



Social inequalities in multimorbidity patterns in Europe: A multilevel latent class analysis using the European Social Survey (ESS)

Javier Álvarez-Gálvez^{a,b,e}, Jesús Carretero-Bravo^{a,*}, Víctor Suárez-Lledó^a,
Esther Ortega-Martín^a, Begoña Ramos-Fiol^a, Carolina Lagares-Franco^{c,e},
Cristina O’Ferrall-González^d, José Almenara-Barrios^{a,e}, Juan Luis González-Caballero^c

^a Department of Biomedicine, Biotechnology and Public Health, University of Cadiz, Avda. Ana de Viya, 52, 11009, Cádiz, Spain

^b University Institute of Research for Sustainable Social Development (INDESS), University of Cadiz, Jerez de la Frontera, CP 11405, Spain

^c Department of Statistics and Operations Research, University of Cadiz, Polígono Río San Pedro, 11510, Puerto Real, Cádiz, Spain

^d Department of Nursing and Physiotherapy, University of Cadiz, Avda. Ana de Viya 52, 11009, Cádiz, Spain

^e Research Group of Healthcare Information Systems (PAIDI CTS553), Spain

ARTICLE INFO

Keywords:

Multimorbidity
Health inequalities
Socioeconomic status
Multilevel latent class analysis
Patterns of chronic conditions
European countries

ABSTRACT

Multimorbidity is associated with lower quality of life, greater disability and higher use of health services and is one of the main challenges facing governments in Europe. There is a need to identify and characterize patterns of chronic conditions and analyse their association with social determinants not only from an individual point of view but also from a collective point of view. This paper aims to respond to this knowledge gap by detecting patterns of chronic conditions and their social determinants in 19 European countries from a multilevel perspective. We used data from the ESS round 7. The final sample consisted of 18,933 individuals over 18 years of age, and patterns of multimorbidity from 14 chronic conditions were detected through Multilevel Latent Class Analysis, which also allows detecting similarities between countries. Gender, Age, Housing Location, Income Level and Educational Level were used as individual covariates to determine possible associations with social inequalities. The goodness-of-fit indices derived in a model with six multimorbidity patterns and five countries clusters. The six patterns were “Back, Digestive and Headaches”, “Allergies and Respiratory”, “Complex Multimorbidity”, “Cancer and Cardiovascular”, “Musculoskeletal” and “Cardiovascular”; the five clusters could be associated with some geographical areas or welfare states. Patterns showed significant differences in the covariates of interest, with differences in education and income being of particular interest. Some significant differences were found among patterns and the country groupings. Our findings show that chronic diseases tend to appear in a combined and interactive way, and socioeconomic differences in the occurrence of patterns are not only of the individual but also of group importance, emphasising how the welfare states in each country can influence in the health of their inhabitants.

1. Introduction

The number of people suffering (or at risk of) long-term conditions, such as diabetes, heart disease, musculoskeletal disorders, mental health conditions, or cancer is rising rapidly in Europe (Barnett et al., 2012). One of the main reasons for this is the rapid increase in life expectancy in all regions of the world over the last few years. The average life expectancy in European Union was 78.4 years for males and 83.8 years for females in 2020 (Eurostat, 2022a). This accelerated growth of the elderly is causing the accumulation of chronic diseases, with the

consequent increase in aspects such as health and social costs and poly-medication. In addition, the problem of multimorbidity is not only a problem of older people, but also occurs, albeit less frequently, among young people and adults, considering that the multimorbidity at this age could have different etiology from those that appear among older people (Barnett et al., 2012), which may be due to changing lifestyles and the increasing prevalence of mental disorders (Koné Pefoyo et al., 2015).

Multimorbidity can be defined generically as the accumulation of two or more chronic health conditions (van den Akker et al., 1996; WHO, 2008), and due to the situation caused by the ageing of the

* Corresponding author. Department of Biomedicine, Biotechnology and Public Health, University of Cadiz, Avda. Ana de Viya, 52, 11009 Cádiz, Spain.
E-mail address: jesus.carretero@uca.es (J. Carretero-Bravo).

<https://doi.org/10.1016/j.ssmph.2022.101268>

Received 25 July 2022; Received in revised form 16 September 2022; Accepted 11 October 2022

Available online 12 October 2022

2352-8273/© 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

European population is one of the main challenges facing governments and healthcare systems (Fortin et al., 2005; Kuzuya, 2019; Onder et al., 2015). This health condition is associated with a lower quality of life, increased disability, functional decline, higher healthcare utilisation and fragmentation of care, complex treatment, and higher mortality (Gallacher et al., 2014; Gijzen et al., 2001). In this field of research, one of the problems to be addressed is that adverse health outcomes associated with multimorbidity are partly determined by the fact that healthcare delivery and measurements are defined and organised based on patients with single diseases (Moffat & Mercer, 2015).

Some studies have highlighted the incapacity of current clinical guidelines to tackle the complex needs of patients with multimorbidity because of the inadequate or modest attention to co-occurring diseases (Moffat & Mercer, 2015; Sevick et al., 2007). Common problems among these patients with multimorbidity are, for instance: treatment incompatibility, negative interactions among medications for multiple diseases, or undertreatment for second-order diseases (Wallace et al., 2015). Given this fact, new ways of addressing the complex problem of multimorbidity are needed. The usual way of measuring this problem has been using disease accumulation indices, such as Charlson-Deyo comorbidity index (Charlson et al., 1987), Elixhauser comorbidity score (Elixhauser et al., 1998) or the count of each individual's chronic conditions. However, this approach does not allow the detection of possible recurrent patterns of chronic conditions in the population, and in recent years numerous studies have emerged with the aim of detecting specific patterns of multimorbidity within European countries (Hanlon et al., 2018; Hernández et al., 2021; Olaya et al., 2017; Violan et al., 2014). Identifying these patterns allows for a more targeted approach to the problem of multimorbidity and for targeted interventions that consider the common recurrence of certain diseases.

In addition, another major challenge to be addressed in this research problem is how to provide new evidence-based knowledge on the complex relationship between co-joint chronic diseases and how their patterns of association with social inequalities in health might vary depending on disparities in contextual circumstances linked to structural or intermediary factors (Alvarez-Galvez, 2018, 2019). It is known that non-communicable diseases are influenced by social and economic differences between populations (socioeconomic status, educational level, or economic hardship) (Bono & Matranga, 2019; GBD 2016 DALYs and HALE Collaborators, 2017), and the influence of these factors can be expected to extrapolate even more clearly in the presence of multimorbidity.

Although the impact of social determinant of health, understood as the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life (World Health Organization, 2021) have been identified in the specialized literature, the pattern of association of the different chronic conditions together (physical and mental) that makeup multimorbidity and their respective drivers is not so well defined (Arokiasamy et al., 2015; Barnett et al., 2012). Recent work shows that multimorbidity is strongly associated with social and economic factors that condition the early onset of chronicity and subsequent multimorbidity in disadvantaged social groups (Arokiasamy et al., 2015; Nielsen et al., 2017).

Studies in Europe have shown that multimorbidity patterns are related to social and demographic determinants such as gender, age, education, income level and living area (Díaz et al., 2015; Foguet-Boreu et al., 2015; Hernández et al., 2021), factors that may predispose to the appearance of different co-joint chronic conditions and health outcomes in individuals with similar physical characteristics. Depending on gender and age, different studies in particular regions of Europe have identified some interesting relations. For example, a higher prevalence of mental multimorbidity patterns in younger women (Larsen et al., 2017), while cardiovascular patterns are more prevalent in older men (Nguyen et al., 2020). Musculoskeletal and cardiometabolic patterns are more prevalent among men of low socio-economic status (Larsen et al., 2017; Møller et al., 2020). Complex patterns, those with a high

combination of chronic diseases, are more frequent in older age groups (Olaya et al., 2017), while younger groups of medium-high socio-economic status have a higher prevalence of mental health problems (Chmiel et al., 2014). This fact indicates that the way to deal with multimorbidity should be related to the analysis from the point of view of patterns or groups of conditions and their association to possible social inequalities and not so much from the point of view of multimorbidity as a mere accumulation of conditions (Busija et al., 2019; Pearson-Stuttard et al., 2019).

Other studies have shown how the place of birth and the area where one lives can influence the appearance of different patterns (Kringos et al., 2016; Lai et al., 2021; Larsen et al., 2017) associated with specific characteristics and politics of the regions or countries. However, few studies have focused on the differences between patterns across European countries and their associations with individual social determinants from a multilevel paradigm, focusing not only on the perspective of individual characteristics but also the collective perspective of the country of belonging.

This study is aimed to identify the patterns of multimorbidity in European countries and their association with social inequalities. Specifically, our research objectives are the following: (1) to identify classes of multimorbidity among the European population, (2) to study the prevalence of the resulting multimorbidity classes and their differences among European countries from a multilevel perspective, and (3) to know how these patterns are associated with socioeconomic status and possible inequalities at individual level in these countries.

2. Methods

2.1. Study design and participants

To carry out this study, we use the data obtained by The European Social Survey (ESS) in Round 7, for which data collection was carried out between 2014 and 2015. The ESS is an academically driven multi-country survey which has been administered in over 30 countries to date. The survey covers 22 countries in the seventh round and employs the most rigorous methodologies (European Social Survey Data Archive, 2016). The survey involves strict random probability sampling, a minimum target response rate of 70% and rigorous translation protocols. The hour-long face-to-face interview includes questions on various core topics repeated from previous rounds of the survey and a specific module developed for Round 7 covering Social Inequalities in Health.

From the specific health module of round 7, the 14 chronic conditions of interest for our study were selected: heart problems, high blood pressure, breathing problems, allergies, back or neck pain, muscular or joint pain in hand or arm, muscular pain in foot or leg, stomach or digestion related, skin conditions, severe headaches, diabetes, cancer, obesity, and severe depression. The selection of these chronic conditions was based on their serious nature (i.e. those potentially fatal or limiting for daily activities) and their elevated economic cost (e.g. cancer).

About the social inequalities in health, we selected available covariates in ESS Round 7 at the individual level that could be related to the multimorbidity patterns and established in the literature as possible social determinants. In addition, we selected those whose categories were similarly distributed within the selected European countries and did not present anomalous data.

Specifically, the covariates chosen were Gender (Male and Female), Age (18–39, 40–54, 54–69 and over 69), Income Level (divided into quartiles of the individual's income within each specific country, with Q1 being the lowest income group and Q4 the highest income group), Educational Level (normalised to the equivalent in each European country, with Primary or No Education being the lowest level of education and University being the highest level) and Housing Location (grouped into three categories, Big City, Small City or Town and Country Village or Rural Place).

As inclusion conditions, we chose those countries within the 22 in

which the survey was conducted that had sufficient information on the chronic conditions of interest. In turn, only individuals with multimorbidity were selected so that the patterns of conditions obtained would consist only of individuals with two or more conditions, as has been done in other similar studies (Bendayan et al., 2021). Finally, only individuals over 18 years of age were chosen.

The final sample size was composed of 18,933 individuals of legal age with two or more chronic conditions (truly multimorbidity) that were selected from 19 European countries: Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Israel, Lithuania, the Netherlands, Norway, Poland, Portugal, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom.

2.2. Statistical analysis

Firstly, a descriptive analysis of the sample was carried out (Means, SDs with continuous variables, Frequencies and Percentages with categorical). Missing values were analysed and imputed in those variables where they were small (less than 1%). Only in the income variable, the high number of missing values (due to unwillingness to answer) lead to the category do not know/no answer being considered within this variable.

After descriptive analysis, the data were prepared to obtain the patterns by means of Latent Class Analysis (LCA). LCA is a multivariate technique used to classify observations based on patterns of categorical or continuous observed variables (Bartholomew et al., 2011). Classification is associated with unobserved groups of individuals called latent classes. This technique has often been used to identify multimorbidity patterns and their association with social determinants (Jacob et al., 2020; Tazzeo et al., 2021; Zhu et al., 2020).

The usual approach to LCA assumes independence between observations across individuals. This independence can break down in hierarchical data, such as those from the European survey we are analysing, making a multilevel approach necessary. We used multilevel latent class analysis (MLCA) (Vermunt, 2003) to identify multimorbidity subgroups within the European countries, incorporating two levels of classes, one at the level of individuals (level 1) and a second level associated with the 19 countries (level 2). The statistical model with MLCA was based on 14 observed chronic conditions of interest.

In MLCA, two types of categorisation were obtained: on the one hand, patterns or classes of multimorbidity, at the level of the individual (level 1) and on the other hand, sets of European countries with similar

patterns of chronic conditions (level 2). The variable grouping was the 19 countries, with the number of subjects per country ranging from 652 (Slovenia) to 1,979 (Germany), with a mean value of 996.47 subjects and a deviation of 260.98. These values show that the number of groups is enough for the average size of each group (Park & Yu, 2017).

The process of obtaining the appropriate number of level 1 patterns and level 2 country groups is done through 3 steps (Lukociene et al., 2010): (1) Determination of the latent classes without taking into account the hierarchical structure of the data, (2) determination of the country groups by fixing the latent classes obtained in the previous step and (3) fixing the number of country groups and checking whether the latent classes obtained in the first step are appropriate.

We chase successive models in each pass by the Bayesian information criterion (BIC), the adjusted BIC and the Akaike Information Criterion Three (AIC3), three of the indices that best fit the data in the MLCA models (Lukociene et al., 2010). The lower the BIC, ABIC, and AIC3, the better the fit is. Sometimes it is helpful to use an elbow plot to mark the point beyond which the improvement in the goodness-of-fit indices is not much since raising the number of classes raises the number of model parameters and the parsimony of the model is lost (Weller et al., 2020).

To check the relationship between social determinants and localised multimorbidity patterns, covariates for each individual were incorporated into the latent class model. Incorporating covariates into the global model may change the number of latent classes of both levels, so it is recommended to perform the covariate analysis following the 3-Step approach (Bolck et al., 2004), according to which it is recommended to (1) estimate the latent class model (2) calculate the latent class of membership of the individual and (3) relate these membership classes to the desired covariates through multinomial logistic regression models. In addition, the multinomial models proposed were also performed stratifying according to the cluster of European countries obtained by MLCA, with the aim of detecting possible differences between groups of countries.

All statistical computations were performed using R and RStudio, and MPlus version 7.2.

3. Results

The descriptive statistics of the sample characteristics and the chronic conditions categorised by country can be found in Table S1 of the supplementary material. As characteristics to mention, there were 18,933 individuals with multimorbidity with a mean of 3.46 conditions

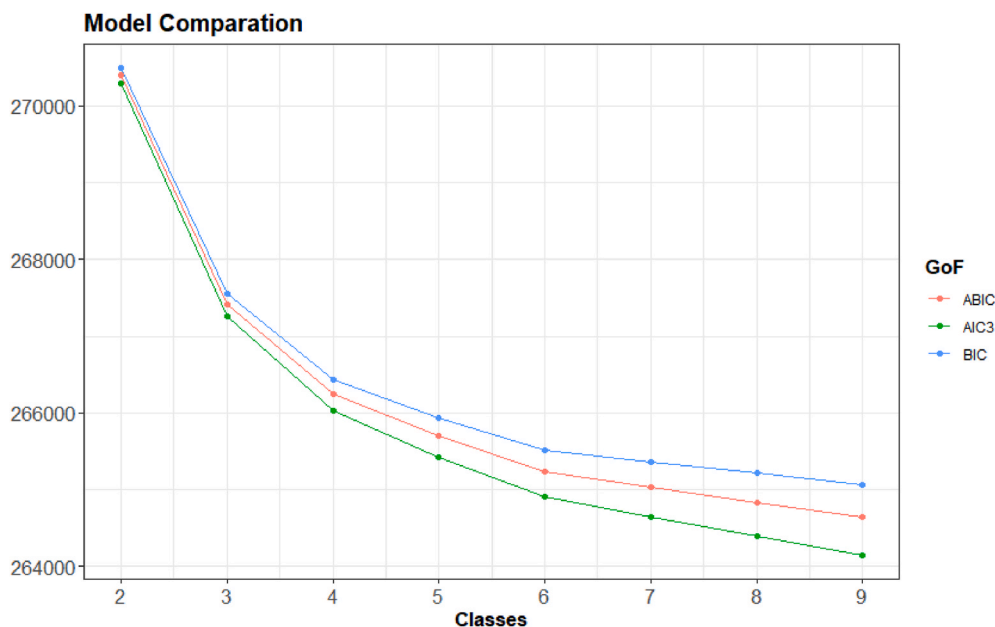


Fig. 1. Elbowplot of LCA with 2–9 classes.

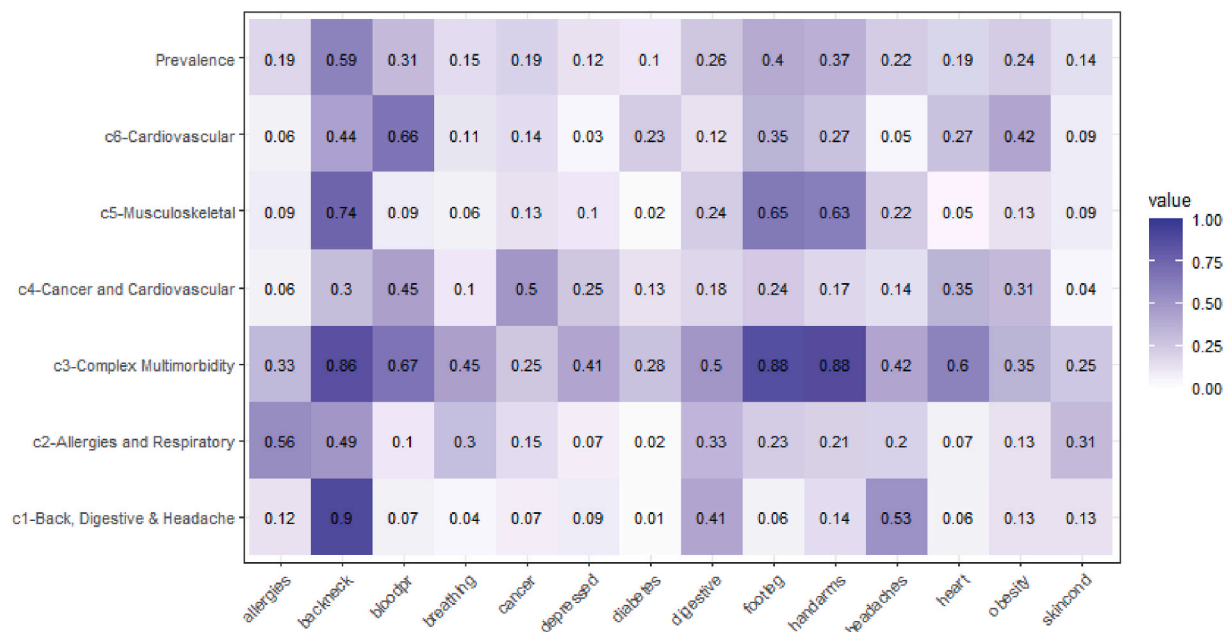


Fig. 2. Final model of chronic conditions among six classes and overall prevalence.

per individual. There are most women, with 56% and the distribution by age group is similar, with all four age groups having sizes above 20%.

3.1. Model selection

The process of selecting the appropriate latent class model through MLCA was as follows: first, the number of latent classes at the individual level was selected without considering the multilevel structure. For this purpose, the BIC, ABIC, AIC3, and entropy were obtained for the two-nine class models, and their values were analysed, which can be seen in Table S3. An elbowplot graph in Fig. 1 was then produced to analyse the chosen model.

In the elbowplot we could see that from six classes onwards, the curve becomes smoother. Taking this into account, the multimorbidity patterns were analysed reviewing their clinical interpretability, an adequate sample size and trying to obtain as many coherent patterns as possible. In this way, the six-pattern multimorbidity model was selected, as extracting additional classes did not improve the overall fit of the model.

This model has somewhat low entropy (0.589), but it should be noted that the multilevel structure of the data has not been considered. The patterns of chronic conditions and the prevalence of these health problems can be seen in Fig. 2. The first class is people with back problems, digestive problems and headaches, second class is associated with allergies, skin problems and respiratory conditions, third class is a kind of complex multimorbidity (with musculoskeletal, allergies, cardiovascular and mental together), fourth class is mainly cancer with metabolic syndrome (diabetes, hypertension and obesity), fifth class is

Table 1
Goodness-of-fit index in MLCA with 6 classes and 2–9 clusters.

Classes	Clusters	BIC	BICK	ABICK	entropy
6	2	264,540.9	263,885.0	263,583.1	0.705
	3	264,389.1	263,691.8	263,370.8	0.716
	4	264,327.7	263,588.9	263,248.9	0.744
	5	264,218.2	263,438.0	263,078.9	0.771
	6	264,299.7	263,478.1	263,099.9	0.797
	7	264,312.1	263,449.1	263,051.8	0.805
	8	264,217.8	263,313.3	262,897.0	0.789
	9	264,276.9	263,331.0	262,895.6	0.794

people with musculoskeletal (back, neck or muscular pain) and finally sixth class is associated only with cardiovascular conditions and metabolic syndrome.

After setting classes, the number of clusters of European countries was analysed, thus including the multilevel information of the model. For this purpose, the goodness-of-fit indices were rechecked, and the elbowplot (Table 1 and Fig. S1) was performed for models with six classes and two to nine clusters. In addition to BIC, two other multilevel goodness-of-fit indices were calculated, substituting sample size for the number of clusters (BICK and ABICK). The AIC3 was discarded because its values were similar to the BICK values.

In this case, the models with five, eight and nine clusters show the best indices, so these clusters were revised to choose the one with the fewest groups and the best interpretability. The groupings of eight and nine clusters were discarded because they left some groups with only one country. The solution chosen was that of five clusters, in which the country groupings presented a certain coherence due to their geographical proximity, E1 (Ireland, Israel, Poland), E2 (Austria, Finland, Germany, Netherlands, United Kingdom, Sweden), E3 (Belgium, Denmark, France, Norway, Slovenia, Switzerland), E4 (Hungary, Lithuania) and E5 (Portugal, Spain). This distribution of cluster condition patterns across European countries can be seen in Fig. 3. The model has an entropy of 0.771, which is higher than the previous model when the hierarchical structure of the data is incorporated.

With the model of six classes and five clusters chosen, the appropriate number of patterns was tested in a third step by fixing the number of clusters (see Table S3 and Fig. S2 in the supplementary material). Again, it was more consistent to choose six classes, as both the elbowplot and the clinical interpretation indicated that this was the most parsimonious model. The proportion of each pattern of chronic conditions within the European country clusters can be seen in Fig. 4. The prevalence of patterns of chronic conditions in each European country can be seen in Fig. 5.

3.2. Social determinants and chronic conditions

Table 2 summarises the social determinants of the sample individuals in each class and the distribution of the clusters in each class. This table is complemented by Table 3, which shows the multinomial logistic

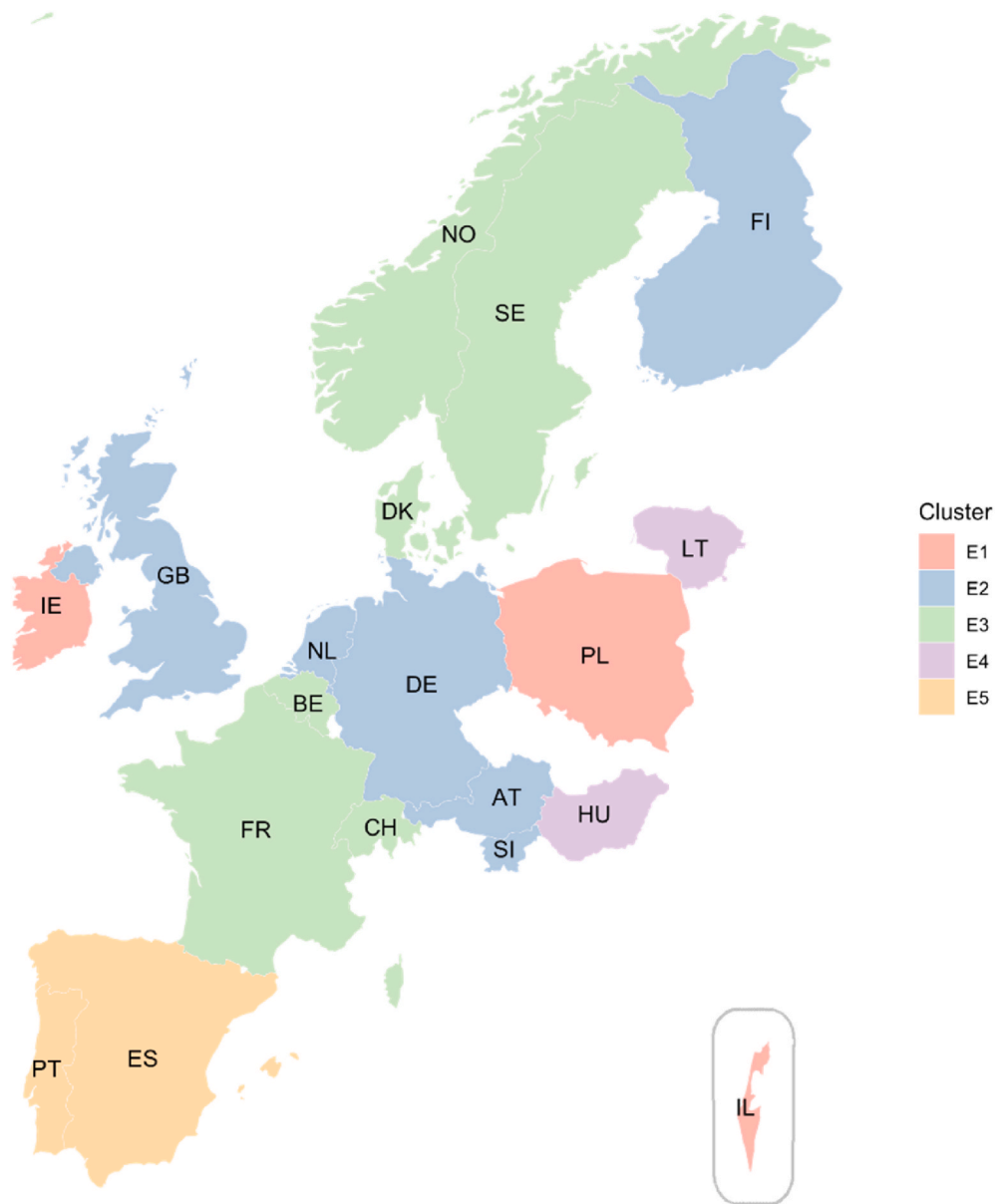


Fig. 3. Map with clusters of European countries associated with chronic conditions, ISO2 coding.

regression results associating the four variables of interest with the class of membership in each condition following the 3-step approach.

Analysing the regression results, the following distribution of the determinants within each class can be posited, taking into account we have significant results considering the reference class. Pattern “Back, Digestive and Headaches”, that is taken as a reference because it is the class with the lowest average number of chronic conditions, consists of young and middle-aged people, women, and with higher-than-average income. “Allergies and Respiratory” pattern comprise middle-aged men with a medium/high level of education and higher than average income. “Complex Multimorbidity” class consists of older people with lower income and primary education. “Cancer and Cardiovascular” is made up of older men with a low income and primary or secondary education. Class “Musculoskeletal” is made up of older people (although somewhat younger than those in classes C3 and C4) with low level of education (primary) and more inclined to live in the countryside. Finally, “Cardiovascular” pattern is mainly made up of older men with a low level of education. This pattern is the one with the highest mean age together with the “Complex Multimorbidity” class.

Looking at the distribution of the country clusters combined with the condition patterns in Fig. 4, the “Allergies and Respiratory” pattern is significantly more prevalent in cluster E5, the “Cancer and Cardiovascular” pattern is more prevalent in clusters E1 and E5, the “Musculoskeletal” pattern is less prevalent significantly in cluster E2, and the “Cardiovascular” pattern is the most prevalent in E2 and E4 clusters. “Complex Multimorbidity” is the only pattern without significant differences among clusters (see Fig. 5).

Finally, the influence of the covariates was analysed according to each MLCA-derived country cluster. Table S5 shows the results of the multinomial regression stratified by cluster. In general, the determinants act in a similar way in each cluster as they do globally. By gender, similar trends are observed, although cluster E5 (Spain and Portugal) does not show significant differences by pattern with respect to men except in the “Complex Multimorbidity” pattern, while in the other clusters women seem to have more protection in certain patterns. It is also interesting to note in cluster E5 that people with lower incomes do not have significant differences in the appearance of the six patterns, unlike in the rest of the European countries.

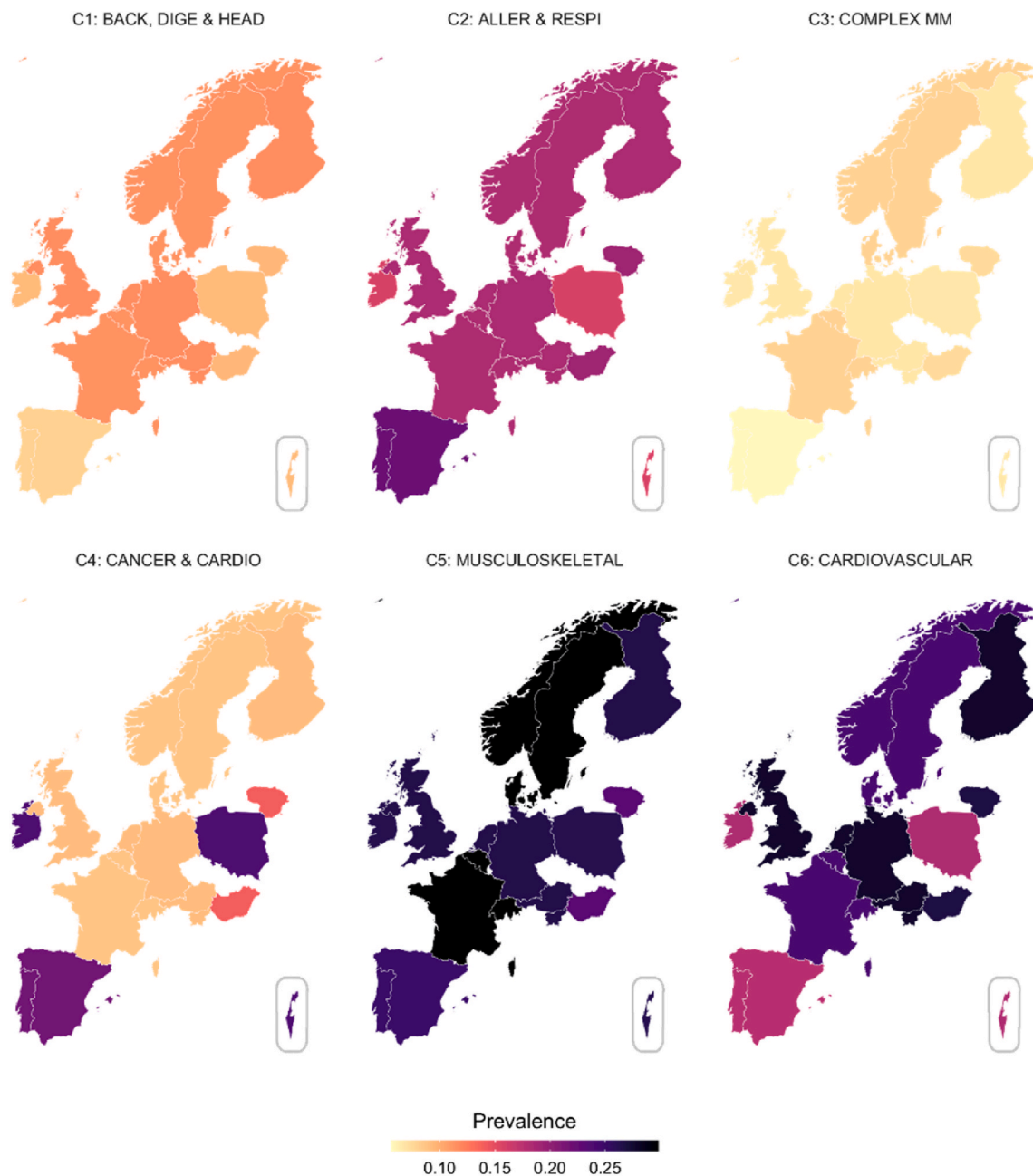


Fig. 4. Maps with the prevalence of multimorbidity patterns by European countries.

The most notable difference in this analysis comes in the Housing Location variable. In the “Cancer and Cardiovascular” pattern, while in clusters E2 and E5 living in places with fewer inhabitants is a risk factor, in clusters E3 and E4 it is a protective factor. It should also be noted that in cluster E5 the “Musculoskeletal” pattern is significantly more prevalent in rural areas.

4. Discussion

This study has aimed to explore multimorbidity patterns among European countries through the MLCA technique, which allows multi-level information to be introduced into a latent class model. In our results, 14 Chronic conditions have been grouped into six different patterns within those with two or more chronic conditions.

While classical clustering and factor analysis techniques have been used for pattern detection, it is interesting to highlight the use of LCA as

one of the most widespread techniques in recent years in the search for multimorbidity classes (Craig et al., 2021; Marengoni et al., 2020; Olaya et al., 2017). In our case, other studies that have made use of LCA in European countries, but our study is one of the first to make use of the multilevel version of LCA in a large set of European countries for the detection of multimorbidity patterns and possible similarities between countries and social determinants.

Overall, the six multimorbidity patterns obtained in the European population were in line with those obtained in previous studies, although comparison with other studies is limited given the differences in regions, chronic conditions measured, and technique used for the patterns (Busija et al., 2019). In a systematic review of 14 studies of multimorbidity patterns, the three most common patterns were found to be musculoskeletal, mental health and cardiovascular (Prados-Torres et al., 2014), while in another review in developed countries (Ng et al., 2018) the three most common were cardiovascular, mental health and

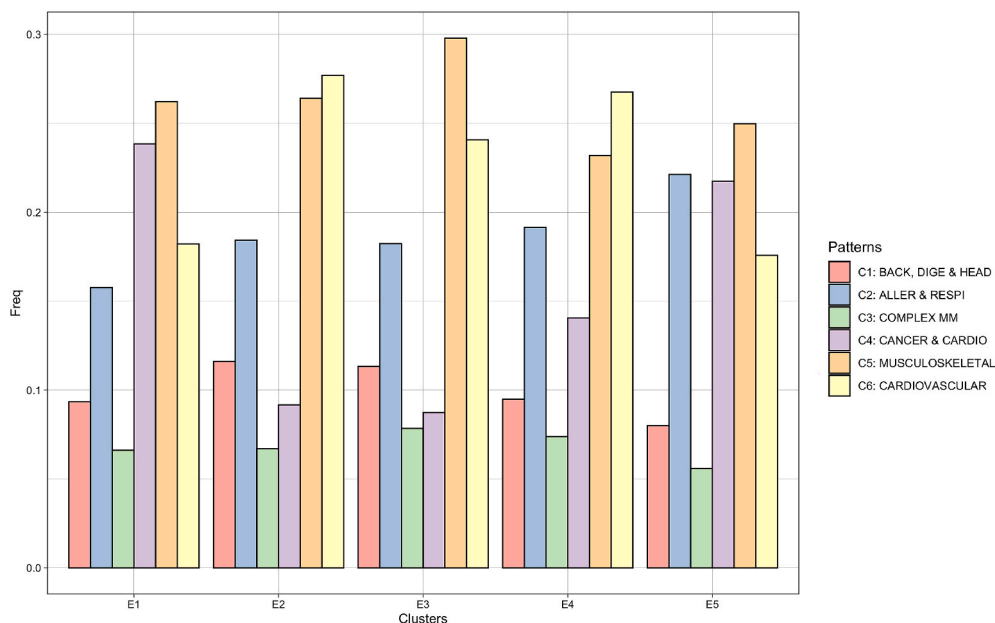


Fig. 5. Prevalence of multimorbidity patterns by clusters of European countries.

allergic disease. In our study, three of the six localised patterns (“Cardiovascular”, “Musculoskeletal”, and “Allergies”) are in line with these reviews. However, the mental pattern has not emerged, which may be caused by the fact that only one of the 14 conditions analysed is mental and its highest prevalence is in the “Complex Multimorbidity” group.

On the other hand, this complex pattern has the most chronic conditions on average (7.51) and groups parts of several other patterns such as musculoskeletal, cardiovascular or allergies, as well as depression. It is a typical pattern associated with the progressive ageing of society and also appears in other studies (Garin et al., 2016; Olaya et al., 2017), including physical conditions and mental health problems, which are mostly caused by the physical deterioration and activity limitation that comes with accumulating so many chronic conditions. In fact, the relationship between the conditions that make it up this pattern is referenced and is a large part of the current problem stemming from the health expenditure associated with high old age in Europe.

A somewhat different pattern to that found in other studies is “Cancer and Cardiovascular”. This is a pattern that combines diseases that are part of the metabolic syndrome (heart problems, hypertension, and obesity) with cancer in its various forms. These types of cardiovascular problems can lead to the development of cancer (Esposito et al., 2014), and in our study their occurrence shows signs of this relationship.

Our results highlight the association of multimorbidity patterns with socioeconomic determinants (Palladino et al., 2016). Two interesting patterns to highlight this difference are “Back, Digestive, and Headaches” and “Musculoskeletal”. Significant differences are found between the two patterns, as while people with headaches or back pain have above-average income and medium/high educational levels, most of the population with musculoskeletal problems is older, poorly educated, and rural.

It can be hypothesised that educational level and place of origin may have been critical factors in these differences. Like we have said, the “Back, Digestive and Headaches” pattern is a typical pattern of young/medium age people and it could be related with medium/high skilled technical work, with these pathologies being some of the most frequent in office/technique jobs (Madeleine et al., 2013; Nunes et al., 2021), while the “Musculoskeletal” patterns are associated with manual and low skilled jobs and rural areas (Docking et al., 2015; Stewart et al., 2014), as well as being associated with lower incomes.

These social differences also occur in patterns associated with

metabolic syndrome (in our study, “Cardiovascular” and “Cancer and Cardiovascular”). These patterns are significant in men in our sample, who have the highest prevalence of metabolic syndrome in Europe (Regitz-Zagrosek et al., 2006), although this difference becomes less pronounced from the age of 50 onwards (Abbate et al., 2021). They have a somewhat lower educational level than other patterns and have lower overall incomes, more pronouncedly in the case of the “Cancer and Cardiovascular” pattern. These patterns are associated with poor diet and poor lifestyles, which tend to be associated with low levels of education and income (Blanquet et al., 2016; Khambaty et al., 2020).

On the other hand, the “Allergies and Respiratory” pattern is made up of people younger than the other patterns, with a higher level of income and education than the other patterns. It is a frequent pattern in other studies in developed countries (Jones et al., 2022; Larsen et al., 2017) and young people (Violán et al., 2016). Together with pattern “Back, digestive and headache”, it is the pattern with the youngest people. Studies on multimorbidity patterns in young people are not very extensive, so finding these patterns is essential in the approach to prevention campaigns, given the possibility of the origin of these chronic conditions in habits such as smoking and poor diet (Andrianasolo et al., 2018; Hisinger-Mölkänen et al., 2022) or environmental factors related with climate change issues (Luschkova et al., 2022).

Finally, the “Complex Multimorbidity” pattern is difficult to categorise at the level of chronic conditions due to their great variety, but it is easy to see at the level of social determinants. It is made up of older people, with low/middle income and a lower educational level than the other patterns. It is clearly related to the ageing process and appears in other studies, where it is also related to low income (Olaya et al., 2017). It is also related to low educational level, thus higher education was significantly associated with a decreased risk of general multimorbidity (Afshar et al., 2015). Given the advanced ageing process in Europe, determining the characteristics that can lead to this type of pattern is fundamental when establishing health protection policies.

The differential contribution of our study is thanks to MLCA being able to group countries into clusters according to the prevalence of the patterns of multimorbidity. Analysing the similarities and differences between clusters seeing Figs. 3 and 5, E2 and E3 are two of the most similar country clusters, consisting mainly of central and northern European countries. The main difference was “Cardiovascular” pattern were more prevalent in E2. Statistics show that in Germany, Austria, and

Table 2
Summary of the sample characteristics in each class in all countries (n = 18,933).

Characteristics	Overall, N = 18,933	C1, Back, Digestive & Headache N = 2,022 (11%)	C2, Allergies and Respiratory N = 3,490 (18%)	C3, Complex Multimorbidity N = 1,323 (7%)	C4, Cancer and Cardiovascular N = 2,394 (13%)	C5, Musculoskeletal N = 5,108 (27%)	C6, Cardiovascular N = 4,596 (24%)
Conditions	3.46 (1.68)	2.65 (0.91)	3.16 (1.32)	7.51 (1.53)	3.20 (1.29)	3.27 (1.18)	3.23 (1.27)
Gender							
Male	8,281 (44%)	697 (34%)	1,517 (43%)	407 (31%)	959 (40%)	2,242 (44%)	2,459 (54%)
Female	10,652 (56%)	1,325 (66%)	1,973 (57%)	916 (69%)	1,435 (60%)	2,866 (56%)	2,137 (46%)
Age							
18-39	4,484 (24%)	999 (49%)	1,425 (41%)	106 (8.0%)	240 (10%)	1,397 (27%)	317 (6.9%)
40-54	4,602 (24%)	619 (31%)	920 (26%)	220 (17%)	483 (20%)	1,517 (30%)	843 (18%)
55-69	5,674 (30%)	312 (15%)	753 (22%)	441 (33%)	901 (38%)	1,414 (28%)	1,853 (40%)
>69	4,173 (22%)	92 (4.5%)	392 (11%)	556 (42%)	770 (32%)	780 (15%)	1,583 (34%)
Housing Location							
Big city	6,047 (32%)	673 (33%)	1,282 (37%)	410 (31%)	754 (32%)	1,589 (31%)	1,339 (29%)
Town	5,924 (31%)	663 (33%)	1,083 (31%)	411 (31%)	853 (36%)	1,511 (30%)	1,403 (31%)
Rural Area	6,949 (37%)	685 (34%)	1,125 (32%)	497 (38%)	785 (33%)	2,006 (39%)	1,851 (40%)
Education							
Basic	5,689 (30%)	370 (18%)	669 (19%)	720 (55%)	863 (36%)	1,422 (28%)	1,645 (36%)
Secondary	9,080 (48%)	1,075 (53%)	1,706 (49%)	479 (37%)	1,163 (49%)	2,516 (49%)	2,141 (47%)
University	4,074 (22%)	571 (28%)	1,103 (32%)	111 (8.5%)	354 (15%)	1,155 (23%)	780 (17%)
Income							
Q1	3,873 (20%)	302 (15%)	629 (18%)	485 (37%)	581 (24%)	920 (18%)	956 (21%)
Q2	3,866 (20%)	332 (16%)	593 (17%)	310 (23%)	529 (22%)	1,062 (21%)	1,040 (23%)
Q3	5,050 (27%)	609 (30%)	997 (29%)	217 (16%)	513 (21%)	1,436 (28%)	1,278 (28%)
Q4	4,197 (22%)	592 (29%)	959 (27%)	136 (10%)	367 (15%)	1,231 (24%)	912 (20%)
N/A	1,947 (10%)	187 (9%)	312 (9%)	175 (13%)	404 (17%)	459 (9%)	410 (9%)
Cluster							
E1	2,525 (13%)	236 (12%)	398 (11%)	167 (13%)	602 (25%)	662 (13%)	460 (10%)
E2	7,137 (38%)	828 (41%)	1,315 (38%)	478 (36%)	654 (27%)	1,885 (37%)	1,977 (43%)
E3	5,737 (30%)	650 (32%)	1,046 (30%)	450 (34%)	501 (21%)	1,709 (33%)	1,381 (30%)
E4	1,708 (9.0%)	162 (8.0%)	327 (9.4%)	126 (9.5%)	240 (10%)	396 (7.8%)	457 (9.9%)
E5	1,826 (9.6%)	146 (7.2%)	404 (12%)	102 (7.7%)	397 (17%)	456 (8.9%)	321 (7.0%)

Hungary, the percentage of the population with this type of problem is higher than in other European countries (Eurostat, 2019a). Other studies also found that hypertension and the multimorbidity associated with it were more prevalent in central and eastern European countries (Nielsen et al., 2017).

In this respect, cluster E4, formed by Eastern European countries (Hungary and Lithuania), has similarities with cluster E2, the clusters with the highest “Cardiovascular” pattern. It differs from cluster E2 mainly in having a higher prevalence of the “Cancer and Cardiovascular” pattern. Eastern European countries tend to have higher cancer rates (Eurostat, 2019b), with Hungary and Lithuania being the countries with the highest cancer prevalence in our sample. In turn, we can relate cluster E4 to cluster E1, to which Poland (also an Eastern European country) belongs, as well as Israel and Ireland. The pattern “Cancer and Cardiovascular” is also relevant in cluster E5 (Spain and Portugal), but this fact is due more to the cardiovascular part, as the prevalence of cancer as a single condition is low in these Mediterranean countries in our study (see Tables S1 and S4). However, it is interesting to note that this pattern, frequent in E5, is made up of people with low-income levels, with these two countries being among those with the lowest average salaries in Europe (Eurostat, 2022b).

The E1 and E5 clusters are similar in the prevalence of the patterns, the difference being in the “Allergies” pattern. Allergies and their association with respiratory problems are more common in Mediterranean countries. These two clusters are countries that could be called peripheral to central/northern Europe (Ireland, Poland and Israel in E1, Portugal and Spain in E5) and with a somewhat lower socioeconomic status than the countries in clusters E2 and E3 (UNDP (United Nations Development Programme), 2020). In addition to geographical proximity, a relationship could be observed between the obtained country grouping and welfare state characteristics. Clusters E2 and E3 contain countries that could be encompassed within two well-established welfare regimes: Scandinavian or social democratic and Bismarckian or conservative (Alvarez-Galvez et al., 2014; Castles & Obinger, 2008). In turn, cluster E4 would be formed by post-Soviet countries from the East

and E5 by Mediterranean countries.

Within these differences among clusters of European countries and patterns, a similarity of interest for our study emerges. The only pattern that is similarly distributed across clusters is “Complex Multimorbidity”. This pattern, which as we have hypothesised is clearly associated with ageing, affects clusters of countries in a similar way whatever their welfare status or geographical area. This shows ageing to be a key factor in the emergence of this type of multimorbidity and makes clear the importance of acting preventively on the problem of multimorbidity, since countries will have less opportunity to address this health problem as age increases.

Finally, some differences have been detected in the influence of social determinants at the individual level according to the cluster to which the individual belongs. On the one hand, the appearance of patterns in cluster E5 seems not to be influenced by gender and income level. This fact may be due to a smaller sample size than the rest of the clusters (which have more countries) since, although they are not significant, the ORs of the covariates Gender and Income Level are like the others.

On the other hand, it is observed that while in clusters E2 and E5 living in places with fewer inhabitants is a risk factor, in clusters E3 and E4 it is a protective factor in the appearance of the pattern “Cancer and Cardiovascular”. The difference between cluster E5 and E2, with very opposite ORs, is remarkable. This fact may be due to the social difference between the rural and urban environment, especially important in countries such as Spain (in E5), with a clear separation between very dense areas and sparsely populated areas, with a scarcity of services, especially health services (Latorre-Arteaga et al., 2018), which are so important in the early diagnosis of diseases such as cancer.

All the above highlights the evidence in the importance of the socioeconomic context in explaining the differences in health determinants (Alvarez-Galvez et al., 2014) and more specifically in our study in the emergence of multimorbidity patterns. It is observed that the relationship of multimorbidity patterns with economic inequalities should be analysed not only at the individual level but also at the group

Table 3
Multilevel multinomial logistic regression of social determinants. OR compared C1 class (Back, Digestive & Headache) with the others.

C1 – Back, Digestive & Headache (Ref.) Category	C2 – Allergies and Respiratory		C3 – Complex Multimorbidity		C4 – Cancer and Cardiovascular		C5 - Musculo-skeletal		C6 – Cardiovascular	
	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value
(Intercept)	2.009	0.000*	0.394	0.000*	0.980	0.893	2.601	0.000*	0.584	0.000*
<i>Level 1 Covariates</i>										
Gender										
Male (Ref.)	1		1		1		1		1	
Female	0.653	0.000*	0.965	0.660	0.671	0.000*	0.641	0.000*	0.420	0.000*
Age										
18-39 (Ref.)	1		1		1		1		1	
40-54	1.064	0.359	3.524	0.000*	3.338	0.000*	1.756	0.000*	4.319	0.000*
55-69	1.733	0.000*	11.174	0.000*	11.505	0.000*	3.121	0.000*	18.052	0.000*
>69	3.043	0.000*	34.184	0.000*	29.021	0.000*	5.362	0.000*	48.879	0.000*
Housing Location										
Big City (Ref.)	1		1		1		1		1	
Town	0.887	0.086	0.873	0.148	1.049	0.543	0.941	0.365	4.319	0.000*
Rural Area	0.899	0.126	0.920	0.364	0.917	0.280	1.157	0.028*	18.052	0.000*
Education										
Primary (Ref.)	1		1		1		1		1	
Secondary	1.062	0.448	0.487	0.000*	0.843	0.038*	0.801	0.002*	0.793	0.002*
University	1.349	0.001*	0.276	0.000*	0.568	0.000*	0.773	0.003*	0.656	0.000*
Income										
Q1 (Ref.)	1		1		1		1		1	
Q2	0.847	0.094	0.709	0.003*	0.943	0.577	1.078	0.423	1.021	0.830
Q3	0.807	0.017*	0.408	0.000*	0.664	0.000*	0.890	0.175	0.905	0.269
Q4	0.772	0.006*	0.379	0.000*	0.611	0.000*	0.845	0.061	0.826	0.047*
N/A	0.864	0.154	0.810	0.123	1.603	0.000*	0.906	0.380	0.848	0.167
<i>Level 2 Covariates</i>										
Cluster										
E1 (Ref.)	1		1		1		1		1	
E2	0.972	0.767	0.935	0.586	0.337	0.000*	0.825	0.030*	1.294	0.008*
E3	0.962	0.688	0.955	0.711	0.289	0.000*	0.907	0.283	1.020	0.845
E4	1.189	0.176	1.110	0.529	0.578	0.000*	0.853	0.195	1.364	0.017*
E5	1.656	0.000*	1.125	0.492	1.156	0.266	1.118	0.369	1.158	0.280

level, taking age as a fundamental factor and as a mediator for the prevention strategies that can be taken.

In this sense, it is interesting to analyse how multimorbidity patterns such as “Cardiovascular” or “Back, Digestive and Headaches” are more prevalent in countries in clusters E2 and E3. These patterns are formed by individuals with a medium/high level of education and a high level of income and are more frequent in our study in countries with well-consolidated and more protectionist welfare states. This shows how the problem of multimorbidity occurs in all European countries, given the general ageing of the population and the advance of new diseases, but it occurs in different ways depending on the socioeconomic differences not only to individual characteristics, but also to social determinants specific to each country.

4.1. Strengths and limitations

The main strength of this study is its novelty, as it is one of the first studies to analyse differences in multimorbidity patterns across European countries. To do so, it applies a technique (LCA) that has been widely used in recent years and has been the basis for other studies of multimorbidity patterns. Another of its strengths has been the incorporation of multilevel information, which has allowed us to improve the entropy and classification of the model, giving greater strength to our results. Finally, the study is based on data from the European Social Survey, a survey with a solid methodological basis and which has been used in numerous prestigious studies.

It is important to mention that this study has some limitations. The number of chronic conditions used to determine multimorbidity patterns is 14, somewhat lower than in other similar studies, which means that some common patterns such as mental health do not appear. On the other hand, the sample size per country is sufficient for the groups in the

MLCA technique but somewhat short of achieving the desired variability in chronic conditions. Moreover, the sample of European countries (19) is representative mainly of central and northern Europe, but some Mediterranean and eastern European countries are missing to be able to consolidate the results obtained.

In future similar studies, a larger sample size per country and a more significant number of European countries would strengthen our initial results and better refine the main patterns of multimorbidity in each European area.

5. Conclusions

This initial study shows that some disease combinations are more prevalent among different socioeconomic groups. The MLCA technique identifies well-defined and common multimorbidity profiles, but at the same time classifies mixed complementary profiles that present a combined and more complex characterization (e.g. allergies and respiratory conditions and complex multimorbidity). In particular, our analysis provides new evidence on how MLCA models could be used to address the problematic study of the complex combinations of co-occurring diseases among the elderly population in Europe. Furthermore, our findings show that socioeconomic differences in the occurrence of patterns are not only of the individual but also of group importance, emphasising the importance of the protective measures that European countries should apply and how the welfare states in each country can influence in the health of their inhabitants.

These main findings show that chronic diseases tend to appear in a combined and interactive way, indicating that a multidimensional and integrative public health strategy is needed to address multimorbidity and their social inequalities in Europe. These preliminary models suggest that tailored public health strategies are needed to address social

inequalities in multimorbidity.

Ethical statement

- 1) This material is the authors' own original work, which has not been previously published elsewhere.
- 2) The paper is not currently being considered for publication elsewhere.
- 3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
- 4) The paper properly credits the meaningful contributions of co-authors and co-researchers.
- 5) The results are appropriately placed in the context of prior and existing research.
- 6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
- 7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

Author statement

JAG: Conceptualization, Methodology and Revision, Project Administration, JCB: Writing – Original Draft, Formal Analysis, VSL: Software, Writing – Original Draft, EOM: Investigation, Writing - Review & Editing, BRF: Investigation, Writing - Review & Editing, CLF: Formal Analysis, Methodology, COG and JAB: Supervision and Visualization and JLG: Conceptualization, Methodology and Formal Analysis.

Data availability

The data used in this study is publicly available on the European Social Survey website.

Acknowledgements

This research has been granted by the University Institute of Research for Sustainable Social Development (INDESS, Jerez de la Frontera, CP 11405, University of Cadiz, Spain), the Research Group of Healthcare Information Systems (PAIDI CTS553), Ramon & Cajal program operated by the Spanish Ministry of Science and Innovation (RYC-2016-19353) and public funds of the ITI call (Integrated Territorial Investment), developed by the Health Department of the Andalusian Government. The DEMMOCAD project has been 80% co-financed by funds from the European Regional Development Fund (ERDF) operational program of Andalusia 2014–2020.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ssmph.2022.101268>.

References

- Abbate, M., Pericas, J., Yañez, A. M., López-González, A. A., de Pedro-Gómez, J., Aguilo, A., Morales-Asencio, J. M., & Bennasar-Veny, M. (2021). Socioeconomic inequalities in metabolic syndrome by age and gender in a Spanish working population. *International Journal of Environmental Research and Public Health* 2021, 18, Article 10333. <https://doi.org/10.3390/IJERPH181910333>, 10333–18.
- Afshar, S., Roderick, P. J., Kowal, P., Dimitrov, B. D., & Hill, A. G. (2015). Multimorbidity and the inequalities of global ageing: A cross-sectional study of 28 countries using the world health surveys. <https://doi.org/10.1186/s12889-015-2008-7>.
- van den Akker, M., Buntinx, F., & Knottnerus, J. A. (1996). Comorbidity or multimorbidity: What's in a name? A review of literature. *The European Journal of General Practice*, 2, 65–70. <https://doi.org/10.3109/13814789609162146>
- Alvarez-Galvez, J. (2018). Multidimensionality of Health Inequalities: A Cross-Country Identification of Health Clusters through Multivariate Classification Techniques.

- International Journal of Environmental Research and Public Health*, 15(9). <https://doi.org/10.3390/IJERPH15091900>.
- Alvarez-Galvez, J., Rodero-Cosano, M. L., García-Alonso, C., & Salvador-Carulla, L. (2014). Changes in socioeconomic determinants of health: Comparing the effect of social and economic indicators through European welfare state regimes. *Journal of Public Health (Germany)*, 22(4), 305–311. <https://doi.org/10.1007/s10389-014-0623-x>.
- Álvarez-Gálvez, J., Rodero-Cosano, M. L., Salinas-Pérez, J. A., & Gómez-Baya, D. (2019). Exploring the Complex Associations Among Social Determinants of Health in Andalusia After the 2008 Financial Crisis. *Social Indicators Research*, 141(2), 873–893. <https://doi.org/10.1007/s11205-018-1845-z>.
- Andrianasolo, R. M., Kesse-Guyot, E., Adjibade, M., Hercberg, S., Galan, P., & Varraso, R. (2018). Associations between dietary scores with asthma symptoms and asthma control in adults. *European Respiratory Journal*, 52, Article 1702572. <https://doi.org/10.1183/13993003.02572-2017>
- Arokiasamy, P., Uttamacharya, U., Jain, K., Biritwum, R. B., Yawson, A. E., Wu, F., Guo, Y., Maximova, T., Espinoza, B. M., Salinas Rodriguez, A., Afshar, S., Pati, S., Ice, G., Banerjee, S., Liebert, M. A., Snodgrass, J. J., Naidoo, N., Chatterji, S., & Kowal, P. (2015). The impact of multimorbidity on adult physical and mental health in low- and middle-income countries: What does the study on global ageing and adult health (SAGE) reveal? *BMC Medicine*, 13. <https://doi.org/10.1186/s12916-015-0402-8>
- Barnett, K., Mercer, S. W., Norbury, M., Watt, G., Wyke, S., & Guthrie, B. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. *Lancet*, 380, 37–43. [https://doi.org/10.1016/S0140-6736\(12\)60240-2](https://doi.org/10.1016/S0140-6736(12)60240-2)
- Bartholomew, D., Knott, M., & Moustaki, I. (2011). Latent variable models and factor Analysis: A unified approach. In *Latent variable models and factor Analysis: A unified approach* (3rd ed.). John Wiley and Sons Ltd. <https://doi.org/10.1002/9781119970583>.
- Bendayan, R., Zhu, Y., Federman, A. D., & Dobson, R. J. B. (2021). Multimorbidity patterns and memory trajectories in older adults: Evidence from the English longitudinal study of aging. *J Gerontol A Biol Sci Med Sci*, 76, 867–875. <https://doi.org/10.1093/GERONA/GLAB009>
- Blanquet, M., Debost-Légrand, A., Gerbaud, L., de La Celle, C., Brigand, A., Mioche, L., Sass, C., Hazart, J., & Aw, A. (2016). Metabolic syndrome and social deprivation: Results of a French observational multicentre survey. *Family Practice*, 33, 17–22. <https://doi.org/10.1093/FAMPRA/CMV086>
- Bolck, A., Croon, M., & Hagenaars, J. (2004). Estimating latent structure models with categorical variables: One-step versus three-step estimators. *Political Analysis*, 12, 3–27. <https://doi.org/10.1093/PAN/MPH001>
- Bono, F., & Matrangola, D. (2019). Socioeconomic inequality in non-communicable diseases in Europe between 2004 and 2015: Evidence from the SHARE survey. *The European Journal of Public Health*, 29, 105–110. <https://doi.org/10.1093/EURPUB/CKY165>
- Busija, L., Lim, K., Szoek, C., Sanders, K. M., & McCabe, M. P. (2019). Do replicable profiles of multimorbidity exist? Systematic review and synthesis. *European Journal of Epidemiology*, 34, 1025–1053. <https://doi.org/10.1007/s10654-019-00568-5>
- Castles, F. G., & Obinger, H. (2008). Worlds, families, regimes: Country clusters in European and OECD area public policy. <https://doi.org/10.1080/01402380701835140> 31, 321–344. <https://doi.org/10.1080/01402380701835140>
- Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases*, 40, 373–383. [https://doi.org/10.1016/0021-9681\(87\)90171-8](https://doi.org/10.1016/0021-9681(87)90171-8)
- Chmiel, A., Klimek, P., & Thurner, S. (2014). Spreading of diseases through comorbidity networks across life and gender. *New Journal of Physics*, 16, Article 115013. <https://doi.org/10.1088/1367-2630/16/11/115013>
- Craig, L. S., Cunningham-Myrie, C. A., Hotchkiss, D. R., Hernandez, J. H., Gustat, J., & Theall, K. P. (2021). Social determinants of multimorbidity in Jamaica: Application of latent class analysis in a cross-sectional study. *BMC Public Health*, 21, 1197. <https://doi.org/10.1186/s12889-021-11225-6>
- Diaz, E., Poblador-Pou, B., Gimeno-Feliu, L. A., Calderón-Larrañaga, A., Kumar, B. N., & Prados-Torres, A. (2015). Multimorbidity and its patterns according to immigrant origin. A nationwide register-based study in Norway. *PLoS One*, 10, Article e0145233. <https://doi.org/10.1371/JOURNAL.PONE.0145233>
- Docking, R. E., Beasley, M., Steinerowski, A., Jones, E. A., Farmer, J., Macfarlane, G. J., & Jones, G. T. (2015). The epidemiology of regional and widespread musculoskeletal pain in rural versus urban settings in those ≥55 years. *Br J Pain*, 9, 86–95. <https://doi.org/10.1177/2049463714527438>
- Elixhauser, A., Steiner, C., Harris, D. R., & Coffey, R. M. (1998). Comorbidity measures for use with administrative data. *Medical Care*, 36, 8–27. <https://doi.org/10.1097/00005650-199801000-00004>
- Esposito, K., Capuano, A., & Giugliano, D. (2014). Metabolic syndrome and cancer: Holistic or reductionist? *Endocrine*, 45, 362–364. <https://doi.org/10.1007/s12020-013-0056-2>
- European Social Survey Data Archive. (2016). *European social survey (2016): ESS-7 2014 documentation report*, 3.2. Bergen.
- Eurostat. (2019a). Cardiovascular diseases statistics [WWW document]. Eurostat, statistic explained, 7.1.22 https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cardiovascular_diseases_statistics.
- Eurostat. (2019b). Cancer statistics [WWW document]. Eurostat, statistics explained, 7.1.22 https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cancer_statistics#Deaths_from_cancer.

- Eurostat. (2022a). Life expectancy across EU regions in 2020 [WWW document]. Eurostat news, 7.1.22 <https://ec.europa.eu/eurostat/web/products-eurostat-news/-/ddn-20220427-1>.
- Eurostat. (2022b). Mean and median income by household type [WWW Document]. EU-SILC and ECHP surveys, 7.14.22 https://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=ilc_di04.
- Foguet-Boreu, Q., Violán, C., Rodríguez-Blanco, T., Roso-Llorach, A., Pons-Vigués, M., Pujol-Ribera, E., Gil, Y. C., & Valderas, J. M. (2015). Multimorbidity patterns in elderly primary health care patients in a south mediterranean European region: A cluster Analysis. *PLoS One*, 10. <https://doi.org/10.1371/JOURNAL.PONE.0141155>
- Fortin, M., Lapointe, L., Hudon, C., & Vanasse, A. (2005). Multimorbidity is common to family practice: Is it commonly researched? *Canadian Family Physician*, 51, 245.
- Gallacher, K. I., Batty, G. D., McLean, G., Mercer, S. W., Guthrie, B., May, C. R., Langhorne, P., & Mair, F. S. (2014). Stroke, multimorbidity and polypharmacy in a nationally representative sample of 1,424,378 patients in scotland: Implications for treatment burden. *BMC Medicine*, 12. <https://doi.org/10.1186/S12916-014-0151-0>
- Garin, N., Koyanagi, A., Chatterji, S., Tyrovolas, S., Olaya, B., Leonardi, M., Lara, E., Koskinen, S., Tobiasz-Adamczyk, B., Ayuso-Mateos, J. L., & Haro, J. M. (2016). Global multimorbidity patterns: A cross-sectional, population-based, multi-country study. *J Gerontol A Biol Sci Med Sci*, 71, 205–214. <https://doi.org/10.1093/GERONA/GLV128>
- GBD 2016 DALYs and HALE Collaborators. (2017). Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: A systematic analysis for the global burden of disease study 2016. *Lancet*, 390, 1260–1344. [https://doi.org/10.1016/S0140-6736\(17\)32130-X](https://doi.org/10.1016/S0140-6736(17)32130-X)
- Gijzen, R., Hoeymans, N., Schellevis, F. G., Ruwaard, D., Satariano, W. A., & van den Bos, G. A. M. (2001). Causes and consequences of comorbidity: A review. *Journal of Clinical Epidemiology*, 54, 661–674. [https://doi.org/10.1016/S0895-4356\(00\)00363-2](https://doi.org/10.1016/S0895-4356(00)00363-2)
- Hanlon, P., Nicholl, B. I., Jani, B. D., McQueenie, R., Lee, D., Gallacher, K. I., & Mair, F. S. (2018). Examining patterns of multimorbidity, polypharmacy and risk of adverse drug reactions in chronic obstructive pulmonary disease: A cross-sectional UK biobank study. *BMJ Open*, 8, Article e018404. <https://doi.org/10.1136/bmjopen-2017-018404>
- Hernández, B., Voll, S., Lewis, N. A., McCrory, C., White, A., Stirland, L., Kenny, R. A., Reilly, R., Hutton, C. P., Griffith, L. E., Kirkland, C. A., Terrera, G. M., & Hofer, S. M. (2021). Comparisons of disease cluster patterns, prevalence and health factors in the USA, Canada, England and Ireland. *BMC Public Health*, 21. <https://doi.org/10.1186/S12889-021-11706-8>
- Hisinger-Mölkänen, H., Kankaanranta, J. H., Haahela, T., Sovijärvi, J. A., Tuomisto, L., Andersén, H., Lindqvist, A., Backman, H., Langhammer, A., Rönmark, E., Pinja, I., Pallasaho, P., & Piirilä, J. P. (2022). The combined effect of exposures to vapours, gases, dusts, fumes and tobacco smoke on current asthma. *Clinical Research J*, 16, 467–474. <https://doi.org/10.1111/CRJ.13512>
- Jacob, M. E., Ni, P., Driver, J., Lertz, E., Leveille, S. G., Jette, A. M., & Bean, J. F. (2020). Burden and patterns of multimorbidity: Impact on disablement in older adults. *American Journal of Physical Medicine & Rehabilitation*, 99, 359–365. <https://doi.org/10.1097/PHM.0000000000001388>
- Jones, C. J., Paudyal, P., West, R. M., Mansur, A. H., Jay, N., Makwana, N., Baker, S., & Krishna, M. T. (2022). Burden of allergic disease among ethnic minority groups in high-income countries. *Clinical and Experimental Allergy*, 52, 604–615. <https://doi.org/10.1111/CEA.14131>
- Khambaty, T., Schneiderman, N., Llabre, M. M., Elfassy, T., Moncrieff, A. E., Daviglus, M., Talavera, G. A., Isasi, C. R., Gallo, L. C., Reina, S. A., Vidot, D., & Heiss, G. (2020). Elucidating the multidimensionality of socioeconomic status in relation to metabolic syndrome in the hispanic community health study/study of latinos (HCHS/SOL). *International Journal of Behavioral Medicine* 2020, 27(2 27), 188–199. <https://doi.org/10.1007/S12529-020-09847-Y>
- Koné Pefoyo, A. J., Bronskill, S. E., Gruneir, A., Calzavara, A., Thavorn, K., Petrosyan, Y., Maxwell, C. J., Bai, Y. Q., & Wodchis, W. P. (2015). The increasing burden and complexity of multimorbidity disease epidemiology - Chronic. *BMC Public Health*, 15, 1–11. <https://doi.org/10.1186/S12889-015-1733-2/TABLES/3>
- Kringos, D. S., van den Broeke, J. R., van der Lee, A. P. M., Plochg, T., & Stronks, K. (2016). How does an integrated primary care approach for patients in deprived neighbourhoods impact utilization patterns? An explorative study. *BMC Public Health*, 16. <https://doi.org/10.1186/s12889-016-3246-z>
- Kuzuya, M. (2019). Era of geriatric medical challenges: Multimorbidity among older patients. *Geriatrics and Gerontology International*, 19, 699–704. <https://doi.org/10.1111/GGI.13742>
- Lai, F. T. T., Beeler, P. E., Yip, B. H. K., Cheetham, M., Chau, P. Y. K., Chung, R. Y., Wong, E. L. Y., Yeoh, E. K., Betteguy, E., & Wong, S. Y. S. (2021). Comparing multimorbidity patterns among discharged middle-aged and older inpatients between Hong Kong and zurich: A hierarchical agglomerative clustering analysis of routine hospital records. *Frontiers of Medicine*, 8. <https://doi.org/10.3389/FMED.2021.651925>
- Larsen, F. B., Pedersen, M. H., Friis, K., Gluèmer, C., & Lasgaard, M. (2017). A latent class Analysis of multimorbidity and the relationship to socio-demographic factors and health-related quality of life. A national population-based study of 162,283 Danish adults. *PLoS One*, 12. <https://doi.org/10.1371/JOURNAL.PONE.0169426>
- Latorre-Arteaga, S., Fernández-Sáez, J., & Gil-González, D. (2018). Inequities in visual health and health services use in a rural region in Spain. *Gaceta Sanitaria*, 32, 439–446. <https://doi.org/10.1016/J.GACETA.2017.03.009>
- Lukoclene, O., Varriale, R., & Vermunt, J. K. (2010). The simultaneous decision(S) about the number of lower- and higher-level classes in multilevel latent class Analysis. *Sociological Methodology*, 40, 247–283. <https://doi.org/10.1111/J.1467-9531.2010.01231.X>
- Luschkova, D., Traidl-Hoffmann, C., & Bayr, D. (2022). Climate change and allergies. *Allergo J Int*, 31, 26–30. <https://doi.org/10.1007/S40629-022-00212-X>
- Madeleine, P., Vangsgaard, S., Hviid Andersen, J., Ge, H. Y., & Arendt-Nielsen, L. (2013). Computer work and self-reported variables on anthropometrics, computer usage, work ability, productivity, pain, and physical activity. *BMC Musculoskeletal Disorders*, 14. <https://doi.org/10.1186/1471-2474-14-226>
- Marengoni, A., Roso-Llorach, A., Vetrano, D. L., Fernández-Bertolin, S., Guisado-Clavero, M., Violán, C., & Calderón-Larrañaga, A. (2020). Patterns of multimorbidity in a population-based cohort of older people: Sociodemographic, lifestyle, clinical, and functional differences. *J Gerontol A Biol Sci Med Sci*, 75, 798–805. <https://doi.org/10.1093/gerona/glz137>
- Moffat, K., & Mercer, S. W. (2015). Challenges of managing people with multimorbidity in today's healthcare systems. *BMC Family Practice*, 16, 129. <https://doi.org/10.1186/s12875-015-0344-4>
- Møller, S. P., Laursen, B., Johannesen, C. K., Tolstrup, J. S., & Schramm, S. (2020). Patterns of multimorbidity and demographic profile of latent classes in a Danish population-A register-based study. *PLoS One*, 15. <https://doi.org/10.1371/JOURNAL.PONE.0237375>
- Ng, S. K., Tawiah, R., Sawyer, M., & Scuffham, P. (2018). Patterns of multimorbid health conditions: A systematic review of analytical methods and comparison analysis. *International Journal of Epidemiology*, 47, 1687–1704. <https://doi.org/10.1093/IJE/DYY134>
- Nguyen, H., Chua, K. C., Dregan, A., Vitoratou, S., Bayes-Marin, I., Olaya, B., & Prina, A. M. (2020). Factors associated with multimorbidity patterns in older adults in england: Findings from the English longitudinal study of aging (ELSA). *Journal of Aging and Health*, 32, 1120–1132. <https://doi.org/10.1177/0898264319891026>
- Nielsen, C. R., Halling, A., & Andersen-Ranberg, K. (2017). Disparities in multimorbidity across Europe – findings from the SHARE survey. *Eur Geriatr Med*, 8, 16–21. <https://doi.org/10.1016/J.EURGER.2016.11.010>
- Nunes, A. M. P., Moita, J. P. A. M., Espanha, M. M. M. R., Petersen, K. K., & Arendt-Nielsen, L. (2021). Pressure pain thresholds in office workers with chronic neck pain: A systematic review and meta-analysis. *Pain Practice*, 21, 799–814. <https://doi.org/10.1111/PAPR.13014>
- Olaya, B., Moneta, M. V., Caballero, F. F., Tyrovolas, S., Bayes, I., Ayuso-Mateos, J. L., & Haro, J. M. (2017). Latent class analysis of multimorbidity patterns and associated outcomes in Spanish older adults: A prospective cohort study. *BMC Geriatrics*, 17, 1–10. <https://doi.org/10.1186/S12877-017-0586-1/TABLES/3>
- Onder, G., Palmer, K., Navickas, R., Jureviciene, E., Mammarella, F., Strandzheva, M., Mannucci, P., Pecorelli, S., & Marengoni, A. (2015). Time to face the challenge of multimorbidity. A European perspective from the joint action on chronic diseases and promoting healthy ageing across the life cycle (JA-CHRODIS). *European Journal of Internal Medicine*, 26, 157–159. <https://doi.org/10.1016/J.EJIM.2015.02.020>
- Palladino, R., Lee, J. T., Ashworth, M., Triassi, M., & Millett, C. (2016). Associations between multimorbidity, healthcare utilisation and health status: Evidence from 16 European countries. *Age and Ageing*, 45, 431–435. <https://doi.org/10.1093/AGEING/AFW044>
- Park, J., & Yu, H. T. (2017). Recommendations on the sample sizes for multilevel latent class models. <https://doi.org/10.1177/0013164417719111> 78, 737–761 <https://doi.org/10.1177/0013164417719111>
- Pearson-Stuttard, J., Ezzati, M., & Gregg, E. W. (2019). Multimorbidity-a defining challenge for health systems. *The Lancet Public Health*, 4, e599–e600. [https://doi.org/10.1016/S2468-2667\(19\)30222-1](https://doi.org/10.1016/S2468-2667(19)30222-1)
- Prados-Torres, A., Calderón-Larrañaga, A., Hanco-Saavedra, J., Poblador-Plou, B., & van den Akker, M. (2014). Multimorbidity patterns: A systematic review. *Journal of Clinical Epidemiology*, 67, 254–266. <https://doi.org/10.1016/J.JCLINEPI.2013.09.021>
- Regitz-Zagrosek, V., Lehmküh, E., & Weickert, M. O. (2006). Gender differences in the metabolic syndrome and their role for cardiovascular disease. *Clinical Research in Cardiology*, 95, 136–147. <https://doi.org/10.1007/s00392-006-0351-5>
- Sevick, M. A., Trauth, J. M., Ling, B. S., Anderson, R. T., Piatt, G. A., Kilbourne, A. M., & Goodman, R. M. (2007). Patients with complex chronic diseases: Perspectives on supporting self-management. *Journal of General Internal Medicine*, 22(Suppl 3), 438–444. <https://doi.org/10.1007/S11606-007-0316-Z>
- Stewart, S. K., Rothmore, P. R., Doda, D.v.d., Hiller, J. E., Mahmood, M. A., & Pisanelli, D. L. (2014). Musculoskeletal pain and discomfort and associated worker and organizational factors: A cross-sectional study. *Work*, 48, 261–271. <https://doi.org/10.3233/WOR-131622>
- Tazzeo, C., Rizzuto, D., Calderón-Larrañaga, A., Roso-Llorach, A., Marengoni, A., Welmer, A. K., Onder, G., Trevisan, C., & Vetrano, D. L. (2021). Multimorbidity patterns and risk of frailty in older community-dwelling adults: A population-based cohort study. *Age and Ageing*, 50, 2183–2191. <https://doi.org/10.1093/AGEING/AFAB138>
- UNDP (United Nations Development Programme). (2020). *Human development report 2020. The next frontier: Human development and the anthropocene*. New York.
- Vermunt, J. K. (2003). Multilevel latent class models. *Sociological Methodology*, 33, 213–239. <https://doi.org/10.1111/J.0081-1750.2003.T01-1-00131.X>
- Violán, C., Foguet-Boreu, Q., Flores-Mateo, G., Salisbury, C., Blom, J., Freitag, M., Glynn, L., Muth, C., & Valderas, J. M. (2014). Prevalence, determinants and patterns of multimorbidity in primary care: A systematic review of observational studies. *PLoS One*, 9, Article e102149. <https://doi.org/10.1371/journal.pone.0102149>
- Violán, C., Foguet-Boreu, Q., Roso-Llorach, A., Rodríguez-Blanco, T., Pons-Vigués, M., Pujol-Ribera, E., & Valderas, J. M. (2016). Patrones de multimorbilidad en adultos jóvenes en cataluña: Un análisis de clústeres. *Atención Primaria*, 48, 479–492. <https://doi.org/10.1016/J.APRIM.2015.10.006>

- Wallace, E., Salisbury, C., Guthrie, B., Lewis, C., Fahey, T., & Smith, S. M. (2015). Managing patients with multimorbidity in primary care. *BMJ*, 350. <https://doi.org/10.1136/BMJ.H176>
- Weller, B. E., Bowen, N. K., & Faubert, S. J. (2020). *Latent class Analysis: A guide to best practice*. <https://doi.org/10.1177/0095798420930932>. <https://doi-org.bibezproxy.uca.es/10.1177/0095798420930932> 46, 287–311.
- Who. (2008). *The world health report 2008 - primary health care: Now more than ever*. Geneva.
- World Health Organization. (2021). *COVID-19 and the social determinants of health and health equity: Evidence brief* (pp. 1–32). World Health Organization.
- Zhu, Y., Edwards, D., Mant, J., Payne, R. A., & Kiddle, S. (2020). Characteristics, service use and mortality of clusters of multimorbid patients in england: A population-based study. *BMC Medicine*, 18, 1–11. <https://doi.org/10.1186/S12916-020-01543-8/TABLES/4>