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Understanding patterns of multimorbidity: perspectives from interdisciplinary research

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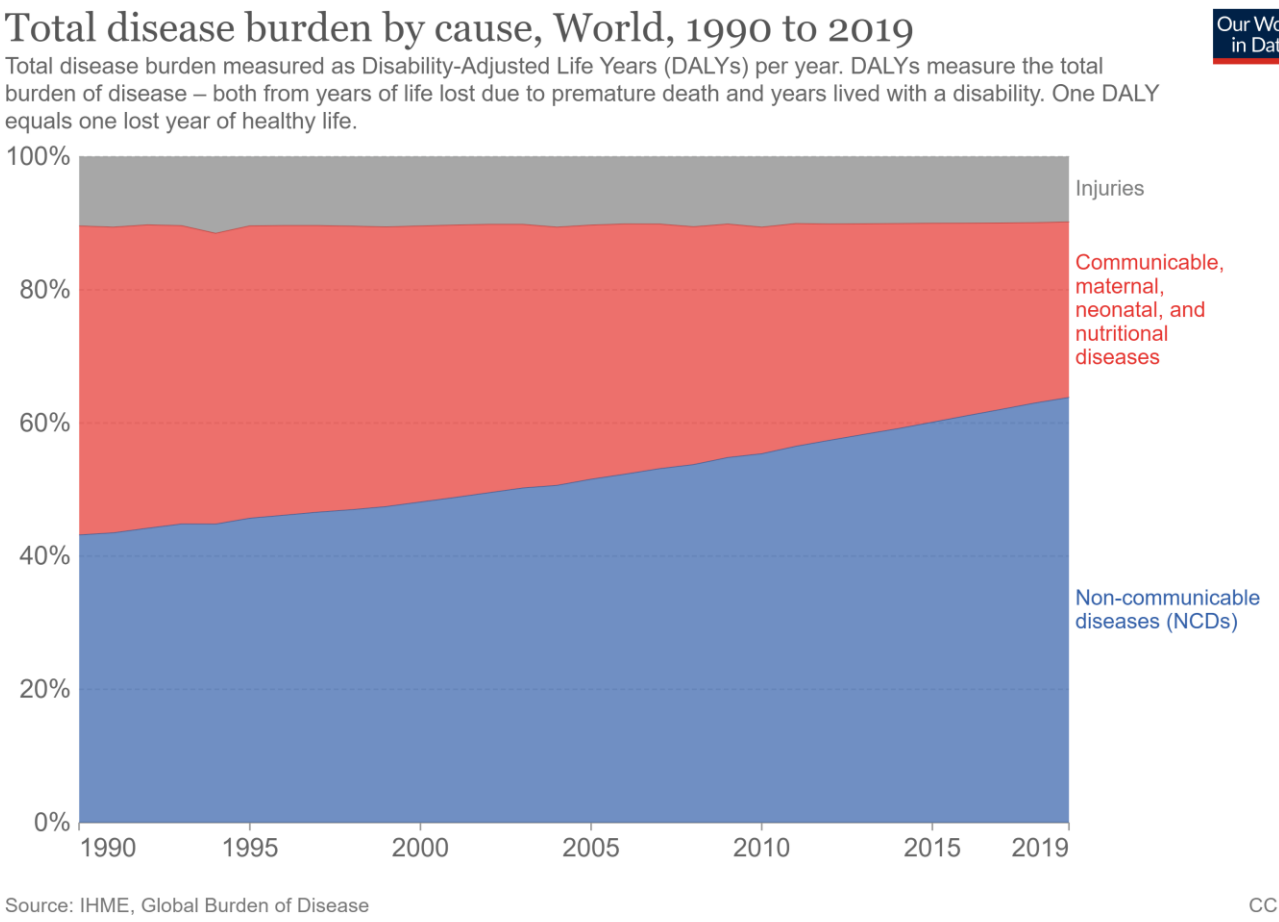
Perspectives from interdisciplinary research

- Challenges in multimorbidity measurement
- Conceptualising multimorbidity: processes, networks, states
- Modelling longitudinal relations
- Examples:
  - Disease sequencing
  - Life course accumulation
  - Multimorbid life expectancy and projection

The epidemiological and demographic context of the multimorbidity 'epidemic'

- Increased longevity
- Shift in disease burden from infectious to non-communicable or dual burdens
- Better diagnosis and treatment management for NCDs
- Increased health inequality



How do we measure multimorbidity?

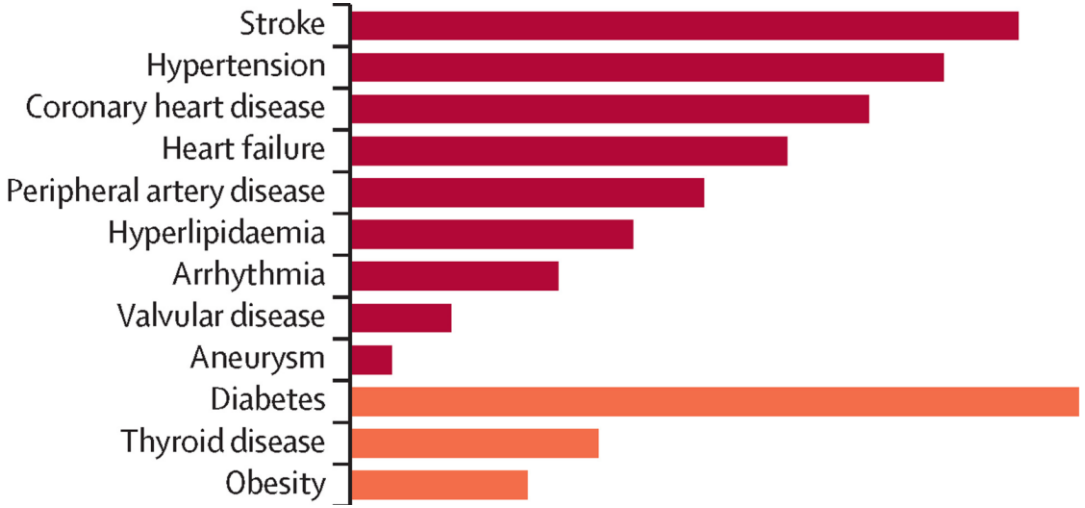
2 or more concurrent chronic diseases in the same individual

- What is chronic?
- What diseases count?
- Who and what reports /diagnoses these diseases and their onset
- how accurate and complete is this?

Measurement inconsistencies are ubiquitous

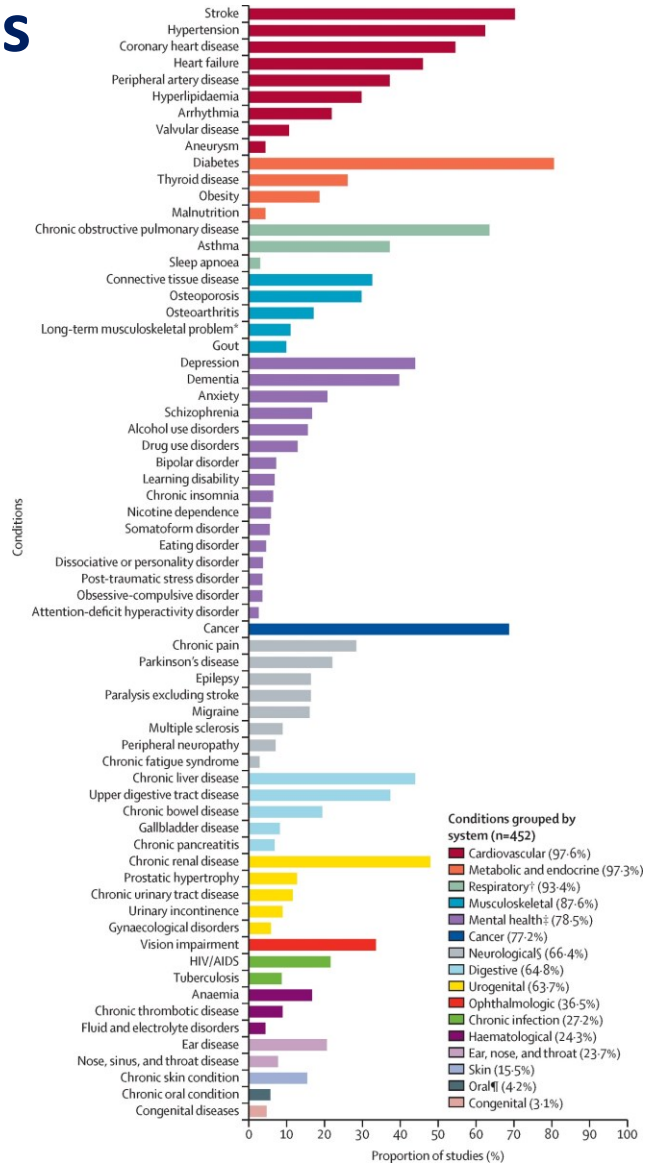
- **Which diseases count as a morbidity?**
  - Classic definitions / lists e.g. **Charlson comorbidity index (CCI), Elixhauser** were designed to capture hospitalisation co-morbidities; in using admin data from other sources or surveys these lists have been expanded
  - Depends on what's available in the data
  - Depends on what the authors consider a chronic disease worth counting

Review of common conditions considered in multimorbidity studies



- Only 8 conditions are included in more than half of studies (diabetes, stroke, cancer, COPD, hypertension, coronary heart disease, chronic kidney disease, heart failure)

- Are hypertension and obesity diseases or risk factors?



Ho et al, 2021

Suggested core set of conditions based on DALYs

Potential core conditions with high disability-adjusted life-years or high years of life lost

(1) Cancer
(2) Coronary heart disease
(3) Stroke
(4) Heart failure
(5) Diabetes
(6) Dementia
(7) Depression
(8) Schizophrenia
(9) Anxiety
(10) Alcohol use disorders
(11) Drug use disorders
(12) Chronic liver disease
(13) Chronic renal disease
(14) Chronic obstructive pulmonary disease
(15) Asthma
(16) Vision impairment
(17) Musculoskeletal impairment due to injury
(18) Osteoarthritis
(19) Chronic pain
(20) Gynaecological disorders

Potential considerations for including other conditions

Particularly relevant in some countries
- Tuberculosis
- Malnutrition
- HIV/AIDS

Particularly relevant in children
- Congenital disease
- Learning disability

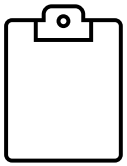
Particularly relevant if the focus is quality of life
- Eczema
- Psoriasis
- Migraine
- Oral disorders
- For some

For some purposes
- More detailed condition definition might be relevant (eg, myocardial infarction or stable angina)
- Inclusion of rare conditions might be appropriate

- Are depression and anxiety chronic?
- What if people recover from cancer?

Ho et al, 2021

Data source influences measurement



Surveys

+ Population data
+ Repeat measures
+ Rich social, environmental and sociodemographic data

- Population ? Bias
- Lack of clinical precision
- 'Self-reported doctor diagnoses'
-Limited number of conditions

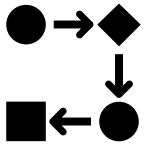
Medical records (primary/secondary care)

+ Population data
+ Clinical precision (full ICD10 codes)
+ *may* record date of onset

- Some diseases /conditions are never recorded in secondary care
- Identifying *chronic* diseases (disease recovery?)
- Recording depends on care seeking behaviour, medical referrals and recording accuracy
- Date of onset tricky (e.g 'simultaneous' diagnoses)
- Limited information beyond age and sex

Multimorbidity as a life course process

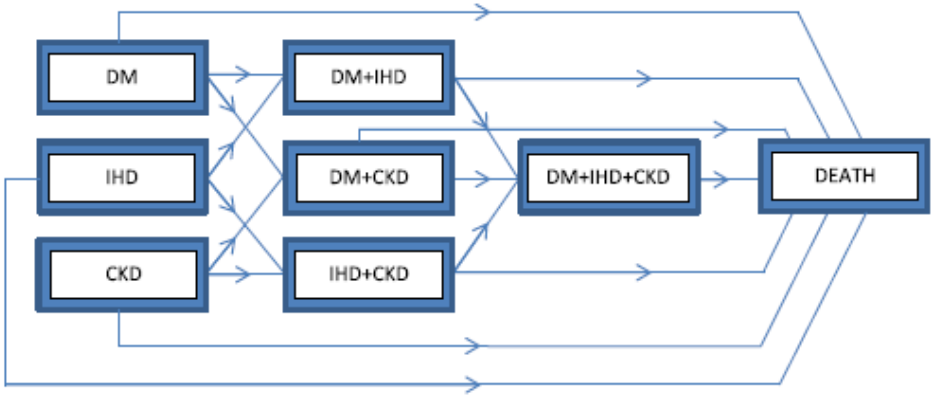
- Concern with definitions (epidemiological concern with prevalence) skates over the *processual nature* of multimorbidity
- This is about the development of illness over the life course; to some extent the process of biological ageing
- From a measurement perspective, we need to consider how to model MM longitudinally


Conceptualisation: multimorbidity as a set of states

Progressive chronic disease network (8 states)

by Siriwardana et al. (2018)

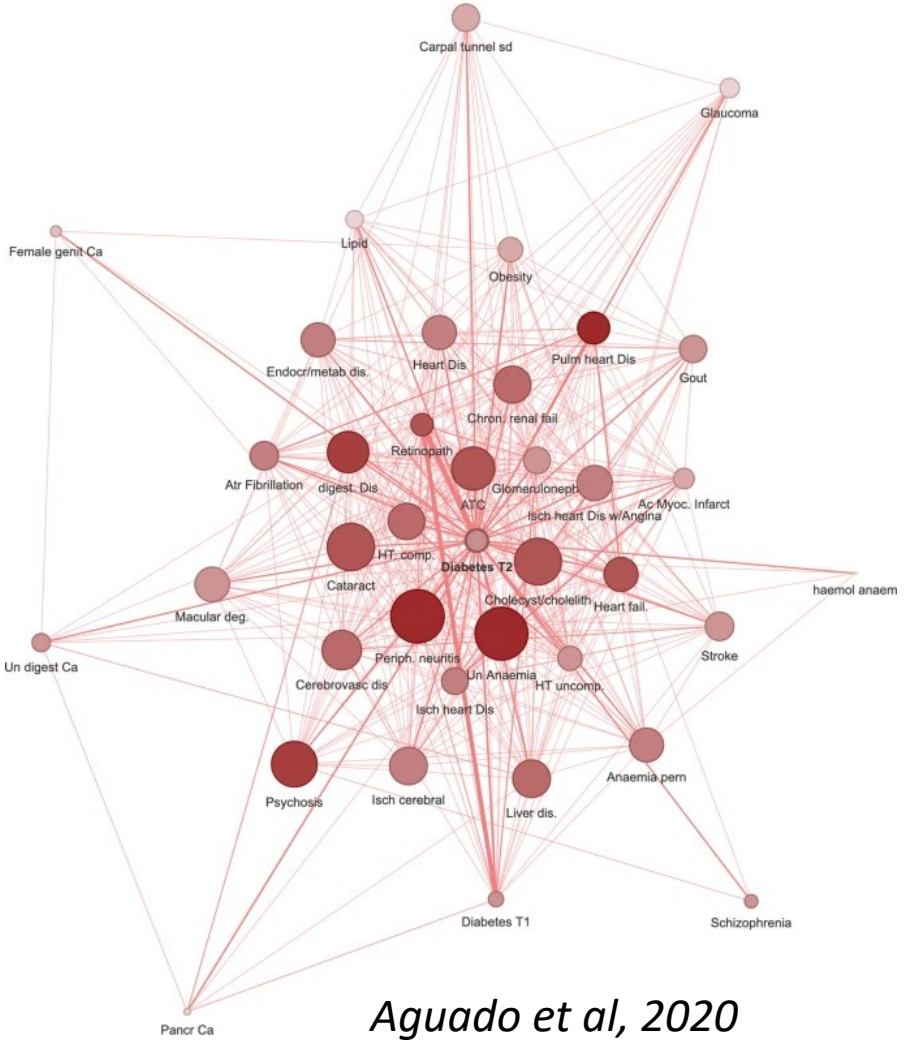


- Relies on accurate measurement of onset /diagnosis and possible recovery
- Simply disease occurrence- severity, medication, management etc not accounted for
- Allows modelling of 'transition probabilities' conditional on other factors i.e. the things that make transitioning more or less likely
- Can be expanded to take into account individual diseases but number is limited
- Therefore, useful for understanding

Multimorbidity as a network or system

- Takes account of the likelihood of diseases being more likely to co-occur
- Can uncover possible etiological links

- Clustering algorithms/ network-based approaches
- Largely cross-sectional



Aguado et al, 2020

Systematic scoping review - Longitudinal approaches to analysing multimorbidity and disease trajectories

Cezard et al, 2021

Included articles: 34 papers published

- All published in the last decade (since 2011), mostly based on data from high-income countries

Measurement of Multimorbidity

- List of diseases range from 3 to over 900 conditions
- Various disease ascertainment: self-reported, clinical diagnosis, cognitive test, laboratory test, medication use.

Multimorbidity approaches

- Disease accumulation
- Disease combination
- Disease transition

Methodological groups

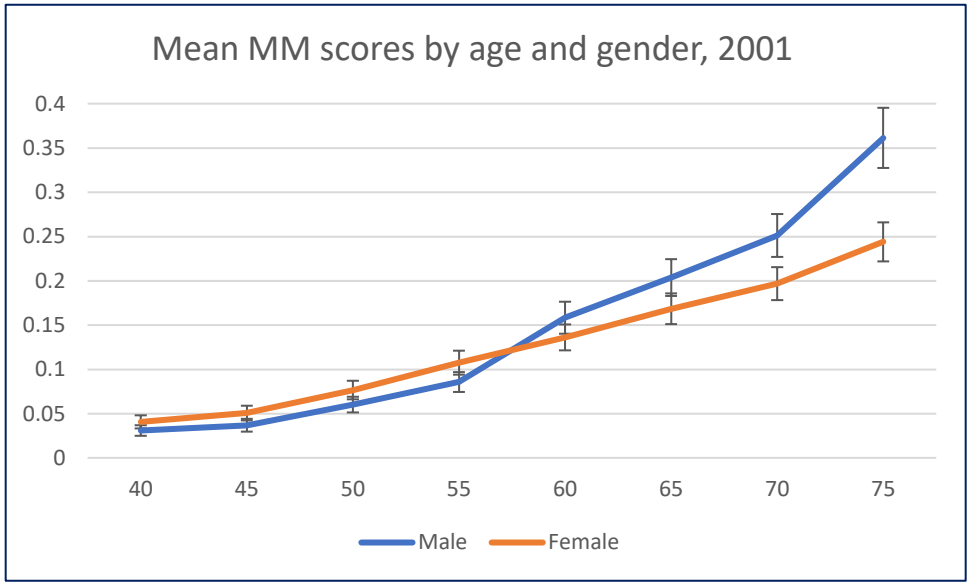
- Constructed variable of multimorbidity change
- Regressions: linear mixed models, growth curve models, multilevel models
- Clusters of trajectories
- Disease transitions approaches: complex modelling, data mining
- Visualisation techniques

Disease accumulation and sequencing in Scotland

Data sources

- **Scottish Longitudinal Study (SLS)**
  - Scottish censuses conducted in 1991, 2001 and 2011 for a 5.3 % sample
  - Linked to health register data (inpatient hospitalisations, diabetes and cancer diseases registers)
  - Linked to vital records: mortality, marriages and in/out migration data
  - **Cohort description**
  - Aged 40-69 years at 2001, followed until 2019 or until death / exit from the study
  - After missing data exclusions (1.6% of sample); c. 97,000 individuals
- **Multimorbidity**
  - 17 diseases of the Charlson comorbidity index, weighted (Quan 2011)- range 0-17
  - Extracted ICD10 codes, their timing from health records
  - Disease specific sequences and transitions
- **Sociodemographic factors in 2001**
  - gender, age, marital status, household size, education, household tenure, Scottish Index of Multiple Deprivation (SIMD)

Age, period, gender



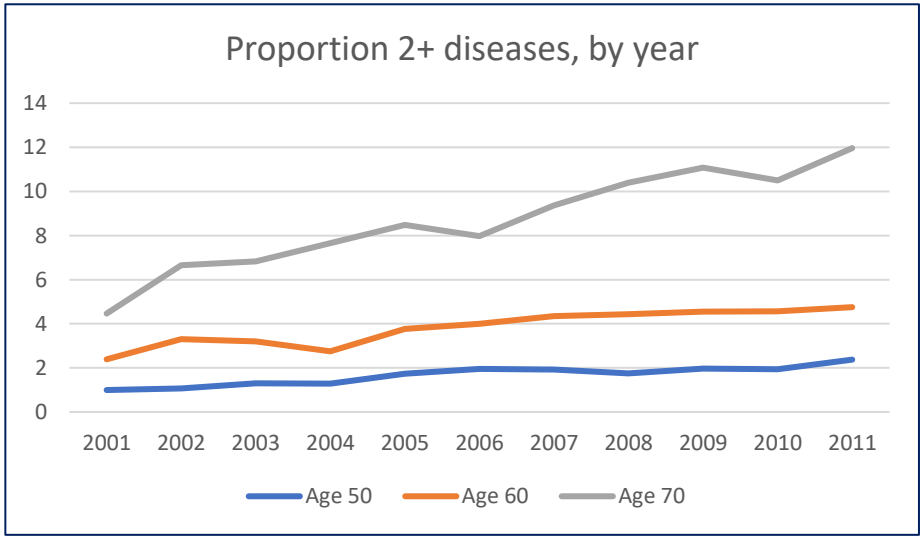
Source: Scottish Longitudinal Study

Age effects

- Mid-life shift in gender patterns

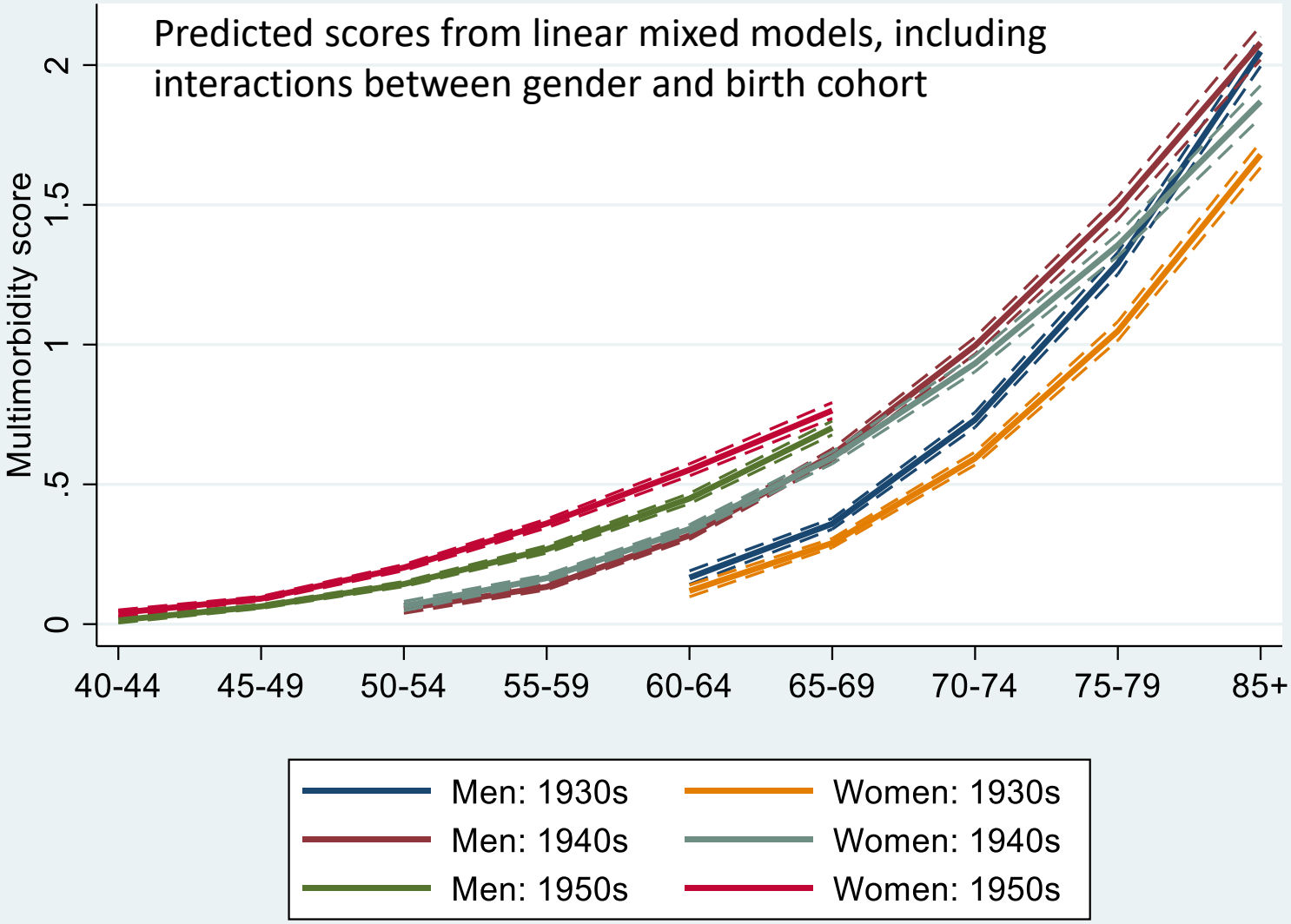
Period effects?

- Steady increase over time in the % adults with MM at any given age
- (most obvious at older ages)
- No abrupt changes



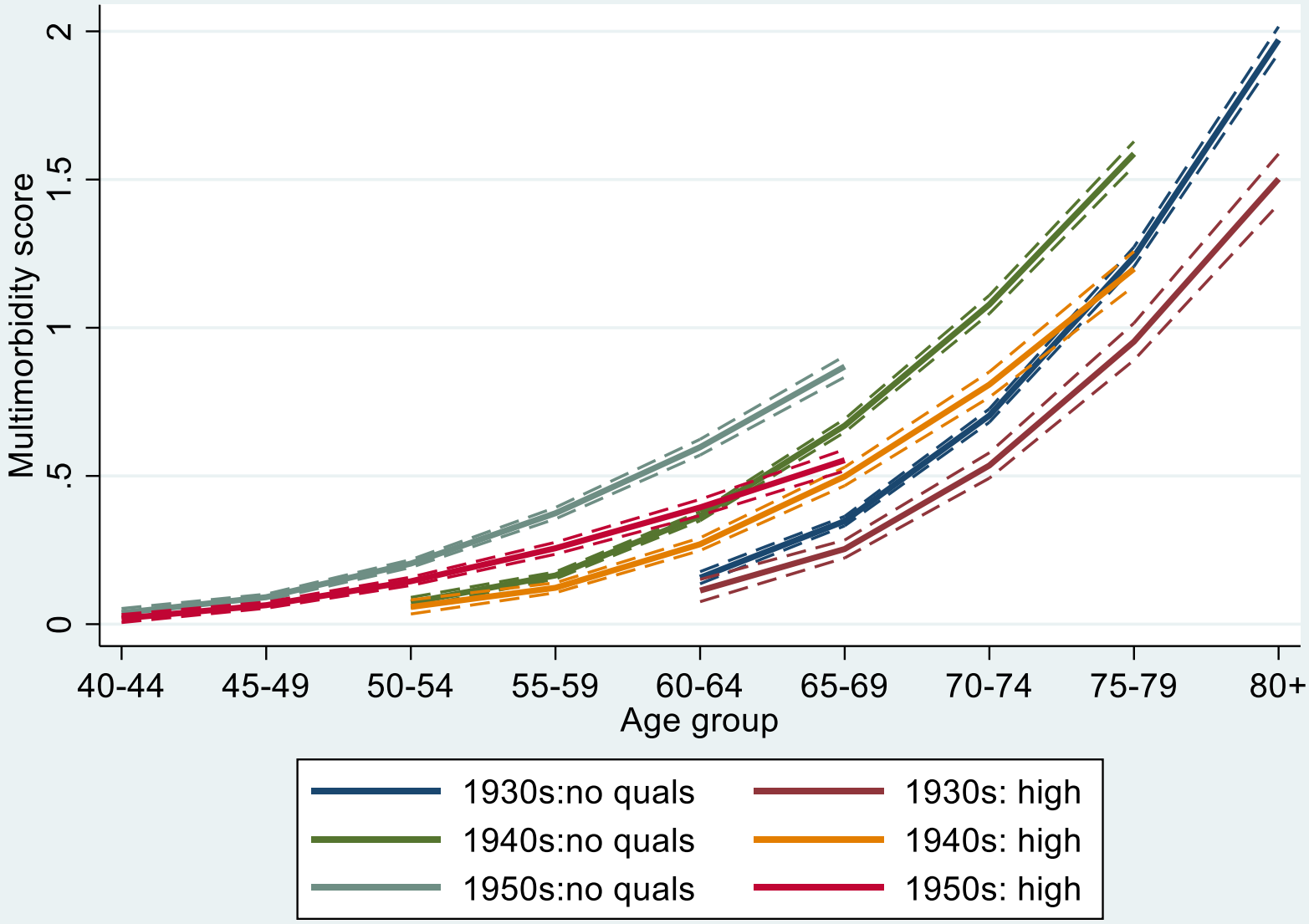
Source: Scottish Longitudinal Study

Age, gender and birth cohort trajectories



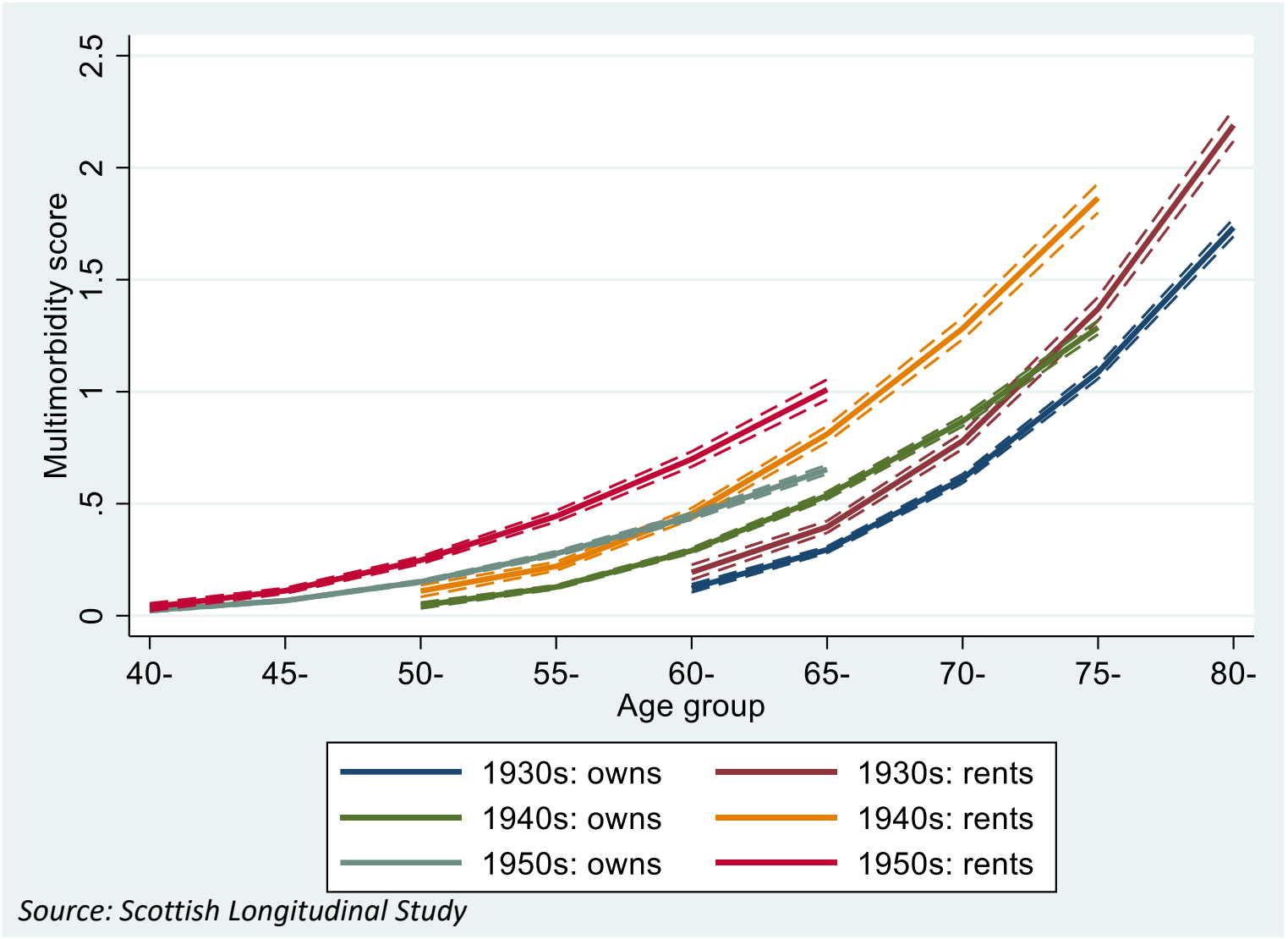
Source: Scottish Longitudinal Study

Age, cohort and education



Source: Scottish Longitudinal Study

Age, cohort and housing tenure (adjusted for deprivation and education)



Source: Scottish Longitudinal Study

1st disease characteristics and onset by birth cohort

Among all adults aged 40-69 in 2001, hospitalisation data from 1997-2019

	Born 1930s	Born 1940s	Born 1950s
1	Cancer	Cancer	Chronic pulmonary disease
2	Chronic pulmonary disease	Chronic pulmonary disease	Cancer
3	Myocardial infarction	Myocardial infarction	**Diabetes**
4	Cerebrovascular disease	**Diabetes**	Myocardial infarction
5	**Diabetes**	Cerebrovascular disease	Ulcer disease
6	Peripheral vascular disease	Ulcer disease	Cerebrovascular disease
7	Congestive heart failure	Peripheral vascular disease	**Mild liver disease**
8	Ulcer disease	Congestive heart failure	Connective tissue disease
9	Connective tissue disease	**Mild liver disease**	Peripheral vascular disease
10	Dementia	Connective tissue disease	Congestive heart failure

Source: Scottish Longitudinal Study

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2	Chronic pulmonary disease	Chronic pulmonary disease	Cancer
3	Myocardial infarction	Myocardial infarction	Diabetes
4	**Cerebrovascular disease**	Diabetes	Myocardial infarction
5	Diabetes	**Cerebrovascular disease**	Ulcer disease
6	Peripheral vascular disease	Ulcer disease	**Cerebrovascular disease**
7	**Congestive heart failure**	Peripheral vascular disease	Mild liver disease
8	Ulcer disease	**Congestive heart failure**	Connective tissue disease
9	Connective tissue disease	Mild liver disease	Peripheral vascular disease
10	Dementia	Connective tissue disease	**Congestive heart failure**

Source: Scottish Longitudinal Study

Disease sequencing

- 3 diseases: CVD, cancer, diabetes
- 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
- 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

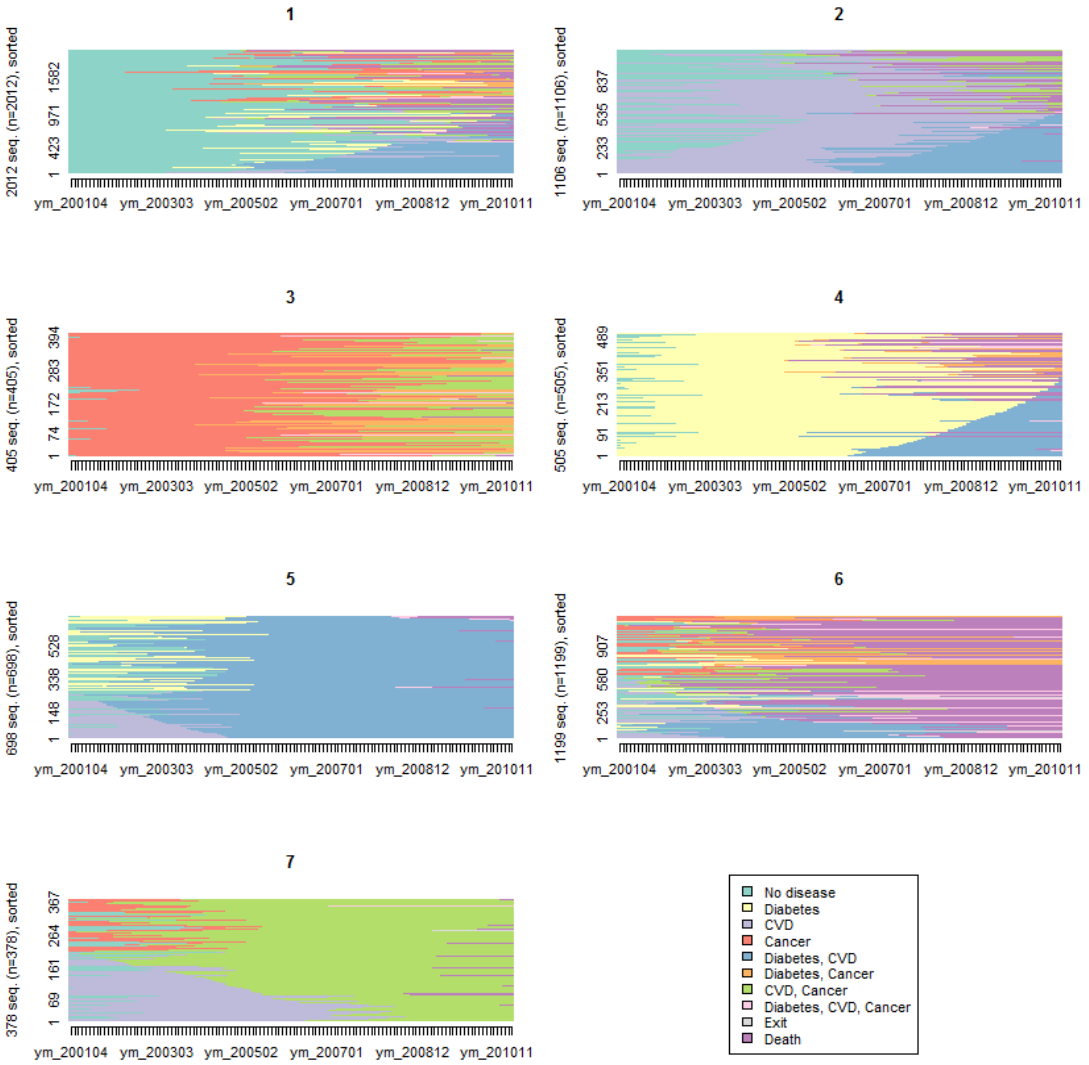
MM trajectory clusters

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 by the end of the follow-up period) (N = 6,300; 6%)

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



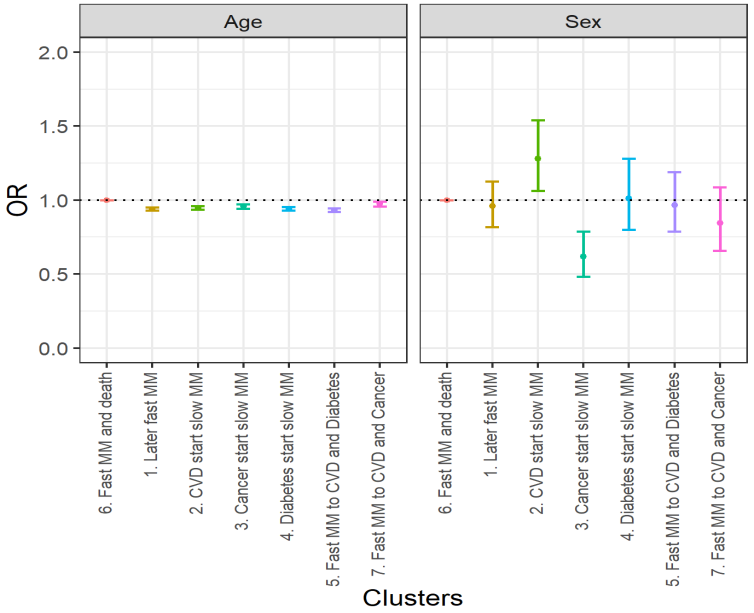
Joint work with Cezard, G & Sullivan, F. (2022)

Association between sociodemographic factors and typical MM trajectories

- Sociodemographic profile of typical trajectories
- Identification of sociodemographic differences in multimorbidity trajectories

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.



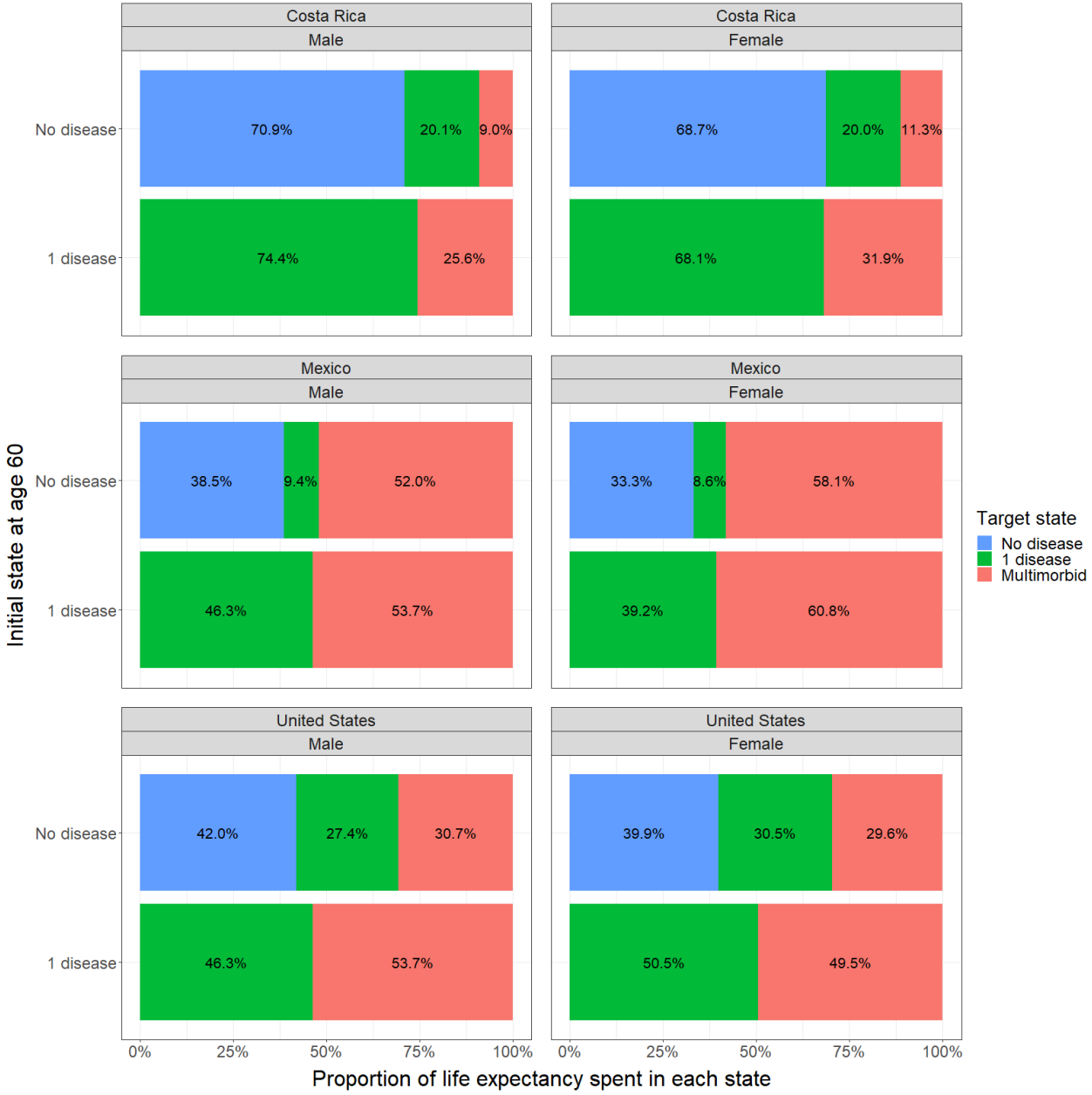
Joint work with Cezard, G & Sullivan, F. (2022)

How much our of lifetime do we spend multimorbid?

- While life expectancy may be rising globally, is this bonus time spent in good health?
- And how does multimorbidity fit into the picture?
- We explored this using sources of comparable longitudinal survey data, which capture the time people become multimorbid and mortality trends, and allow adjustment for a range of covariates
- This includes data from Health and Retirement Survey- US (2004-18); Costa Rican Study on Longevity and Healthy Aging (2005-09), Mexican Health and Aging Study (2012-18)

Comparing Costa Rica, Mexico and the US

- % of LE at age 60 spent with 0, 1, and 2+ diseases
- CR has the highest LE, and spend the least time living with MM
- Mexicans have the lowest LE but spend more- about half of that time with MM
- In CR & US, having no disease at age 60 makes you less likely to be MM; in Mexico this doesn't matter



Joint work with Lam, A, Kulu, H; Myrskylä, M & Cezard, G. (unpublished)

Important future challenges

Measurement

- Multimorbidity = complexity; for researchers; for clinicians; for patients
- Role of infectious diseases/ NCD interactions crucial
- Ways of conceptualising and dealing with multimorbidity have to become more agile and adaptable

Research focus for understanding impact

- The proportion of multimorbid which this is debilitating is key (quality of life /disability)
- From a research perspective: we need to find more nuanced measures of capturing severity and its impact
- From a policy perspective: we have to find ways to narrow health inequalities and prevent disease progression

Thank you for listening!

Feel free to contact me:

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