

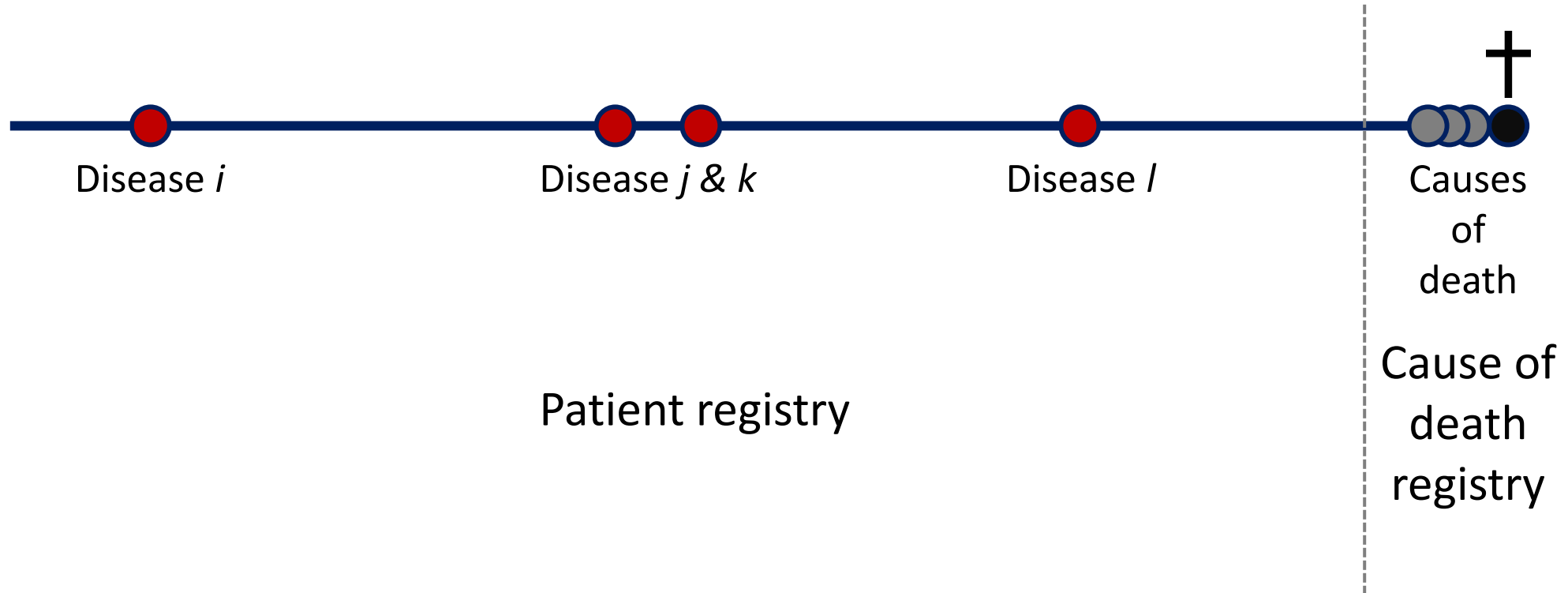
Is end-of-life Morbidity Different in Deaths with Multiple versus Single Causes?

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MultiCause Network meeting, Barcelona, 16 & 17 October 2025



Multiple causes of death: A way how to account for multimorbidity at death

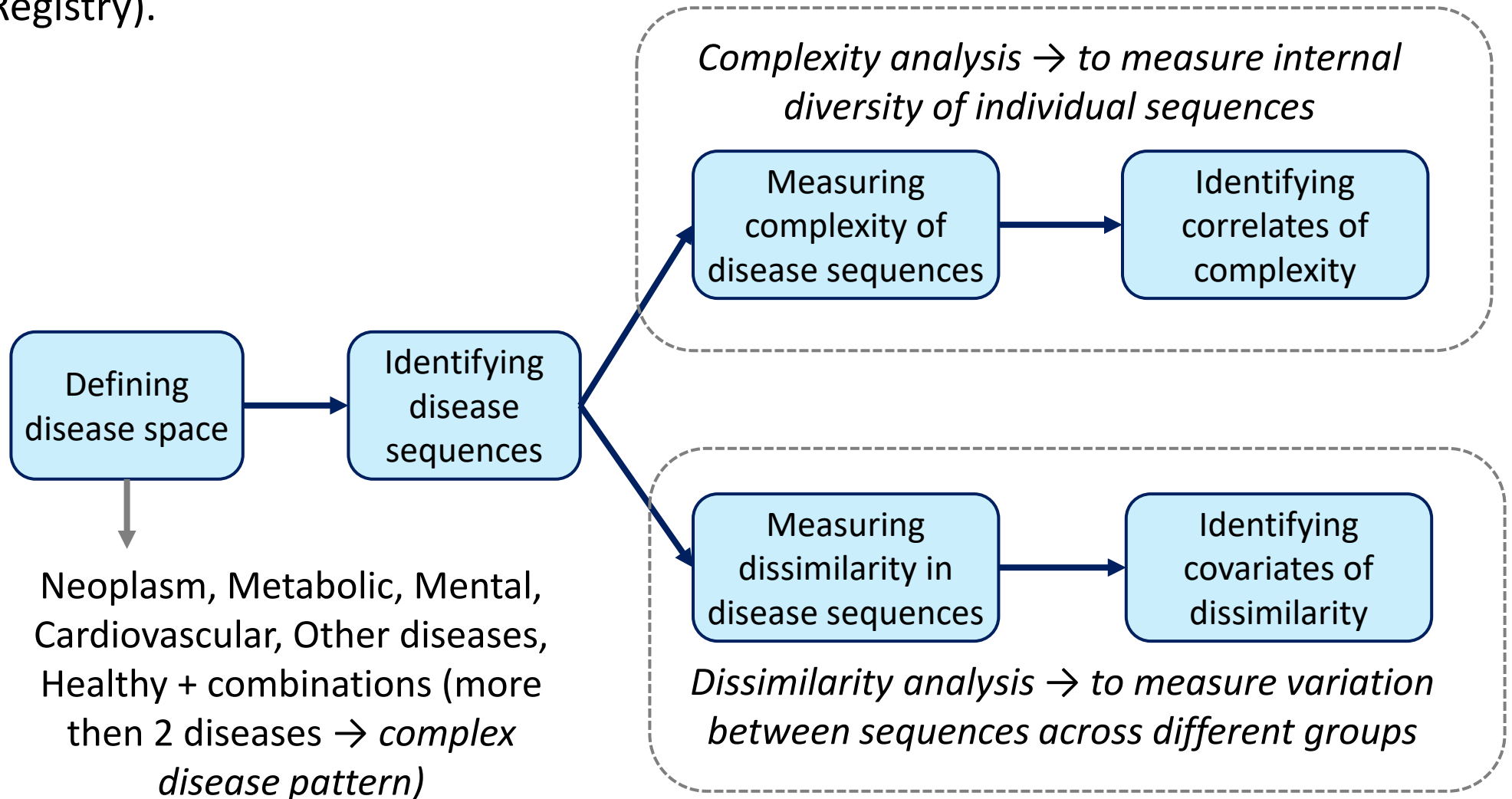


Aim:

Look into differences in disease sequences in death with multiple and single causes, focusing on:

1. Differences in complexity of disease sequences;
2. Dissimilarity in disease sequences by information recorded on death certificate.

We took cohort of death aged 65+ in 2019 in Denmark and tracked their diseases since 1995 (~ combination of Danish Cause of Death Registry and Danish Patient Registry).



Identifying disease sequences

Standard procedure: dissimilarity matrix using Optimal Matching method, CLARA algorithm to cluster disease sequences

Measuring complexity of disease sequences

Longitudinal entropy, complexity index, sequence turbulence (this is what literature identifies as the most usable indices)

Identifying correlates of complexity

Linear regression (Dependent: measure of complexity; Independent: demographic characteristics of the deceased, death certification data)

Measuring dissimilarity in disease sequences

Dissimilarity matrix used to identify disease sequences

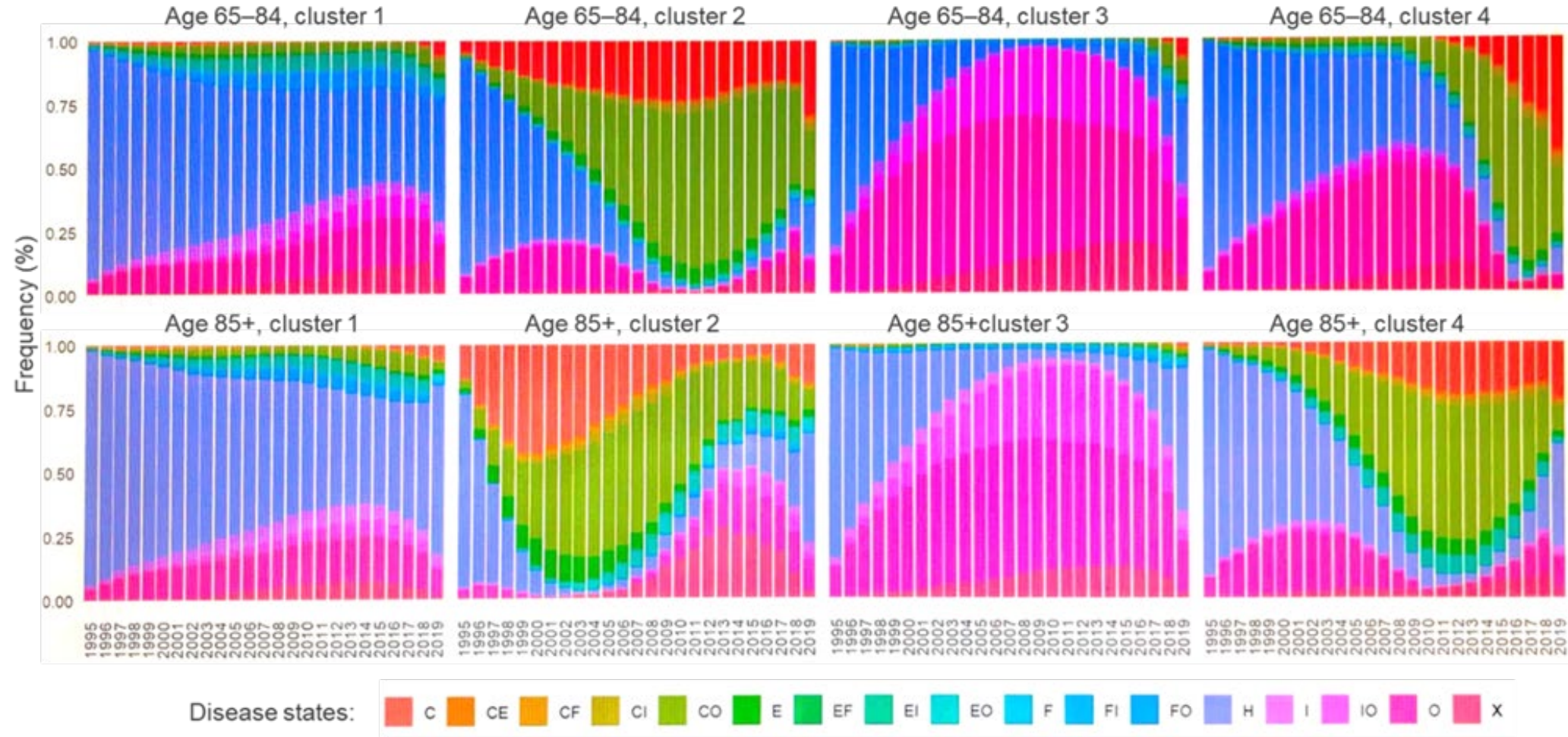
Identifying covariates of dissimilarity

ANOVA-like analysis, to compare within-group and between-group sequence dissimilarities (Levene tests)

Covariates used in the analysis:

- Has a contributory cause in Part 2
- Has a „*due to*“ relationship in Part 1
- Died in any type of medical facility
- The death certifier knew the deceased during their life
- The deceased was a male
- Underlying cause of death
 - Cardiovascular disease
 - Neoplasm
 - Respiratory disease
 - Mental or nervous disease
 - Ill-defined cause of death
 - Other
- Disease sequence cluster
 - 1
 - 2
 - 3
 - 4

Figure: Types of disease sequences (disease clusters)



C = neoplasm; E = metabolic; F = mental; H = healthy; O = other diseases;
I = cardiovascular; X = complex disease pattern (3+ diseases)

Figure: Distribution of longitudinal entropy

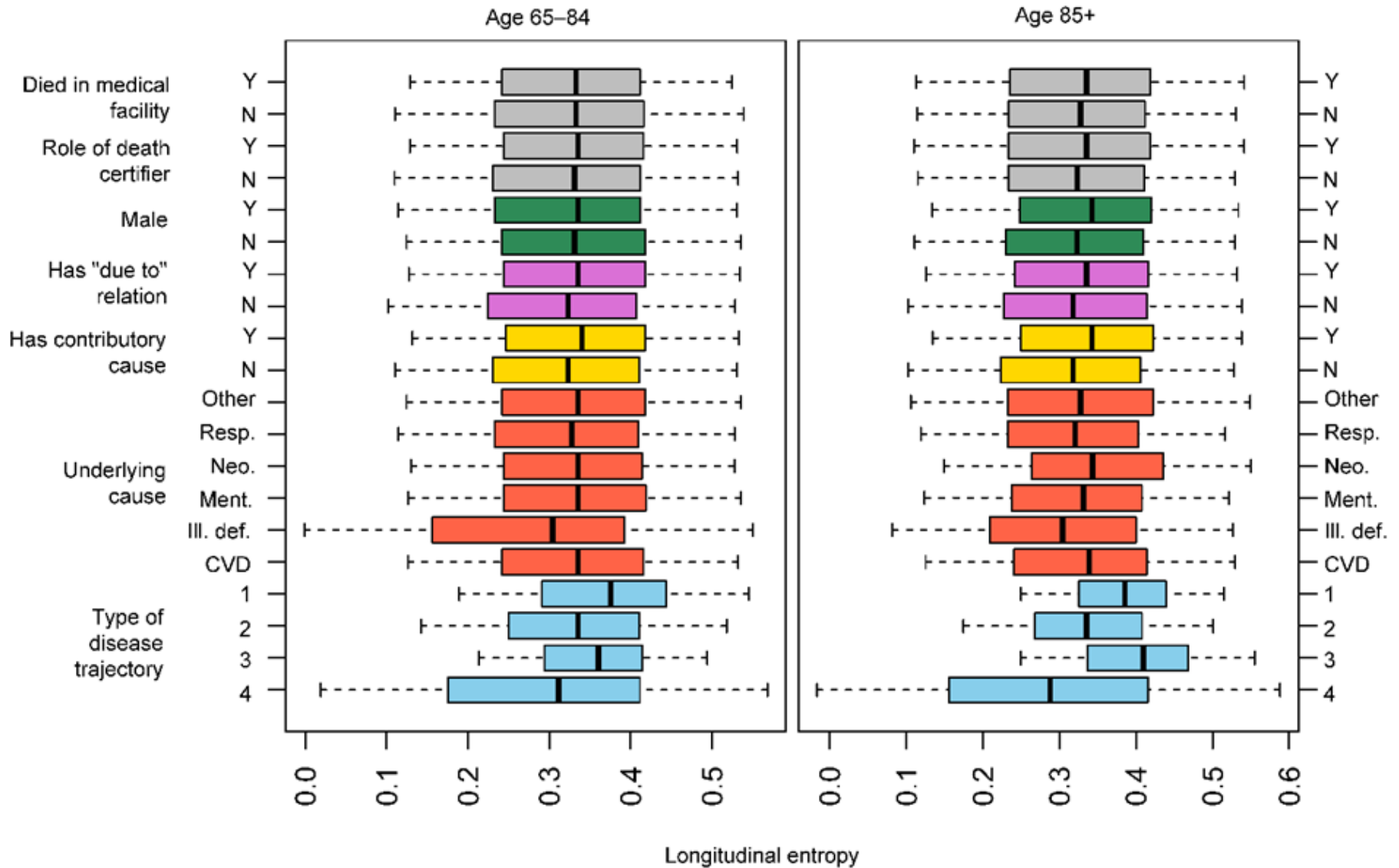


Table: Factors associated with complexity of disease sequences

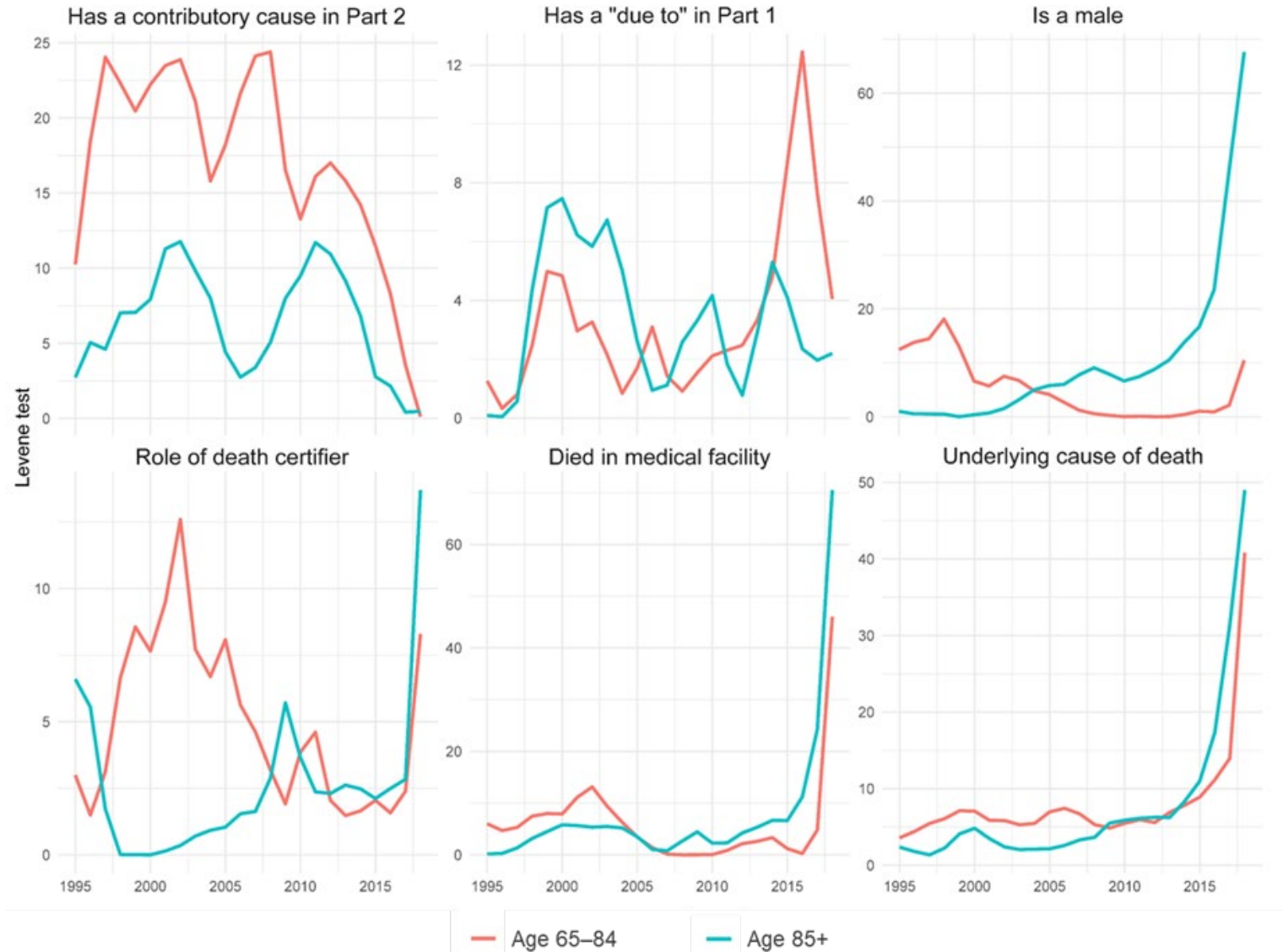
		Age 65–84		Age 85+	
		Coefficient	p-value	Coefficient	p-value
	Has a contributory cause in Part 2	0.0195	0.0000	0.0157	0.0002
	Has a "due to" relation in Part 1	0.0084	0.0489	<i>0.0039</i>	<i>0.4245</i>
	The deceased was a male	0.0074	0.0360	0.0108	0.0097
	Died in any type of medical facility	<i>-0.0039</i>	<i>0.3140</i>	<i>-0.0060</i>	<i>0.2337</i>
	Role of death certifier	<i>0.0064</i>	<i>0.1096</i>	<i>0.0058</i>	<i>0.2052</i>
Underlying cause of death	Ill-defined	<i>-0.0045</i>	<i>0.6221</i>	<i>-0.0154</i>	<i>0.0626</i>
	Mental	0.0195	0.0044	<i>-0.0071</i>	<i>0.2666</i>
	Neoplasm	<i>0.0026</i>	<i>0.6003</i>	<i>0.0017</i>	<i>0.7884</i>
	Respiratory	<i>0.0058</i>	<i>0.3615</i>	<i>-0.0074</i>	<i>0.2826</i>
	Other	0.0136	0.0222	-0.0122	0.0450
Type of disease trajectory	2	0.0660	0.0000	0.1231	2.00E-16
	3	0.0353	0.0000	0.0460	2.00E-16
	4	0.0803	0.0000	0.0777	2.00E-16

Table: Results of multifactor discrepancy analysis

	Age 65–84		Age 85+	
	F	p-value	F	p-value
Has a contributory cause in Part 2	4.61	0.002	3.00	0.002
Has a "due to" relation in Part 1	<i>0.97</i>	<i>0.432</i>	<i>0.90</i>	<i>0.538</i>
Died in any type of medical facility	1.85	0.022	2.35	0.004
The death certifier knew the deceased during their live	<i>1.20</i>	<i>0.204</i>	<i>1.15</i>	<i>0.256</i>
The deceased was a male	7.30	0.002	4.65	0.002
Underlying cause of death	12.77	0.002	5.35	0.002

Figure: Time evolution of Levene test

Association between sequence dissimilarity and a covariate



The **complexity of these sequences differs primarily between individuals who do and do not have a contributory cause recorded in Part 2** of the certificate, then by UCD: among younger deaths, complexity is lower if UCD was an ill-defined condition, whereas among older deaths, complexity is higher in death with UCD cancer. The multifactor discrepancy analysis showed that, **in both the younger and older cohorts, there were no significant differences in disease sequences based on whether a “due to” relationship was indicated between conditions in Part 1**, or whether the certifying physician had also been the deceased’s treating physician prior to death. Both medical and non-medical covariates recorded on the death certificate explain only a negligible portion of the overall variability in disease sequences. The strength of the association between the contributory cause covariate and disease trajectories does not increase as death approaches, suggesting that the greatest differences in sequences by MCD occur well before death in 2019.

Too simplistic definition of disease states...

Too much focus on „quantity“ of causes rather than which causes are combined...

Retrospective analysis: losing people who died before the age of 65

Underrecording of some diagnosis in Danish registries...

Healthy of not using medical services even if ill?

Etc.

Thank you.

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It seems to depend on in which Part these causes are recorded, among other.

