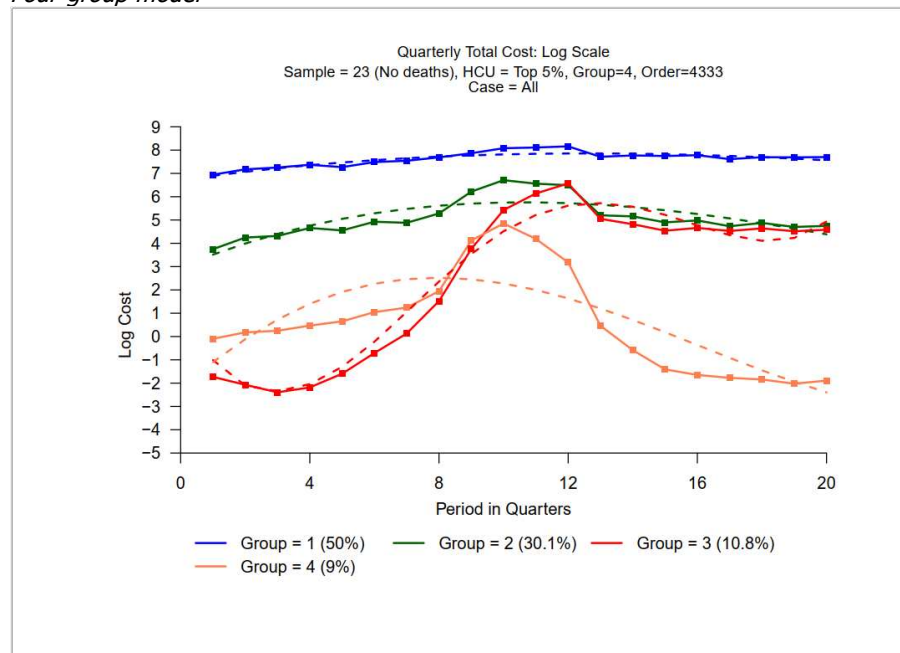


## Appendix

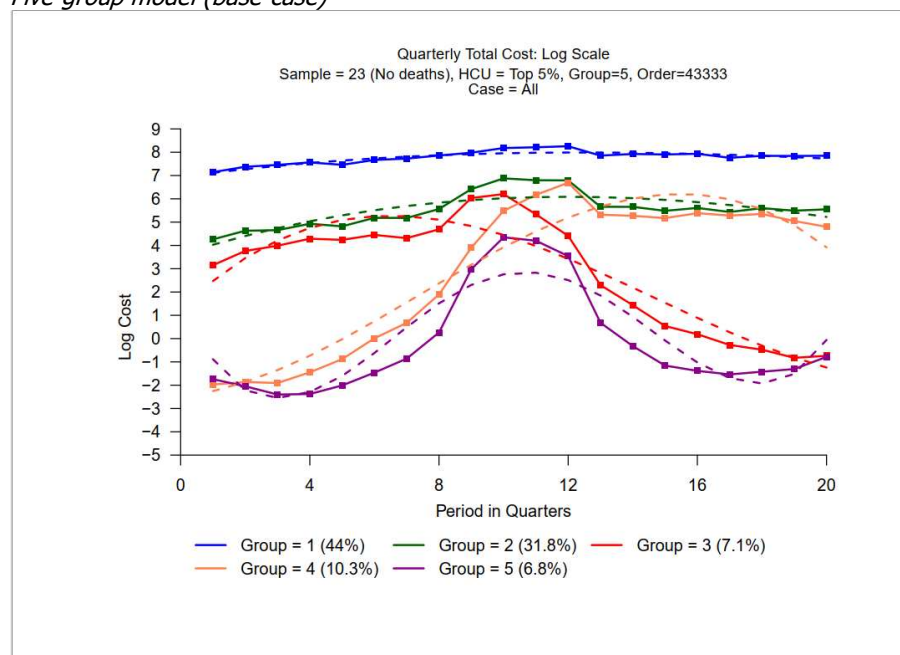
- Figure A1. Actual (solid line) and predicted (dashed line) five-year cost trajectories from group-based trajectory models with four to seven latent groups
- Table A1. Model fit statistics for group-based trajectory models with four to seven latent groups
- Table A2. Table A2. Average and predicted values (with 95 % confidence intervals) for the five-group trajectory model, by time period
- Figure A2. Mean trajectories for each latent group alongside individual trajectories (1% sample)
- Table A3. Parameters for five-group trajectory model
- Figure A3. Five-group trajectory model of HNHC patients based on alternative HNHC years (Sensitivity analysis 1)
- Figure A4. Five-group trajectory model of HNHC patients based on alternative HNHC thresholds (Sensitivity analysis 2)
- Table A4. Demographic and clinical characteristics by trajectory group
- Table A5. Factors associated with group membership (adjusted odds ratio and 95% confidence interval) from multivariate multinomial logistic regression
- Figure A5. Forest plot of factors associated with group membership, relative to the 'very-high-cost' trajectory group, from multinomial logistic regression (adjusted Odds Ratios, 95% CI)

**Figure A1. Actual (solid line) and predicted (dashed line) five-year cost trajectories from group-based trajectory models with four to seven latent groups**

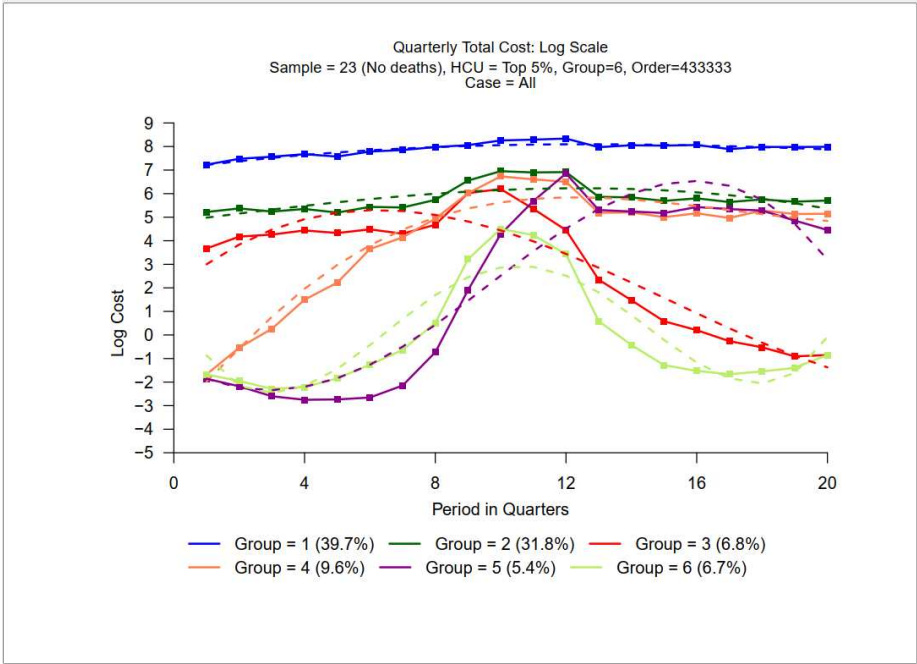
*Four-group model*



*Five-group model (base-case)*



*Six-group model*



Seven-group model

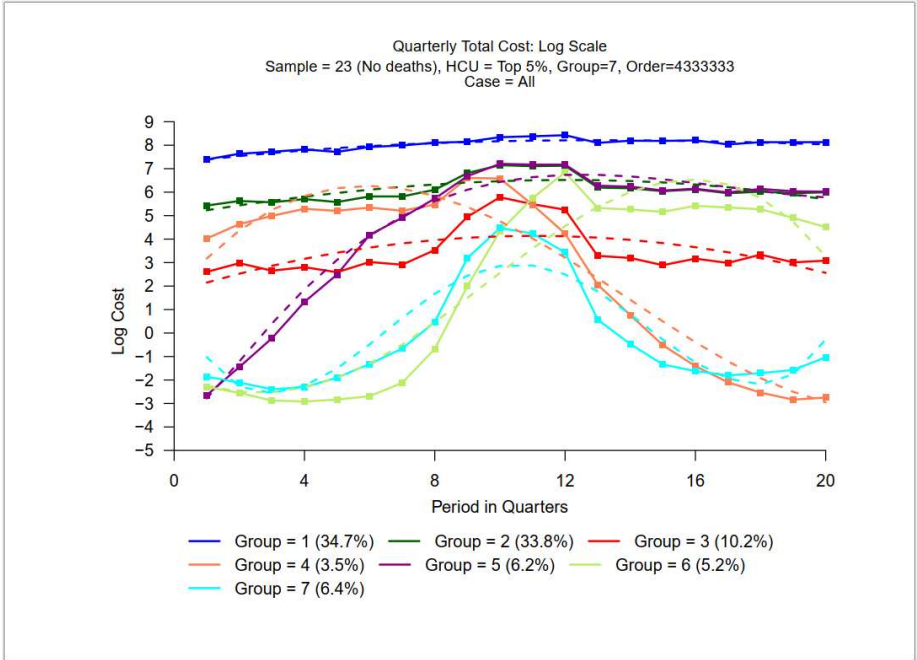


Table A1. Model fit statistics for group-based trajectory models with four to seven latent groups and 2<sup>nd</sup> to 4<sup>th</sup> degree polynomials\*

groups	polynomials	BIC1	BIC2	AIC	LL	Change in BIC1	Change in BIC2	Entropy
4	4333	-11550175	-11550206	-11550066	-11550045			0.903
5	<b>43333</b>	<b>-11472689</b>	<b>-11472728</b>	<b>-11472555</b>	<b>-11472529</b>	<b>23891</b>	<b>23890</b>	<b>0.898</b>
6	433333	-11433127	-11433174	-11432967	-11432936	25155	25154	0.889
7	4333333	-11401437	-11401491	-11401252	-11401216	24975	24974	0.883

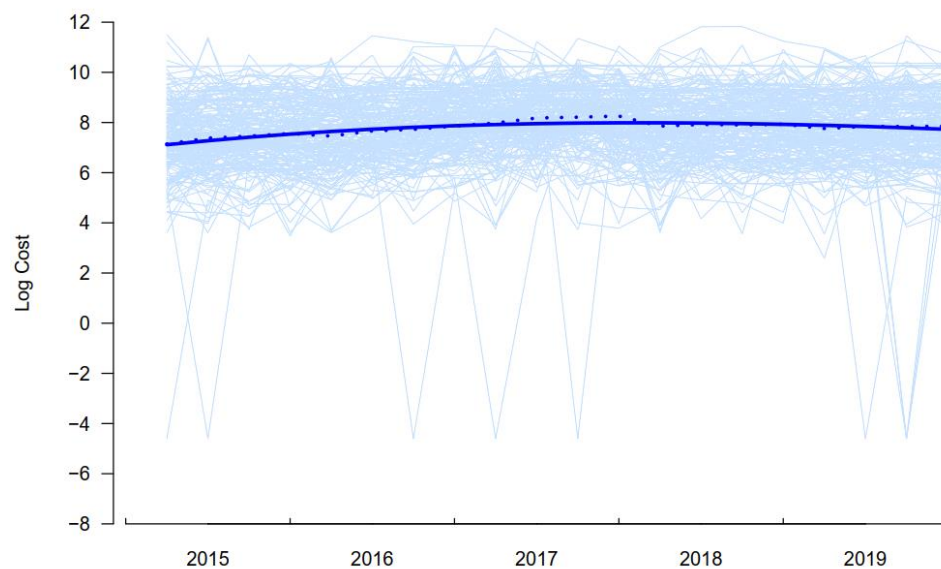
AIC: Akaike information criteria; BIC: Bayesian information criteria; LL: log-likelihood  
\* bolded model was selected as the base case

Table A2. Average and predicted values (with 95 % confidence intervals) for the five-group trajectory model, by time period

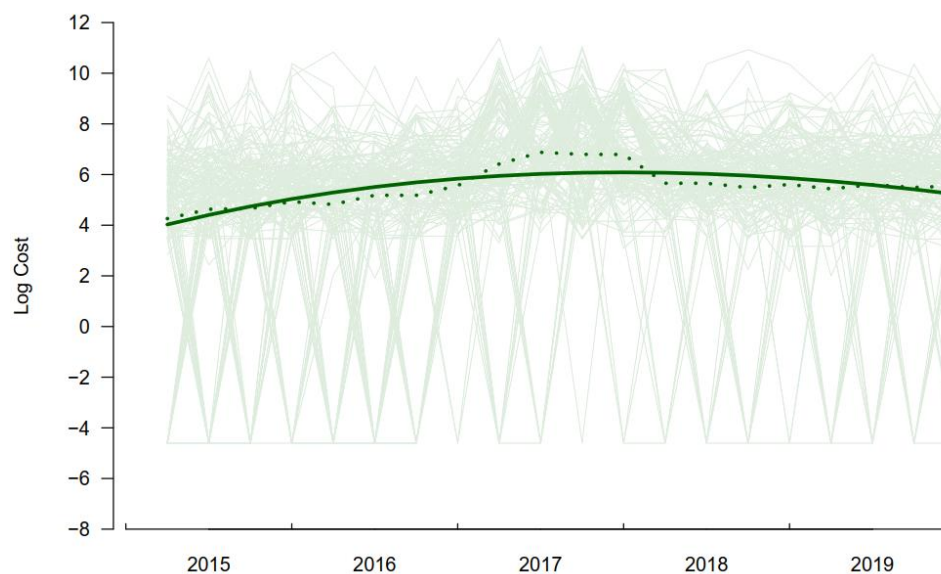
Time period	Persistent very-high cost				Persistent high cost				Rising cost				Declining cost				Cost spike			
	Avg.	Pred.	2.5%	97.5%	Avg.	Pred.	2.5%	97.5%	Avg.	Pred.	2.5%	97.5%	Avg.	Pred.	2.5%	97.5%	Avg.	Pred.	2.5%	97.5%
1	7.14	7.12	7.10	7.13	4.26	4.03	4.00	4.05	-1.97	-2.25	-2.29	-2.21	3.15	2.47	2.42	2.52	-1.74	-0.89	-0.95	-0.82
2	7.38	7.27	7.26	7.29	4.63	4.40	4.38	4.43	-1.87	-1.86	-1.90	-1.83	3.76	3.46	3.42	3.49	-2.05	-2.22	-2.25	-2.18
3	7.46	7.41	7.40	7.42	4.65	4.74	4.72	4.76	-1.91	-1.35	-1.38	-1.32	3.99	4.21	4.18	4.24	-2.40	-2.55	-2.58	-2.52
4	7.56	7.54	7.53	7.55	4.93	5.03	5.02	5.05	-1.45	-0.74	-0.77	-0.70	4.29	4.75	4.72	4.78	-2.38	-2.29	-2.33	-2.26
5	7.46	7.64	7.63	7.65	4.82	5.29	5.28	5.31	-0.88	-0.03	-0.06	0.00	4.24	5.09	5.07	5.12	-2.01	-1.61	-1.64	-1.57
6	7.67	7.73	7.72	7.74	5.18	5.51	5.49	5.52	0.01	0.74	0.71	0.77	4.45	5.25	5.23	5.28	-1.46	-0.62	-0.65	-0.58
7	7.73	7.81	7.80	7.82	5.18	5.69	5.68	5.70	0.67	1.55	1.53	1.58	4.31	5.25	5.23	5.28	-0.86	0.49	0.46	0.52
8	7.86	7.87	7.86	7.88	5.56	5.84	5.82	5.85	1.90	2.37	2.35	2.39	4.69	5.10	5.08	5.13	0.26	1.51	1.49	1.54
9	7.98	7.92	7.91	7.93	6.42	5.95	5.93	5.96	3.90	3.17	3.15	3.19	6.03	4.83	4.81	4.85	2.98	2.30	2.28	2.33
10	8.18	7.95	7.94	7.96	6.88	6.03	6.01	6.04	5.48	3.92	3.90	3.94	6.20	4.45	4.43	4.47	4.35	2.76	2.73	2.78
11	8.21	7.98	7.97	7.99	6.80	6.07	6.06	6.08	6.17	4.60	4.59	4.62	5.34	3.97	3.95	4.00	4.20	2.83	2.80	2.85
12	8.26	7.99	7.98	8.00	6.79	6.09	6.07	6.10	6.69	5.20	5.18	5.21	4.41	3.43	3.40	3.45	3.54	2.51	2.49	2.54
13	7.86	7.99	7.98	8.00	5.66	6.07	6.06	6.08	5.32	5.67	5.65	5.69	2.30	2.83	2.80	2.85	0.68	1.85	1.82	1.88
14	7.92	7.98	7.97	7.99	5.66	6.03	6.01	6.04	5.27	6.01	5.99	6.03	1.44	2.19	2.16	2.22	-0.32	0.94	0.91	0.97
15	7.90	7.96	7.95	7.97	5.48	5.96	5.94	5.97	5.17	6.19	6.17	6.21	0.54	1.54	1.50	1.57	-1.16	-0.08	-0.12	-0.05
16	7.93	7.93	7.92	7.94	5.61	5.86	5.84	5.87	5.38	6.19	6.17	6.21	0.19	0.89	0.86	0.93	-1.38	-1.02	-1.06	-0.98
17	7.76	7.89	7.88	7.90	5.44	5.73	5.72	5.75	5.28	5.98	5.96	6.00	-0.27	0.27	0.23	0.31	-1.54	-1.69	-1.73	-1.65
18	7.85	7.84	7.83	7.85	5.60	5.59	5.57	5.60	5.35	5.55	5.53	5.57	-0.48	-0.30	-0.35	-0.26	-1.42	-1.93	-1.96	-1.89
19	7.84	7.79	7.78	7.80	5.49	5.42	5.40	5.43	5.05	4.87	4.84	4.90	-0.82	-0.81	-0.87	-0.76	-1.31	-1.52	-1.56	-1.48
20	7.85	7.73	7.71	7.75	5.55	5.22	5.20	5.25	4.80	3.92	3.88	3.95	-0.74	-1.24	-1.31	-1.17	-0.79	-0.06	-0.12	0.00

**Figure A2. Mean trajectories for each latent group alongside individual trajectories (1% sample)**

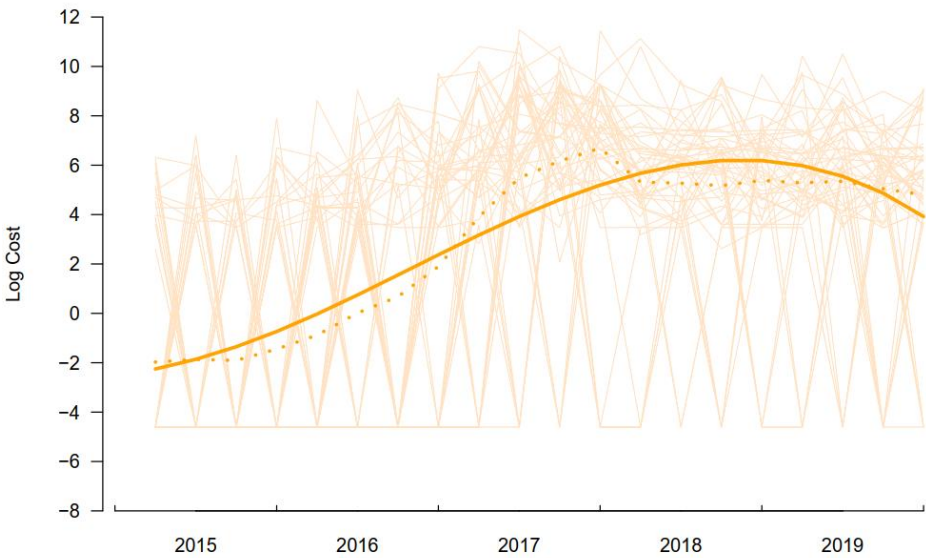
**Group 1: Persistent very-high-cost**



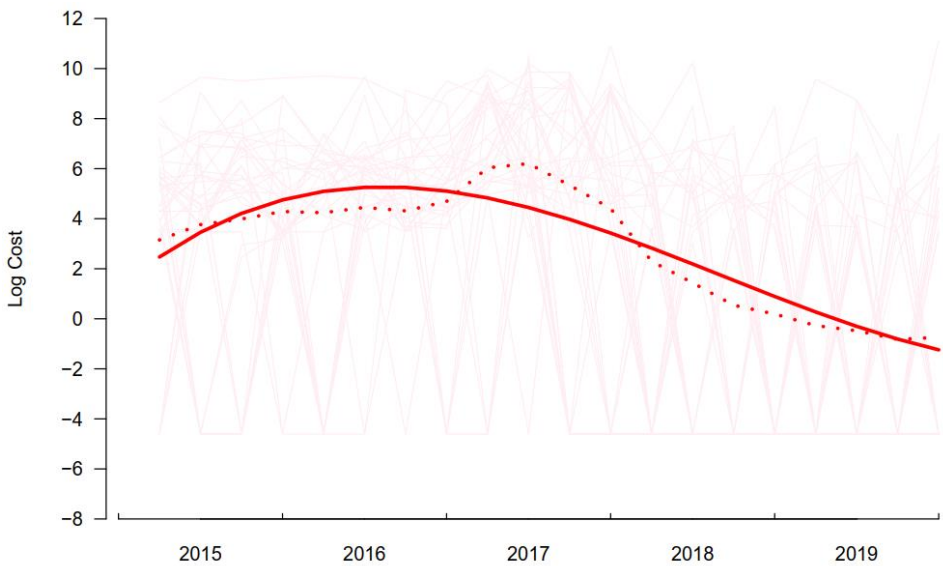
**Group 2: Persistent high-cost**



**Group 3: Rising cost**



**Group 4: Declining cost**



Group 5: Cost spike

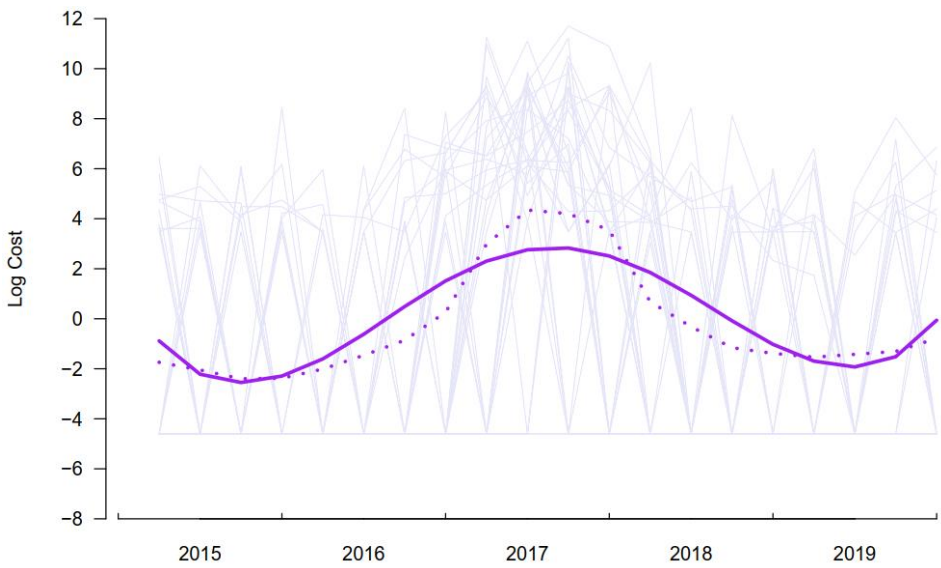


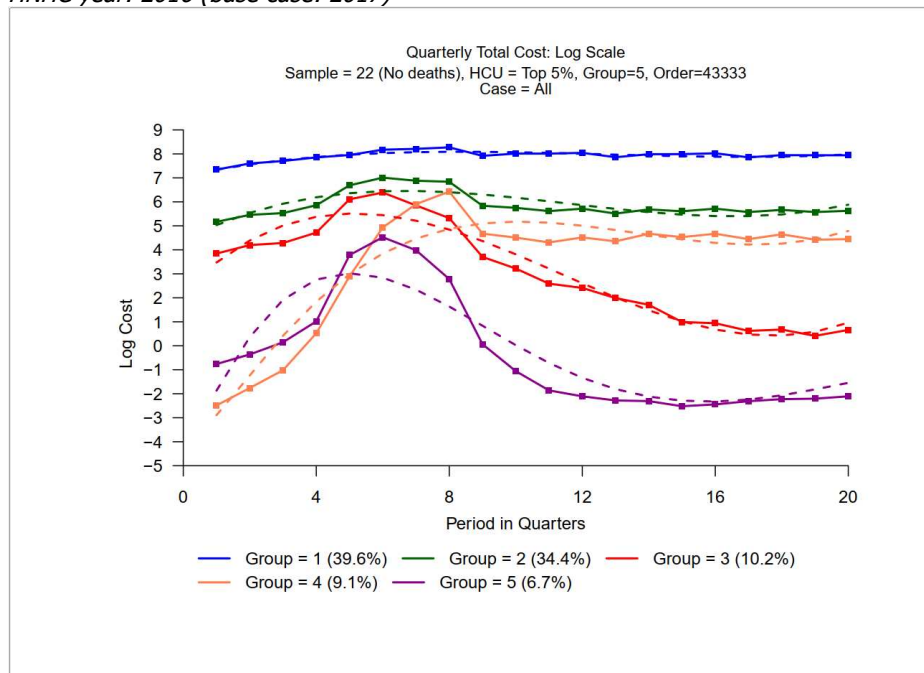


Table A3. Parameters for five-group trajectory model

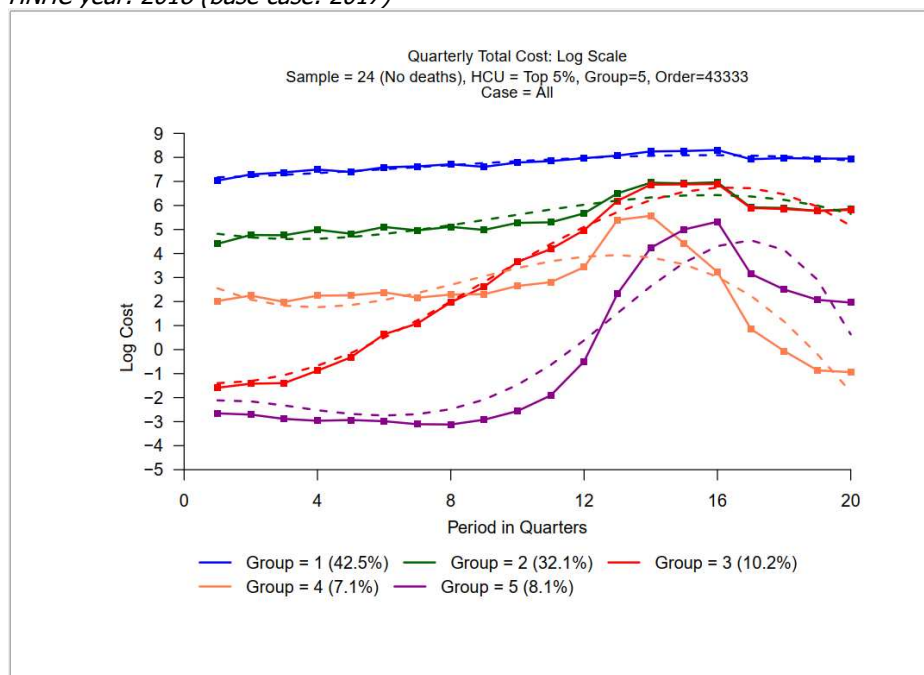
Group	Parameter	Estimate	SE	t-value	pvalue
Cost spike	Intercept	2.1234	0.0414	51.2940	0.0000
Cost spike	Linear	-4.0860	0.0258	-158.1330	0.0000
Cost spike	Quadratic	0.9875	0.0048	205.4800	0.0000
Cost spike	Cubic	-0.0751	0.0003	-221.7470	0.0000
Cost spike	Quartic	0.0018	0.0000	222.7400	0.0000
Rising cost	Intercept	-3.0978	0.0258	-120.2160	0.0000
Rising cost	Linear	0.3070	0.0106	29.0050	0.0000
Rising cost	Quadratic	0.0768	0.0012	65.9070	0.0000
Rising cost	Cubic	-0.0037	0.0000	-102.8930	0.0000
Declining cost	Intercept	1.2173	0.0329	37.0040	0.0000
Declining cost	Linear	1.3766	0.0129	106.9220	0.0000
Declining cost	Quadratic	-0.1352	0.0014	-94.6240	0.0000
Declining cost	Cubic	0.0030	0.0000	66.4530	0.0000
Persistent high-cost	Intercept	3.6075	0.0166	216.9270	0.0000
Persistent high-cost	Linear	0.4412	0.0055	80.1070	0.0000
Persistent high-cost	Quadratic	-0.0218	0.0006	-36.9620	0.0000
Persistent high-cost	Cubic	0.0002	0.0000	10.2930	0.0000
Persistent very-high-cost	Intercept	6.9499	0.0112	620.3540	0.0000
Persistent very-high-cost	Linear	0.1873	0.0042	44.0910	0.0000
Persistent very-high-cost	Quadratic	-0.0095	0.0005	-20.5020	0.0000
Persistent very-high-cost	Cubic	0.0001	0.0000	7.3060	0.0000

**Figure A3. Five-group trajectory model of HNHC patients based on alternative HNHC years (Sensitivity analysis 1)**

*HNHC year: 2016 (base case: 2017)*

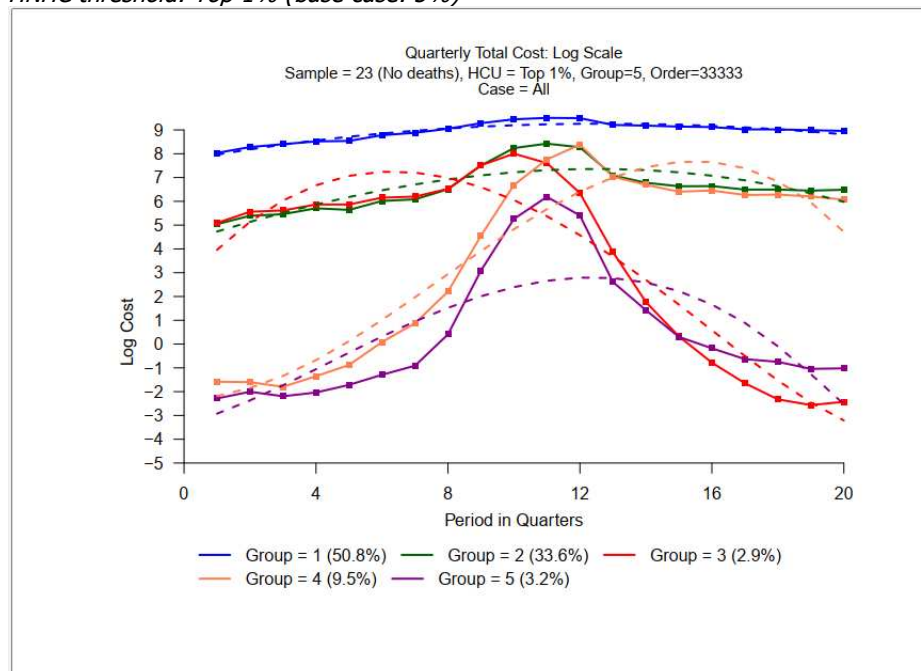


*HNHC year: 2018 (base case: 2017)*



**Figure A4. Five-group trajectory model of HNHC patients based on alternative HNHC thresholds (Sensitivity analysis 2)**

*HNHC threshold: Top 1% (base case: 5%)*



*HNHC threshold: Top 10% (base case: 5%)*

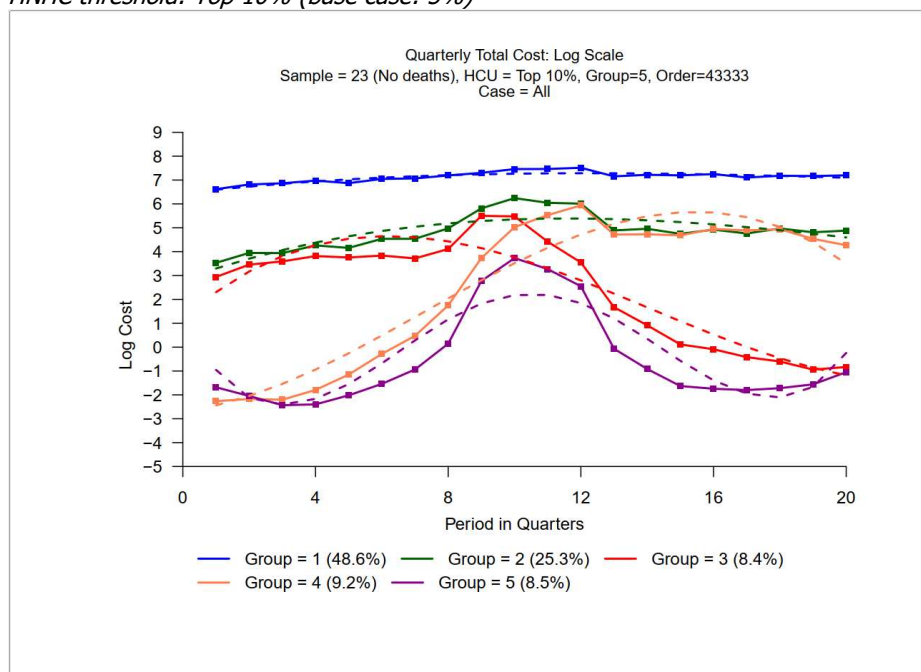


Table A4. Demographic and clinical characteristics (proportion) by trajectory group

	Persistently very-high-cost	Persistently high-cost	Rising cost	Declining cost	Cost spike
Age Group					
0-44	20.0%	26.0%	44.0%	53.0%	65.0%
45-64	31.0%	34.0%	36.0%	28.0%	26.0%
65-74	20.0%	24.0%	14.0%	11.0%	6.0%
≥75	30.0%	16.0%	6.2%	7.8%	2.1%
Sex					
Male	44.0%	44.0%	51.0%	38.0%	48.0%
Female	56.0%	56.0%	49.0%	62.0%	52.0%
Income Quintile					
1st	28.0%	20.0%	17.0%	21.0%	17.0%
2nd	21.0%	19.0%	16.0%	20.0%	17.0%
3rd	19.0%	19.0%	16.0%	19.0%	16.0%
4th	17.0%	20.0%	16.0%	19.0%	16.0%
5th	14.0%	19.0%	15.0%	17.0%	15.0%
Missing	1.5%	2.4%	21.0%	3.4%	19.3%
Geographic Region					
Metropolitan	56.0%	52.0%	43.0%	51.0%	42.0%
Non-metropolitan (hub hospital)	37.0%	38.0%	30.0%	37.0%	30.0%
Non-metropolitan (small/no hospital)	6.5%	7.8%	7.2%	8.7%	8.4%
Remote	0.2%	0.5%	0.5%	0.6%	0.8%
Missing	0.4%	1.3%	20.0%	2.1%	18.0%
Comorbidities (Elixhauser)					
0	27.0%	40.0%	42.0%	61.0%	68.0%
1	19.0%	28.0%	28.0%	20.0%	20.0%
2	17.0%	16.0%	16.0%	9.4%	7.9%
3	13.0%	8.1%	7.6%	4.7%	2.8%
≥4	24.0%	6.8%	6.8%	5.0%	1.6%

**Table A5. Factors associated with group membership (adjusted odds ratio and 95% confidence interval) from multivariate multinomial logistic regression**

	Persistently very-high-cost	Persistently high-cost	Rising cost	Declining cost	Cost spike
Age (per 10 years)	Ref	0.87 (0.87, 0.88)*	0.69 (0.68, 0.69)*	0.69 (0.68, 0.70)*	0.59 (0.58, 0.60)*
Male (ref: female)		1.10 (1.08, 1.13)*	1.70 (1.64, 1.76)*	1.07 (1.03, 1.11)*	1.89 (1.81, 1.97)*
Rural region (ref: metropolitan)		1.16 (1.13, 1.18)*	1.16 (1.13, 1.20)*	1.23 (1.18, 1.27)*	1.28 (1.23, 1.34)*
Lowest neighborhood income quintile		0.72 (0.70, 0.74)*	0.78 (0.75, 0.81)*	0.78 (0.75, 0.81)*	0.77 (0.74, 0.81)*
Comorbidities (count; ref=0)					
One		1.34 (1.29, 1.39)*	1.37 (1.29, 1.46)*	0.63 (0.59, 0.68)*	0.66 (0.59, 0.74)*
Two		1.18 (1.11, 1.24)*	1.09 (0.99, 1.21)	0.40 (0.36, 0.45)*	0.36 (0.30, 0.45)*
Three		0.97 (0.90, 1.04)	0.84 (0.73, 0.97)*	0.29 (0.25, 0.34)*	0.20 (0.15, 0.27)*
Four		0.69 (0.62, 0.77)*	0.59 (0.48, 0.72)*	0.22 (0.17, 0.28)*	0.12 (0.07, 0.19)*
Comorbidities					
Congestive Heart Failure		0.83 (0.79, 0.88)*	1.30 (1.19, 1.43)*	1.01 (0.89, 1.14)	1.05 (0.85, 1.28)
Chronic Pulmonary Disease		0.51 (0.48, 0.53)*	0.41 (0.37, 0.45)*	0.67 (0.60, 0.75)*	0.36 (0.30, 0.44)*
Diabetes		0.65 (0.63, 0.68)*	0.40 (0.37, 0.43)*	0.56 (0.51, 0.62)*	0.31 (0.26, 0.36)*
Hypothyroidism		0.89 (0.79, 1.01)	0.89 (0.71, 1.12)	1.28 (1.00, 1.62)*	0.84 (0.54, 1.28)
Renal Failure		0.49 (0.46, 0.51)*	0.40 (0.36, 0.45)*	0.62 (0.55, 0.70)*	0.27 (0.21, 0.36)*
Liver Disease		0.77 (0.71, 0.84)*	1.03 (0.92, 1.17)	0.93 (0.80, 1.08)	0.98 (0.80, 1.21)
Peptic Ulcer Disease		0.87 (0.79, 0.96)*	0.80 (0.68, 0.96)*	0.89 (0.71, 1.10)	0.78 (0.56, 1.07)
AIDS/HIV		0.63 (0.48, 0.84)*	0.43 (0.26, 0.71)*	0.55 (0.30, 1.01)	0.38 (0.15, 0.98)*
Lymphoma		1.29 (1.14, 1.46)*	1.54 (1.28, 1.87)*	1.00 (0.74, 1.35)	0.77 (0.51, 1.18)
Metastatic Cancer		1.13 (1.04, 1.22)*	1.57 (1.40, 1.76)*	1.36 (1.15, 1.61)*	1.35 (1.07, 1.70)*
Cardiac Arrhythmia		1.01 (0.97, 1.05)	1.00 (0.93, 1.08)	1.23 (1.12, 1.34)*	1.05 (0.91, 1.22)
Solid Tumor without Metastasis		1.47 (1.40, 1.53)*	2.12 (1.96, 2.28)*	1.42 (1.28, 1.57)*	1.72 (1.48, 1.98)*
Rheumatoid Arthritis		0.30 (0.27, 0.33)*	0.19 (0.15, 0.24)*	0.32 (0.25, 0.41)*	0.14 (0.09, 0.21)*

Coagulopathy		0.80 (0.73, 0.88)*	0.87 (0.75, 1.01)	1.14 (0.96, 1.36)	0.99 (0.77, 1.28)
Obesity		1.03 (0.94, 1.12)	0.61 (0.51, 0.72)*	1.67 (1.45, 1.93)*	0.93 (0.74, 1.17)
Weight Loss		0.62 (0.57, 0.67)*	0.80 (0.69, 0.92)*	0.85 (0.72, 1.02)	0.86 (0.67, 1.11)
Fluid/Electrolyte Disorders		0.72 (0.69, 0.75)*	0.78 (0.72, 0.84)*	0.94 (0.86, 1.03)	0.96 (0.83, 1.11)
Blood Loss Anemia		0.82 (0.72, 0.93)*	1.01 (0.81, 1.24)	1.05 (0.81, 1.37)	1.41 (1.00, 1.98)*
Deficiency Anemia		0.79 (0.74, 0.84)*	0.81 (0.72, 0.92)*	0.97 (0.84, 1.11)	0.86 (0.70, 1.06)
Alcohol Abuse		1.47 (1.39, 1.56)*	1.69 (1.54, 1.84)*	2.21 (1.99, 2.45)*	2.49 (2.16, 2.88)*
Drug Abuse		0.47 (0.44, 0.49)*	0.48 (0.44, 0.52)*	0.69 (0.63, 0.76)*	0.49 (0.43, 0.57)*
Valvular Disease		1.16 (1.08, 1.25)*	1.11 (0.97, 1.26)	1.14 (0.96, 1.35)	1.11 (0.84, 1.46)
Mental		0.47 (0.45, 0.49)*	0.57 (0.53, 0.61)*	0.54 (0.49, 0.59)*	0.54 (0.47, 0.61)*
Pulmonary Circulation Disorders		0.89 (0.82, 0.96)*	1.23 (1.08, 1.39)*	0.94 (0.79, 1.12)	1.26 (1.00, 1.58)*
Hypertension		1.15 (1.11, 1.20)*	1.36 (1.27, 1.46)*	1.23 (1.12, 1.34)*	1.27 (1.11, 1.47)*
Paralysis		0.82 (0.75, 0.89)*	1.58 (1.40, 1.79)*	0.98 (0.81, 1.19)	0.94 (0.72, 1.24)
Other Neurological Disorders		0.49 (0.46, 0.52)*	0.51 (0.46, 0.56)*	0.55 (0.49, 0.63)*	0.31 (0.25, 0.37)*

**Figure A5. Forest plot of factors associated with group membership, relative to the 'very-high-cost' trajectory group, from multinomial logistic regression with *forward variable selection* (adjusted Odds Ratios, 95% CI)**

