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Prognostic factors for poor recovery after trauma: a prospective multicentre cohort study

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Abstract

Objectives: to determine (I) prognostic factors for poor health status and (II) recovery patterns during the first two years after injury in the clinical trauma population.

Design: a prospective longitudinal cohort study.

Setting: Ten participating hospitals in Brabant, the Netherlands

Participants: adult injury patients admitted to a hospital between August 2015 and November 2016 were followed. 4883 (50%) patients participated.

Main outcome measures: Primary outcome was health status (measured with the EuroQol-5-dimensions-3-level [EQ-5D-3L] and a cognition item and the EuroQol Visual Analogue Scale [EQ-VAS]) and were collected at 1 week, 1, 3, 6, 12, and 24 months after injury.

Results. Health status was especially low during the first six months after injury (mean EQ-5D utility[SD] ranged from 0.49[0.32] at 1 week to 0.79[0.25] at 24 months). The dimensions mobility, pain/discomfort and usual activities improved up to 2 years after injury. Lower pre-injury health status, frailty and longer length of stay were important prognostic factors for poor recovery. Spine injury, lower and upper extremity injury showed to be prognostic factors for problems after injury. Traumatic brain injury was a prognostic factor for problems with cognition.

Conclusion. This study contributes to the increase in knowledge of recovery patterns and could be a starting point to develop prediction models for specific injury classifications for the implementation of personalized medicine.

Trial registration number: NCT02508675

Strengths and limitations of the study

- a strength of the study was the short- and long-term follow-up measurements to obtain essential recovery data of the trauma patients.

- a strength of the study is the high number of participants in this prospective cohort study.

- a limitation of this study is the possibility of selective drop-out, which could have resulted in an overestimation of complaints after injury

- a limitation of this study is the possibility of selection bias, suggesting that more severely injured patients were more likely to participated.

Introduction

Trauma, defined as a physical injury, is one of the leading causes of disability and affects millions of people worldwide each year. The number of survivors after trauma increased the last decades, due to the improvement of trauma care[1-3]. Many patients suffer physical, psychological or cognitive impairments, resulting in a reduction of their health status (HS).

The trauma population is a heterogeneous group of patients. Patients are from various age groups with many different injury patterns, in both severity and body region. In addition, type of accident (e.g. falls, road traffic accident) and mechanism of injury (e.g. bleeding, fracture) can be diverse. The identification of patients at high risk of poor health status outcome could enable clinicians to tailor treatment in which patients are referred to specialized care and rehabilitation at an early stage of their recovery.

Previous research identified several prognostic factors for poor outcome after injury[4-16]. Most previous studies on prognostic factors for poor recovery were conducted in major or severe trauma patients population[4-12], traumatic brain injury patients[7,13] or assessed on a small follow-up trauma population[14]. In addition, one study focused on long-term follow-up measurement, two to seven years after injury[10]. Last, pre-injury health status was not measured or taken into account by determining the prognostic factors for health status in previous studies. Research that take into account the total clinical trauma population during the first two years of their recovery is scarce[15]. In addition, different recovery patterns can be expected in, for example, brain injury patients and patients suffering from lower/upper extremity injury.

This study aimed (I) to determine prognostic factors for poor health status and (II) determine recovery patterns after injury during the first two years after injury in the clinical trauma population and in specific injury classifications.

Methods

Study design and participants

Data was obtained from the Brabant Injury Outcome Surveillance (BIOS)[17]. The BIOS-study is a prospective observational cohort study in which health status, costs, functional and psychological outcomes were assessed in the first 24 months after trauma in injured patients. The study was approved by the Medical Ethics Committee Brabant (NL50258.028.14). Patients were not involved in the study design.

All adult (≥18 years) patients admitted to a hospital in the region Noord-Brabant (the Netherlands) from 1 August 2015 to 30 November 2016 due to an injury and who survived to hospital discharge were included in this study. Patients without sufficient knowledge of the Dutch language or with pathological fractures were excluded. A proxy informant (caregiver or family member) was asked to complete the self-administered questionnaires if patients were incapable of participating in the BIOS-study. The questionnaires were sent by post or electronically at one week, one month, three months, six months, twelve months and 24 months after injury. All participants, patients or proxy informants, signed informed consent. Patients were asked to complete a shorter version of the questionnaire at three months, six months, twelve months and 24 months after injury to increase response. This short version incorporates only a small collection of the questions that are included in the BIOS-study. Injury characteristics were collected in the Brabant Trauma Registry and, for participating patients, merged to the BIOS-data.

Outcome

Health status was measured with the EuroQol-5D-3L (EQ-5D)[18]. This questionnaire consists of the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D descriptive system comprised the following five dimensions: mobility, self-care, usual

activities, pain/discomfort and anxiety/depression. Each dimension could be answered in three levels: no problems, some problems and severe/extreme problems.

A summary score of the EQ-5D (EQ-5D utility) can be calculated by using the Dutch tariffs[19]. This utility score ranged from 0 (death) to 1 (perfect health). The EQ-VAS is a vertical visual analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state.

Cognition was added as additional dimension to the EQ-5D questionnaire. Respondents were asked to describe their or, in case of proxy, the patients' state of health, concerning cognition (e.g. memory, concentration). Similar to the other dimensions, answer options were based on three levels: no problems, some problems and severe problems.

HS was measured at each time point during follow-up in both patient and proxy questionnaires. The EQ-5D (including the cognition dimension) and EQ-VAS were also measured pre-injury, by asking participants at one week or one month and proxy informants at one month for the patients' health status before sustaining the injury. The EQ-VAS was not included in the short questionnaire.

Prognostic factors

Sociodemographic variables

Possible prognostic factors for health status that were measured in the BIOS-study were sex, age, educational level (low, middle or high), pre-injury work status (yes/no), frailty and pre-injury health status. Educational level was categorized in three levels as the highest completed degree, diploma of education; low (primary education, preparatory secondary vocational education or without diploma), middle (university preparatory education, senior general secondary education or senior secondary vocational education and training), and high (academic degree or university of applied science). Frailty was measured at one week or one month after injury with the Groningen Frailty Index (GFI) in patients ≥65 years[20]. A sum-score

of ≥4 was considered frail. Patients <65 years were considered not frail. Pre-injury health status was measured at 1 week or 1 month after injury with the EQ-5D-3L, referring to the health status of the patients prior to injury.

Clinical variables

Possible other clinical prognostic factors for health status were length of hospital stay, injury severity score, admission to the intensive care (yes/no), presence of comorbidities and the functional capacity index. Comorbidities were measured with the American Society of Anaesthesiologists (ASA) physical status classification system ranging from 1 (healthy patient) to 4 (severe systemic disease that is a constant threat to life). The functional capacity index and injury severity score were based on the Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)[21].

Injury Classification

The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)[21] were used to create injury group classifications representing the most common types of injuries. In total, 14 injury groups were created: 3 lower extremity injury groups (pelvic injury, hip fracture, and tibia fracture/complex foot fracture or distal/shaft femur fracture), 2 upper extremity injury groups (shoulder and upper arm injury, and radius, ulna or hand fracture), 2 head injury groups(AIS-head≤2, and AIS-head≥3), 1 face injury group, 2 thorax injury groups (thorax injury, and rib fracture), 2 abdomen injury (AIS-abdomen≤2, and AIS-abdomen≥3) and 2 spine injury (spinal cord injury/brachial plexus lesion, and stable vertebral fracture/disc injury). Patients who suffer multiple injuries could be classified in one or more injury group classifications.

Data analysis

Baseline characteristics of participants were compared with non-participants, using chi-square for categorical variables or the Mann-Whitney U test for non-normal distributed data.

Descriptive statistics included the median with the interquartile range (IQR) for continuous variables. Missing baseline characteristics (0.9% for ISS and 6.8% for length of stay at hospital) and missing utility scores for participants (ranging from 1.8% at 1 week follow-up to 6.9% at 12 months follow-up) were imputed according to multiple imputation by using the Multivariate Imputations by Chained Equations (MICE) procedure with 15 imputations and 5 iterations[22]. The imputation model included baseline characteristics, injury characteristics and summary scores of the follow-up questionnaires to capture associations with missingness as completely as possible.

Multicollinearity was checked based on the Variance Inflation Factor (criterion: VIF > 10). Prognostic factors were assessed for poor health status outcome with EQ-5D utility and EQ-VAS as outcome measures. Regression coefficients with corresponding 95% confidence interval (CI) were reported. The dimensions of the EQ-5D descriptive system were dichotomized into 0=no problems and 1=some problems/extreme problems. Logistic mixed models with random intercepts were used to assess prognostic factors for poor outcome for the six dimensions of the EQ-5D (e.g. mobility, self-care, usual activities, pain/discomfort, anxiety/depression and cognition). All potential prognostic factors were included in the multivariable regression models to calculate adjusted Odds Ratios and corresponding 95% CI. Age and LOS were included as categorical variables, because of the non-linear relation between factor and outcome.

Recovery patterns were determined by changing the reference category of the categorical time variable in linear mixed models for health status and logistic mixed models for the dimensions of health status, adjusted for the prognostic factors. Recovery patterns for the items of the EQ-5D were assessed in detail for injury classifications that showed to be statistically significant for the dimensions in the total multivariable model.

Analyses were conducted in the statistical programs R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS version 24 (Chicago, USA) and results were reported according to the TRIPOD guidelines[23].

Results

Baseline characteristics

A total of 4883 patients (50% of total, N=9774) completed at least one questionnaire of the BIOS study of whom 48% (N=2,329) was male **(Figure 1, Table 1)**. The median age was 68 years with an IQR of 53-80 years. Responders had a median injury severity score of 5 (IQR [4-9]) and most of the patients were classified as healthy or as patients with mild systemic disease (N=3,879, 79%). A total of 358 patients (7%) were admitted to the intensive care unit. Compared to the non-responders, participants were more severely injured, were more often admitted to a level I trauma centre, were more often admitted to the intensive care unit, had lower functional capacity index values, and were more often healthy (measured with the ASA classification). The majority of the responders had low educational level (N=2,670, 55%) and 38% of the responders (N=1,278) had a job prior to injury.

Health status over time

The mean (SD) EQ-5D utility score ranged from 0.49 (0.32), 0.56 (0.30), 0.69 (0.27), 0.76 (0.25), 0.77 (0.26) and 0.79 (0.25) at 1 week, 1, 3, 6, 12 and 24 months respectively **(Figure 2A)**. The mean (SD) EQ-VAS score ranged from 58.26 (20.45), 63.02 (20.46), 69.48 (18.56), 72.97 (17.28), 73.50 (18.08) and 75.58 (17.88) at 1 week, 1, 3, 6, 12 and 24 months respectively. Patients reported the most recovery during the first 6 months, with a little improvement up to 12 months. The first month, patients reported most problems for pain/discomfort, usual activities, mobility and self-care **(Figure 2B)**. During the 24 month follow-up, the percentage of patients reporting problems for pain/discomfort, usual activities and mobility were highest. Two years after injury 49% (95% CI: 47, 51) of the patients reported problems for pain/discomfort, 43% (95% CI: 41, 45) reported problems for mobility, 41% (95% CI: 39, 43)

reported problems for usual activities, 25% (95% CI: 23, 27) reported for cognition, 20% (95% CI: 18, 22) reported problems for anxiety/depression and 19% (95% CI: 17, 21) for self-care.

Prognostic factors

Almost all variables were prognostic factors for recovery in the univariable analyses (**Supplemental Table 1**). Lower pre-injury health status, frailty and longer length of stay at hospital were important significant prognostic factors for decreased health status during the first two years after trauma in the multivariable analyses (**Table 2**). Higher age is a prognostic factor for less problems on self-care, usual activities, pain/discomfort, anxiety/depression and cognition, but no significant association was found for mobility. Female sex showed to be a significant prognostic factor for all outcomes, except for mobility.

Lower extremity injury showed to be a prognostic factor for health status , mobility, self-care, usual activities and pain-discomfort. Upper extremity injury was a prognostic factor for health status, self-care, usual activities and pain/discomfort. Spine injury showed to be a prognostic factor, although not always significant, for health status, and the dimensions mobility, self-care, usual activities and pain/discomfort. Traumatic brain injury showed to be a prognostic factor for problems with cognition.

Recovery patterns

Most recovery occurred in the first 6 months (**Table 3**). Health status measured with the EQ-5D utility improved significantly during the first year after injury and health status measured with the EQ-VAS significantly increased during the 24 months after injury (although not significant at twelve months compared to six months). Patients reported to have significantly less problems with mobility, usual activities and pain/discomfort 24 months after injury compared to twelve months after injury.

Patients with spine injury showed improved mobility up to three months after injury, whereas patients with lower extremity injury showed less mobility problems up to twelve months after injury **(Table 4)**. Upper and lower extremity injury showed the same recovery pattern during the first two years for self-care. Patients with spine injury showed improvement up to six months compared with three months after injury for self-care.

Patients with upper extremity and spine injury reported less problems for usual activities at twelve months after injury compared with six months after injury. Recovery mostly occurred up until twelve months after injury, except for pain/discomfort. Patients with lower extremity injury reported significant less problems at 24 months compared to twelve months for pain/discomfort.

Discussion

In this multicentre prospective cohort study, we found that patients reported problems up until two years after injury. Health status was especially low during the first six months after injury, in which patients often reported problems in most of the dimensions of health status. Lower pre-injury health status, frailty and longer length of stay at hospital were prognostic factors for both decreased health status and reporting problems in the dimensions during the first two years after trauma. For the EQ-5D dimensions mobility, usual activities and pain/discomfort less problems were reported at two years compared to one year after trauma, as for the other dimensions we found no decrease in reported problems after one year.

Previous research showed that age is a prognostic factor for reduced health status[9,15,24]. In contrast, results from this study showed improved overall health status. This could be explained by the addition of the strong prognostic factors pre-injury health status and frailty in the multivariable adjusted models. Indicating that not the increase of age is a prognostic factor for poor health status, but the patients' health status before injury. Not all elderly patients are frail nor are they in poor health. With the ageing population, frailty and pre-injury health status are essential to consider when assessing recovery patterns in injury patients. Higher age was a prognostic factor for problems with mobility and self-care but showed to be a negative associated with other dimensions of the EQ-5D. The latter is in line with a recent study, stating that the relationship between age and the dimensions of EQ-5D differed[4].

The addition of the cognitive dimension on the EQ-5D has previously been shown to improve classification and validity, especially in patients with TBI[25,26]. In line with these findings, this study showed that patients with TBI were at risk on developing cognitive problems after injury. It has been suggested previously that most patients with mild TBI patients recover fully within three to six month, although some patients with mild TBI and patients with more severe TBI

suffer persistent cognitive problems[27-29]. Our study showed that TBI patients reported to be recovered after six months, in line with the recovery pattern of mild TBI patients. This is possibly due to the fact that most responders of the BIOS-study suffered mostly mild TBI (27%) compared to moderate/severe TBI (4%). Further evaluation of these subgroups with more specific outcome measures are necessary to determine their recovery patterns.

In line with previous studies, this study showed that female sex is a prognostic factor for poor health status after injury[4,5,7,8,12,15,30]. It has been suggested that problems were more often reported in females, in contrast to males, who dismiss there complaints more often. Another explanation could be that women experience more psychological impact, resulting in lower health status.

Except for longer length of stay at the hospital, no injury related characteristics were found to be prognostic factors for anxiety/depression complaints. These results suggest that psychological problems after injury are mainly based on patient characteristics, which is confirmed in previous research[31,32].

Although the large prospective longitudinal design of this study is a major strength, there are also some limitations. First, only 50% of the patients responded to the BIOS-study. We found differences in injury and patient characteristics between responders and non-responders of the BIOS-study, e.g. responders were more severely injured compared to the non-responders, indicating selection bias. Next, it is also possible that selective dropout has occurred. We suspect that patients who were fully recovered were less likely to respond to the follow-up questions, resulting in an overestimation of complaints after injury. Last, frailty was only assessed in patients aged ≥65 years. This could have introduced bias, because younger patients may be frail. However, we believe this would only affect a small proportion in this large cohort.

Next, generalisability of the study results can be questioned, because inclusion criteria for injured patients could be different from other registries. This study included all injury severities and elderly patients with hip fracture.

We acknowledge that long-term non-fatal outcomes should be incorporated in the trauma registry[33]. These outcomes could be used to inform caregivers and patients about their expected recovery patterns. However, pre-injury health status is essential in predicting short and long-term outcome after injury and should therefore also be included in the registry. Furthermore, the dimensions of the EQ-5D and health status showed to have different recovery patterns for different injury classifications. Non-fatal outcome should not only be focused on health status, but especially on the different dimensions.

Although patients showed to be recovered after six months for the dimensions anxiety/depression and cognition, the dimensions mobility, pain/discomfort and usual activities still improved 2 years after injury. These results contribute to the increase in knowledge of recovery patterns and could be a starting point to develop prediction models for specific injury classifications for the implementation of personalized medicine.

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Contributors

LM, SP and MJ contributed to conception and design of this study. LM and MJ contributed to data collection. LM, SP, RH, ES, MJ contributed to analyses and interpretation. LM, SP, RH, ES and MJ contributed to preparation of the manuscript. The final version of the article was approved by all the authors.

Table 1. Patient characteristics tables of responders and non-responders of the BIOS-study

	Responders[a]	Non-responders	p-value
N (%)	4883	4891	
Male (%)	2329 (48)	2407 (49)	0.13
Age (median, IQR)	68 (53-80)	70 (46-84)	0.26
ASA classification (N, %)			
1 (healthy)	1531 (31)	1195 (24)	0.00
2	2348 (48)	1657 (34)	
3	950 (19)	1046 (21)	
4 (severe systemic disease)	54 (1)	40 (1)	
Missing	-	953 (20)	
Injury Severity Score (median, IQR)	5 (4-9)	5 (2-9)	0.00
Length of stay at hospital (median, IQR)	4 (2-8)	4 (2-8)	0.02
Functional capacity index (N, %)			0.00
1-2 (worse state)	248 (5)	169 (4)	
3-4	2074 (42)	1721 (35)	
5 (best possible state)	2561 (52)	2473 (51)	
Missing	-	528 (11)	
Injury classification (N, %)			
Pelvic injury	293 (6)	151 (3)	
Hip fracture	1266 (26)	1099 (23)	
Tibia, complex foot or femur fracture	569 (12)	505 (10)	
Shoulder and upper arm injury	473 (10)	417 (9)	
Radius, ulna or hand fracture	308 (6)	283 (6)	
Head injury with AIS <=2	1324 (27)	1443 (30)	
Head injury with AIS >=3	186 (4)	181 (4)	
Facial injury	249 (5)	303 (6)	
Thoracic injury	198 (4)	162 (3)	
Rib fracture	451 (11)	398 (8)	
Abdominal injury	87 (2)	89 (2)	
Spinal cord injury	36 (1)	30 (1)	
Stable vertebral fracture or disc injury	27 (1)	10 (0)	
Pelvic injury	301 (6)	249 (5)	
Mechanism of injury			
Home and leisure	2957 (61)	2582 (53)	
Traffic	1272 (26)	895 (18)	
Occupational	205 (4)	144 (3)	
Sport	321 (7)	165 (3)	
Self-harm	18 (0)	27 (1)	
Violence	64 (1)	149 (3)	
Other	46 (1)	42 (1)	
missing		887 (18)	
Admission to intensive care unit (N, %)	358 (7)	292 (6)	0.00
Educational level (N, %)*			
Low	2670 (55)	-	
Middle	1305 (27)	-	
High	908 (19)	-	
Pre-injury work status*	1278 (38)	-	

[a]patients who completed at least one follow-up questionnaire. Missing variables were imputed.
*variables were only collected in responders
Abbreviations: ASA, American Society of Anaesthesiologists Classification; IQR, Inter Quartile Range; N, Number.

Table 2. Regression coefficients in multivariable linear mixed models for the EQ-5D utility and the EQ-VAS and odds ratios in multivariable logistic mixed models for the dimensions of HS.

	During the first two years after injury							
	Linear regression coefficients (95% CI)		Odds Ratios (95% CI)					
	EQ-5D utility	EQ-VAS	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/ depression	Cognition
Female sex	-0.03 (-0.04, -0.01)	-1.43 (-2.30, -0.55)	1.08 (0.91, 1.29)	1.08 (0.95, 1.22)	1.51 (1.32, 1.72)	1.56 (1.35, 1.80)	2.02 (1.62, 2.51)	2.01 (1.54, 2.63)
Age (years)								
18 - 24	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25 - 44	0.01 (-0.03, 0.04)	-0.32 (-2.87, 2.24)	1.13 (0.70, 1.83)	0.88 (0.61, 1.28)	1.18 (0.82, 1.71)	1.08 (0.72, 1.61)	0.97 (0.53, 1.77)	0.84 (0.41, 1.72)
45 - 64	0.05 (0.02, 0.09)	1.22 (-1.15, 3.60)	1.20 (0.76, 1.87)	0.79 (0.56, 1.13)	0.89 (0.63, 1.26)	0.81 (0.55, 1.18)	0.37 (0.21, 0.66)	0.37 (0.19, 0.73)
65 - 74	0.12 (0.08, 0.16)	6.43 (3.76, 9.10)	0.84 (0.51, 1.38)	0.55 (0.38, 0.82)	0.53 (0.36, 0.78)	0.51 (0.33, 0.78)	0.10 (0.05, 0.20)	0.14 (0.07, 0.31)
≥ 75	0.09 (0.05, 0.13)	4.98 (2.22, 7.73)	1.39 (0.82, 2.33)	0.98 (0.66, 1.46)	0.64 (0.43, 0.96)	0.45 (0.29, 0.70)	0.13 (0.07, 0.26)	0.42 (0.19, 0.92)
Nr of comorbidities								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-0.03 (-0.04, -0.01)	-2.72 (-3.79, -1.65)	1.45 (1.18, 1.77)	1.19 (1.03, 1.39)	1.29 (1.11, 1.51)	1.23 (1.04, 1.46)	1.65 (1.27, 2.15)	1.36 (0.99, 1.88)
≥2	-0.05 (-0.07, -0.04)	-4.08 (-5.30, -2.87)	2.13 (1.69, 2.68)	1.62 (1.38, 1.91)	1.84 (1.54, 2.20)	1.80 (1.47, 2.20)	2.34 (1.74, 3.13)	2.01 (1.40, 2.87)
Injury Severity Score[b]	-0.01 (-0.02, 0.00)	-0.93 (-1.53, -0.33)	1.10 (0.98, 1.23)	1 (0.92, 1.09)	1.08 (0.99, 1.18)	0.92 (0.83, 1.01)	1.12 (0.97, 1.30)	1.27 (1.05, 1.52)
Length of stay at hospital (days)								
1 - 2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3 - 7	-0.05 (-0.07, -0.03)	-3.40 (-4.52, -2.29)	2.14 (1.73, 2.64)	1.56 (1.33, 1.84)	1.72 (1.47, 2.03)	1.69 (1.40, 2.04)	1.69 (1.27, 2.25)	1.15 (0.81, 1.62)
8 - 14	-0.10 (-0.12, -0.08)	-6.24 (-7.70, -4.77)	3.21 (2.39, 4.29)	2.60 (2.12, 3.19)	2.67 (2.13, 3.35)	2.15 (1.68, 2.75)	2.73 (1.90, 3.92)	1.77 (1.13, 2.76)
≥ 15	-0.15 (-0.18, -0.12)	-9.32 (-11.43, -7.22)	6.07 (3.80, 9.69)	3.42 (2.51, 4.66)	3.97 (2.77, 5.71)	2.43 (1.66, 3.55)	4.15 (2.48, 6.95)	2.81 (1.47, 5.37)
Functional Capacity Index								
1 (worse state)	-0.07 (-0.15, 0.00)	-0.89 (-6.27, 4.48)	1.51 (0.57, 4.06)	1.79 (0.87, 3.71)	1.14 (0.51, 2.54)	1.00 (0.42, 2.41)	1.46 (0.41, 5.19)	1.63 (0.31, 8.57)
2	-0.06 (-0.10, -0.03)	-1.22 (-3.57, 1.12)	1.89 (1.19, 3.01)	1.94 (1.42, 2.66)	1.59 (1.12, 2.27)	1.28 (0.87, 1.89)	1.57 (0.89, 2.77)	0.67 (0.32, 1.38)
3	-0.03 (-0.07, 0.00)	-0.48 (-2.84, 1.89)	2.11 (1.34, 3.31)	1.47 (1.08, 2.02)	1.88 (1.32, 2.68)	1.14 (0.78, 1.66)	1.10 (0.62, 1.95)	0.91 (0.44, 1.86)
4	-0.03 (-0.05, -0.01)	-0.04 (-1.50, 1.43)	1.62 (1.22, 2.15)	1.57 (1.29, 1.93)	1.42 (1.14, 1.77)	1.28 (1.01, 1.63)	1.03 (0.72, 1.48)	0.57 (0.36, 0.91)
5 (best possible state)[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Injury classification[c]								
Pelvic injury	-0.04 (-0.07, -0.02)	-1.64 (-3.37, 0.10)	2.74 (1.96, 3.83)	1.29 (1.02, 1.64)	0.97 (0.74, 1.25)	1.33 (0.99, 1.78)	0.67 (0.43, 1.04)	0.57 (0.33, 0.98)
Hip fracture	-0.01 (-0.04, 0.02)	-0.34 (-2.20, 1.52)	2.62 (1.82, 3.79)	1.28 (0.99, 1.66)	1.05 (0.79, 1.40)	1.04 (0.76, 1.41)	0.90 (0.57, 1.42)	1.00 (0.57, 1.77)
Tibia, complex foot or femur fracture	-0.05 (-0.07, -0.02)	-1.14 (-2.75, 0.48)	6.85 (4.97, 9.44)	1.27 (1.02, 1.58)	1.71 (1.33, 2.18)	1.34 (1.03, 1.76)	0.8 (0.53, 1.19)	0.71 (0.43, 1.18)
Shoulder and upper arm injury	-0.03 (-0.06, -0.01)	-2.00 (-3.44, -0.55)	0.56 (0.42, 0.74)	2.22 (1.82, 2.71)	1.58 (1.28, 1.96)	2.05 (1.60, 2.61)	1.01 (0.7, 1.44)	0.71 (0.46, 1.12)
Radius, ulna or hand fracture	-0.02 (-0.04, 0.00)	-0.59 (-2.31, 1.12)	0.42 (0.30, 0.58)	1.46 (1.16, 1.85)	1.22 (0.95, 1.57)	1.23 (0.93, 1.63)	1.44 (0.94, 2.19)	0.87 (0.51, 1.48)
Head injury with AIS <=2	0.02 (0.01, 0.04)	0.64 (-0.41, 1.70)	0.78 (0.64, 0.96)	0.57 (0.49, 0.67)	0.77 (0.66, 0.90)	0.85 (0.72, 1.01)	1.15 (0.88, 1.49)	2.91 (2.12, 4.01)
Head injury with AIS >=3	0.04 (0.00, 0.08)	2.07 (-0.66, 4.80)	0.86 (0.51, 1.43)	0.92 (0.62, 1.37)	0.78 (0.52, 1.17)	0.90 (0.58, 1.39)	1.20 (0.62, 2.34)	3.29 (1.45, 7.49)
Facial injury	0.02 (0.00, 0.05)	0.78 (-1.15, 2.70)	0.52 (0.35, 0.75)	0.75 (0.56, 1.00)	0.67 (0.51, 0.89)	0.67 (0.49, 0.91)	1.10 (0.68, 1.78)	1.21 (0.68, 2.16)
Thoracic injury	0.06 (0.03, 0.10)	3.11 (0.77, 5.46)	0.54 (0.35, 0.84)	0.56 (0.40, 0.78)	0.55 (0.40, 0.78)	0.68 (0.47, 1.00)	0.58 (0.32, 1.05)	0.60 (0.29, 1.24)
Rib fracture	-0.01 (-0.03, 0.01)	-0.07 (-1.61, 1.48)	1.07 (0.80, 1.43)	1.02 (0.81, 1.27)	0.93 (0.74, 1.16)	1.63 (1.26, 2.11)	0.96 (0.65, 1.41)	0.85 (0.53, 1.36)
Abdominal injury	0.02 (-0.02, 0.06)	1.68 (-1.27, 4.63)	0.63 (0.36, 1.09)	0.57 (0.36, 0.88)	0.67 (0.44, 1.02)	0.56 (0.35, 0.90)	0.93 (0.45, 1.95)	1.55 (0.65, 3.69)
Spinal cord injury	-0.06 (-0.16, 0.04)	-3.03 (-9.85, 3.80)	1.86 (0.53, 6.60)	1.33 (0.53, 3.33)	1.35 (0.47, 3.88)	11.61 (2.86, 47.17)	0.92 (0.18, 4.71)	0.30 (0.04, 2.35)

Stable vertebral fracture or disc injury	-0.06 (-0.08, -0.03)	-4.16 (-5.99, -2.33)	1.31 (0.93, 1.84)	1.67 (1.30, 2.15)	1.79 (1.37, 2.34)	2.45 (1.79, 3.35)	1.14 (0.72, 1.79)	0.82 (0.47, 1.42)
Admission to Intensive Care Unit	0.00 (-0.02, 0.03)	-0.47 (-2.35, 1.41)	0.81 (0.56, 1.18)	1.01 (0.77, 1.32)	1.04 (0.78, 1.38)	1.08 (0.79, 1.49)	0.77 (0.48, 1.23)	2.22 (1.26, 3.91)
Pre-injury work status	0.00 (-0.02, 0.02)	-0.23 (-1.62, 1.17)	0.73 (0.57, 0.95)	0.94 (0.78, 1.14)	1.01 (0.83, 1.23)	1.12 (0.90, 1.40)	0.74 (0.53, 1.04)	0.92 (0.61, 1.39)
Educational level								
Low[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle	0.00 (-0.01, 0.02)	0.39 (-0.66, 1.43)	0.94 (0.77, 1.15)	0.96 (0.83, 1.11)	0.93 (0.80, 1.08)	1.07 (0.90, 1.26)	0.71 (0.55, 0.92)	1.05 (0.77, 1.45)
High	0.02 (0.00, 0.03)	0.36 (-0.76, 1.49)	0.91 (0.73, 1.13)	0.99 (0.84, 1.15)	0.75 (0.64, 0.89)	0.82 (0.68, 0.98)	0.64 (0.48, 0.86)	1.06 (0.75, 1.51)
Frailty	-0.09 (-0.11, -0.07)	-5.12 (-6.54, -3.71)	2.38 (1.75, 3.24)	1.79 (1.46, 2.20)	2.07 (1.63, 2.62)	1.48 (1.18, 1.87)	4.94 (3.55, 6.86)	4.37 (2.89, 6.61)
Pre-injury status[d]	0.49 (0.45, 0.53)	0.47 (0.44, 0.50)						
No problems[a]			Ref	Ref	Ref	Ref	Ref	Ref
Moderate/severe problems			13.58 (10.62, 17.36)	20.02 (15.50, 25.86)	6.39 (5.20, 7.86)	6.12 (5.09, 7.36)	30.22 (21.62, 42.25)	371.77 (224.34, 616.10)

[a]Reference category

[b]Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

[c]Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

[d]Regression coefficients (95% CI) for pre-injury EQ-5D utility score and the pre-injury EQ-VAS for EQ-5D utility and EQ-VAS respectively. Odds ratios (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort, Anxiety/depression and cognition respectively for the columns).

Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.

Table 3. Change in health status and the dimensions of health status over time in multivariable linear and logistic mixed models.

	1 month vs 1 week	3 months vs 1 month	6 months vs 3 months	12 months vs 6 months	24 months vs 12 months
Linear regression coefficients (95% Confidence Interval)*					
EQ-5D utility	0.13 (0.12, 0.14)	0.12 (0.11, 0.13)	0.06 (0.05, 0.07)	0.01 (0.00, 0.02)	0.00 (-0.01, 0.02)
EQ-VAS	8.48 (7.70, 9.26)	5.97 (5.28, 6.69)	3.12 (2.36, 3.87)	0.24 (-0.52, 1.01)	0.98 (0.19, 1.76)
Odds Ratios (95% Confidence Interval)*					
Mobility	0.51 (0.41, 0.63)	0.38 (0.32, 0.46)	0.38 (0.31, 0.46)	0.85 (0.70, 1.03)	0.79 (0.65, 0.97)
Self-care	0.25 (0.21, 0.30)	0.14 (0.12, 0.17)	0.34 (0.28, 0.41)	0.73 (0.59, 0.91)	1.03 (0.82, 1.30)
Usual activities	0.67 (0.54, 0.83)	0.22 (0.19, 0.27)	0.31 (0.26, 0.37)	0.61 (0.52, 0.73)	0.82 (0.69, 0.98)
Pain/discomfort	0.46 (0.37, 0.56)	0.36 (0.30, 0.42)	0.51 (0.44, 0.61)	0.68 (0.58, 0.80)	0.84 (0.71, 1.00)
Anxiety/depression	0.99 (0.82, 1.21)	0.70 (0.59, 0.84)	0.70 (0.58, 0.85)	0.83 (0.68, 1.02)	0.89 (0.72, 1.11)
Cognition	0.85 (0.68, 1.06)	0.91 (0.75, 1.12)	0.62 (0.49, 0.77)	1.09 (0.86, 1.38)	1.15 (0.91, 1.45)

Time was included as categorical variable in the analyses

*Regression coefficients and odds ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level, frailty and pre-injury status

Table 4. Change in the dimensions of health status over time in multivariable logistic mixed models for different injury classifications

	Adjusted Odds Ratios (95% Confidence Interval)*				
	1 month vs 1 week	**3 months vs 1 month**	**6 months vs 3 months**	**12 months vs 6 months**	**24 months vs 12 months**
Mobility					
Lower extremity[1]	0.78 (0.48, 1.27)	0.24 (0.16, 0.35)	0.17 (0.12, 0.23)	0.54 (0.41, 0.70)	0.79 (0.60, 1.03)
Spine[2]	0.12 (0.05, 0.30)	0.18 (0.08, 0.37)	0.37 (0.17, 0.81)	1.01 (0.47, 2.22)	0.70 (0.31, 1.60)
Self-care					
Lower extremity[1]	0.33 (0.24, 0.44)	0.66 (0.52, 0.84)	0.75 (0.58, 0.95)	0.66 (0.49, 0.88)	1.05 (0.77, 1.43)
Upper extremity[3]	0.19 (0.11, 0.32)	0.09 (0.06, 0.15)	0.25 (0.16, 0.40)	0.51 (0.30, 0.87)	0.72 (0.40, 1.31)
Spine[2]	0.25 (0.11, 0.57)	0.05 (0.02, 0.11)	0.15 (0.06, 0.34)	0.55 (0.21, 1.43)	1.43 (0.52, 3.93)
Usual activities					
Upper extremity[3]	0.40 (0.22, 0.73)	0.20 (0.13, 0.32)	0.25 (0.17, 0.38)	0.61 (0.40, 0.90)	0.76 (0.50, 1.15)
Spine[2]	0.48 (0.17, 1.30)	0.11 (0.05, 0.25)	0.24 (0.12, 0.49)	0.30 (0.15, 0.60)	1.71 (0.58, 2.38)
Pain/discomfort					
Lower extremity[1]	0.42 (0.30, 0.59)	0.53 (0.41, 0.69)	0.49 (0.39, 0.63)	0.66 (0.52, 0.84)	0.75 (0.59, 0.96)
Upper extremity[3]	0.49 (0.27, 0.87)	0.27 (0.17, 0.43)	0.48 (0.32, 0.73)	0.52 (0.35, 0.78)	0.78 (0.52, 1.18)
Spine[2]	0.35 (0.12, 0.98)	0.29 (0.13, 0.64)	0.62 (0.30, 1.27)	0.19 (0.09, 0.39)	1.27 (0.64, 2.50)
Anxiety/depression					
Spine[2]	0.69 (0.33, 1.43)	0.92 (0.49, 1.74)	0.64 (0.32, 1.27)	0.81 (0.40, 1.64)	0.87 (0.41, 1.85)
Cognition					
Traumtic Brain Injury[4]	0.72 (0.50, 1.02)	0.85 (0.60, 1.18)	0.69 (0.48, 0.99)	0.91 (0.63, 1.32)	1.15 (0.79, 1.68)

Time was included as categorical variable in all analyses

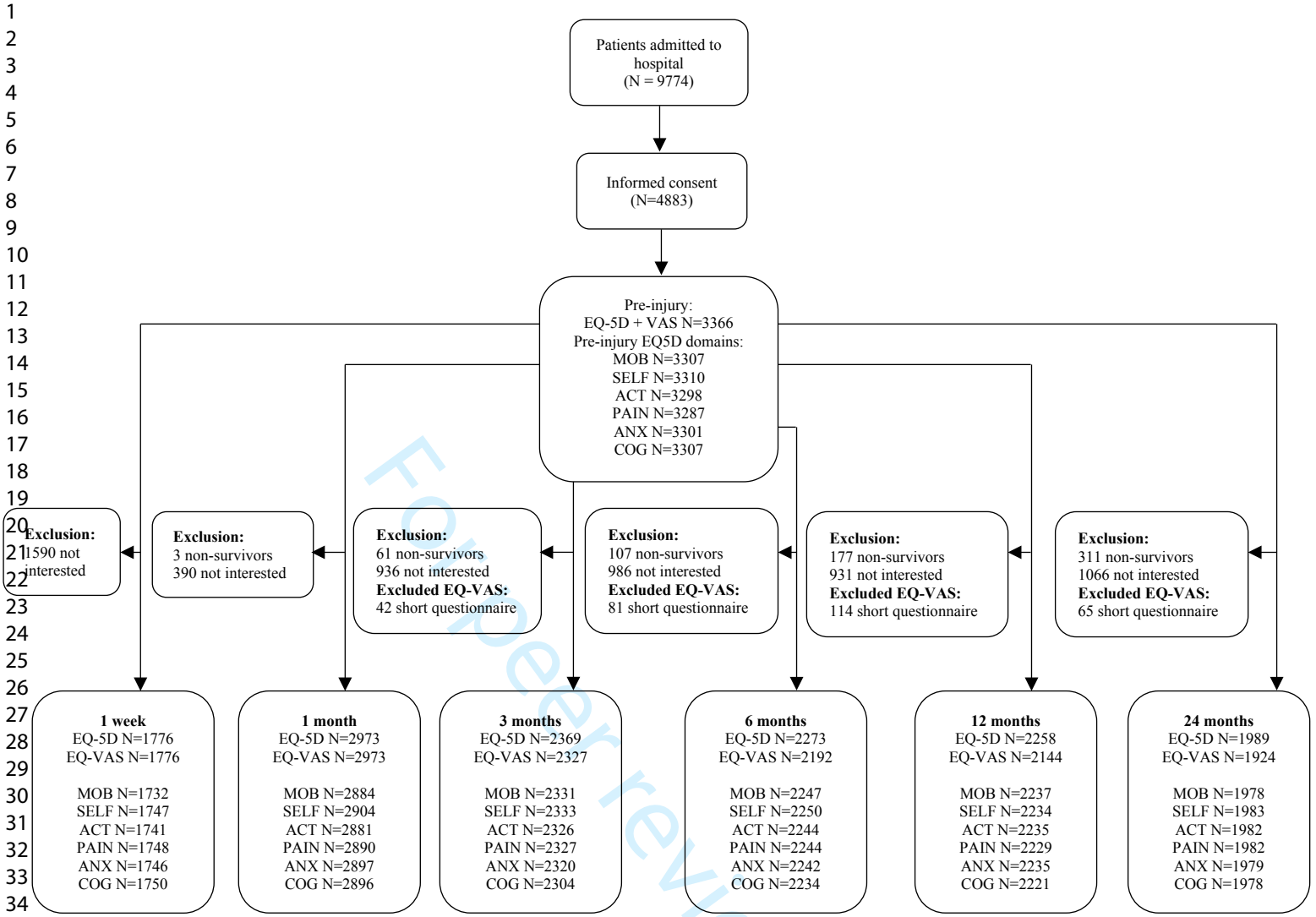
*Odds Ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level, frailty and pre-injury status

[1]Patients with pelvic injury, hip fracture or tibia, complex foot or femur fracture

[2]Patients with spinal cord injury or stable vertebral fracture or disc injury

[3]Patients with shoulder and upper arm injury or radius, ulna or hand fracture

[4]Patients with Traumatic brain injury, independent of injury severity



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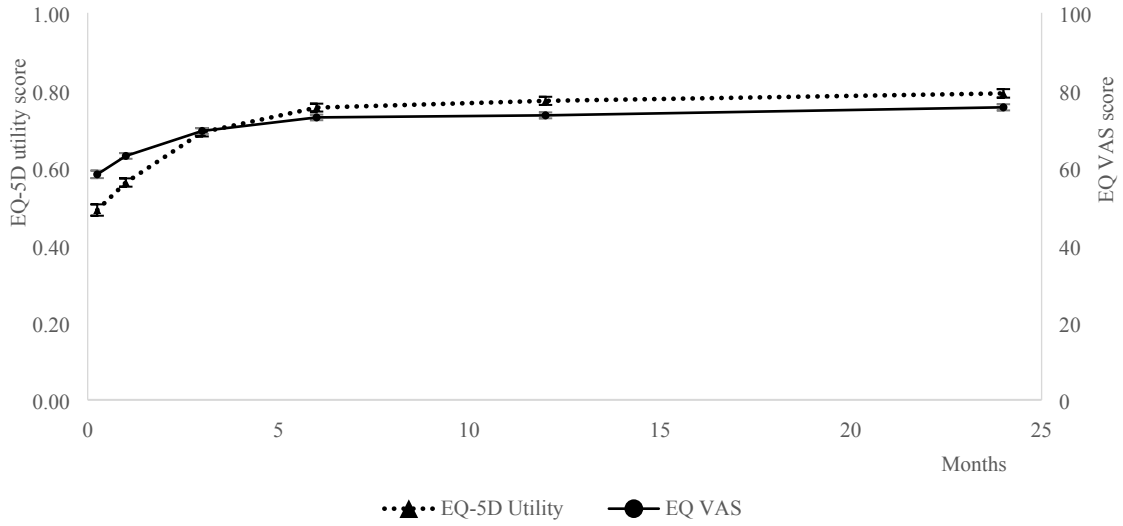
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0.80
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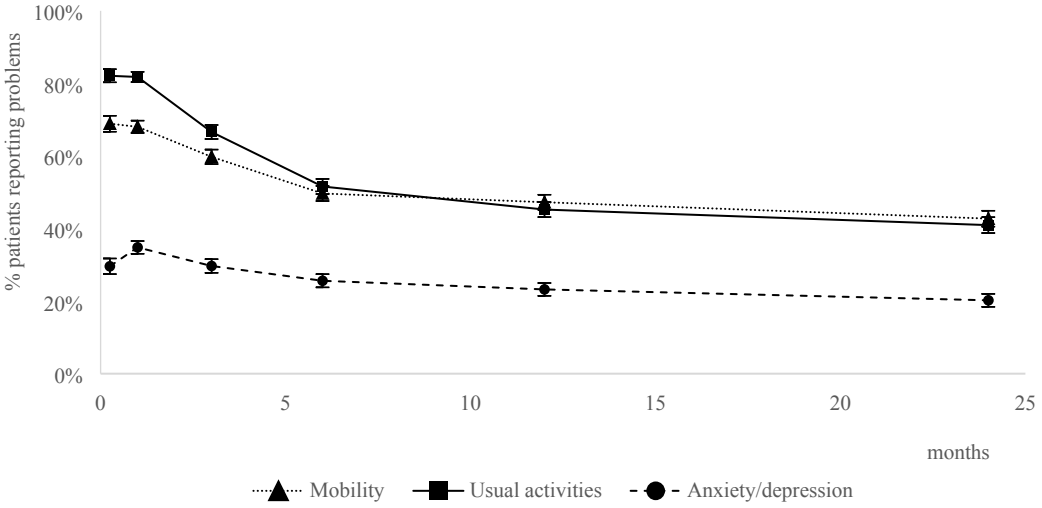
25
Months
EQ-5D Utility
EQ VAS

B.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Mobility
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Anxiety/depression

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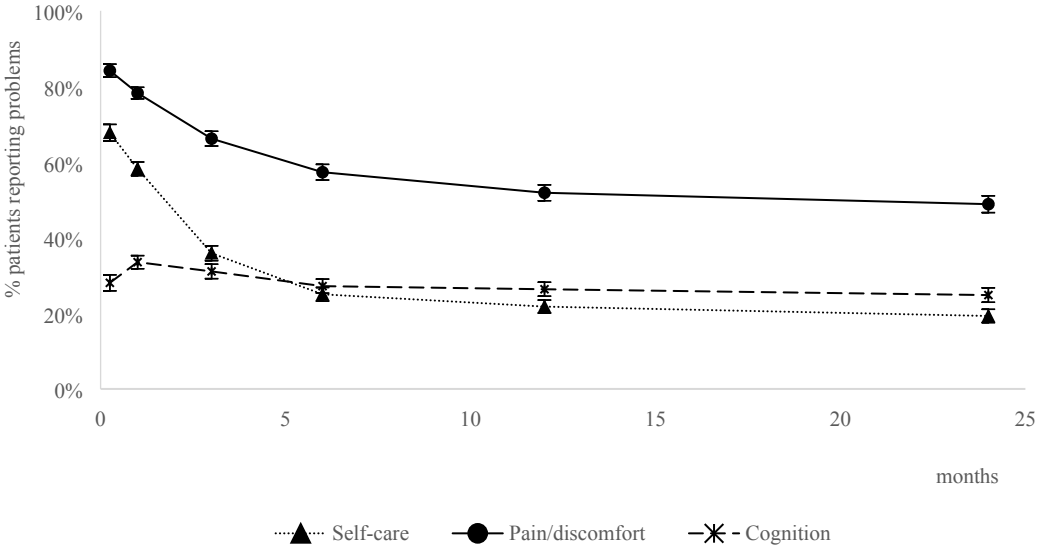
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Self-care
Pain/discomfort
Cognition

Supplemental Table . Regression coefficients in univariable linear mixed models for the EQ-5D utility and the EQ-VAS and odds ratios in univariable logistic mixed models for the dimensions of HS.

	During the first two years after injury							
	Linear regression coefficients (95% CI)		Odds Ratios (95% CI)					
	EQ-5D utility	EQ-VAS	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/ depression	Cognition
Female sex	-0.11 (-0.12, -0.10)	-6.37 (-7.42, -5.32)	4.57 (3.73, 5.61)	3.04 (2.62, 3.53)	3.20 (2.78, 3.68)	2.46 (2.15, 2.82)	4.28 (3.48, 5.28)	4.95 (3.71, 6.60)
Age (years)								
18 - 24	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25 - 44	-0.03 (-0.07, 0.01)	-1.59 (-4.66, 1.47)	2.08 (1.18, 3.64)	1.59 (1.03, 2.46)	1.83 (1.22, 2.74)	1.72 (1.15, 2.59)	0.93 (0.52, 1.67)	0.71 (0.34, 1.52)
45 - 64	-0.02 (-0.06, 0.01)	-3.69 (-6.50, -0.88)	4.59 (2.74, 7.68)	2.08 (1.40, 3.10)	1.86 (1.29, 2.69)	1.82 (1.26, 2.63)	0.58 (0.34, 0.98)	0.43 (0.22, 0.86)
65 - 74	-0.02 (-0.06, 0.02)	-2.47 (-5.35, 0.41)	10.91 (6.42, 18.56)	2.78 (1.85, 4.18)	1.77 (1.21, 2.58)	1.63 (1.12, 2.37)	0.39 (0.23, 0.68)	0.39 (0.20, 0.79)
≥ 75	-0.16 (-0.19, -0.12)	-12.78 (-15.58, -9.98)	105.71 (61.48, 181.77)	14.70 (9.83, 21.98)	6.29 (4.34, 9.1)	2.50 (1.73, 3.60)	2.07 (1.23, 3.49)	12.86 (6.37, 25.98)
Nr of comorbidities								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-0.08 (-0.10, -0.06)	-7.86 (-9.05, -6.66)	5.41 (4.26, 6.87)	2.45 (2.06, 2.91)	2.14 (1.82, 2.51)	1.75 (1.49, 2.05)	2.54 (1.98, 3.24)	5.41 (3.88, 7.53)
≥2	-0.21 (-0.22, -0.19)	-16.02 (-17.20, -14.84)	36.44 (27.79, 47.78)	8.45 (7.07, 10.10)	7.16 (6.03, 8.51)	4.70 (3.97, 5.57)	9.32 (7.25, 11.97)	45.33 (30.83, 66.64)
Injury Severity Score[b]	-0.03 (-0.03,-0.02)	-2.07 (-2.49, -1.65)	1.58 (1.45, 1.71)	1.34 (1.27, 1.43)	1.35 (1.27, 1.43)	1.12 (1.06, 1.18)	1.25 (1.15, 1.36)	1.52 (1.36, 1.70)
Length of stay at hospital (days)								
1 - 2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3 - 7	-0.10 (-0.12, -0.09)	-6.46 (-7.70, -5.22)	10.61 (8.31, 13.53)	3.72 (3.11, 4.45)	3.11 (2.65, 3.66)	2.19 (1.86, 2.59)	2.23 (1.72, 2.88)	2.22 (1.57, 3.13)
8 - 14	-0.20 (-0.22, -0.18)	-13.00 (-14.52, -11.48)	39.48 (28.73, 54.26)	11.04 (8.87, 13.73)	8.06 (6.54, 9.93)	3.73 (3.05, 4.57)	5.73 (4.23, 7.76)	9.12 (5.96, 13.97)
≥ 15	-0.28 (-0.31, -0.26)	-18.39 (-20.52, -16.25)	103.66 (65.98, 162.88)	22.75 (16.73, 30.93)	14.88 (10.88, 20.36)	4.91 (3.63, 6.65)	11.30 (7.41, 17.24)	24.69 (13.58, 44.90)
Functional Capacity Index								
1 (worse state)	-0.13 (-0.20, -0.06)	-7.63 (-13.18, -2.08)	4.12 (1.62, 10.48)	2.95 (1.45, 5.99)	3.04 (1.52, 6.08)	1.43 (0.72, 2.85)	3.97 (1.46, 10.75)	8.96 (2.28, 35.20)

2	-0.10 (-0.13, -0.06)	-3.73 (-6.41, -1.05)	9.85 (6.00, 16.17)	2.47 (1.74, 3.52)	2.85 (2.00, 4.05)	2.16 (1.51, 3.09)	1.88 (1.12, 3.17)	0.33 (0.16, 0.65)
3	-0.10 (-0.13, -0.06)	-2.74 (-5.57, 0.08)	7.83 (4.70, 13.06)	2.91 (2.00, 4.25)	3.93 (2.69, 5.75)	1.63 (1.13, 2.36)	1.67 (0.96, 2.92)	0.69 (0.33, 1.45)
4	-0.11 (-0.12, -0.10)	-6.01 (-7.15, -4.88)	13.22 (10.56, 16.56)	4.62 (3.94, 5.43)	3.27 (2.82, 3.80)	1.71 (1.48, 1.98)	2.05 (1.64, 2.56)	1.37 (1.02, 1.84)
5 (best possible state)[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Injury classification[c]								
Pelvic injury	0.71 (0.70, 0.72)	-4.60 (-6.70, -2.51)	6.17 (4.27, 8.92)	2.27 (1.71, 3.00)	1.93 (1.47, 2.54)	1.57 (1.19, 2.08)	1.37 (0.9, 2.1)	1.19 (0.68, 2.09)
Hip fracture	-0.09 (-0.12, -0.06)	-9.15 (-10.55, -7.74)	20.99 (16.05, 27.46)	5.59 (4.60, 6.81)	3.77 (3.12, 4.55)	1.68 (1.4, 2.02)	2.68 (2.04, 3.53)	5.48 (3.75, 8.02)
Tibia, complex foot or femur fracture	-0.13 (-0.15, -0.11)	-2.37 (-4.09, -0.65)	12.24 (8.98, 16.69)	1.79 (1.42, 2.24)	2.84 (2.27, 3.57)	1.81 (1.44, 2.27)	1.26 (0.9, 1.76)	0.53 (0.34, 0.82)
Shoulder and upper arm injury	-0.07 (-0.10, -0.05)	-2.57 (-4.40, -0.74)	0.75 (0.55, 1.01)	2.47 (1.95, 3.14)	1.8 (1.43, 2.27)	2.21 (1.74, 2.8)	1.21 (0.85, 1.72)	0.75 (0.47, 1.18)
Radius, ulna or hand fracture	-0.04 (-0.07, -0.02)	0.60 (-1.54, 2.74)	0.35 (0.24, 0.5)	1.22 (0.92, 1.62)	1.06 (0.81, 1.38)	1.03 (0.78, 1.35)	0.77 (0.5, 1.17)	0.36 (0.21, 0.63)
Head injury with AIS <=2	0.01 (-0.02, 0.03)	1.40 (0.10, 2.69)	0.66 (0.53, 0.82)	0.50 (0.41, 0.59)	0.63 (0.53, 0.74)	0.67 (0.57, 0.8)	0.82 (0.64, 1.06)	2.52 (1.8, 3.53)
Head injury with AIS >=3	0.04 (0.03, 0.06)	-2.77 (-5.54, 0.00)	1.84 (1.16, 2.91)	1.17 (0.80, 1.71)	1.66 (1.16, 2.36)	0.86 (0.61, 1.22)	2.44 (1.43, 4.15)	13.11 (6.35, 27.06)
Facial injury	-0.03 (-0.06, 0.01)	1.99 (-0.40, 4.37)	0.37 (0.25, 0.56)	0.64 (0.46, 0.90)	0.65 (0.48, 0.88)	0.6 (0.44, 0.81)	0.99 (0.61, 1.58)	1.34 (0.72, 2.47)
Thoracic injury	0.04 (0.00, 0.07)	2.37 (-0.49, 5.23)	0.54 (0.33, 0.87)	0.62 (0.42, 0.93)	0.73 (0.51, 1.05)	0.61 (0.42, 0.89)	0.83 (0.47, 1.48)	0.8 (0.38, 1.68)
Rib fracture	0.04 (0.00, 0.07)	-0.80 (-2.68, 1.09)	1 (0.73, 1.37)	0.81 (0.63, 1.05)	0.94 (0.74, 1.19)	1.35 (1.06, 1.72)	0.65 (0.45, 0.95)	1.05 (0.65, 1.71)
Abdominal injury	0.00 (-0.02, 0.03)	1.24 (-2.24, 4.73)	0.44 (0.24, 0.81)	0.58 (0.35, 0.95)	0.66 (0.42, 1.04)	0.56 (0.35, 0.88)	1.06 (0.53, 2.14)	1.27 (0.51, 3.14)
Spinal cord injury	-0.18 (-0.27, -0.09)	-7.32 (-14.94, 0.29)	5.97 (1.8, 19.76)	3.55 (1.41, 8.98)	5.03 (1.95, 13)	23.14 (6.63, 80.76)	2.97 (0.78, 11.27)	0.94 (0.16, 5.48)
Stable vertebral fracture or disc injury	-0.05 (-0.08, -0.03)	-4.10 (-6.27, -1.93)	1.22 (0.85, 1.76)	1.57 (1.17, 2.10)	1.88 (1.42, 2.49)	2.43 (1.82, 3.25)	1.23 (0.8, 1.87)	0.96 (0.55, 1.68)
Admission to Intensive Care Unit	-0.02 (-0.05, 0.01)	-2.88 (-4.90, -0.86)	0.80 (0.55, 1.16)	0.94 (0.72, 1.25)	1.26 (0.97, 1.65)	1.10 (0.84, 1.43)	1.16 (0.79, 1.71)	4.15 (2.51, 6.83)
Pre-injury work status	0.11 (0.09, 0.12)	7.58 (6.40, 8.76)	0.06 (0.05, 0.08)	0.23 (0.19, 0.27)	0.38 (0.33, 0.45)	0.63 (0.54, 0.73)	0.35 (0.28, 0.45)	0.10 (0.07, 0.15)
Educational level								
Low[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle	0.07 (0.06, 0.09)	5.42 (4.15, 6.70)	0.22 (0.17, 0.28)	0.38 (0.32, 0.46)	0.51 (0.43, 0.6)	0.76 (0.65, 0.90)	0.39 (0.31, 0.50)	0.25 (0.18, 0.35)
High	0.11 (0.09, 0.13)	6.74 (5.35, 8.13)	0.18 (0.13, 0.23)	0.35 (0.29, 0.43)	0.37 (0.31, 0.45)	0.48 (0.40, 0.57)	0.25 (0.19, 0.33)	0.18 (0.12, 0.26)
Frailty	-0.28 (-0.30, -0.26)	-17.00 (-18.28, -15.73)	42.04 (30.13, 58.65)	17.43 (13.8, 22.02)	10.32 (8.11, 13.12)	3.53 (2.84, 4.39)	20.90 (15.31, 28.54)	181.79 (99.22, 333.08)

Pre-injury status[d]	0.67 (0.64, 0.70)	0.58 (0.55, 0.60)						
No problems[a]			Ref	Ref	Ref	Ref	Ref	Ref
Moderate/severe problems			71.89 (54.53, 94.77)	61.03 (47.05, 79.17)	15.01 (12.27, 18.36)	8.69 (7.29, 10.36)	114.45 (79.19, 165.42)	3613.12 (1619.40, 8061.43)

[a]Reference category

[b]Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

[c]Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

[d]Regression coefficients (95% CI) for pre-injury EQ-5D utility score and the pre-injury EQ-VAS for EQ-5D utility and EQ-VAS respectively. Odds ratios (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort, Anxiety/depression and cognition respectively for the columns).

Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-6
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
-Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	Report numbers of outcome events or summary measures over time	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prognostic factors for recovery of health status after injury: a prospective multicentre cohort study

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Running head: Prognostic factors for recovery after injury

Key words: injury; longitudinal cohort study; health status; prognostic factors; recovery;

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Abstract

Objectives: to determine (I) prognostic factors for poor health status and (II) recovery patterns during the first two years after injury in the clinical trauma population.

Design: a prospective longitudinal cohort study.

Setting: Ten participating hospitals in Brabant, the Netherlands

Participants: adult injury patients admitted to a hospital between August 2015 and November 2016 were followed: 4883 (50%) patients participated.

Main outcome measures: Primary outcome was health status, measured with the EuroQol-5-dimensions-3-level (EQ-5D), including a cognition item and the EuroQol Visual Analogue Scale (EQ-VAS). Health status was collected at 1 week, 1, 3, 6, 12, and 24 months after injury. Potential prognostic factors were based on literature and clinical experience (e.g. age, sex, pre-injury frailty (Groningen Frailty Index), pre-injury EQ-5D).

Results. Health status increased strongly during the first six months after injury with a mean EQ-5D utility score at 1 week of 0.49 and 0.79 at 24 months. The dimensions mobility, pain/discomfort and usual activities improved up to 2 years after injury. Lower pre-injury health status, frailty and longer length of stay at the hospital were important prognostic factors for poor recovery. Spine injury, lower and upper extremity injury showed to be prognostic factors for problems after injury. Traumatic brain injury was a prognostic factor for problems with cognition.

Conclusion. This study contributes to the increase in knowledge of health recovery after injury. It could be a starting point to develop prediction models for specific injury classifications and implementation of personalized medicine.

Trial registration number: NCT02508675

Strengths and limitations of the study

- a strength of the study was the short- and long-term follow-up measurements to obtain essential recovery data of the injury patients.

- a strength of the study is the high number of participants in this prospective cohort study.

- a limitation of this study is the possibility of selective drop-out, which could have resulted in an overestimation of complaints after injury

- a limitation of this study is the possibility of selection bias, suggesting that more severely injured patients were more likely to participate.

Introduction

Trauma, defined as a physical injury, is one of the leading causes of disability and affects millions of people worldwide each year. The number of survivors after trauma has increased over several decades, due to the improvement of trauma care[1-3]. Many patients suffer physical, psychological or cognitive impairments, resulting in a reduction of their health status.

The trauma population is a heterogeneous group of patients. Patients are from various age groups with many different injury patterns, in both severity and body region. In addition, type of accident (e.g. falls, road traffic accident) and mechanism of injury (e.g. bleeding, fracture) can be diverse. The identification of patients at high risk of poor health status could enable clinicians to tailor treatment in which patients are referred to specialized care and rehabilitation at an early stage of their recovery or to lifelong treatment or lifestyle changes.

Previous research identified several prognostic factors for poor outcome after injury, e.g. age, gender, educational level, comorbidity, pre-injury work status[4-16]. Most previous studies on prognostic factors for health status studied major or severe trauma patients population[4,6-9,12-15], traumatic brain injury patients[5,14] or a small follow-up trauma population[11]. In addition, one study focused on long-term follow-up measurement, two to seven years after injury[8]. Last, pre-injury health status was not assessed as prognostic factor for health status in previous studies. Although recovery after injury is not only determined by injury severity or injury in specific body regions, research that takes into account the total clinical trauma population during their recovery is scarce[16]. In addition, different recovery patterns can be expected in, for example, brain injury patients and patients suffering from lower/upper extremity injury.

This study aimed to determine prognostic factors for health status and determine recovery patterns of health status after injury during the first two years after injury in the clinical trauma population and in specific injury classifications.

Methods

Study design and participants

Data was obtained from the Brabant Injury Outcome Surveillance (BIOS). The BIOS-study is a prospective observational cohort study in which health status, costs, functional and psychological outcomes were assessed in the first 24 months after injury. A detailed description of the methods of the BIOS-study can be found in the published research protocol[17].

All adult (≥18 years) patients admitted to a hospital in the region Noord-Brabant (the Netherlands) from 1 August 2015 to 30 November 2016 due to an injury and who survived to hospital discharge were included in this study. Patients without sufficient knowledge of the Dutch language or with pathological fractures (e.g. osteoporosis) were excluded. A proxy informant (caregiver or family member) was asked to complete the self-administered questionnaires if patients were incapable of completing the questionnaires in the BIOS-study from 1 month onwards. Proxy use of the EQ-5D-3L was validated previously in an injury cohort[18]. The questionnaires were sent by post or electronically at one week, one month, three months, six months, 12 months and 24 months after injury. All participants, patients or proxy informants, signed informed consent. Patients were asked to complete a shorter version of the questionnaire at three months, six months, 12 months and 24 months after injury to increase response, if patients did not complete the corresponding BIOS-questionnaire. This short version incorporates only a small collection of the questionnaires that are included in the BIOS-study (e.g. EQ-5D, demographics and return to work). Patients who did not respond to a questionnaire were considered a non-responder for that time point, but could participate again in the following questionnaires. Injury characteristics were collected in the Brabant Trauma Registry and were merged to the BIOS-data for all participating patients. The study was approved by the Medical Ethics Committee Brabant (project number BIOS-study: NL50258.028.14 and short questionnaire: NW2016-09).

Patient and public involvement

No patient involved.

Outcome

Health status was measured with the EuroQol-5D-3L (EQ-5D)[19]. This questionnaire consists of the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D descriptive system comprised the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension could be answered in three levels: no problems, some problems and severe/extreme problems.

A summary score of the EQ-5D (i.e. EQ-5D utility score) can be calculated by using the Dutch tariffs[20]. The EQ-5D utility score ranged from 0 (death) to 1 (perfect health). The EQ-VAS is a vertical visual analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state.

Cognition was added as an additional dimension to the EQ-5D questionnaire. Respondents were asked to describe their or, in case of proxy, the patients' state of health, concerning cognition (e.g. memory, concentration). Similar to the other dimensions, answer options were based on three levels: no problems, some problems and severe problems.

Health status was measured at each time point during follow-up in both patient and proxy questionnaires. The EQ-5D (including the cognition dimension) and EQ-VAS were also measured pre-injury, by asking participants at one week or one month and proxy informants at one month for the patients' health status before sustaining the injury. The EQ-5D with cognition dimension and EQ-VAS were botch included in the BIOS-study. The short questionnaire only included the EQ-5D and cognition dimension..

Prognostic factors

Prognostic factors can be subdivided into sociodemographic variables and clinical variables and were chosen based on previous literature and clinical experience[4-16]. *Sociodemographic variables*

Possible prognostic factors for health status that were measured in the BIOS-study were sex, age, educational level (low, middle or high), pre-injury work status (yes/no), frailty and pre-injury health status. Educational level was categorized in three levels as the highest completed degree, diploma of education; low (primary education, preparatory secondary vocational education or without diploma), middle (university preparatory education, senior general secondary education or senior secondary vocational education and training), and high (academic degree or university of applied science). Frailty was measured at one week or one month after injury with the Groningen Frailty Index (GFI) in patients ≥65 years[21]. A sum-score of ≥4 was considered frail. Patients <65 years were considered not frail.

Clinical variables

Possible clinical prognostic factors for health status were length of hospital stay, injury severity score (ranging from 1; mild injury to 75; fatal injury), admission to the intensive care (yes/no), presence of comorbidities and the functional capacity index. Comorbidities were measured with the American Society of Anaesthesiologists (ASA) physical status classification system ranging from 1 (healthy patient) to 4 (severe systemic disease that is a constant threat to life). The functional capacity index and injury severity score were based on the Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)[22]. All clinical variables were extracted from the trauma registry.

Injury Classification

The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)[22] were used to create injury group classifications representing the most common types of injuries. In total, 14 injury groups

were created: 3 lower extremity injury groups (pelvic injury, hip fracture, and tibia fracture/complex foot fracture or distal/shaft femur fracture), 2 upper extremity injury groups (shoulder and upper arm injury, and radius, ulna or hand fracture), 2 traumatic brain injury groups (AIS-head≤2, and AIS-head≥3), 1 face injury group, 2 thorax injury groups (thorax injury, and rib fracture), 2 abdomen injury groups (AIS-abdomen≤2, and AIS-abdomen≥3) and 2 spine injury groups (spinal cord injury/brachial plexus lesion, and stable vertebral fracture/disc injury) (**Supplemental File 1**). Patients who suffer multiple injuries could be classified in one or more injury group classifications.

Data analysis

Baseline characteristics of participants were compared with characteristics of non-responders, using chi-square for categorical variables or the Mann-Whitney U test for non-normal distributed data Normality was checked visually with a normal Q-Q plot. Descriptive statistics included the median with the interquartile range (IQR), mean with standard deviation (SD) for continuous variables and number with percentage for categorical variables. Missing baseline characteristics (0.9% for the Injury Severity Score and 6.8% for length of stay at hospital) and missing EQ-5D utility scores for participants (ranging from 1.8% at 1 week follow-up to 6.9% at 12 months follow-up) were imputed according to multiple imputation by using the Multivariate Imputations by Chained Equations (MICE) procedure with 15 imputations and 5 iterations[23]. The imputation model included baseline characteristics, injury characteristics and summary scores of the follow-up questionnaires to capture associations with missingness as completely as possible. Detailed description of the imputation model and imputed values were previously published[24]. No large differences were found between imputed data analyses and complete case analyses.

Multicollinearity was checked based on the Variance Inflation Factor (criterion: VIF > 10). Prognostic factors were assessed for poor health status outcome with EQ-5D utility scores and

EQ-VAS as outcome measures. Regression coefficients with corresponding 95% confidence interval (CI) were reported. The dimensions of the EQ-5D descriptive system were dichotomized into 0=no problems and 1=some problems/extreme problems. Logistic mixed models with random intercepts were used to assess prognostic factors for poor outcome for the six dimensions of the EQ-5D (e.g. mobility, self-care, usual activities, pain/discomfort, anxiety/depression and cognition). All potential prognostic factors were included in the multivariable regression models to calculate adjusted Odds Ratios and corresponding 95% CI. Age and length of stay at the hospital were included as categorical variables, because of the non-linear relation between factor and outcome.

Recovery patterns of health status were determined by changing the reference category of the categorical time variable in linear mixed models for health status and logistic mixed models for the dimensions of health status, adjusted for the prognostic factors. Recovery patterns for the items of the EQ-5D were assessed in detail for injury classifications that showed to be statistically significant for the dimensions in the total multivariable model.

Analyses were conducted in the statistical programs R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS version 24 (Chicago, USA) and results were reported according to the TRIPOD guidelines[25]. A p-value of $\leq .05$ was considered statistically significant.

Results

Baseline characteristics

A total of 4883 patients (50% of total, N=9774) completed at least one questionnaire of the BIOS study of whom 48% (N=2,329) was male **(Figure 1, Table 1)**. The median age was 68 years with an IQR of 53-80 years. Participants had a median injury severity score of 5 (IQR [4-9]) and most of the patients were classified as healthy or as patients with mild systemic disease (N= 3,879, 79%). A total of 358 patients (7%) were admitted to the intensive care unit. The majority of the participants had low educational level (N=2,670, 55%) and 38% of the participants (N=1,278) had a job prior to injury. Mean pre-injury EQ-5D utility score (SD) was 0.85 (0.23). A total of 762 participants (16%) of the patients reported to be frail.

Compared to the non-responders, participants were more severely injured, were more often admitted to the intensive care unit (7% vs 6%), had lower functional capacity index values, and were more often healthy (measured with the ASA classification).

A total of 1,105 participants (22.6% of the study population) completed all BIOS-questionnaires at each time point. The main reason for lost to follow-up was that completing the questionnaire was too time consuming. Patients who reported to be fully recovered and patients aged 18-24 were most likely to be lost to follow-up.

EQ-5D over time

The mean EQ-5D utility (SD) score was 0.49 (0.32), 0.56 (0.30), 0.69 (0.27), 0.76 (0.25), 0.77 (0.26) and 0.79 (0.25) at 1 week, 1, 3, 6, 12 and 24 months respectively **(Figure 2A, Supplemental File 2)**. The mean EQ-VAS (SD) score was 58.26 (20.45), 63.02 (20.46), 69.48 (18.56), 72.97 (17.28), 73.50 (18.08) and 75.58 (17.88) at 1 week, 1, 3, 6, 12 and 24 months

respectively. Patients reported the most increase in EQ-5D utility scores during the first 6 months, with a little improvement up to 12 months.

The first month, patients reported most problems for the following dimensions of the EQ-5D: pain/discomfort, usual activities, mobility and self-care **(Figure 2B and 2C, Supplemental File 2)**. During the 24 month follow-up, the percentage of patients reporting problems for pain/discomfort, usual activities and mobility were highest. Two years after injury 49% (95% CI: 47, 51) of the patients reported problems for pain/discomfort, 43% (95% CI: 41, 45) reported problems for mobility, 41% (95% CI: 39, 43) reported problems for usual activities, 25% (95% CI: 23, 27) reported for cognition, 20% (95% CI: 18, 22) reported problems for anxiety/depression and 19% (95% CI: 17, 21) for self-care.

Prognostic factors

Almost all variables were prognostic factors for an increase of the EQ-5D utility score in the univariable analyses (**Supplemental File 3**). Lower pre-injury health status, frailty and longer length of stay at hospital were important significant prognostic factors for decreased EQ-5D utility score, decreased EQ-VAS and its' dimensions during the first two years after injury in the multivariable analyses (**Table 2**). Age is a prognostic factor for self-care, usual activities, pain/discomfort, anxiety/depression and cognition, but no significant association was found for mobility. Sex showed to be a significant prognostic factor for all outcomes, except for mobility and self-care.

Lower extremity injury (Pelvic injury, hip fracture and tibia, complex foot or femur fracture) was a prognostic factor for the EQ-5D utility score, mobility, self-care, usual activities and pain-discomfort. Upper extremity injury (shoulder and upper arm injury, radius, ulna or hand fracture) was a prognostic factor for the EQ-5D utility score, mobility and self-care. Spine injury (spinal cord injury or stable vertebral fracture or disc injury) was a prognostic factor, although not always significant, for health status, and the dimensions mobility, self-care, usual

activities and pain/discomfort. Traumatic brain injury was a prognostic factor for problems with cognition.

Recovery patterns for injury classifications

Recovery for dimensions of health status amongst different injury classifications mostly occurred up until twelve months after injury, except for pain/discomfort (**Table 3**). Patients with lower extremity injury reported significant less problems at 24 months compared to twelve months for pain/discomfort.

Patients with spine injury showed improved mobility up to six months for mobility and self-care, and up to twelve months for pain/discomfort and usual activities. Upper and lower extremity injury showed the same recovery pattern during the first two years for self-care, with significant improvement up to twelve months after inury.

Discussion

In this multicentre prospective cohort study, we found that patients reported problems up until two years after injury. Health status was especially low during the first six months after injury, in which patients often reported problems in most of the dimensions of health status. Lower pre-injury health status, frailty and longer length of stay at hospital were prognostic factors for both decreased health status during the first two years after injury. For the EQ-5D dimensions mobility, usual activities and pain/discomfort less problems were reported at two years compared to one year after injury, as for the other dimensions we found no decrease in reported problems after one year.

The prevalence of problems in the dimensions of health status decreased during two years follow up. Although a recent study in severely injured patients demonstrated higher prevalence of problems in the health status dimensions[6], our results are in line with another study in the general clinical trauma population[16].

Previous research showed that age is a prognostic factor for reduced health status[9,16,26]. In contrast, results from this study showed improved overall health status. This could be explained by the addition of the strong prognostic factors pre-injury health status and frailty in the multivariable adjusted models. Indicating that not the increase of age is a prognostic factor for poor health status, but the patients' health status before injury. Not all elderly patients are frail nor are they in poor health. With the ageing population, frailty and pre-injury health status are essential to consider when assessing recovery patterns in injury patients. We found that increasing age was a prognostic factor for less problems with usual activities, pain/discomfort, anxiety/depression and cognition. This is also in contrast with a recent study, stating that the relationship between age and the dimensions of EQ-5D differed[6]. Again, the different findings can be attributed to the additional strong predictors. This is confirmed by the univariate analyses

which demonstrate that increasing age is associated with more problems on all dimensions of health status, except anxiety/depression and cognition.

The addition of the cognitive dimension on the EQ-5D has previously been shown to improve classification and validity, especially in patients with TBI[27,28]. In line with these findings, this study showed that patients with TBI were at risk of developing cognitive problems after injury. It has been suggested previously that most patients with mild TBI patients recover fully within three to six month, although some patients with mild TBI and patients with more severe TBI suffer persistent cognitive problems[29-31]. Our study showed that TBI patients reported no further improvement in health status after six months, in line with the recovery pattern of mild TBI patients. This is possibly due to the fact that most participants of the BIOS-study suffered mild TBI (27%) compared to moderate/severe TBI (4%). Further evaluation of these subgroups with more specific outcome measures are necessary to determine their recovery patterns.

In line with previous studies, this study showed that female sex is a prognostic factor for poor health status after injury[4,6,13-16,32]. It has been suggested that problems were more often reported in females, in contrast to males, who dismiss there complaints more often. Another explanation could be that women experience more psychological impact, resulting in lower health status. Except for longer length of stay at the hospital, no injury related characteristics were found to be prognostic factors for anxiety/depression complaints. These results suggest that psychological problems after injury are mainly based on patient characteristics, which is confirmed in previous research[33,34].

Although the large prospective longitudinal design of this study is a major strength, there are also some limitations. First, only 50% of the patients responded to the BIOS-study. We found differences in injury and patient characteristics between participants and non-responders of the BIOS-study, e.g. participants were more severely injured compared to the non-responders,

indicating selection bias. Next, it is also possible that selective dropout has occurred. We suspect that patients who were fully recovered were less likely to respond to the follow-up questions, resulting in an overestimation of complaints after injury. In addition, retrospectively collected preinjury health status scores are prone to recall bias and response shift[35]. However, they are considered more appropriate compared to general population norm scores[36]. Last, frailty was only assessed in patients aged ≥65 years. This could have introduced bias, because younger patients may be frail. However, we believe this would only affect a small proportion in this large cohort.

Next, generalisability of the study results can be questioned, because inclusion criteria for injured patients could be different from other registries. This study included all injury severities and elderly patients with hip fracture.

We acknowledge that long-term non-fatal outcomes should be incorporated in the trauma registry[37]. These outcomes could be used to inform caregivers and patients about their expected recovery patterns. However, pre-injury health status is essential in predicting short and long-term outcome after injury and should therefore also be included in the registry. Furthermore, the dimensions of the EQ-5D and health status showed to have different recovery patterns for different injury classifications. Non-fatal outcome should not only be focused on health status, but especially on the different dimensions.

Although patients demonstrated recovery after six months for the dimensions anxiety/depression and cognition, the dimensions mobility, pain/discomfort and usual activities still improved up to 2 years after injury. These results contribute to the increase in knowledge of recovery patterns of health status after injury and could be a starting point to develop prediction models for specific injury classifications and implementation of personalized medicine.

342

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Author contributions

LM, SP and MJ contributed to conception and design of this study. LM and MJ contributed to data collection. LM, SP, RH, ES, MJ contributed to analyses and interpretation. LM, SP, RH, ES and MJ contributed to preparation of the manuscript. The final version of the article was approved by all the authors.

Data sharing

Data from this study can contain potentially identifying or sensitive patient information. Data is anonymized, but due to relatively few severe cases, patients could be identified. Therefore, data from the BIOS-study will be made available for researchers who provide a methodologically sound proposal. Requests may be sent to secretariaat@nazb.nl.

Figure legends

Figure 1. Flow diagram of study participation

Abbreviations: ACT, Usual activities; ANX, Anxiety/depression; COG, Cognition; EQ-5D, EuroQol-5-Dimension; EQ-VAS, EuroQol Visual Analogue Scale; MOB, Mobility; N, Number; PAIN, Pain/discomfort; SELF, Self-care;

Figure 2. (A) Health status scores (95% CI) and (B and C) % patients reporting problems (95% CI) on the dimensions of the EQ-5D-3L, including whether there was a significant change in health status scores compared to the previous time-point.

Table 1. Patient characteristics tables of participants and non-responders of the BIOS-study

[a]patients who completed at least one follow-up questionnaire. Missing variables were imputed.

	Participants[a]	Non-responders	p-value
N (%)	4883	4891	
Male (%)	2329 (48)	2407 (49)	0.13
Age (median, IQR)	68 (53-80)	70 (46-84)	0.26
18-24 yrs (N, %)	217 (4)	400 (8)	
25-44 yrs (N, %)	516 (11)	767 (16)	
45-64 yrs (N, %)	1364 (28)	1006 (21)	
65-74 yrs (N, %)	963 (20)	563 (12)	
≥ 75 yrs (N, %)	1823 (37)	2155 (44)	
ASA classification (N, %)			
1 (healthy)	1531 (31)	1195 (24)	0.00
2	2348 (48)	1657 (34)	
3	950 (19)	1046 (21)	
4 (severe systemic disease)	54 (1)	40 (1)	
Missing	-	953 (20)	
Injury Severity Score (median, IQR)	5 (4-9)	5 (2-9)	0.00
Length of stay at hospital (median, IQR)	4 (2-8)	4 (2-8)	0.02
1-2 days (N, %)	1444 (30)	1528 (31)	
3-7 days (N, %)	2081 (43)	1642 (34)	
8-14 days (N, %)	995 (20)	911 (19)	
≥15 days (N, %)	363 (7)	421 (9)	
Missing	-	389 (8)	
Functional capacity index (N, %)			0.00
1-2 (worse state)	248 (5)	169 (4)	
3-4	2074 (42)	1721 (35)	
5 (best possible state)	2561 (52)	2473 (51)	
Missing	-	528 (11)	
Injury classification (N, %)			
Pelvic injury	293 (6)	151 (3)	
Hip fracture	1266 (26)	1099 (23)	
Tibia, complex foot or femur fracture	569 (12)	505 (10)	
Shoulder and upper arm injury	473 (10)	417 (9)	
Radius, ulna or hand fracture	308 (6)	283 (6)	
Head injury with AIS <=2	1324 (27)	1443 (30)	
Head injury with AIS >=3	186 (4)	181 (4)	
Facial injury	249 (5)	303 (6)	
Thoracic injury	198 (4)	162 (3)	
Rib fracture	451 (11)	398 (8)	
Mild abdominal injury	87 (2)	89 (2)	
Severe abdominal injury	36 (1)	30 (1)	
Spinal cord injury	27 (1)	10 (0)	
Stable vertebral fracture or disc injury	301 (6)	249 (5)	
Admission to intensive care unit (N, %)	358 (7)	292 (6)	0.00
Educational level (N, %)*			
Low	2670 (55)	-	
Middle	1305 (27)	-	
High	908 (19)	-	
Pre-injury work status*	1278 (38)	-	
Pre-injury frailty*	762 (16)		
Pre-injury health status*			
EQ-5D utility (mean, SD)	0.85 (0.23)	-	
EQ-VAS (mean, SD)	79.4 (18.2)	-	
% problems mobility	1051 (32)	-	
% problems self-care	530 (16)	-	
% problems usual activities	856 (26)	-	
% problems pain/discomfort	1044 (32)	-	
% problems anxiety/depression	540 (16)	-	
% problems cognition	651 (19)	-	
Missing	1517 (31)		

*variables were only collected in responders

Abbreviations: ASA, American Society of Anaesthesiologists Classification; IQR, Inter Quartile Range; N, Number.

Table 2. Regression coefficients in multivariable linear mixed models for the EQ-5D utility score and the EQ-VAS and odds ratios in multivariable logistic mixed models for the dimensions of health status.

	During the first two years after injury							
	Linear regression coefficients (95% CI)		Odds Ratios (95% CI)					
	EQ-5D utility	EQ-VAS	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/ depression	Cognition
Female sex	-0.03 (-0.04, -0.01)*	-1.43 (-2.30, -0.55)*	1.08 (0.91, 1.29)	1.08 (0.95, 1.22)	1.51 (1.32, 1.72)*	1.56 (1.35, 1.80)*	2.02 (1.62, 2.51)*	2.01 (1.54, 2.63)*
Age (years)								
18 - 24	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25 - 44	0.01 (-0.03, 0.04)	-0.32 (-2.87, 2.24)	1.13 (0.70, 1.83)	0.88 (0.61, 1.28)	1.18 (0.82, 1.71)	1.08 (0.72, 1.61)	0.97 (0.53, 1.77)	0.84 (0.41, 1.72)
45 - 64	0.05 (0.02, 0.09)*	1.22 (-1.15, 3.60)	1.20 (0.76, 1.87)	0.79 (0.56, 1.13)	0.89 (0.63, 1.26)	0.81 (0.55, 1.18)	0.37 (0.21, 0.66)*	0.37 (0.19, 0.73)*
65 - 74	0.12 (0.08, 0.16)*	6.43 (3.76, 9.10)*	0.84 (0.51, 1.38)	0.55 (0.38, 0.82)*	0.53 (0.36, 0.78)*	0.51 (0.33, 0.78)*	0.10 (0.05, 0.20)*	0.14 (0.07, 0.31)*
≥ 75	0.09 (0.05, 0.13)*	4.98 (2.22, 7.73)*	1.39 (0.82, 2.33)	0.98 (0.66, 1.46)	0.64 (0.43, 0.96)*	0.45 (0.29, 0.70)*	0.13 (0.07, 0.26)*	0.42 (0.19, 0.92)*
Nr of comorbidities								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-0.03 (-0.04, -0.01)*	-2.72 (-3.79, -1.65)*	1.45 (1.18, 1.77)*	1.19 (1.03, 1.39)*	1.29 (1.11, 1.51)*	1.23 (1.04, 1.46)*	1.65 (1.27, 2.15)*	1.36 (0.99, 1.88)
≥2	-0.05 (-0.07, -0.04)*	-4.08 (-5.30, -2.87)*	2.13 (1.69, 2.68)*	1.62 (1.38, 1.91)*	1.84 (1.54, 2.20)*	1.80 (1.47, 2.20)*	2.34 (1.74, 3.13)*	2.01 (1.40, 2.87)*
Injury Severity Score[b]	-0.01 (-0.02, 0.00)*	-0.93 (-1.53, -0.33)*	1.10 (0.98, 1.23)	1 (0.92, 1.09)	1.08 (0.99, 1.18)	0.92 (0.83, 1.01)	1.12 (0.97, 1.30)	1.27 (1.05, 1.52)*
Length of stay at hospital (days)								
1 - 2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3 - 7	-0.05 (-0.07, -0.03)*	-3.40 (-4.52, -2.29)*	2.14 (1.73, 2.64)*	1.56 (1.33, 1.84)*	1.72 (1.47, 2.03)*	1.69 (1.40, 2.04)*	1.69 (1.27, 2.25)*	1.15 (0.81, 1.62)
8 - 14	-0.10 (-0.12, -0.08)*	-6.24 (-7.70, -4.77)*	3.21 (2.39, 4.29)*	2.60 (2.12, 3.19)*	2.67 (2.13, 3.35)*	2.15 (1.68, 2.75)*	2.73 (1.90, 3.92)*	1.77 (1.13, 2.76)*
≥ 15	-0.15 (-0.18, -0.12)*	-9.32 (-11.43, -7.22)*	6.07 (3.80, 9.69)*	3.42 (2.51, 4.66)*	3.97 (2.77, 5.71)*	2.43 (1.66, 3.55)*	4.15 (2.48, 6.95)*	2.81 (1.47, 5.37)*
Functional Capacity Index								
1 (worse state)	-0.07 (-0.15, 0.00)*	-0.89 (-6.27, 4.48)	1.51 (0.57, 4.06)	1.79 (0.87, 3.71)	1.14 (0.51, 2.54)	1.00 (0.42, 2.41)	1.46 (0.41, 5.19)	1.63 (0.31, 8.57)
2	-0.06 (-0.10, -0.03)*	-1.22 (-3.57, 1.12)	1.89 (1.19, 3.01)*	1.94 (1.42, 2.66)*	1.59 (1.12, 2.27)*	1.28 (0.87, 1.89)	1.57 (0.89, 2.77)	0.67 (0.32, 1.38)
3	-0.03 (-0.07, 0.00)*	-0.48 (-2.84, 1.89)	2.11 (1.34, 3.31)*	1.47 (1.08, 2.02)*	1.88 (1.32, 2.68)*	1.14 (0.78, 1.66)	1.10 (0.62, 1.95)	0.91 (0.44, 1.86)
4	-0.03 (-0.05, -0.01)*	-0.04 (-1.50, 1.43)	1.62 (1.22, 2.15)*	1.57 (1.29, 1.93)*	1.42 (1.14, 1.77)*	1.28 (1.01, 1.63)*	1.03 (0.72, 1.48)	0.57 (0.36, 0.91)*
5 (best possible state)[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Injury classification[c]								
Lower extremity injury								
Pelvic injury	-0.04 (-0.07, -0.02)*	-1.64 (-3.37, 0.10)	2.74 (1.96, 3.83)*	1.29 (1.02, 1.64)*	0.97 (0.74, 1.25)	1.33 (0.99, 1.78)	0.67 (0.43, 1.04)	0.57 (0.33, 0.98)*
Hip fracture	-0.01 (-0.04, 0.02)	-0.34 (-2.20, 1.52)	2.62 (1.82, 3.79)*	1.28 (0.99, 1.66)	1.05 (0.79, 1.40)	1.04 (0.76, 1.41)	0.90 (0.57, 1.42)	1.00 (0.57, 1.77)
Tibia, complex foot or femur fracture	-0.05 (-0.07, -0.02)*	-1.14 (-2.75, 0.48)	6.85 (4.97, 9.44)*	1.27 (1.02, 1.58)*	1.71 (1.33, 2.18)*	1.34 (1.03, 1.76)*	0.8 (0.53, 1.19)	0.71 (0.43, 1.18)
Upper extremity injury								
Shoulder and upper arm injury	-0.03 (-0.06, -0.01)*	-2.00 (-3.44, -0.55)*	0.56 (0.42, 0.74)*	2.22 (1.82, 2.71)*	1.58 (1.28, 1.96)*	2.05 (1.60, 2.61)*	1.01 (0.70, 1.44)	0.71 (0.46, 1.12)

Radius, ulna or hand fracture	-0.02 (-0.04, 0.00)*	-0.59 (-2.31, 1.12)	0.42 (0.30, 0.58)*	1.46 (1.16, 1.85)*	1.22 (0.95, 1.57)	1.23 (0.93, 1.63)	1.44 (0.94, 2.19)	0.87 (0.51, 1.48)
Traumatic brain injury								
Head injury with AIS <=2	0.02 (0.01, 0.04)*	0.64 (-0.41, 1.70)	0.78 (0.64, 0.96)*	0.57 (0.49, 0.67)*	0.77 (0.66, 0.90)*	0.85 (0.72, 1.01)	1.15 (0.88, 1.49)	2.91 (2.12, 4.01)*
Head injury with AIS >=3	0.04 (0.00, 0.08)*	2.07 (-0.66, 4.80)	0.86 (0.51, 1.43)	0.92 (0.62, 1.37)	0.78 (0.52, 1.17)	0.90 (0.58, 1.39)	1.20 (0.62, 2.34)	3.29 (1.45, 7.49)*
Facial injury	0.02 (0.00, 0.05)*	0.78 (-1.15, 2.70)	0.52 (0.35, 0.75)*	0.75 (0.56, 1.00)*	0.67 (0.51, 0.89)*	0.67 (0.49, 0.91)*	1.10 (0.68, 1.78)	1.21 (0.68, 2.16)
Thoracic injury	0.06 (0.03, 0.10)*	3.11 (0.77, 5.46)*	0.54 (0.35, 0.84)*	0.56 (0.40, 0.78)*	0.55 (0.40, 0.78)*	0.68 (0.47, 1.00)*	0.58 (0.32, 1.05)	0.60 (0.29, 1.24)
Rib fracture	-0.01 (-0.03, 0.01)	-0.07 (-1.61, 1.48)	1.07 (0.80, 1.43)	1.02 (0.81, 1.27)	0.93 (0.74, 1.16)	1.63 (1.26, 2.11)*	0.96 (0.65, 1.41)	0.85 (0.53, 1.36)
Abdominal injury	0.02 (-0.02, 0.06)	1.68 (-1.27, 4.63)	0.63 (0.36, 1.09)	0.57 (0.36, 0.88)*	0.67 (0.44, 1.02)	0.56 (0.35, 0.90)*	0.93 (0.45, 1.95)	1.55 (0.65, 3.69)
Spine injury								
Spinal cord injury	-0.06 (-0.16, 0.04)	-3.03 (-9.85, 3.80)	1.86 (0.53, 6.60)	1.33 (0.53, 3.33)	1.35 (0.47, 3.88)	11.61 (2.86, 47.17)*	0.92 (0.18, 4.71)	0.30 (0.04, 2.35)
Stable vertebral fracture or disc injury	-0.06 (-0.08, -0.03)*	-4.16 (-5.99, -2.33)*	1.31 (0.93, 1.84)	1.67 (1.30, 2.15)*	1.79 (1.37, 2.34)*	2.45 (1.79, 3.35)*	1.14 (0.72, 1.79)	0.82 (0.47, 1.42)
Admission to Intensive Care Unit	0.00 (-0.02, 0.03)	-0.47 (-2.35, 1.41)	0.81 (0.56, 1.18)	1.01 (0.77, 1.32)	1.04 (0.78, 1.38)	1.08 (0.79, 1.49)	0.77 (0.48, 1.23)	2.22 (1.26, 3.91)*
Pre-injury work status	0.00 (-0.02, 0.02)	-0.23 (-1.62, 1.17)	0.73 (0.57, 0.95)*	0.94 (0.78, 1.14)	1.01 (0.83, 1.23)	1.12 (0.90, 1.40)	0.74 (0.53, 1.04)	0.92 (0.61, 1.39)
Educational level								
Low[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle	0.00 (-0.01, 0.02)	0.39 (-0.66, 1.43)	0.94 (0.77, 1.15)	0.96 (0.83, 1.11)	0.93 (0.80, 1.08)	1.07 (0.90, 1.26)	0.71 (0.55, 0.92)*	1.05 (0.77, 1.45)
High	0.02 (0.00, 0.03)*	0.36 (-0.76, 1.49)	0.91 (0.73, 1.13)	0.99 (0.84, 1.15)	0.75 (0.64, 0.89)*	0.82 (0.68, 0.98)*	0.64 (0.48, 0.86)*	1.06 (0.75, 1.51)
Frailty	-0.09 (-0.11, -0.07)*	-5.12 (-6.54, -3.71)*	2.38 (1.75, 3.24)*	1.79 (1.46, 2.20)*	2.07 (1.63, 2.62)*	1.48 (1.18, 1.87)*	4.94 (3.55, 6.86)*	4.37 (2.89, 6.61)*
Pre-injury status[d]	0.49 (0.45, 0.53)*	0.47 (0.44, 0.50)*						
No problems[a]			Ref	Ref	Ref	Ref	Ref	Ref
Moderate/severe problems			13.58 (10.62, 17.36)*	20.02 (15.50, 25.86)*	6.39 (5.20, 7.86)*	6.12 (5.09, 7.36)*	30.22 (21.62, 42.25)*	371.77 (224.34, 616.10)*

*p-value≤.05

[a]Reference category

[b]Regression coefficients and odds ratios (95%) represents a 4 unit increase on the Injury Severity Score.

[c]Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

[d]Regression coefficients (95% CI) for pre-injury EQ-5D utility score and the pre-injury EQ-VAS for EQ-5D utility score and EQ-VAS respectively. Odds ratios (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort, Anxiety/depression and cognition respectively for the columns).

Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.

Table 3. Change in the dimensions of the EQ-5D over time in multivariable logistic mixed models for different injury classifications

	Adjusted Odds Ratios (95% Confidence Interval)[a]				
	1 month vs 1 week	**3 months vs 1 month**	**6 months vs 3 months**	**12 months vs 6 months**	**24 months vs 12 months**
Mobility					
Lower extremity[1]	0.78 (0.48, 1.27)	0.24 (0.16, 0.35)*	0.17 (0.12, 0.23)*	0.54 (0.41, 0.70)	0.79 (0.60, 1.03)
Spine[2]	0.12 (0.05, 0.30)*	0.18 (0.08, 0.37)*	0.37 (0.17, 0.81)*	1.01 (0.47, 2.22)	0.70 (0.31, 1.60)
Self-care					
Lower extremity[1]	0.33 (0.24, 0.44)*	0.66 (0.52, 0.84)*	0.75 (0.58, 0.95)*	0.66 (0.49, 0.88)*	1.05 (0.77, 1.43)
Upper extremity[3]	0.19 (0.11, 0.32)*	0.09 (0.06, 0.15)*	0.25 (0.16, 0.40)*	0.51 (0.30, 0.87)*	0.72 (0.40, 1.31)
Spine[2]	0.25 (0.11, 0.57)*	0.05 (0.02, 0.11)*	0.15 (0.06, 0.34)*	0.55 (0.21, 1.43)	1.43 (0.52, 3.93)
Usual activities					
Upper extremity[3]	0.40 (0.22, 0.73)*	0.20 (0.13, 0.32)*	0.25 (0.17, 0.38)*	0.61 (0.40, 0.90)*	0.76 (0.50, 1.15)
Spine[2]	0.48 (0.17, 1.30)	0.11 (0.05, 0.25)*	0.24 (0.12, 0.49)*	0.30 (0.15, 0.60)*	1.71 (0.58, 2.38)
Pain/discomfort					
Lower extremity[1]	0.42 (0.30, 0.59)*	0.53 (0.41, 0.69)*	0.49 (0.39, 0.63)*	0.66 (0.52, 0.84)*	0.75 (0.59, 0.96)*
Upper extremity[3]	0.49 (0.27, 0.87)*	0.27 (0.17, 0.43)*	0.48 (0.32, 0.73)*	0.52 (0.35, 0.78)*	0.78 (0.52, 1.18)
Spine[2]	0.35 (0.12, 0.98)*	0.29 (0.13, 0.64)*	0.62 (0.30, 1.27)	0.19 (0.09, 0.39)*	1.27 (0.64, 2.50)
Anxiety/depression					
Spine[2]	0.69 (0.33, 1.43)	0.92 (0.49, 1.74)	0.64 (0.32, 1.27)	0.81 (0.40, 1.64)	0.87 (0.41, 1.85)
Cognition					
Traumtic Brain Injury[4]	0.72 (0.50, 1.02)	0.85 (0.60, 1.18)	0.69 (0.48, 0.99)*	0.91 (0.63, 1.32)	1.15 (0.79, 1.68)

Time was included as categorical variable in all analyses

*p-value≤.05

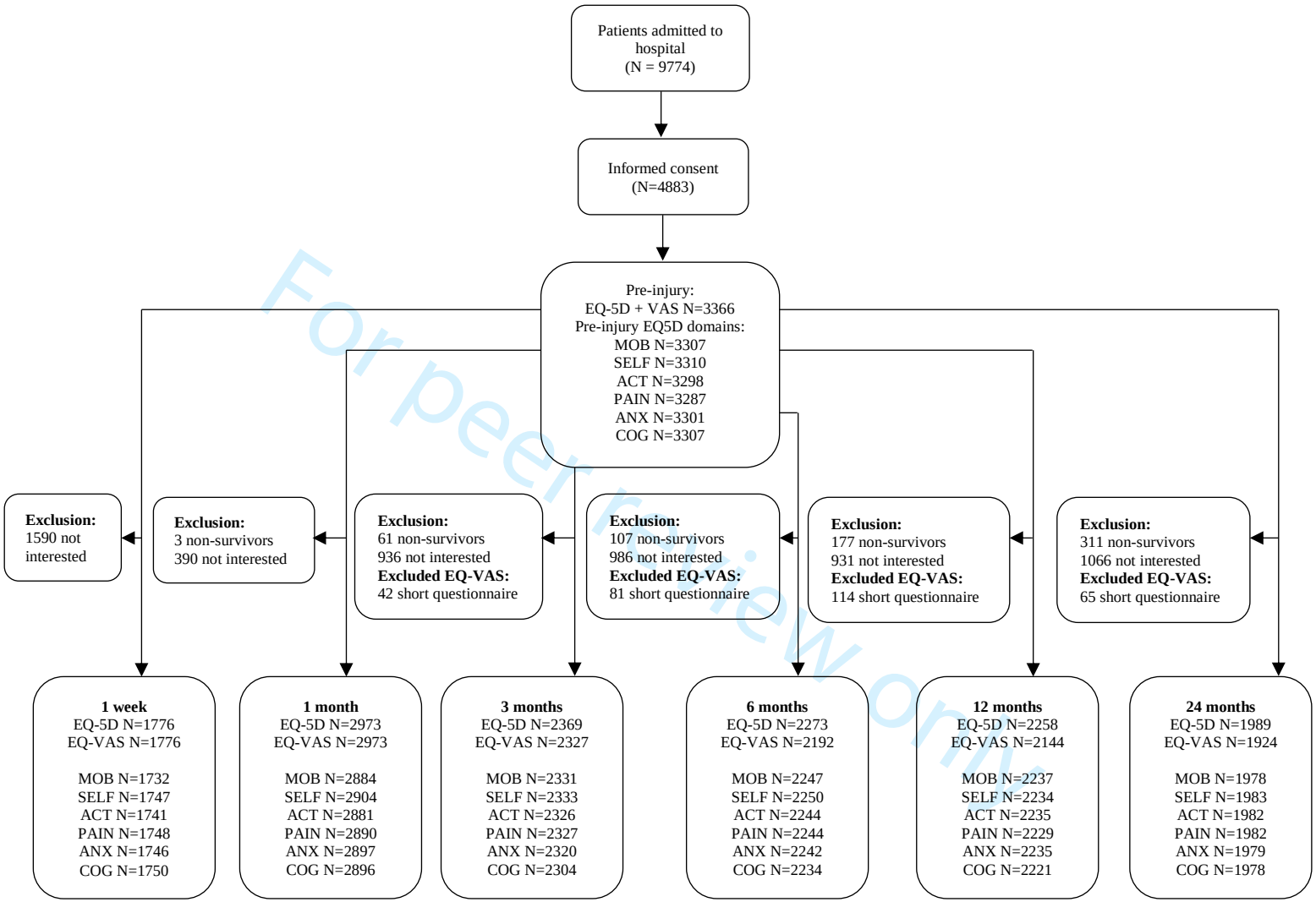
[a]Odds Ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level, frailty and pre-injury status

[1]Patients with pelvic injury, hip fracture or tibia, complex foot or femur fracture

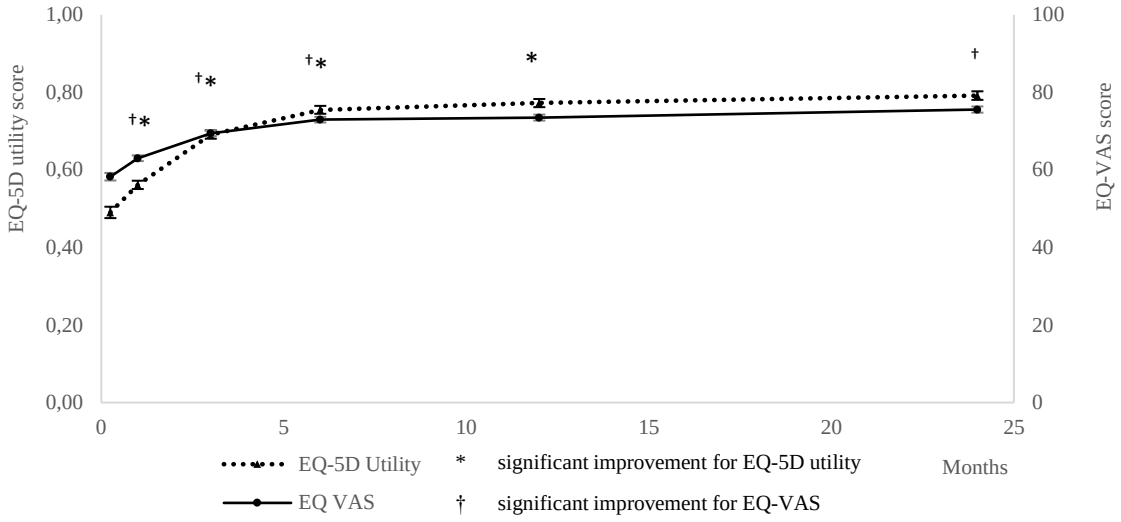
[2]Patients with spinal cord injury or stable vertebral fracture or disc injury

[3]Patients with shoulder and upper arm injury or radius, ulna or hand fracture

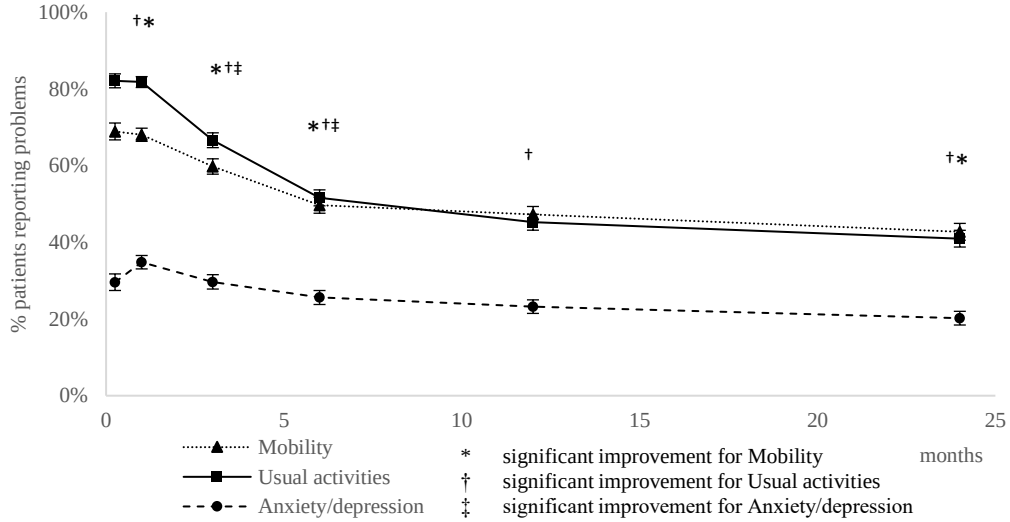
[4]Patients with Traumatic brain injury, independent of injury severity



A.


1,00
0,80
0,60
0,40
0,20
0,00
EQ-5D utility score
100
80
60
40
20
0
EQ-VAS score
0
5
10
15
20
25
Months
†*
†*
†*
*
†
EQ-5D Utility
EQ VAS
* significant improvement for EQ-5D utility
† significant improvement for EQ-VAS

B.


100%
80%
60%
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% patients reporting problems
0
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25
months
†*
*†‡
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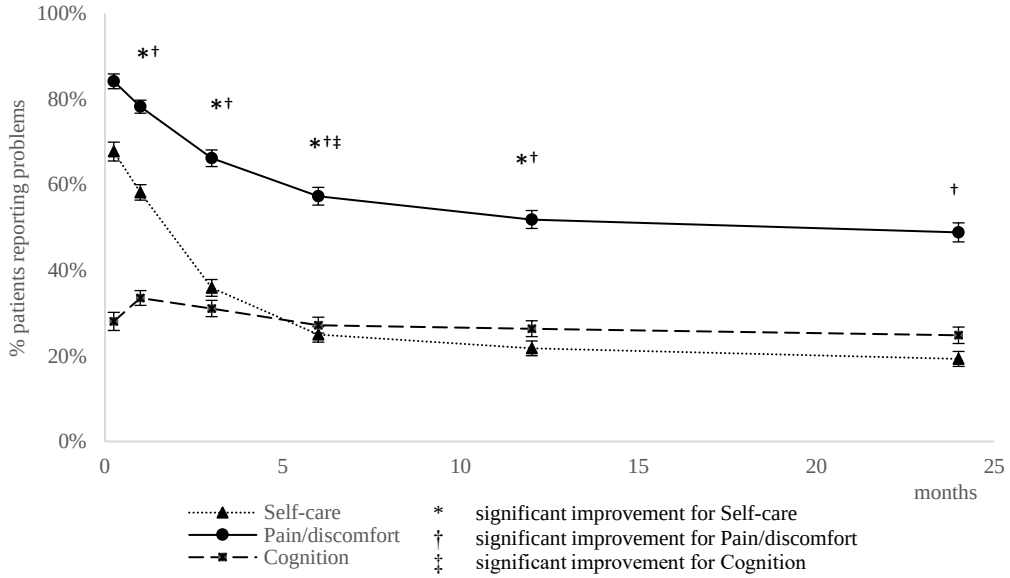
†
†*
Mobility
Usual activities
Anxiety/depression
* significant improvement for Mobility
† significant improvement for Usual activities
‡ significant improvement for Anxiety/depression

C.


100%
80%
60%
40%
20%
0%
% patients reporting problems
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15
20
25
months
*†
*†
*†‡
*†
†
Self-care
Pain/discomfort
Cognition
* significant improvement for Self-care
† significant improvement for Pain/discomfort
‡ significant improvement for Cognition

S1 Table. Injury group classification of the most common types of injury, based on the Abbreviated Injury Score[22].

Type of trauma	First three numbers of the AIS-code	Injury severity (.1=minor, .6=maximal)
Pelvic injury	856	.2, .3, .4, .5
Hip fracture	853	.3
Tibia, complex foot or femur fracture	854	.2
	857	.2
	858	.2
Shoulder and upper arm injury	770	.1, .2
	771	.1, .2
	750	.2
	751	.2
Radius, ulna or hand fracture	752	.1, .2, .3
	753	.2
Mild TBI*	110	.1, .2
	140	.2
	161	.1, .2
Severe TBI**	110	.3
	140	.3, .4, .5, .6
	161	.3, .4, .5
Facial fracture	250	.1, .2, .3
	251	.1, .2, .3
Thoracic injury	441	.1, .2, .3, .4, .5
	419	.2, .3, .4, .5
	442	.2, .3, .4, .5
Rib fracture	450	.1, .2, .3, .4
Mild abdominal injury	516	.1, .2
	510	.1, .2
	521	.2
	530	.1
	540	.1, .2
	541	.2
	542	.1, .2
	543	.1, .2
	544	.1, .2
	545	.1, .2
Severe abdominal injury	516	.3
	510	.3
	520	.3
	520	.4, .5
	521	.3, .4
	540	.3, .4
	541	.3, .4, .5
	542	.3, .4, .5
	543	.3, .4, .5
	544	.3, .4, .5
	545	.3, .4, .5
Spinal cord injury	640	3, .4, .5
Stable vertebral fracture or disc injury	650	.2, .3

Abbreviations: AIS, Abbreviated Injury Score; TBI, traumatic brain injury.

* Concussion/ commotio cerebri, sequelae of intracranial injury. Sequelae of injury classifiable to S06.

** Traumatic cerebral oedema, focal brain injury, epidural haemorrhage, traumatic subdural heamorrhage, traumatic subarachnoid haemorrhage, intercranial injury unspecified, crushing injury of face, crushing injury of skull, crushing injury of other parts of head, crushing injury of head part unspecified, diffuse brain injury, intracranial injury with prolonged coma, other intracranial injuries traumatic haemorrhage (cerebellar/intracranial not specified).

Supplemental Table 2. Change in EQ-5D and the dimensions of the EQ-5D over time in multivariable linear and logistic mixed models.

	1 month vs 1 week	3 months vs 1 month	6 months vs 3 months	12 months vs 6 months	24 months vs 12 months
Linear regression coefficients (95% Confidence Interval)[a]					
EQ-5D utility score	0.13 (0.12, 0.14)*	0.12 (0.11, 0.13)*	0.06 (0.05, 0.07)*	0.01 (0.00, 0.02)*	0.00 (-0.01, 0.02)
EQ-VAS	8.48 (7.70, 9.26)*	5.97 (5.28, 6.69)*	3.12 (2.36, 3.87)*	0.24 (-0.52, 1.01)	0.98 (0.19, 1.76)*
Odds Ratios (95% Confidence Interval)[a]					
Mobility	0.51 (0.41, 0.63)*	0.38 (0.32, 0.46)*	0.38 (0.31, 0.46)*	0.85 (0.70, 1.03)	0.79 (0.65, 0.97)*
Self-care	0.25 (0.21, 0.30)*	0.14 (0.12, 0.17)*	0.34 (0.28, 0.41)*	0.73 (0.59, 0.91)*	1.03 (0.82, 1.30)
Usual activities	0.67 (0.54, 0.83)*	0.22 (0.19, 0.27)*	0.31 (0.26, 0.37)*	0.61 (0.52, 0.73)*	0.82 (0.69, 0.98)*
Pain/discomfort	0.46 (0.37, 0.56)*	0.36 (0.30, 0.42)*	0.51 (0.44, 0.61)*	0.68 (0.58, 0.80)*	0.84 (0.71, 1.00)*
Anxiety/depression	0.99 (0.82, 1.21)	0.70 (0.59, 0.84)*	0.70 (0.58, 0.85)*	0.83 (0.68, 1.02)	0.89 (0.72, 1.11)
Cognition	0.85 (0.68, 1.06)	0.91 (0.75, 1.12)	0.62 (0.49, 0.77)*	1.09 (0.86, 1.38)	1.15 (0.91, 1.45)

Time was included as categorical variable in the analyses

*p-value≤.05

[a]Regression coefficients and odds ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level, frailty and pre-injury status

Supplemental Table 3. Regression coefficients in univariable linear mixed models for the EQ-5D utility and the EQ-VAS and odds ratios in univariable logistic mixed models for the dimensions of HS.

	During the first two years after injury							
	Linear regression coefficients (95% CI)		Odds Ratios (95% CI)					
	EQ-5D utility	EQ-VAS	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/ depression	Cognition
Female sex	-0.11 (-0.12, -0.10)*	-6.37 (-7.42, -5.32)*	4.57 (3.73, 5.61)*	3.04 (2.62, 3.53)*	3.20 (2.78, 3.68)*	2.46 (2.15, 2.82)*	4.28 (3.48, 5.28)*	4.95 (3.71, 6.60)*
Age (years)								
18 - 24	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25 - 44	-0.03 (-0.07, 0.01)	-1.59 (-4.66, 1.47)	2.08 (1.18, 3.64)*	1.59 (1.03, 2.46)*	1.83 (1.22, 2.74)*	1.72 (1.15, 2.59)*	0.93 (0.52, 1.67)	0.71 (0.34, 1.52)
45 - 64	-0.02 (-0.06, 0.01)	-3.69 (-6.50, -0.88)*	4.59 (2.74, 7.68)*	2.08 (1.40, 3.10)*	1.86 (1.29, 2.69)*	1.82 (1.26, 2.63)*	0.58 (0.34, 0.98)*	0.43 (0.22, 0.86)*
65 - 74	-0.02 (-0.06, 0.02)	-2.47 (-5.35, 0.41)	10.91 (6.42, 18.56)*	2.78 (1.85, 4.18)*	1.77 (1.21, 2.58)*	1.63 (1.12, 2.37)*	0.39 (0.23, 0.68)*	0.39 (0.20, 0.79)*
≥ 75	-0.16 (-0.19, -0.12)*	-12.78 (-15.58, -9.98)*	105.71 (61.48, 181.77)*	14.70 (9.83, 21.98)*	6.29 (4.34, 9.1)*	2.50 (1.73, 3.60)*	2.07 (1.23, 3.49)*	12.86 (6.37, 25.98)*
Nr of comorbidities								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-0.08 (-0.10, -0.06)*	-7.86 (-9.05, -6.66)*	5.41 (4.26, 6.87)*	2.45 (2.06, 2.91)*	2.14 (1.82, 2.51)*	1.75 (1.49, 2.05)*	2.54 (1.98, 3.24)*	5.41 (3.88, 7.53)*
≥2	-0.21 (-0.22, -0.19)*	-16.02 (-17.20, -14.84)*	36.44 (27.79, 47.78)*	8.45 (7.07, 10.10)*	7.16 (6.03, 8.51)*	4.70 (3.97, 5.57)*	9.32 (7.25, 11.97)*	45.33 (30.83, 66.64)*
Injury Severity Score[b]	-0.03 (-0.03,-0.02)*	-2.07 (-2.49, -1.65)*	1.58 (1.45, 1.71)*	1.34 (1.27, 1.43)*	1.35 (1.27, 1.43)*	1.12 (1.06, 1.18)*	1.25 (1.15, 1.36)*	1.52 (1.36, 1.70)*
Length of stay at hospital (days)								
1 - 2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3 - 7	-0.10 (-0.12, -0.09)*	-6.46 (-7.70, -5.22)*	10.61 (8.31, 13.53)*	3.72 (3.11, 4.45)*	3.11 (2.65, 3.66)*	2.19 (1.86, 2.59)*	2.23 (1.72, 2.88)*	2.22 (1.57, 3.13)*
8 - 14	-0.20 (-0.22, -0.18)*	-13.00 (-14.52, -11.48)*	39.48 (28.73, 54.26)*	11.04 (8.87, 13.73)*	8.06 (6.54, 9.93)*	3.73 (3.05, 4.57)*	5.73 (4.23, 7.76)*	9.12 (5.96, 13.97)*
≥ 15	-0.28 (-0.31, -0.26)*	-18.39 (-20.52, -16.25)*	103.66 (65.98, 162.88)*	22.75 (16.73, 30.93)*	14.88 (10.88, 20.36)*	4.91 (3.63, 6.65)*	11.30 (7.41, 17.24)*	24.69 (13.58, 44.90)*
Functional Capacity Index								
1 (worse state)	-0.13 (-0.20, -0.06)*	-7.63 (-13.18, -2.08)*	4.12 (1.62, 10.48)*	2.95 (1.45, 5.99)*	3.04 (1.52, 6.08)*	1.43 (0.72, 2.85)	3.97 (1.46, 10.75)*	8.96 (2.28, 35.20)*
2	-0.10 (-0.13, -0.06)*	-3.73 (-6.41, -1.05)*	9.85 (6.00, 16.17)*	2.47 (1.74, 3.52)*	2.85 (2.00, 4.05)*	2.16 (1.51, 3.09)*	1.88 (1.12, 3.17)*	0.33 (0.16, 0.65)*
3	-0.10 (-0.13, -0.06)*	-2.74 (-5.57, 0.08)	7.83 (4.70, 13.06)*	2.91 (2.00, 4.25)*	3.93 (2.69, 5.75)*	1.63 (1.13, 2.36)*	1.67 (0.96, 2.92)	0.69 (0.33, 1.45)
4	-0.11 (-0.12, -0.10)*	-6.01 (-7.15, -4.88)*	13.22 (10.56, 16.56)*	4.62 (3.94, 5.43)*	3.27 (2.82, 3.80)*	1.71 (1.48, 1.98)*	2.05 (1.64, 2.56)*	1.37 (1.02, 1.84)*
5 (best possible state)[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Injury classification[c]								
Lower extremity injury								
Pelvic injury	0.71 (0.70, 0.72)	-4.60 (-6.70, -2.51)*	6.17 (4.27, 8.92)*	2.27 (1.71, 3.00)*	1.93 (1.47, 2.54)*	1.57 (1.19, 2.08)*	1.37 (0.90, 2.10)	1.19 (0.68, 2.09)
Hip fracture	-0.09 (-0.12, -0.06)*	-9.15 (-10.55, -7.74)*	20.99 (16.05, 27.46)*	5.59 (4.60, 6.81)*	3.77 (3.12, 4.55)*	1.68 (1.40, 2.02)*	2.68 (2.04, 3.53)*	5.48 (3.75, 8.02)*

Tibia, complex foot or femur fracture	-0.13 (-0.15, -0.11)*	-2.37 (-4.09, -0.65)*	12.24 (8.98, 16.69)*	1.79 (1.42, 2.24)*	2.84 (2.27, 3.57)*	1.81 (1.44, 2.27)*	1.26 (0.90, 1.76)	0.53 (0.34, 0.82)*
Upper extremity injury								
Shoulder and upper arm injury	-0.07 (-0.10, -0.05)*	-2.57 (-4.40, -0.74)*	0.75 (0.55, 1.01)	2.47 (1.95, 3.14)*	1.8 (1.43, 2.27)*	2.21 (1.74, 2.80)*	1.21 (0.85, 1.72)	0.75 (0.47, 1.18)
Radius, ulna or hand fracture	-0.04 (-0.07, -0.02)*	0.60 (-1.54, 2.74)	0.35 (0.24, 0.50)*	1.22 (0.92, 1.62)	1.06 (0.81, 1.38)	1.03 (0.78, 1.35)	0.77 (0.5, 1.17)	0.36 (0.21, 0.63)*
Traumatic brain injury								
Head injury with AIS <=2	0.01 (-0.02, 0.03)	1.40 (0.10, 2.69)*	0.66 (0.53, 0.82)*	0.50 (0.41, 0.59)*	0.63 (0.53, 0.74)*	0.67 (0.57, 0.80)*	0.82 (0.64, 1.06)	2.52 (1.80, 3.53)*
Head injury with AIS >=3	0.04 (0.03, 0.06)*	-2.77 (-5.54, 0.00)*	1.84 (1.16, 2.91)*	1.17 (0.80, 1.71)	1.66 (1.16, 2.36)*	0.86 (0.61, 1.22)	2.44 (1.43, 4.15)*	13.11 (6.35, 27.06)*
Facial injury	-0.03 (-0.06, 0.01)	1.99 (-0.40, 4.37)	0.37 (0.25, 0.56)*	0.64 (0.46, 0.90)*	0.65 (0.48, 0.88)	0.6 (0.44, 0.81)*	0.99 (0.61, 1.58)	1.34 (0.72, 2.47)
Thoracic injury	0.04 (0.00, 0.07)*	2.37 (-0.49, 5.23)	0.54 (0.33, 0.87)*	0.62 (0.42, 0.93)*	0.73 (0.51, 1.05)	0.61 (0.42, 0.89)*	0.83 (0.47, 1.48)	0.8 (0.38, 1.68)
Rib fracture	0.04 (0.00, 0.07)*	-0.80 (-2.68, 1.09)	1 (0.73, 1.37)	0.81 (0.63, 1.05)	0.94 (0.74, 1.19)	1.35 (1.06, 1.72)*	0.65 (0.45, 0.95)*	1.05 (0.65, 1.71)
Abdominal injury	0.00 (-0.02, 0.03)	1.24 (-2.24, 4.73)	0.44 (0.24, 0.81)*	0.58 (0.35, 0.95)*	0.66 (0.42, 1.04)	0.56 (0.35, 0.88)*	1.06 (0.53, 2.14)	1.27 (0.51, 3.14)
Spine injury								
Spinal cord injury	-0.18 (-0.27, -0.09)*	-7.32 (-14.94, 0.29)	5.97 (1.8, 19.76)*	3.55 (1.41, 8.98)*	5.03 (1.95, 13.00)*	23.14 (6.63, 80.76)*	2.97 (0.78, 11.27)	0.94 (0.16, 5.48)
Stable vertebral fracture or disc injury	-0.05 (-0.08, -0.03)*	-4.10 (-6.27, -1.93)*	1.22 (0.85, 1.76)	1.57 (1.17, 2.10)*	1.88 (1.42, 2.49)*	2.43 (1.82, 3.25)*	1.23 (0.8, 1.87)	0.96 (0.55, 1.68)
Admission to Intensive Care Unit	-0.02 (-0.05, 0.01)	-2.88 (-4.90, -0.86)*	0.80 (0.55, 1.16)	0.94 (0.72, 1.25)	1.26 (0.97, 1.65)	1.10 (0.84, 1.43)	1.16 (0.79, 1.71)	4.15 (2.51, 6.83)*
Pre-injury work status	0.11 (0.09, 0.12)*	7.58 (6.40, 8.76)*	0.06 (0.05, 0.08)*	0.23 (0.19, 0.27)*	0.38 (0.33, 0.45)*	0.63 (0.54, 0.73)*	0.35 (0.28, 0.45)*	0.10 (0.07, 0.15)*
Educational level								
Low[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle	0.07 (0.06, 0.09)*	5.42 (4.15, 6.70)*	0.22 (0.17, 0.28)*	0.38 (0.32, 0.46)*	0.51 (0.43, 0.60)*	0.76 (0.65, 0.90)*	0.39 (0.31, 0.50)*	0.25 (0.18, 0.35)*
High	0.11 (0.09, 0.13)*	6.74 (5.35, 8.13)*	0.18 (0.13, 0.23)*	0.35 (0.29, 0.43)*	0.37 (0.31, 0.45)*	0.48 (0.40, 0.57)*	0.25 (0.19, 0.33)*	0.18 (0.12, 0.26)*
Frailty	-0.28 (-0.30, -0.26)*	-17.00 (-18.28, -15.73)*	42.04 (30.13, 58.65)*	17.43 (13.8, 22.02)*	10.32 (8.11, 13.12)*	3.53 (2.84, 4.39)*	20.90 (15.31, 28.54)*	181.79 (99.22, 333.08)*
Pre-injury status[d]	0.67 (0.64, 0.70)*	0.58 (0.55, 0.60)*						
No problems[a]			Ref	Ref	Ref	Ref	Ref	Ref
Moderate/severe problems			71.89 (54.53, 94.77)*	61.03 (47.05, 79.17)*	15.01 (12.27, 18.36)*	8.69 (7.29, 10.36)*	114.45 (79.19, 165.42)*	3613.12 (1619.40, 8061.43)*

*p-value≤.05

[a]Reference category

[b]Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

[c]Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

[d]Regression coefficients (95% CI) for pre-injury EQ-5D utility score and the pre-injury EQ-VAS for EQ-5D utility and EQ-VAS respectively. Odds ratios (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort, Anxiety/depression and cognition respectively for the columns).

Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	4,9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
-Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, explain how loss to follow-up was addressed	7-8
		(*e*) Describe any sensitivity analyses	7-8
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	7,9
		(c) Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	Report numbers of outcome events or summary measures over time	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prognostic factors for recovery of health status after injury: a prospective multicentre cohort study

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Running head: Prognostic factors for recovery after injury

Key words: injury; longitudinal cohort study; health status; prognostic factors; recovery;

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Abstract

Objectives: to determine prognostic factors for health status and recovery patterns during the first two years after injury in the clinical trauma population.

Design: a prospective longitudinal cohort study.

Setting: Ten participating hospitals in Brabant, the Netherlands

Participants: adult injured patients admitted to a hospital between August 2015 and November 2016 were followed: 4883 (50%) patients participated.

Main outcome measures: Primary outcome was health status, measured with the EuroQol-5-dimensions-3-level (EQ-5D), including a cognition item and the EuroQol Visual Analogue Scale (EQ-VAS). Health status was collected at 1 week, 1, 3, 6, 12, and 24 months after injury. Potential prognostic factors were based on literature and clinical experience (e.g. age, sex, pre-injury frailty (Groningen Frailty Index), pre-injury EQ-5D).

Results. Health status increased mainly during the first six months after injury with a mean EQ-5D utility score at 1 week of 0.49 and 0.79 at 24 months. The dimensions mobility, pain/discomfort and usual activities improved up to 2 years after injury. Lower pre-injury health status, frailty and longer length of stay at the hospital were important prognostic factors for poor recovery. Spine injury, lower and upper extremity injury showed to be prognostic factors for problems after injury. Traumatic brain injury was a prognostic factor for cognitive problems.

Conclusion. This study contributes to the increase in knowledge of health recovery after injury. It could be a starting point to develop prediction models for specific injury classifications and implementation of personalized medicine.

Trial registration number: NCT02508675

Strengths and limitations of the study

- a strength of the study was the short- and long-term follow-up measurements to obtain essential recovery data of the injury patients.

- a strength of the study is the high number of participants in this prospective cohort study.

- a limitation of this study is the possibility of selective drop-out, which could have resulted in an overestimation of complaints after injury

- a limitation of this study is the possibility of selection bias, suggesting that more severely injured patients were more likely to participate.

Introduction

Trauma, defined as a physical injury, is one of the leading causes of disability and affects millions of people worldwide each year. The number of survivors after trauma has increased over several decades, due to the improvement of trauma care[1-3]. However, many patients suffer physical, psychological or cognitive impairments, resulting in a reduction of their health status. The trauma population is a heterogeneous group of patients. Patients are from various age groups with many different injury patterns, in both severity and body region. In addition, type of accident (e.g. falls, road traffic accident) and mechanism of injury (e.g. bleeding, fracture) can be diverse. The identification of patients at high risk of poor health status could enable clinicians to tailor treatment in which patients are referred to specialized care and rehabilitation at an early stage of their recovery or to lifelong treatment or lifestyle changes.

Previous research identified several prognostic factors for poor outcome after injury, e.g. age, gender, educational level, comorbidity, pre-injury work status[4-16]. Most previous studies on prognostic factors for health status evaluated major or severe trauma patients population[4,6-9,12-15], traumatic brain injury patients[5,14] or a small follow-up trauma population[11]. In addition, one study focused on long-term follow-up measurement, two to seven years after injury[8]. Last, pre-injury health status was not assessed as prognostic factor for health status in previous studies. Although recovery after injury is not only determined by injury severity or injury in specific body regions, research that takes into account the total clinical trauma population during their recovery is scarce[16]. In addition, different recovery patterns can be expected in, for example, brain injury patients and patients suffering from lower/upper extremity injury.

This study aimed to determine prognostic factors for health status and determine recovery patterns of health status after injury in the clinical trauma population and in specific injury classifications.

Methods

Study design and participants

Data was obtained from the Brabant Injury Outcome Surveillance (BIOS). The BIOS-study is a prospective observational cohort study in which health status, costs, functional and psychological outcomes were assessed in the first 24 months after injury. A detailed description of the methods of the BIOS-study can be found in the published research protocol[17].

All adult (≥18 years) patients admitted to a hospital in the region Noord-Brabant (the Netherlands) from 1 August 2015 to 30 November 2016 due to an injury and who survived to hospital discharge were included in this study. Patients without sufficient knowledge of the Dutch language or with pathological fractures (e.g. osteoporosis) were excluded. A proxy informant (caregiver or family member) was asked to complete the self-administered questionnaires if patients were incapable of completing the questionnaires in the BIOS-study from 1 month onwards. Proxy informant use of the EQ-5D-3L was validated previously in an injury cohort[18]. The questionnaires were sent by post or electronically at one week, one month, three months, six months, 12 months and 24 months after injury. All participants, patients or proxy informants, signed informed consent. If patients did not complete the corresponding BIOS-questionnaire, they were asked to complete a shorter version of the questionnaire at three months, six months, 12 months and 24 months after injury to increase the response rate. This short version incorporates only a small collection of the questionnaires that are included in the BIOS-study (e.g. EQ-5D, demographics and return to work). Patients who did not respond to a questionnaire were considered a non-participant for that time point, but could participate again in the following questionnaires. Patients were called to inform them about the BIOS-study and were asked for reasons of non-participating. Non-responders were patients who did not completed informed consent nor completed a follow-up questionnaire. Injury characteristics were collected in the Brabant Trauma Registry and were merged to the BIOS-data for all

participating patients. The study was approved by the Medical Ethics Committee Brabant (project number BIOS-study: NL50258.028.14 and short questionnaire: NW2016-09).

Patient and public involvement

No patient involved.

Outcome

Health status was measured with the EuroQol-5D-3L (EQ-5D)[19]. This questionnaire consists of the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D descriptive system comprised the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension could be answered in three levels: no problems, some problems and severe/extreme problems.

A summary score of the EQ-5D (i.e. EQ-5D utility score) can be calculated by using the Dutch tariffs[20]. The EQ-5D utility score ranged from 0 (death) to 1 (perfect health). The EQ-VAS is a vertical visual analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state.

Cognition was added as an additional dimension to the EQ-5D questionnaire. Respondents were asked to describe their or, in case of proxy, the patients' state of health, concerning cognition (e.g. memory, concentration). Similar to the other dimensions, answer options were based on three levels: no problems, some problems and severe problems.

Health status was measured at each time point during follow-up in both patient and proxy questionnaires. The EQ-5D (including the cognition dimension) and EQ-VAS were also measured pre-injury, by asking participants at one week or one month and proxy informants at one month for the patients' health status before sustaining the injury. The EQ-5D with cognition dimension and EQ-VAS were both included in the BIOS-study. The short questionnaire only included the EQ-5D and cognition dimension.

Prognostic factors

Prognostic factors can be subdivided into sociodemographic variables and clinical variables and were chosen based on previous literature and clinical experience[4-16].

Sociodemographic variables

Possible prognostic factors for health status that were measured in the BIOS-study were sex, age, educational level (low, middle or high), pre-injury work status (yes/no), frailty and pre-injury health status. Educational level was categorized in three levels as the highest completed degree, diploma of education; low (primary education, preparatory secondary vocational education or without diploma), middle (university preparatory education, senior general secondary education or senior secondary vocational education and training), and high (academic degree or university of applied science). Frailty was measured at one week or one month after injury with the Groningen Frailty Index (GFI) in patients ≥65 years[21]. A sum-score of ≥4 was considered frail.

Clinical variables

Possible clinical prognostic factors for health status were length of hospital stay, injury severity score (ranging from 1; mild injury to 75; fatal injury), admission to the intensive care (yes/no), presence of comorbidities and the functional capacity index. Comorbidities were measured with the American Society of Anaesthesiologists (ASA) physical status classification system ranging from 1 (healthy patient) to 4 (severe systemic disease that is a constant threat to life). The functional capacity index and injury severity score were based on the Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)[22]. All clinical variables were extracted from the trauma registry.

Injury Classification

The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)[22] were used to create injury group classifications representing the most common types of injuries. In total, 14 injury groups were created: 3 lower extremity injury groups (pelvic injury, hip fracture, and tibia fracture/complex foot fracture or distal/shaft femur fracture), 2 upper extremity injury groups (shoulder and upper arm injury, and radius, ulna or hand fracture), 2 traumatic brain injury groups (AIS-head≤2, and AIS-head≥3), 1 face injury group, 2 thorax injury groups (thorax injury, and rib fracture), 2 abdomen injury groups (AIS-abdomen≤2, and AIS-abdomen≥3) and 2 spine injury groups (spinal cord injury/brachial plexus lesion, and stable vertebral fracture/disc injury) (**Supplemental File 1**). Patients who suffer multiple injuries could be classified in one or more injury group classifications.

Data analysis

Baseline characteristics of participants were compared with characteristics of non-responders, using chi-square for categorical variables or the Mann-Whitney U test for non-normal distributed data. Normality was checked visually with a normal Q-Q plot. Descriptive statistics included the median with the interquartile range (IQR), mean with standard deviation (SD) for continuous variables and number with percentage for categorical variables. Missing baseline characteristics (0.9% for the Injury Severity Score and 6.8% for length of stay at hospital) and missing EQ-5D utility scores for participants (ranging from 1.8% at 1 week follow-up to 6.9% at 12 months follow-up) were imputed according to multiple imputation by using the Multivariate Imputations by Chained Equations (MICE) procedure with 15 imputations and 5 iterations[23]. The imputation model included baseline characteristics, injury characteristics and summary scores of the follow-up questionnaires to capture associations with missingness as completely as possible. Detailed description of the imputation model and imputed values were previously published[24]. No large differences were found between imputed data analyses and complete case analyses.

Multicollinearity was checked based on the Variance Inflation Factor (criterion: VIF > 10). Prognostic factors were assessed for poor health status outcome with EQ-5D utility scores and EQ-VAS as outcome measures. Regression coefficients with corresponding 95% confidence interval (CI) were reported. The dimensions of the EQ-5D descriptive system were dichotomized into 0=no problems and 1=some problems/extreme problems. Logistic mixed models with random intercepts were used to assess prognostic factors for poor outcome for the six dimensions of the EQ-5D (e.g. mobility, self-care, usual activities, pain/discomfort, anxiety/depression and cognition). All potential prognostic factors were included in the multivariable regression models to calculate adjusted Odds Ratios and corresponding 95% CI. Age and length of stay at the hospital were included as categorical variables, because of the non-linear relation between factor and outcome.

Recovery patterns of health status were determined by changing the reference category of the categorical time variable in linear mixed models for health status and logistic mixed models for the dimensions of health status, adjusted for the prognostic factors. Recovery patterns for the items of the EQ-5D were assessed in detail for injury classifications that showed to be statistically significant for the dimensions in the total multivariable model.

Analyses were conducted in the statistical programs R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS version 24 (Chicago, USA) and results were reported according to the TRIPOD guidelines[25]. A p-value of ≤.05 was considered statistically significant.

Results

Baseline characteristics

A total of 4883 patients (50% of total, N=9774) completed at least one questionnaire of the BIOS study of whom 48% (N=2,329) was male **(Figure 1, Table 1)**. The median age was 68 years with an IQR of 53-80 years. Participants had a median injury severity score of 5 (IQR [4-9]) and most of the patients were classified as healthy or as patients with mild systemic disease (N= 3,879, 79%). A total of 358 patients (7%) were admitted to the intensive care unit. The majority of the participants had low educational level (N=2,670, 55%) and 38% of the participants (N=1,278) had a job prior to injury. Mean pre-injury EQ-5D utility score (SD) was 0.85 (0.23). A total of 762 participants (27% of participants ≥65years) reported to be frail.

Compared to the non-responders, participants were more severely injured, were more often admitted to the intensive care unit (7% vs 6%), had lower functional capacity index values, and were more often healthy (measured with the ASA classification).

A total of 1,105 participants (22.6% of the study population) completed all BIOS-questionnaires at each time point. The main reason for not participating was that completing the questionnaire was too time consuming. Patients who reported to be fully recovered and patients aged 18-24 were most likely to be lost to follow-up.

EQ-5D over time

The mean EQ-5D utility (SD) score was 0.49 (0.32), 0.56 (0.30), 0.69 (0.27), 0.76 (0.25), 0.77 (0.26) and 0.79 (0.25) at 1 week, 1, 3, 6, 12 and 24 months respectively **(Figure 2A, Supplemental File 2)**. The mean EQ-VAS (SD) score was 58.26 (20.45), 63.02 (20.46), 69.48 (18.56), 72.97 (17.28), 73.50 (18.08) and 75.58 (17.88) at 1 week, 1, 3, 6, 12 and 24 months

respectively. Patients reported the most increase in EQ-5D utility scores during the first 6 months, with a little improvement up to 12 months.

The first month, patients reported most problems for the following dimensions of the EQ-5D: pain/discomfort, usual activities, mobility and self-care **(Figure 2B and 2C, Supplemental File 2)**. During the 24 month follow-up, the percentage of patients reporting problems for pain/discomfort, usual activities and mobility were highest. Two years after injury 49% (95% CI: 47, 51) of the patients reported problems for pain/discomfort, 43% (95% CI: 41, 45) reported problems for mobility, 41% (95% CI: 39, 43) reported problems for usual activities, 25% (95% CI: 23, 27) reported for cognition, 20% (95% CI: 18, 22) reported problems for anxiety/depression and 19% (95% CI: 17, 21) for self-care.

Prognostic factors

Almost all variables were prognostic factors for an increase of the EQ-5D utility score in the univariable analyses (**Supplemental File 3**). Lower pre-injury health status, frailty and longer length of stay at hospital were important significant prognostic factors for decreased EQ-5D utility score, decreased EQ-VAS and its' dimensions during the first two years after injury in the multivariable analyses (**Table 2**). Age is a prognostic factor for self-care, usual activities, pain/discomfort, anxiety/depression and cognition, but no significant association was found for mobility. Sex showed to be a significant prognostic factor for all outcomes, except for mobility and self-care.

Lower extremity injury (Pelvic injury, hip fracture and tibia, complex foot or femur fracture) was a prognostic factor for the EQ-5D utility score, mobility, self-care, usual activities and pain-discomfort. Upper extremity injury (shoulder and upper arm injury, radius, ulna or hand fracture) was a prognostic factor for the EQ-5D utility score, mobility and self-care. Spine injury (spinal cord injury or stable vertebral fracture or disc injury) was a prognostic factor, although not always significant, for health status, and the dimensions mobility, self-care, usual

activities and pain/discomfort. Traumatic brain injury was a prognostic factor for problems with cognition.

Recovery patterns for injury classifications

Recovery for dimensions of health status amongst different injury classifications mostly occurred up until twelve months after injury, except for pain/discomfort (**Table 3**). Patients with lower extremity injury reported significant less problems at 24 months compared to twelve months for pain/discomfort.

Patients with spine injury showed improved mobility up to six months for mobility and self-care, and up to twelve months for pain/discomfort and usual activities. Upper and lower extremity injury showed the same recovery pattern during the first two years for self-care, with significant improvement up to twelve months after injury.

Discussion

In this multicentre prospective cohort study, we found that patients reported problems up until two years after injury. Health status was especially low during the first six months after injury, in which patients often reported problems in most of the dimensions of health status. Lower pre-injury health status, frailty and longer length of stay at hospital were prognostic factors for both decreased health status during the first two years after injury. For the EQ-5D dimensions mobility, usual activities and pain/discomfort less problems were reported at two years compared to one year after injury, as for the other dimensions we found no decrease in reported problems after one year.

The prevalence of problems in the dimensions of health status decreased during two years follow up. Although a recent study in severely injured patients demonstrated higher prevalence of problems in the health status dimensions[6], our results are in line with another study in the general clinical trauma population[16].

Previous research showed that age is a prognostic factor for reduced health status[9,16,26]. In contrast, results from this study showed improved overall health status. This could be explained by the addition of the strong prognostic factors pre-injury health status and frailty in the multivariable adjusted models. Indicating that not the increase of age is a prognostic factor for poor health status, but the patients' health status before injury. Not all elderly patients are frail nor are they in poor health. With the ageing population, frailty and pre-injury health status are essential to consider when assessing recovery patterns in injury patients. We found that increasing age was a prognostic factor for less problems with usual activities, pain/discomfort, anxiety/depression and cognition. This is also in contrast with a recent study, stating that the relationship between age and the dimensions of EQ-5D differed[6]. Again, the different findings can be attributed to the additional strong predictors. This is confirmed by the univariate analyses

which demonstrate that increasing age is associated with more problems on all dimensions of health status, except anxiety/depression and cognition.

The addition of the cognitive dimension on the EQ-5D has previously been shown to improve classification and validity, especially in patients with TBI[27,28]. In line with these findings, this study showed that patients with TBI were at risk of developing cognitive problems after injury. It has been suggested previously that most patients with mild TBI patients recover fully within three to six month, although some patients with mild TBI and patients with more severe TBI suffer persistent cognitive problems[29-31]. Our study showed that TBI patients reported no further improvement in health status after six months, in line with the recovery pattern of mild TBI patients. This is possibly due to the fact that most participants of the BIOS-study suffered mild TBI (27%) compared to moderate/severe TBI (4%). Further evaluation of these subgroups with more specific outcome measures are necessary to determine their recovery patterns.

In line with previous studies, this study showed that female sex is a prognostic factor for poor health status after injury[4,6,13-16,32]. It has been suggested that problems were more often reported in females, in contrast to males, who dismiss there complaints more often. Another explanation could be that women experience more psychological impact, resulting in lower health status. Except for longer length of stay at the hospital, no injury related characteristics were found to be prognostic factors for anxiety/depression complaints. These results suggest that psychological problems after injury are mainly based on patient characteristics, which is confirmed in previous research[33,34].

Although the large prospective longitudinal design of this study is a major strength, there are also some limitations. First, only 50% of the patients responded to the BIOS-study. We found differences in injury and patient characteristics between participants and non-responders of the BIOS-study, e.g. participants were more severely injured compared to the non-responders,

indicating selection bias. Next, it is also possible that selective dropout has occurred. We suspect that patients who were fully recovered were less likely to respond to the follow-up questions, resulting in an overestimation of complaints after injury. In addition, retrospectively collected preinjury health status scores are prone to recall bias and response shift[35]. However, they are considered more appropriate compared to general population norm scores[36]. Last, frailty was only assessed in patients aged ≥65 years. This could have introduced bias, because younger patients may be frail. However, we believe this would only affect a small proportion in this large cohort.

Next, generalisability of the study results can be questioned, because inclusion criteria for injured patients could be different from other registries. This study included all injury severities and elderly patients with hip fracture.

We acknowledge that long-term non-fatal outcomes should be incorporated in the trauma registry[37]. These outcomes could be used to inform caregivers and patients about their expected recovery patterns. However, pre-injury health status is essential in predicting short and long-term outcome after injury and should therefore also be included in the registry. Furthermore, the dimensions of the EQ-5D and health status showed to have different recovery patterns for different injury classifications. Non-fatal outcome should not only be focused on health status, but especially on the different dimensions.

Knowledge about individual recovery patterns can induce specific interventions to increase health status and improve recovery after injury. For example, previous research demonstrated a need to identify patients who may be experiencing mental health issues for timely referral and appropriate care after injury[38]. In addition, the prediction models can contribute to realistic expectations of their recovery for injury patients[38,39].

Although the responding patients demonstrated recovery after six months for the dimensions anxiety/depression and cognition, the dimensions mobility, pain/discomfort and usual activities

still improved up to 2 years after injury. These results contribute to the increase in knowledge of recovery patterns of health status after injury and could be a starting point to develop prediction models for specific injury classifications and implementation of personalized medicine.

Author contributions

LM, SP and MJ contributed to conception and design of this study. LM and MJ contributed to data collection. LM, SP, RH, ES, MJ contributed to analyses and interpretation. LM, SP, RH, ES and MJ contributed to preparation of the manuscript. The final version of the article was approved by all the authors.

Conflict of interest statement

The authors declare no conflict of interest.

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Data sharing

Data from this study can contain potentially identifying or sensitive patient information. Data is anonymized, but due to relatively few severe cases, patients could be identified. Therefore, data from the BIOS-study will be made available for researchers who provide a methodologically sound proposal. Requests may be sent to secretariaat@nazb.nl.

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Figure legends

Figure 1. Flow diagram of study participation

Abbreviations: ACT, Usual activities; ANX, Anxiety/depression; COG, Cognition; EQ-5D, EuroQol-5-Dimension; EQ-VAS, EuroQol Visual Analogue Scale; MOB, Mobility; N, Number; PAIN, Pain/discomofort; SELF, Self-care;

Non-survivors are participants that died during the follow-up period.

Figure 2. (A) Health status scores (95% CI) and (B and C) % patients reporting problems (95% CI) on the dimensions of the EQ-5D-3L, including whether there was a significant change in health status scores compared to the previous time-point.

Table 1. Patient characteristics tables of participants and non-responders of the BIOS-study

	Participants[a]	Non-responders	p-value
N (%)	4883	4891	
Male (%)	2329 (48)	2407 (49)	0.13
Age (median, IQR)	68 (53-80)	70 (46-84)	0.26
18-24 yrs (N, %)	217 (4)	400 (8)	
25-44 yrs (N, %)	516 (11)	767 (16)	
45-64 yrs (N, %)	1364 (28)	1006 (21)	
65-74 yrs (N, %)	963 (20)	563 (12)	
≥ 75 yrs (N, %)	1823 (37)	2155 (44)	
ASA classification (N, %)			
1 (healthy)	1531 (31)	1195 (24)	0.00
2	2348 (48)	1657 (34)	
3	950 (19)	1046 (21)	
4 (severe systemic disease)	54 (1)	40 (1)	
Missing	-	953 (20)	
Injury Severity Score (median, IQR)	5 (4-9)	5 (2-9)	0.00
Length of stay at hospital (median, IQR)	4 (2-8)	4 (2-8)	0.02
1-2 days (N, %)	1444 (30)	1528 (31)	
3-7 days (N, %)	2081 (43)	1642 (34)	
8-14 days (N, %)	995 (20)	911 (19)	
≥15 days (N, %)	363 (7)	421 (9)	
Missing	-	389 (8)	
Functional capacity index (N, %)			0.00
1-2 (worse state)	248 (5)	169 (4)	
3-4	2074 (42)	1721 (35)	
5 (best possible state)	2561 (52)	2473 (51)	
Missing	-	528 (11)	
Injury classification (N, %)			
Pelvic injury	293 (6)	151 (3)	
Hip fracture	1266 (26)	1099 (23)	
Tibia, complex foot or femur fracture	569 (12)	505 (10)	
Shoulder and upper arm injury	473 (10)	417 (9)	
Radius, ulna or hand fracture	308 (6)	283 (6)	
Head injury with AIS <=2	1324 (27)	1443 (30)	
Head injury with AIS >=3	186 (4)	181 (4)	
Facial injury	249 (5)	303 (6)	
Thoracic injury	198 (4)	162 (3)	
Rib fracture	451 (11)	398 (8)	
Mild abdominal injury	87 (2)	89 (2)	
Severe abdominal injury	36 (1)	30 (1)	
Spinal cord injury	27 (1)	10 (0)	
Stable vertebral fracture or disc injury	301 (6)	249 (5)	
Admission to intensive care unit (N, %)	358 (7)	292 (6)	0.00
Educational level (N, %)*			
Low	2670 (55)	-	
Middle	1305 (27)	-	
High	908 (19)	-	
Pre-injury work status*	1278 (38)	-	
Pre-injury frailty*	762 (16)		
Pre-injury health status*			
EQ-5D utility (mean, SD)	0.85 (0.23)	-	
EQ-VAS (mean, SD)	79.4 (18.2)	-	
% problems mobility	1051 (32)	-	
% problems self-care	530 (16)	-	
% problems usual activities	856 (26)	-	
% problems pain/discomfort	1044 (32)	-	
% problems anxiety/depression	540 (16)	-	
% problems cognition	651 (19)	-	
Missing	1517 (31)		

[a]patients who completed at least one follow-up questionnaire. Missing variables were imputed.
*variables were only collected in responders
Abbreviations: ASA, American Society of Anaesthesiologists Classification; IQR, Inter Quartile Range; N, Number.

Table 2. Regression coefficients in multivariable linear mixed models for the EQ-5D utility score and the EQ-VAS and odds ratios in multivariable logistic mixed models for the dimensions of health status.

	During the first two years after injury							
	Linear regression coefficients (95% CI)		Odds Ratios (95% CI)					
	EQ-5D utility	EQ-VAS	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/ depression	Cognition
Female sex	-0.03 (-0.04, -0.01)*	-1.43 (-2.30, -0.55)*	1.08 (0.91, 1.29)	1.08 (0.95, 1.22)	1.51 (1.32, 1.72)*	1.56 (1.35, 1.80)*	2.02 (1.62, 2.51)*	2.01 (1.54, 2.63)*
Age (years)								
18 - 24	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25 - 44	0.01 (-0.03, 0.04)	-0.32 (-2.87, 2.24)	1.13 (0.70, 1.83)	0.88 (0.61, 1.28)	1.18 (0.82, 1.71)	1.08 (0.72, 1.61)	0.97 (0.53, 1.77)	0.84 (0.41, 1.72)
45 - 64	0.05 (0.02, 0.09)*	1.22 (-1.15, 3.60)	1.20 (0.76, 1.87)	0.79 (0.56, 1.13)	0.89 (0.63, 1.26)	0.81 (0.55, 1.18)	0.37 (0.21, 0.66)*	0.37 (0.19, 0.73)*
65 - 74	0.12 (0.08, 0.16)*	6.43 (3.76, 9.10)*	0.84 (0.51, 1.38)	0.55 (0.38, 0.82)*	0.53 (0.36, 0.78)*	0.51 (0.33, 0.78)*	0.10 (0.05, 0.20)*	0.14 (0.07, 0.31)*
≥ 75	0.09 (0.05, 0.13)*	4.98 (2.22, 7.73)*	1.39 (0.82, 2.33)	0.98 (0.66, 1.46)	0.64 (0.43, 0.96)*	0.45 (0.29, 0.70)*	0.13 (0.07, 0.26)*	0.42 (0.19, 0.92)*
Nr of comorbidities								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-0.03 (-0.04, -0.01)*	-2.72 (-3.79, -1.65)*	1.45 (1.18, 1.77)*	1.19 (1.03, 1.39)*	1.29 (1.11, 1.51)*	1.23 (1.04, 1.46)*	1.65 (1.27, 2.15)*	1.36 (0.99, 1.88)
≥2	-0.05 (-0.07, -0.04)*	-4.08 (-5.30, -2.87)*	2.13 (1.69, 2.68)*	1.62 (1.38, 1.91)*	1.84 (1.54, 2.20)*	1.80 (1.47, 2.20)*	2.34 (1.74, 3.13)*	2.01 (1.40, 2.87)*
Injury Severity Score[b]	-0.01 (-0.02, 0.00)*	-0.93 (-1.53, -0.33)*	1.10 (0.98, 1.23)	1 (0.92, 1.09)	1.08 (0.99, 1.18)	0.92 (0.83, 1.01)	1.12 (0.97, 1.30)	1.27 (1.05, 1.52)*
Length of stay at hospital (days)								
1 - 2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3 - 7	-0.05 (-0.07, -0.03)*	-3.40 (-4.52, -2.29)*	2.14 (1.73, 2.64)*	1.56 (1.33, 1.84)*	1.72 (1.47, 2.03)*	1.69 (1.40, 2.04)*	1.69 (1.27, 2.25)*	1.15 (0.81, 1.62)
8 - 14	-0.10 (-0.12, -0.08)*	-6.24 (-7.70, -4.77)*	3.21 (2.39, 4.29)*	2.60 (2.12, 3.19)*	2.67 (2.13, 3.35)*	2.15 (1.68, 2.75)*	2.73 (1.90, 3.92)*	1.77 (1.13, 2.76)*
≥ 15	-0.15 (-0.18, -0.12)*	-9.32 (-11.43, -7.22)*	6.07 (3.80, 9.69)*	3.42 (2.51, 4.66)*	3.97 (2.77, 5.71)*	2.43 (1.66, 3.55)*	4.15 (2.48, 6.95)*	2.81 (1.47, 5.37)*
Functional Capacity Index								
1 (worse state)	-0.07 (-0.15, 0.00)*	-0.89 (-6.27, 4.48)	1.51 (0.57, 4.06)	1.79 (0.87, 3.71)	1.14 (0.51, 2.54)	1.00 (0.42, 2.41)	1.46 (0.41, 5.19)	1.63 (0.31, 8.57)
2	-0.06 (-0.10, -0.03)*	-1.22 (-3.57, 1.12)	1.89 (1.19, 3.01)*	1.94 (1.42, 2.66)*	1.59 (1.12, 2.27)*	1.28 (0.87, 1.89)	1.57 (0.89, 2.77)	0.67 (0.32, 1.38)
3	-0.03 (-0.07, 0.00)*	-0.48 (-2.84, 1.89)	2.11 (1.34, 3.31)*	1.47 (1.08, 2.02)*	1.88 (1.32, 2.68)*	1.14 (0.78, 1.66)	1.10 (0.62, 1.95)	0.91 (0.44, 1.86)
4	-0.03 (-0.05, -0.01)*	-0.04 (-1.50, 1.43)	1.62 (1.22, 2.15)*	1.57 (1.29, 1.93)*	1.42 (1.14, 1.77)*	1.28 (1.01, 1.63)*	1.03 (0.72, 1.48)	0.57 (0.36, 0.91)*
5 (best possible state)[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Injury classification[c]								
Lower extremity injury								
Pelvic injury	-0.04 (-0.07, -0.02)*	-1.64 (-3.37, 0.10)	2.74 (1.96, 3.83)*	1.29 (1.02, 1.64)*	0.97 (0.74, 1.25)	1.33 (0.99, 1.78)	0.67 (0.43, 1.04)	0.57 (0.33, 0.98)*
Hip fracture	-0.01 (-0.04, 0.02)	-0.34 (-2.20, 1.52)	2.62 (1.82, 3.79)*	1.28 (0.99, 1.66)	1.05 (0.79, 1.40)	1.04 (0.76, 1.41)	0.90 (0.57, 1.42)	1.00 (0.57, 1.77)
Tibia, complex foot or femur fracture	-0.05 (-0.07, -0.02)*	-1.14 (-2.75, 0.48)	6.85 (4.97, 9.44)*	1.27 (1.02, 1.58)*	1.71 (1.33, 2.18)*	1.34 (1.03, 1.76)*	0.8 (0.53, 1.19)	0.71 (0.43, 1.18)
Upper extremity injury								
Shoulder and upper arm injury	-0.03 (-0.06, -0.01)*	-2.00 (-3.44, -0.55)*	0.56 (0.42, 0.74)*	2.22 (1.82, 2.71)*	1.58 (1.28, 1.96)*	2.05 (1.60, 2.61)*	1.01 (0.70, 1.44)	0.71 (0.46, 1.12)
Radius, ulna or hand fracture	-0.02 (-0.04, 0.00)*	-0.59 (-2.31, 1.12)	0.42 (0.30, 0.58)*	1.46 (1.16, 1.85)*	1.22 (0.95, 1.57)	1.23 (0.93, 1.63)	1.44 (0.94, 2.19)	0.87 (0.51, 1.48)
Traumatic brain injury								
Head injury with AIS <=2	0.02 (0.01, 0.04)*	0.64 (-0.41, 1.70)	0.78 (0.64, 0.96)*	0.57 (0.49, 0.67)*	0.77 (0.66, 0.90)*	0.85 (0.72, 1.01)	1.15 (0.88, 1.49)	2.91 (2.12, 4.01)*
Head injury with AIS >=3	0.04 (0.00, 0.08)*	2.07 (-0.66, 4.80)	0.86 (0.51, 1.43)	0.92 (0.62, 1.37)	0.78 (0.52, 1.17)	0.90 (0.58, 1.39)	1.20 (0.62, 2.34)	3.29 (1.45, 7.49)*
Facial injury	0.02 (0.00, 0.05)*	0.78 (-1.15, 2.70)	0.52 (0.35, 0.75)*	0.75 (0.56, 1.00)*	0.67 (0.51, 0.89)*	0.67 (0.49, 0.91)*	1.10 (0.68, 1.78)	1.21 (0.68, 2.16)
Thoracic injury	0.06 (0.03, 0.10)*	3.11 (0.77, 5.46)*	0.54 (0.35, 0.84)*	0.56 (0.40, 0.78)*	0.55 (0.40, 0.78)*	0.68 (0.47, 1.00)*	0.58 (0.32, 1.05)	0.60 (0.29, 1.24)

Rib fracture	-0.01 (-0.03, 0.01)	-0.07 (-1.61, 1.48)	1.07 (0.80, 1.43)	1.02 (0.81, 1.27)	0.93 (0.74, 1.16)	1.63 (1.26, 2.11)*	0.96 (0.65, 1.41)	0.85 (0.53, 1.36)
Abdominal injury	0.02 (-0.02, 0.06)	1.68 (-1.27, 4.63)	0.63 (0.36, 1.09)	0.57 (0.36, 0.88)*	0.67 (0.44, 1.02)	0.56 (0.35, 0.90)*	0.93 (0.45, 1.95)	1.55 (0.65, 3.69)
Spine injury								
Spinal cord injury	-0.06 (-0.16, 0.04)	-3.03 (-9.85, 3.80)	1.86 (0.53, 6.60)	1.33 (0.53, 3.33)	1.35 (0.47, 3.88)	11.61 (2.86, 47.17)*	0.92 (0.18, 4.71)	0.30 (0.04, 2.35)
Stable vertebral fracture or disc injury	-0.06 (-0.08, -0.03)*	-4.16 (-5.99, -2.33)*	1.31 (0.93, 1.84)	1.67 (1.30, 2.15)*	1.79 (1.37, 2.34)*	2.45 (1.79, 3.35)*	1.14 (0.72, 1.79)	0.82 (0.47, 1.42)
Admission to Intensive Care Unit	0.00 (-0.02, 0.03)	-0.47 (-2.35, 1.41)	0.81 (0.56, 1.18)	1.01 (0.77, 1.32)	1.04 (0.78, 1.38)	1.08 (0.79, 1.49)	0.77 (0.48, 1.23)	2.22 (1.26, 3.91)*
Pre-injury work status	0.00 (-0.02, 0.02)	-0.23 (-1.62, 1.17)	0.73 (0.57, 0.95)*	0.94 (0.78, 1.14)	1.01 (0.83, 1.23)	1.12 (0.90, 1.40)	0.74 (0.53, 1.04)	0.92 (0.61, 1.39)
Educational level								
Low[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle	0.00 (-0.01, 0.02)	0.39 (-0.66, 1.43)	0.94 (0.77, 1.15)	0.96 (0.83, 1.11)	0.93 (0.80, 1.08)	1.07 (0.90, 1.26)	0.71 (0.55, 0.92)*	1.05 (0.77, 1.45)
High	0.02 (0.00, 0.03)*	0.36 (-0.76, 1.49)	0.91 (0.73, 1.13)	0.99 (0.84, 1.15)	0.75 (0.64, 0.89)*	0.82 (0.68, 0.98)*	0.64 (0.48, 0.86)*	1.06 (0.75, 1.51)
Frailty	-0.09 (-0.11, -0.07)*	-5.12 (-6.54, -3.71)*	2.38 (1.75, 3.24)*	1.79 (1.46, 2.20)*	2.07 (1.63, 2.62)*	1.48 (1.18, 1.87)*	4.94 (3.55, 6.86)*	4.37 (2.89, 6.61)*
Pre-injury status[d]	0.49 (0.45, 0.53)*	0.47 (0.44, 0.50)*						
No problems[a]			Ref	Ref	Ref	Ref	Ref	Ref
Moderate/severe problems			13.58 (10.62, 17.36)*	20.02 (15.50, 25.86)*	6.39 (5.20, 7.86)*	6.12 (5.09, 7.36)*	30.22 (21.62, 42.25)*	371.77 (224.34, 616.10)*

*p-value≤.05

[a]Reference category

[b]Regression coefficients and odds ratios (95%) represents a 4 unit increase on the Injury Severity Score.

[c]Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

[d]Regression coefficients (95% CI) for pre-injury EQ-5D utility score and the pre-injury EQ-VAS for EQ-5D utility score and EQ-VAS respectively. Odds ratios (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort, Anxiety/depression and cognition respectively for the columns).

Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.

Table 3. Change in the dimensions of the EQ-5D over time in multivariable logistic mixed models for different injury classifications

	Adjusted Odds Ratios (95% Confidence Interval)[a]				
	1 month vs 1 week	**3 months vs 1 month**	**6 months vs 3 months**	**12 months vs 6 months**	**24 months vs 12 months**
Mobility					
Lower extremity[1]	0.78 (0.48, 1.27)	0.24 (0.16, 0.35)*	0.17 (0.12, 0.23)*	0.54 (0.41, 0.70)	0.79 (0.60, 1.03)
Spine[2]	0.12 (0.05, 0.30)*	0.18 (0.08, 0.37)*	0.37 (0.17, 0.81)*	1.01 (0.47, 2.22)	0.70 (0.31, 1.60)
Self-care					
Lower extremity[1]	0.33 (0.24, 0.44)*	0.66 (0.52, 0.84)*	0.75 (0.58, 0.95)*	0.66 (0.49, 0.88)*	1.05 (0.77, 1.43)
Upper extremity[3]	0.19 (0.11, 0.32)*	0.09 (0.06, 0.15)*	0.25 (0.16, 0.40)*	0.51 (0.30, 0.87)*	0.72 (0.40, 1.31)
Spine[2]	0.25 (0.11, 0.57)*	0.05 (0.02, 0.11)*	0.15 (0.06, 0.34)*	0.55 (0.21, 1.43)	1.43 (0.52, 3.93)
Usual activities					
Upper extremity[3]	0.40 (0.22, 0.73)*	0.20 (0.13, 0.32)*	0.25 (0.17, 0.38)*	0.61 (0.40, 0.90)*	0.76 (0.50, 1.15)
Spine[2]	0.48 (0.17, 1.30)	0.11 (0.05, 0.25)*	0.24 (0.12, 0.49)*	0.30 (0.15, 0.60)*	1.71 (0.58, 2.38)
Pain/discomfort					
Lower extremity[1]	0.42 (0.30, 0.59)*	0.53 (0.41, 0.69)*	0.49 (0.39, 0.63)*	0.66 (0.52, 0.84)*	0.75 (0.59, 0.96)*
Upper extremity[3]	0.49 (0.27, 0.87)*	0.27 (0.17, 0.43)*	0.48 (0.32, 0.73)*	0.52 (0.35, 0.78)*	0.78 (0.52, 1.18)
Spine[2]	0.35 (0.12, 0.98)*	0.29 (0.13, 0.64)*	0.62 (0.30, 1.27)	0.19 (0.09, 0.39)*	1.27 (0.64, 2.50)
Anxiety/depression					
Spine[2]	0.69 (0.33, 1.43)	0.92 (0.49, 1.74)	0.64 (0.32, 1.27)	0.81 (0.40, 1.64)	0.87 (0.41, 1.85)
Cognition					
Traumtic Brain Injury[4]	0.72 (0.50, 1.02)	0.85 (0.60, 1.18)	0.69 (0.48, 0.99)*	0.91 (0.63, 1.32)	1.15 (0.79, 1.68)

Time was included as categorical variable in all analyses

*p-value≤.05

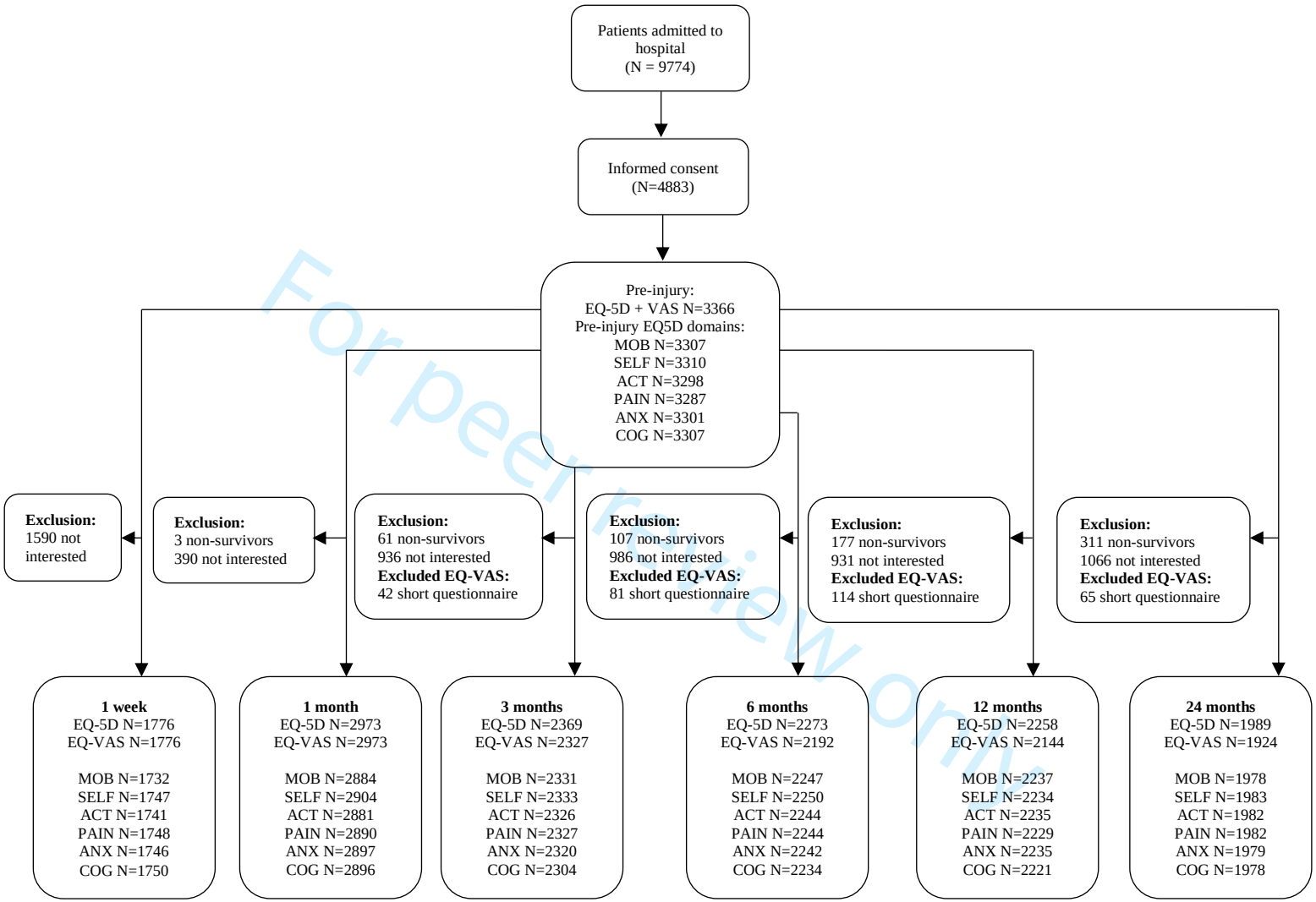
[a]Odds Ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level, frailty and pre-injury status

[1]Patients with pelvic injury, hip fracture or tibia, complex foot or femur fracture

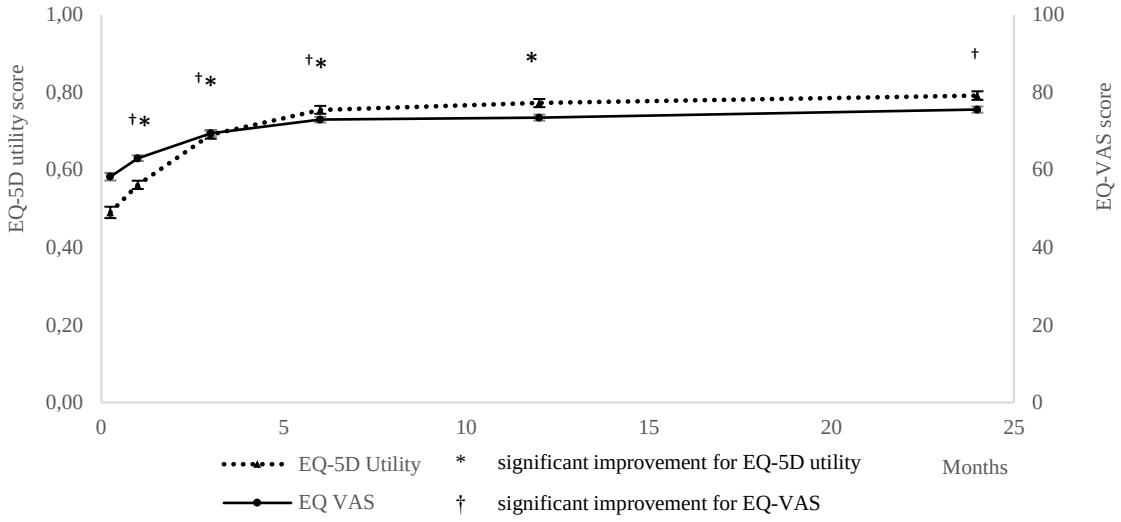
[2]Patients with spinal cord injury or stable vertebral fracture or disc injury

[3]Patients with shoulder and upper arm injury or radius, ulna or hand fracture

[4]Patients with Traumatic brain injury, independent of injury severity



A.


1,00
0,80
0,60
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EQ-5D utility score
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EQ-VAS score
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15
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Months
†*
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*
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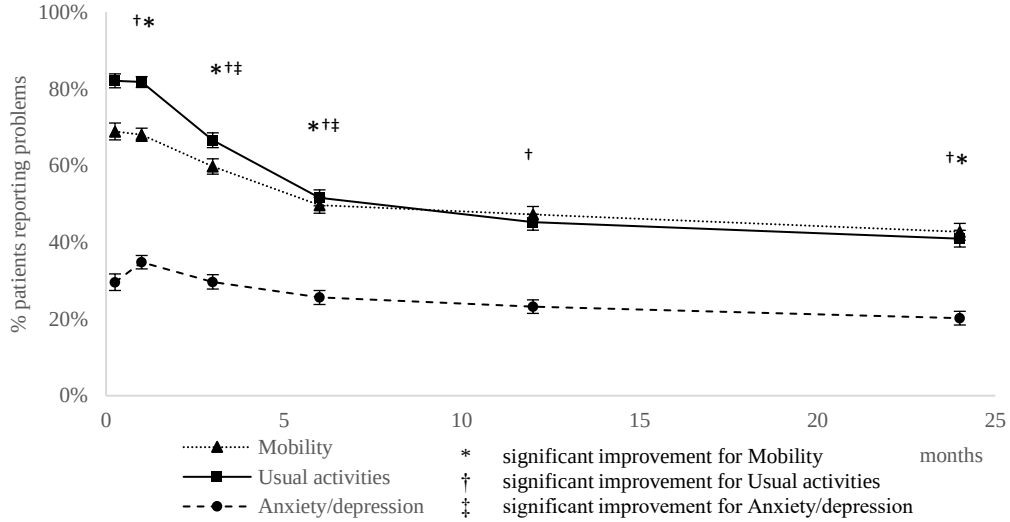
EQ-5D Utility
EQ VAS
* significant improvement for EQ-5D utility
† significant improvement for EQ-VAS

B.


100%
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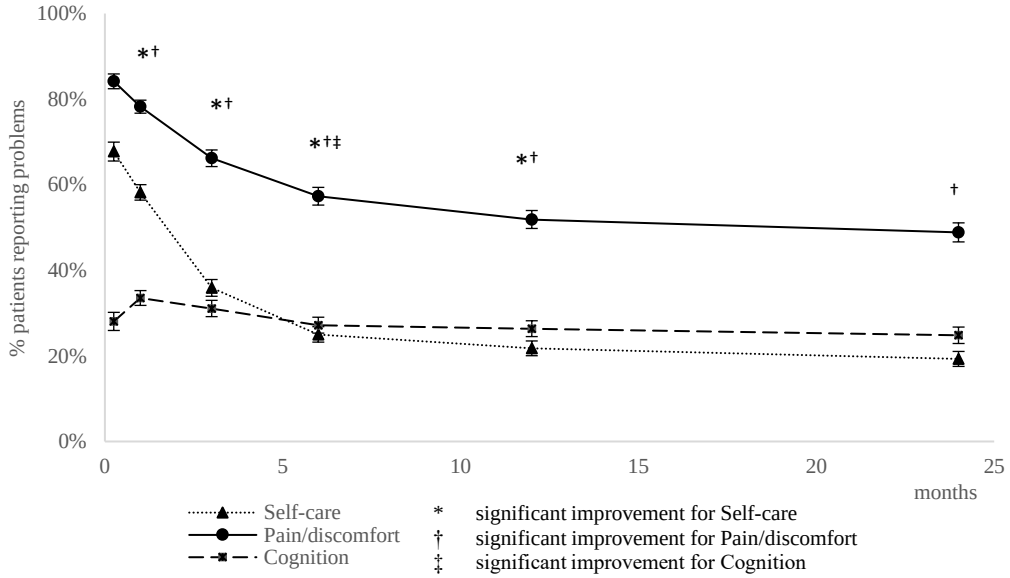
Mobility
Usual activities
Anxiety/depression
* significant improvement for Mobility
† significant improvement for Usual activities
‡ significant improvement for Anxiety/depression

C.


100%
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months
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Self-care
Pain/discomfort
Cognition
* significant improvement for Self-care
† significant improvement for Pain/discomfort
‡ significant improvement for Cognition

S1 Table. Injury group classification of the most common types of injury, based on the Abbreviated Injury Score[22].

Type of trauma	First three numbers of the AIS-code	Injury severity (.1=minor, .6=maximal)
Pelvic injury	856	.2, .3, .4, .5
Hip fracture	853	.3
Tibia, complex foot or femur fracture	854	.2
	857	.2
	858	.2
Shoulder and upper arm injury	770	.1, .2
	771	.1, .2
	750	.2
	751	.2
Radius, ulna or hand fracture	752	.1, .2, .3
	753	.2
Mild TBI*	110	.1, .2
	140	.2
	161	.1, .2
Severe TBI**	110	.3
	140	.3, .4, .5, .6
	161	.3, .4, .5
Facial fracture	250	.1, .2, .3
	251	.1, .2, .3
Thoracic injury	441	.1, .2, .3, .4, .5
	419	.2, .3, .4, .5
	442	.2, .3, .4, .5
Rib fracture	450	.1, .2, .3, .4
Mild abdominal injury	516	.1, .2
	510	.1, .2
	521	.2
	530	.1
	540	.1, .2
	541	.2
	542	.1, .2
	543	.1, .2
	544	.1, .2
	545	.1, .2
Severe abdominal injury	516	.3
	510	.3
	520	.3
	520	.4, .5
	521	.3, .4
	540	.3, .4
	541	.3, .4, .5
	542	.3, .4, .5
	543	.3, .4, .5
	544	.3, .4, .5
	545	.3, .4, .5
Spinal cord injury	640	3, .4, .5
Stable vertebral fracture or disc injury	650	.2, .3

Abbreviations: AIS, Abbreviated Injury Score; TBI, traumatic brain injury.

* Concussion/ commotio cerebri, sequelae of intracranial injury. Sequelae of injury classifiable to S06.

** Traumatic cerebral oedema, focal brain injury, epidural haemorrhage, traumatic subdural heamorrhage, traumatic subarachnoid haemorrhage, intercranial injury unspecified, crushing injury of face, crushing injury of skull, crushing injury of other parts of head, crushing injury of head part unspecified, diffuse brain injury, intracranial injury with prolonged coma, other intracranial injuries traumatic haemorrhage (cerebellar/intracranial not specified).

Supplemental Table 2. Change in EQ-5D and the dimensions of the EQ-5D over time in multivariable linear and logistic mixed models.

	1 month vs 1 week	3 months vs 1 month	6 months vs 3 months	12 months vs 6 months	24 months vs 12 months
Linear regression coefficients (95% Confidence Interval)[a]					
EQ-5D utility score	0.13 (0.12, 0.14)*	0.12 (0.11, 0.13)*	0.06 (0.05, 0.07)*	0.01 (0.00, 0.02)*	0.00 (-0.01, 0.02)
EQ-VAS	8.48 (7.70, 9.26)*	5.97 (5.28, 6.69)*	3.12 (2.36, 3.87)*	0.24 (-0.52, 1.01)	0.98 (0.19, 1.76)*
Odds Ratios (95% Confidence Interval)[a]					
Mobility	0.51 (0.41, 0.63)*	0.38 (0.32, 0.46)*	0.38 (0.31, 0.46)*	0.85 (0.70, 1.03)	0.79 (0.65, 0.97)*
Self-care	0.25 (0.21, 0.30)*	0.14 (0.12, 0.17)*	0.34 (0.28, 0.41)*	0.73 (0.59, 0.91)*	1.03 (0.82, 1.30)
Usual activities	0.67 (0.54, 0.83)*	0.22 (0.19, 0.27)*	0.31 (0.26, 0.37)*	0.61 (0.52, 0.73)*	0.82 (0.69, 0.98)*
Pain/discomfort	0.46 (0.37, 0.56)*	0.36 (0.30, 0.42)*	0.51 (0.44, 0.61)*	0.68 (0.58, 0.80)*	0.84 (0.71, 1.00)*
Anxiety/depression	0.99 (0.82, 1.21)	0.70 (0.59, 0.84)*	0.70 (0.58, 0.85)*	0.83 (0.68, 1.02)	0.89 (0.72, 1.11)
Cognition	0.85 (0.68, 1.06)	0.91 (0.75, 1.12)	0.62 (0.49, 0.77)*	1.09 (0.86, 1.38)	1.15 (0.91, 1.45)

Time was included as categorical variable in the analyses

*p-value≤.05

[a]Regression coefficients and odds ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level, frailty and pre-injury status

Supplemental Table 3. Regression coefficients in univariable linear mixed models for the EQ-5D utility and the EQ-VAS and odds ratios in univariable logistic mixed models for the dimensions of HS.

	During the first two years after injury							
	Linear regression coefficients (95% CI)		Odds Ratios (95% CI)					
	EQ-5D utility	EQ-VAS	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/ depression	Cognition
Female sex	-0.11 (-0.12, -0.10)*	-6.37 (-7.42, -5.32)*	4.57 (3.73, 5.61)*	3.04 (2.62, 3.53)*	3.20 (2.78, 3.68)*	2.46 (2.15, 2.82)*	4.28 (3.48, 5.28)*	4.95 (3.71, 6.60)*
Age (years)								
18 - 24	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
25 - 44	-0.03 (-0.07, 0.01)	-1.59 (-4.66, 1.47)	2.08 (1.18, 3.64)*	1.59 (1.03, 2.46)*	1.83 (1.22, 2.74)*	1.72 (1.15, 2.59)*	0.93 (0.52, 1.67)	0.71 (0.34, 1.52)
45 - 64	-0.02 (-0.06, 0.01)	-3.69 (-6.50, -0.88)*	4.59 (2.74, 7.68)*	2.08 (1.40, 3.10)*	1.86 (1.29, 2.69)*	1.82 (1.26, 2.63)*	0.58 (0.34, 0.98)*	0.43 (0.22, 0.86)*
65 - 74	-0.02 (-0.06, 0.02)	-2.47 (-5.35, 0.41)	10.91 (6.42, 18.56)*	2.78 (1.85, 4.18)*	1.77 (1.21, 2.58)*	1.63 (1.12, 2.37)*	0.39 (0.23, 0.68)*	0.39 (0.20, 0.79)*
≥ 75	-0.16 (-0.19, -0.12)*	-12.78 (-15.58, -9.98)*	105.71 (61.48, 181.77)*	14.70 (9.83, 21.98)*	6.29 (4.34, 9.1)*	2.50 (1.73, 3.60)*	2.07 (1.23, 3.49)*	12.86 (6.37, 25.98)*
Nr of comorbidities								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	-0.08 (-0.10, -0.06)*	-7.86 (-9.05, -6.66)*	5.41 (4.26, 6.87)*	2.45 (2.06, 2.91)*	2.14 (1.82, 2.51)*	1.75 (1.49, 2.05)*	2.54 (1.98, 3.24)*	5.41 (3.88, 7.53)*
≥2	-0.21 (-0.22, -0.19)*	-16.02 (-17.20, -14.84)*	36.44 (27.79, 47.78)*	8.45 (7.07, 10.10)*	7.16 (6.03, 8.51)*	4.70 (3.97, 5.57)*	9.32 (7.25, 11.97)*	45.33 (30.83, 66.64)*
Injury Severity Score[b]	-0.03 (-0.03,-0.02)*	-2.07 (-2.49, -1.65)*	1.58 (1.45, 1.71)*	1.34 (1.27, 1.43)*	1.35 (1.27, 1.43)*	1.12 (1.06, 1.18)*	1.25 (1.15, 1.36)*	1.52 (1.36, 1.70)*
Length of stay at hospital (days)								
1 - 2	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3 - 7	-0.10 (-0.12, -0.09)*	-6.46 (-7.70, -5.22)*	10.61 (8.31, 13.53)*	3.72 (3.11, 4.45)*	3.11 (2.65, 3.66)*	2.19 (1.86, 2.59)*	2.23 (1.72, 2.88)*	2.22 (1.57, 3.13)*
8 - 14	-0.20 (-0.22, -0.18)*	-13.00 (-14.52, -11.48)*	39.48 (28.73, 54.26)*	11.04 (8.87, 13.73)*	8.06 (6.54, 9.93)*	3.73 (3.05, 4.57)*	5.73 (4.23, 7.76)*	9.12 (5.96, 13.97)*
≥ 15	-0.28 (-0.31, -0.26)*	-18.39 (-20.52, -16.25)*	103.66 (65.98, 162.88)*	22.75 (16.73, 30.93)*	14.88 (10.88, 20.36)*	4.91 (3.63, 6.65)*	11.30 (7.41, 17.24)*	24.69 (13.58, 44.90)*
Functional Capacity Index								
1 (worse state)	-0.13 (-0.20, -0.06)*	-7.63 (-13.18, -2.08)*	4.12 (1.62, 10.48)*	2.95 (1.45, 5.99)*	3.04 (1.52, 6.08)*	1.43 (0.72, 2.85)	3.97 (1.46, 10.75)*	8.96 (2.28, 35.20)*
2	-0.10 (-0.13, -0.06)*	-3.73 (-6.41, -1.05)*	9.85 (6.00, 16.17)*	2.47 (1.74, 3.52)*	2.85 (2.00, 4.05)*	2.16 (1.51, 3.09)*	1.88 (1.12, 3.17)*	0.33 (0.16, 0.65)*
3	-0.10 (-0.13, -0.06)*	-2.74 (-5.57, 0.08)	7.83 (4.70, 13.06)*	2.91 (2.00, 4.25)*	3.93 (2.69, 5.75)*	1.63 (1.13, 2.36)*	1.67 (0.96, 2.92)	0.69 (0.33, 1.45)
4	-0.11 (-0.12, -0.10)*	-6.01 (-7.15, -4.88)*	13.22 (10.56, 16.56)*	4.62 (3.94, 5.43)*	3.27 (2.82, 3.80)*	1.71 (1.48, 1.98)*	2.05 (1.64, 2.56)*	1.37 (1.02, 1.84)*
5 (best possible state)[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Injury classification[c]								
Lower extremity injury								
Pelvic injury	0.71 (0.70, 0.72)	-4.60 (-6.70, -2.51)*	6.17 (4.27, 8.92)*	2.27 (1.71, 3.00)*	1.93 (1.47, 2.54)*	1.57 (1.19, 2.08)*	1.37 (0.90, 2.10)	1.19 (0.68, 2.09)
Hip fracture	-0.09 (-0.12, -0.06)*	-9.15 (-10.55, -7.74)*	20.99 (16.05, 27.46)*	5.59 (4.60, 6.81)*	3.77 (3.12, 4.55)*	1.68 (1.40, 2.02)*	2.68 (2.04, 3.53)*	5.48 (3.75, 8.02)*

Tibia, complex foot or femur fracture	-0.13 (-0.15, -0.11)*	-2.37 (-4.09, -0.65)*	12.24 (8.98, 16.69)*	1.79 (1.42, 2.24)*	2.84 (2.27, 3.57)*	1.81 (1.44, 2.27)*	1.26 (0.90, 1.76)	0.53 (0.34, 0.82)*
Upper extremity injury								
Shoulder and upper arm injury	-0.07 (-0.10, -0.05)*	-2.57 (-4.40, -0.74)*	0.75 (0.55, 1.01)	2.47 (1.95, 3.14)*	1.8 (1.43, 2.27)*	2.21 (1.74, 2.80)*	1.21 (0.85, 1.72)	0.75 (0.47, 1.18)
Radius, ulna or hand fracture	-0.04 (-0.07, -0.02)*	0.60 (-1.54, 2.74)	0.35 (0.24, 0.50)*	1.22 (0.92, 1.62)	1.06 (0.81, 1.38)	1.03 (0.78, 1.35)	0.77 (0.5, 1.17)	0.36 (0.21, 0.63)*
Traumatic brain injury								
Head injury with AIS <=2	0.01 (-0.02, 0.03)	1.40 (0.10, 2.69)*	0.66 (0.53, 0.82)*	0.50 (0.41, 0.59)*	0.63 (0.53, 0.74)*	0.67 (0.57, 0.80)*	0.82 (0.64, 1.06)	2.52 (1.80, 3.53)*
Head injury with AIS >=3	0.04 (0.03, 0.06)*	-2.77 (-5.54, 0.00)*	1.84 (1.16, 2.91)*	1.17 (0.80, 1.71)	1.66 (1.16, 2.36)*	0.86 (0.61, 1.22)	2.44 (1.43, 4.15)*	13.11 (6.35, 27.06)*
Facial injury	-0.03 (-0.06, 0.01)	1.99 (-0.40, 4.37)	0.37 (0.25, 0.56)*	0.64 (0.46, 0.90)*	0.65 (0.48, 0.88)	0.6 (0.44, 0.81)*	0.99 (0.61, 1.58)	1.34 (0.72, 2.47)
Thoracic injury	0.04 (0.00, 0.07)*	2.37 (-0.49, 5.23)	0.54 (0.33, 0.87)*	0.62 (0.42, 0.93)*	0.73 (0.51, 1.05)	0.61 (0.42, 0.89)*	0.83 (0.47, 1.48)	0.8 (0.38, 1.68)
Rib fracture	0.04 (0.00, 0.07)*	-0.80 (-2.68, 1.09)	1 (0.73, 1.37)	0.81 (0.63, 1.05)	0.94 (0.74, 1.19)	1.35 (1.06, 1.72)*	0.65 (0.45, 0.95)*	1.05 (0.65, 1.71)
Abdominal injury	0.00 (-0.02, 0.03)	1.24 (-2.24, 4.73)	0.44 (0.24, 0.81)*	0.58 (0.35, 0.95)*	0.66 (0.42, 1.04)	0.56 (0.35, 0.88)*	1.06 (0.53, 2.14)	1.27 (0.51, 3.14)
Spine injury								
Spinal cord injury	-0.18 (-0.27, -0.09)*	-7.32 (-14.94, 0.29)	5.97 (1.8, 19.76)*	3.55 (1.41, 8.98)*	5.03 (1.95, 13.00)*	23.14 (6.63, 80.76)*	2.97 (0.78, 11.27)	0.94 (0.16, 5.48)
Stable vertebral fracture or disc injury	-0.05 (-0.08, -0.03)*	-4.10 (-6.27, -1.93)*	1.22 (0.85, 1.76)	1.57 (1.17, 2.10)*	1.88 (1.42, 2.49)*	2.43 (1.82, 3.25)*	1.23 (0.8, 1.87)	0.96 (0.55, 1.68)
Admission to Intensive Care Unit	-0.02 (-0.05, 0.01)	-2.88 (-4.90, -0.86)*	0.80 (0.55, 1.16)	0.94 (0.72, 1.25)	1.26 (0.97, 1.65)	1.10 (0.84, 1.43)	1.16 (0.79, 1.71)	4.15 (2.51, 6.83)*
Pre-injury work status	0.11 (0.09, 0.12)*	7.58 (6.40, 8.76)*	0.06 (0.05, 0.08)*	0.23 (0.19, 0.27)*	0.38 (0.33, 0.45)*	0.63 (0.54, 0.73)*	0.35 (0.28, 0.45)*	0.10 (0.07, 0.15)*
Educational level								
Low[a]	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle	0.07 (0.06, 0.09)*	5.42 (4.15, 6.70)*	0.22 (0.17, 0.28)*	0.38 (0.32, 0.46)*	0.51 (0.43, 0.60)*	0.76 (0.65, 0.90)*	0.39 (0.31, 0.50)*	0.25 (0.18, 0.35)*
High	0.11 (0.09, 0.13)*	6.74 (5.35, 8.13)*	0.18 (0.13, 0.23)*	0.35 (0.29, 0.43)*	0.37 (0.31, 0.45)*	0.48 (0.40, 0.57)*	0.25 (0.19, 0.33)*	0.18 (0.12, 0.26)*
Frailty	-0.28 (-0.30, -0.26)*	-17.00 (-18.28, -15.73)*	42.04 (30.13, 58.65)*	17.43 (13.8, 22.02)*	10.32 (8.11, 13.12)*	3.53 (2.84, 4.39)*	20.90 (15.31, 28.54)*	181.79 (99.22, 333.08)*
Pre-injury status[d]	0.67 (0.64, 0.70)*	0.58 (0.55, 0.60)*						
No problems[a]			Ref	Ref	Ref	Ref	Ref	Ref
Moderate/severe problems			71.89 (54.53, 94.77)*	61.03 (47.05, 79.17)*	15.01 (12.27, 18.36)*	8.69 (7.29, 10.36)*	114.45 (79.19, 165.42)*	3613.12 (1619.40, 8061.43)*

*p-value≤.05

[a]Reference category

[b]Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

[c]Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

[d]Regression coefficients (95% CI) for pre-injury EQ-5D utility score and the pre-injury EQ-VAS for EQ-5D utility and EQ-VAS respectively. Odds ratios (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort, Anxiety/depression and cognition respectively for the columns).

Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	4,9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
-Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, explain how loss to follow-up was addressed	7-8
		(*e*) Describe any sensitivity analyses	7-8
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	7,9
		(c) Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	Report numbers of outcome events or summary measures over time	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.