Health status and psychological outcomes after trauma; a prospective multicenter cohort study

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Full Title: Health status and psychological outcomes after trauma; a prospective multicenter cohort study

Short Title: Health status and psychological outcomes after trauma

Corresponding Author: Nena Kruithof
Elisabeth-TweeSteden Ziekenhuis
Tilburg, NETHERLANDS

Keywords: injury; Trauma; hospitalization; longitudinal cohort study; health status; psychological outcome; Determinants; prognostic factors

Abstract: Introduction: Survival after trauma has considerably improved. This warrants research on non-fatal outcome. We aimed to describe the recovery patterns of health status (HS) and psychological outcomes during 24 months of follow-up and to identify subgroups at risk of both short and long-term HS after trauma. Methods: Hospitalized patients with all types of injuries were included. Data were collected at 1 week 1, 3, 6, 12, and 24 months post-trauma. HS was assessed with the EuroQol-5D-3L (EQ-5D-3L) and the Health Utilities Index Mark 2 and 3 (HUI2/3). For the screening of symptoms of post-traumatic stress, anxiety and depression, the Impact of Event Scale (IES) and the Hospital Anxiety and Depression Scale (HADS) subscale anxiety (HADSA) and subscale depression (HADSD) were used. Recovery patterns of HS and psychological outcomes were examined with linear mixed model analyses. Results: A total of 4,883 patients participated (median age 68 (Interquartile range 53-80); 50% response rate). The mean (Standard Deviation (SD)) pre-injury EQ-5D-3L score was 0.85 (0.23). One week post-trauma, mean (SD) EQ-5D-3L, HUI2 and HUI3 scores were 0.49 (0.32), 0.61 (0.22) and 0.38 (0.31), respectively. These scores significantly improved to 0.77 (0.26), 0.77 (0.21) and 0.62 (0.35), respectively, at 24 months. Most recovery occurred up until 3 months. At long-term follow-up, patients of higher age, with comorbidities, longer hospital stay, lower extremity fracture and spine injury showed lower HS. The mean (SD) scores of the IES, HADSA and HADSD were respectively 14.80 (15.80), 4.92 (3.98) and 5.00 (4.28), respectively, at 1 week post-trauma and slightly improved over 24 months post-trauma to 10.35 (14.72), 4.31 (3.76) and 3.62 (3.87), respectively. Discussion: HS and psychological symptoms improved over time and most improvements occurred within 3 months post-trauma. The effect of severity and type of injury faded out over time. Patients frequently reported symptoms of post-traumatic stress.

Order of Authors:

Nena Kruithof
Suzanne Polinder
Leonie de Munter
Cornelis van de Ree
Koen Lansink
Mariska de Jong

Opposed Reviewers:

Blerina Kellezi
Nottingham Trent University
Blerina.kellezi@ntu.ac.uk
Blerina recently published a comparable study.

Helen Harcombe
Dunedin School of Medicine
helen.harcombe@otago.ac.nz
A few years ago, Helen published a comparable study.
Response to Reviews:

Response to comments

Additional Editor Comments
- The additional explanation of SES needs to describe whether higher or lower scores indicate greater disadvantage to avoid potential mis-interpretation.
A: In the 'statistical analyses' paragraph, we described the following sentence: a lower status score indicates a lower SES whereas a higher status score indicates a higher SES. Furthermore, we described in the discussion and conclusion paragraphs that a lower status scores is an indicator of a lower SES-level (lines 425 and 473).

- The axes on Figure 5 are not clear. Which data do the titles on the left and right-hand x axes correspond to? Moreover, are these truly demonstrating "differences" or mean values? Ideally it is a good idea to depict variability (e.g., sd, se or 95%CI around the mean).
A: We changed Figure 3 as supposed by the editor. Furthermore, we made the description of the y-axis more clear.

- Supplementary Figure 5 does not appear to have been uploaded.
A: In this manuscript, there is no supplementary Figure 5. In the text, we did not refer to Supplementary Figure 5.

- The explanation of how to interpret a beta score is not sufficient. I suggest you follow the recommendation of Reviewer 2 in providing a clearer explanation of the beta value.
A: See the comment of reviewer 2: we have changed the sentence as supposed by the reviewer.

Comments reviewer 1
- There is still some language editing required which can be done at the proofing stage if the manuscript is accepted by the journal.
A: We did made several improvements in language editing throughout the manuscript.

- One sentence that is important to address in the abstract is: ‘We aimed to describe the recovery patterns of health status (HS) and psychological outcomes during 24 months of follow-up and to identify subgroups at risk of both short and long-term HS after trauma’. The authors should make it clear that the focus is on identification of subgroups at risk of poor health status.
A: In the abstract and manuscript, we now described: ‘We aimed to 1) identify subgroups at risk of both short and long-term health status (HS) after trauma and 2) to describe the recovery patterns of HS and psychological outcomes during 24 months of follow-up.’

Comments reviewer 2
- The manuscript still requires significant editing for grammatical and spelling errors. For example, in line 71, no comma is required; line 106 should read ‘complies’ and not ‘comproise’; line 140 should read ‘comprise’ and not ‘comproise’. Errors are too extensive to list them all. Spelling/gramma correction software should help (not just the Word tool).
A: We have deleted the comma in line 71, we have changed the word ‘complies’ into ‘complies’ and changed the word ‘comproise’ into ‘comprise’. Furthermore, we made several improvements in language editing throughout the manuscript.

- Line 108. Please explain ‘randomly controlled the data’ in the data verification process more detail. All patient files or a sample? Did you check completeness, consistency, coherence and/or chronology?
A: We now described the following sentence: ‘Quality of the data of the BTR and BIOS was checked on outliers and completeness by a trauma coordinator and researcher respectively. Furthermore, data from a sample of the trauma registry was checked manually by a trauma surgeon.’

- Line 240. Spell out FU. Again, using too many acronyms that are not widely recognized makes reading very arduous.
A: We have spelled out the FU as ‘follow-up’ as suggested by the reviewer.

- Table 4 ‘Beta: measures how strong each predictor variable influences the dependent
variable’ could be replaced by ‘mean increase in EQ-5D-3L score (improvement in quality of life) compared to the reference category.

A: We thank the reviewer for this suggestion. We changed the sentence as supposed by the reviewer.

Comments reviewer 3
-I am still a little confused by the status-scores.
A: In the ‘statistical analyses’ paragraph, we described the following sentence: a lower status score indicates a lower SES whereas a higher status score indicates a higher SES. Hopefully, this will lead to a better interpretation of the status score. Furthermore, we described in the discussion and conclusion paragraphs that a lower status scores is an indicator of a lower SES-level (lines 425 and 473). To interpret the results, we added the minimum and maximum scores.

-Some of the confidence intervals contains negative figures. What are the extremes of the scale? As this seems to be a Dutch scale, you could explain this better to international readers.
A: We added the minimum and maximum score of the EQ-5D-3L under Table 4.

-In the study design and participants section it is stated: “The Brabant Trauma Registry (BTR) compiles pre-hospital and hospital data of all trauma patients admitted after presentation to the ED in the Noord-Brabant region.” You probably intended to say compiles?
A: Indeed, we intened to say ‘compile’ instead of ‘complies’. We changed the word ‘complies’ into ‘compiles’.

Same paragraph: “Before the data of the BTR and data of the BIOS-study were merged, the researchers randomly controlled the data of the trauma registry.” This is commendable, but what was “randomly”? 1 of 100, 1 of 1000, 20%? Please elaborate, otherwise this statement is not very descriptive.
A: We deleted the following text: ‘Before the data of the BTR and data of the BIOS-study were merged, the researchers randomly controlled the data of the trauma registry’. We replaced this text with the following sentence: ‘Quality of the data of the BTR and BIOS was checked on outliers and completeness by a trauma coordinator and researcher respectively. Furthermore, data from a sample of the trauma registry was checked manually by a trauma surgeon.’

Additional Information:

| Question | Response |
|----------|----------|
| **Financial Disclosure** | This work was supported by The Netherlands Organization for Health Research and Development (ZonMw) under grant number 80-84200-98-14225. |
| Enter a financial disclosure statement that describes the sources of funding for the work included in this submission. Review the [submission guidelines](https://www.zonmw.nl/nl/) for detailed requirements. View published research articles from [PLOS ONE](https://journals.plos.org) for specific examples. | The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. |
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Ethics committee: Medical Ethics Committee Brabant (project number NL50258.028.14 and NW2016-09).

Prior to participation, participants signed an informed consent form.
Format for specific study types

**Human Subject Research (involving human participants and/or tissue)**
- Give the name of the institutional review board or ethics committee that approved the study
- Include the approval number and/or a statement indicating approval of this research
- Indicate the form of consent obtained (written/oral) or the reason that consent was not obtained (e.g. the data were analyzed anonymously)

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- If the study involved non-human primates, add additional details about animal welfare and steps taken to ameliorate suffering
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  *The data underlying the results presented in the study are available from [include the name of the third party]*

Data of the BIOS are unsuitable for public deposition due to the privacy of participant data. Data are anonymized, but due to relatively few severe cases, patients could be identified. Therefore, BIOS data are available for any interested researcher who meets the criteria for access to confidential data. The Brabant Trauma Registry (e-mail: secretariaat@nazb.nl) may be contacted to request data.
and contact information or URL).

- This text is appropriate if the data are owned by a third party and authors do not have permission to share the data.

Additional data availability information:
Dear Dr. M.J. Giummarra,

Please find enclosed the second revised version of our manuscript entitled ‘Health status and psychological outcomes after trauma: a prospective multicenter cohort study’ (PONE-D-19-21191). The text of the original manuscript has been modified entirely in line with the valuable comments and recommendations of you and the three reviewers. The changes will be addressed one by one in the addendum. We trust that the changes and improvements made this completely revised manuscript suitable for publication in PlosOne.

On behalf of all authors, I am looking forward to hearing from you.

Yours sincerely,

Nena Kruithof, PhD

Addendum: Response to comments
Health status and psychological outcomes after trauma; a prospective multicenter cohort study

Nena Kruithof1*, Suzanne Polinder2, Leonie de Munter1, Cornelis L.P. van de Ree1, Koen W.W. Lansink1,3,4, Mariska A.C. de Jongh1,4, BIOS-group

1ETZ Hospital (Elisabeth-TweeSteden Ziekenhuis), Department Trauma TopCare, Tilburg, the Netherlands

2Erasmus University Medical Centre, Department of Public Health, Rotterdam, the Netherlands

3ETZ Hospital (Elisabeth-TweeSteden Ziekenhuis), Department of Surgery, Tilburg, the Netherlands

4Brabant Trauma Registry, Network Emergency Care Brabant, Tilburg, the Netherlands

*Corresponding author:
Email: nenakruithof@hotmail.com

Membership of the BIOS group is provided in the Acknowledgements
Abstract

Introduction: Survival after trauma has considerably improved. This warrants research on non-fatal outcome. We aimed to identify subgroups at risk of both short and long-term health status (HS) after trauma and to describe the recovery patterns of HS and psychological outcomes during 24 months of follow-up. Methods: Hospitalized patients with all types of injuries were included. Data were collected at 1 week, 1, 3, 6, 12, and 24 months post-trauma. HS was assessed with the EuroQol-5D-3L (EQ-5D-3L) and the Health Utilities Index Mark 2 and 3 (HUI2/3). For the screening of symptoms of post-traumatic stress, anxiety and depression, the Impact of Event Scale (IES) and the Hospital Anxiety and Depression Scale (HADS) subscale anxiety (HADSA) and subscale depression (HADSD) were used. Recovery patterns of HS and psychological outcomes were examined with linear mixed model analyses. Results: A total of 4,883 patients participated (median age 68 (Interquartile range 53-80); 50% response rate). The mean (Standard Deviation (SD)) pre-injury EQ-5D-3L score was 0.85 (0.23). One week post-trauma, mean (SD) EQ-5D-3L, HUI2 and HUI3 scores were 0.49 (0.32), 0.61 (0.22) and 0.38 (0.31), respectively. These scores significantly improved to 0.77 (0.26), 0.77 (0.21) and 0.62 (0.35), respectively, at 24 months. Most recovery occurred up until 3 months. At long-term follow-up, patients of higher age, with comorbidities, longer hospital stay, lower extremity fracture and spine injury showed lower HS. The mean (SD) scores of the IES, HADSA and HADSD were respectively 14.80 (15.80), 4.92 (3.98) and 5.00 (4.28), respectively, at 1 week post-trauma and slightly improved over 24 months post-trauma to 10.35 (14.72), 4.31 (3.76) and 3.62 (3.87), respectively. Discussion: HS and psychological symptoms improved over time and most improvements occurred within 3 months post-trauma. The effects of severity and type of injury faded out over time. Patients frequently reported symptoms of post-traumatic stress.

Trail registration: ClinicalTrials.gov identifier: NCT02508675

Keywords: injury, trauma, hospitalization, longitudinal cohort study, health status, psychological outcome, determinants, prognostic factors
Introduction

Trauma poses a large burden on public health [1]. Reduction of trauma-related mortality in high-income countries [2] has resulted in increased numbers of trauma survivors with long-term injury impact [3], including reduced health status (HS) [4]. An improved understanding of the quality of survival of patients is critically important for improving health care quality and in evaluating trauma care. Furthermore, it is important to understand short and long-term recovery patterns of HS in terms of injured patient characteristics and to identify predictors of outcome of seriously injured patients [5, 6].

Establishing recovery patterns in the short and long-term requires longitudinal data [7]. Non-fatal outcomes after trauma can be assessed with an overall measure of HS. HS includes patients’ physical functioning, state of mind and social activities [8]. In general, trauma has a large impact on HS [4, 9-12], but large variations between patients have been observed [11, 12].

In addition, several relevant non-fatal outcomes after trauma may be assessed more specifically. These include psychological outcomes, such as anxiety and depression. Psychological problems are often reported among trauma patients [13-18] and are associated with worse HS [9, 16].

The fact that trauma has an impact on diverse aspects of patient health, illustrates that a multidimensional approach is necessary for a comprehensive understanding of non-fatal outcomes after trauma. This also allows studying the mutual relations between non-fatal outcomes. Using a multidimensional approach to measure outcomes including HS and symptoms of depression, anxiety and post-traumatic stress will result in a comprehensive understanding of non-fatal outcomes after trauma. In addition, to assess prognostic factors for a poor outcome it is important to cover the entire spectrum of the trauma population without exclusion of particular patient groups (e.g. elderly). The number of longitudinal cohort studies that examine multiple non-fatal outcomes in a large sample with a broad inclusion of type and severity of injury is limited [12, 19-23]. Most studies start measuring outcomes at least 3 months after trauma, resulting in little knowledge about the real short-term consequences [11, 24-27].

The overall aim of the Brabant Injury Outcome Surveillance (BIOS), a population based longitudinal study, is to provide more insight into recovery patterns and determinants of non-fatal outcomes after trauma. The aims of this population-based study are 1. to identify prognostic factors for decreased short, mid and long-term HS and 2. to describe the 2 year recovery patterns of HS and
psychological outcome for different categories of trauma patients. This information is important for understanding the short and long-term recovery patterns and for best informing provision of trauma care to injured patients with long-term disability.

**Methods**

**Study design and participants**

Data were obtained from the BIOS. The BIOS-study is a prospective observational cohort study in which HS and psychological outcomes are assessed in injured patients in the first 24 months after trauma. The methods of the BIOS have been described in detail in a published research protocol (doi: 10.1136/injuryprev-2016-042032) [28].

Recruitment occurred in all ten hospitals of the Noord-Brabant region (the Netherlands) from August 2015 until November 2016. Adults (≥18 years) who visited an emergency department ≤48 hours after trauma and who were admitted to the hospital, were invited to participate. All types of injuries were included regardless of the intent or severity of the injury. Patients who died between hospital discharge and the first week post-trauma, non-Dutch speaking patients, patients with no permanent address or patients with a pathological fracture were excluded. A proxy informant (caregiver or family member) was asked to complete the self-administered questionnaires if the patient was incapable of participating in the BIOS study him- or herself. Proxy informants were invited to enroll in the study 1 month post-trauma. Informal caregivers (e.g. family members) and paid caregivers (e.g. nurses) were allowed to function as proxy informants.

The Brabant Trauma Registry (BTR) compiles pre-hospital and hospital data of all trauma patients admitted after presentation to the ED in the Noord-Brabant region. Quality of the data of the BTR and BIOS was checked on outliers and completeness by a trauma coordinator and researcher respectively. Furthermore, data from a sample of the trauma registry was checked manually by a trauma surgeon.

The study was approved by the Medical Ethics Committee Brabant, the Netherlands (project numbers NL50258.028.14 and NW2016-09). Prior to participation, participants signed an informed consent form.
**Data collection**

Questionnaires were sent at 1 week and 1, 3, 6, 12 and 24 months after trauma. Based on the participants’ preference, follow-up questionnaires were either completed by paper and pencil or digitally. The questionnaires collected data on general patient characteristics (date of birth, gender), self-reported comorbidities (by using a modified version of the Cumulative Illness Rating Scale [29]), self-reported HS (i.e. EuroQol-5D-3L (EQ-5D-3L) [30], the Health Utilities Index (HUI) Mark 2 and Mark 3 [31]) and self-reported psychological functioning (i.e., Hospital Anxiety and Depression Scale (HADS) [32] and the Impact of Event Scale (IES) [33]). Proxy informants did not complete questionnaires regarding psychological outcome.

To increase the response rate, patients who did not complete a questionnaire up until 3 or 6 months post-trauma were asked to complete a short version of the BIOS-questionnaire. Patients who completed the shortened questionnaire included those who could not be reached by phone and did not return a BIOS questionnaire. In this short questionnaire, educational level, comorbidities, the EQ-5D-3L and the IES were included. This short questionnaire did not include proxy assessments. In the shortened questionnaire, pre-injury HS was not collected.

If participants did not complete the questionnaire, they were not excluded from the study but they were still invited at the subsequent time points.

**Outcome measures**

The EQ-5D and HUI are used in various studies measuring HS after trauma [9, 11, 24, 26, 34-39]. The EQ-5D provides valid results for trauma patients when it is completed by a proxy informant [40]. Moreover, a combination of the EQ-5D and the HUI is recommended for use in trauma patients since the combination of these measures covers all relevant dimensions of health [37, 41].

The EQ-5D consists of the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D comprises the following five dimensions: ‘mobility’, ‘self-care’, ‘usual activities’, ‘pain/discomfort’ and ‘anxiety/depression’. Each dimension can be scored as ‘no problems’, ‘moderate problems’ or ‘severe problems’ [30]. A scoring algorithm is available by which each HS description can be expressed as a summary score. This summary score ranges from 0 for death and 1 for full health and can be interpreted as a judgment on the relative desirability of an HS compared with perfect health. A summary score of these five dimensions (EQ-5D utility) can be calculated by using the Dutch
The EQ-VAS is a vertical visual analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state. The EQ-5D and EQ-VAS were also measured pre-injury, by asking participants 1 week or 1 month and proxy informants 1 month after the trauma for the patients’ HS before sustaining the injury. The EQ-VAS was not included in the short questionnaire.

The HUI is a self-administered HS questionnaire that covers the main health domains that are affected by injury, with a particular focus on functional capacities. The HUI consists of 15 questions, classifying respondents into either the HUI2 or HUI3 health states [31]. Single-attribute and overall HS utility scores are calculated using the respective HUI2 and HUI3 utility functions. The results of the HUI questionnaires are converted by an algorithm into the levels of the complementary HUI2 and HUI3 classification system to form seven-element and eight-element health state vectors. From these vectors, single-attribute and overall health state utility scores are calculated [31].

For both the EQ-5D and the HUI, a scoring algorithm is used in which a score of 1 represents full health, 0 represents death and negative values indicate a HS of worse than death [30, 31].

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression [32]. The HADS consists of 14 questions, 7 for symptoms of anxiety (HADSA) and 7 for depressive symptoms (HADSD). All questions have a 4-point response scale (0-3) and the scores for both subscales ranged from 0 to 21. A higher subscale score indicates greater severity of symptoms for anxiety and depression with a subscale value of ≥11 indicating a probable case (i.e., clinical symptoms) [32].

The IES was used to assess self-reported symptoms of post-traumatic stress [33]. The IES consists of 15 items of which the patient could use a 4-point scale (0=not at all, 1=rarely, 3=sometimes and 5=often) to determine whether the statement is present during the last seven days. The IES measures intrusive re-experience of the trauma and avoidance of trauma-related stimuli. A total sum score for the IES could be calculated ranging from 0 to 75. A score of ≥35 is considered as having symptoms of post-traumatic stress [33].

**Prognostic factors**

Hospital length of stay (LOS), admission to an Intensive Care Unit (ICU) and type and severity of injury were collected from the Brabant Trauma Registry and merged with the BIOS-data. The
Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008) [43] were used to create 14 injury group classifications (e.g. hip fracture, severe abdominal injury) representing the most common types of injuries (see S1 Table). Patients who suffer multiple injuries could be classified into one or more injury group classifications.

Trauma severity was based on the Injury Severity Score (ISS). The ISS is based on the square of the highest Abbreviated Injury Scales (AIS) scores of the three most severely injured body regions with a range of 1 to 75. An ISS of ≥16 is considered severely injured [43].

To determine socio-economic status (SES), educational level was used. Educational level was categorized into three levels; low (primary education, preparatory secondary vocational education or without diploma), middle (university preparatory education, senior general secondary education or senior secondary vocational education and training), and high (academic degree or university of applied science).

Statistical analyses

Patients were included in the analyses if they completed a questionnaire for at least one of the predetermined time points. For the non-responders of the BIOS, we could not obtain educational level. Therefore, in the non-responders analysis, status scores from 2014 were used as a proxy to indicate SES. Status scores were based on the mean income, % of people with a low income, % of people with low educational level and % of unemployed people in the neighborhood. In 2014, the mean status score in the Netherlands was 0.28 [44]. A lower status score indicates a lower SES whereas a higher status score indicates a higher SES. Responders and non-responders were compared on age, gender, status score, ISS, type of trauma, LOS and admission to an ICU using Mann-Whitney U tests and Chi-square tests ($\chi^2$).

Means and standard deviations (SDs) of the EQ-5D-3L, HUI2, HUI3, HADSD, HADSA and IES summary scores were calculated and reported for the total BIOS population and for the different subcategories.

Multiple imputation was conducted with the Multivariate Imputation by Chained Equations procedure [45] to handle missing baseline characteristics and sum scores of the questionnaires due to missing item scores (see S2). The dataset was imputed 15 times with 5 iterations. Sensitivity analysis
was performed in which only complete cases were included to compare results with the imputed datasets. S3 shows the differences between the original and imputed data.

Score options from each dimension of the EQ-5D were dichotomized into 0='no problems' and 1='moderate problems'/severe problems'.

Four linear mixed models [46] with a random intercepts were performed to assess longitudinal association between prognostic factors and HS over the 24 months after trauma, which were divided into short-term (1 week and 1 month), mid-term (3 and 6 months) and long-term (12 and 24 months) associations. HS was measured with the EQ-5D-3L summary score.

The results were considered statistically significant at a level of p<0.05. All analyses were conducted in SPSS V.24 (Statistical Package for Social Sciences, Chicago, Illinois, USA), except of the multiple imputation which was performed in R version 3.4.0 (The R Project for Statistical Computing).

Results

BIOS cohort

During the inclusion period of the BIOS, a total of 10,227 patients were hospitalized because of trauma in one of the participating study centers. Patients were excluded if they did not speak the Dutch language (n=194), had no permanent address (n=32), died during their hospital stay within the first week after trauma (n=219) or had other reasons (n=8) (e.g., living abroad). Thus, 9,774 patients were eligible for participation in the BIOS, of whom 4,883 patients provided informed consent and were included (50% response rate). Of these 4,883 participants, 1,099 filled out the shortened questionnaires (see Fig 1).

At 1 week and 1, 3, 6, 12 and 24 months following the trauma, we collected data from of 1,776, 2,971, 3,109, 3,418, 3,105 and 2,734 participants (36.4%, 60.8%, 63.7%, 69.9%, 63.6% and 56.0%, respectively, of the study population) (see Fig 1). A total of 1,105 participants (22.6% of the study population) completed all BIOS questionnaires at each time point. In addition, data on pre-injury HS were obtained from 3,366 participants (69% of the study population). After the first week assessment, missing questionnaires were the result of non-response (i.e., patients who had provided no data at any of the previous time points) and loss to follow-up (i.e., patients who had provided data
for at least one of the previous time points). The main reason for participants to be lost to follow-up during the study period was that completing the questionnaires was too time consuming. Elderly, participants with low educational levels, longer hospital LOS, moderate injury (ISS 9-15), a hip fracture, severe traumatic brain injury (TBI) and those with severe abdominal trauma showed lower response rates to the 1 week questionnaire but provided data thereafter. In the BIOS, patients aged 18-24 and those who recovered completely were most likely to be lost to follow-up.

-insert Fig1 here-

Study population

The median age of the study population was 68 years (IQR 53-80) (Table 1). Responders had a median ISS of 5 (IQR [4-9]) and a large part of the population reported comorbidities. Mild TBI (27.1%) and hip fracture (25.9%) were the most common types of trauma among the participants included in the BIOS. The majority of the participants (n=2,562, 52.5%) had a low educational level. A total of 407 participants (8% of the study population) were represented by a proxy informant.

Compared to the non-responders, participants were more severely injured and had a higher probability of being admitted to the ICU. In addition, responders had a higher median status score (based on the mean income, % of people with a low income, % of people with low educational level and % of unemployed people in the neighborhood) compared to the general Dutch population (mean 0.28) and compared to the median status score of the non-responders (median 0.33, min. score -3.03, max. score 2.58). Patients aged 18-44 and ≥85 years showed relatively low response rates (35%-40% and 39%, respectively). Patients with minor injuries (ISS 1-3) revealed a low response rate (46%), as well as patients with a hospital LOS of ≤2 or ≥15 days (46% and 45%, respectively).

Table 1. Characteristics of responders and non-responders of the Brabant Injury Outcome Surveillance.

| Characteristics          | Responders (n=4,883) % | Non-responders (n=4,891) % |
|--------------------------|------------------------|-----------------------------|
| Gender (male)            | 2,329 (47.7%)          | 2,407 (49.0%)               |
| Median age (yrs)         | 68 (IQR 53-80)         | 70 (IQR 46-84)              |
| 18-24                    | 217 (4.4%)             | 400 (8.2%)                  |
| 25-44                    | 516 (10.6%)            | 767 (15.7%)                 |
| 45-64                    | 1,364 (27.9%)          | 1,006 (20.6%)               |
| 65-74                    | 963 (19.7%)            | 563 (11.6%)                 |
| 75-84                    | 1,102 (22.6%)          | 1,030 (21.1%)               |
| ≥85                      | 721 (14.8%)            | 1,125 (23.0%)               |
| Missing                  | 0 (0.0%)               | 0 (0.0%)                    |
| Median SES status score  | 0.33 (IQR -0.24-0.84)  | 0.13 (IQR -0.36-0.73)       |
| Missing                  | 60 (1.2%)              | 68 (1.4%)                   |
| Median days hospital LOS | 4 (IQR 2-8)            | 4 (IQR 2-8)                 |
The mean EQ-5D-3L summary score increased from 0.49 (SD 0.32) at 1 week post-trauma to 0.77 (SD 0.26) at 24 months post-trauma. The mean pre-injury EQ-5D score was 0.85 (SD 0.23). In addition, the mean (SD) HUI2 and HUI3 scores increased from 0.61 (0.22) and 0.38 (0.31) at 1 week post-trauma to 0.77 (0.21) and 0.62 (0.35) at 24 months post-trauma, respectively (see Table 2). With regard to the individual domains of the EQ-5D, trauma patients reported various problems on the ‘mobility’, ‘usual activities’ and ‘pain/discomfort’ dimensions during the 24 months of follow-up (see Fig 2). In addition, during the 24 months, the prevalence of problems on all dimensions of the EQ-5D decreased, but remained higher at 24 months compared to pre-injury (46% and 32%, respectively for mobility, 23% and 16%, respectively for self-care, 44% and 26%, respectively for usual activities, 52% and 32%, respectively for pain/discomfort and 22% and 16%, respectively for anxiety/depression).

Table 2. Mean (SD) summary scores of self-reported health status and psychological outcomes up to 2 years post-trauma.

| Time post-trauma | EQ-5D-3L* N Mean (SD) | HUI2** N Mean (SD) | HUI3** N Mean (SD) | HADSA*** N Mean (SD) | HADSD*** N Mean (SD) | IES**** N Mean (SD) |
|------------------|------------------------|-------------------|-------------------|----------------------|---------------------|---------------------|
| 1 week           | 1,77 0.49 (0.32)       | 1,77 0.61 (0.22)  | 1,77 0.38 (0.31)  | 1,77 4.92 (3.98)     | 1,77 5.00 (4.28)    | 1,77 14.80 (15.80)  |
| 1 month          | 2,97 0.56 (0.26)       | 2,97 0.67 (0.26)  | 2,97 0.45 (0.26)  | 2,64 4.81 (3.81)     | 2,64 4.77 (4.47)    | 2,64 14.44 (14.24)  |

Abbreviations: SES, social-economic status; ICU, intensive care unit; ISS, Injury Severity Score; IQR, Interquartile range; LOS, length of stay; TBI, traumatic brain injury; yrs, years.
clinical

Female patients had a lower HS compared to males with a hip fracture who completed only the short questionnaire. The prevalence rates of clinical symptoms of anxiety (HADSA≥11), depression (HADSD≥11) and post-traumatic stress (IES≥35) reported at 1 week post-trauma were 10.2%, 12.3% and 13.5%, respectively, and showed a small decrease over time to 7.8%, 6.8% and 11.0% at 24 months post-trauma, respectively.

The results revealed that patients with symptoms of post-traumatic stress (IES≥35) showed worse outcomes on the EQ-5D-3L than patients with no symptoms of post-traumatic stress (Fig. 3).

Prognostic factors of health status

Overall, HS measured as with the EQ-5D-3L increased over at least up until 6 months for all groups of patients and stabilized between 6 and 12 months post-trauma for most groups (see Table 3). Female patients had a lower HS compared to males at every time point.

At all time points, patients aged 85 and older had the lowest HS compared to the other age categories. At 3 and 6 months, all patient groups between 25 and 74 years reported the same HS
whereas patients aged between 18 and 24 reported a higher EQ-5D summary score. HS stabilized at 6 or 12 months for every age group, except for patients between 25 and 44 years for whom HS increased further.

Except for 1 week, patients with a high educational level had the highest HS.

With an increasing number of comorbidities, HS decreased. Patients with moderate injuries (ISS 9-15) showed on almost each time point the lowest HS. At 1 week, severely injured patients (ISS ≥16) showed the lowest mean HS (0.28, SD 0.35).

Patients with the longest hospital LOS (≥15 days) had the lowest mean HS at all time points, ranging from 0.28 (SD 0.34) at 1 week up to 0.62 (SD 0.28) at 24 months after trauma.

Table 3. Mean (SD) of the self-reported health status for patient and injury characteristics as measured with the EQ-5D-3L.

| Characteristics | Pre-injury | 1 week | 1 month | 3 months | 6 months | 12 months | 24 months |
|-----------------|------------|--------|---------|----------|----------|-----------|-----------|
| Gender          |            |        |         |          |          |           |           |
| Male            | 0.90 (0.19)| 0.54 (0.32)| 0.62 (0.28)| 0.74 (0.25)| 0.79 (0.23)| 0.83 (0.21)| 0.84 (0.21)|
| Female          | 0.80 (0.25)| 0.43 (0.31)| 0.50 (0.30)| 0.64 (0.28)| 0.69 (0.26)| 0.70 (0.27)| 0.72 (0.28)|
| Age (yrs)       |            |        |         |          |          |           |           |
| 18-24           | 0.95 (0.13)| 0.50 (0.32)| 0.63 (0.24)| 0.79 (0.24)| 0.85 (0.21)| 0.86 (0.21)| 0.86 (0.22)|
| 25-44           | 0.95 (0.12)| 0.45 (0.30)| 0.59 (0.29)| 0.74 (0.24)| 0.79 (0.24)| 0.84 (0.22)| 0.87 (0.19)|
| 45-64           | 0.91 (0.17)| 0.49 (0.31)| 0.60 (0.27)| 0.73 (0.24)| 0.79 (0.21)| 0.83 (0.21)| 0.83 (0.22)|
| 65-74           | 0.88 (0.20)| 0.51 (0.31)| 0.62 (0.28)| 0.73 (0.24)| 0.79 (0.22)| 0.80 (0.22)| 0.81 (0.23)|
| ≥75             | 0.78 (0.26)| 0.52 (0.33)| 0.53 (0.31)| 0.66 (0.27)| 0.70 (0.25)| 0.70 (0.26)| 0.70 (0.28)|
| Comorbidity     |            |        |         |          |          |           |           |
| 0               | 0.96 (0.12)| 0.53 (0.30)| 0.65 (0.26)| 0.77 (0.20)| 0.83 (0.19)| 0.86 (0.18)| 0.87 (0.18)|
| 1               | 0.85 (0.21)| 0.49 (0.32)| 0.56 (0.29)| 0.69 (0.25)| 0.75 (0.24)| 0.77 (0.24)| 0.78 (0.25)|
| ≥2              | 0.75 (0.24)| 0.45 (0.30)| 0.47 (0.31)| 0.61 (0.29)| 0.66 (0.26)| 0.67 (0.27)| 0.68 (0.28)|
| ISS             |            |        |         |          |          |           |           |
| 1-3             | 0.86 (0.22)| 0.63 (0.29)| 0.69 (0.27)| 0.78 (0.23)| 0.79 (0.24)| 0.79 (0.25)| 0.81 (0.25)|
| 4-8             | 0.89 (0.20)| 0.46 (0.31)| 0.56 (0.29)| 0.71 (0.25)| 0.77 (0.23)| 0.80 (0.22)| 0.81 (0.23)|
| 9-15            | 0.80 (0.26)| 0.43 (0.30)| 0.50 (0.30)| 0.63 (0.28)| 0.68 (0.27)| 0.70 (0.28)| 0.72 (0.28)|
| ≥16             | 0.90 (0.19)| 0.37 (0.35)| 0.50 (0.31)| 0.65 (0.20)| 0.74 (0.25)| 0.77 (0.24)| 0.77 (0.25)|
| LOS (days)      |            |        |         |          |          |           |           |
| ≤2              | 0.91 (0.18)| 0.61 (0.29)| 0.70 (0.25)| 0.81 (0.21)| 0.83 (0.20)| 0.84 (0.22)| 0.86 (0.21)|
| 3-7             | 0.85 (0.23)| 0.47 (0.30)| 0.55 (0.28)| 0.69 (0.25)| 0.74 (0.24)| 0.77 (0.24)| 0.79 (0.24)|
| 8-14            | 0.78 (0.27)| 0.31 (0.31)| 0.46 (0.29)| 0.59 (0.29)| 0.65 (0.27)| 0.68 (0.28)| 0.67 (0.29)|
| ≥15             | 0.74 (0.28)| 0.28 (0.34)| 0.32 (0.31)| 0.50 (0.29)| 0.58 (0.28)| 0.60 (0.28)| 0.62 (0.28)|

Range of EQ-5D-3L: 0-1. Mean EQ-5D-3L of the general Dutch population: 0.87.

Abbreviations: SES, socio-economic status; SD, standard deviation; EQ-5D, EuroQol-5D-3L; ISS, Injury Severity Score; LOS, length of hospital stay; yrs, years

After adjustment for confounding factors, short-term (1 week and 1 month) prognostic factors for a significant lower EQ-5D summary score were female gender, a higher number of comorbidities, a longer LOS, a higher ISS, pelvic injury, tibia/complex foot or femur fracture, radius/ulna/hand fracture, shoulder/upper arm injury, rib fracture, spinal cord injury and stable vertebral fracture/disc injury (see Table 4). Mid-term (3 and 6 months) prognostic factors were a higher number of comorbidities, an ISS between 4 and 15, a longer LOS, radius/ulna/hand fracture, tibia/complex foot or femur fracture, severe TBI, spinal cord injury and...
stable vertebral fracture/disc injury. Long-term (12 and 24 months) prognostic factors for a lower HS were: age 75 and above, 2 or more comorbidities, a longer LOS, tibia/complex foot or femur fracture, spinal cord injury and stable vertebral fracture/disc injury were prognostic factors. A high educational level was associated with higher HS in the long-term analysis.

Table 4. Multivariable longitudinal analysis of short, mid and long-term prognostic factors for decreased health status as measured with the EQ-5D-3L.

| Characteristics | Number of patients | Total (1 week-24 months) | Short-term (1 week-1 month) | Mid-term (3-6 months) | Long-term (12-24 months) |
|-----------------|-------------------|--------------------------|-----------------------------|----------------------|--------------------------|
|                 |                   | * Beta (95% C.I.)         | * Beta (95% C.I.)           | * Beta (95% C.I.)    | * Beta (95% C.I.)        |
| **Gender**      |                   |                          |                             |                      |                          |
| Male            | 2,291             | ref                      | ref                         | ref                  | ref                      |
| Female          | 2,518             | -0.05 (-0.06; -0.04)     | -0.06 (-0.08; -0.05)        | -0.05 (-0.06; -0.03) | -0.06 (-0.08; -0.05)     |
| **Age (yrs)**   |                   |                          |                             |                      |                          |
| 18-44           | 721               | ref                      | ref                         | ref                  | ref                      |
| 45-64           | 1,345             | 0.04 (0.02; 0.05)        | 0.06 (0.04; 0.09)           | 0.02 (0.00; 0.04)    | 0.01 (-0.01; 0.03)       |
| 65-74           | 956               | 0.09 (0.08; 0.11)        | 0.14 (0.11; 0.17)           | 0.07 (0.05; 0.09)    | 0.04 (0.02; 0.06)        |
| ≥75             | 1,787             | 0.02 (0.01; 0.04)        | 0.09 (0.06; 0.12)           | -0.01 (-0.03; 0.01)  | -0.05 (-0.07; -0.02)     |
| **Educational level** |         |                          |                             |                      |                          |
| Low             | 2,637             | ref                      | ref                         | ref                  | ref                      |
| Middle          | 1,280             | 0.02 (0.00; 0.03)        | 0.01 (-0.01; 0.03)          | 0.01 (-0.00; 0.02)   | 0.03 (0.01; 0.04)        |
| High            | 893               | 0.03 (0.02; 0.05)        | 0.02 (-0.01; 0.04)          | 0.04 (0.02; 0.05)    | 0.05 (0.04; 0.07)        |
| **Number of comorbidities** |        |                          |                             |                      |                          |
| None            | 1,801             | ref                      | ref                         | ref                  | ref                      |
| 1               | 1,426             | -0.06 (-0.07; -0.05)     | -0.06 (-0.08; -0.04)        | -0.06 (-0.07; -0.04) | -0.05 (-0.07; -0.04)     |
| ≥2              | 1,582             | -0.15 (-0.16; -0.14)     | -0.14 (-0.17; -0.12)        | -0.14 (-0.16; -0.13) | -0.16 (-0.18; -0.15)     |
| **ISS**         |                   |                          |                             |                      |                          |
| 1-3             | 1,139             | ref                      | ref                         | ref                  | ref                      |
| 4-8             | 1,596             | 0.00 (-0.01; 0.02)       | -0.03 (-0.06; -0.01)        | 0.01 (-0.05; 0.03)   | 0.03 (0.01; 0.05)        |
| 9-15            | 1,838             | -0.02 (-0.04; -0.00)     | -0.06 (-0.09; -0.02)        | -0.02 (-0.04; -0.01) | 0.00 (-0.02; 0.03)       |
| ≥16             | 235               | 0.01 (-0.01; 0.04)       | -0.02 (-0.08; -0.04)        | 0.01 (-0.04; 0.05)   | 0.04 (-0.01; 0.08)       |
| **LOS**         |                   |                          |                             |                      |                          |
| ≤2              | 1,425             | ref                      | ref                         | ref                  | ref                      |
| 3-7             | 2,053             | -0.05 (-0.06; -0.04)     | -0.08 (-0.10; -0.06)        | -0.06 (-0.07; -0.04) | -0.03 (-0.04; -0.01)     |
| 8-14            | 975               | -0.11 (-0.12; -0.09)     | -0.15 (-0.18; -0.12)        | -0.11 (-0.13; 0.09)  | -0.08 (-0.11; 0.06)      |
| ≥15             | 357               | -0.20 (-0.22; -0.18)     | -0.24 (-0.28; -0.20)        | -0.20 (-0.23; 0.17)  | -0.17 (-0.20; 0.14)      |
| **Injury**      |                   |                          |                             |                      |                          |
| Pelvic injury   | 286               | -0.05 (-0.07; -0.03)     | -0.13 (-0.16; -0.10)        | -0.01 (-0.04; 0.01)  | 0.00 (-0.02; 0.03)       |
| Hip fracture    | 1,242             | -0.02 (-0.04; -0.01)     | -0.02 (-0.05; 0.01)         | -0.03 (-0.05; 0.00)  | -0.02 (-0.05; 0.00)      |
| Tibia, complex foot or femur fracture | 561 | -0.05 (-0.06; -0.04) | -0.11 (-0.14; -0.08) | -0.05 (-0.07; -0.02) | -0.02 (-0.04; 0.00) |
| Shoulder and upper arm injury | 469 | -0.03 (-0.04; -0.01) | -0.07 (-0.10; -0.05) | -0.02 (-0.04; 0.00) | -0.00 (-0.02; 0.00) |
| Radius, ulna or hand fracture | 304 | 0.00 (-0.02; 0.02) | -0.03 (-0.06; 0.00) | 0.00 (-0.02; 0.03) | 0.02 (-0.00; 0.05) |
| Mild TBI (AIS 1-2) | 1,302 | 0.03 (0.02; 0.04) | 0.06 (0.04; 0.08) | 0.03 (0.02; 0.05) | 0.02 (-0.00; 0.03) |
| Serious TBI (AIS 3) | 125 | 0.04 (0.01; 0.07) | 0.07 (0.02; 0.13) | 0.05 (0.01; 0.10) | 0.01 (-0.03; 0.05) |
| Severe TBI (≥ 4) | 76 | -0.03 (-0.06; -0.02) | -0.02 (-0.10; -0.07) | -0.06 (-0.12; 0.00) | -0.01 (-0.07; -0.05) |
| Facial fracture | 243 | 0.02 (0.01; 0.04) | 0.05 (0.01; 0.09) | 0.02 (-0.01; 0.04) | 0.01 (-0.01; 0.04) |
| Thoracic injury | 198 | 0.04 (0.02; 0.06) | 0.05 (0.01; 0.10) | 0.04 (0.02; 0.07) | 0.03 (-0.01; 0.01) |
Discussion

This study describes HS and psychological outcomes over 24 months after trauma. HS markedly improved during the 24 months after trauma, most of which occurred within the first 3 months. Compared to pre-injury HS, a large decrease in HS was found 1 week post-trauma. The prevalence rates of symptoms of anxiety and depression were relatively low. In contrast, symptoms of post-traumatic stress were highly prevalent and were present five times as often as compared with the Dutch general population [48]. Additionally, in line with the literature, having symptoms of post-traumatic stress were associated with a lower HS [27]. The addition of an assessment at 1 week post-trauma in the present study adds detailed insight into (baseline) functioning shortly after trauma. Therefore, it provides a more valid assessment of the magnitude of recovery thereafter.

Between 1 week and 3 months, the percentage of patients who reported problems on the ‘pain/discomfort’ and ‘self-care’ dimensions of the EQ-5D decreased steeply. For the ‘mobility’ and ‘usual activities’ dimensions, this decrease started 1 month after trauma. The percentage of patients who reported problems on the ‘anxiety and depression’ dimension was the highest at 1 month after trauma. Within 6 months post-trauma, patients showed the most recovery. From 6 months post-trauma onwards, little improvement in overall HS was found. The percentage of patients who reported improvements on the different EQ-5D domains increased through the 24 months of follow-up.

However, the vast majority of trauma patients did not recover to their pre-injury HS. The mean EQ-5D-3L summary score for the total Dutch adult population is considered 0.87 (SD 0.18) (for males 0.89 (SD 0.16) and for females 0.85 (SD 0.19)) [47].

At short-term (up to 1 month post-trauma) female gender, lower extremity, spine, shoulder and upper arm injuries, injury severity, comorbidities and a longer hospital stay were associated with lower
HS. At mid-term (3 and 6 months), almost the same prognostic factors were significant and relevant, however, only injury severity seemed to be less important. In the long-term a greater age, two or more comorbidities, a longer hospital stay and only a few injuries (i.e., lower extremity fracture and spine injury) showed a significantly lower HS. The effect of injury severity seemed to fade over time. Spinal cord injury patients had the highest risk (long-term Beta = -0.18, CI = -0.27; -0.08) of a lower HS during both the short (not significant), mid and long-term post-trauma. Middle and high educational levels were associated with a higher HS in the long term compared to those with low educational levels.

Most recovery in HS occurs up to 3 months post-trauma, which is in agreement with previous studies on this topic [9, 10, 19]. In this regard, the addition of an assessment at 1 week post-trauma in the present study adds detailed insight into (baseline) functioning shortly after trauma. Prior work also confirms the finding that a large proportion of patients have a considerably lower HS 1 year post-trauma compared to pre-injury HS [9, 11, 16] or compared to the HS of the general population [49].

In addition to the physical injury itself, other characteristics largely affect HS after trauma. This was particularly in the long-term. This finding extends those of previous studies [15, 35], confirming that patients who were the most severely injured, were not necessarily those with the lowest HS.

In this study, the prevalence of symptoms of anxiety and depression was slightly higher compared to the prevalence of an anxiety disorder or depression in the general Dutch population (both disorders are estimated to be present in 10.0% of the Dutch population) [50, 51]. As a result, the prevalence of symptoms of anxiety and depression slightly decreased over time. Recent and comparable studies have documented a slightly higher prevalences of symptoms of anxiety and depression [9, 16].

The prevalence of symptoms of post-traumatic stress was high as compared with the Dutch population (11.0% at 2 years post-trauma versus 2.6-3.3%) [48]. Our prevalence rate of long-term symptoms of post-traumatic stress is in line with previous research that also uses the ≥35 cut-off point for the IES [13]. However, the systematic review by Haagsma et al. [52] revealed prevalence of post-traumatic stress in hospitalized trauma patients that ranged from 30% (90% CI 27%-33%) within 3 months post-trauma to 6% (90% CI 4%-10%) at 1 year. Compared to those results, we found a lower prevalence of symptoms of post-traumatic stress early post-trauma whereas a higher prevalence was found at the 1 year follow-up. This discrepancy may be due to studies using various instruments and different cut-off points to indicate post-traumatic stress.
This study was conducted according to the recommended guidelines for measuring non-fatal outcomes after trauma [41]. The BIOS included a broad study population, measured both short-term and long-term outcomes, measured functioning prior to the trauma, included a large number of patient and injury-related characteristics and requested information from proxy informants for patients who were incapable of completing the set of questionnaires themselves. Recruitment for the BIOS occurred in all hospitals of the Dutch Noord-Brabant region, covering both urban and rural populations.

The inclusion of elderly individuals with a hip fracture in the current study improves the generalizability of the study findings. In this study, one out of four participants was aged 65 or older and had a hip fracture. We are aware that recovery patterns (due to comorbidities and functional decline) in the elderly population are different from recovery patterns in younger patients.

This study also has several limitations. First, there was selection bias since younger patients, elderly patients, patients with very minor injuries (ISS 1-3) and those with a low status score (used as a proxy to indicate SES; a low status score indicate a lower SES-level) were less likely to participate. It is challenging to include these specific groups. Previous studies also reported lower response rates from younger and elderly patients [7, 10, 24, 35], from patients with minor injuries [10] and from those with low educational level [53, 54]. Second, only a selected group of patients (18% of the eligible population) completed the 1 week assessment. Since most recovery occurs within the first 3 months post-trauma, it is vital to examine very early recovery patterns. This study provides unique data since it incorporates the use of a standardized 1 week assessment in a comprehensive group of trauma patients. Nevertheless in most cases, non-responders at this time point felt too disabled to complete a long questionnaire. Therefore, this most likely led to an underestimations of the reported HS and psychological outcomes 1 week post-trauma. Third, there were many missing data, especially early post-trauma. However, we were able to impute missing sum scores in several cases. Fourth, we did not correct for pre-injury HS in the longitudinal analyses since we were not able to collect pre-injury HS in all participants. Fifth, we did not include a pre-injury assessment of the symptoms of anxiety or depression. Sixth, we cannot exclude change findings due to multiple testing. Change findings might have occurred for the results of the longitudinal analyses as presented in Table 4.

Given the acute nature of trauma, it is difficult to include patients soon after they experience trauma in order to examine very early recovery patterns. To increase the response rate and to reduce loss to follow-up, future research should minimize the large number of questionnaires that patients
have to complete at each time point, especially early post-trauma. A promising technique includes computerized adaptive testing. In this already proven valid technique, tailored-made short and precise domain-specific data can be collected [55-58].

We are aware that recall bias and response shift most likely led to an overestimation of the pre-injury HS as measured in this study. However, to produce valid estimates of the health impact and the decrease in functioning after trauma, information on patients functioning prior to the trauma is crucial [59-62]. Future research should focus on the effects of recall bias and response shift on retrospectively collected data.

**Implications for health-care**

According to the literature, early recognition, treatment and monitoring of psychological problems improve non-fatal outcomes after trauma [16, 63-66]. Therefore, early screening and interventions to reduce symptoms of post-traumatic stress should be part of standard care. Furthermore in the long long-term, patients aged ≥75 years, patients with a longer length of hospital stay and patients with ≥2 comorbidities are more likely to have a poor HS. For these patients, standard aftercare should be extended to screen for remaining problems that the patients should address after their trauma. For example by a follow-up appointment with a case manager.

Symptoms of post-traumatic stress were frequently reported in this study. Patients need to be better informed about the psychological problems they may experience after trauma. Health-care providers should not solely focus on the physical consequences but should also be aware of all other possible consequences that may occur after trauma. To achieve this, a more holistic approach towards the treatment of trauma patients should be aimed in which the patients’ own perspectives on their recovery should play a crucial role.

**Conclusion**

Hospitalized trauma patients experience substantial reductions in HS and frequently report symptoms of post-traumatic stress. The results of this study should be interpreted with caution since younger patients, patients with very minor injuries and those with a lower status score (used as an proxy to indicate SES, a lower status score indicates a lower SES-level) were less likely to participate.
Most improvements in HS and psychological symptoms occurred within the first 3 months post-trauma. After two years post trauma, the vast majority of trauma patients did not achieve their pre-injury HS. Recovery trajectories varied widely in which female gender, age ≥75 years, spinal cord injury, having more comorbidities, low educational level, a longer hospital stay and symptoms of post-traumatic stress were associated with a higher risk of decreased HS in the long-term after trauma. In the short-term, also several lower extremity injuries are prognostic factors for decreased HS.

Acknowledgements

Membership list of the BIOS-group: P.V. van Eerten (Maxima Medical Center, department of surgery, Eindhoven, the Netherlands), F.C. van Eijck (Bravis Hospital, department of surgery, Bergen op Zoom and Roosendaal, the Netherlands), H.J. van Geffen (Jeroen Bosch Hospital, department of surgery, ’s-Hertogenbosch, the Netherlands), W.A. Haagh (St. Anna Hospital, department of surgery, Geldrop, the Netherlands), L.M. Poelhekke (Maasziekenhuis Pantein Hospital, department of surgery, Boxmeer, the Netherlands), J.B. Sintenie (Elkerliek Hospital, department of surgery, Helmond, the Netherlands, C.T. Stevens (Bernhoven Hospital, department of surgery, Uden, the Netherlands), A.H. van der Veen (Catharina Hospital, department of surgery, Eindhoven, the Netherlands), C.H. van der Vlies (Maasstad Hospital, department of surgery, Rotterdam, Eindhoven, D.I. Vos (Amphia Hospital, department of surgery, Breda, the Netherlands). Contact person of the BIOS-group: A.H. van der Veen: alexander.vd.veen@catharinaziekenhuis.nl
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Compliance with ethical standards

Ethical approval and informed consent: The BIOS was approved by the Medical Ethics Committee Brabant, the Netherlands (project number NL50258.028.14 and NW2016-09). This study was conducted according to the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all individual participants included in the study.

Availability of data and material: Data of the BIOS are unsuitable for public deposition due to the privacy of participant data. Data are anonymized, but due to relatively few severe cases, patients could be identified. Therefore, BIOS data are available for any interested researcher who meets the criteria for access to confidential data. The Brabant Trauma Registry (e-mail: secretariaat@nazb.nl) may be contacted to request data.

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Author’s contributions:

NK: conception and design, acquisition of data, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

SP: conception and design, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

LM: conception and design, acquisition of data, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

CR: conception and design, acquisition of data, analysis and interpretation of data, critical revision of the article, final approval of the version to be published

KL: conception and design, analysis and interpretation of data, published

MJ: conception and design, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

BIOS-group: conception and design, final approval of the version to be published
Supporting information

S1 Table. Injury group classification of the most common types of injury, based on the Abbreviated Injury Score [67].

S2 File. Methods of imputed data of the Brabant Injury Outcome Surveillance.

S3 Table. Missing sum scores of the original data and imputed data of the self-reported health status and psychological measures of the participants of the Brabant Injury Outcome Surveillance (n=4,883).
**Fig 1.** Number of participants throughout the Brabant Injury Outcome Surveillance (n=4,883).

**Abbreviations:** EQ-5D, EuroQol-5D-3L; HUI, Health Utilities Index Mark 2/3; HADS, Hospital Anxiety and Depression Scale; IES, Impact of Event Scale; VAS, Visual Analogue Scale.
Fig 21. Prevalence of moderate or severe problems (%) on each EuroQol-5D-3L dimension up until 2 years of follow-up.
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Health status and psychological outcomes after trauma; a prospective multicenter cohort study

Nena Kruithof1*, Suzanne Polinder2, Leonie de Munter1, Cornelis L.P. van de Ree1, Koen W.W. Lansink1,3,4, Mariska A.C. de Jongh1,4, BIOS-group

1ETZ Hospital (Elisabeth-TweeSteden Ziekenhuis), Department Trauma TopCare, Tilburg, the Netherlands

2Erasmus University Medical Centre, Department of Public Health, Rotterdam, the Netherlands

3ETZ Hospital (Elisabeth-TweeSteden Ziekenhuis), Department of Surgery, Tilburg, the Netherlands

4Brabant Trauma Registry, Network Emergency Care Brabant, Tilburg, the Netherlands

*Corresponding author:
Email: nenakruithof@hotmail.com

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Abstract

Introduction: Survival after trauma has considerably improved. This warrants research on non-fatal outcome. We aimed to describe the recovery patterns of health status (HS) and psychological outcomes during 24 months of follow-up and to identify subgroups at risk of both short and long-term health status (HS) after trauma and to describe the recovery patterns of HS and psychological outcomes during 24 months of follow-up. Methods: Hospitalized patients with all types of injuries were included. Data were collected at 1 week, 3, 6, 12, and 24 months post-trauma. HS was assessed with the EuroQol-5D-3L (EQ-5D-3L) and the Health Utilities Index Mark 2 and 3 (HUI2/3). For the screening of symptoms of post-traumatic stress, anxiety and depression, the Impact of Event Scale (IES) and the Hospital Anxiety and Depression Scale (HADS) subscale anxiety (HADSA) and subscale depression (HADSD) were used. Recovery patterns of HS and psychological outcomes were examined with linear mixed model analyses. Results: A total of 4,883 patients participated (median age 68 (Interquartile range 53-80); 50% response rate). The mean (Standard Deviation (SD)) pre-injury EQ-5D-3L score was 0.85 (0.23). One week post-trauma, mean (SD) EQ-5D-3L, HUI2 and HUI3 scores were 0.49 (0.32), 0.61 (0.22) and 0.38 (0.31), respectively. These scores significantly improved to 0.77 (0.26), 0.77 (0.21) and 0.62 (0.35), respectively, at 24 months. Most recovery occurred up until 3 months. At long-term follow-up, patients of higher age, with comorbidities, longer hospital stay, lower extremity fracture and spine injury showed lower HS. The mean (SD) scores of the IES, HADSA and HADSD were respectively 14.80 (15.80), 4.92 (3.98) and 5.00 (4.28), respectively, at 1 week post-trauma and slightly improved over 24 months post-trauma to 10.35 (14.72), 4.31 (3.76) and 3.62 (3.87), respectively. Discussion: HS and psychological symptoms improved over time and most improvements occurred within 3 months post-trauma. The effects of severity and type of injury faded out over time. Patients frequently reported symptoms of post-traumatic stress. Trail registration: ClinicalTrials.gov identifier: NCT02508675

Keywords: injury, trauma, hospitalization, longitudinal cohort study, health status, psychological outcome, determinants, prognostic factors
Introduction

Trauma poses a large burden on public health [1]. Reduction of trauma-related mortality in high-income countries [2] has resulted in increased numbers of trauma survivors with long-term injury impact [3], including reduced health status (HS) [4]. An improved understanding of the quality of survival of patients is critically important for improving health care quality and in evaluating trauma care. Furthermore, it is important to understand short and long-term recovery patterns of HS in terms of injured patient characteristics and to identify predictors of outcome of seriously injured patients [5, 6].

Establishing recovery patterns in the short and long-term requires longitudinal data [7]. Non-fatal outcomes after trauma can be assessed with an overall measure of HS. HS includes patients' physical functioning, state of mind and social activities [8]. In general, trauma has a large impact on HS [4, 9-12], but large variations between patients have been observed [11, 12].

In addition, several relevant non-fatal outcomes after trauma may be assessed more specifically. These include psychological outcomes, such as anxiety and depression. Psychological problems are often reported among trauma patients [13-18] and are associated with worse HS [9, 16].

The fact that trauma has an impact on diverse aspects of patient health, illustrates that a multidimensional approach is necessary for a comprehensive understanding of non-fatal outcomes after trauma. This also allows studying the mutual relations between non-fatal outcomes. Using a multidimensional approach to measure outcomes including HS and symptoms of depression, anxiety and post-traumatic stress will result in a comprehensive understanding of non-fatal outcomes after trauma. In addition, to assess prognostic factors for a poor outcome, it is important to cover the entire spectrum of the trauma population without exclusion of particular patient groups (e.g. elderly). The number of longitudinal cohort studies that examine multiple non-fatal outcomes in a large sample with a broad inclusion of type and severity of injury is limited [12, 19-23]. Most studies start measuring outcomes at least 3 months after trauma, resulting in little knowledge about the real short-term consequences [11, 24-27].

The overall aim of the Brabant Injury Outcome Surveillance (BIOS), a population based longitudinal study, is to provide more insight into recovery patterns and determinants of non-fatal outcomes after trauma. The aims of this population-based study are 1. to identify prognostic factors for decreased short, mid and long-term HS and to describe the 2-year recovery patterns of HS and...
psychological outcome for different categories of trauma patients and 2. to describe the 2 year recovery patterns of HS and psychological outcome for different categories of trauma patients. To identify prognostic factors for decreased short, mid and long-term HS. This information is important for understanding the short- and long-term recovery patterns and for best informing provision of trauma care to injured patients with long-term disability.

Methods

Study design and participants

Data were obtained from the BIOS. The BIOS-study is a prospective observational cohort study in which HS and psychological outcomes are assessed in injured patients in the first 24 months after trauma. The methods of the BIOS have been described in detail in a published research protocol (doi: 10.1136/injuryprev-2016-042032) [28].

Recruitment occurred in all ten hospitals of the Noord-Brabant region (the Netherlands) from August 2015 until November 2016. Adults (≥18 years) who visited an emergency department ≤48 hours after trauma and who were admitted to the hospital, were invited to participate. All types of injuries were included, regardless of the intent or severity of the injury. Patients who died between hospital discharge and the first week post-trauma, non-Dutch speaking patients, patients with no permanent address or patients with a pathological fracture were excluded. A proxy informant (caregiver or family member) was asked to complete the self-administered questionnaires if the patient was incapable of participating in the BIOS study him- or herself. Proxy informants were invited to enroll in the study 1 month post-trauma. Informal caregivers (e.g. family members) and paid caregivers (e.g. nurses) were allowed to function as proxy informants.

The Brabant Trauma Registry (BTR) complies pre-hospital and hospital data of all trauma patients admitted after presentation to the ED in the Noord-Brabant region. Before the data of the BTR and data of the BIOS study were merged, the researchers randomly controlled the data of the trauma registry. Quality of the data of the BTR and BIOS was checked on outliers and completeness by a trauma coordinator and researcher respectively. Furthermore, data from a sample of the trauma registry was checked manually by a trauma surgeon.
The study was approved by the Medical Ethics Committee Brabant, the Netherlands (project numbers NL50258.028.14 and NW2016-09). Prior to participation, participants signed an informed consent form.

**Data collection**

Questionnaires were sent at 1 week and 1, 3, 6, 12 and 24 months after trauma. Based on the participants’ preference, follow-up questionnaires were either completed by paper and pencil or digitally. The questionnaires collected data on general patient characteristics (date of birth, gender), self-reported comorbidities (by using a modified version of the Cumulative Illness Rating Scale [29]), self-reported HS (i.e. EuroQol-5D-3L (EQ-5D-3L) [30], the Health Utilities Index (HUI) Mark 2 and Mark 3 [31]) and self-reported psychological functioning (i.e., Hospital Anxiety and Depression Scale (HADS) [32] and the Impact of Event Scale (IES) [33]). Proxy informants did not complete questionnaires regarding psychological outcome.

To increase the response rate, patients who did not complete a questionnaire up until 3 or 6 months post-trauma were asked to complete a short version of the BIOS questionnaire. Patients who completed the shortened questionnaire included those who could not be reached by phone and did not return a BIOS questionnaire. In this short questionnaire, educational level, comorbidities, the EQ-5D-3L and the IES were included. This short questionnaire did not include proxy assessments. In the shortened questionnaire, pre-injury HS was not collected.

If participants did not complete the questionnaire, they were not excluded from the study but they were still invited at the subsequent time points.

**Outcome measures**

The EQ-5D and HUI are used in various studies measuring HS after trauma [9, 11, 24, 26, 34-39]. The EQ-5D provides valid results for trauma patients when it is completed by a proxy informant [40]. Moreover, a combination of the EQ-5D and the HUI is recommended for use in trauma patients since the combination of these measures covers all relevant dimensions of health [37, 41].

The EQ-5D consists of the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D comprises the following five dimensions: ‘mobility’, ‘self-care’, ‘usual activities’, ‘pain/discomfort’ and ‘anxiety/depression’. Each dimension can be scored as ‘no problems’, ‘moderate
problems’ or ‘severe problems’ [30]. A scoring algorithm is available by which each HS description can be expressed as a summary score. This summary score ranges from 0 for death and 1 for full health and can be interpreted as a judgment on the relative desirability of an HS compared with perfect health. A summary score of these five dimensions (EQ-5D utility) can be calculated by using the Dutch tariffs [42]. The EQ-VAS is a vertical visual analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state. The EQ-5D and EQ-VAS were also measured pre-injury, by asking participants 1 week or 1 month and proxy informants 1 month after the trauma for the patients’ HS before sustaining the injury. The EQ-VAS was not included in the short questionnaire.

The HUI is a self-administered HS questionnaire that covers the main health domains that are affected by injury, with a particular focus on functional capacities. The HUI consists of 15 questions, classifying respondents into either the HUI2 or HUI3 health states [31]. Single-attribute and overall HS utility scores are calculated using the respective HUI2 and HUI3 utility functions. The results of the HUI questionnaires are converted by an algorithm into the levels of the complementary HUI2 and HUI3 classification system to form seven-element and eight-element health state vectors. From these vectors, single-attribute and overall health state utility scores are calculated [31].

For both the EQ-5D and the HUI, a scoring algorithm is used in which a score of 1 represents full health, 0 represents death and negative values indicate a HS of worse than death [30, 31].

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression [32]. The HADS consists of 14 questions, 7 for symptoms of anxiety (HADSA) and 7 for depressive symptoms (HADSD). All questions have a 4-point response scale (0=not at all, 1=rarely, 3=sometimes and 5=often) to determine whether the statement is present during the last seven days. A higher subscale score indicates greater severity of symptoms for anxiety and depression with a subscale value of ≥11 indicating a probable case (i.e., clinical symptoms) [32].

The IES was used to assess self-reported symptoms of post-traumatic stress [33]. The IES consists of 15 items of which the patient could use a 4-point scale (0=not at all, 1=rarely, 3=sometimes and 5=often) to determine whether the statement is present during the last seven days. The IES measures intrusive re-experience of the trauma and avoidance of trauma-related stimuli. A total sum score for the IES could be calculated ranging from 0 to 75. A score of ≥35 is considered as having symptoms of post-traumatic stress [33].
Prognostic factors

Hospital length of stay (LOS), admission to an Intensive Care Unit (ICU) and type and severity of injury were collected from the Brabant Trauma Registry and merged with the BIOS-data. The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008) [43] were used to create 14 injury group classifications (e.g. hip fracture, severe abdominal injury) representing the most common types of injuries (see S1 Table). Patients who suffer multiple injuries could be classified into one or more injury group classifications.

Trauma severity was based on the Injury Severity Score (ISS). The ISS is based on the square of the highest Abbreviated Injury Scales (AIS) scores of the three most severely injured body regions with a range of 1 to 75. An ISS of ≥16 is considered severely injured [43].

To determine socio-economic status (SES), educational level was used. Educational level was categorized into three levels; low (primary education, preparatory secondary vocational education or without diploma), middle (university preparatory education, senior general secondary education or senior secondary vocational education and training), and high (academic degree or university of applied science). Statistical analyses

Patients were included in the analyses if they completed a questionnaire for at least one of the predetermined time points. For the non-responders of the BIOS, we could not obtain educational level. Therefore, in the non-responders analysis, status scores from 2014 were used as a proxy to indicate SES. Status scores were based on the mean income, % of people with a low income, % of people with low educational level and % of unemployed people in the neighborhood. In 2014, the mean status score in the Netherlands was 0.28 [44]. A lower status score indicates a lower SES, whereas a higher status score indicates a higher SES. Responders and non-responders were compared on age, gender, status score, ISS, type of trauma, LOS and admission to an ICU using Mann-Whitney U tests and Chi-square tests ($\chi^2$).

Means and standard deviations (SDs) of the EQ-5D-3L, HUI2, HUI3, HADSD, HADSA and IES summary scores were calculated and reported for the total BIOS population and for the different subcategories.
Multiple imputation was conducted with the Multivariate Imputation by Chained Equations procedure [45] to handle missing baseline characteristics and sum scores of the questionnaires due to missing item scores (see S2). The dataset was imputed 15 times with 5 iterations. Sensitivity analysis was performed in which only complete cases were included to compare results with the imputed datasets. S3 shows the differences between the original and imputed data.

Score options from each dimension of the EQ-5D were dichotomized into 0='no problems' and 1='moderate problems/severe problems'.

Four linear mixed models [46] with a random intercepts were performed to assess longitudinal association between prognostic factors and HS over the 24 months after trauma, which were divided into short-term (1 week and 1 month), mid-term (3 and 6 months) and long-term (12 and 24 months) associations. HS was measured with the EQ-5D-3L summary score.

The results were considered statistically significant at a level of p<0.05. All analyses were conducted in SPSS V.24 (Statistical Package for Social Sciences, Chicago, Illinois, USA), except of the multiple imputation which was performed in R version 3.4.0 (The R Project for Statistical Computing).

Results

BIOS cohort

During the inclusion period of the BIOS, a total of 10,227 patients were hospitalized because of trauma in one of the participating study centers. Patients were excluded if they did not speak the Dutch language (n=194), had no permanent address (n=32), died during their hospital stay within the first week after trauma (n=219) or had other reasons (n=8) (e.g., living abroad). Thus, 9,774 patients were eligible for participation in the BIOS, of whom 4,883 patients provided informed consent and were included (50% response rate). Of these 4,883 participants, 1,099 filled out the shortened questionnaires (see Fig 1).

At 1 week and 1, 3, 6, 12 and 24 months following the trauma, we collected data from of 1,776, 2,971, 3,109, 3,418, 3,105 and 2,734 participants (36.4%, 60.8%, 63.7%, 69.9%, 63.6% and 56.0%, respectively, of the study population) (see Fig 1). A total of 1,105 participants (22.6% of the study population) completed all BIOS questionnaires at each time point. In addition, data on pre-injury

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HS were obtained from 3,366 participants (69% of the study population). After the first week assessment, missing questionnaires were the result of non-response (i.e., patients who had provided no data at any of the previous time points) and loss to follow-up (i.e., patients who had provided data for at least one of the previous time points). The main reason for participants to be lost to follow-up during the study period was that completing the questionnaires was too time consuming. Elderly, participants with low educational levels, longer hospital LOS, moderate injury (ISS 9-15), a hip fracture, severe traumatic brain injury (TBI) and those with severe abdominal trauma showed lower response rates to the 1 week questionnaire but provided data thereafter. In the BIOS, patients aged 18-24 and those who recovered completely were most likely to be lost to follow-up.

-Insert Fig1 here-

**Study population**

The median age of the study population was 68 years (IQR 53-80) (Table 1). Responders had a median ISS of 5 (IQR 4-9) and a large part of the population reported comorbidities. Mild TBI (27.1%) and hip fracture (25.9%) were the most common types of trauma among the participants included in the BIOS. The majority of the participants (n=2,562, 52.5%) had a low educational level. A total of 407 participants (8% of the study population) were represented by a proxy informant.

Compared to the non-responders, participants were more severely injured and had a higher probability of being admitted to the ICU. In addition, responders had a higher median status score (based on the mean income, % of people with a low income, % of people with low educational level and % of unemployed people in the neighborhood) compared to the general Dutch population (mean 0.28) and compared to the median status score of the non-responders (median 0.33, min. score -3.03, max. score 2.58). Patients aged 18-44 and ≥85 years showed relatively low response rates (35%-40% and 39%, respectively). Patients with minor injuries (ISS 1-3) revealed a low response rate (46%), as well as patients with a hospital LOS of ≤2 or ≥15 days (46% and 45%, respectively).

**Table 1.** Characteristics of responders and non-responders of the Brabant Injury Outcome Surveillance.

| Characteristics | Responders (n=4,883) | Non-responders (n=4,891) |
|-----------------|-----------------------|--------------------------|
| Gender (male)   | 2,329 (47.7%)         | 2,407 (49.0%)            |
| Median age (yrs)| 68 (IQR 53-68)        | 70 (IQR 46-84)           |
| 18-24           | 217 (4.4%)            | 400 (8.2%)               |
| 25-44           | 516 (10.6%)           | 767 (15.7%)              |
| 45-64           | 1,394 (27.9%)         | 1,098 (22.6%)            |
| Age group | Median SES status score | Median days hospital LOS | Injury severity |
|-----------|-------------------------|--------------------------|-----------------|
| 65-74     | 0.33 (IQR 0.24-0.84)    | 1,325 (27.1%)            | 5 (IQR 4-9)     |
| 75-84     | 0.13 (IQR 0.36-0.73)    | 1,528 (31.2%)            | 5 (IQR 2-9)     |
| ≥85       | 0.00 (IQR 0.00-0.00)     | 2,125 (43.2%)            | 5 (IQR 2-9)     |

### Type of injury

| Type of injury | Frequency | Percentage |
|----------------|-----------|------------|
| Pelvic injury  | 293       | 6.0%       |
| Hip fracture   | 1,266     | 25.9%      |
| Shoulder and upper arm injury | 472 | 9.7% |
| Tibia, tibia fracture or hand fracture | 308 | 6.3% |
| Mild TBI       | 1,324     | 27.1%      |
| Severe TBI     | 126       | 2.6%       |
| Facial fracture | 249      | 5.1%       |
| Thoracic injury| 198       | 4.1%       |
| Mild abdominal injury | 87    | 1.8%       |
| Severe abdominal injury | 36      | 0.7%       |
| Spinal cord injury | 27    | 0.6%       |
| Stable vertebral fracture or disc injury | 201  | 4.2%       |

### Injury severity

| ISS 1-3 | 1,149 | 23.4% |
| ISS 4-8 | 1,597 | 32.7% |
| ISS ≥9 | 1,857 | 36.0% |

### Health status

The mean EQ-5D-3L summary score increased from 0.49 (SD 0.32) at 1 week post-trauma to 0.77 (SD 0.26) at 24 months post-trauma. The mean pre-injury EQ-5D score was 0.85 (SD 0.23). In addition, the mean (SD) HUI2 and HUI3 scores increased from 0.61 (0.22) and 0.38 (0.31) at 1 week post-trauma to 0.77 (0.21) and 0.62 (0.35) at 24 months post-trauma, respectively (see Table 2). With regard to the individual domains of the EQ-5D, trauma patients reported various problems on the ‘mobility,’ ‘usual activities’ and ‘pain/discomfort’ dimensions during the 24 months of follow-up (see Fig 2). In addition, during the 24 months, the prevalence of problems on all dimensions of the EQ-5D decreased, but remained higher at 24 months compared to pre-injury (46% and 32%, respectively for mobility, 23% and 16%, respectively for self-care, 44% and 26%, respectively for usual activities, 52% and 32%, respectively for pain/discomfort and 22% and 16%, respectively for anxiety/depression).

### Table 2

Mean (SD) summary scores of self-reported health status and psychological outcomes up to 2 years post-trauma.
Clinical evaluation that patients with worse outcomes and post-traumatic stress (IES≥35) showed worse outcomes on the EQ-SD-3L than patients with no symptoms of post-traumatic stress (Fig. 3).
At all time points, patients aged 85 and older had the lowest HS compared to the other age categories. At 3 and 6 months, all patient groups between 25 and 74 years reported the same HS whereas patients aged between 18 and 24 reported a higher EQ-5D summary score. HS stabilized at 6 or 12 months for every age group, except for patients between 25 and 44 years for whom HS increased further.

Except for 1 week, at all time points, patients with a high educational level had the highest HS.

With an increasing number of comorbidities, HS decreased. Patients with moderate injuries (ISS 9-15) showed, on, almost each time point the lowest HS. At 1 week, severely injured patients (ISS ≥16) showed the lowest mean HS (0.28, SD 0.35).

Patients with the longest hospital LOSstay (≥15 days) had the lowest mean HS at all time points, ranging from 0.28 (SD 0.34) at 1 week up to 0.62 (SD 0.28) at 24 months after trauma.

### Table 3. Mean (SD) of the self-reported health status for patient and injury characteristics as measured with the EQ-5D-3L.

| Characteristics | Pre-injury | 1 week | 1 month | 3 months | 6 months | 12 months | 24 months |
|-----------------|------------|--------|---------|----------|----------|-----------|----------|
| **Gender**      |            |        |         |          |          |           |          |
| Male            | 0.90 (0.19)| 0.54 (0.32)| 0.62 (0.28)| 0.74 (0.25)| 0.79 (0.23)| 0.83 (0.21)| 0.84 (0.21)|
| Female          | 0.80 (0.25)| 0.43 (0.31)| 0.50 (0.30)| 0.64 (0.26)| 0.69 (0.26)| 0.70 (0.27)| 0.72 (0.28)|
| **Age (yrs)**   |            |        |         |          |          |           |          |
| 18-24           | 0.95 (0.13)| 0.50 (0.32)| 0.63 (0.24)| 0.79 (0.24)| 0.85 (0.21)| 0.86 (0.21)| 0.86 (0.22)|
| 25-44           | 0.95 (0.12)| 0.46 (0.30)| 0.59 (0.29)| 0.74 (0.24)| 0.79 (0.24)| 0.84 (0.23)| 0.87 (0.19)|
| 45-74           | 0.88 (0.20)| 0.51 (0.31)| 0.62 (0.28)| 0.76 (0.24)| 0.79 (0.22)| 0.80 (0.22)| 0.81 (0.23)|
| 75-84           | 0.78 (0.26)| 0.52 (0.33)| 0.63 (0.31)| 0.66 (0.27)| 0.70 (0.25)| 0.70 (0.26)| 0.70 (0.29)|
| ≥85             | 0.63 (0.28)| 0.48 (0.30)| 0.59 (0.32)| 0.65 (0.29)| 0.66 (0.32)| 0.73 (0.29)| 0.57 (0.29)|
| **Educational level** |     |        |         |          |          |           |          |
| Low             | 0.78 (0.27)| 0.49 (0.33)| 0.52 (0.31)| 0.65 (0.28)| 0.70 (0.27)| 0.71 (0.27)| 0.72 (0.28)|
| Middle          | 0.90 (0.17)| 0.50 (0.31)| 0.59 (0.29)| 0.71 (0.26)| 0.71 (0.24)| 0.80 (0.23)| 0.81 (0.23)|
| High            | 0.93 (0.13)| 0.48 (0.30)| 0.62 (0.26)| 0.75 (0.23)| 0.80 (0.21)| 0.84 (0.20)| 0.86 (0.20)|
| **Comorbidity** |            |        |         |          |          |           |          |
| 1               | 0.96 (0.12)| 0.52 (0.30)| 0.65 (0.26)| 0.77 (0.23)| 0.83 (0.19)| 0.86 (0.18)| 0.87 (0.18)|
| 2               | 0.95 (0.21)| 0.49 (0.33)| 0.56 (0.29)| 0.69 (0.25)| 0.75 (0.24)| 0.77 (0.24)| 0.78 (0.35)|
| 3               | 0.94 (0.24)| 0.46 (0.30)| 0.47 (0.31)| 0.57 (0.29)| 0.66 (0.26)| 0.67 (0.27)| 0.68 (0.28)|
| **ISS**         |            |        |         |          |          |           |          |
| 1-3             | 0.86 (0.22)| 0.63 (0.29)| 0.69 (0.27)| 0.78 (0.22)| 0.79 (0.24)| 0.79 (0.25)| 0.81 (0.25)|
| 4-8             | 0.88 (0.20)| 0.56 (0.31)| 0.56 (0.29)| 0.71 (0.24)| 0.77 (0.23)| 0.80 (0.22)| 0.81 (0.23)|
| 9-15            | 0.80 (0.26)| 0.44 (0.30)| 0.50 (0.30)| 0.63 (0.28)| 0.68 (0.27)| 0.70 (0.28)| 0.72 (0.28)|
| ≥16             | 0.90 (0.18)| 0.47 (0.30)| 0.50 (0.31)| 0.66 (0.30)| 0.74 (0.26)| 0.77 (0.24)| 0.77 (0.26)|
| **LOS (days)**  |            |        |         |          |          |           |          |
| 1               | 0.91 (0.18)| 0.61 (0.29)| 0.70 (0.25)| 0.81 (0.21)| 0.83 (0.20)| 0.84 (0.22)| 0.86 (0.21)|
| 2               | 0.85 (0.23)| 0.47 (0.30)| 0.55 (0.28)| 0.69 (0.25)| 0.74 (0.24)| 0.77 (0.24)| 0.79 (0.24)|
| ≥3              | 0.88 (0.27)| 0.31 (0.31)| 0.46 (0.30)| 0.59 (0.29)| 0.65 (0.27)| 0.68 (0.28)| 0.67 (0.29)|

Range of EQ-5D-3L: 0-1. Mean EQ-5D-3L of the general Dutch population: 0.87.

Abbreviations: SES, socio-economic status; SD, standard deviation; EQ-5D, EuroQol-5D-3L; ISS, Injury Severity Score; LOS, length of hospital stay; yrs, years

After adjustment for confounding factors, short-term (1 week and 1 month) prognostic factors for a significant lower EQ-5D summary score were female gender, a higher number of comorbidities, a longer LOS, a higher ISS, pelvic injury, tibia/complex foot or femur fracture, radius/ulna/hand fracture, shoulder/upper arm injury, rib fracture, spinal cord injury and stable vertebral fracture/disc injury (see Table 4). Mid-term (3 and 6 months)
prognostic factors were a higher number of comorbidities, an ISS between 4 and 15, a longer LOS, radius/ulna/hand fracture, tibia/complex foot or femur fracture, severe TBI, spinal cord injury and stable vertebral fracture/disc injury. Long-term (12 and 24 months) prognostic factors for a lower HS were: age 75 and above, 2 or more comorbidities, a longer LOS, tibia/complex foot or femur fracture, spinal cord injury and stable vertebral fracture/disc injury were prognostic factors for a lower HS. A high educational level was associated with higher HS in the long-term analysis.

Table 4. Multivariable longitudinal analysis of short, mid and long-term prognostic factors for decreased health status as measured with the EQ-5D-3L.

| Characteristics          | Number of patients | Total (1 week-24 months) | Short-term (1 week-1 month) | Mid-term (3-6 months) | Long-term (12-24 months) |
|--------------------------|--------------------|--------------------------|-----------------------------|-----------------------|--------------------------|
|                          |                    | * Beta (95% C.I.)        | * Beta (95% C.I.)           | * Beta (95% C.I.)      | * Beta (95% C.I.)        |
| Gender                   |                    |                          |                             |                       |                          |
| Male                     | 2,291              | ref                      | ref                         | ref                   | ref                      |
| Female                   | 2,518              | -0.05 (-0.06; -0.04)     | -0.06 (-0.08; -0.05)        | -0.05 (-0.06; -0.03)  | -0.06 (-0.08; -0.06)    |
| Age (yrs)                |                    |                          |                             |                       |                          |
| 18-44                    | 721                | ref                      | ref                         | ref                   | ref                      |
| 45-64                    | 1,345              | 0.04 (0.02; 0.06)        | 0.06 (0.04; 0.09)           | 0.02 (0.01; 0.04)     | 0.01 (0.01; 0.04)       |
| 65-74                    | 956                | 0.09 (0.08; 0.11)        | 0.14 (0.11; 0.17)           | 0.07 (0.06; 0.09)     | 0.04 (0.02; 0.06)       |
| ≥75                      | 1,767              | 0.02 (0.01; 0.04)        | 0.09 (0.06; 0.12)           | -0.01 (0.03; 0.01)    | -0.05 (0.07; 0.02)      |
| Educational level        |                    |                          |                             |                       |                          |
| Low                      | 2,637              | ref                      | ref                         | ref                   | ref                      |
| Middle                   | 1,280              | 0.02 (0.00; 0.03)        | 0.01 (0.01; 0.03)           | 0.01 (0.02; 0.02)     | 0.03 (0.01; 0.04)       |
| High                     | 893                | 0.03 (0.02; 0.05)        | 0.02 (0.01; 0.04)           | 0.04 (0.02; 0.05)     | 0.05 (0.04; 0.07)       |
| Number of comorbidities  |                    |                          |                             |                       |                          |
| 1                        | 1,426              | -0.06 (-0.07; -0.05)     | -0.06 (-0.08; -0.04)        | -0.06 (-0.07; -0.04)  | -0.05 (-0.07; -0.04)    |
| 2                        | 1,582              | -0.15 (-0.16; -0.14)     | -0.14 (-0.17; -0.12)        | -0.14 (-0.18; -0.13)  | -0.16 (-0.18; -0.15)    |
| ISS                      |                    |                          |                             |                       |                          |
| 1-3                      | 1,139              | ref                      | ref                         | ref                   | ref                      |
| 4-8                      | 1,596              | 0.00 (-0.01; 0.02)       | -0.03 (-0.06; -0.01)        | 0.01 (0.05; 0.03)     | 0.03 (0.01; 0.05)       |
| 9-15                     | 1,838              | -0.02 (-0.04; 0.00)      | -0.06 (-0.09; -0.02)        | -0.02 (-0.04; -0.01)  | 0.00 (-0.02; 0.03)      |
| ≥16                      | 255                | 0.01 (0.00; 0.02)        | 0.02 (0.01; 0.03)           | 0.01 (0.03; 0.01)     | 0.04 (0.03; 0.01)       |
| LOS                      |                    |                          |                             |                       |                          |
| 3-7                      | 2,053              | -0.05 (-0.06; -0.04)     | -0.08 (-0.10; -0.06)        | -0.08 (-0.07; -0.04)  | -0.03 (-0.04; -0.01)    |
| 8-14                     | 975                | -0.11 (-0.12; -0.09)     | -0.15 (-0.18; -0.12)        | -0.11 (-0.13; -0.09)  | -0.09 (-0.11; -0.06)    |
| ≥15                      | 357                | -0.20 (-0.22; -0.18)     | -0.24 (-0.28; -0.20)        | -0.20 (-0.23; -0.17)  | -0.17 (-0.20; -0.14)    |
| Injury                   |                    |                          |                             |                       |                          |
| Pelvic injury            | 286                | -0.06 (-0.07; -0.03)     | -0.13 (-0.16; -0.10)        | -0.01 (-0.04; -0.01)  | 0.00 (-0.02; 0.03)      |
| Hip fracture             | 1,242              | -0.02 (-0.04; -0.01)     | -0.02 (-0.05; -0.01)        | -0.03 (-0.05; 0.00)   | 0.02 (-0.05; 0.00)      |
| Tibia, complex foot or femur fracture | 561 | -0.05 (-0.06; -0.04) | -0.11 (-0.14; -0.08) | -0.05 (-0.07; -0.02) | -0.02 (-0.04; -0.00) |
| Shoulder and upper arm injury | 469 | -0.03 (-0.04; -0.01) | -0.07 (-0.10; -0.05) | -0.02 (-0.04; -0.00) | -0.00 (-0.02; 0.00) |
| Radius, ulna or hand fracture | 304 | 0.00 (-0.02; 0.00) | -0.03 (-0.06; -0.00) | 0.00 (-0.02; 0.00) | 0.02 (-0.00; 0.02) |
| Mild TBI (AIS 1-2)       | 1,302              | 0.03 (0.02; 0.04)        | 0.06 (0.04; 0.08)           | 0.03 (0.02; 0.05)     | 0.02 (0.00; 0.03)       |
| Serious TBI (AIS 3)      | 125                | 0.04 (0.01; 0.07)        | 0.07 (0.02; 0.13)           | 0.05 (0.01; 0.18)     | 0.01 (0.03; 0.05)       |
**Discussion**

This study describes HS and psychological outcomes over 24 months after trauma. HS markedly improved during the 24 months after trauma, most of which occurred within the first 3 months. Compared to pre-injury HS, a large decrease in HS was found 1 week post-trauma. The prevalence rates of symptoms of anxiety and depression were relatively low. In contrast, symptoms of post-traumatic stress were highly prevalent and were present five times as often as compared with the Dutch general population [48]. Additionally, in line with the literature, having symptoms of post-traumatic stress was associated with a lower HS [27]. The addition of an assessment at 1 week post-trauma in the present study adds detailed insight into (baseline) functioning shortly after trauma. Therefore, it provides a more valid assessment of the magnitude of recovery thereafter.

Between 1 week and 3 months, the percentage of patients who reported problems on the ‘pain/discomfort’ and ‘self-care’ dimensions of the EQ-5D decreased steeply. For the ‘mobility’ and ‘usual activities’ dimensions, this decrease started 1 month after trauma. The percentage of patients who reported problems on the ‘anxiety and depression’ dimension was the highest at 1 month after trauma. Within 6 months post-trauma, patients showed the most recovery. From 6 months post-trauma onwards, little improvement in overall HS was found. The percentage of patients who reported improvements on the different EQ-5D domains increased through the 24 months of follow-up.

However, the vast majority of trauma patients did not recover to their pre-injury HS. The mean EQ-5D-3L score (improvement of Health Status) compared to pre-trauma in the present study adds detailed insight into (baseline) functioning shortly after trauma.

### Abbreviations

- ISS, Injury Severity Score
- AIS, Abbreviated Injury Scale
- LOS, Hospital length of stay
- yrs, years
- TBI, traumatic brain injury
- months
- weeks
- pre, pre-injury

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**Table 1:**

| Injury Type                      | Sample Size | β (95% CI)       |
|---------------------------------|-------------|-----------------|
| Severe TBI (≥ 4)                | 76          | -0.03 (-0.06; 0.02) |
| Facial fracture                 | 243         | 0.02 (0.01; 0.04) |
| Thoracic injury                 | 198         | 0.04 (0.02; 0.06) |
| Rib fracture                    | 533         | 0.01 (-0.00; 0.02) |
| Mild abdominal injury           | 85          | 0.02 (0.00; 0.05) |
| Severe abdominal injury         | 38          | 0.03 (-0.02; 0.08) |
| Spinal cord injury              | 27          | -0.11 (-0.17; -0.05) |
| Stable vertebral fracture or disc injury | 256 | 0.06 (-0.01; 0.03) |

* Mixed models, adjusted for all other variables

Beta: mean increase in EQ-5D-3L score (improvement of Health Status) compared to the reference category.

Range of EQ-5D-3L: 0–1. Mean EQ-5D-3L of the general Dutch population: 0.87 [47]. Higher EQ-5D-3L model scores indicate better QoL. Each predictor variable influences the dependent variable.

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**Notes:**

- Adjust space between Latin and Asian text.
- Adjust space between Asian text and numbers.

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**Figure:**

- Adjust space between Latin and Asian text.
- Adjust space between Asian text and numbers.
3L summary score for the total Dutch adult population is considered 0.87 (SD 0.18) (for males 0.89 (SD 0.16) and for females 0.85 (SD 0.19)) [47].

At short-term (up to 1 month post-trauma) female gender, lower extremity, spine, shoulder and upper arm injuries, injury severity, comorbidities and a longer hospital stay were associated with lower HS. At mid-term (3 and 6 months), almost the same prognostic factors were significant and relevant, however, only injury severity seemed to be less important. In the long-term a greater age, two or more comorbidities, a longer hospital stay and only a few injuries (i.e., lower extremity fracture and spine injury) showed a significantly lower HS. The effect of injury severity seemed to fade over time. Spinal cord injury patients had the highest risk (long-term Beta -0.18, CI -0.27;-0.08) of a lower HS during both the short (not significant), mid and long-term post-trauma periods. Middle and high educational levels were associated with a higher HS in the long term compared to those with low educational levels.

Most recovery in HS occurs up to 3 months post-trauma, which is in agreement with previous studies on this topic [9, 10, 19]. In this regard, the addition of an assessment at 1 week post-trauma in the present study adds detailed insight into (baseline) functioning shortly after trauma. Thereby, it provides a more valid assessment of the magnitude of recovery. Prior work also confirms the finding that a large proportion of patients have a considerably lower HS 1 year post-trauma compared to pre-injury HS [9, 11, 16] or compared to the HS of the general population [49].

In addition to the physical injury itself, other characteristics largely affect HS after trauma. This was, in particular, in the long-term. This finding extends those of previous studies [15, 35], confirming that patients who were the most severely injured, were not necessarily those with the lowest HS.

In this study, the prevalence of symptoms of anxiety and depression was slightly higher compared to the prevalence of an anxiety disorder or depression in the general Dutch population (both disorders are estimated to be present in 10.0% of the Dutch population) [50, 51]. As a result, the prevalence of symptoms of anxiety and depression slightly decreased over time. Recent and comparable studies have documented a slightly higher prevalences of symptoms of anxiety and depression [9, 16].

The prevalence of symptoms of post-traumatic stress was high as compared with the Dutch population (11.0% at 2 years post-trauma versus 2.6-3.3%) [48]. Our prevalence rate of long-term
symptoms of post-traumatic stress is in line with previous research that also uses the ≥35 cut-off point for the IES [13]. However, the systematic review by Haagsma et al. [52] revealed prevalence of post-traumatic stress in hospitalized trauma patients that ranged from 30% (90% CI 27%-33%) within 3 months post-trauma to 6% (90% CI 4%-10%) at 1 year. Compared to those results, we found a lower prevalence of symptoms of post-traumatic stress early post-trauma whereas a higher prevalence was found at the 1 year follow-up. This discrepancy may be due to studies using various instruments and different cut-off points to indicate post-traumatic stress.

This study was conducted according to the recommended guidelines for measuring non-fatal outcomes after trauma [41]. The BIOS included a broad study population, measured both short-term and long-term outcomes, measured functioning prior to the trauma, included a large number of patient and injury-related characteristics and requested information from proxy informants for patients who were incapable of completing the set of questionnaires themselves. Recruitment for the BIOS occurred in all hospitals of the Dutch Noord-Brabant region, covering both urban and rural populations.

The inclusion of elderly individuals with a hip fracture in the current study improves the generalizability of the study findings. In this study, one out of four participants was aged 65 or older and had a hip fracture. We are aware that recovery patterns (due to comorbidities and functional decline) in the elderly population are different from recovery patterns in younger patients. However, this study also has several limitations. First, there was selection bias since younger patients, elderly patients, patients with very minor injuries (ISS 1-3) and those with a low status score (used as a proxy to indicate SES; a low status score indicate a lower SES-level) were less likely to participate. It is challenging to include these specific groups. Previous studies also reported lower response rates from younger and elderly patients [7, 10, 24, 35], from patients with minor injuries [10] and from those with low educational level [53, 54]. Second, only a selected group of patients (18% of the eligible population) completed the 1 week assessment. Since most recovery occurs within the first 3 months post-trauma, it is vital to examine very early recovery patterns. This study provides unique data since it incorporates the use of a standardized 1 week assessment in a comprehensive group of trauma patients. Nevertheless, in most cases, non-responders at this time point felt too disabled to complete a long questionnaire. Therefore, this most likely led to an underestimations of the reported HS and psychological outcomes 1 week post-trauma. Third, there were many missing data, especially early post-trauma. However, we were able to impute missing sum scores in several cases. Fourth, we
did not correct for pre-injury HS in the longitudinal analyses since we were not able to collect pre-injury
HS in all participants. Fifth, we did not include a pre-injury assessment of the symptoms of anxiety or
depression. Sixth, we cannot exclude change findings due to multiple testing. Change findings might
have occurred for the results of the longitudinal analyses as presented in Table 4.

Given the acute nature of trauma, it is difficult to include patients soon after they experience
trauma in order to examine very early recovery patterns. To increase the response rate and to reduce
loss to follow-up, future research should minimize the large number of questionnaires that patients
have to complete at each time point, especially early post-trauma. A promising technique includes
computerized adaptive testing (CAT). In this already proven valid technique, tailored-made short and
precise domain-specific data can be collected [55-58].

We are aware that recall bias and response shift most likely led to an overestimation of the
pre-injury HS as measured in this study. However, to produce valid estimates of the health impact and
the decrease in functioning after trauma, information on patients functioning prior to the trauma is
crucial [59-62]. Future research should focus on the effects of recall bias and response shift on
retrospectively collected data.

**Implications for health-care**

According to the literature, early recognition, treatment and monitoring of psychological
problems improve non-fatal outcomes after trauma [16, 63-66]. Therefore, early screening and
interventions to reduce symptoms of post-traumatic stress should be part of standard care.
Furthermore in the long long-term, patients aged ≥75 years, patients with a longer length of hospital
stay and patients with ≥2 comorbidities are more likely to have a poor HS. For these patients, standard
aftercare should be extended to screen for remaining problems that the patients should address after
their trauma. For example, e.g., by a follow-up appointment with a case manager.

Symptoms of post-traumatic stress were frequently reported in this study. Patients need to be
better informed about the psychological problems they may experience after trauma. Health-care
providers should not solely focus on the physical consequences but should also be aware of all other
possible consequences that may occur after trauma. To achieve this, a more holistic approach
towards the treatment of trauma patients should be aimed in which the patients’ own perspectives on
their recovery should play a crucial role.
Conclusion

Hospitalized trauma patients experience substantial reductions in HS and frequently report symptoms of post-traumatic stress. The results of this study should be interpreted with caution since younger patients, patients with very minor injuries and those with a lower status score (used as an proxy to indicate SES, a lower status score indicates a lower SES-level) were less likely to participate. Most improvements in HS and psychological symptoms occurred within the first 3 months post-trauma. After two years post trauma, the vast majority of trauma patients did not achieve their pre-injury HS. Recovery trajectories varied widely in which female gender, age ≥75 years, spinal cord injury, having more comorbidities, low educational level, a longer hospital stay and symptoms of post-traumatic stress were associated with a higher risk of decreased HS in the long-term after trauma. In the short-term, also several lower extremity injuries are prognostic factors for decreased HS.

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Membership list of the BIOS-group: P.V. van Eerten (Maxima Medical Center, department of surgery, Eindhoven, the Netherlands), F.C. van Eijck (Bravis Hospital, department of surgery, Bergen op Zoom and Roosendaal, the Netherlands), H.J. van Geffen (Jeroen Bosch Hospital, department of surgery, ’s-Hertogenbosch, the Netherlands), W.A. Haagh (St. Anna Hospital, department of surgery, Geldrop, the Netherlands), L.M. Poelhekke (Maasziekenhuis Pantein Hospital, department of surgery, Boxmeer, the Netherlands), J.B. Sintenie (Elkerliek Hospital, department of surgery, Helmond, the Netherlands, C.T. Stevens (Bernhoven Hospital, department of surgery, Uden, the Netherlands), A.H. van der Veen (Catharina Hospital, department of surgery, Eindhoven, the Netherlands), C.H. van der Vlies (Maasstad Hospital, department of surgery, Rotterdam, Eindhoven, D.I. Vos (Amphia Hospital, department of surgery, Breda, the Netherlands). Contact person of the BIOS-group: A.H. van der Veen: alexander.vd.veen@catharinaziekenhuis.nl
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Compliance with ethical standards

Ethical approval and informed consent: The BIOS was approved by the Medical Ethics Committee Brabant, the Netherlands (project number NL50258.028.14 and NW2016-09). This study was conducted according to the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all individual participants included in the study.

Availability of data and material: Data of the BIOS are unsuitable for public deposition due to the privacy of participant data. Data are anonymized, but due to relatively few severe cases, patients could be identified. Therefore, BIOS data are available for any interested researcher who meets the criteria for access to confidential data. The Brabant Trauma Registry (e-mail: secretariaat@nazb.nl) may be contacted to request data.

Competing interests: The authors declare that there is no conflict of interest.

Author's contributions:

NK: conception and design, acquisition of data, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

SP: conception and design, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

LM: conception and design, acquisition of data, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

CR: conception and design, acquisition of data, analysis and interpretation of data, critical revision of the article, final approval of the version to be published

KL: conception and design, analysis and interpretation of data, final approval of the version to be published

MJ: conception and design, analysis and interpretation of data, drafting the article, critical revision of the article, final approval of the version to be published

BIOS-group: conception and design, final approval of the version to be published
Supporting information

S1 Table. Injury group classification of the most common types of injury, based on the Abbreviated Injury Score [67].

S2 File. Methods of imputed data of the Brabant Injury Outcome Surveillance.

S3 Table. Missing sum scores of the original data and imputed data of the self-reported health status and psychological measures of the participants of the Brabant Injury Outcome Surveillance (n=4,883).
Rebuttal letter

Response to comments

Additional Editor Comments
- The additional explanation of SES needs to describe whether higher or lower scores indicate greater disadvantage to avoid potential mis-interpretation.
  A: In the ‘statistical analyses’ paragraph, we described the following sentence: a lower status score indicates a lower SES whereas a higher status score indicates a higher SES. Furthermore, we described in the discussion and conclusion paragraphs that a lower status scores is an indicator of a lower SES-level (lines 425 and 473).

- The axes on Figure 5 are not clear. Which data do the titles on the left and right-hand x axes correspond to? Moreover, are these truly demonstrating “differences” or mean values? Ideally it is a good idea to depict variability (e.g., sd, se or 95%CI around the mean).
  A: We changed Figure 3 as supposed by the editor. Furthermore, we made the description of the y-axis more clear.

- Supplementary Figure 5 does not appear to have been uploaded.
  A: In this manuscript, there is no supplementary Figure 5. In the text, we did not refer to Supplementary Figure 5.

- The explanation of how to interpret a beta score is not sufficient. I suggest you follow the recommendation of Reviewer 2 in providing a clearer explanation of the beta value.
  A: See the comment of reviewer 2: we have changed the sentence as supposed by the reviewer.

Comments reviewer 1
- There is still some language editing required which can be done at the proofing stage if the manuscript is accepted by the journal.
  A: We did made several improvements in language editing throughout the manuscript.

- One sentence that is important to address in the abstract is: ‘We aimed to describe the recovery patterns of health status (HS) and psychological outcomes during 24 months of follow-up and to identify subgroups at risk of both short and long-term HS after trauma’. The authors should make it clear that the focus is on identification of sub-groups at risk of poor health status.
  A: In the abstract and manuscript, we now described: ‘We aimed to 1) identify subgroups at risk of both short and long-term health status (HS) after trauma and 2) to describe the recovery patterns of HS and psychological outcomes during 24 months of follow-up.’

Comments reviewer 2
- The manuscript still requires significant editing for grammatical and spelling errors. For example, in line 71, no comma is required; line 106 should read ‘compiles’ and not ‘complies’; line 140 should read ‘comprise’ and not ‘comproise’. Errors are too extensive to list them all. Spelling/grammar correction software should help (not just the Word tool).
  A: We have deleted the comma in line 71, we have changed the word ‘complies’ into ‘compiles’ and changed the word ‘comproise’ into ‘comprise’. Furthermore, we made several improvements in language editing throughout the manuscript.

- Line 108. Please explain ‘randomly controlled the data’ in the data verification process more detail. All patient files or a sample? Did you check completeness, consistency, coherence and/or chronology?
A: We now described the following sentence: ‘Quality of the data of the BTR and BIOS was checked on outliers and completeness by a trauma coordinator and researcher respectively. Furthermore, data from a sample of the trauma registry was checked manually by a trauma surgeon.’

-Line 240. Spell out FU. Again, using too many acronyms that are not widely recognized makes reading very arduous
A: We have spelled out the FU as ‘follow-up’ as suggested by the reviewer.

-Table 4 ‘Beta: measures how strong each predictor variable influences the dependent variable’ could be replaced by ‘mean increase in EQ-5D-3L score (improvement in quality of life) compared to the reference category.
A: We thank the reviewer for this suggestion. We changed the sentence as supposed by the reviewer.

Comments reviewer 3
-I am still a little confused by the status scores.
A: In the ‘statistical analyses’ paragraph, we described the following sentence: a lower status score indicates a lower SES whereas a higher status score indicates a higher SES. Hopefully, this will lead to a better interpretation of the status score. Furthermore, we described in the discussion and conclusion paragraphs that a lower status scores is an indicator of a lower SES-level (lines 425 and 473). To interpret the results, we added the minimum and maximum scores.

-Some of the confidence intervals contain negative figures. What are the extremes of the scale? As this seems to be a Dutch scale, you could explain this better to international readers.
A: We added the minimum and maximum score of the EQ-5D-3L under Table 4.

-In the study design and participants section it is stated: “The Brabant Trauma Registry (BTR) complies pre-hospital and hospital data of all trauma patients admitted after presentation to the ED in the Noord-Brabant region.” You probably intended to say compiles?
A: Indeed, we intended to say ‘compile’ instead of ‘compiles’. We changed the word ‘compiles’ into ‘compiles’.

Same paragraph: “Before the data of the BTR and data of the BIOS-study were merged, the researchers randomly controlled the data of the trauma registry.” This is commendable, but what was “randomly”? 1 of 100, 1 of 1000, 20%? Please elaborate, otherwise this statement is not very descriptive.
A: We deleted the following text: ‘Before the data of the BTR and data of the BIOS-study were merged, the researchers randomly controlled the data of the trauma registry’. We replaced this text with the following sentence: ‘Quality of the data of the BTR and BIOS was checked on outliers and completeness by a trauma coordinator and researcher respectively. Furthermore, data from a sample of the trauma registry was checked manually by a trauma surgeon.’