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Health related quality of life at hospital discharge as a predictor for six-month unplanned readmission and all-cause mortality of acutely admitted older medical patients

## Introduction

A substantial part of the growing older population will need care and treatment at some point in time. This provides challenges for the established healthcare systems due to capacity issues [1]. The older population is heterogeneous, the majority of older people have multi morbidities, therefore specialized and disease specific approaches may fall short in both the diagnostic and the treatment phase [2]. The substantial part of older persons, that will be in need of care and treatment are more often frail, have an affected health status and an affected health related quality of life (HRQOL) [3]. Self-reported HRQOL is a subjective measure that has been shown to be a predictor for hospitalization, functional decline and all-cause mortality in large population-based cohorts of older community-dwelling persons [4-9].

Acutely hospitalized older medical patients, defined as an unplanned and non-elective sudden hospitalization, with an affected HRQOL, being frail or having decreased functional status are generally at a higher risk of hospitalization with associated disability, functional decline, readmissions or death shortly after a hospitalization [10-14]. If the individual patient's HRQOL is associated with severe negative outcomes, HRQOL may be helpful in making customized treatment decisions for patients at risk. Only a few studies have been identified, that examined HRQOL in a heterogeneous population of acutely admitted older medical patients as a prognostic factor for negative adverse outcomes after a hospitalization [15-19]. No large study has investigated the association of health-related quality of life and readmission in this population. Two of the aforementioned studies, with relatively small sample sizes (N = 210, N = 163), assessed the association with readmission within six and twelve months after hospitalization [16, 18]. Four studies have examined the prognostic value in relation to mortality at 3, 12 months and one study at 5 years [15, 17-19]. The findings

of these limited number of studies suggest that poorer HRQOL may be associated with a greater likelihood of readmission or death in admitted older medical patients. Previous research has shown that readmission in acutely admitted older medical patients is particularly difficult to predict, even though associations between exposure variables as frailty and functional measures and readmission were identified [13, 20-26]. This may be due to the complex nature of readmission. Therefore, it is relevant to examine whether subjective HRQOL may contribute with a prognostic value to be utilized in clinical practice in general medical wards. Studies have shown that the predictive value in relation to mortality in acutely admitted frail older medical patients is stronger [27-29], than the predictive performance for readmission. Still, if self-reported HRQOL can predict mortality it may be helpful in relation to individualized patient treatment decisions. The findings from a large cohort study will contribute to establish a knowledge base regarding a vulnerable population and adverse consequences of a lower HRQOL compared to a higher HRQOL.

HRQOL is a construct focusing on individuals' physical, psychological and social aspects of living, as well as role functioning and activities of daily living. It represents elements of life directly affected by morbidity and thereby might be associated with negative outcomes. A widely used instrument, which evaluates and converts HRQOL measures into a utility index, is the EQ5D [30], a generic instrument suitable to be administered to different populations, performing as well as other instruments and has been found to be simpler to use [31]. Regarding HRQOL gender and age differences have been described; women generally report lower HRQOL compared to men and younger citizens report higher HRQOL than older citizens in Denmark and in other countries as well [6, 32].

The first aim of this study was to assess whether patient-reported HRQOL in acutely admitted older medical patients, assessed by EQ5D, was associated with a combined end-point including first unplanned readmission or death without prior readmission, within six months after discharge. Secondly, to explore if HRQOL was associated with death within six months after discharge regardless of previous readmissions.

## **Methods**

#### Study design

The recruitment for this cohort of acutely admitted older medical patients has previously been described in detail [13]. The manuscript is written in accordance with the STROBE guidelines [33]. In brief, recruitment took place at two acute receiving medical units and seven medical wards at Aalborg University Hospital in Denmark from May 2014 to May 2015. The medical subspecialties at the seven wards were: endocrinology, gastroenterology, hematology, infectious disease, nephrology, pulmonology and geriatrics [13]. All patients were admitted through the two acute medical wards and within 24 hours they were allocated to the specialty wards or discharged. Each specialty ward also received a fraction of internal medical patients as these patients were allocated to wards having available beds.

In Denmark, health care is free, but restricted. A patient cannot enter the emergency room, without a referral from a general practitioner or the physician from the emergency service. It is always a medical decision to admit the patient or not. In acute

## Study population

situations patients may call 911 (in Denmark 112) [34].

Patients aged 65 years and older, acutely admitted to one of the seven medical wards or the two acute medical units were approached when scheduled for discharge. By being able to provide informed consent they were eligible for inclusion. Exclusion criteria were terminal illness, severe cognitive impairment and inability to speak Danish. The Short Portal Mental Status Questionnaire (SPMSQ), which is validated for a population of older persons, was used to screen the patients for cognitive deficits [35]. We did not use proxies and informed consent was given by the patients. In a previous study assessing the mental status of older hospitalized patients the sensitivity, specificity and predictive positive value for the test was found to be 0.73, 0.91 and 0.89, respectively [36]. Patients were also excluded if still hospitalized for more than 2 days after baseline testing. It was verified for a 2-month period, that patients

discharged during the early or late hours of the days or at weekends did not differ from the included patients regarding age and gender.

#### **Data Collection and Primary Outcomes**

After informed consent was obtained from the patients, trained physiotherapists obtained data from the patients at the respective wards. Due to different bed capacities and thereby different discharge rates at the wards, a prepared random testing sequence defined which wards were approached more frequently, as limited assessor resources made it impossible to approach all eligible patients. On weekdays, two testers included and tested eligible patients using the random testing sequence. Patients that were planned for discharge were approached at the specific wards

Patient-reported HRQOL was assessed using EQ5D, which is a descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which, in the version EQ5D-5L, can take one of five responses; no problems, slight problems, moderate problems, severe problems and unable to/extreme problems. The EQ5D is a generic instrument with well-established psychometric properties [37]. The EQ5D VAS score is a part of EQ5D and records a self-rated health scale of "health today" on a 20-cm visual analogue scale with endpoints of "the best health you can imagine" and "worst health you can imagine" [30]. By using responses from the five dimensions from each respondent, an EQ5D index can be calculated [38]. The index score can vary from 1 (full health) to 0 (death) and – 0.54 (conditions regarded worse than death) [39].

Covariates were registered at baseline and included gender, age, time since previous admission, length of stay, place of discharge and educational level. Data from the patient administrative system regarding diagnoses was used for calculating the Charlson's Comorbidity Index [40].

The primary outcome was combined first unplanned readmission or death without prior readmission within six months. We defined this combined outcome as a registered death of an older patient included in the cohort was considered a

readmission, that was not reached on time. An unplanned readmission was defined as an acute readmission, if a patient had been discharged for more than 4 hours before a readmission. The readmission was unspecific and could be at any hospital in Denmark. The second outcome measure was all-cause mortality within six months regardless the previous number of readmissions, to investigate if HRQOL was associated with the worst outcome. In Denmark, all patient contacts with hospitals, also readmissions and mortality, are registered in the National Patient Register and the outcomes for this study were extracted by using the patients' unique identification numbers, which are assigned to them at birth or immigration by the Danish Civil Registration System.

### Statistical Analysis

Medians and 10th and 90th percentiles were presented as summary measures to describe sociodemographic and clinical baseline characteristics of all patients included in the study. Cox regression or time-to-event statistics [41, 42] was used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the association between HRQOL (EQ5D) and readmission or all-cause mortality combined or all-course mortality within six months. The utility index of EQ5D status was modelled as continuous spline variables using the data within 5% and 95% of the range and model default settings were used to define knots for the utility index of EQ5D [43]. Two Cox regression models were constructed: a gender- and age-adjusted model and a gender-, age- and comorbidity-adjusted model, as these covariates were considered the main potential confounders [14]. This was done for both readmission or mortality and mortality regardless of previous readmissions. The model knots defined three categories and a reference value. The analyses were performed for all participants and stratified according to gender and age +/- 75 years. Due to little missing data a complete cases data analysis approach was used. Statistical significance level was set at 0.05. The discriminant capacity of the models was measured by the Harrell's C- statistic.

Stata version 14 (StataCorp. 2013. Stata Statistical software: Release 14. College Station, TX: StataCorp LP) was used for statistical analyses.

## Results

In total, 6,132 patients aged 65 years or more were acutely admitted during the 12-month period. Out of these, 2,793 patients were consecutively screened for eligibility of which 1,328 patients were included and tested during the enrolment period (Fig. 1). Complete follow-up information was achieved for all included patients. The median (10/90 percentiles) age of the participants was 77.1 (67.5; 87.7) years, 50.4% were women and the median (10/90 percentiles) length of stay in hospital was 5 (1;15) days. Baseline characteristics for the total sample and stratified by gender and age are presented in Table 1.

The overall combined proportion of patients readmitted or dying without prior readmission was 21.9% (n=291) after 30 days and 50% (n=664) after six months. In total, 635 patients were readmitted and only twenty-nine patients died without prior readmission. In total, 202 patients (15.2%) died within six months. Among men, unplanned readmission or death was slightly more frequent than among women, 52.8% versus 47.2% (difference 5.6%, CI 0.2;10.9) and among patients aged 75 or more readmission or death was slightly more frequent than among those below 75 years of age, 51.4% versus 48.0% (difference 3.4%, CI –2.0;8.9).

The EQ5D calculated index score median (10/90 percentiles) was 0.74 (0.44;1.0) for the total sample, for women it was 0.72 (0.39; 0.87) and for men 0.75 (0.50;1.00), respectively. The index score was calculated for the 1,271 patients with complete data. For the overall health on the visual analog scale the median (10/90 percentiles) for the total sample was 50.0 (35;85), for women it was 50 (32.5;80) and for men 60 (35;90). In relation to the five dimensions of the EQ5D, the highest proportions of patients reporting moderate or severe problems were reported in the mobility dimension and the pain/discomfort dimension. See Table 2 for the results in the five dimensions for the total sample and stratified for gender and age.

When the gender and age-adjusted EQ5D index score was categorized with the optimal index score 1 as the reference value, a lower index score was associated with a higher HR of combined unplanned first readmission or all-cause mortality in all three index score categories (<1 to 0.741, <0.741 to 0.438 and <0.438 to -0.40); HR 1.60 (CI

1.18;2.18), 1.93 (CI 1.42;2.62) and 2.02 (CI 1.40;2.91). When additionally adjusting for comorbidity, the HRs were 1.55 (CI 1.14;2.11), 1.82 (CI 1.34;2.47) and 1.90 (1.32;2.75). In gender- and age-stratified analyses the associations were present in all subgroups (Table 3).

When the gender and age-adjusted EQ5D index score was categorized with 1 as the reference value, a lower index score was associated with a higher HR of all-cause mortality in all three index score categories (<1 to 0.741, <0.741 to 0.438 and <0.438 to -0.40); HR 1.72 (CI 0.90;3.28), 2.54 (CI 1.36;4.75) and 3.79 (CI 1.90;7.55). When additionally adjusting for comorbidity, the HR s were 1.61 (CI 0.85;3.08), 2.26 (CI 1.20;4.23) and 3.43 (1.72;6.83). In the gender- and age-stratified analyses the associations were present in all subgroups (Table 4).

The Harrell's C values for the EQ5D index for combined readmission or all-cause mortality was 0.56 for the gender- and age adjusted model and 0.60 for the gender-, age- and comorbidity adjusted model. For all-cause mortality, the Harrell's C for gender- and age adjusted and for the gender-, age-, and comorbidity adjusted models were 0.63 and 0.68, respectively.

#### Discussion

Patient-reported HRQOL assessed using the EQ5D index adjusted for gender and age, was associated with combined first unplanned readmission or death without prior readmission within six months after discharge in a heterogeneous population of acutely admitted older medical patients, with a lower index score indicating a higher risk. Likewise, the HRQOL was associated with all-cause mortality. A lower index score in the gender-, age- and comorbidity adjusted models was also associated with a higher combined unplanned readmission or death and associated with all-cause mortality within six months. These findings demonstrate that the EQ5D is able to differentiate between groups with higher and lower risks of readmission or all-cause mortality. The predictive performance indicated by Harrell's C values were fair and the highest values were seen in the models adjusted for comorbidities. The Harrell's C

values indicate a predictive performance equivalent to other instruments aiming at predicting readmission or death [13, 20, 25, 44, 45].

The strengths of the current study include the prospective character, the large sample size and the complete register-based follow-up on outcome for all included patients. The included patients constituted a random sample of the total patient population with few patients declining to participate. Due to complete follow-up on first unplanned readmission and death after six months outcomes selection bias seems unlikely. Information regarding the outcomes was obtained from central registers and independently from the exposure information. The presented findings should, however, be generalized to other populations or settings with caution, as the study was undertaken only at Medical Departments at one University Hospital in Denmark. To explore the importance of morbidity, we adjusted for Charlson's Comorbidity Index in the Cox regression analyses. The exact number of medications for each patient could not be extracted. This is unfortunate as the number of medications indicates the morbidity burden of the patient. The Charlson's Comorbidity Index was instead included as a proxy for morbidity, although not a feasible measure in daily clinical practice. When morbidity is included in the model, the interpretation of the results becomes difficult, as the variation in the HRQOL measure after adjustment can no longer be due to morbidity. The relevance of these analyses is thus open for discussion.

There were limitations of the current study as well. Even though the positive predictive value of SPMSQ was 0.89 in a study assessing older hospitalized patients [36], the test measures memory and orientation without testing visuospatial and language aspects of cognition and therefore it may not have been sensitive enough regarding cognitive deficits. We did in this study use the CCI to indicate the burden of illness, however length of stay may be linked to the health status as well. We did not look into length of stay in the present analysis, however, this could also be an important confounding factor to look into in future studies.

The median index score of 0.74 at discharge for the study population was lower than the score for a general Danish reference population aged between 60 and 79 years of

age, having an average score of 0.87 [32]. Karampampa et al. (2016) showed that HRQOL measured by EQ5D among persons 65 years or older was not affected by one single hospital admission, whilst multiple all-cause admissions resulted in a decline in HRQOL and this was especially significant in women [46]. Hospital readmissions in old age may therefore indicate a shift from a healthy life to a life of compromised health measured by EQ5D [46]. It has been stated, that the psychometric performance of EQ5D is under investigated in the older population [47]. However, the findings of this study showed that EQ5D can identify important associations with severe negative outcomes in acutely admitted older medical patients and therefore seem justifiable to use. This is supported by the recent studies of Parlevliet et al. (2016) and Belayachi et al. (2018) [15, 17].

The associative findings of the present study resemble findings in the former identified studies [15-19] investigating readmission or all-cause mortality in general medical wards, although some of the studies applied different HRQOL questions or instruments such as SF 36 [16], selected items from the Dukes Health Profile [19] and the Assessment of Quality of Life instrument [18]. There were, however, differences in population age, wards included, HRQOL instruments and the utility index values were also different as well as were the frequency of events, which complicates the comparison across the studies, but the trend showing an inverse association between the level of EQ5D index and risk of readmission or death. None of the aforementioned studies reported the predictive performance of EQ5D in relation to readmission or mortality using C-statistics [15-19].

Prognostic factors identified using relevant and feasible non-specialist measures is highly needed in clinical practice, especially due to an increasing population of older inpatients in risk. The components of EQ5D are easily understandable for both patients and health professionals and may be utilized in both the secondary and the primary sector.

In conclusion, lower HRQOL in acutely admitted older medical patients assessed at discharge, using EQ5D, was associated with a higher risk of combined readmission or death without prior readmission within six months and with six months mortality after

discharge. The C-statistics showed a fair predictive performance. Therefore, HRQOL, using EQ5D, may contribute with a prognostic value to be utilized in clinical practice in general medical wards. Further research should replicate the findings and research is needed to assess ways of improving this non-disease specific risk stratification tool.

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## **Compliance with ethical standards**

#### **Conflicts of interest**

The authors declare that they have no conflict of interest.

## **Ethical approval**

The Danish Regional Ethics Committee assessed the study and stated that no approval was required (ID-number N-20140016). The Danish Data Protection Agency approved the study (2008-58-0028). The study complied with the Declaration of Helsinki.

## **Informed consent**

Informed consent was obtained from all individual participants included in the study.

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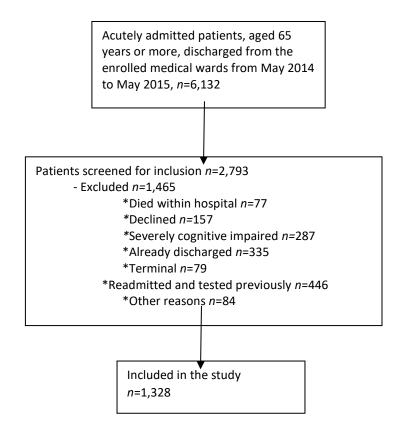
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Fig. 1 Project flowchart



**Table 1** Baseline characteristics for the acutely admitted older medical patients at discharge in total, gender and age stratified

		T-1-1	14/	14/	14/			
		Total	<u>Women</u>	Women	<u>Women</u>	<u>Men</u>	<u>Men</u>	<u>Men</u>
				Age 65-74	Age 75+		Age 65-74	Age 75+
Median (10/	/90) or %	n=1,328	n=669	n=261	n=408	n=659	n=283	n=376
(n)								
Age, Median	n (10/90)	77.1	77.4	70.2	81.9	76.9	69.5	81.2
		(67.5;87.7)	(67.6;88.7)	(66.4;74.1)	(76.3;91.1)	(67.3;86.7)	(66.0;74.3)	(76.6;88.7)
No. of como	orbities,	1 (0;3)	1 (0;3)	1 (0;3)	1 (0;3)	1 (0;3)	1 (0;3)	1 (0;3)
Median (10/	/90)							
Charlson Cor	morbidity	1 (0;4)	1 (0;4)	1 (0;4)	1 (0;4)	2 (0;5)	2 (0;5)	2 (0;5)
Index Score,	, Median							
(10/90)								
BMI⁵, Media	an (10/90)	25.0	24.4	24.8	24.1	25.6	26.8	25.0
		(19.2;33.1)	(18.4;33.6)	(18.3;35.5)	(18.6;32.5)	(20.4;33.0)	(21.0;34.4)	(20.1;31.3)
Length of sta	ay in days,	5 (1;15)	5 (1;17)	5 (1;15)	5 (1;17)	5 (1;15)	5 (1;15)	6 (1;15)
Median (10/90)								
Discharged to own		89.9	88.2	93.9	84.6	91.7	94.7	89.4
home, % (n)		(1,194)	(590)	(245)	(345)	(604)	(268)	(336)
Living alone, % (n)		50.5	63.1	46.4	73.8	37.8	32.9	41.5
		(671)	(422)	(121)	(301)	(249)	(93)	(156)
Level of edu	cation <sup>&amp;</sup> , %							
(n)								
- P	Public	83.6	85.7 (573)	80.5 (210)	89.0 (363)	81.5 (537)	80.2 (227)	82.5 (310)
S	chool/short	(1,110)						
e	education							
- N	Medium edu.	10.8 (144)	11.7 (78)	17.2 (45)	8.1 (33)	10 (66)	12.7 (36)	8 (30)
- Lo	ong edu.	4.7 (63)	1.8 (12)	2.3 (6)	1.5 (6)	7.7 (51)	6.7 (19)	8.5 (32)

<sup>§</sup>Body Mass Index. & Public school/short education = up to ten years, Medium education = up to 13 years, Long education = more than 13 years.

 Table 2 Baseline values for EQ5D-5L in total, gender and age stratified

EQ5D-5L, %, N	Total	Women	Women 65-74	Women 75+	Men	Men 65-74	Men 75+
Mobility/	n=1,328	n=669	n=261	n=408	n=659	n=283	n=376
walking							
-no problems	34.2 (451)	35.1 (233)	36.8 (96)	34.0 (137)	33.3 (218)	39.7 (112)	28.4 (106)
-slight	27.1 (358)	27.9 (185)	26.8 (70)	28.5 (115)	26.4 (173)	21.6 (61)	30.0 (112)
problems	00 = (0=0)	100(105)	04.4 (==)	4= 4 (=0)	00.5 (4.40)	(==)	0.1.0 (0.0)
-moderate	20.7 (273)	18.8 (125)	21.1 (55)	17.4 (70)	22.6 (148)	19.5 (55)	24.9 (93)
-severe -unable	12.2 (161) 5.8 (76)	11.6 (77) 6.6 (44)	10.7 (28) 4.6 (12)	12.2 (49) 7.9 (32)	12.8 (84) 4.9 (32)	15.3 (43) 3.9 (11)	11.0 (41) 5.6 (21)
-missing, N	(9)	(5)	(0)	(5)	(4)	(1)	(3)
Self-care	F2 0 (CO7)	E4 2 (220)	FC 4 /44C\	40.0 (403)	E 4 7 (2E0)	C1 0 (172)	40.0 (400)
-no problems -slight	53.0 (697) 20.1 (264)	51.3 (339) 18.3 (121)	56.4 (146) 18.2 (47)	48.0 (193) 18.4 (74)	54.7 (358) 21.8 (143)	61.0 (172) 16.7 (47)	49.9 (186) 25.7 (96)
problems	20.1 (204)	10.5 (121)	10.2 (47)	10.4 (74)	21.0 (143)	10.7 (47)	23.7 (30)
-moderate	13.3 (175)	14.4 (95)	12.7 (33)	15.4 (62)	12.2 (80)	12.1 (34)	12.3 (46)
-severe	6.9 (91)	7.9 (52)	7.7 (20)	8.0 (32)	6.0 (39)	7.1 (20)	5.1 (19)
-unable	6.8 (89)	8.2 (54)	5.0 (13)	10.2(41)	5.3 (35)	3.2 (9)	7.0 (26)
-missing, N	(12)	(8)	(2)	(6)	(4)	(1)	(3)
Usual activities							
-no problems	43.3 (560)	36.8 (238)	39.9 (101)	34.9 (137)	49.9 (322)	50.5 (141)	49.3 (181)
-slight	24.6 (318)	27.2 (176)	25.3 (64)	28.5 (112)	22.0 (142)	22.9 (64)	21.3 (78)
problems	.= . (00.1)			4= 0 (60)		( )	4= 4 (64)
-moderate	17.1 (221)	18.1 (117)	19.4 (49)	17.3 (68)	16.1 (104)	14.3 (40)	17.4 (64)
-severe -unable	8.0 (103) 7.0 (90)	8.5 (55) 9.3 (60)	7.5 (19) 7.9 (20)	9.2 (36) 10.2 (40)	7.4 (48) 4.6 (30)	7.5 (21) 4.7 (13)	7.4 (27) 4.6 (17)
-missing, N	(36)	(23)	(8)	(15)	(13)	(4)	(9)
Pain/							
discomfort -no problems	41.0 (538)	37.3 (246)	35.8 (93)	38.3 (153)	44.8 (292)	43.6 (123)	45.7 (169)
-slight	23.9 (313)	24.2 (160)	22.3 (58)	25.5 (102)	23.5 (153)	25.9 (73)	21.6 (80)
-moderate	22.8 (299)	24.1 (159)	28.5 (74)	21.3 (85)	21.5 (140)	21.3 (60)	21.6 (80)
-severe	11.3 (148)	13.2 (87)	10.8 (28)	14.8 (59)	9.4 (61)	8.5 (24)	10.0 (37)
-extreme	1.1 (14)	1.2 (8)	2.7 (7)	0.3 (1)	0.9 (6)	0.7 (2)	1.1 (4)
-missing, N	(16)	(9)	(1)	(8)	(7)	(1)	(6)
Anxiety/							
Depression							
-not anxious/	71.1 (934)	67.4 (447)	64.0 (167)	69.7 (280)	74.9 (487)	72.2 (203)	77.0 (284)
depressed							
-slightly	18.1 (237)	20.5 (136)	21.5 (56)	19.9 (80)	15.5 (101)	17.8 (50)	13.8 (51)
-moderately	7.2 (95)	6.6 (44)	8.4 (22)	5.5 (22)	7.9 (51) 1.4 (9)	7.1 (20)	8.4 (31) 0.8 (3)
-severe -extreme	3.4 (44) 0.2 (3)	5.3 (35) 0.2 (1)	6.1 (16) 0 (0.0)	4.7 (19) 0.3 (1)	0.3 (2)	2.1 (6) 0.7 (2)	0.8 (3)
-missing,N	(15)	(6)	(0)	(6)	(9)	(2)	(7)
VAC	E0 /3E 0E'	F0	F7 F	E0 /20 00\	CO (25 00)	(0 (20 00)	CO (25 00)
VAS overall, Median	50 (35;85)	50 (32.5;80)	57.5 (35;85)	50 (30;80)	60.(35;90)	60 (30;90)	60 (35;90)
(10/90)		(32.3,00)	(33,33)				
N=1,256							
FOED Indian	0.74	0.72	0.74	0.72	0.75	0.77	0.74
EQ5D Index value,	0.74 (0.44;1)	0.72 (0.39;0.87)	0.74 (0.40;1)	0.72 (0.38;0.87)	0.75 (0.50;1)	0.77 (0.50;1)	0.74 (0.48;1)
value,	(0.44,1)	(0.33,0.67)	(0.40,1)	(0.30,0.07)	(0.30,1)	(0.50,1)	(U.+U, I)

Median (10/90) N=1,271

**Table 3** Hazard Ratios and 95% Confidence intervals for combined readmission or mortality without prior readmission using Cox regression with cubic splines. N=1,271

	EQ5D-5L <sup>†</sup> Index value 1.0	EQ5D-5L Index value from 1.0 to 0.741	EQ5D-5L Index value from 0.741 to 0.438	EQ5D-5L Index value from 0.438 to - 0.4
	Reference value	HR (CI)	HR (CI)	HR (CI)
Total sample adjusted for sex, age	1.0	1.60 (1.18;2.18)	1.93 (1.42;2.62)	2.02 (1.40;2.91)
Total sample adjusted for sex, age, comorbidity	1.0	1.55 (1.14;2.11)	1.82 (1.34;2.47)	1.90 (1.32;2.75)
Male adjusted for age	1.0	1.52 (1.03;2.25)	1.77 (1.20;2.61)	1.65 (0.99;2.75)
Male adjusted for age, comorbidity	1.0	1.40 (0.95;2.08)	1.59 (1.07;2.35)	1.49 (0.89;2.49)
Female adjusted for age	1.0	1.74 (1.05;2.88)	2.20 (1.35;3.59)	2.50 (1.44;4.34)
Female adjusted for age, comorbidity	1.0	1.77 (1.07;2.92)	2.18 (1.33;3.56)	2.46 (1.42;4.28)
Age 65-74 adjusted for sex	1.0	1.69 (1.07;2.66)	1.99 (1.26;3.13)	2.79 (1.63;4.80)
Age 65-74 adjusted for sex, comorbidity	1.0	1.59 (1.0;2.50)	1.87 (1.19;3.0)	2.49 (1.45;4.28)
Age 75+ adjusted for sex	1.0	1.52 (1.0;2.31)	1.84 (1.22;2.77)	1.6 (0.97;2.63)
Age 75+ adjusted for sex comorbidity	1.0	1.49 (0.98;2.28)	1.75 (1.16;2.63)	1.55 (0.94;2.55)

<sup>†</sup>EQ5D-5L: Health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of five responses.

**Table 4** Hazard Ratios and 95% Confidence intervals for all-cause mortality using Cox regression with cubic splines. N=1,271

	EQ5D-5L <sup>†</sup> Index value 1.0	EQ5D-5L Index value from 1.0 to 0.741	EQ5D-5L Index value from 0.741 to 0.438	EQ5D-5L Index value from 0.438 to - 0.4
	Reference value	HR (CI)	HR (CI)	HR (CI)
Total sample adjusted for sex, age	1.0	1.72 (0.90;3.28)	2.54 (1.36;4.75)	3.79 (1.90;7.55)
Total sample adjusted for sex, age, comorbidity	1.0	1.61 (0.85;3.08)	2.26 (1.20;4.23)	3.43 (1.72;6.83)
Male adjusted for age	1.0	1.47 (0.68;3.18)	2.40 (1.14;5.06)	2.37 (0.95;5.90)
Male adjusted for age, comorbidity	1.0	1.30 (0.60;2.82)	2.02 (0.95;4.29)	2.02 (0.81;5.06)
Female adjusted for age	1.0	2.41 (0.72;8.03)	3.11 (0.96;10.08)	5.65 (1.95;22.10)
Female adjusted for age, comorbidity	1.0	2.55 (0.76;8.50)	3.06 (0.94;9.94)	6.59 (1.96;22.21)
Age 65-74 adjusted for sex	1.0	4.16 (0.97;17.82)	5.47 (1.29;23.17)	11.75 (2.60;53.15)
Age 65-74 adjusted for sex, comorbidity	1.0	3.61 (0.84;15.48)	4.67 (1.10;19.84)	8.85 (1.94;40.31)
Age +75 adjusted for sex	1.0	1.21 (0.58;2.51)	1.87 (0.93;3.75)	2.38 (1.08;5.23)
Age +75 adjusted for sex comorbidity	1.0	1.18 (0.57;2.44)	1.71 (0.85;3.44)	2.28 (1.04;5.02)

<sup>†</sup>EQ5D-5L: Health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of five responses.