Understanding the development and accumulation of chronic diseases over time in older adults

Introduction

Multimorbidity, the coexistence of multiple chronic conditions, is emerging as a new challenge facing the global ageing population. The advancements in healthcare and medicine have significantly extended life expectancies, allowing individuals to live long enough to develop multiple chronic ailments. Multi-morbidity has been shown to be associated with mortality and poor quality of life, and also with increased health service utilisation (Makovski et al., 2019; Marengoni et al., 2011). Understanding the trajectories that lead to multi-morbidity and subsequent mortality is crucial for prevention, and for understanding how different diseases interact and accumulate. Specifically, identifying which conditions are the first to emerge and whether or not they lead to multi-morbidity may provide insights for targeted preventive measures.

Sequence analysis presents itself as a well suited method to addressing the development and accumulation of diseases in the population. The method is gaining popularity with the advent of high quality longitudinal data sets which allow for sequence analysis. Cluster analysis is also a useful method that has been applied on its own or in combination with sequence analysis. It's main advantage lies in its ability to identify groups that experience similar trajectories, or diseases that commonly cluster together. Both sequence and clustering methods have been used to study multi-morbidity – broadly defined – in different contexts, including in Scotland, Spain and Taiwan (Guisado-Clavero et al., 2018) (Cezard et al., 2022; Hsu, 2015) In this current study we aim to contribute to the literature, by leveraging a longitudinal register data, the Public Data Analysis for Health Research and Innovation Program (PADRIS) database from Catalunya, in Spain . We apply a combination of sequence analysis and clustering to understand disease emergence and trajectories in the studied population, an approach similar to that employed by (Cezard et al., 2022) in Scotland.

This analysis is preliminary, and substantial modifications maybe done to further develop the paper.

Objectives:

- To identify describe the trajectories leading to multi-morbidity and mortality
- To identify common patterns of morbidity and multi-morbidity
- To identify any demographic characteristics that are associated with specific morbidity and multi-morbidity patterns or trajectories

Methods

Data source

This study uses data from Public Data Analysis for Health Research and Innovation Program (PADRIS) database. This database comprehensively collects the diagnosis history of a large number of diseases as well as mortality for a representative sample of the entire population of Catalonia from 2005 onwards. In the current study, individuals are followed over a 15 years period, from Jan 2005 to December 2020. We select participants aged 45–74 years old at the start of the follow-up period (2005), to focus on understanding the emergence of multimorbidity from a healthy state. We expect this to be of higher utility to prevention efforts

Outcome identification

In this analysis we study the emergence of three chronic disease categories that commonly occur in the population, and which are unlikely to subside after diagnosis. These include cardiovascular diseases (including hypertension), cancer, and metabolic disorders (diabetes and lipid metabolism disorders). These conditions were identified using their ICD-10 codes obtained from hospital registers, which also provide a date of diagnosis. In the final paper, we aim to expand the list of conditions so as to make better use of the available data.

Sequence creation

The current analysis takes into account the accumulation of diseases overtime. All individuals start as 'Healthy', or with no disease. After one unit of time passes, this individual can transition to any of the 9 possible states: "no disease", "metabolic conditions", "CVD", "cancer", "metabolic+ CVD", "metabolic+ cancer", "CVD + cancer", "metabolic, CVD, cancer", and "death".

For the current analysis, the unit of transition was one year, however this will be modified to one month in the final paper.

Statistical analysis

We use single channel sequence analysis with one sequence per person. Sequences show the accumulation and combination the three diseases of interest based on their diagnosis for each individual. First, we describe the sequences using descriptive statistics of the most common reduced sequences. To identify distinct groups of sequences, we use Optimal matching (OM) to assess the dissimilarity between all pairs of sequence. For the current analysis we use and Indel cost of xx, as the we believe both the sequence and timing of transition is important for this study. In the final paper, we aim to conduct sensitivity analysis using multiple indel costs.

For cluster analysis, we used hierarchical cluster analysis applied to the dissimilarity matrix. We used a range of measures that are available in R for choosing the optimal number of clusters, PBC - Point Biserial Correlation, HG - Hubert's Gamma, HGSD - Hubert's Somers D, ASW - the average value of the silhouette, ASWw - the average value of the silhouette weighted. These measures seemed to converge on a range of 6 to 8 cluster, thus we chose 7 clusters.

In the final paper, we will extend this analysis to investigate whether certain trajectories are associated with earlier or later mortality, and with more sever forms of multimorbidity.

Results[1]

Characteristics of the sample

From the 13024 individuals aged 45 – 75, we selected 12065 participants who were healthy (no disease diagnosed) at the beginning of the follow up period. This sub sample consisted of 49.6% male. Most (52%) were in the age range from 45 to 55, and majority were Spanish nationals (Table 1).

Table 1: Characteristics of the sample:

Category	Male	Female
Age group		
45-54	4459 (41.4%)	4476 (39.3%)
55-64	3513 (32.7%)	3695 (32.4%)
65-74	2786 (25.9%)	3219 (28.3%)
Nationality		
Spanish	10028 (93.2%)	10660 (93.6%)
Other	730 (6.8%)	730 (6.4%)
Health status at the end of 2005		
Healthy	5990 (55.7%)	6075 (53.3%)
One disease	2634 (24.5%)	2960 (26.0%)
Two diseases	1811 (16.8%)	2127 (18.7%)
Three or more	115 (1.1%)	142 (1.2%)
Dead	208 (1.9%)	86 (0.8)
Total	10758 (48.6%)	11390 (51.4%)

The findings in the following graphs are based on the sample of indivuduals aged 45-64 and with no disease in 2005.

[1] Due to technical issues and time constraints, we are only able to present low quality images of the figures in this abstract. The final study will include better quality images.

Figure 1 in the final paper will show a bar graph of the average period spent in each state. On average, Catalonians spent 8 years (out of 15) without any of the three diseases considered here. The combination of cardiovascular and metabolic conditions were the occupied the second longest time, of almost two years, followed by cardiovascular conditions alone.

Figure 1: mean time spent in each state

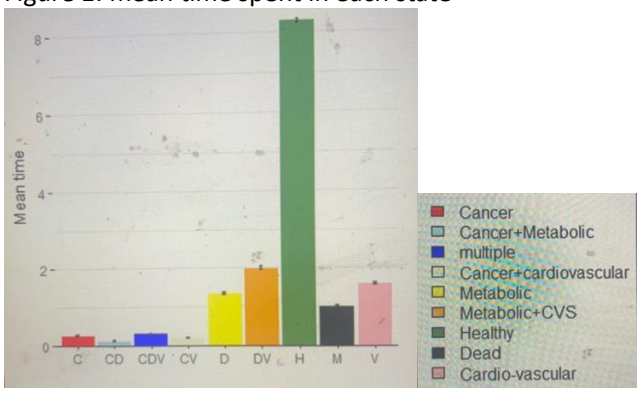
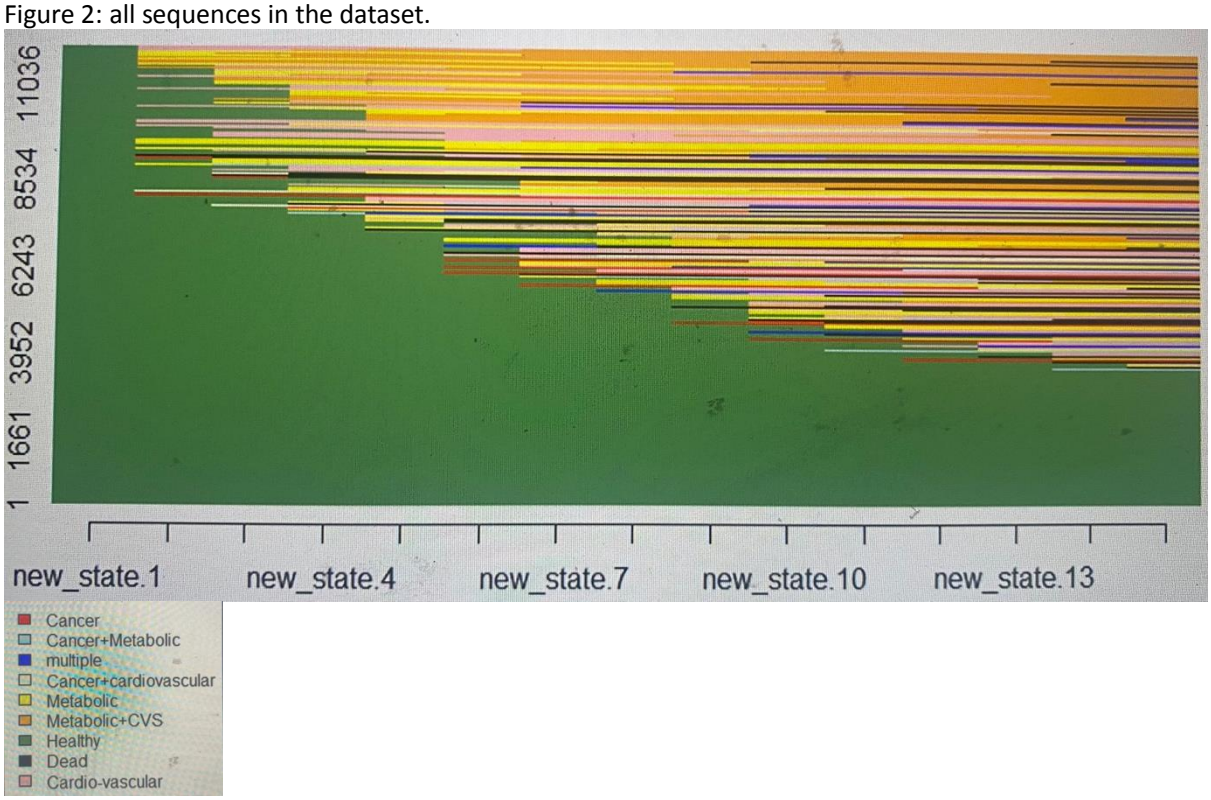


Figure 2 below shows all the sequences in the dataset. It confirms what we see in figure 1, namely long periods spent in health, but also long periods spent with a single metabolic or cardiovascular condition or in a state of multimorbidity from a combination of cardiovascular and metabolic conditions.
When summarising the most common sequences in the dataset, we found that that 38.9% of all sequences involve a transition from health to either a metabolic or a cardiovascular condition, with long periods before transitioning to multimorbidity.

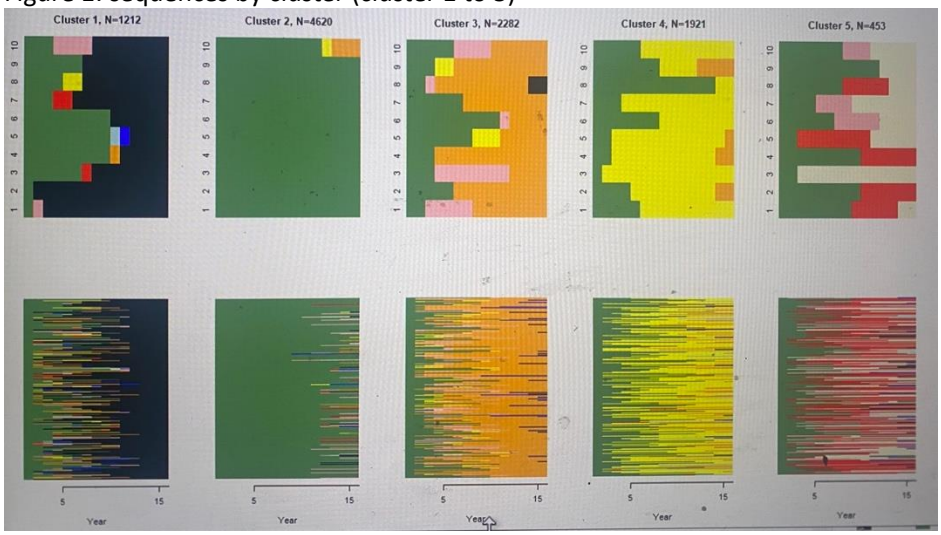
Figure 2: all sequences in the dataset.



The highest transition rate is observed for the transition from having all three conditions to death (1.0), followed by the transition from only a metabolic condition to a combination of cardiovascular and metabolic (0.81), and the transition from only a cardiovascular condition to a combination of metabolic and cardiovascular (0.71)

The cluster analysis uncovered 7 distinct clusters in the dataset (graph 4). Cluster 1 comprises 10% of the sample and is characterised by a relatively short period of health that is followed by a transition to one condition (often cancer) and a quick transition to mortality. 67% of sequences in this cluster were for men, 45% of them were in the age range of 65-75

Figure 1: sequences by cluster (cluster 1 to 5)



Cluster 2 is the largest cluster, comprising 30% of the sequences, and it involves a long period with no disease for most members, with a few transitioning to a metabolic condition followed by a quick transition to multimorbidity with the development of a cardiovascular condition. Cluster 2 was roughly equally distributed between men women, however 60% were in the youngest age group (45-55).
Cluster 3 involves a quick transition from health to multimorbidity, specifically the combination of cardiovascular and metabolic diseases, though sometimes the cardiovascular conditions precede it. Individuals in this cluster spend a long period with multiple conditions. They are mostly of the younger age group, and equally distributed across sex.
Cluster 4 is characterised by a quick transition to a metabolic condition and a very late transition to multimorbidity. Individuals in this cluster spend most of the period with one disease. This cluster is mostly made of younger age groups (60% in the 45-55 age group), and a slightly higher percentage of women (57%). In Cluster 5, like cluster 3, though the multimorbidity starts with either cancer or a cardiovascular disease. Cluster 6, a transition from one, to two, and to three conditions. This cluster has a higher percentage of men (58%). Cluster 7 is similar to cluster 4, but with a cardiovascular condition.

Interpretation:

The study highlighted trajectories leading to multi-morbidity and mortality among individuals aged 45-75 in Catalunya. A notable proportion of individuals maintained a healthy state, averting the onset of the considered diseases for substantial periods. However, cardiovascular and metabolic conditions emerged as prevalent adversaries, frequently characterizing the initial steps away from a healthy state.
Clustering of the disease sequences unveiled several distinct narratives. For instance, one cluster manifested a short journey from health to mortality, characterized predominantly by male participants and an initial onset of cancer. In contrast, another cluster exhibited a prolonged period of multi-morbidity, primarily among female participants, with gradual transitions through metabolic and cardiovascular conditions. Each cluster tells a story, echoing the differential impacts of age and gender in the odyssey through health, disease, and mortality.

References

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