Understanding multimorbidity trajectories in Scotland

An application of sequence analysis

Dr Genevieve Cezard

University of St Andrews, gc79@st-andrews.ac.uk
University of Cambridge, gic30@medschl.cam.ac.uk

Co-authors: Frank Sullivan, Katy Keenan

BSPS conference – September 15th 2021

Introduction

- Multimorbidity (MM)– an introduction
  - MM: co-occurrence of two or more chronic conditions in a single individual.
  - MM is linked to higher health care use/cost and worse outcomes for individuals (e.g. higher risk of mortality and worse quality of life)

- Gaps
  - Research on multimorbidity primarily cross-sectional
  - Need to better understand multimorbidity development and progression.

- Systematic scoping review
  - Type of longitudinal methods used to analyse multimorbidity over time within individuals
  - **Studying trajectories of multimorbidity: a systematic scoping review of longitudinal approaches and evidence**
  - Preprint: https://www.medrxiv.org/content/10.1101/2020.11.16.20232363v2

  - Lack of studies based on ordering and sequencing of diseases
  - Little development in the field of longitudinal associative multimorbidity (how diseases cluster over time)

Aim and research questions

- General aims
  - To explore how sequence analysis can be used to understand the sequencing of common chronic diseases that lead to multimorbidity
  - To assess what are the factors associated with typical multimorbidity trajectories

- Selected chronic diseases
  - Example of the value of sequence analysis in MM research based on 3 chronic diseases: Diabetes (DM), cardiovascular disease (CVD) and Cancer

- Research questions
  1. What are the typical trajectories to MM (using DM/CVD/Cancer as an example)?
  2. Are there sociodemographic differences in distinct trajectories to MM?
  3. Are specific trajectories to MM associated with higher health care utilisation and worse mortality outcome?
  4. What is the value of sequence analysis in researching multiple chronic disease trajectories?

Data source: Scottish Longitudinal Study (SLS)

- SLS: Linkage of Scottish Censuses (1991, 2001, 2011) to other data sources for about 5.3% of Scotland population

- Cohort
  - Linkage of the Scottish Census 2001 to health data (hospitalisation, disease registry and death records)
  - Aged 40-74 years old on the day of the Scottish Census 2001 (N=109,510)
  - Follow-up period: 10 years (2001-2011)
  - Selected participants who transitioned to MM (from 0-1 disease to at least 2 of DM/CVD/Cancer at some point during the follow-up period) (N = 6,300; 6%)

- Sociodemographic determinants in 2001
  - sex, age, marital status, household size, education, household tenure, Scottish Index of Multiple Deprivation (SIMD)

- Outcomes
  - Health care utilisation: Number of hospitalisation and number of overnight stay
  - Mortality

Methods: sequence analysis

- Sequence creation
  - ➢ Single channel sequence analysis -> one sequence per individual
  - ➢ It relies on the accurate identification of onset of disease
  - 8 states based on the combination of 3 diseases : “no disease”, “DM”, “CVD”, “Cancer”, “DM-CVD”, “DM-Cancer”, “CVD-Cancer”, “DM-CVD-Cancer”
  - Added 2 states “Death”, “Exit”
  - Time unit: month; Sequences are made of 120 consecutive states

- Description of the sequences (order in which diseases occur)
- Assess how similar sequences are
  - Dissimilarity matrix based on optimal matching with a constant substitution matrix (assumption that “all states are equally different”) and an single indel cost of 1.5 (considering sequencing as well as the speed of transition as relevant when assessing similarities)
- Hierarchical cluster analysis
  - Best number of clusters based on cluster quality measures available in R

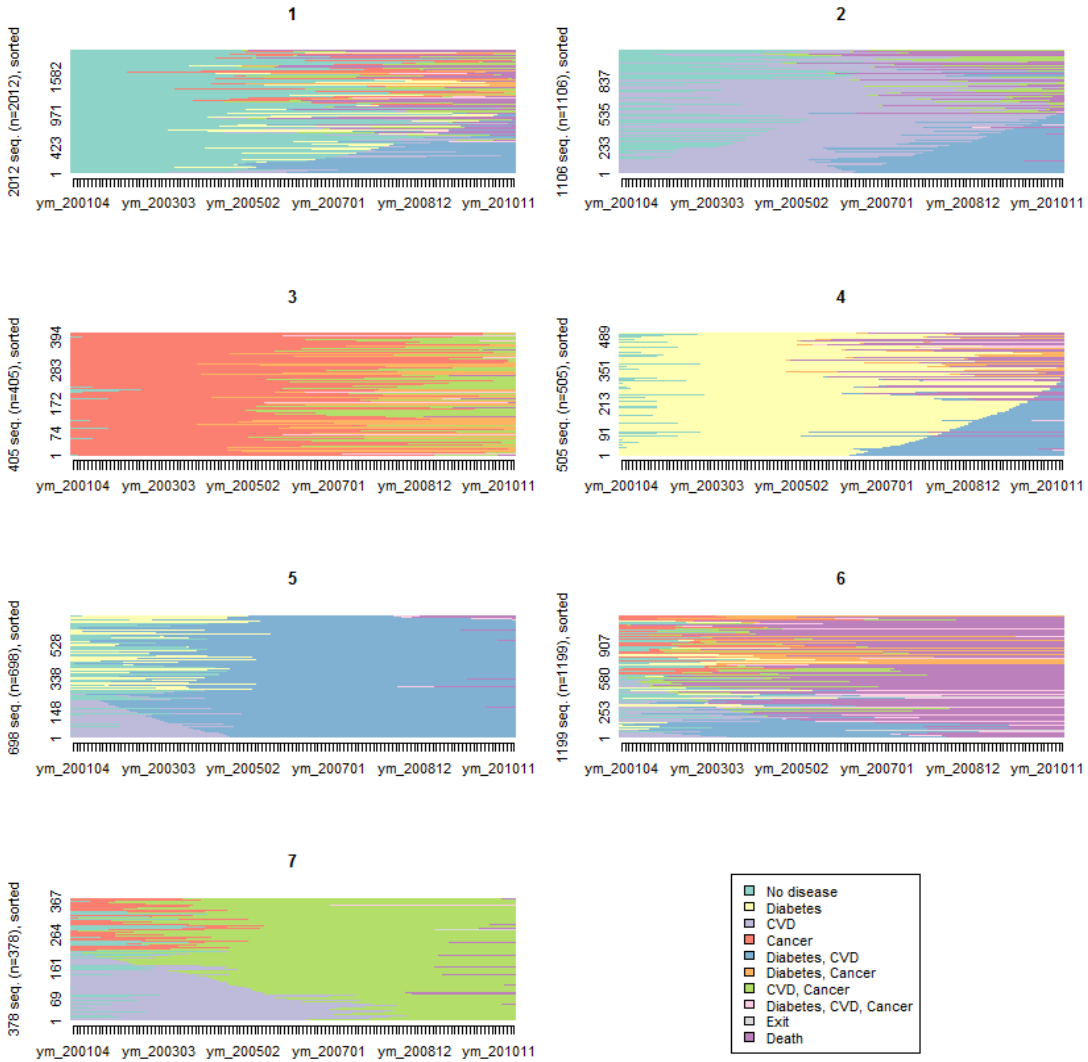
  - ➢ It distinguishes typical groups of multimorbidity trajectories

Results RQ1: MM trajectories clusters

7 clusters

1. later fast transition to MM
2. CVD start with slow transition to MM
3. cancer start with slow transition to MM
4. diabetes start with slow transition to MM
5. fast transition to both diabetes and CVD
6. fast transition to MM and death
7. fast transition to both cancer and CVD

sequence index plots



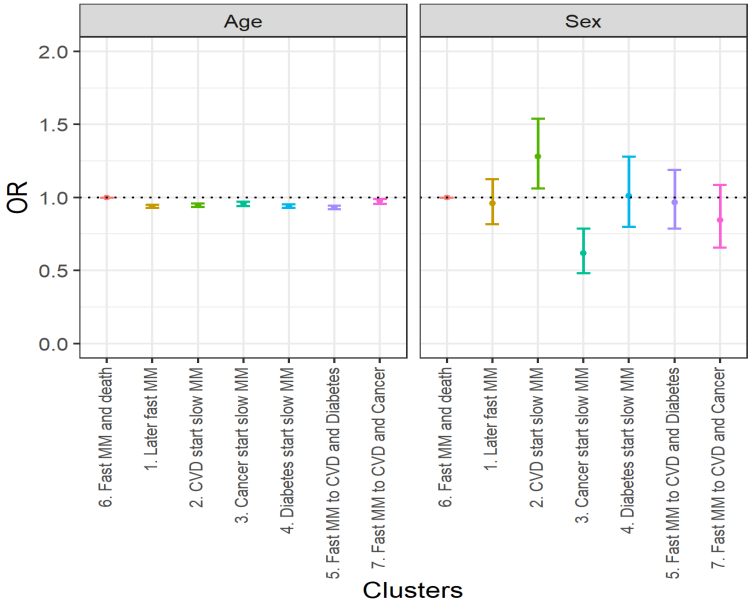
Source: Scottish Longitudinal Study

Results RQ2: Association between sociodemographic factors and typical MM trajectories

- Sociodemographic profile of typical trajectories
- Identification of sociodemographic differences in multimorbidity trajectories
- Method: Multinomial logistic regression
- Findings:

Reference cluster : cluster 6 (fast transition to MM and death)

- Individuals of cluster 6 significantly older, more likely to be single.
- Individuals of cluster 3 (cancer start) more likely to be women while those of cluster 2 (CVD start) more likely to be men.
- Individuals of clusters 1 (late MM), 3 (cancer start) and 7 (transition to both CVD/Cancer) showed a better SES profile with higher level of education, more likely to own than rent and less likely to live in more deprived areas.



Source: Scottish Longitudinal Study

Results RQ3: Association between typical MM trajectories and outcomes

- Methods
  - Within 5 years post MM onset, adjusted for death/exit -> comparable exposure time
  - Hospitalisation (Number of hospitalisations and overnight stay): Poisson regression
  - Mortality: Survival analysis (Cox regression)
  - Adjusted for sociodemographic factors and other comorbidities

- Findings
  - Individuals of cluster 6 (fast transition to MM and death) had the worst hospitalisation outcome with significantly higher number of hospitalisation and overnight stay relative to their exposure time. They had the higher mortality risk too.

  Within the other clusters, there are differences
  - Individuals of cluster 4 (diabetes start) had significantly more hospitalisation/over night stay compared to individuals of other clusters.
  - Individuals of cluster 5 (transition to both diabetes/CVD) had the lowest risk of hospitalisation within 5 years both MM onset.
  - Individuals of cluster 5 (transition to both diabetes/CVD) and those with typical trajectories including cancer (clusters 3 and 7) had better mortality outcome than the other clusters (1, 2, 4).

Conclusion

- Sequence analysis with cluster analysis is useful to research multimorbidity trajectories
  - To understand the sequencing of disease that lead to MM
  - To distinguish typical trajectories to MM

- Association analyses of typical trajectories to MM
  - These typical trajectories have different sociodemographic profiles

e.g. trajectories to MM starting with CVD are more likely to be in men and those starting with cancer in women.

  - Specific trajectories are associated with more frequent hospitalisations and overnight stays (post MM onset).
  - Mortality risk (post MM onset) differs across the different typical MM trajectories

- <u>Limitation:</u> Based on a small number of diseases
  - Sequence analysis on 4-5 diseases will generate 16-32 states which can not be interpreted and visualised meaningfully with this method.
- <u>Future avenues:</u>
  - Multiple channel sequence analysis: parallel disease trajectories.
  - Machine learning methods to assess trajectories using a greater number of diseases

Thank you!