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

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

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**Running head:** Prognostic factors for recovery after trauma

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

**Word count:**

## 27 Abstract

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

30 **Design:** a prospective longitudinal cohort study.

31 **Setting:** Ten participating hospitals in Brabant, the Netherlands

32 **Participants:** adult injury patients admitted to a hospital between August 2015 and November  
33 2016 were followed. 4883 (50%) patients participated.

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

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

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

47 **Trial registration number:** NCT02508675

## 48 **Strengths and limitations of the study**

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

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

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

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

56

## 57 Introduction

58  
59 Trauma, defined as a physical injury, is one of the leading causes of disability and affects  
60 millions of people worldwide each year. The number of survivors after trauma increased the  
61 last decades, due to the improvement of trauma care<sup>1-3</sup>. Many patients suffer physical,  
62 psychological or cognitive impairments, resulting in a reduction of their health status (HS).

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

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

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

## 81 **Methods**

### 83 **Study design and participants**

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

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

### 102 **Outcome**

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



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3 106 activities, pain/discomfort and anxiety/depression. Each dimension could be answered in three  
4  
5 107 levels: no problems, some problems and severe/extreme problems.

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8 108 A summary score of the EQ-5D (EQ-5D utility) can be calculated by using the Dutch tariffs<sup>19</sup>.  
9  
10 109 This utility score ranged from 0 (death) to 1 (perfect health). The EQ-VAS is a vertical visual  
11  
12 110 analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best  
13  
14 111 imaginable health state.

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16  
17 112 Cognition was added as additional dimension to the EQ-5D questionnaire. Respondents were  
18  
19 113 asked to describe their or, in case of proxy, the patients' state of health, concerning cognition  
20  
21 114 (e.g. memory, concentration). Similar to the other dimensions, answer options were based on  
22  
23 115 three levels: no problems, some problems and severe problems.

24  
25  
26 116 HS was measured at each time point during follow-up in both patient and proxy questionnaires.  
27  
28 117 The EQ-5D (including the cognition dimension) and EQ-VAS were also measured pre-injury,  
29  
30 118 by asking participants at one week or one month and proxy informants at one month for the  
31  
32 119 patients' health status before sustaining the injury. The EQ-VAS was not included in the short  
33  
34 120 questionnaire.

## 35 36 37 38 121 **Prognostic factors**

### 39 40 41 122 *Sociodemographic variables*

42  
43 123 Possible prognostic factors for health status that were measured in the BIOS-study were sex,  
44  
45 124 age, educational level (low, middle or high), pre-injury work status (yes/no), frailty and pre-  
46  
47 125 injury health status. Educational level was categorized in three levels as the highest completed  
48  
49 126 degree, diploma of education; low (primary education, preparatory secondary vocational  
50  
51 127 education or without diploma), middle (university preparatory education, senior general  
52  
53 128 secondary education or senior secondary vocational education and training), and high  
54  
55 129 (academic degree or university of applied science). Frailty was measured at one week or one  
56  
57 130 month after injury with the Groningen Frailty Index (GFI) in patients  $\geq 65$  years<sup>20</sup>. A sum-score

1  
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3 131 of  $\geq 4$  was considered frail. Patients  $< 65$  years were considered not frail. Pre-injury health status  
4  
5 132 was measured at 1 week or 1 month after injury with the EQ-5D-3L, referring to the health  
6  
7 133 status of the patients prior to injury.  
8  
9

#### 10 134 *Clinical variables*

11  
12  
13 135 Possible other clinical prognostic factors for health status were length of hospital stay, injury  
14  
15 136 severity score, admission to the intensive care (yes/no), presence of comorbidities and the  
16  
17 137 functional capacity index. Comorbidities were measured with the American Society of  
18  
19 138 Anaesthesiologists (ASA) physical status classification system ranging from 1 (healthy patient)  
20  
21 139 to 4 (severe systemic disease that is a constant threat to life). The functional capacity index and  
22  
23 140 injury severity score were based on the Abbreviated Injury Scale (AIS) codes (AIS-90, update  
24  
25 141 2008)<sup>21</sup>.  
26  
27  
28  
29

#### 30 142 *Injury Classification*

31  
32 143 The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)<sup>21</sup> were used to create injury  
33  
34 144 group classifications representing the most common types of injuries. In total, 14 injury groups  
35  
36 145 were created: 3 lower extremity injury groups (pelvic injury, hip fracture, and tibia  
37  
38 146 fracture/complex foot fracture or distal/shaft femur fracture), 2 upper extremity injury groups  
39  
40 147 (shoulder and upper arm injury, and radius, ulna or hand fracture), 2 head injury groups (AIS-  
41  
42 148 head  $\leq 2$ , and AIS-head  $\geq 3$ ), 1 face injury group, 2 thorax injury groups (thorax injury, and rib  
43  
44 149 fracture), 2 abdomen injury (AIS-abdomen  $\leq 2$ , and AIS-abdomen  $\geq 3$ ) and 2 spine injury (spinal  
45  
46 150 cord injury/brachial plexus lesion, and stable vertebral fracture/disc injury). Patients who suffer  
47  
48 151 multiple injuries could be classified in one or more injury group classifications.  
49  
50  
51  
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#### 53 152 **Data analysis**

54  
55  
56 153 Baseline characteristics of participants were compared with non-participants, using chi-square  
57  
58 154 for categorical variables or the Mann-Whitney U test for non-normal distributed data.  
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3 155 Descriptive statistics included the median with the interquartile range (IQR) for continuous  
4  
5 156 variables. Missing baseline characteristics (0.9% for ISS and 6.8% for length of stay at hospital)  
6  
7 157 and missing utility scores for participants (ranging from 1.8% at 1 week follow-up to 6.9% at  
8  
9 158 12 months follow-up) were imputed according to multiple imputation by using the Multivariate  
10  
11 159 Imputations by Chained Equations (MICE) procedure with 15 imputations and 5 iterations<sup>22</sup>.  
12  
13 160 The imputation model included baseline characteristics, injury characteristics and summary  
14  
15 161 scores of the follow-up questionnaires to capture associations with missingness as completely  
16  
17 162 as possible.  
18  
19 163 Multicollinearity was checked based on the Variance Inflation Factor (criterion:  $VIF > 10$ ).  
20  
21 164 Prognostic factors were assessed for poor health status outcome with EQ-5D utility and EQ-  
22  
23 165 VAS as outcome measures. Regression coefficients with corresponding 95% confidence  
24  
25 166 interval (CI) were reported. The dimensions of the EQ-5D descriptive system were  
26  
27 167 dichotomized into 0=no problems and 1=some problems/extreme problems. Logistic mixed  
28  
29 168 models with random intercepts were used to assess prognostic factors for poor outcome for the  
30  
31 169 six dimensions of the EQ-5D (e.g. mobility, self-care, usual activities, pain/discomfort,  
32  
33 170 anxiety/depression and cognition). All potential prognostic factors were included in the  
34  
35 171 multivariable regression models to calculate adjusted Odds Ratios and corresponding 95% CI.  
36  
37 172 Age and LOS were included as categorical variables, because of the non-linear relation between  
38  
39 173 factor and outcome.  
40  
41 174 Recovery patterns were determined by changing the reference category of the categorical time  
42  
43 175 variable in linear mixed models for health status and logistic mixed models for the dimensions  
44  
45 176 of health status, adjusted for the prognostic factors. Recovery patterns for the items of the EQ-  
46  
47 177 5D were assessed in detail for injury classifications that showed to be statistically significant  
48  
49 178 for the dimensions in the total multivariable model.  
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3 179 Analyses were conducted in the statistical programs R version 3.4.0 (R Foundation for  
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5 180 Statistical Computing, Vienna, Austria) and IBM SPSS version 24 (Chicago, USA) and results  
6  
7  
8 181 were reported according to the TRIPOD guidelines<sup>23</sup>.  
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## 183 **Results**

### 185 **Baseline characteristics**

186 A total of 4883 patients (50% of total, N=9774) completed at least one questionnaire of the  
187 BIOS study of whom 48% (N=2,329) was male (**Figure 1, Table 1**). The median age was 68  
188 years with an IQR of 53-80 years. Responders had a median injury severity score of 5 (IQR [4-  
189 9]) and most of the patients were classified as healthy or as patients with mild systemic disease  
190 (N=3,879, 79%). A total of 358 patients (7%) were admitted to the intensive care unit.  
191 Compared to the non-responders, participants were more severely injured, were more often  
192 admitted to a level I trauma centre, were more often admitted to the intensive care unit, had  
193 lower functional capacity index values, and were more often healthy (measured with the ASA  
194 classification). The majority of the responders had low educational level (N=2,670, 55%) and  
195 38% of the responders (N=1,278) had a job prior to injury.

### 197 **Health status over time**

198 The mean (SD) EQ-5D utility score ranged from 0.49 (0.32), 0.56 (0.30), 0.69 (0.27), 0.76  
199 (0.25), 0.77 (0.26) and 0.79 (0.25) at 1 week, 1, 3, 6, 12 and 24 months respectively (**Figure**  
200 **2A**). The mean (SD) EQ-VAS score ranged from 58.26 (20.45), 63.02 (20.46), 69.48 (18.56),  
201 72.97 (17.28), 73.50 (18.08) and 75.58 (17.88) at 1 week, 1, 3, 6, 12 and 24 months respectively.  
202 Patients reported the most recovery during the first 6 months, with a little improvement up to  
203 12 months. The first month, patients reported most problems for pain/discomfort, usual  
204 activities, mobility and self-care (**Figure 2B**). During the 24 month follow-up, the percentage  
205 of patients reporting problems for pain/discomfort, usual activities and mobility were highest.  
206 Two years after injury 49% (95% CI: 47, 51) of the patients reported problems for  
207 pain/discomfort, 43% (95% CI: 41, 45) reported problems for mobility, 41% (95% CI: 39, 43)

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3 208 reported problems for usual activities, 25% (95% CI: 23, 27) reported for cognition, 20% (95%  
4  
5 209 CI: 18, 22) reported problems for anxiety/depression and 19% (95% CI: 17, 21) for self-care.  
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### 211 **Prognostic factors**

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

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

### 226 **Recovery patterns**

227 Most recovery occurred in the first 6 months (**Table 3**). Health status measured with the EQ-  
228 5D utility improved significantly during the first year after injury and health status measured  
229 with the EQ-VAS significantly increased during the 24 months after injury (although not  
230 significant at twelve months compared to six months). Patients reported to have significantly  
231 less problems with mobility, usual activities and pain/discomfort 24 months after injury  
232 compared to twelve months after injury.

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3 233 Patients with spine injury showed improved mobility up to three months after injury, whereas  
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5 234 patients with lower extremity injury showed less mobility problems up to twelve months after  
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8 235 injury (**Table 4**). Upper and lower extremity injury showed the same recovery pattern during  
9  
10 236 the first two years for self-care. Patients with spine injury showed improvement up to six  
11  
12 237 months compared with three months after injury for self-care.  
13  
14 238 Patients with upper extremity and spine injury reported less problems for usual activities at  
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17 239 twelve months after injury compared with six months after injury. Recovery mostly occurred  
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19 240 up until twelve months after injury, except for pain/discomfort. Patients with lower extremity  
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21 241 injury reported significant less problems at 24 months compared to twelve months for  
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24 242 pain/discomfort.  
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## 243 Discussion

244  
245 In this multicentre prospective cohort study, we found that patients reported problems up until  
246 two years after injury. Health status was especially low during the first six months after injury,  
247 in which patients often reported problems in most of the dimensions of health status. Lower  
248 pre-injury health status, frailty and longer length of stay at hospital were prognostic factors for  
249 both decreased health status and reporting problems in the dimensions during the first two years  
250 after trauma. For the EQ-5D dimensions mobility, usual activities and pain/discomfort less  
251 problems were reported at two years compared to one year after trauma, as for the other  
252 dimensions we found no decrease in reported problems after one year.

253  
254 Previous research showed that age is a prognostic factor for reduced health status<sup>9,15,24</sup>. In  
255 contrast, results from this study showed improved overall health status. This could be explained  
256 by the addition of the strong prognostic factors pre-injury health status and frailty in the  
257 multivariable adjusted models. Indicating that not the increase of age is a prognostic factor for  
258 poor health status, but the patients' health status before injury. Not all elderly patients are frail  
259 nor are they in poor health. With the ageing population, frailty and pre-injury health status are  
260 essential to consider when assessing recovery patterns in injury patients. Higher age was a  
261 prognostic factor for problems with mobility and self-care but showed to be a negative  
262 associated with other dimensions of the EQ-5D. The latter is in line with a recent study, stating  
263 that the relationship between age and the dimensions of EQ-5D differed<sup>4</sup>.

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



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3 269 suffer persistent cognitive problems<sup>27-29</sup>. Our study showed that TBI patients reported to be  
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5 270 recovered after six months, in line with the recovery pattern of mild TBI patients. This is  
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8 271 possibly due to the fact that most responders of the BIOS-study suffered mostly mild TBI (27%)  
9  
10 272 compared to moderate/severe TBI (4%). Further evaluation of these subgroups with more  
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12 273 specific outcome measures are necessary to determine their recovery patterns.  
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16  
17 275 In line with previous studies, this study showed that female sex is a prognostic factor for poor  
18  
19 276 health status after injury<sup>4,5,7,8,12,15,30</sup>. It has been suggested that problems were more often  
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21 277 reported in females, in contrast to males, who dismiss their complaints more often. Another  
22  
23 278 explanation could be that women experience more psychological impact, resulting in lower  
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26 279 health status.

27  
28 280 Except for longer length of stay at the hospital, no injury related characteristics were found to  
29  
30 281 be prognostic factors for anxiety/depression complaints. These results suggest that  
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32 282 psychological problems after injury are mainly based on patient characteristics, which is  
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35 283 confirmed in previous research<sup>31,32</sup>.  
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39 285 Although the large prospective longitudinal design of this study is a major strength, there are  
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41 286 also some limitations. First, only 50% of the patients responded to the BIOS-study. We found  
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43 287 differences in injury and patient characteristics between responders and non-responders of the  
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45  
46 288 BIOS-study, e.g. responders were more severely injured compared to the non-responders,  
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48 289 indicating selection bias. Next, it is also possible that selective dropout has occurred. We  
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51 290 suspect that patients who were fully recovered were less likely to respond to the follow-up  
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53 291 questions, resulting in an overestimation of complaints after injury. Last, frailty was only  
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55 292 assessed in patients aged  $\geq 65$  years. This could have introduced bias, because younger patients  
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58 293 may be frail. However, we believe this would only affect a small proportion in this large cohort.  
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3 294 Next, generalisability of the study results can be questioned, because inclusion criteria for  
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5 295 injured patients could be different from other registries. This study included all injury severities  
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7  
8 296 and elderly patients with hip fracture.

9  
10 297 We acknowledge that long-term non-fatal outcomes should be incorporated in the trauma  
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12 298 registry<sup>33</sup>. These outcomes could be used to inform caregivers and patients about their expected  
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14 299 recovery patterns. However, pre-injury health status is essential in predicting short and long-  
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17 300 term outcome after injury and should therefore also be included in the registry. Furthermore,  
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19 301 the dimensions of the EQ-5D and health status showed to have different recovery patterns for  
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21 302 different injury classifications. Non-fatal outcome should not only be focused on health status,  
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23  
24 303 but especially on the different dimensions.

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26 304  
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28 305 Although patients showed to be recovered after six months for the dimensions  
29  
30 306 anxiety/depression and cognition, the dimensions mobility, pain/discomfort and usual activities  
31  
32 307 still improved 2 years after injury. These results contribute to the increase in knowledge of  
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35 308 recovery patterns and could be a starting point to develop prediction models for specific injury  
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37 309 classifications for the implementation of personalized medicine.

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4 400 **Contributors**

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6  
7 402 LM, SP and MJ contributed to conception and design of this study. LM and MJ contributed to data

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9 403 collection. LM, SP, RH, ES, MJ contributed to analyses and interpretation. LM, SP, RH, ES and MJ

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11 404 contributed to preparation of the manuscript. The final version of the article was approved by all the

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

	Responders <sup>a</sup>	Non-responders	p-value
<b>N (%)</b>	4883	4891	
<b>Male (%)</b>	2329 (48)	2407 (49)	0.13
<b>Age (median, IQR)</b>	68 (53-80)	70 (46-84)	0.26
<b>ASA classification (N, %)</b>			
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)	
<b>Injury Severity Score (median, IQR)</b>	5 (4-9)	5 (2-9)	0.00
<b>Length of stay at hospital (median, IQR)</b>	4 (2-8)	4 (2-8)	0.02
<b>Functional capacity index (N, %)</b>			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)	
<b>Injury classification (N, %)</b>			
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)	
<b>Mechanism of injury</b>			
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)	
<b>Admission to intensive care unit (N, %)</b>	358 (7)	292 (6)	0.00
<b>Educational level (N, %)*</b>			
Low	2670 (55)	-	
Middle	1305 (27)	-	
High	908 (19)	-	
<b>Pre-injury work status*</b>	1278 (38)	-	

<sup>a</sup>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
<b>Female sex</b>	-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)
<b>Age (years)</b>								
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)
<b>Nr of comorbidities</b>								
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)
<b>Injury Severity Score<sup>b</sup></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)
<b>Length of stay at hospital (days)</b>								
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)
<b>Functional Capacity Index</b>								
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) <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<b>Injury classification<sup>c</sup></b>								
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)
<b>Admission to Intensive Care Unit</b>	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)
<b>Pre-injury work status</b>	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)
<b>Educational level</b>								
Low <sup>a</sup>	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)
<b>Frailty</b>	-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)
<b>Pre-injury status<sup>d</sup></b>	0.49 (0.45, 0.53)	0.47 (0.44, 0.50)						
No problems <sup>a</sup>			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)

<sup>a</sup>Reference category

<sup>b</sup>Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

<sup>c</sup>Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

<sup>d</sup>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.

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**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
<b>Linear regression coefficients (95% Confidence Interval)*</b>					
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)
<b>Odds Ratios (95% Confidence Interval)*</b>					
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
<b>Mobility</b>					
Lower extremity <sup>1</sup>	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 <sup>2</sup>	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)
<b>Self-care</b>					
Lower extremity <sup>1</sup>	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 <sup>3</sup>	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 <sup>2</sup>	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)
<b>Usual activities</b>					
Upper extremity <sup>3</sup>	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 <sup>2</sup>	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)
<b>Pain/discomfort</b>					
Lower extremity <sup>1</sup>	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 <sup>3</sup>	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 <sup>2</sup>	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)
<b>Anxiety/depression</b>					
Spine <sup>2</sup>	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)
<b>Cognition</b>					
Traumatic Brain Injury <sup>4</sup>	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

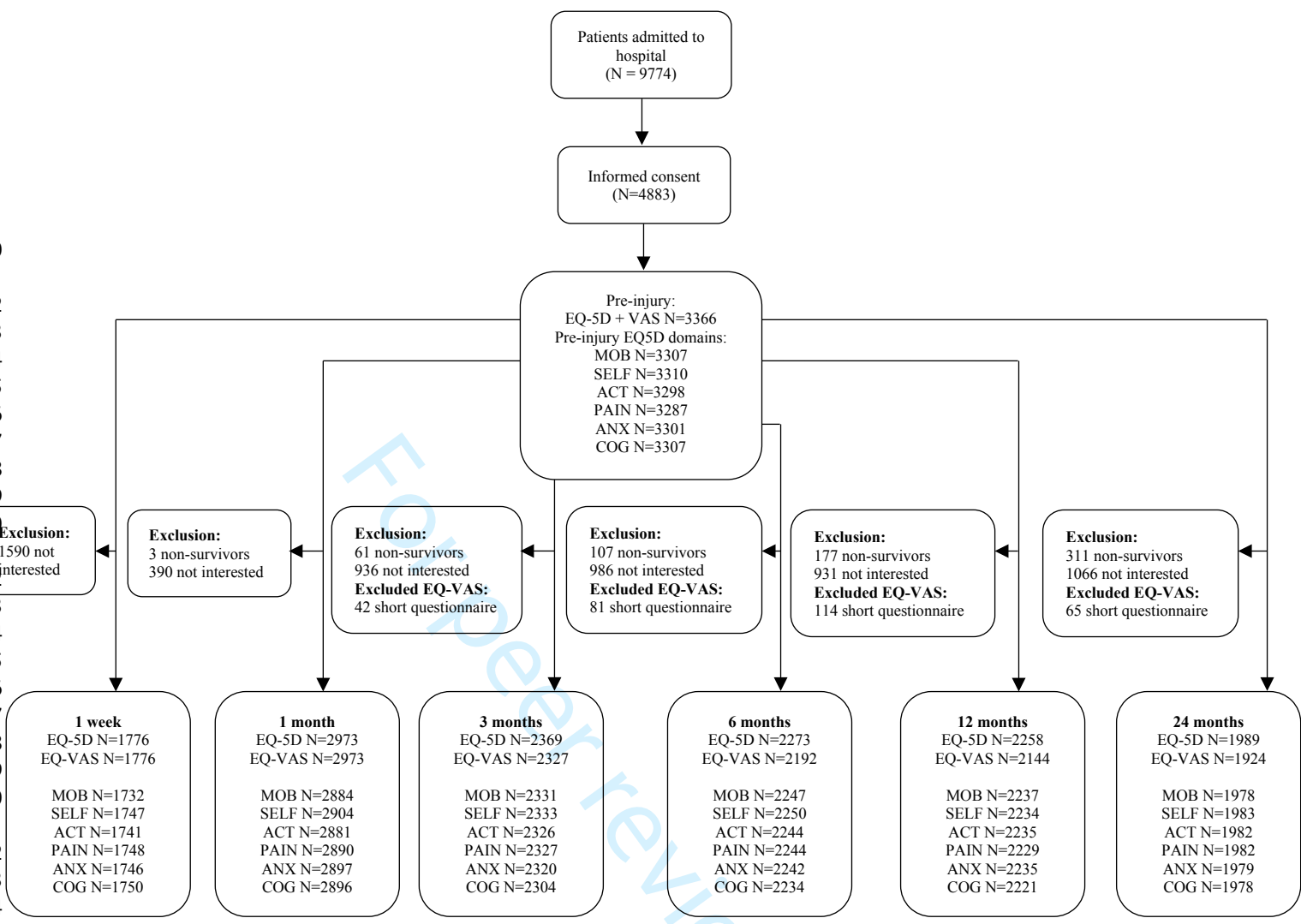
<sup>1</sup>Patients with pelvic injury, hip fracture or tibia, complex foot or femur fracture

<sup>2</sup>Patients with spinal cord injury or stable vertebral fracture or disc injury

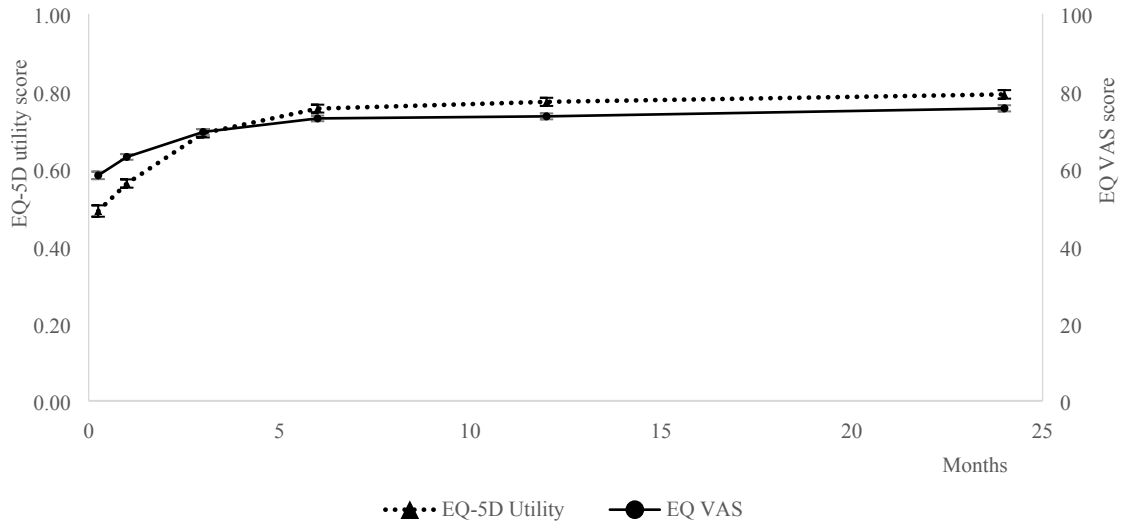
<sup>3</sup>Patients with shoulder and upper arm injury or radius, ulna or hand fracture

<sup>4</sup>Patients with Traumatic brain injury, independent of injury severity

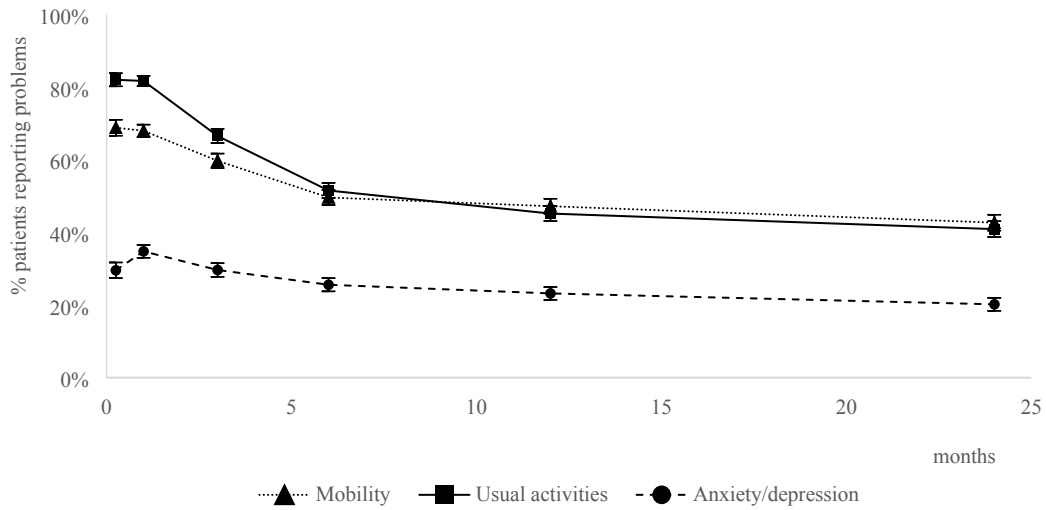
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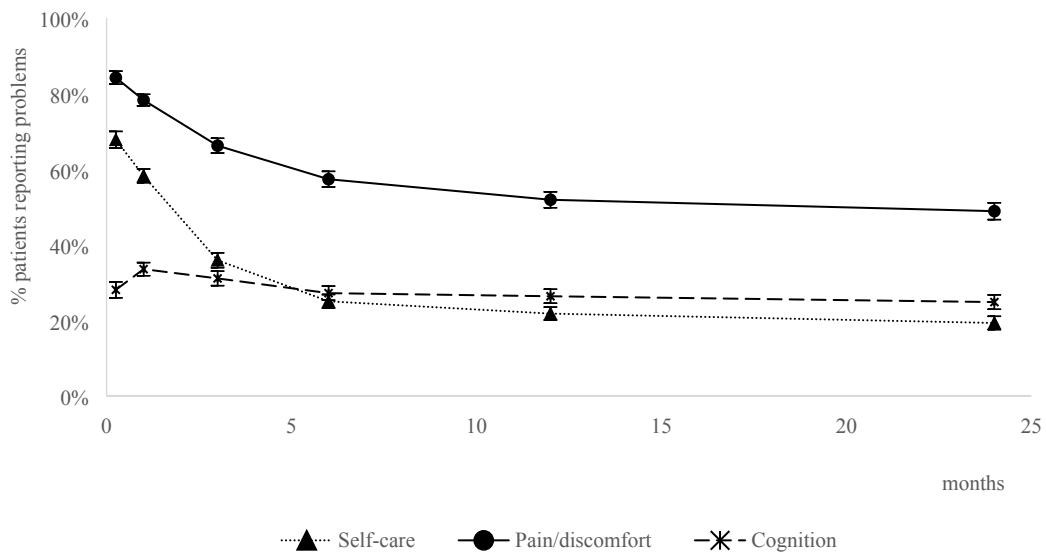
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**Supplemental Table .** Regression coefficients in univariable linear mixed models for the EQ-5D utility and the EQ-VAS and odds ratios in univariable logistic mixed models for the dimensions of HS.

	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
<b>Female sex</b>	-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)
<b>Age (years)</b>								
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)
<b>Nr of comorbidities</b>								
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)
<b>Injury Severity Score<sup>b</sup></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)
<b>Length of stay at hospital (days)</b>								
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)
<b>Functional Capacity Index</b>								
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) <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	
<b>Injury classification<sup>c</sup></b>									
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)	
<b>Admission to Intensive Care Unit</b>	-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)	
<b>Pre-injury work status</b>	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)	
<b>Educational level</b>									
Low <sup>a</sup>	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)	
<b>Frailty</b>	-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)	



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<b>Pre-injury status<sup>d</sup></b>	0.67 (0.64, 0.70)	0.58 (0.55, 0.60)						
No problems <sup>a</sup>			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)

<sup>a</sup>Reference category

<sup>b</sup>Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

<sup>c</sup>Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

<sup>d</sup>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 #
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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
<b>Results</b>			

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
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12
<b>Limitations</b>			
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
<b>Other information</b>			
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.

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

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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;

**Word count:** 3256

## 27 **Abstract**

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

30 **Design:** a prospective longitudinal cohort study.

31 **Setting:** Ten participating hospitals in Brabant, the Netherlands

32 **Participants:** adult injury patients admitted to a hospital between August 2015 and November  
33 2016 were followed: 4883 (50%) patients participated.

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

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

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

49 **Trial registration number:** NCT02508675

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4 50 **Strengths and limitations of the study**  
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6 51 - a strength of the study was the short- and long-term follow-up measurements to obtain  
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8 52 essential recovery data of the injury patients.  
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11 53 - a strength of the study is the high number of participants in this prospective cohort study.  
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13  
14 54 - a limitation of this study is the possibility of selective drop-out, which could have resulted in  
15  
16 55 an overestimation of complaints after injury  
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19 56 - a limitation of this study is the possibility of selection bias, suggesting that more severely  
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21 57 injured patients were more likely to participate.  
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## 59 Introduction

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

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

71 Previous research identified several prognostic factors for poor outcome after injury, e.g. age,  
72 gender, educational level, comorbidity, pre-injury work status<sup>4-16</sup>. Most previous studies on  
73 prognostic factors for health status studied major or severe trauma patients population<sup>4,6-9,12-15</sup>,  
74 traumatic brain injury patients<sup>5,14</sup> or a small follow-up trauma population<sup>11</sup>. In addition, one  
75 study focused on long-term follow-up measurement, two to seven years after injury<sup>8</sup>. Last, pre-  
76 injury health status was not assessed as prognostic factor for health status in previous studies.

77 Although recovery after injury is not only determined by injury severity or injury in specific  
78 body regions, research that takes into account the total clinical trauma population during their  
79 recovery is scarce<sup>16</sup>. In addition, different recovery patterns can be expected in, for example,  
80 brain injury patients and patients suffering from lower/upper extremity injury.

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

## 84 **Methods**

### 86 **Study design and participants**

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

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

## 110 **Patient and public involvement**

111 No patient involved.

## 113 **Outcome**

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

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

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

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

## 133 **Prognostic factors**

134 Prognostic factors can be subdivided into sociodemographic variables and clinical variables  
135 and were chosen based on previous literature and clinical experience<sup>4-16</sup>. *Sociodemographic*  
136 *variables*

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

### 146 *Clinical variables*

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

### 155 *Injury Classification*

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

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3 158 were created: 3 lower extremity injury groups (pelvic injury, hip fracture, and tibia  
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5 159 fracture/complex foot fracture or distal/shaft femur fracture), 2 upper extremity injury groups  
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7 160 (shoulder and upper arm injury, and radius, ulna or hand fracture), 2 traumatic brain injury  
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9 161 groups (AIS-head $\leq$ 2, and AIS-head $\geq$ 3), 1 face injury group, 2 thorax injury groups (thorax  
10  
11 162 injury, and rib fracture), 2 abdomen injury groups (AIS-abdomen $\leq$ 2, and AIS-abdomen $\geq$ 3) and  
12  
13 163 2 spine injury groups (spinal cord injury/brachial plexus lesion, and stable vertebral  
14  
15 164 fracture/disc injury) (**Supplemental File 1**). Patients who suffer multiple injuries could be  
16  
17 165 classified in one or more injury group classifications.  
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## 22 166 **Data analysis**

23  
24 167 Baseline characteristics of participants were compared with characteristics of non-responders,  
25  
26 168 using chi-square for categorical variables or the Mann-Whitney U test for non-normal  
27  
28 169 distributed data Normality was checked visually with a normal Q-Q plot. Descriptive statistics  
29  
30 170 included the median with the interquartile range (IQR), mean with standard deviation (SD) for  
31  
32 171 continuous variables and number with percentage for categorical variables. Missing baseline  
33  
34 172 characteristics (0.9% for the Injury Severity Score and 6.8% for length of stay at hospital) and  
35  
36 173 missing EQ-5D utility scores for participants (ranging from 1.8% at 1 week follow-up to 6.9%  
37  
38 174 at 12 months follow-up) were imputed according to multiple imputation by using the  
39  
40 175 Multivariate Imputations by Chained Equations (MICE) procedure with 15 imputations and 5  
41  
42 176 iterations<sup>23</sup>. The imputation model included baseline characteristics, injury characteristics and  
43  
44 177 summary scores of the follow-up questionnaires to capture associations with missingness as  
45  
46 178 completely as possible. Detailed description of the imputation model and imputed values were  
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48 179 previously published<sup>24</sup>. No large differences were found between imputed data analyses and  
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50 180 complete case analyses.  
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56 181 Multicollinearity was checked based on the Variance Inflation Factor (criterion: VIF > 10).

57 182 Prognostic factors were assessed for poor health status outcome with EQ-5D utility scores and  
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3 183 EQ-VAS as outcome measures. Regression coefficients with corresponding 95% confidence  
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5 184 interval (CI) were reported. The dimensions of the EQ-5D descriptive system were  
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7 185 dichotomized into 0=no problems and 1=some problems/extreme problems. Logistic mixed  
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9 186 models with random intercepts were used to assess prognostic factors for poor outcome for the  
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11 187 six dimensions of the EQ-5D (e.g. mobility, self-care, usual activities, pain/discomfort,  
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13 188 anxiety/depression and cognition). All potential prognostic factors were included in the  
14  
15 189 multivariable regression models to calculate adjusted Odds Ratios and corresponding 95% CI.  
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17 190 Age and length of stay at the hospital were included as categorical variables, because of the  
18  
19 191 non-linear relation between factor and outcome.  
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23 192 Recovery patterns of health status were determined by changing the reference category of the  
24  
25 193 categorical time variable in linear mixed models for health status and logistic mixed models for  
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27 194 the dimensions of health status, adjusted for the prognostic factors. Recovery patterns for the  
28  
29 195 items of the EQ-5D were assessed in detail for injury classifications that showed to be  
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31 196 statistically significant for the dimensions in the total multivariable model.  
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34 197 Analyses were conducted in the statistical programs R version 3.4.0 (R Foundation for  
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36 198 Statistical Computing, Vienna, Austria) and IBM SPSS version 24 (Chicago, USA) and results  
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38 199 were reported according to the TRIPOD guidelines<sup>25</sup>. A p-value of  $\leq 0.05$  was considered  
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40 200 statistically significant.  
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## 202 **Results**

### 204 **Baseline characteristics**

205 A total of 4883 patients (50% of total, N=9774) completed at least one questionnaire of the  
206 BIOS study of whom 48% (N=2,329) was male (**Figure 1, Table 1**). The median age was 68  
207 years with an IQR of 53-80 years. Participants had a median injury severity score of 5 (IQR [4-  
208 9]) and most of the patients were classified as healthy or as patients with mild systemic disease  
209 (N= 3,879, 79%). A total of 358 patients (7%) were admitted to the intensive care unit. The  
210 majority of the participants had low educational level (N=2,670, 55%) and 38% of the  
211 participants (N=1,278) had a job prior to injury. Mean pre-injury EQ-5D utility score (SD) was  
212 0.85 (0.23). A total of 762 participants (16%) of the patients reported to be frail.

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

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

### 221 **EQ-5D over time**

222 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  
223 (0.26) and 0.79 (0.25) at 1 week, 1, 3, 6, 12 and 24 months respectively (**Figure 2A,**  
224 **Supplemental File 2**). The mean EQ-VAS (SD) score was 58.26 (20.45), 63.02 (20.46), 69.48  
225 (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



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

228 The first month, patients reported most problems for the following dimensions of the EQ-5D:  
229 pain/discomfort, usual activities, mobility and self-care (**Figure 2B and 2C, Supplemental**  
230 **File 2**). During the 24 month follow-up, the percentage of patients reporting problems for  
231 pain/discomfort, usual activities and mobility were highest. Two years after injury 49% (95%  
232 CI: 47, 51) of the patients reported problems for pain/discomfort, 43% (95% CI: 41, 45)  
233 reported problems for mobility, 41% (95% CI: 39, 43) reported problems for usual activities,  
234 25% (95% CI: 23, 27) reported for cognition, 20% (95% CI: 18, 22) reported problems for  
235 anxiety/depression and 19% (95% CI: 17, 21) for self-care.

### 237 **Prognostic factors**

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

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



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3 252 activities and pain/discomfort. Traumatic brain injury was a prognostic factor for problems with  
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5 253 cognition.  
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### 10 255 **Recovery patterns for injury classifications**

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12 256 Recovery for dimensions of health status amongst different injury classifications mostly  
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14 257 occurred up until twelve months after injury, except for pain/discomfort (**Table 3**). Patients  
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16 258 with lower extremity injury reported significant less problems at 24 months compared to twelve  
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18 259 months for pain/discomfort.  
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21 260 Patients with spine injury showed improved mobility up to six months for mobility and self-  
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23 261 care, and up to twelve months for pain/discomfort and usual activities. Upper and lower  
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25 262 extremity injury showed the same recovery pattern during the first two years for self-care, with  
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27 263 significant improvement up to twelve months after injury.  
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## 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<sup>6</sup>, our results are in line with another study in the general clinical trauma population<sup>16</sup>.

Previous research showed that age is a prognostic factor for reduced health status<sup>9,16,26</sup>. 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<sup>6</sup>. Again, the different findings can be attributed to the additional strong predictors. This is confirmed by the univariate analyses

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3 291 which demonstrate that increasing age is associated with more problems on all dimensions of  
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5 292 health status, except anxiety/depression and cognition.

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8 293 The addition of the cognitive dimension on the EQ-5D has previously been shown to improve  
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10 294 classification and validity, especially in patients with TBI<sup>27,28</sup>. In line with these findings, this  
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12 295 study showed that patients with TBI were at risk of developing cognitive problems after injury.  
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14 296 It has been suggested previously that most patients with mild TBI patients recover fully within  
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16 297 three to six month, although some patients with mild TBI and patients with more severe TBI  
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18 298 suffer persistent cognitive problems<sup>29-31</sup>. Our study showed that TBI patients reported no further  
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20 299 improvement in health status after six months, in line with the recovery pattern of mild TBI  
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22 300 patients. This is possibly due to the fact that most participants of the BIOS-study suffered mild  
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24 301 TBI (27%) compared to moderate/severe TBI (4%). Further evaluation of these subgroups with  
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26 302 more specific outcome measures are necessary to determine their recovery patterns.  
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35 304 In line with previous studies, this study showed that female sex is a prognostic factor for poor  
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37 305 health status after injury<sup>4,6,13-16,32</sup>. It has been suggested that problems were more often reported  
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39 306 in females, in contrast to males, who dismiss there complaints more often. Another explanation  
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41 307 could be that women experience more psychological impact, resulting in lower health status.  
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43 308 Except for longer length of stay at the hospital, no injury related characteristics were found to  
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45 309 be prognostic factors for anxiety/depression complaints. These results suggest that  
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47 310 psychological problems after injury are mainly based on patient characteristics, which is  
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49 311 confirmed in previous research<sup>33,34</sup>.

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53 313 Although the large prospective longitudinal design of this study is a major strength, there are  
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55 314 also some limitations. First, only 50% of the patients responded to the BIOS-study. We found  
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57 315 differences in injury and patient characteristics between participants and non-responders of the  
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59 316 BIOS-study, e.g. participants were more severely injured compared to the non-responders,

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3 317 indicating selection bias. Next, it is also possible that selective dropout has occurred. We  
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5 318 suspect that patients who were fully recovered were less likely to respond to the follow-up  
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7 319 questions, resulting in an overestimation of complaints after injury. In addition, retrospectively  
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9 320 collected preinjury health status scores are prone to recall bias and response shift<sup>35</sup>. However,  
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11 321 they are considered more appropriate compared to general population norm scores<sup>36</sup>. Last,  
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13 322 frailty was only assessed in patients aged  $\geq 65$  years. This could have introduced bias, because  
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15 323 younger patients may be frail. However, we believe this would only affect a small proportion  
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17 324 in this large cohort.

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19 325 Next, generalisability of the study results can be questioned, because inclusion criteria for  
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21 326 injured patients could be different from other registries. This study included all injury severities  
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23 327 and elderly patients with hip fracture.

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25 328 We acknowledge that long-term non-fatal outcomes should be incorporated in the trauma  
26  
27 329 registry<sup>37</sup>. These outcomes could be used to inform caregivers and patients about their expected  
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29 330 recovery patterns. However, pre-injury health status is essential in predicting short and long-  
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31 331 term outcome after injury and should therefore also be included in the registry. Furthermore,  
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33 332 the dimensions of the EQ-5D and health status showed to have different recovery patterns for  
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35 333 different injury classifications. Non-fatal outcome should not only be focused on health status,  
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37 334 but especially on the different dimensions.

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41 336 Although patients demonstrated recovery after six months for the dimensions  
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43 337 anxiety/depression and cognition, the dimensions mobility, pain/discomfort and usual activities  
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45 338 still improved up to 2 years after injury. These results contribute to the increase in knowledge  
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47 339 of recovery patterns of health status after injury and could be a starting point to develop  
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49 340 prediction models for specific injury classifications and implementation of personalized  
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51 341 medicine.

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## 446 **Author contributions**

447  
448 LM, SP and MJ contributed to conception and design of this study. LM and MJ contributed to data  
449 collection. LM, SP, RH, ES, MJ contributed to analyses and interpretation. LM, SP, RH, ES and MJ  
450 contributed to preparation of the manuscript. The final version of the article was approved by all the  
451 authors.

## 453 **Data sharing**

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

## 459 **Figure legends**

460 **Figure 1.** Flow diagram of study participation

461 Abbreviations: ACT, Usual activities; ANX, Anxiety/depression; COG, Cognition; EQ-5D, EuroQol-  
462 5-Dimension; EQ-VAS, EuroQol Visual Analogue Scale; MOB, Mobility; N, Number; PAIN,  
463 Pain/discomfort; SELF, Self-care;

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

467

**Table 1.** Patient characteristics tables of participants and non-responders of the BIOS-study<sup>a</sup>patients who completed at least one follow-up questionnaire. Missing variables were imputed.

	Participants <sup>a</sup>	Non-responders	p-value
<b>N (%)</b>	4883	4891	
<b>Male (%)</b>	2329 (48)	2407 (49)	0.13
<b>Age (median, IQR)</b>	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)	
<b>ASA classification (N, %)</b>			
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)	
<b>Injury Severity Score (median, IQR)</b>	5 (4-9)	5 (2-9)	0.00
<b>Length of stay at hospital (median, IQR)</b>	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)	
<b>Functional capacity index (N, %)</b>			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)	
<b>Injury classification (N, %)</b>			
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)	
<b>Admission to intensive care unit (N, %)</b>	358 (7)	292 (6)	0.00
<b>Educational level (N, %)*</b>			
Low	2670 (55)	-	
Middle	1305 (27)	-	
High	908 (19)	-	
<b>Pre-injury work status*</b>	1278 (38)	-	
<b>Pre-injury frailty*</b>	762 (16)	-	
<b>Pre-injury health status*</b>			
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
<b>Female sex</b>	-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)*
<b>Age (years)</b>								
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)*
<b>Nr of comorbidities</b>								
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)*
<b>Injury Severity Score<sup>b</sup></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)*
<b>Length of stay at hospital (days)</b>								
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)*
<b>Functional Capacity Index</b>								
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) <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<b>Injury classification<sup>c</sup></b>								
<b>Lower extremity injury</b>								
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)
<b>Upper extremity injury</b>								
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)
<b>Traumatic brain injury</b>								
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)*
<b>Facial injury</b>	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)
<b>Thoracic injury</b>	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)
<b>Rib fracture</b>	-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)
<b>Abdominal injury</b>	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)
<b>Spine injury</b>								
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)
<b>Admission to Intensive Care Unit</b>	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)*
<b>Pre-injury work status</b>	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)
<b>Educational level</b>								
Low <sup>a</sup>	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)
<b>Frailty</b>	-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)*
<b>Pre-injury status<sup>d</sup></b>	0.49 (0.45, 0.53)*	0.47 (0.44, 0.50)*						
No problems <sup>a</sup>			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

<sup>a</sup>Reference category

<sup>b</sup>Regression coefficients and odds ratios (95%) represents a 4 unit increase on the Injury Severity Score.

<sup>c</sup>Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

<sup>d</sup>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) <sup>a</sup>				
	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
<b>Mobility</b>					
Lower extremity <sup>1</sup>	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 <sup>2</sup>	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)
<b>Self-care</b>					
Lower extremity <sup>1</sup>	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 <sup>3</sup>	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 <sup>2</sup>	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)
<b>Usual activities</b>					
Upper extremity <sup>3</sup>	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 <sup>2</sup>	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)
<b>Pain/discomfort</b>					
Lower extremity <sup>1</sup>	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 <sup>3</sup>	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 <sup>2</sup>	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)
<b>Anxiety/depression</b>					
Spine <sup>2</sup>	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)
<b>Cognition</b>					
Traumatic Brain Injury <sup>4</sup>	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

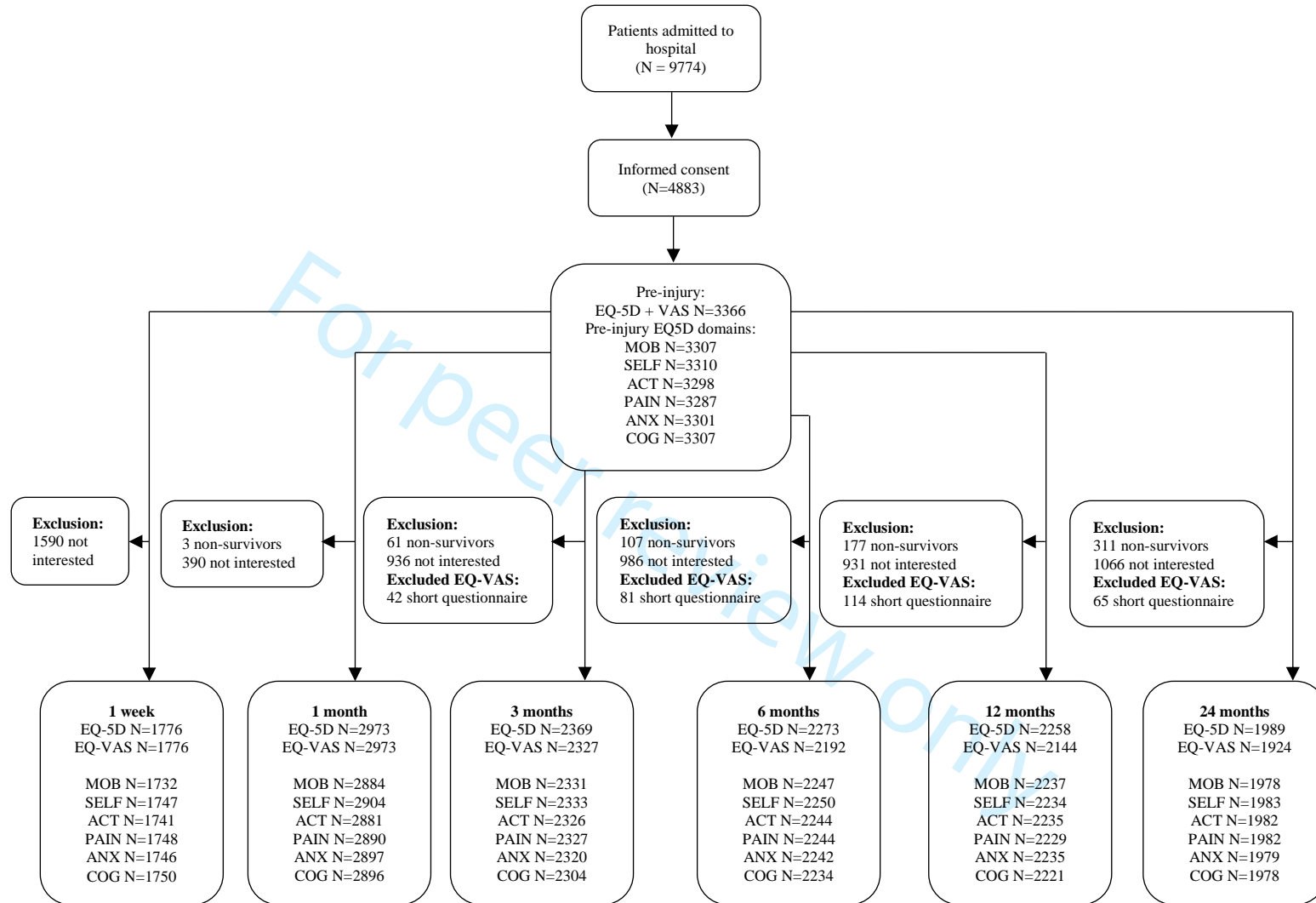
<sup>a</sup>Odds Ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level,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

<sup>1</sup>Patients with pelvic injury, hip fracture or tibia, complex foot or femur fracture

<sup>2</sup>Patients with spinal cord injury or stable vertebral fracture or disc injury

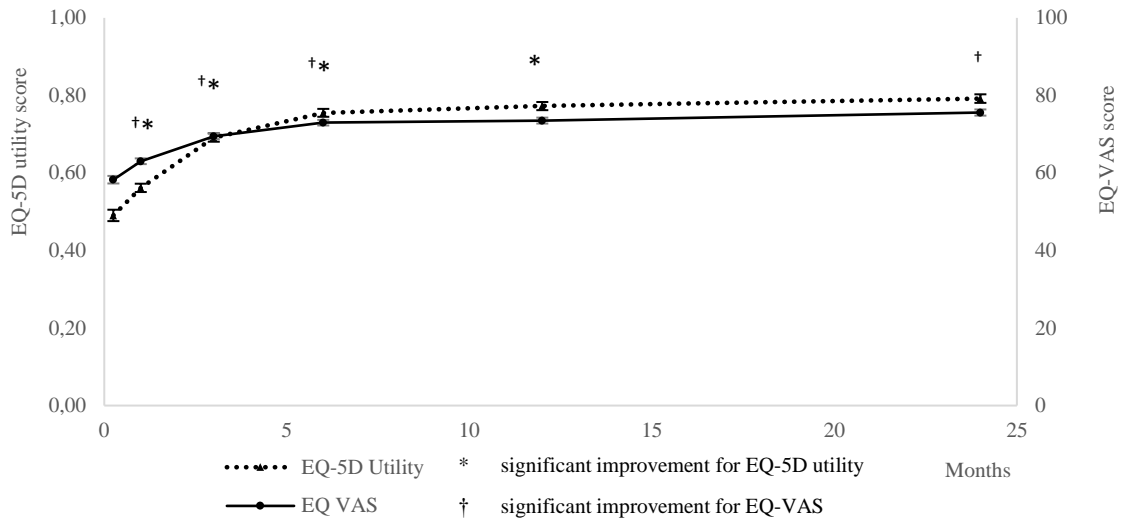
<sup>3</sup>Patients with shoulder and upper arm injury or radius, ulna or hand fracture

<sup>4</sup>Patients with Traumatic brain injury, independent of injury severity

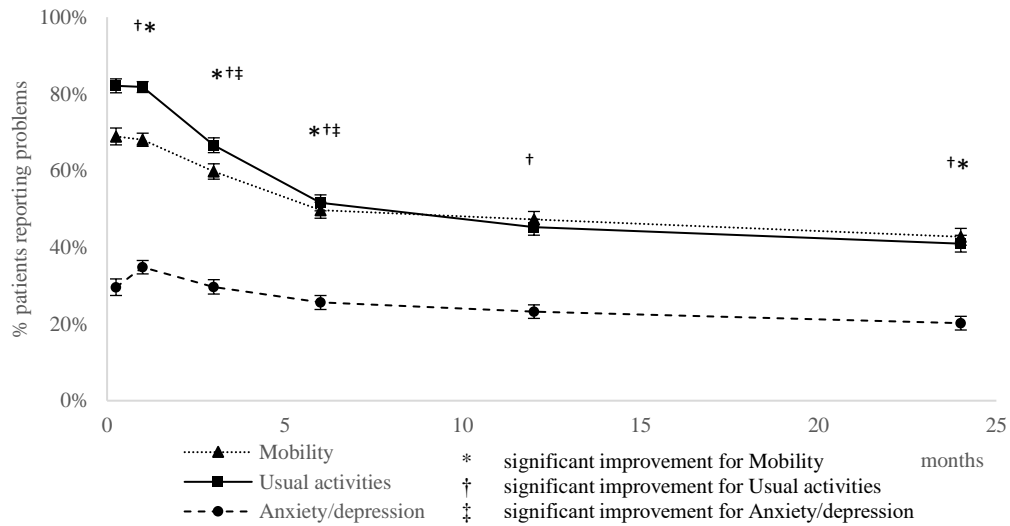




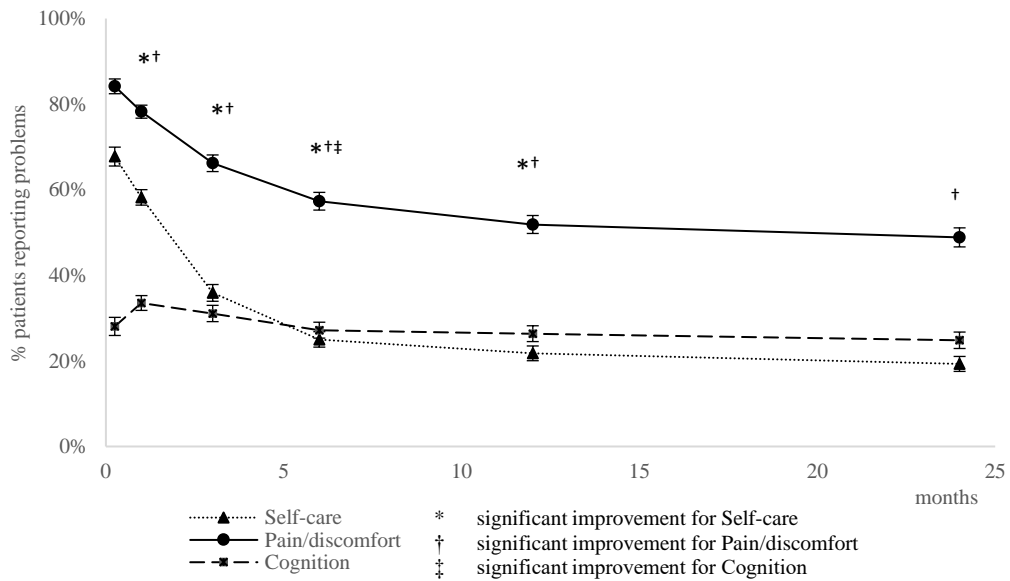
A.



B.



C.



**S1 Table.** Injury group classification of the most common types of injury, based on the Abbreviated Injury Score<sup>22</sup>.

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 haemorrhage, 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).

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**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
<b>Linear regression coefficients (95% Confidence Interval)<sup>a</sup></b>					
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)*
<b>Odds Ratios (95% Confidence Interval)<sup>a</sup></b>					
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

<sup>a</sup>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
<b>Female sex</b>	-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)*
<b>Age (years)</b>								
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)*
<b>Nr of comorbidities</b>								
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)*
<b>Injury Severity Score<sup>b</sup></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)*
<b>Length of stay at hospital (days)</b>								
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)*
<b>Functional Capacity Index</b>								
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) <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<b>Injury classification<sup>c</sup></b>								
<b>Lower extremity injury</b>								
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)*

1									
2									
3	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)*
4	<b>Upper extremity injury</b>								
5	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)
6	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)*
7	<b>Traumatic brain injury</b>								
8	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)*
9	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)*
10	<b>Facial injury</b>	-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)
11	<b>Thoracic injury</b>	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)
12	<b>Rib fracture</b>	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)
13	<b>Abdominal injury</b>	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)
14	<b>Spine injury</b>								
15	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)
16	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)
17	<b>Admission to Intensive Care Unit</b>	-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)*
18	<b>Pre-injury work status</b>	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)*
19	<b>Educational level</b>								
20	Low <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
21	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)*
22	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)*
23	<b>Frailty</b>	-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)*
24	<b>Pre-injury status<sup>d</sup></b>	0.67 (0.64, 0.70)*	0.58 (0.55, 0.60)*						
25	No problems <sup>a</sup>			Ref	Ref	Ref	Ref	Ref	Ref
26	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

<sup>a</sup>Reference category<sup>b</sup>Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.<sup>c</sup>Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

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3 <sup>d</sup>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  
4 (95% CI) for pre-injury moderate and severe problems on the dimensions of the EQ-5D questionnaire (pre-injury mobility, Self-care, Pain/discomfort,  
5 Anxiety/depression and cognition respectively for the columns).  
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7 *Abbreviations: AIS, Abbreviated Injury scale; ASA, American Society of Anaesthesiologists Classification; CI, Confidence Interval; Ref, Reference Category.*  
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**STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies***

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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
<b>Results</b>			

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
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12
<b>Limitations</b>			
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
<b>Other information</b>			
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](http://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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# 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;

**Word count:** 3336

## 27 **Abstract**

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

30 **Design:** a prospective longitudinal cohort study.

31 **Setting:** Ten participating hospitals in Brabant, the Netherlands

32 **Participants:** adult injured patients admitted to a hospital between August 2015 and November  
33 2016 were followed: 4883 (50%) patients participated.

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

39 **Results.** Health status increased mainly during the first six months after injury with a mean EQ-  
40 5D utility score at 1 week of 0.49 and 0.79 at 24 months. The dimensions mobility,  
41 pain/discomfort and usual activities improved up to 2 years after injury. Lower pre-injury health  
42 status, frailty and longer length of stay at the hospital were important prognostic factors for  
43 poor recovery. Spine injury, lower and upper extremity injury showed to be prognostic factors  
44 for problems after injury. Traumatic brain injury was a prognostic factor for cognitive problems.

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

48 **Trial registration number:** NCT02508675

## 49 **Strengths and limitations of the study**

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

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

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

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

57

## 58 Introduction

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

70 Previous research identified several prognostic factors for poor outcome after injury, e.g. age,  
71 gender, educational level, comorbidity, pre-injury work status<sup>4-16</sup>. Most previous studies on  
72 prognostic factors for health status evaluated major or severe trauma patients population<sup>4,6-9,12-</sup>  
73 <sup>15</sup>, traumatic brain injury patients<sup>5,14</sup> or a small follow-up trauma population<sup>11</sup>. In addition, one  
74 study focused on long-term follow-up measurement, two to seven years after injury<sup>8</sup>. Last, pre-  
75 injury health status was not assessed as prognostic factor for health status in previous studies.

76 Although recovery after injury is not only determined by injury severity or injury in specific  
77 body regions, research that takes into account the total clinical trauma population during their  
78 recovery is scarce<sup>16</sup>. In addition, different recovery patterns can be expected in, for example,  
79 brain injury patients and patients suffering from lower/upper extremity injury.

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

## 83 **Methods**

### 85 **Study design and participants**

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

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

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2  
3 109 participating patients. The study was approved by the Medical Ethics Committee Brabant  
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5 110 (project number BIOS-study: NL50258.028.14 and short questionnaire: NW2016-09).  
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## 8 111 **Patient and public involvement**

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10 112 No patient involved.  
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## 14 114 **Outcome**

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17 115 Health status was measured with the EuroQol-5D-3L (EQ-5D)<sup>19</sup>. This questionnaire consists of  
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19 116 the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D  
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21 117 descriptive system comprised the following five dimensions: mobility, self-care, usual  
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23 118 activities, pain/discomfort and anxiety/depression. Each dimension could be answered in three  
24  
25 119 levels: no problems, some problems and severe/extreme problems.  
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28  
29 120 A summary score of the EQ-5D (i.e. EQ-5D utility score) can be calculated by using the Dutch  
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31 121 tariffs<sup>20</sup>. The EQ-5D utility score ranged from 0 (death) to 1 (perfect health). The EQ-VAS is a  
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33 122 vertical visual analogue scale with 0 indicating the worst imaginable health state and 100  
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35 123 indicating the best imaginable health state.  
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38 124 Cognition was added as an additional dimension to the EQ-5D questionnaire. Respondents were  
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40 125 asked to describe their or, in case of proxy, the patients' state of health, concerning cognition  
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42 126 (e.g. memory, concentration). Similar to the other dimensions, answer options were based on  
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44 127 three levels: no problems, some problems and severe problems.  
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47 128 Health status was measured at each time point during follow-up in both patient and proxy  
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49 129 questionnaires. The EQ-5D (including the cognition dimension) and EQ-VAS were also  
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51 130 measured pre-injury, by asking participants at one week or one month and proxy informants at  
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53 131 one month for the patients' health status before sustaining the injury. The EQ-5D with cognition  
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55 132 dimension and EQ-VAS were both included in the BIOS-study. The short questionnaire only  
56  
57 133 included the EQ-5D and cognition dimension.  
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## 134 **Prognostic factors**

135 Prognostic factors can be subdivided into sociodemographic variables and clinical variables  
136 and were chosen based on previous literature and clinical experience<sup>4-16</sup>.

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### 138 *Sociodemographic variables*

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

### 148 *Clinical variables*

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

### 157 *Injury Classification*

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3 158 The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008)<sup>22</sup> were used to create injury  
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5 159 group classifications representing the most common types of injuries. In total, 14 injury groups  
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7 160 were created: 3 lower extremity injury groups (pelvic injury, hip fracture, and tibia  
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9 161 fracture/complex foot fracture or distal/shaft femur fracture), 2 upper extremity injury groups  
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11 162 (shoulder and upper arm injury, and radius, ulna or hand fracture), 2 traumatic brain injury  
12  
13 163 groups (AIS-head $\leq$ 2, and AIS-head $\geq$ 3), 1 face injury group, 2 thorax injury groups (thorax  
14  
15 164 injury, and rib fracture), 2 abdomen injury groups (AIS-abdomen $\leq$ 2, and AIS-abdomen $\geq$ 3) and  
16  
17 165 2 spine injury groups (spinal cord injury/brachial plexus lesion, and stable vertebral  
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19 166 fracture/disc injury) (**Supplemental File 1**). Patients who suffer multiple injuries could be  
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23 167 classified in one or more injury group classifications.

## 27 168 **Data analysis**

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29 169 Baseline characteristics of participants were compared with characteristics of non-responders,  
30  
31 170 using chi-square for categorical variables or the Mann-Whitney U test for non-normal  
32  
33 171 distributed data. Normality was checked visually with a normal Q-Q plot. Descriptive statistics  
34  
35 172 included the median with the interquartile range (IQR), mean with standard deviation (SD) for  
36  
37 173 continuous variables and number with percentage for categorical variables. Missing baseline  
38  
39 174 characteristics (0.9% for the Injury Severity Score and 6.8% for length of stay at hospital) and  
40  
41 175 missing EQ-5D utility scores for participants (ranging from 1.8% at 1 week follow-up to 6.9%  
42  
43 176 at 12 months follow-up) were imputed according to multiple imputation by using the  
44  
45 177 Multivariate Imputations by Chained Equations (MICE) procedure with 15 imputations and 5  
46  
47 178 iterations<sup>23</sup>. The imputation model included baseline characteristics, injury characteristics and  
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49 179 summary scores of the follow-up questionnaires to capture associations with missingness as  
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51 180 completely as possible. Detailed description of the imputation model and imputed values were  
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53 181 previously published<sup>24</sup>. No large differences were found between imputed data analyses and  
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55 182 complete case analyses.  
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3 183 Multicollinearity was checked based on the Variance Inflation Factor (criterion:  $VIF > 10$ ).  
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5 184 Prognostic factors were assessed for poor health status outcome with EQ-5D utility scores and  
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7 185 EQ-VAS as outcome measures. Regression coefficients with corresponding 95% confidence  
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9 186 interval (CI) were reported. The dimensions of the EQ-5D descriptive system were  
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11 187 dichotomized into 0=no problems and 1=some problems/extreme problems. Logistic mixed  
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13 188 models with random intercepts were used to assess prognostic factors for poor outcome for the  
14  
15 189 six dimensions of the EQ-5D (e.g. mobility, self-care, usual activities, pain/discomfort,  
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17 190 anxiety/depression and cognition). All potential prognostic factors were included in the  
18  
19 191 multivariable regression models to calculate adjusted Odds Ratios and corresponding 95% CI.  
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21 192 Age and length of stay at the hospital were included as categorical variables, because of the  
22  
23 193 non-linear relation between factor and outcome.  
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25 194 Recovery patterns of health status were determined by changing the reference category of the  
26  
27 195 categorical time variable in linear mixed models for health status and logistic mixed models for  
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29 196 the dimensions of health status, adjusted for the prognostic factors. Recovery patterns for the  
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31 197 items of the EQ-5D were assessed in detail for injury classifications that showed to be  
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33 198 statistically significant for the dimensions in the total multivariable model.  
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35 199 Analyses were conducted in the statistical programs R version 3.4.0 (R Foundation for  
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37 200 Statistical Computing, Vienna, Austria) and IBM SPSS version 24 (Chicago, USA) and results  
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39 201 were reported according to the TRIPOD guidelines<sup>25</sup>. A p-value of  $\leq 0.05$  was considered  
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41 202 statistically significant.  
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## 204 **Results**

### 206 **Baseline characteristics**

207 A total of 4883 patients (50% of total, N=9774) completed at least one questionnaire of the  
208 BIOS study of whom 48% (N=2,329) was male (**Figure 1, Table 1**). The median age was 68  
209 years with an IQR of 53-80 years. Participants had a median injury severity score of 5 (IQR [4-  
210 9]) and most of the patients were classified as healthy or as patients with mild systemic disease  
211 (N= 3,879, 79%). A total of 358 patients (7%) were admitted to the intensive care unit. The  
212 majority of the participants had low educational level (N=2,670, 55%) and 38% of the  
213 participants (N=1,278) had a job prior to injury. Mean pre-injury EQ-5D utility score (SD) was  
214 0.85 (0.23). A total of 762 participants (27% of participants  $\geq 65$  years) reported to be frail.  
215 Compared to the non-responders, participants were more severely injured, were more often  
216 admitted to the intensive care unit (7% vs 6%), had lower functional capacity index values, and  
217 were more often healthy (measured with the ASA classification).

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

### 223 **EQ-5D over time**

224 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  
225 (0.26) and 0.79 (0.25) at 1 week, 1, 3, 6, 12 and 24 months respectively (**Figure 2A,**  
226 **Supplemental File 2**). The mean EQ-VAS (SD) score was 58.26 (20.45), 63.02 (20.46), 69.48  
227 (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

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

230 The first month, patients reported most problems for the following dimensions of the EQ-5D:  
231 pain/discomfort, usual activities, mobility and self-care (**Figure 2B and 2C, Supplemental**  
232 **File 2**). During the 24 month follow-up, the percentage of patients reporting problems for  
233 pain/discomfort, usual activities and mobility were highest. Two years after injury 49% (95%  
234 CI: 47, 51) of the patients reported problems for pain/discomfort, 43% (95% CI: 41, 45)  
235 reported problems for mobility, 41% (95% CI: 39, 43) reported problems for usual activities,  
236 25% (95% CI: 23, 27) reported for cognition, 20% (95% CI: 18, 22) reported problems for  
237 anxiety/depression and 19% (95% CI: 17, 21) for self-care.

### 239 **Prognostic factors**

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

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

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3 254 activities and pain/discomfort. Traumatic brain injury was a prognostic factor for problems with  
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5 255 cognition.  
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10 257 **Recovery patterns for injury classifications**  
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13 258 Recovery for dimensions of health status amongst different injury classifications mostly  
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15 259 occurred up until twelve months after injury, except for pain/discomfort (**Table 3**). Patients  
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17 260 with lower extremity injury reported significant less problems at 24 months compared to twelve  
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20 261 months for pain/discomfort.  
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22 262 Patients with spine injury showed improved mobility up to six months for mobility and self-  
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24 263 care, and up to twelve months for pain/discomfort and usual activities. Upper and lower  
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27 264 extremity injury showed the same recovery pattern during the first two years for self-care, with  
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29 265 significant improvement up to twelve months after injury.  
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## 267 Discussion

268  
269 In this multicentre prospective cohort study, we found that patients reported problems up until  
270 two years after injury. Health status was especially low during the first six months after injury,  
271 in which patients often reported problems in most of the dimensions of health status. Lower  
272 pre-injury health status, frailty and longer length of stay at hospital were prognostic factors for  
273 both decreased health status during the first two years after injury. For the EQ-5D dimensions  
274 mobility, usual activities and pain/discomfort less problems were reported at two years  
275 compared to one year after injury, as for the other dimensions we found no decrease in reported  
276 problems after one year.

277  
278 The prevalence of problems in the dimensions of health status decreased during two years  
279 follow up. Although a recent study in severely injured patients demonstrated higher prevalence  
280 of problems in the health status dimensions<sup>6</sup>, our results are in line with another study in the  
281 general clinical trauma population<sup>16</sup>.

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

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3 293 which demonstrate that increasing age is associated with more problems on all dimensions of  
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5 294 health status, except anxiety/depression and cognition.

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8 295 The addition of the cognitive dimension on the EQ-5D has previously been shown to improve  
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10 296 classification and validity, especially in patients with TBI<sup>27,28</sup>. In line with these findings, this  
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12 297 study showed that patients with TBI were at risk of developing cognitive problems after injury.  
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14 298 It has been suggested previously that most patients with mild TBI patients recover fully within  
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16 299 three to six month, although some patients with mild TBI and patients with more severe TBI  
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18 300 suffer persistent cognitive problems<sup>29-31</sup>. Our study showed that TBI patients reported no further  
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20 301 improvement in health status after six months, in line with the recovery pattern of mild TBI  
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22 302 patients. This is possibly due to the fact that most participants of the BIOS-study suffered mild  
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24 303 TBI (27%) compared to moderate/severe TBI (4%). Further evaluation of these subgroups with  
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26 304 more specific outcome measures are necessary to determine their recovery patterns.  
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33 306 In line with previous studies, this study showed that female sex is a prognostic factor for poor  
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35 307 health status after injury<sup>4,6,13-16,32</sup>. It has been suggested that problems were more often reported  
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37 308 in females, in contrast to males, who dismiss there complaints more often. Another explanation  
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39 309 could be that women experience more psychological impact, resulting in lower health status.

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41 310 Except for longer length of stay at the hospital, no injury related characteristics were found to  
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43 311 be prognostic factors for anxiety/depression complaints. These results suggest that  
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45 312 psychological problems after injury are mainly based on patient characteristics, which is  
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47 313 confirmed in previous research<sup>33,34</sup>.

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52 315 Although the large prospective longitudinal design of this study is a major strength, there are  
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54 316 also some limitations. First, only 50% of the patients responded to the BIOS-study. We found  
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56 317 differences in injury and patient characteristics between participants and non-responders of the  
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58 318 BIOS-study, e.g. participants were more severely injured compared to the non-responders,  
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3 319 indicating selection bias. Next, it is also possible that selective dropout has occurred. We  
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5 320 suspect that patients who were fully recovered were less likely to respond to the follow-up  
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7 321 questions, resulting in an overestimation of complaints after injury. In addition, retrospectively  
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9 322 collected preinjury health status scores are prone to recall bias and response shift<sup>35</sup>. However,  
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11 323 they are considered more appropriate compared to general population norm scores<sup>36</sup>. Last,  
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13 324 frailty was only assessed in patients aged  $\geq 65$  years. This could have introduced bias, because  
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15 325 younger patients may be frail. However, we believe this would only affect a small proportion  
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17 326 in this large cohort.

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21 327 Next, generalisability of the study results can be questioned, because inclusion criteria for  
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23 328 injured patients could be different from other registries. This study included all injury severities  
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25 329 and elderly patients with hip fracture.

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28 330 We acknowledge that long-term non-fatal outcomes should be incorporated in the trauma  
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30 331 registry<sup>37</sup>. These outcomes could be used to inform caregivers and patients about their expected  
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32 332 recovery patterns. However, pre-injury health status is essential in predicting short and long-  
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34 333 term outcome after injury and should therefore also be included in the registry. Furthermore,  
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36 334 the dimensions of the EQ-5D and health status showed to have different recovery patterns for  
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38 335 different injury classifications. Non-fatal outcome should not only be focused on health status,  
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40 336 but especially on the different dimensions.

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44 337 Knowledge about individual recovery patterns can induce specific interventions to increase  
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46 338 health status and improve recovery after injury. For example, previous research demonstrated  
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48 339 a need to identify patients who may be experiencing mental health issues for timely referral and  
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50 340 appropriate care after injury<sup>38</sup>. In addition, the prediction models can contribute to realistic  
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52 341 expectations of their recovery for injury patients<sup>38,39</sup>.

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56 342 Although the responding patients demonstrated recovery after six months for the dimensions  
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58 343 anxiety/depression and cognition, the dimensions mobility, pain/discomfort and usual activities  
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344 still improved up to 2 years after injury. These results contribute to the increase in knowledge  
345 of recovery patterns of health status after injury and could be a starting point to develop  
346 prediction models for specific injury classifications and implementation of personalized  
347 medicine.  
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For peer review only

## 349 **Author contributions**

350

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

## 355 **Conflict of interest statement**

356 The authors declare no conflict of interest.

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## 360 **Data sharing**

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

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9 **471 Figure legends**

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11 **472 Figure 1.** Flow diagram of study participation

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13 **473** Abbreviations: ACT, Usual activities; ANX, Anxiety/depression; COG, Cognition; EQ-5D, EuroQol-  
14 **474** 5-Dimension; EQ-VAS, EuroQol Visual Analogue Scale; MOB, Mobility; N, Number; PAIN,  
15 **475** Pain/discomfort; SELF, Self-care;

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19 **476** Non-survivors are participants that died during the follow-up period.

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21 **477 Figure 2.** (A) Health status scores (95% CI) and (B and C) % patients reporting problems (95% CI) on  
22 **478** the dimensions of the EQ-5D-3L, including whether there was a significant change in health status  
23 **479** scores compared to the previous time-point.

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

	Participants <sup>a</sup>	Non-responders	p-value
<b>N (%)</b>	4883	4891	
<b>Male (%)</b>	2329 (48)	2407 (49)	0.13
<b>Age (median, IQR)</b>	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)	
<b>ASA classification (N, %)</b>			
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)	
<b>Injury Severity Score (median, IQR)</b>	5 (4-9)	5 (2-9)	0.00
<b>Length of stay at hospital (median, IQR)</b>	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)	
<b>Functional capacity index (N, %)</b>			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)	
<b>Injury classification (N, %)</b>			
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)	
<b>Admission to intensive care unit (N, %)</b>	358 (7)	292 (6)	0.00
<b>Educational level (N, %)*</b>			
Low	2670 (55)	-	
Middle	1305 (27)	-	
High	908 (19)	-	
<b>Pre-injury work status*</b>	1278 (38)	-	
<b>Pre-injury frailty*</b>	762 (16)	-	
<b>Pre-injury health status*</b>			
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)	-	

<sup>a</sup>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
<b>Female sex</b>	-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)*
<b>Age (years)</b>								
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)*
<b>Nr of comorbidities</b>								
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)*
<b>Injury Severity Score<sup>b</sup></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)*
<b>Length of stay at hospital (days)</b>								
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)*
<b>Functional Capacity Index</b>								
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) <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<b>Injury classification<sup>c</sup></b>								
<b>Lower extremity injury</b>								
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)
<b>Upper extremity injury</b>								
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)
<b>Traumatic brain injury</b>								
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)*
<b>Facial injury</b>	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)
<b>Thoracic injury</b>	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)

	<b>Rib fracture</b>	-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)
	<b>Abdominal injury</b>	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)
	<b>Spine injury</b>								
	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)
	<b>Admission to Intensive Care Unit</b>	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)*
	<b>Pre-injury work status</b>	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)
	<b>Educational level</b>								
	Low <sup>a</sup>	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)
	<b>Frailty</b>	-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)*
	<b>Pre-injury status<sup>d</sup></b>	0.49 (0.45, 0.53)*	0.47 (0.44, 0.50)*						
	No problems <sup>a</sup>			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 ≤ 0.05

<sup>a</sup>Reference category

<sup>b</sup>Regression coefficients and odds ratios (95%) represents a 4 unit increase on the Injury Severity Score.

<sup>c</sup>Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

<sup>d</sup>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) <sup>a</sup>				
	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
<b>Mobility</b>					
Lower extremity <sup>1</sup>	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 <sup>2</sup>	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)
<b>Self-care</b>					
Lower extremity <sup>1</sup>	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 <sup>3</sup>	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 <sup>2</sup>	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)
<b>Usual activities</b>					
Upper extremity <sup>3</sup>	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 <sup>2</sup>	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)
<b>Pain/discomfort</b>					
Lower extremity <sup>1</sup>	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 <sup>3</sup>	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 <sup>2</sup>	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)
<b>Anxiety/depression</b>					
Spine <sup>2</sup>	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)
<b>Cognition</b>					
Traumatic Brain Injury <sup>4</sup>	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

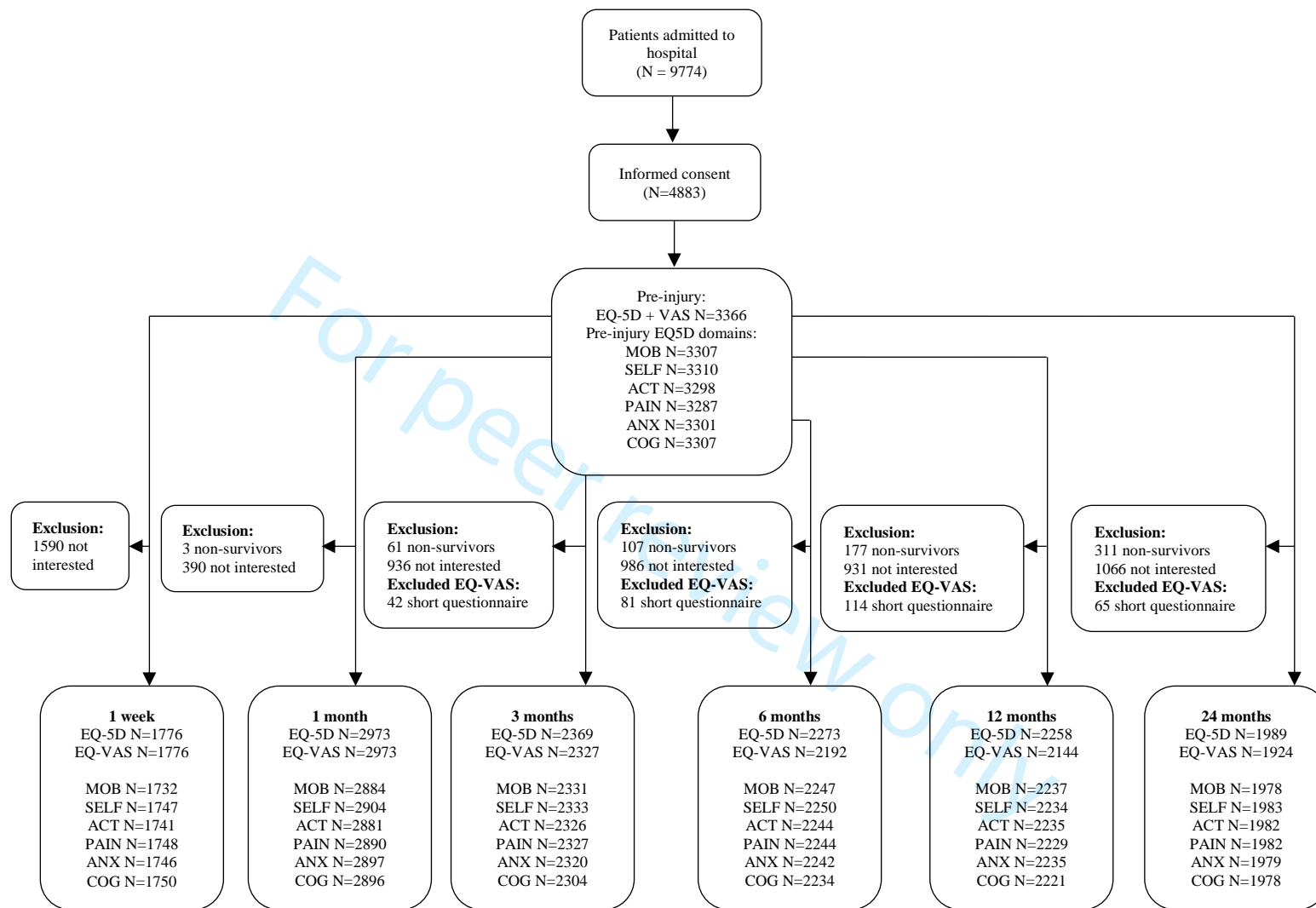
<sup>a</sup>Odds Ratios in longitudinal analyses adjusted for sex, age, American Society of Anaesthesiologists Classification, Injury Severity Score, length of stay at hospital, Functional Capacity Index, Injury classifications, admission to intensive care unit, pre-injury work status, educational level,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

<sup>1</sup>Patients with pelvic injury, hip fracture or tibia, complex foot or femur fracture

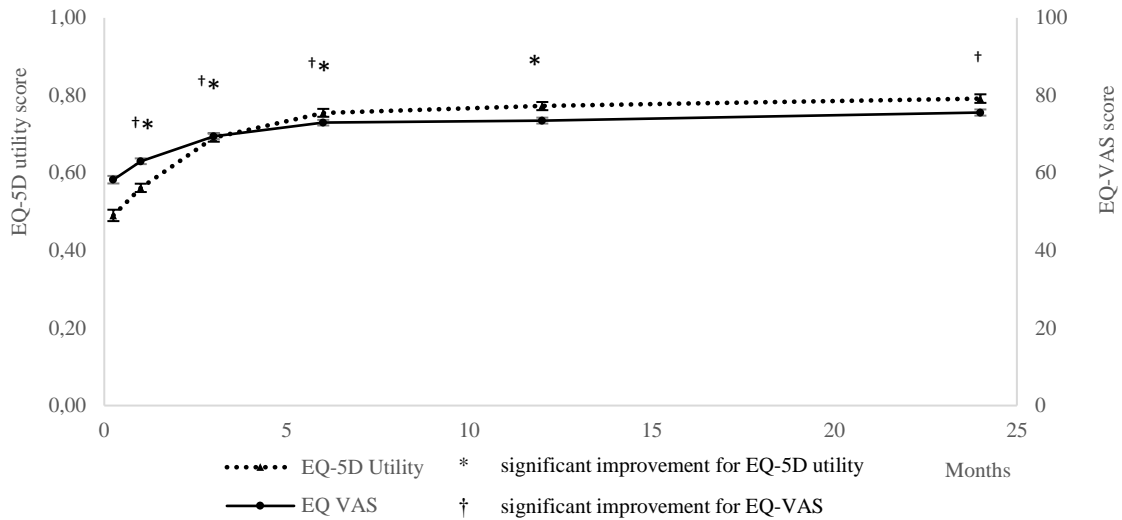
<sup>2</sup>Patients with spinal cord injury or stable vertebral fracture or disc injury

<sup>3</sup>Patients with shoulder and upper arm injury or radius, ulna or hand fracture

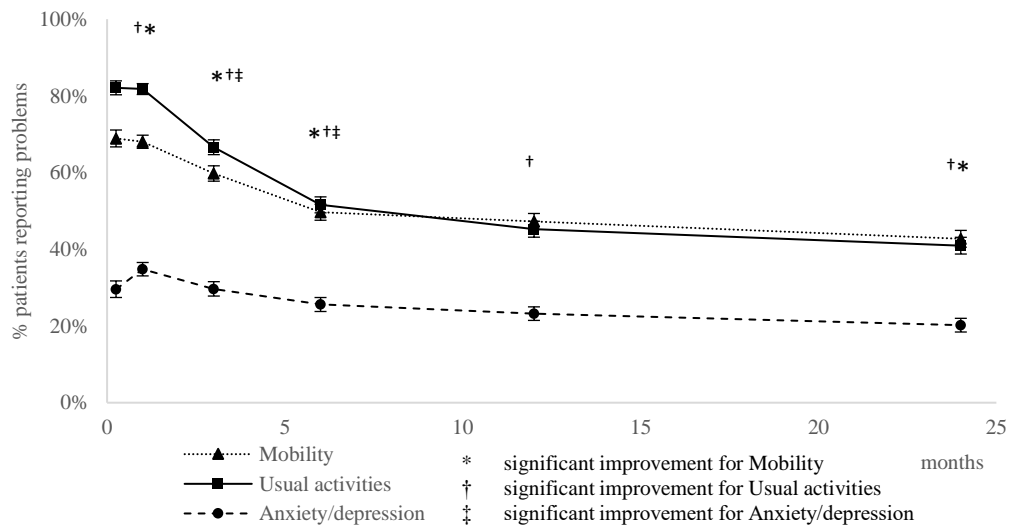
<sup>4</sup>Patients with Traumatic brain injury, independent of injury severity



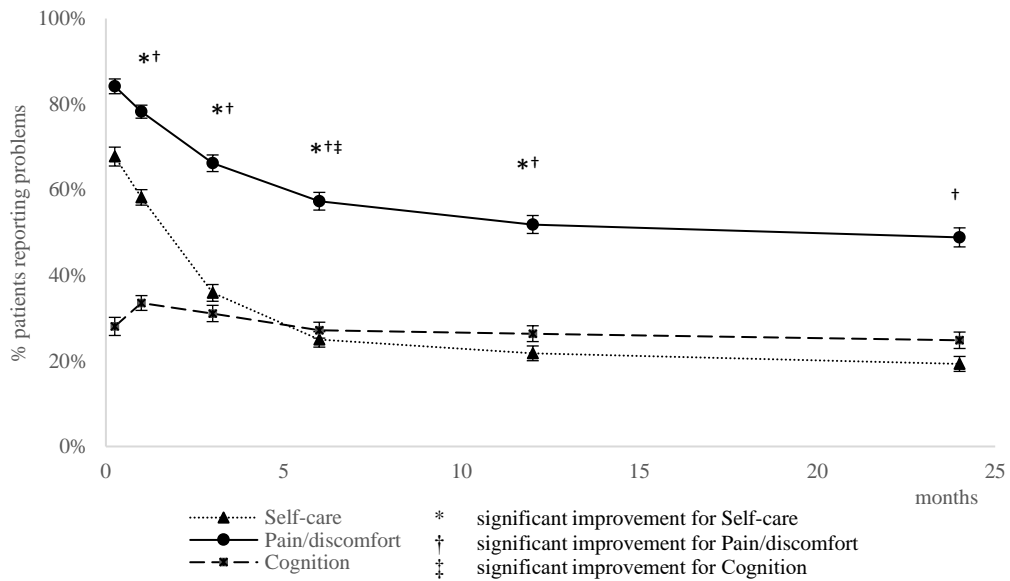
A.



B.



C.



**S1 Table.** Injury group classification of the most common types of injury, based on the Abbreviated Injury Score<sup>22</sup>.

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 haemorrhage, 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
<b>Linear regression coefficients (95% Confidence Interval)<sup>a</sup></b>					
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)*
<b>Odds Ratios (95% Confidence Interval)<sup>a</sup></b>					
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

<sup>a</sup>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
<b>Female sex</b>	-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)*
<b>Age (years)</b>								
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)*
<b>Nr of comorbidities</b>								
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)*
<b>Injury Severity Score<sup>b</sup></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)*
<b>Length of stay at hospital (days)</b>								
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)*
<b>Functional Capacity Index</b>								
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) <sup>a</sup>	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<b>Injury classification<sup>c</sup></b>								
<b>Lower extremity injury</b>								
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)*
	<b>Upper extremity injury</b>								
	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)*
	<b>Traumatic brain injury</b>								
	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)*
	<b>Facial injury</b>	-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)
	<b>Thoracic injury</b>	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)
	<b>Rib fracture</b>	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)
	<b>Abdominal injury</b>	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)
	<b>Spine injury</b>								
	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)
	<b>Admission to Intensive Care Unit</b>	-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)*
	<b>Pre-injury work status</b>	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)*
	<b>Educational level</b>								
	Low <sup>a</sup>	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)*
	<b>Frailty</b>	-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)*
	<b>Pre-injury status<sup>d</sup></b>	0.67 (0.64, 0.70)*	0.58 (0.55, 0.60)*						
	No problems <sup>a</sup>			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

<sup>a</sup>Reference category

<sup>b</sup>Regression coefficients and odds ratios (95%) represents a 4 unit increase on the ISS scale.

<sup>c</sup>Regression coefficients and odds ratios (95% CI) for patients suffering the injury compared to patients not having the injury.

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<sup>d</sup>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.*

For peer review only

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

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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
<b>Results</b>			

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
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	12
<b>Limitations</b>			
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
<b>Other information</b>			
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](http://www.strobe-statement.org).