Quality of life near the end-of-life: the relationship between self-rated overall health and the five EQ-5D domains

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Introduction

- Valuation of health states varies between individuals according to various factors and over time with aging.[1,2,3]

- Patient's experienced assessment of their well-being maybe a more appropriate measure of quality of life.[4]

- As patients near the end of life (EoL) HRQoL measures (such as the EQ-5D) may not adequately capture domains of importance.[5]

- Longitudinal, questionnaire based data, collected in the Dutch Bone Metastasis Study (DBMS) is used.[6]

- **We aim to investigate the relationship between the measured domains of the EQ-5D and patient's self-rated overall health with proximity to death.**

Methods

- EQ-5D questionnaires completed by 849 patients in the DBMS were used. Questionnaires were at baseline, weekly (for 12 weeks) and subsequently monthly for up to two years.

- The number of completed questionnaires ranged from 1 to 35 (median 11). 23.5% of individuals returned less than 5 questionnaires.

- The fitted model was as follows:

$$EQVAS_{it} = \alpha + \beta_1 Mobility_{it} + \beta_2 Selfcare_{it} + \beta_3 Activity_{it} + \beta_4 Pain_{it} + \beta_5 Anxiety_{it} + \gamma TTD_{it} + \delta_1 Mobility_{it} \times TTD_{it} + \ldots + \delta_5 Anxiety_{it} \times TTD_{it} + c_i + \mu_{it}$$

- A generalised least squares, fixed effects model was used guided by the Hausman test (p<0.001).

- Time to death was incorporated using a restricted cubic spline with 4 knots placed at 1, 6, 27 and 77 weeks.

- Robustness checks assessed the consequences of heterogeneity and unbalanced panels.

Results

- Median survival was 18.9 weeks (95% CI 16.9-20.3 weeks).

- Mean EQ-VAS was 45.9 (SD 23.8).

- EQ-VAS varied with proximity to the EoL from 53.4 (SD 22.7) 24-52 weeks from death to 33.1 (SD 22.7) in the final six weeks of life.

- Missingness increased with proximity to the EoL from 8.67% more than two years from the EoL up to 56% in in the last 6 weeks of life. No difference was observed between domains in relation to missingness (table 1).

Table 1. EQ-5D levels at varying time to death.

	Full sample		<6 wks		6w-3 mths		3-6 mths		6-9 mths		9-12 mths		1-2 years		>2 yrs	
Mobility																
No problems	3,974	47%	265	23%	621	38%	1,041	50%	640	51%	423	51%	890	62%	94	78%
Some problems	3,397	40%	478	41%	702	43%	810	39%	520	41%	373	45%	492	34%	22	18%
Severe problems	1,142	13%	424	36%	296	18%	227	11%	104	8%	30	4%	56	4%	5	4%
Missing	3,622		1,346		707		702		349		223		289		6	
Usual activities																
No problems	1,059	12%	37	3%	103	6%	300	14%	191	15%	146	18%	265	18%	17	13%
Some problems	3,254	38%	188	16%	487	30%	800	39%	582	46%	403	49%	740	51%	54	43%
Severe problems	4,190	49%	935	81%	1,026	63%	970	47%	488	39%	277	34%	438	30%	56	44%
Missing	3,632		1,353		710		710		352		223		284		0	
Anxiety/depression																
No problems	3,757	44%	390	33%	654	40%	965	46%	583	46%	431	52%	684	47%	50	39%
Some problems	4,141	48%	588	50%	829	51%	1,010	48%	622	49%	367	44%	657	45%	68	54%
Severe problems	696	8%	199	17%	147	9%	121	6%	64	5%	36	4%	120	8%	9	7%
Missing	3,541		1,336		696		684		344		215		266		0	
Pain/discomfort																
No problems	792	9%	50	4%	112	7%	201	10%	134	11%	98	12%	164	11%	33	26%
Some problems	6,080	71%	696	60%	1,111	68%	1,519	72%	905	71%	639	77%	1,126	77%	84	66%
Severe problems	1,721	20%	422	36%	410	25%	380	18%	231	18%	95	11%	173	12%	10	8%
Missing	3,542		1,345		693		680		343		217		264		0	
Self-care																
No problems	3,713	43%	201	17%	484	30%	931	44%	619	49%	465	56%	941	64%	72	57%
Some problems	3,600	42%	482	41%	833	51%	941	45%	542	43%	309	37%	444	30%	49	39%
Severe problems	1,295	15%	494	42%	318	19%	229	11%	108	9%	60	7%	80	5%	6	5%
Missing	3,527		1,336		691		679		344		215		262		0	
Total of observations	12,135		2,513		2,326		2,780		1,613		1,049		1,727		127	

- TTD remains a significant independent predictor of EQ-VAS.

- The pain/discomfort domain is associated with the largest decrement in the EQ-VAS, with mobility the smallest (table 2).

- The deterioration in EQ-VAS with proximity to death accelerates markedly in the final months of life (figure 1).
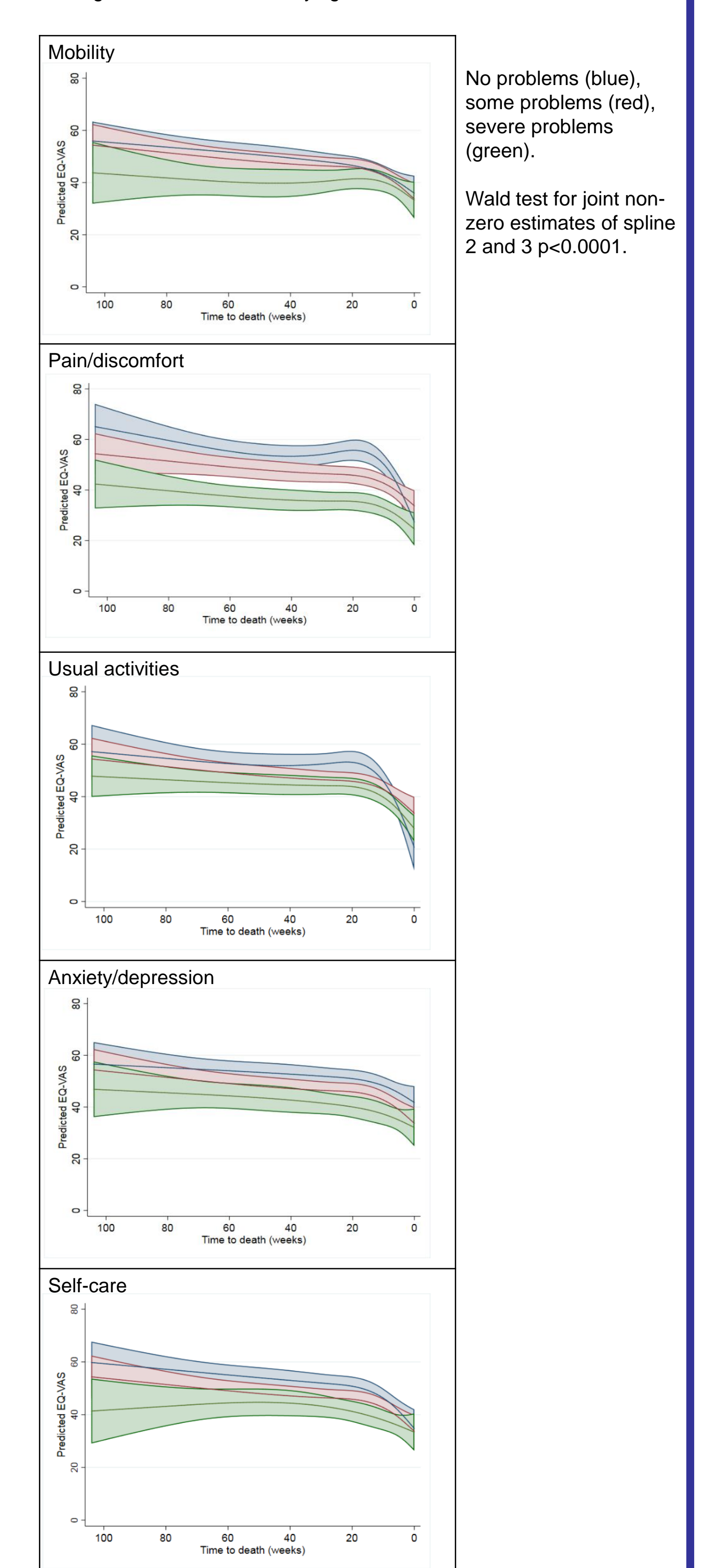
Table 2. Fixed effects model of EQ-VAS with EQ-5D domains and varying proximity to death

	TTD only		EQ-5D domains only		TTD and domains	
	Coef	SE	Coef	SE	Coef	SE
TTD - (1 week)	1.827***	0.174			1.209***	0.161
TTD - (6 weeks)	-22.965***	3.525			-16.277***	3.183
TTD - (27 weeks)	28.277***	4.483			20.102***	4.043
Mobility						
Some problems			-1.520*	0.719	-0.933	0.714
Severe problems			-5.242***	0.968	-3.957***	0.967
Pain						
Some problems			-6.652***	0.750	-6.717***	0.744
Severe problems			-17.062***	0.918	-16.931***	0.911
Usual activities						
Some problems			-4.011***	0.886	-3.793***	0.879
Severe problems			-7.595***	1.052	-6.795***	1.047
Anxiety/depression						
Some problems			-5.352***	0.598	-5.144***	0.593
Severe problems			-10.742***	1.018	-9.860***	1.012
Self-care						
Some problems			-5.455***	0.670	-4.660***	0.670
Severe problems			-9.753***	1.010	-7.522***	1.021
Constant	25.126***	0.723	68.738***	0.638	53.984***	1.036
R^2	0.087		0.348		0.346	

Table 3. Fixed effects model of EQ-VAS with EQ-5D domains interacted with varying proximity to death.
a) main effects

	Coef	SE		Coef	SE
TTD - (1 week)	4.546***	0.446			
TTD - (6 weeks)	-71.827***	8.72			
TTD - (27 weeks)	89.469***	11.052			
Mobility			**Self-care**		
Some problems	-2.217	2.875	Some problems	-1.052	2.914
Severe problems	-2.698	3.271	Severe problems	-1.388	3.477
Pain			**Anxiety/depression**		
Some problems	6.406	3.405	Some problems	-8.066***	1.971
Severe problems	-2.774	3.679	Severe problems	-9.673***	2.75
Usual activities					
Some problems	13.009***	4.324			
Severe problems	7.108	4.724			

b) Interaction terms

	Coef	SE		Coef	SE
Pain-Spline 1 interaction			**Anxiety-Spline 1 interaction**		
Some problems	-1.748***	0.427	Some problems	0.320	0.260
Severe problems	-1.809***	0.479	Severe problems	-0.173	0.408
Pain-Spline 2 interaction			**Anxiety-Spline 2 interaction**		
Some problems	31.681***	7.973	Some problems	-5.932	5.109
Severe problems	31.719***	9.186	Severe problems	3.731	8.472
Pain-Spline 3 interaction			**Anxiety-Spline 3 interaction**		
Some problems	-39.868***	10.061	Some problems	7.528	6.478
Severe problems	-39.852***	11.623	Severe problems	-4.723	10.789
Usual activities-Spline 1 interaction			**Mobility-Spline 1 interaction**		
Some problems	-1.993**	0.512	Some problems	0.241	0.368
Severe problems	-1.626***	0.568	Severe problems	0.040	0.454
Usual activities-Spline 2 interaction			**Mobility-Spline 2 interaction**		
Some problems	32.925***	9.397	Some problems	-5.745	7.029
Severe problems	27.194*	10.565	Severe problems	-5.804	9.337
Usual activities-Spline 3 interaction			**Mobility-Spline 3 interaction**		
Some problems	-41.044***	11.852	Some problems	7.332	8.896
Severe problems	-34.006*	13.338	Severe problems	7.620	11.889
Self-care-Spline 1 interaction			**Self-care-Spline 3 interaction**		
Some problems	-0.290	0.370	Some problems	-3.724	8.784
Severe problems	-0.873	0.475	Severe problems	-20.166	12.03
Self-care-Spline 2 interaction					
Some problems	3.106	6.954	Constant	25.621***	2.147
Severe problems	15.89	9.474	R^2	0.346	

Figure 1. Predicted average EQ-VAS in the final 2 years of life with differing domain levels and varying time-to-death.

No problems (blue), some problems (red), severe problems (green).

Wald test for joint non-zero estimates of spline 2 and 3 p<0.0001.

Conclusions

- The relationship between the EQ-5D domains and overall self-rated health changes with proximity to death; as patients near the EoL their overall self-rated health falls independently of the EQ-5D domains.

- This finding reinforces the view that the EQ-VAS captures a broader construct of health than that captured by the EQ-5D domains.

- Not only is the global relationship between the EQ-VAS and the domains not constant with proximity to death but in addition within domains the relationship between levels varies. Most markedly, the overall self-rated health (EQ-VAS) associated with no problems in the pain and usual activities domains drops, relative to the other levels, in the final months of life.

- These findings call into question the use of a single societal value set irrespective of proximity to the EoL, particularly given the documented challenges of reference dependency.

- Given the clear change in self-rated overall health with proximity to death there is a now a need to assess the extent to which the valuation of these health states varies over this period.

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