Characterizing the individual course of HrQoL after subarachnoid hemorrhage:
a latent growth mixture model

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Objective

- Methodological approaches to reflect individual differences are limited
- Clinical trials do not consider interindividual differences
- Linear models assume the average trajectory of disease course
- Latent growth mixture model (LGMM) for a chronic disease (Parkinson) in a previous study (Klotsche et al.2011)

Objective: To characterize individual differences in course of HrQoL after subarachnoid hemorrhage by using LGMM

Methods: Design

Study design: Longitudinal HrQoL-study

Study center: Depts. of Neurology, Neurosurgery and Radiology, University of Bonn, Germany

Study population: 113 incident patients with aneurysmal subarachnoid hemorrhage

Study visits: Baseline (hospital), 6 and 12 months after discharge

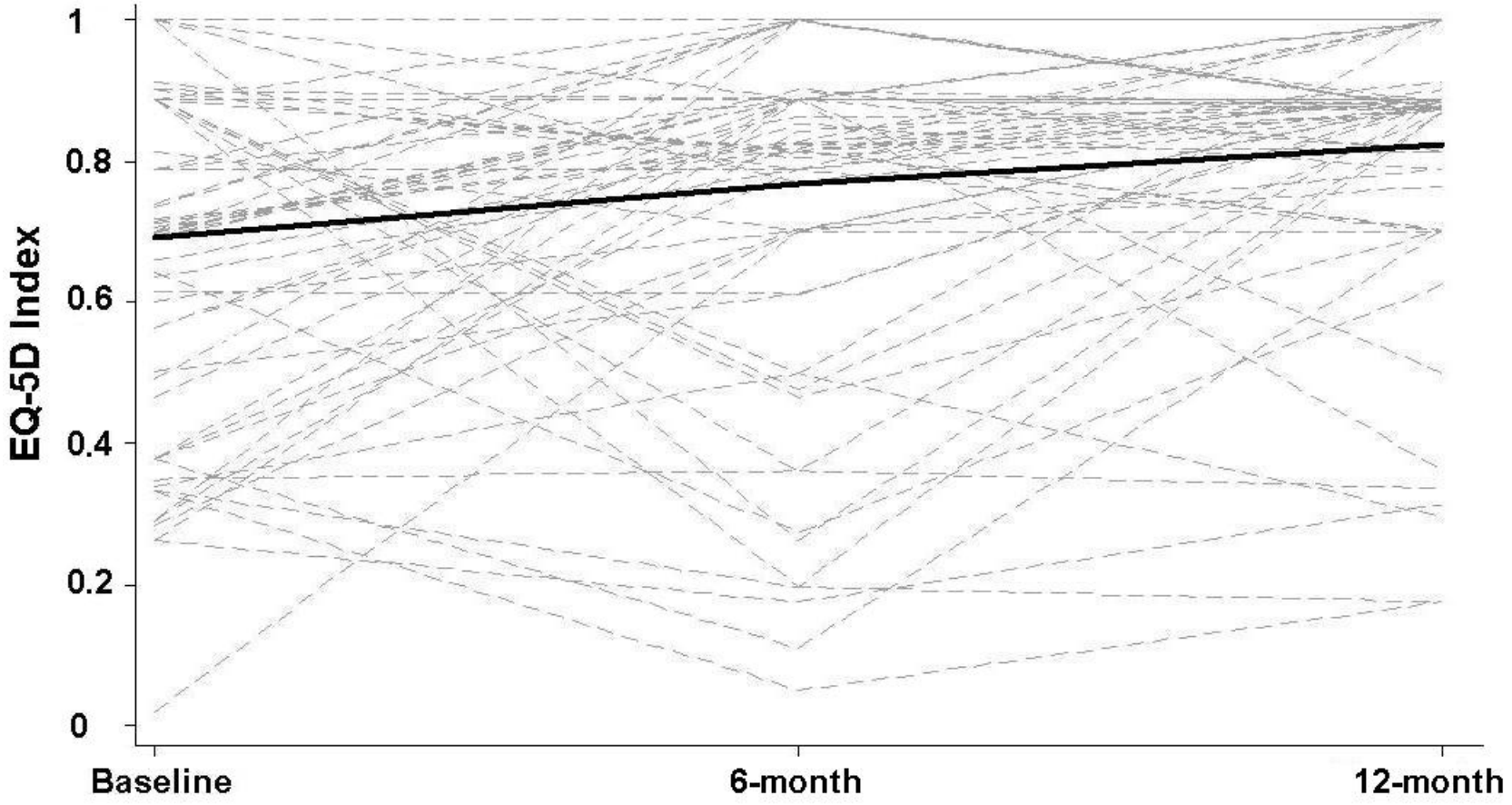
Clinical parameters: Stroke severity scales (Hunt and Hess scale, Barthel-Index, Rankin Scale), depression (Beck Depression Inventory), cognitive impairment (Mini Mental State Examination)

HrQoL evaluation: EuroQol (EQ-5D, EQ VAS)

Data analysis: Latent growth mixture modeling using MPLUS 5.21

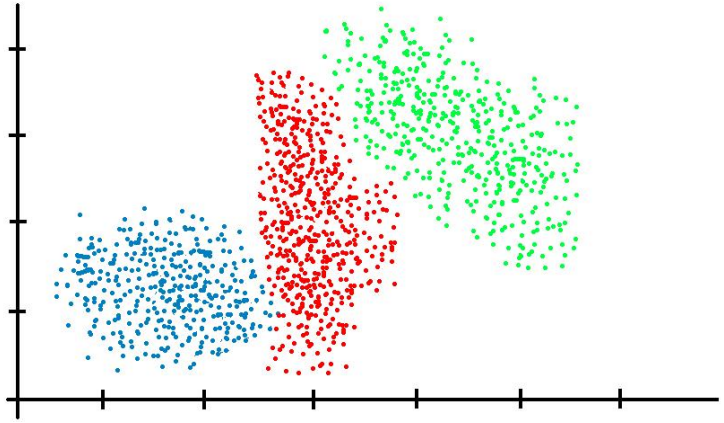
Methods: Latent growth mixture modeling

Growth model: growth function with fixed parts (average development) and random parts (individual variations)



Latent growth mixture modeling (LGMM)

Mixture modeling – modeling a distribution by a mixture of other distributions (subgroups)



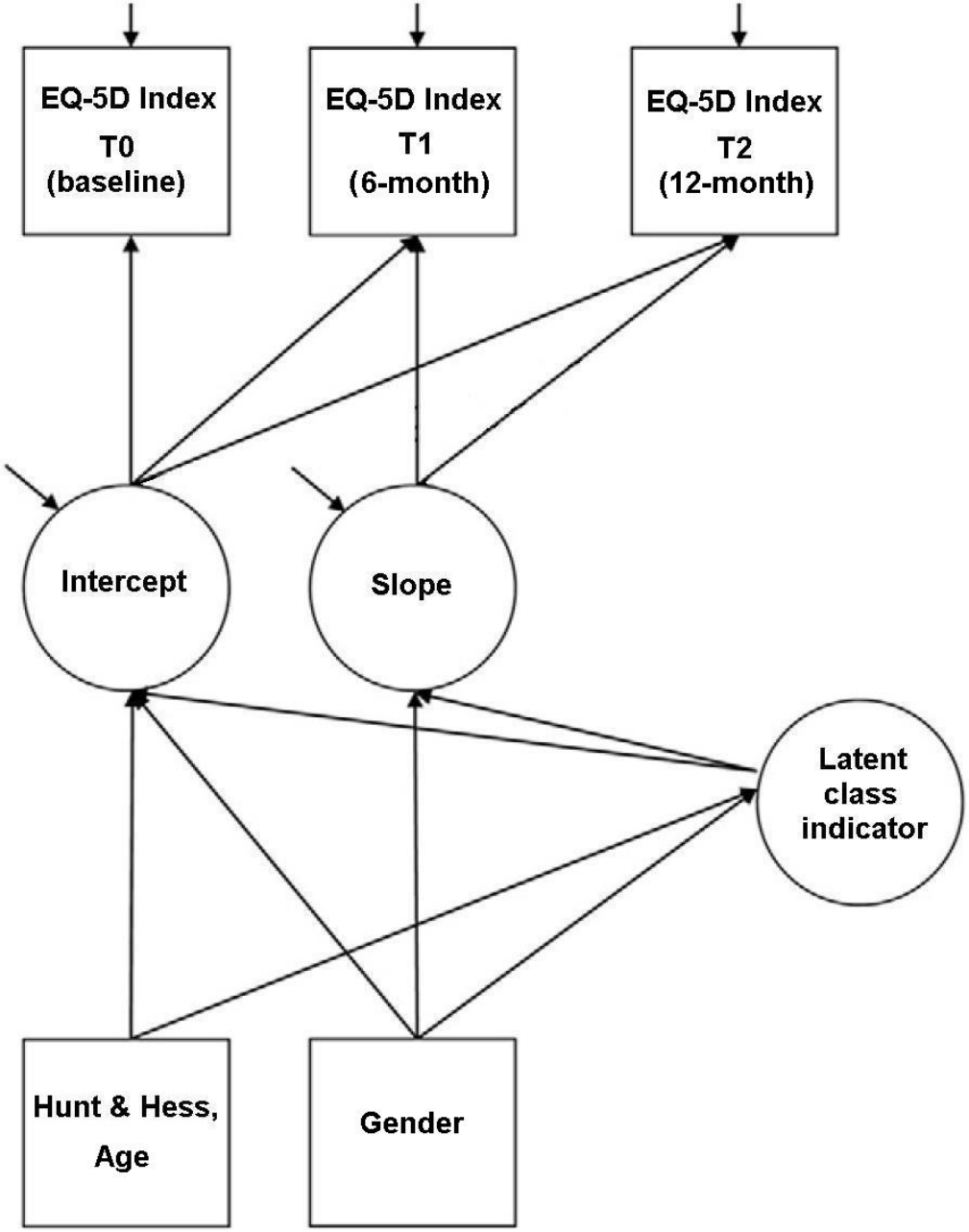
Growth modeling + Mixture modeling = LGMM

...if there is enough homogenity in data heterogeneity to identify classes, which differ according to initial values and their changes over time

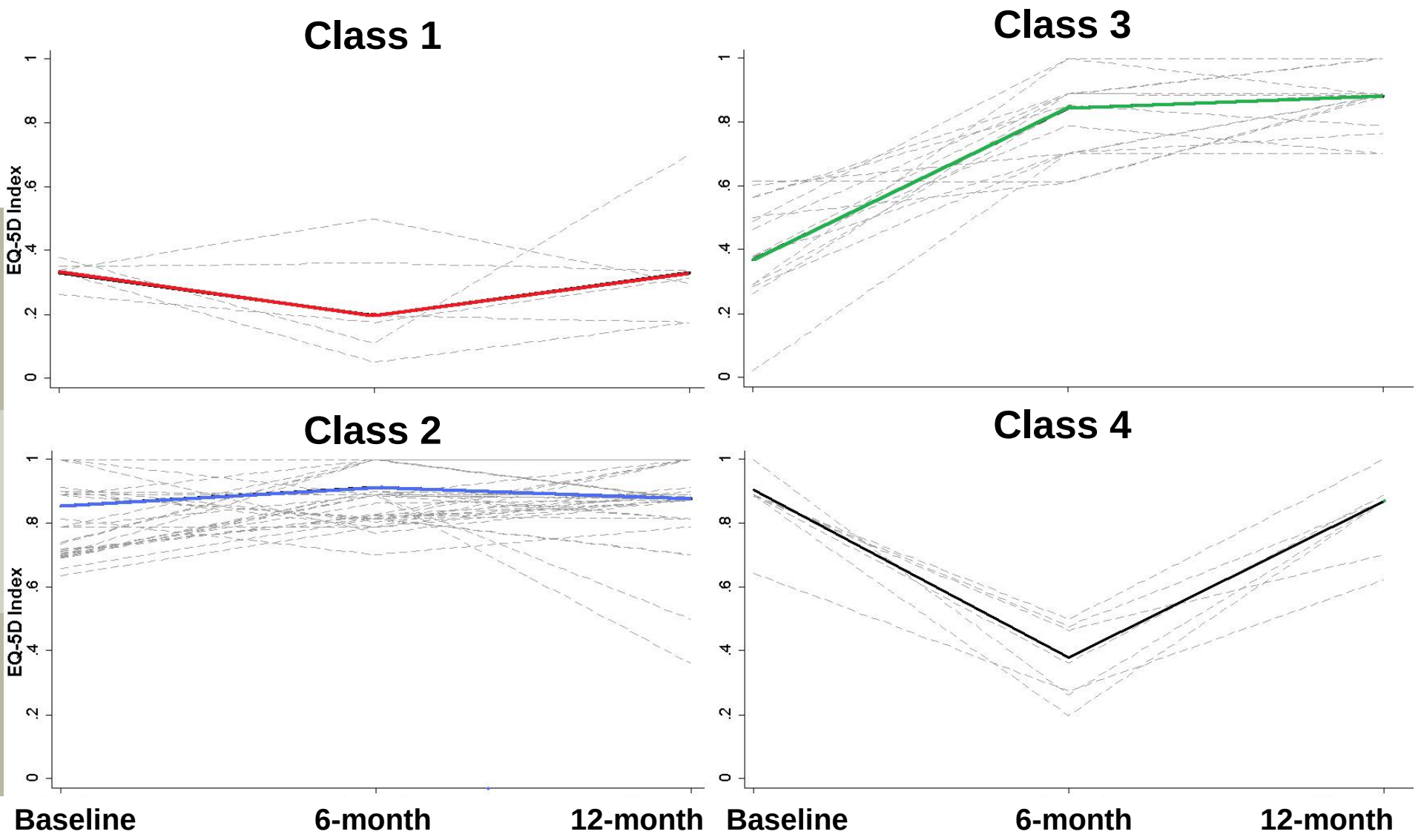
LGMM: Model structure

Parameters of latent classes:

- **Intercept:** baseline score of EQ-5D index
- **Slope** (growth factor): rate of change over time



Results: Latent classes (EQ-5D Index)



Results: Four-class model

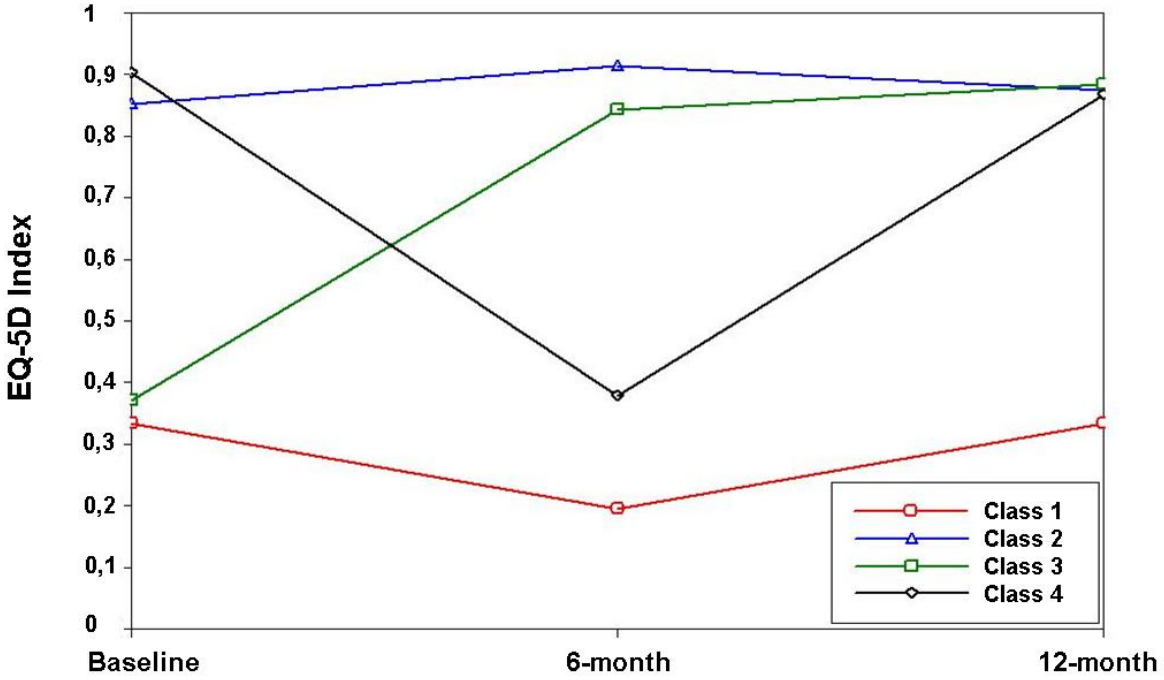
Four-class model: Number of classes was defined based on analysis of the fit indices and visual comparison of individual trajectories with the mean growth curve

Fit indices for models with different number of classes

classes	BIC	aBIC	Entropy	BLRT
1	39.2	20.3		
2	7.3	-24.2	0.923	0.001
3	7.2	-36.9	0.784	0.092
4	0.8	-55.9	0.772	0.038
5	3.1	-66.2	0.766	0.981

BIC: Bayesian information criteria; aBIC: Sample-size adjusted Bayesian information criteria; BLRT: Bootstrapped likelihood ratio test

Results: Parameter estimates of latent classes



EQ-5D index	Class 1 (n=9)		Class 2 (n=69)		Class 3 (n=25)		Class 4 (n=10)	
	beta	95% CI	beta	95% CI	beta	95% CI	beta	95% CI
at baseline	**0.33**	0.28 - 0.39	**0.85**	0.81 - 0.90	**0.37**	0.29 - 0.45	**0.90**	0.87 - 0.94
Δ T0 - T1	-0.14	-0.35 - 0.07	**0.06**	0.00 - 0.12	**0.47**	0.38 - 0.56	**-0.53**	-0.65 - -0.40
Δ T1 - T2	0.14	-0.12 - 0.39	-0.04	-0.10 - 0.02	0.04	-0.02 - 0.10	**0.49**	0.34 - 0.64

bold highlighted beta coefficients are significant at the 5% level
Abbreviations: T0, baseline; T1, 6-month time point; T2, 12-month time point; CI, confidence intervals

Results: Clinical characteristics of latent classes

	Class 1 mean (SD)	Class 2 mean (SD)	Class 3 mean (SD)	Class 4 mean (SD)	p Value Class 1 versus Cl. 2/ Cl. 3 / Cl. 4	p Value Class 2 versus Cl. 3 / Cl. 4	p Value Class 3 versus Cl. 4
H&H at admission	3.5 ± 0.5	2.7 ± 1.1	3.2 ± 0.9	2.6 ± 0.76	**0.04**/ 0.13/ **0.03**	**0.04**/ 0.58	**0.03**
H&H 1-2, N (%)	0 (0.0)	18 (39.2)	4 (22.2)	3 (42.9)			
H&H 3-5, N (%)	6 (100.0)	28 (60.8)	14 (77.8)	4 (57.1)			
Barthel-Index							
discharge	35.83 ± 25.58	70.28 ± 25.12	64.08 ± 35.19	92.14 ± 4.88	**0.04**/ **0.01**/ **<0.01**	**0.04**/ **0.03**	**<0.01**
6-month	76.00 ± 19.81	91.21 ± 8.10	87.00 ± 13.20	87.86 ± 6.99	**0.03**/ **0.04**/ **0.04**	0.68/ 0.11	0.37
12-month	61.00 ± 27.02	85.00 ± 18.8	81.92 ± 26.02	91.67 ± 5.77	**0.01**/ **0.04**/ **0.03**	0.70/ 0.71	0.55
BDI							
discharge	4.00 ± 0.00	6.54 ± 4.68	9.82 ± 6.62	7.33 ± 5.16	**0.04**/ **0.03**/ **0.04**	0.13/ 0.58	**0.04**
6-month	13.20 ± 5.07	7.76 ± 4.99	9.67 ± 5.78	11.00 ± 6.25	**0.02**/ **0.04**/ 0.48	0.26/ **0.04**	**0.04**
12-month	19.75 ± 9.60	7.76 ± 3.89	9.20 ± 7.58	7.67 ± 2.08	**0.01**/ **0.03**/ **0.03**	0.95/ 0.94	0.12
MMSE							
discharge	13.40 ± 8.17	24.17 ± 9.39	24.80 ± 7.32	27.17 ± 3.31	**<0.01**/ **0.02**/ **<0.01**	0.86/ 0.92	0.85
6-month	26.00 ± 6.82	28.36 ± 2.10	27.87 ± 2.90	27.86 ± 1.22	0.41/ 0.53/ 0.52	0.46/ 0.46	0.52
12-month	26.40 ± 4.34	27.97 ± 2.68	29.33 ± 0.89	29.33 ± 1.15	0.41/ 0.12/ 0.13	0.23/ 0.23	0.12

Abbreviations: Cl., Class; H&H, Hunt and Hess scale; mRS, modified Rankin scale; BDI, Beck Depression Inventory; MMSE, Mini-mental state examination

Results: Explorative analysis of EQ-5D Index

		Estimated EQ-5D Index score			
	BDI	Class 1	Class 2	Class 3	Class 4
6-month	2	0,54	0,95	0,85	0,44
	3	0,51	0,95	0,85	0,43
	9	0,30	0,92	0,81	0,38
	10	0,27	0,91	0,80	0,37
	19	0,12	0,86	0,75	0,29
	20	0,09	0,86	0,74	0,28
12-month	2	0,90	0,92	0,91	0,91
	3	0,86	0,91	0,91	0,90
	9	0,66	0,88	0,87	0,85
	10	0,62	0,88	0,86	0,84
	19	0,31	0,83	0,81	0,76
	20	0,28	0,82	0,80	0,75

Conclusions

1. LGMM was at first applied to analyse longitudinal data in an acute disease

2. It is a promising and flexible approach to analyse longitudinal data in HrQol-studies

3. LGMM considers individual patterns of disease course over time

4. It could help to identify treatment responders and to develop individual therapy regimes

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