

Description of multimorbidity clusters of admitted patients in medical departments of a general hospital

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ABSTRACT

Objective We aim to identify patterns of disease clusters among inpatients of a general hospital and to describe the characteristics and evolution of each group.

Methods We used two data sets from the CMBD (Conjunto mínimo básico de datos - Minimum Basic Hospital Data Set (MBDS)) of the Lucus Augusti Hospital (Spain), hospitalisations and patients, realising a retrospective cohort study among the 74 220 patients discharged from the Medic Area between 01 January 2000 and 31 December 2015. We created multimorbidity clusters using multiple correspondence analysis.

Results We identified five clusters for both gender and age. Cluster 1: alcoholic liver disease, alcoholic dependency syndrome, lung and digestive tract malignant neoplasms (age under 50 years). Cluster 2: large intestine, prostate, breast and other malignant neoplasms, lymphoma and myeloma (age over 70, mostly males). Cluster 3: malnutrition, Parkinson disease and other mobility disorders, dementia and other mental health conditions (age over 80 years and mostly women). Cluster 4: atrial fibrillation/flutter, cardiac failure, chronic kidney failure and heart valve disease (age between 70–80 and mostly women). Cluster 5: hypertension/hypertensive heart disease, type 2 diabetes mellitus, ischaemic cardiomyopathy, dyslipidaemia, obesity and sleep apnea, including mostly men (age range 60–80). We assessed significant differences among the clusters when gender, age, number of chronic pathologies, number of rehospitalisations and mortality during the hospitalisation were assessed ($p < 0.001$ in all cases).

Conclusions We identify for the first time in a hospital environment five clusters of disease combinations among the inpatients. These clusters contain several high-incidence diseases related to both age and gender that express their own evolution and clinical characteristics over time.

INTRODUCTION

Background

Hospital care is increasingly focused on patients with both advanced age and multimorbidity (multiple coexisting chronic pathologies). The coexistence of several of these pathologies in the same person makes diagnoses more difficult, modifies treatments and, very probably, makes prognosis worse.^{1–4} We can hypothesise that this combination of diseases is not random but occurs as a result of some interrelated and not always well-recognised processes. That is, the reason behind the emergence of the cluster concept of chronic diseases, defined as the combination of chronic pathologies grouped

in a single patient,^{5,6} a concept associated with well-established parameters as age, socioeconomic status and gender.^{7–9}

Importance

There are not many published works focusing on the hypothesis of multimorbid disease clusters affecting patients clinically during their lives, and the majority of them used data from primary healthcare and general population directories.^{10–11} Despite the importance of this subject works related to multimorbidity clusters remain scarce, all are of exploratory nature and raise the necessity of additional research for them to have a real impact in clinical practice.^{12–14} Despite the fact that studies analysing the associative patterns of multimorbidity are necessary to optimise the evaluation of patients admitted to hospital with higher frequency, there are very few published works extensive and well-designed enough dealing with this issue.^{15–17} The understanding of patterns hidden in the clusters and their behaviour over time have the potential of enabling the conduct of strategic actions to improve medical attention to chronically ill patients.

Goal of this research

Hence, the aim of this work is to test the hypothesis that the aforementioned coexistence of diseases in hospital environments (not in primary care attention or in the general population) is not random but interrelated. Thus, we intend to identify patterns of multimorbidity among inpatients of a general hospital, describing the features of each cluster and their evolution over time.

MATERIAL AND METHODS

Study design and data source

A retrospective cohort study of all patients discharged from all services of the Medic Area of the Lucus Augusti Hospital (Lugo, Spain) between 1 January 2000 and 31 December 2015 was carried out. This is a public (non-private) hospital located in Galicia (Northeast Spain) and provides medical services to an estimated population of 240 000 people. The Medic Area contains 12 services: cardiology, endocrinology, rheumatology, oncology, pneumology, digestive, neurology, nephrology, geriatrics, short-stay unit, infectious diseases and internal medicine. Monitoring of the patients was carried out up to their decease or until 31 December 2017, whichever of the two occurred first.

The main data source was the registry of hospitalisation entries, which includes all diagnoses



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Table 1 Clinical characterisation of the patients

	With multimorbidity (n=52 939)	Without multimorbidity (n=21 281)	P value
	Mean±SD	Mean±SD	
Age	72.2±14.8	58.5±20.6	<0.001
Number of chronic pathologies	3.9±1.8	1.4±1.9	<0.001
Number of acute pathologies	1.7±1.9	1.4±1.6	<0.001
CIRS	10.9±4.6	6.4±3.5	<0.001
Stay time in days (x)	11.5±19.4	8.7±23.2	<0.001
	%	%	
Gender (V)	54.6	56.3	NS
Rural	47.9	48.2	NS
Mortality	6.7	6.1	0.04

carried out by the healthcare professional in charge, codified (by codifying medics) using the Clasificación Internacional de Enfermedades Revisión 9 (modificación clínica) - ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) (CIE.9MC).¹⁸ As additional data sources we used the nursing registries and since 2007 the computerised database IANUS, which gathers all data derived from medical assistance. The study protocols were approved by the Comité

Ético de Investigación Clínica de Galicia (Ethics Committee of Clinic Research of Galicia; registry code CEIC of Galicia 2014 / 409). A computerised database of each hospitalisation event using all the aforementioned registries was created. It includes

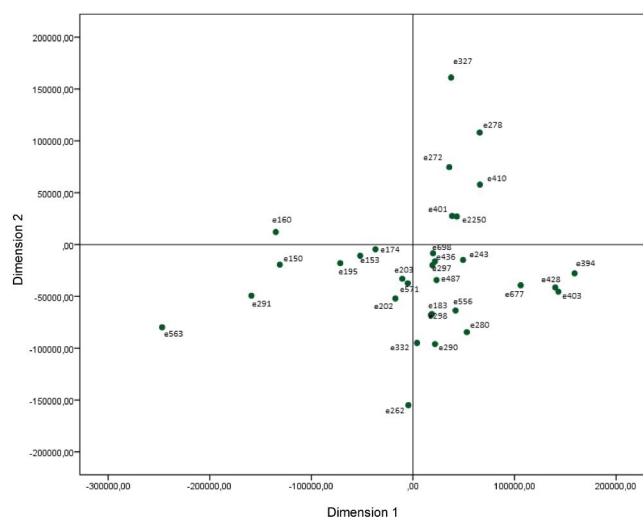


Figure 1 Multiple correspondence analysis of chronic diseases. The quadrant-based distribution of the analysed chronic diseases results as follows. Upper right quadrant: sleep apnea, obesity, dyslipidaemia, ischaemic cardiomyopathy, hypertension/hypertensive cardiomyopathy and type-2 diabetes mellitus. Lower right quadrant: dementia and other mental diseases, anaemia, Parkinson disease, chronic obstructive lung disease, atrial fibrillation/flutter, cardiac failure, chronic kidney failure, heart valve disease, depressive syndrome, stroke, hypothyroidism, rheumatoid arthritis, chronic enterocolitis and prostate malignant neoplasm. Lower left quadrant: malnutrition, lymphoma, myeloma, non-alcoholic liver disease, alcoholic liver disease, alcoholic dependency syndrome, digestive tract malignant neoplasm, large intestine malignant neoplasm, rectum malignant neoplasm and breast malignant neoplasm. Upper left quadrant: lung malignant neoplasm.

Table 2 Studied pathologies and their corresponding numbers

Chronic obstructive lung disease—e487	Congestive heart failure—e428
Cerebrovascular stroke—e436	Alcoholic liver disease—e563
Ischaemic cardiomyopathy—e410	Heart valve disease—e394
Hypertension—e401	Chronic kidney failure—e403
Atrial fibrillation—e677	Depressive syndrome—e297
Type 2 diabetes mellitus—e250	Sleep apnoea—e327
Anaemia—e280	Dyslipidaemia—e272
Dementia—e290	Obesity—e278
Malnutrition—e262	Myeloma—e203
Parkinson disease—e332	Lymphoma—e202
Hypothyroidism—e243	Prostate malignant neoplasm—e183
Rheumatoid arthritis—e698	Breast malignant neoplasm—e174
Chronic enterocolitis—e556	Rectum and large intestine malignant neoplasms—e153
Non-alcoholic liver disease—e571	Lung malignant neoplasm—e160
Other mental diseases—e298	Digestive tract malignant neoplasm—e150
Alcoholic dependency—e291	Other malignant neoplasms—e195

a list of all the hospitalisations and their associated main and secondary medical diagnoses that were thought to be the cause of the hospitalisations. Taking into account the absence of a widely agreed list of chronic pathologies, we referred to a modified version of the German Multicare adapted to the inpatient context.¹⁹ Using this classification methodology, we included 32 common chronic pathologies. Moreover, it was possible to

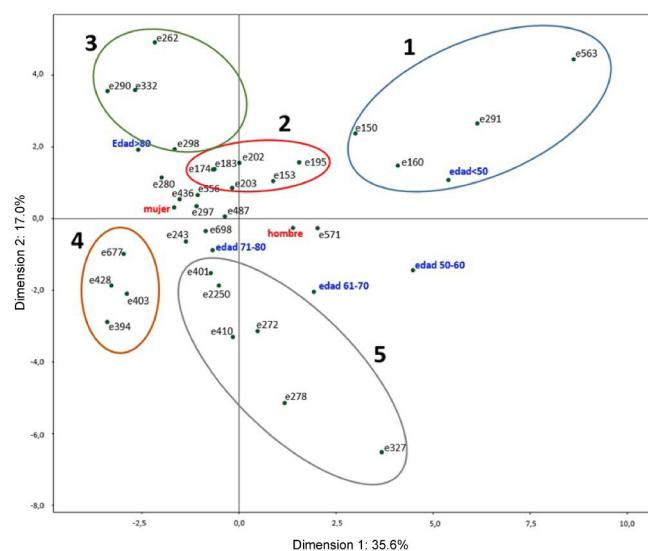


Figure 2 MCA of chronic diseases including age and gender. Cluster 1: alcoholic liver disease, alcoholic dependency syndrome and digestive tract and lung malignant neoplasms associated to a <50 age category. Cluster 2: large intestine malignant neoplasm, lymphoma, myeloma, prostate malignant neoplasm, breast malignant neoplasm and other malignant neoplasms. Cluster 3: malnutrition, Parkinson disease and other motility disorders, dementia and other mental disorders associated with a >80 age category. Cluster 4: atrial fibrillation/flutter, cardiac failure, chronic kidney failure, and heart valve disease, more related to female gender and 71–80 age category. Cluster 5: hypertension/hypertensive cardiomyopathy, type 2 diabetes mellitus, dyslipidaemia, ischaemic cardiomyopathy, obesity, and sleep apnoea, associated with a male gender and 61–70 to 71–80 age categories. MCA, multiple correspondence analysis.

Table 3 Cluster descriptors

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
Sample number	7.654	6.037	16.727	24.925	43.038
Gender (M)	80%	71.3%	44.9%	52%	53.5%
Age*	66.3±13.8	74.6±11.6	78.6±12.4	77.6±11.1	73.8±12.8
Number of hospitalisations	3.2±3.2	3.3±3.2	2.9±2.7	3.1±2.9	2.6±2.5
Exitus during hospitalisation	32.9%	38.8%	27.6%	26.2%	20.3%
Number of chronic pathologies	4.2±2.2	4.5±2.3	4.8±2.3	5.1±2.2	4.3±2.1

classify the disease burden using the CIRS scale.²⁰ Once this first database was completed, a second one was generated where patient data were analysed, allowing us to register main variables (presence/absence of the 32 aforementioned chronic diseases) as well as secondary variables such as gender, date of birth and hospitalisation dates.

Statistical data analysis

We carried out a descriptive analysis of the registered variables. The categorical variables were represented by their absolute and relative frequencies, and the continuous variables by their mean value and SD. We tested the clinical characteristics of the patients regarding the presence/absence of multimorbidity (presence of two or more chronic diseases) using the χ^2 test for categorical variables and the Student’s t-test for continuous variables.

With the aim to determine possible dependent relationships between registered diseases and also to visually identify clusters, we applied the multiple correspondence analysis (MCA). We use this analysis because this exploratory technique allows us to describe and resume a great amount of information within a reduced number of dimensions. The aim of MCA is to map the relative position of the studied diseases identifying combinations of variables and the degree of variation through the estimation of the co-occurrence frequency of diseases in distance terms. Besides the graphic representation we estimated the total inertia, which measures the dispersion of the generated point cloud, that is, the degree of dependence among variables. We calculated the ratio of inertia explained by each dimension and also the accumulated inertia. All tests were carried out taking into account a two-sided approach. All values of $p < 0.05$ were considered significant. We used the computer statistical software SPSS Statistics V.19 (IBM SPSS Statistics) and R 3.3.2 (packages: ca, ade4, ggplot2).^{21 22}

RESULTS

Patients

A total number of 170 978 hospitalisations corresponding to 74 220 patients were included within the time frame of the study. Of the studied individuals 10.8% (7990 patients) did not present

any of the registered 32 chronic diseases, 17.9% were diagnosed with a single disease and the remaining 71.3% (52939 patients) presented between 2 and 18 simultaneous chronic diseases.

The comparison between patients with and without multimorbidity on different clinic variables yielded the following results: the multipathology patients were significantly older than 72.2 years (SD 14.8), median of 76 (15–108) years, with a higher predominance of male individuals (54.6%). The average number of chronic pathologies was also very high in these patients (3.9; SD 1.89). Similar high rates were observed regarding the acute pathologies (1.7; SD 1.9) (table 1).

Statistical results

Significant differences were detected among the mean CIRS (10.9 vs 6.4; SD 4.6 and 3.5, respectively) and the average hospital length of stay calculated in days (11.5 vs 8.7; SD 19.4 and 23.2, respectively). A total of 6.7% of the patients with multimorbidity passed away compared with the 6.1% of deceased patients who did not present several diseases (table 1).

The MCA tried to identify relationships among the aforementioned 32 chronic pathologies. Considering the discriminant power of the obtained dimensions, two of them were extracted, which explains the 50.1% of the total inertia (31.4% and 18.8%, respectively). In the map of correlations (figure 1) each point corresponds to a chronic disease (table 2).

After introducing the secondary variables, gender and age category (<50, 50–60, 61–70, 71–80, >80 years), a scatter plot was obtained using the two first dimensions, which explained a total inertia of 52.7% (35.6% and 17.0%, respectively; figure 2). It is important to highlight that 699 multipathology patients (1.3%) suffer from diseases that are not included in the obtained clusters.

Descriptive analysis

The descriptive analysis of the characteristics of the patients in relation to the five obtained clusters yielded some interesting results. Patients who suffer from cluster 1 diseases are predominantly men (80%). They have an average age at the moment of the first hospitalisation of 66.3 years (SD 13.8) and a mortality

Table 4 Clinical characterisation of the clusters including only the patients with diseases belonging to each cluster

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5
Sample number	1.368	598	1971	1901	12 559
Gender (M)	81.9%	66.6%	46.7%	50.9%	55.9%
Age*	60.0±14.1	69.1±15.4	77.0±16.3	78±13.1	68.3±13.6
Number of hospitalisations	2.69±2.7	3.2±3.6	2.1±1.8	2.1±1.9	1.7±1.45
Exitus during hospitalisation	34.9%	41.8%	23.4%	28.8%	7.4%
Stay time in days (x)	27.7±28.1	29.9±30.4	26.2±31.3	24.8±29.1	15.1±26.9
Time between hospitalisations in days	959.5±1145.4	763.3±981.5	1164.1±1206.5	1117.6±1192.1	1541.2±1402.7
Monitoring time in days	583.2±1002.1	498.4±862.9	592.6±1032.0	546.3±998.6	600.5±1149.1

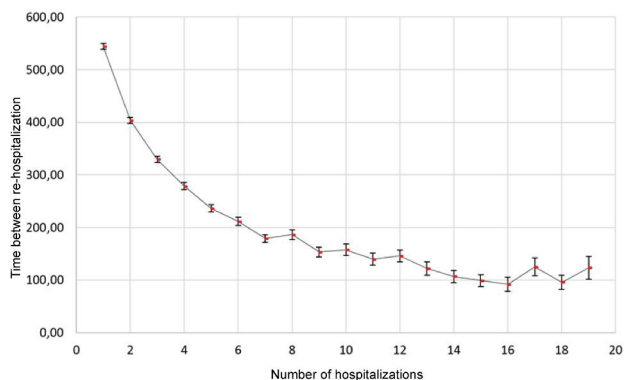


Figure 3 Time between re-hospitalisation relative to the number of hospitalizations, general series. The time elapsed between different hospitalizations of all patients with two or more chronic diseases included in any of the clusters is shown as an average time calculated in days.

of 32.9%. Patients in cluster 2 have an average age of 74.6 years (SD 11.6), mainly men (71.3%) from which 38.8% died cluster 3 shows a higher proportion of women (55.1%) and advanced age individuals (average 78.6; SD 12.4). Clusters 4 and 5 contain a higher proportion of male individuals (52.0% and 53.5%, respectively) with an advanced first hospitalisation age group (77.6 and 73.8; SD 11.1 and 12.8, respectively). Cluster 5 shows the lowest mortality during the hospitalisation (20.3%; table 3). In a subsequent analysis, we selected patients belonging exclusively to the described groups, with diseases that are specific of each cluster. Here, more than 80% of the patients belonging to cluster 1 are men, being comparatively younger at the moment of the first hospitalisation (60.0 years, SD 14.1) and with a mortality rate during the hospitalisation of 34.9%. Cluster 2 has a predominance of male individuals (66.6%) with an average age at the moment of the first hospitalisation of 69.1 years (SD 15.4), showing the highest death ratio (41.8%). Females are preponderant in cluster 3 (53.5%), with an average age of 77.0 years (SD 16.3) and death ratio of 23.4%. Clusters 4–5 have similarly higher ratio of male patients (50.9% and 55.9%, respectively). However, patients with cluster 4 are older at the moment of hospitalisation and cluster 5 shows a lower mortality (see table 4).

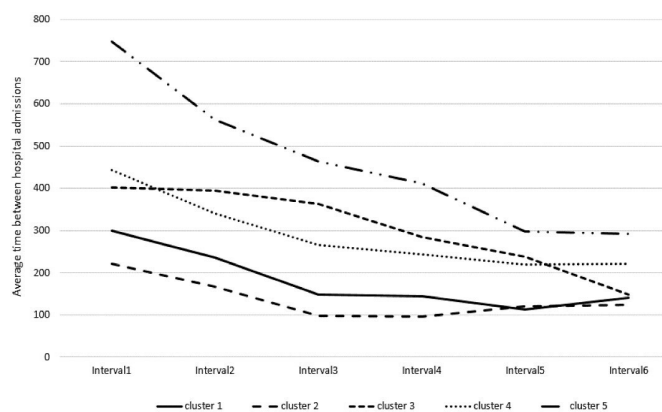


Figure 4 Graphic comparison of the elapsed time between hospitalisations including the five clusters. Only the six first hospitalizations, which contain the highest number of patients, are included.

The elapsed time between successive hospitalisations in all patients included in any of the clusters with two or more chronic diseases becomes progressively shorter (figure 3). This time shortening is more pronounced during the first six rehospitalisations and then becomes more stable (although it is still present). The CIs of successive rehospitalisations do not overlap, at least until the seventh rehospitalisation (figure 3). Also, the average time between hospitalisations is higher in cluster 5 (figure 4).

DISCUSSION

Our results confirm the hypothesis of the presence of disease combinations in hospitalised patients, highlighting the existence of clusters of pathologies associated with age and gender and enable a straightforward interpretation (distance between pathologies) of the possibility that a given set of diseases has to affect the same patient. The results of our work are consistent with other recently published studies conducted in the domain of the primary healthcare or in the general population,^{23–33} some of which used statistical methods different from the MCA to check disease clusters.^{34–45} Despite having many common points regarding the hospital care, these studies differ in the chronic pathologies analysed. Although almost any disease can be relevant in a general population context depending on its impact on the life quality of the patients, it is more logic for the inpatient population to include only the pathologies related to the diagnostic/therapeutic actions that must be applied during the hospitalisation or during a short-term/medium-term follow-up. Thus, our work by combining medical facts together with statistical analysis allows for a very intuitive and simple interpretation of data suitable to perform an exploratory study. The distance among pathologies accounts for the probability of those pathologies appearing together in the same patient. However, there are very common diseases (eg, anaemia and depressive syndrome) that do not appear included in any of the five clusters, since they are equidistant from the different groups. There are several reasons to explain this phenomenon. A similar inertia among several pathologies that belong to different clusters (thus prohibiting their inclusion in any of them) is the most obvious. Since each cluster has its distinctive and own clinical profile, our analysis contributes significantly to the understanding of not only how the different chronic diseases are aggregated into a group but also how they behave as a group. Thus, the identification and characterisation of these clusters become fundamental for the treatment of multimorbid patients.

The multiborbidity analysis among hospitalised patients remains poorly explored, and as such, our work makes further advances in this field. However, the present analysis is still an initial and exploratory approach that can be practical enough to adapt and optimise hospital resources focusing on the detected clusters. Thus, it can be used to design new diagnostic, treatment and monitoring strategies that are well differentiated and adapted to each group. Moreover, the characterisation of the multimorbidity clusters can lead to the creation of clinical practice guidelines for the management of chronic diseases that usually manifest themselves together. Finally, this analysis could be the first step to a better characterisation of the multimorbidity problem, including, for example, the variable ‘time’, which is invaluable for the definition of multimorbidity timing, and for assessing how the different pathologies emerge and progress in a patient. On the other hand, it would be interesting to test in the future whether a patient who develops pathologies pertaining to a particular cluster can evolve to a different one given enough time. There are however a couple of limitations that must be

considered. First, only the characteristics of adult patients with medical pathologies are described, making impossible to extend the results to patients hospitalised due to surgical pathologies. Second, our data come from a single hospital centre, meaning that the results may not always be extrapolated to hospitals from different geographic areas or with different size.

CONCLUSIONS

We detect for the first time in a hospital environment up to five clusters of diseases among inpatients receiving the general services of a hospital. These clusters are constituted of a number of high-incidence diseases related to both age and gender that show their own clinical features and evolution over time. We can assess how the different pathologies in a cluster behave as a group. This becomes fundamental for the treatment of multimorbid patients and also for the optimisation of hospital resources. Also, we show that the distance between pathologies is a straightforward interpretation of the chance that a given set of pathologies has to appear together in a patient. (1; 2)

Main messages

- ▶ We identified five high-incidence diseases clusters in hospitalised patients.
- ▶ Hospitalised patients have their own characteristics different than general population so diseases association clusters are also specific in this environment.
- ▶ Cluster categorisation is essential in treatment and prognosis of multimorbid patients.

Current research questions

- ▶ How do chronic diseases add to each cluster over time?
- ▶ Can one patient change between different clusters during his lifetime?
- ▶ Can we measure economic impact of designing specific care routes and guidelines based on each diseases clusters?

What is already known about this subject

- ▶ Most hospitalized patients are multimorbid
- ▶ Chronic diseases are not randomly associated
- ▶ Clinical practice guidelines should be focused on multimorbid patients

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Competing interests Declaration of competing interest: The authors declare that there are no conflicts of interest regarding this research and publication.

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Data availability statement Data are available upon reasonable request. The main data source was the registry of hospitalisation entries, which includes all diagnoses carried out by the healthcare professional in charge, codified (by codifying medicals) using the CIE.9MC. As additional data sources we used the nursing registries and since 2007 the computerised database IANUS, which gathers all data derived from medical assistance. The study protocols were approved by the Comité Ético de Investigación Clínica de Galicia (Ethics Committee of Clinic Research of Galicia; registry code CEIC of Galicia 2014/409). A computerised database of each

hospitalization event using all the aforementioned registries was created. It includes a list of all the hospitalisations and their associated main and secondary medical diagnoses that were thought to be the cause of the hospitalisations.

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