR)	2 (3)	5 (4)	10 (4)	5 (2)	1 (2)	< 0.001[b]
Probable Anxiety, *n* (%)	49 (0.94)	27 (10.6)	22 (61.1)	0 (0.0)	0 (0.0)	< 0.001[a]
Comorbid, *n* (%)	27 (0.5)	5 (2.0)	22 (61.1)	0 (0.0)	0 (0.0)	< 0.001[a]

Statistical differences among the clusters were evaluated using the Kruskal-Wallis test (b) for continuous variables and the Chi-square test (a) for categorical variables

[a]Chi-Square test

[b]Kruskal-Wallis test

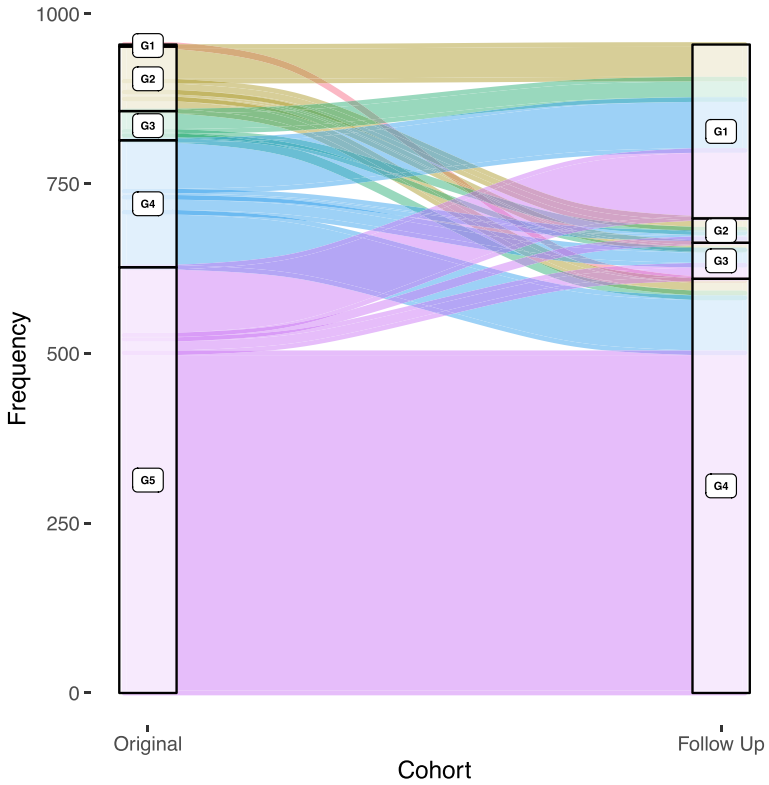


Fig. 8 Visual representation of transitions in mental health row-cluster memberships between the original and follow-up studies. Each row-cluster corresponds to distinct mental health patterns represented by the colored areas, with transitions indicating changes in anxiety and depression symptomatology over time. Key observations include the persistence of symptoms in some clusters and significant changes in others, providing insight into the stability and evolution of mental health profiles in older adults

Table 7 Contingency table illustrating the co-occurrence patterns of mental health groups from the original study with row-clusters identified in the follow-up study

	Follow-Up			
Original	**Row-cluster 1**	**Row-cluster 2**	**Row-cluster 3**	**Row-cluster 4**
Group 1	0	0	0	1
Group 2	51	16	10	18
Group 3	30	5	1	7
Group 4	75	9	22	81
Group 5	100	6	20	501

Each entry represents the number of participants whose mental health profile shifted or remained stable. For example, of the 43 participants originally in Group 3, 30 retained their mental health profile (now classified in Cluster 1), while 13 transitioned to Clusters 2, 3, or 4

the threshold for a diagnosis of anxiety. These figures fall within the ranges reported for community-dwelling adults experiencing anxiety (1.2% - 15%) and depression (4.6% - 9.3%) [14]. Our analysis reveals that 2.75% ($n = 104$) of participants suffer from comorbid depression and anxiety. This translates to 25.7% of those with depression diagnoses having comorbid anxiety, and 30.0% of those with anxiety having comorbid depression. These results are consistent with many previous studies. [17] reported that 27.5% of those with depression also endure anxiety, while [56] found a 29.8% comorbidity rate of anxiety among those with depression. However, some studies report lower comorbidity rates. For example, [16] observed that only 11.6% of individuals with anxiety also have comorbid major depression, although an additional 6.3% exhibit other depressive syndromes. The discrepancy in findings may be attributed to different definitions and diagnostic thresholds for particular syndromes.

A small subset of participants (3%) displayed symptoms of depression (median CES-D 10, median HADS 0) without concurrent anxiety symptoms (Group 1). Predominant manifestations in this group include physical symptoms of depression, such as poor sleep quality and challenges in concentration and effort. With a mean age of 83.1 years, this group was the oldest among the five groups. Additionally, they exhibited the lowest neuropsychological capabilities in the sample (mean RBANS 64.3, median MMSE 24, median FAB 13). Notably, participants in this group showed the highest degree of physical

Table 8 Summary of symptom patterns and associated risk factors across the mental health groups

Mental health group	Depression level	Anxiety level	Co-occurring risk factors
Group 1	Medium	No/Low	older; physically frail; reduced neuropsychological capability; poor sleep; abnormal biomarker levels for liver and bone health
Group 2	High	High	younger; female; no physical frailty; able to complete self-maintenance and daily activities independently
Group 3	Medium	Medium	older; female; reduced neuropsychological capability; more likely to live alone and to smoke; raised level of socioeconomic deprivation
Group 4	No/Low	High	younger; no physical frailty; no signs of cognitive decline; normal biomarker levels
Group 5	No/Low	No/Low	marked by variety

frailty, evidenced by the lengthiest TUG score recorded in any group (mean 25.0s). This suggests that physical symptoms of depression coincide with several typical features of aging. Moreover, this group demonstrated the highest proportion of abnormal biomarker levels for liver health (85.4%) and bone health (52.6%). Additionally, total homocysteine levels were also more likely to be abnormal (48.0%).

Age and physical frailty are linked to diminished mental health, as is living alone [57]. We identified a substantial cluster of patients (Group 3, 20.9%) who were more likely than all groups except Group 1 to live alone (42.8%) and were older and more physically frail than the remaining groups (mean age 78.2 years, mean TUG 21.0s). This group experienced depressive and anxiety symptoms (mean CES-D 12, mean HADS 4) and had the highest number of members meeting the threshold for clinical diagnosis of depression (n = 193) and anxiety (n = 69) among the groups identified. Although this group had the highest proportion of smokers, the overall prevalence was low (14.4%). Both living alone and smoking have been recognized as independent contributors to poorer mental health in older individuals. Additionally, this group had the highest proportion of members residing in areas constituting the bottom two quintiles of deprivation indices. The cognitive function of this group, as measured by the RBANS metric (mean 75.1), was also lower compared to the other groups, except for Group 1. Interestingly, this group had the highest proportion of female members (74.1%), aligning with findings in recent meta-analyses and reviews indicating that women experience depressive symptoms more frequently than men [58–60].

Group 4 participants displayed several symptoms of anxiety, particularly those related to feelings of tension and restlessness. No members of this group met the threshold level for clinical diagnosis of depression, yet symptoms of anxiety were the second highest, on average, among the groups considered (median HADS 5). Moreover, 56 members of this group (9.3%) had HADS scales indicating probable anxiety. This group contrasts with Group 3, as its members are younger (mean age 69.3 years) and significantly less frail. Additionally, this group has the lowest TUG score among all groups (mean 9.2s). Concerning nutritional attainment, this group has the highest proportion of participants with normal B-vitamin biomarker levels (64.1%), bone biomarker levels (68.8%), total homocysteine levels (81.4%), and vitamin D levels (61.8%).

Group 2 exhibits similar patterns to Group 4, skewing younger (mean age 68.4) and less frail (mean TUG 9.9s) compared to the whole sample. Both Group 2 (69.2%) and Group 4 (70.1%) contain a higher proportion of females than the sample as a whole. Moreover, this group is most able to complete self-maintenance and daily activities independently (median IADL 27, median PSMS 24). Group 2, along with Group 4, exhibits no signs of cognitive decline along any metric considered. However, Group 2 exhibits the most acute symptoms of both depression and anxiety among any groups uncovered by the co-cluster analysis. They have the highest CES-D score (median 15), highest HADS score (median 7), and the highest proportion of members satisfying the criteria for clinical diagnoses of depression (28.6%), anxiety (27.0%), and both (11.3%). The major symptom experienced by this group is poor sleep quality (CES-D column-cluster 4, parameter (3, 0.12)). It has been noted that insomnia is often overlooked as a risk factor for late-life depression [12, 61, 62]. The paucity of risk factors typically discussed in the literature, as well as the acute nature of the symptoms experienced, indicate that an exogenous form of mental health disorder exists for a subset of the population. It is not reasonable to expect lifestyle interventions designed for those in Groups 1 and 3 to be effective in ameliorating the symptoms for this group.

Group 5 comprises the largest segment of the population, encompassing approximately 58% of participants.

This group experiences the fewest symptoms of both depression and anxiety. Although some members experienced sleeping issues, feelings of worry, fear, loneliness and tension are almost fully absent. This group is typified mostly by its variety. Those with the fewest symptoms of anxiety and depression exhibit the greatest variation in terms of age, cognitive ability, and physical well-being among all the groups considered. It is noted that, while this study has provided profiles of those suffering from mental health disorders, no clear phenotype for a symptomless person exists.

The profiles of mental health uncovered through the application of the co-clustering method have been demonstrated to persist in a longitudinal study involving a follow-up cohort. This persistence suggests that, while participants may transition between different profiles of mental health disorders over time, the overarching typology of the groups remains consistent. The durability of the mental health profiles offers numerous opportunities: firstly, as the labels given to the sample participants appear robust, we can investigate spatial and socioeconomic clustering of mental health disorder profiles; secondly, the profiles can be used to guide policy and lifestyle interventions best suited to each profile; finally, the findings of this study can be used to motivate further research into the divergence between anxiety and depressive symptoms for some groups, and how acute symptoms are experienced by groups who do not exhibit any prominent risk factors.

The study not only involves grouping the sample participants but also provides insights into the scales used to diagnose depression and anxiety in older adults. The CES-D scale is seen to contain questions aiming at varying levels of severity of depression. For example, questions in the first and third column-clusters capture the feeling of sadness and loneliness, while questions in the second column-cluster have more severe symptoms of depression, namely lack of appetite, feelings of fear, and crying spells. We also note that restless sleeping is experienced by participants in all groups. Similarly, the HADS scale exhibits differing levels of severity, with more prevalent symptoms like tension and worry found in the third column-cluster, and less common symptoms including sudden feelings of panic present in the second column-cluster. In situations where administering the full questionnaires is impractical, sampling questions from each column-cluster could provide an accurate and abridged scale for fast diagnoses. Furthermore, the column-clusters give insights into commonly experienced symptoms and can serve as valuable guides for tailoring treatment plans for patients exhibiting symptoms of depression and anxiety.

The study had several limitations. Firstly, although the cross-sectional sample was large, only 953 individuals underwent repeat cognitive and mental health assessments and were followed longitudinally. This cohort was also younger and had a lower burden of risk factors compared to the original study cohort. This difference may explain why clusters equivalent to mental health Group 1 were not observed in the follow-up study. Despite this, the row-clusters detected in the follow-up data reflected and echoed those found in the original data. If the reassessment included an older sample, the patterns of mental health disorders observed in Group 1 might have been replicated. Moreover, our study cohort recruited from geriatric medicine clinics and general practice is not a population-representative sample, limiting the generalizability of the mental health groups uncovered in this study to the general population. Convenience recruitment from clinic-based populations has known limitations, as highlighted in previous literature [63]. Nevertheless, the mental health profiles discovered remain relevant for clinicians seeking to categorize and understand the mental health of their patients.

In conclusion, our study reveals the presence of distinct and diverse patterns of mental health and co-occurring risk factors in older adults. Utilizing co-clustering analysis, we identified five persistent mental health profiles. Our findings additionally unveil groupings of the assessment questions and risk factors associated with these profiles, facilitating the rapid diagnosis of disorders and enhancing our understanding of population-level trends in community-dwelling older adults. We hope that these insights will inspire and support the development of tailored interventions for successful aging, paving the way for further research in this area.

Supplementary Information

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Supplementary Material 1.

Authors' contributions

J.T. and M.Z. wrote the main manuscript text. J.T. prepared the data analysis results. L.H., H.M., C.H., G.H., and A.M. provided insight regarding the TUDA dataset. All authors reviewed the manuscript.

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Data availability
The data that support the findings of this study are not openly available due to reasons of sensitivity. Further information regarding the data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was obtained from the Office for Research Ethics Committees Northern Ireland (ORECNI; Ref 08/NIR03/113), with corresponding approval from the Northern and Western Health and Social Care Trusts in Northern Ireland, and the Research Ethics Committee of St James's Hospital and The Adelaide and Meath Hospital, Dublin. All participants provided written informed consent at the time of recruitment, ensuring that it conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]School of Computer Science & Statistics, Trinity College Dublin, Dublin, Ireland. [2]School of Computing, Engineering & Intelligent Systems, Ulster University, Derry ~ Londonderry, Northern Ireland, UK. [3]School of Biomedical Sciences, Nutrition Innovation Centre for Food and Health, Ulster University, Coleraine, Northern Ireland, UK. [4]School of Geographic & Environmental Sciences, Ulster University, Coleraine, Northern Ireland, UK. [5]School of Health, Wellbeing & Social Care, The Open University, Belfast, Northern Ireland, UK. [6]School of Medicine, Trinity College Dublin, Dublin, Ireland. [7]School of Computing, Ulster University, Belfast, Northern Ireland, UK.

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