Development of multimorbidity patterns in older adults in Switzerland: A competing risks modeling approach

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Motivation

- **Multimorbidity** represents a **global challenge** with significant implications for individuals, healthcare systems and society (Gastens et al., 2022).

- Multimorbidity is more common in **old age**, and it is associated with **premature death**, **poorer quality of life** and **increased** healthcare **use** and **costs** (Ruckstuhl et al., 2023).

- In **Switzerland**, the **healthcare costs** are 5.5 times **higher** in multimorbid patients than in single-morbid patients (Bähler et al., 2015).

Our research

Research objective

We aim to model the progression of multimorbidity by highlighting the major chronic disease patterns in the Swiss adult population.

- How do different multimorbidity patterns evolve over time?
- Is there any effect of age on the incidence of patterns of multimorbidity?
- Are there specific patterns in which multimorbidity tends to develop depending on gender?

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Competing risks framework

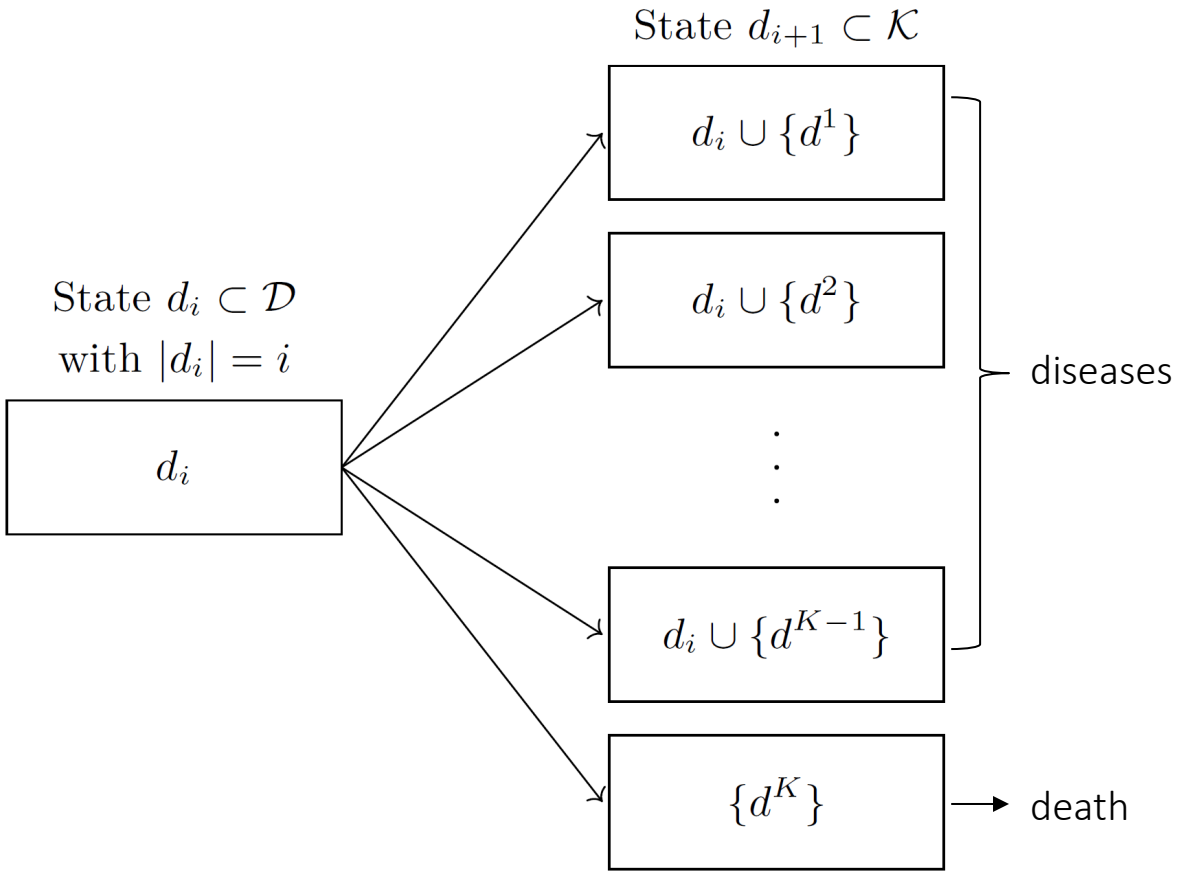

Fig. 1: Illustration of the transition from d_i to d_{i+1}.

Notation

- d_i := initial state
- d_{i+1} := subsequent state
- i := number of diseases
- Set of diseases:
  $\mathcal{D} = \{d^1, \ldots, d^{K-1}\}$.
- Complete set:
  $\mathcal{K} = \mathcal{D} \cup \{d^K\}$.

Subdistribution hazard model (1)

The instantaneous **rate of occurrence**, so-called **subdistribution hazard function** (SHF), for the event of interest $d^{\bar{k}} \, \epsilon \, \mathcal{D} \setminus d_i$ and time-dependent covariate $Z(t)$ (for time-independent $Z(t) = Z$) is as follows (Fine and Gray, 1999):

$$\lambda_{d^{\bar{k}}}(t \mid Z(s), s \leq t) = \underbrace{\lambda_{d^{\bar{k}},0}(t)}_{\substack{\text{Baseline SHF} \\ \text{for } d^{\bar{k}}}} \cdot \exp\left(Z^{\mathrm{T}}(t)\beta_0\right)$$

The estimated **cumulative SHF** at time t for the event of interest $d^{\bar{k}}$ conditional on covariate $Z(t)$ is:

$$\hat{\Lambda}_{d^{\bar{k}}}(t \mid Z(s), s \leq t) = \int_0^t \lambda_{d^{\bar{k}}}(s \mid Z(u), u \leq s)\,\mathrm{d}s = \int_0^t \lambda_{d^{\bar{k}},0}(s) \cdot \exp\left(Z^{\mathrm{T}}(s)\beta_0\right)\,\mathrm{d}s.$$

Subdistribution hazard model (2)

The **cumulative incidence function** (CIF) at time t for the event of interest $d^{\bar{k}}$ conditional on covariate $Z(t)$ is defined as:

$$\underbrace{\mathrm{CIF}_{d^{\bar{k}}}(t \mid Z(s), s \leq t)}_{\text{Marginal probability function: } F_{d^{\bar{k}}}(t \mid Z(t))} = \Pr\left[T \leq t, d^k = d^{\bar{k}} \,\middle|\, Z(s), s \leq t\right] = 1 - \exp\left(-\hat{\Lambda}_{d^{\bar{k}}}(t \mid Z(s), s \leq t)\right)$$

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Data

- A total of **320,679** policyholders aged 50 years or older with **chronic conditions**.
- **Monthly individual** claims data on medication use from 2014 to 2022.
- **Medication** information used to asses the morbidity status of individuals.
- Classification of diseases into **pharmacy cost groups** (PCGs) according to similarities in diagnosis.

Disease groups

PCG	Abbr.	Medical conditions	N
Hypertension	Hyp.	Hypertension	236 568
Asthma	Ast.	Asthma	109 865
Diabetes	Dia.	Diabetes type 1 and type 2	64 720
Glaucoma	Gla.	Glaucoma	55 960
Heart	Heart	Heart disease	46 233
COPD	COPD	Chronic obstructive pulmonary disease/severe asthma	37 732
Cancer	Can.	Cancer, complex cancer, hormone-sensitive tumor	28 236
Inflammatory	Infl.	Crohn's disease/ulcerative colitis, disease of the brain/spinal cord: multiple sclerosis, psoriasis, rheumatism	26 691
Epilepsy	Epi.	Epilepsy	20 686
Parkinson	Park.	Parkinson's disease	14 307
Alzheimer	Alz.	Alzheimer's disease	6 314
Immune	Imm.	Auto-immune disease	5 118
HIV	HIV	Human immunodeficiency virus/acquired immunodeficiency syndrome	1 393
Mental	Men.	Attention deficit hyper-activity disorder	1 195

Table 1: Summary of pharmacy cost groups (PCGs) and medical conditions.

Number of observations for multimorbidity transitions

	$i+1$		$i+2$		$i+z$	
	N	(% lc)	N	(% lc)	N	(% lc)
$i=1$	84 428	(26.5)	3 204	(33.3)	159	(49.1)
$i=2$	46 438	(10.6)	1 334	(15.1)	42	(11.9)
$i\geq 3$	30 934	(3.6)	518	(5.6)	8	(25.0)

(a) Female.

	$i+1$		$i+2$		$i+z$	
	N	(% lc)	N	(% lc)	N	(% lc)
$i=1$	78 712	(26.4)	3 448	(33.9)	215	(37.7)
$i=2$	45 341	(11.0)	1 401	(15.6)	57	(24.6)
$i\geq 3$	33 209	(3.3)	600	(7.8)	15	(0.0)

(b) Male.

80%

Note: The number N in the first column refers to the total number of observations from d_i to d_{i+1}, i.e. $N_{i,i+1}$; the Ns in the second and third columns of the table correspond to $N_{i,i+2}$ and $N_{i,i+z}$ respectively, where $z \geq 3$. Left-censored observations ("lc"), where PCGs are diagnosed before observing the individuals in the data, are reported as a share (in %) in parentheses.

Table 2: Number of observations in the original data for transitions from d_i by gender.

- Algorithm to simulate the occurence of the first next PCG (for cases $i+2$).
- We treat left-censored data with an imputation method.

Number of observations for transitions $d_1 \rightarrow d_2$

d_1 \ d_2	+Hyp.	+Ast.	+Dia.	+Gla.	+Heart	+COPD	+Can.	+Infl.	+Epi.	+Park.	+Alz.	+Imm.	+HIV	+Men.	Death	Total
Hyp.	–	9 621	8 668	5 187	7 200	1 802	2 559	2 096	1 331	973	483	121	68	53	3 560	43 722
Ast.	4 709	–	680	586	302	1 919	356	443	237	127	28	27	19	31	260	9 724
Dia.	6 152	830	–	563	207	130	235	199	124	76	28	15	4	5	295	8 863
Gla.	2 975	701	366	–	122	96	228	145	89	84	71	8	5	6	267	5 163
Heart	1 771	246	94	128	–	44	48	39	22	27	11	4	0	2	123	2 559
COPD	613	727	73	86	41	–	83	48	25	9	13	4	0	1	128	1 851
Can.	1 062	280	142	157	65	103	–	63	86	29	8	4	3	2	900	2 904
Infl.	1 067	402	134	124	44	43	93	–	48	35	12	335	4	9	58	2 408
Epi.	1 038	330	115	127	56	76	111	85	–	51	16	7	4	18	210	2 244
Park.	553	140	64	72	42	28	32	33	97	–	60	4	3	7	188	1 323
Alz.	190	25	16	33	10	8	9	5	28	28	–	0	0	0	159	511
Imm.	114	33	14	11	4	2	3	111	3	2	0	–	0	0	3	300
HIV	213	96	27	17	7	12	23	11	26	7	2	0	–	3	18	462
Men.	53	31	5	3	3	3	3	5	12	4	2	0	0	–	2	126
Total	20 510	13 462	10 398	7 094	8 103	4 266	3 783	3 283	2 128	1 452	734	529	110	137	6 171	82 160

75.8%

(b) Male.

Table 3: Number of observations for transitions $d_1 \rightarrow d_2$ for males.

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Effect of age on the SHF for transitions $d_1 \rightarrow d_2$

	Female			Male		
	SHR (95% CI)	% risk	Sig.	SHR (95% CI)	% risk	Sig.
Hypertension						
+Asthma	0.959 (0.957–0.960)	−4.1	***	0.968 (0.966–0.970)	−3.2	***
+Diabetes	0.970 (0.968–0.972)	−3.0	***	0.969 (0.967–0.971)	−3.1	***
+Glaucoma	1.020 (1.018–1.022)	+2.0	***	1.032 (1.030–1.034)	+3.2	***
+Heart	1.021 (1.019–1.023)	+2.1	***	1.000 (0.998–1.002)	+0.0	
+COPD	1.005 (1.001–1.009)	+0.5	*	1.001 (0.997–1.005)	+0.1	
+Cancer	0.988 (0.985–0.990)	−1.2	***	1.020 (1.017–1.023)	+2.0	***
+Inflammatory	0.968 (0.965–0.972)	−3.2	***	0.971 (0.967–0.975)	−2.9	***
+Epilepsy	0.980 (0.976–0.984)	−2.0	***	0.979 (0.974–0.984)	−2.1	***
+Parkinson	1.014 (1.010–1.018)	+1.4	***	1.023 (1.018–1.029)	+2.3	***
+Alzheimer	1.069 (1.065–1.073)	+6.9	***	1.098 (1.091–1.105)	+9.8	***
Asthma						
+Hypertension	1.005 (1.002–1.007)	+0.5	***	1.000 (0.997–1.003)	+0.0	
+Diabetes	0.958 (0.951–0.966)	−4.2	***	0.964 (0.956–0.972)	−3.6	***
+Glaucoma	1.028 (1.024–1.033)	+2.8	***	1.032 (1.025–1.039)	+3.2	***
+COPD	0.993 (0.989–0.997)	−0.7	***	0.999 (0.995–1.004)	−0.1	
+Cancer	0.991 (0.984–0.998)	−0.9	*	1.014 (1.005–1.024)	+1.4	**
+Inflammatory	0.960 (0.952–0.967)	−4.0	***	0.965 (0.955–0.976)	−3.5	***
Diabetes						
+Hypertension	1.007 (1.004–1.010)	+0.7	***	0.995 (0.992–0.997)	−0.5	***
+Asthma	0.951 (0.944–0.959)	−4.9	***	0.963 (0.956–0.971)	−3.7	***
+Glaucoma	1.012 (1.004–1.021)	+1.2	**	1.026 (1.019–1.034)	+2.6	***

Table 5: Subdistribution hazard ratios for selected transitions $d_1 \rightarrow d_2$.

Relative risk ↘ as age ↗

Relative risk ↗ as age ↗

Relative risk differs by gender

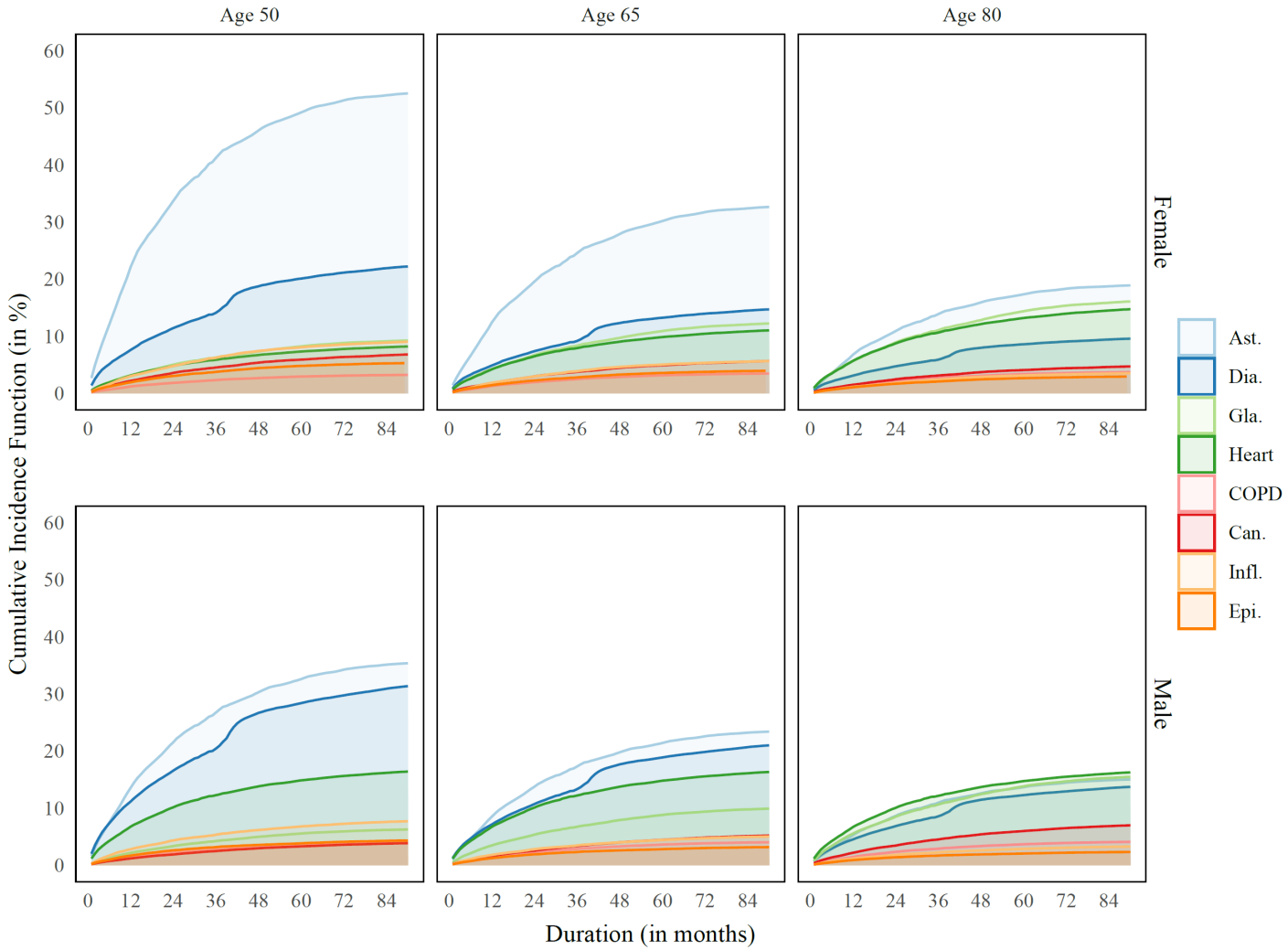
Age as a significant **risk factor** in most models.

Cumulative Incidence Functions for transitions $d_1 \rightarrow d_2$

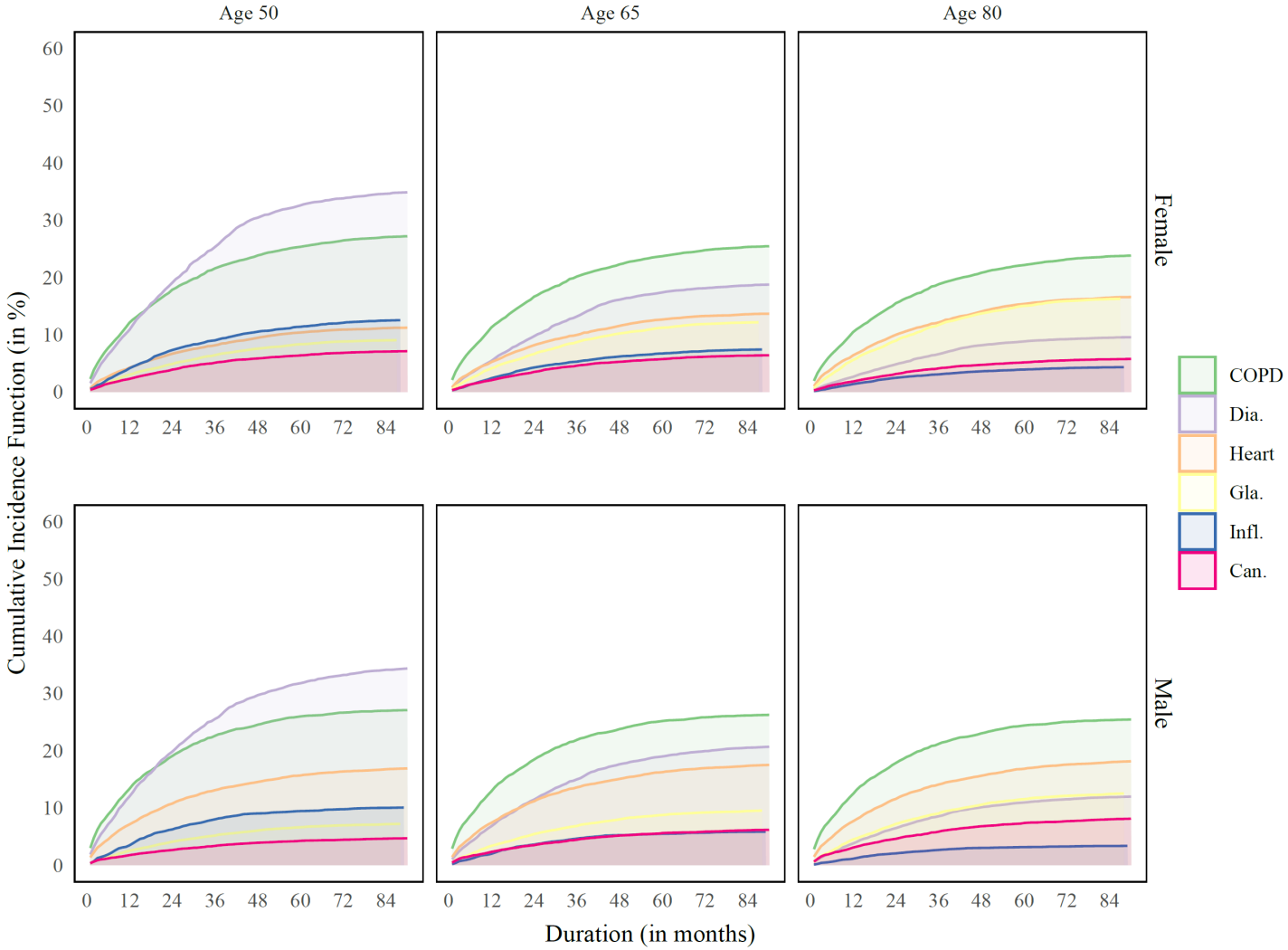
	Female									Male								
Months	12			24			60			12			24			60		
Age	50	65	80	50	65	80	50	65	80	50	65	80	50	65	80	50	65	80
Hypertension																		
+Ast.	22.12	12.42	6.79	33.71	19.60	10.93	49.22	30.20	17.37	13.56	8.51	5.29	21.56	13.78	8.66	32.63	21.43	13.70
+Dia.	7.61	4.89	3.13	11.45	7.41	4.76	20.12	13.26	8.61	11.17	7.15	4.54	16.59	10.75	6.88	28.42	18.90	12.30
+Gla.	3.20	4.27	5.69	5.05	6.73	8.93	8.26	10.93	14.40	2.18	3.49	5.56	3.38	5.38	8.52	5.58	8.83	13.83
+Heart	3.12	4.22	5.71	4.82	6.51	8.77	7.35	9.88	13.22	6.78	6.75	6.72	10.17	10.12	10.07	14.89	14.83	14.76
+COPD	1.23	1.32	1.42	1.86	1.99	2.14	2.97	3.18	3.41	1.42	1.45	1.47	2.30	2.34	2.38	3.58	3.64	3.70
+Can.	2.22	1.84	1.53	3.61	3.00	2.49	5.93	4.93	4.10	1.21	1.64	2.21	1.90	2.57	3.46	3.32	4.48	6.02
+Infl.	3.03	1.87	1.16	4.81	2.99	1.85	8.08	5.06	3.15	2.83	1.83	1.19	4.37	2.84	1.84	6.82	4.46	2.90
+Epi.	1.95	1.45	1.07	3.06	2.28	1.70	4.82	3.60	2.68	1.72	1.25	0.92	2.65	1.94	1.42	3.86	2.83	2.08
+Park.	0.75	0.92	1.13	1.20	1.48	1.81	1.95	2.38	2.92	0.49	0.70	0.99	0.74	1.05	1.48	1.19	1.68	2.36
+Alz.	0.10	0.27	0.72	0.16	0.42	1.14	0.26	0.71	1.92	0.03	0.14	0.56	0.05	0.21	0.85	0.09	0.37	1.51
Asthma																		
+Hyp.	17.96	19.19	20.49	26.67	28.39	30.20	38.44	40.68	43.00	22.73	22.73	22.73	31.93	31.93	31.92	44.83	44.83	44.82
+Dia.	3.33	1.77	0.94	5.39	2.88	1.53	9.18	4.96	2.65	3.84	2.23	1.30	6.38	3.74	2.18	10.01	5.91	3.46
+Gla.	1.82	2.76	4.17	3.11	4.70	7.06	5.26	7.90	11.77	1.32	2.11	3.35	2.15	3.42	5.42	3.42	5.41	8.53
+COPD	9.43	8.48	7.63	14.00	12.63	11.39	19.65	17.79	16.09	10.10	9.97	9.85	14.13	13.96	13.79	18.95	18.73	18.51
+Can.	1.67	1.46	1.28	2.98	2.61	2.29	4.81	4.22	3.70	1.39	1.72	2.12	1.96	2.41	2.97	–	–	–
+Infl.	3.22	1.75	0.95	5.40	2.96	1.61	8.85	4.88	2.67	2.49	1.47	0.87	3.85	2.29	1.36	6.22	3.71	2.21
Diabetes																		
+Hyp.	36.93	39.91	43.04	49.07	52.55	56.12	60.12	63.78	67.45	43.31	40.80	38.39	56.23	53.39	50.59	68.87	65.97	63.06
+Ast.	11.86	5.79	2.78	17.86	8.87	4.29	23.69	11.99	5.85	6.40	3.70	2.13	10.30	6.01	3.47	14.44	8.51	4.94
+Gla.	2.20	2.64	3.16	3.47	4.16	4.97	5.02	5.99	7.15	1.77	2.61	3.83	2.74	4.02	5.89	3.85	5.64	8.22

Table 6: Estimated CIFs for selected combinations of transitions $d_1 \rightarrow d_2$ by gender.

Hypertension-related CIFs at ages 50, 65 and 80 years



Hypertension + Asthma CIFs at ages 50, 65 and 80 years



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Conclusion

- We develop a competing risks framework to analyze the progression of multimorbidity in the elderly population by specifying the disease pattern.
- A few highlights:
  - The complex dynamics of multimorbidity are influenced by interactions between age, gender and initial diagnoses.
  - Overall, asthma and diabetes exhibit a decreasing relative risk with increasing age, while glaucoma becomes more prevalent at older ages.
  - Combinations of hypertension, asthma, diabetes, glaucoma, heart disease and COPD are the most common in the transition from two to three PCGs.
- By identifying multimorbidity trajectories, the study provides insights for prevention strategies and targeted interventions to reduce disease burden and economic impact.

Future research

- Analyzing the impact of cumulative risk of major multimorbidity trajectories on health insurance costs.
- Including other socioeconomic factors in our model, such as deprivation, social status, region.
- Modeling the multimorbidity dynamics from a mental health condition to (physical) chronic diseases.

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