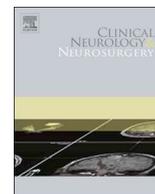




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Global outcome after traumatic brain injury in a prospective cohort

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ABSTRACT

Objectives: Traumatic Brain Injury(TBI) is one of the most common neurosurgical emergencies but the long-term outcome remains unclear. This study investigated the global outcome and return to work after TBI and tried to identify any relationships that exist with injury and demographic features.**Patients & methods:** 1322 consecutive TBI admissions over 4 years, assessed at a specialist neurorehabilitation clinic at 10weeks and 1 yr. The outcomes were Extended Glasgow Outcome Scale(GOSE), return to work, Rivermead Head Injury Follow-up Questionnaire, Rivermead Post-Concussion Symptoms and the Hospital Anxiety and Depression Score.**Results:** 1 year follow-up was achieved in 1207(91.3%). Mean age was 46.9(SD17.3) and 49.2% had mild TBI. The proportion attaining Good Recovery increased from 25.1% to 42.9% by 1 year. However 11.4% deteriorated in GOSE. Only 28.1% of individuals returned to the same pre-morbid level of work by 10 weeks, improving to 45.9% at 1 year. Over a quarter (25.6%) at 1 year were unable to make any return to work or study. Several demographic and injury variables were associated with these outcomes including TBI severity, social class, past psychiatric history and alcohol intoxication. These may allow targeting of vulnerable individuals.**Conclusions:** In a largely representative TBI population including predominantly mild injury, there is still considerable functional disability at 1 year and many individuals are unable to make any return to pre-morbid vocation.

1. Introduction

One of the most common emergencies in neurosurgery is Traumatic Brain Injury(TBI) which is a major cause of worldwide disability and mortality especially in the young [1–3]. It represents a significant public health problem with long lasting repercussions for individuals and their families [4]. The management of TBI and the education of affected individuals and their families, requires an accurate knowledge of the long-term outcomes and prognosis after injury; few individuals report complete symptom resolution [5]. A prediction of outcome would also allow better planning of future care needs and development of TBI services. Given the increasing incidence of TBI, particularly in the developing world, there is a need for reporting of long-term outcomes in order to inform the planning of future services [1,6].

A number of important studies have examined TBI outcomes and the proportion achieving a good response varies considerably. This field is

fraught with pitfalls which can make comparison difficult. Outcome can be measured in many different ways with a variety of measures across health domains e.g. impairment, activity limitation or participation restriction.[8] Studies are often subject to selection bias e.g. young victims or only severe/moderate TBI, ignoring the fact that the majority of injuries are mild. Furthermore, TBI studies are notorious for their attrition of patients to follow-up with up to 70% of cases lost at 6 months[9] resulting in poor representation of the adult TBI population. There is therefore a clear need for further large, prospective, well-designed follow-up studies as many have advocated,[3,6–7] ideally in a non-selected TBI population that is as representative as is possible, of those admitted with the condition [1].

The lack of local neurosurgical expertise or specialist rehabilitation in many areas is likely to affect TBI outcome.[10,11] Post-injury care is often fragmented with a wide range of different specialties involved; patients often end up in the specialty of what is considered the most

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significant injury[12] and TBI often falls in the background to more significant orthopaedic or visceral injury. It has been shown that early rehabilitation input improves the management of TBI[13] and that coordination of an appropriate TBI pathway can improve the medium to long-term outcome and decreased length of stay.[12,14,15] The importance of a “continuous chain” of specialised rehabilitation has been recognised and shown to benefit patients [14,16,17].

In our region (in the North of England), the creation of a new Brain Injury Service facilitated the improved management and coordination of TBI healthcare in 2009.[18] In particular the earlier surveillance of admissions with TBI, afforded the opportunity for Rehabilitation Medicine services to be involved in early management, advice and support for families. Importantly, it also presented the opportunity to follow-up patients, most of whom were previously discharged without any TBI follow-up. Multidisciplinary care in a specialised rehabilitation setting, is known to improve health outcomes [19,20] and it has been shown that follow-up of even mild TBI can reduce long-term symptoms and improve outcomes. [12,21] Hence a key part of the new service was a brain injury clinic to review patients after injury, offer support to patients and family and organise any further treatment or referrals.

While it is important to establish the effect of such neurorehabilitation pathways, this is difficult as traditional randomised controlled trials would not be considered ethical in providing specialised rehabilitation after TBI.[22] Comparison with historical data prior to a pathway creation is possible and has been shown to provide a benefit.¹⁴ However this does not account for recent changes in medical management and resuscitation techniques that may be responsible for changes in outcome.^{1,23}

While it was therefore not possible to prove that the new pathway had improved mortality or other outcomes directly, it did allow the follow-up of a large prospective cohort; the Sheffield Brain Injury after Trauma (SHEFBIT). This constitutes a TBI population admitted with TBI of all severities, ages and aetiologies. We believe that it represents a true depiction of TBI as seen and treated by clinicians and can help to guide professionals and inform patients. As such, it constitutes a “real-world” pathway and is relevant to anyone who has an interest in TBI. Reviews have often called for such pragmatic and realistic studies to demonstrate the outcomes of TBI and effects of any interventions [1].

Our aim was to record the 1 year outcome of TBI and any associations with other variables. We now report on this outcome from the first four years of data collection from the pathway (2011–2015).

2. Patients and methods

2.1. Clinical pathway/population

The design of the TBI clinical pathway has been described previously [12] and was initiated in 2009 to try and reduce the variations in quality of care that patients with TBI received. The brain injury team oversee the care of all admitted TBIs. It facilitates transfers between appropriate services involved in the management of trauma, ensures assessment by all relevant specialists and importantly, arranges follow-up after discharge.

The resulting SHEFBIT (Sheffield Brain Injury after Trauma) cohort is a large prospective group of adult patients admitted by the Emergency Department(ED) in a large teaching hospital in the United Kingdom. Data collection started in August 2011 and patients admitted up to July 2015 were screened for inclusion. All participants had a CT head scan and at least one day as in-patient. Decisions about admission and monitoring were decided by NICE (National Institute for Health and Care Excellence) Guidelines (January 2014) This included neurosurgical review or intervention. [24] Exclusions were for previous TBI requiring hospital treatment, age < 17, dementia or out of area for follow-up. Age was no bar to inclusion thus generating as representative a TBI population as possible. Common Data Elements criteria were used to make a TBI diagnosis. [25] TBI severity was based on the GCS in the

ED rather than at scene.

Follow-up appointments were arranged for 9–10 weeks after injury in a Neurorehabilitation Brain Injury clinic. Attendance was encouraged by letters, a text message and a phone call from clinic staff to patients. Those who failed to attend, were called to encourage attendance and re-appointed. This process was repeated at one year follow-up. The same clinician (RS) saw all patients. Information on demographic features such as employment and gender and injury factors such as GCS and aetiology, were recorded. Psychiatric history was operationally defined as a psychiatric condition or taking medication for a diagnosed psychiatric condition. A record of alcohol intoxication was taken from admission records.

The Trauma Audit and Research Network (TARN) classification was used for mechanism of injury; this lists falls, assault, road traffic collisions (RTC) and “other” mechanisms (work site injuries or falls over 2 m.[26] CT scans were graded by the “overall appearance” system which grades the distribution of CT abnormalities after TBI; these are classed as normal, mild focal injury(one cerebral lobe), medium focal injury(two adjacent cerebral lobes) and diffuse injury.[27] Medical comorbidity was defined by a Cumulative Illness Rating Scale > 10 (CIRS)[28] establishing significant level of comorbidity. The National Statistics Socio-Economic Classification (NS-SEC) [29] was used to classify socioeconomic class. The pre-injury employment status was recorded as those working (including full-time students), unemployed or retired.

The study was approved by both the Hospital Trust and the University of Sheffield Ethics Committees (STH16208).

2.2. Outcome measures

2.2.1. GOSE

The primary outcome measure was the Extended Glasgow Outcome Scale (GOSE).[30] This is the most commonly used primary outcome measure after TBI[31] and the extended scale has been shown to improve distinction between outcome groups and improved differentiation of outcomes.[32] Assessment was by means of a structured clinical interview by a single investigator (RS) to minimise misclassification. To address the small numbers falling into the vegetative state outcome, this level was grouped with severe lower.

There is excellent correlation of GOSE with functional outcomes, measures of injury severity and mood scales. [32] There is also excellent correlation with cognitive scores and neurological examination [33] and between GOSE at discharge and at five to seven years after injury.[34]

2.3. Return to work

Work status at follow-up was ascertained at interview and recorded in three categories; unable to work, partial return to work and a complete return to work or the capacity for work for those who were retired or unemployed. Students were similarly assessed as complete, partial or no return to study.

2.4. Other measures

Patients also completed a Rivermead Head Injury Follow-up Questionnaire and a Rivermead Post-concussion Symptom Score. The former is a ten item participation measure⁸ for psychosocial function after TBI and the latter is a commonly used checklist of sixteen common head injury symptoms. Both are graded in Likert style from 0 to 4 and both have been validated in TBI populations, showing good psychometric properties.[35,36]

Depression and anxiety were assessed using the HADS (Hospital Anxiety and Depression Scale) [37] which has 14 questions in total for both anxiety and depression and produces an overall score of 0–21 for each. This is validated in TBI populations for a score > 8 identifying

depression[38] and a score > 11 as a level signifying severe depression. [38,39]

2.5. Statistics

The results are largely descriptive and presented as frequencies with percentages. Numerical data is presented as mean and standard deviation when approximating to normal distribution or median and range otherwise. With GOSE and Return to Work as ordinal dependent variables, comparison with other variables is made as follows; for binary independent variables (ethnicity, gender, comorbidity, alcohol intoxication, psychiatric history) a Mann-Whitney test was applied; for nominal independents with > 2 categories (aetiology, social support level, pre-injury employment), a Kruskal-Wallis test was applied; for ordinal independent variables (severity, social class, CT scan abnormality) a Kendall- τ was applied as appropriate. Outcome questionnaire scores (RHFUQ, RPCS and HADS) at 10 weeks and 1 year were compared with a Wilcoxon Signed Ranks test as normal distributions could not be assumed. Significance level was $p < 0.05$ and all statistical analyses were performed using version 23 of SPSS.

3. Results

3.1. Population and injury features

Over a four year period (2011 to 2015) a total of 1934 cases with TBI were admitted via the Emergency Department. Exclusions (209 cases) were made for dementia, previous TBI with admission and residence out of area. In 319 cases, the initial diagnosis of TBI could not be confirmed from detailed history. After these exclusions, 1406 individuals had follow-up appointments at 8–10 weeks, of whom 1322 attended their initial appointment. All of these individuals were then followed up at one year as well. At one year there were 60 deaths; 115(8.7%) cases were lost to follow-up despite repeated phone calls, letters and text messages. These individuals lost to one year follow-up, were older by 3.9 years and had slightly lower symptom and participation restriction scores at 10 weeks but there were no other significant differences to the remaining 1147 cases who attended follow-up. Including deaths, this final study population corresponds to a total of 1207 cases with a primary outcome measure at one year, representing a one year follow-up of 91.3% (Fig. 1).

The mean age of the cohort was 46.7 years (SD 20.6); median age was 45.6 (range 17.7–94.1 yrs). Women were older and had less severe TBI with a higher proportion of falls. The majority of the cohort were in employment and there was slight underrepresentation of higher socioeconomic classes compared to the national population in the 2011 census.(Table 1).

Length of stay had a strong positive skew towards short periods of stay as many admissions were overnight stays only. Indeed 86.3% of admissions were < 10days. Median length of stay was 2 days (range 1–163).

Table 2 depicts the injury features; falls and RTC were the most common causes of TBI. Injury severity classified by GCS, was predominantly mild injury; 651 (49.2%) had mild TBI, 448(33.9%) moderate TBI and 223(16.9%) had severe TBI. This represents a closer approximation to the real-life distribution of TBI than many other studies.

Almost 40% of admissions had a normal CT scan; only 6.7% showed widespread or diffuse scan changes (Table 2).

3.2. Outcomes

The primary outcome was the Extended Glasgow Outcome Scale and is shown in Table 3 for both time-points. There was an improvement in outcome scores over this time period with fewer individuals falling into severe disability(SD) outcome and a higher proportion attaining a good recovery(GR). In total, 609 individuals improved their

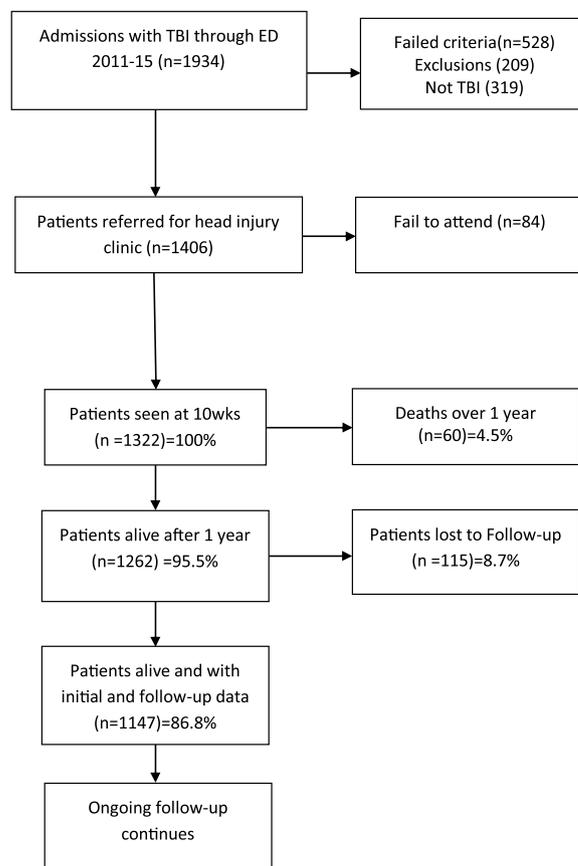


Fig. 1. Study patients and follow-up numbers. Lost numbers and failed criteria explained in text.

GOSE (50.5%). The majority of these only increased by one level on the scale (441, 36.5%) with the remainder experiencing a rise of more than one level.

There was also a large number of individuals who *deteriorated* in GOSE level (138, 11.4%) although 60 of these were deaths. The remainder stayed at the same GOSE level (460, 38.1%).

Furthermore at one year, GR (combining both upper and lower categories) was only achieved by 42.9% of the cohort with 11.8% still showing SD. No one who was in the Severe Lower group at 10 weeks, had managed to improve into the Good Recovery outcome (either lower or upper). Only ten individuals in the Severe Upper group, managed to improve into the Good Lower or second best outcome. This suggests that very few individuals in the Severe Disability group at 10 weeks, are likely to attain a good recovery. These changes are shown in Table 3 which shows the overall outcome categories at 10 weeks and 1 year but also how each group from 10 weeks, progresses after 1 year.

Correlation coefficients were calculated and exhibited negative associations of GOSE with lower GCS, increasing age, medical comorbidity, lower socioeconomic class, pre-injury unemployment and abnormal CT scan ($p < 0.001$). There was no association to gender, ethnicity, aetiology or social isolation (Tables 1,2)

Return to work also showed a marked improvement from ten weeks to one year (Table 4). However, at one year, only 45.9% of the cohort had returned to fulltime work i.e. the exact same capacity prior to injury but over a quarter of the cohort was still unable to return to any form of work whatsoever. There was an association with increasing injury severity and with aetiology of injury($p < 0.001$). There was no association with gender. Individuals in the professional and management grades were more likely to return to work than those in lower SEC as were those who were unemployed pre-injury.

Scores on the Rivermead Head Injury Follow-up Questionnaire

Table 1
demographic features and association with GOSE at 1 yr. Correlation with Kendall- τ for ordinal data, Kruskal-Wallis for nominal variables (> 2 categories) and Mann-Whitney for binary variables, *significance for $p < 0.05$.

| Variable | Number (%) | GOSE at 1 yr | | | | | | | Correlation with GOSE (Mann-Whitney, Kendall- τ , Kruskal Wallis), p-value |
|------------------------------|------------|--------------|--------------|--------------|----------------|----------------|------------|------------|---|
| | | Dead | Severe Lower | Severe Upper | Moderate Lower | Moderate Upper | Good Lower | Good Upper | |
| Gender | | | | | | | | | |
| Male | 909(68.7) | 36(4.4) | 8(1.0) | 86(10.4) | 199(24.1) | 148(17.9) | 136(16.5) | 213(25.8) | 156724, $p = 0.909$ |
| Female | 413(31.3) | 24(6.3) | 3(0.8) | 45(11.8) | 68(17.8) | 72(18.9) | 80(21.0) | 89(23.4) | |
| Ethnicity | | | | | | | | | |
| White | 1226(92.7) | 58(5.2) | 10(0.9) | 122(10.9) | 249(22.3) | 198(17.7) | 201(18) | 279(25) | 48206, $p = 0.509$ |
| Non-white | 96(7.3) | 2(2.2) | 1(1.1) | 9(10.0) | 18(20) | 22(29.4) | 15(16.7) | 23(25.6) | |
| Socio-economic class | | | | | | | | | |
| Professional | 90 (6.8) | 1(1.2) | 1(1.2) | 9(11.0) | 10(12.2) | 15(18.3) | 12(14.6) | 34(41.5) | 41.36, $p < 0.001^*$ |
| Lower Management | 202 (15.3) | 6(3.3) | 0(0) | 17(9.3) | 31(16.9) | 39(21.3) | 38(20.8) | 52(28.4) | |
| Intermediate | 116 (8.8) | 5(4.8) | 0(0) | 9(8.7) | 20(19.2) | 26(25.0) | 21(20.2) | 23(22.1) | |
| Small employer | 100 (7.6) | 7(8.0) | 0(0) | 9(8.7) | 20(19.2) | 26(25.0) | 21(20.2) | 23(22.1) | |
| Lower Supervisory | 229 (17.3) | 14(6.8) | 1(0.5) | 21(10.2) | 44(21.5) | 34(16.6) | 43(21.0) | 48(23.4) | |
| Semi-routine | 296 (22.4) | 14(5.1) | 3(1.1) | 41(14.9) | 67(24.4) | 45(16.4) | 45(16.4) | 60(21.8) | |
| Routine | 165 (12.5) | 4(2.6) | 4(2.6) | 14(9.3) | 43(28.5) | 23(15.2) | 32(21.2) | 31(20.5) | |
| Never-worked | 67 (5.1) | 9(13.6) | 2(3.0) | 12(18.2) | 19(28.8) | 7(10.6) | 8(12.1) | 9(13.6) | |
| Students | 57 (4.3) | 0(0) | 0(0) | 2(3.7) | 5(9.3) | 13(24.1) | 7(13.0) | 27(50.0) | |
| Pre-injury Employment | | | | | | | | | |
| Working | 889 (67.2) | 8(1.0) | 5(0.6) | 67(8.2) | 198(24.3) | 160(19.7) | 138(17.0) | 238(29.2) | 54.10, $p < 0.001^*$ |
| Unemployed | 185 (14.0) | 5(2.9) | 3(1.7) | 44(25.6) | 46(26.7) | 28(16.3) | 29(16.9) | 17(9.9) | |
| Retired | 248 (18.8) | 47(21.3) | 3(1.4) | 20(0.9) | 23(10.4) | 32(14.5) | 49(22.2) | 47(21.3) | |
| Medical Comorbidity | | | | | | | | | |
| Yes | 369 (27.9) | 51(15.0) | 3(0.9) | 42(12.3) | 66(19.4) | 52(15.2) | 63(18.5) | 64(18.8) | 119365, $p < 0.001^*$ |
| No | 953 (72.1) | 9(1.0) | 8(0.9) | 89(10.3) | 201(23.2) | 168(19.4) | 153(17.7) | 238(27.5) | |
| Social isolation | | | | | | | | | |
| Yes | 518 (39.2) | 24(5.1) | 6(1.3) | 56(12.0) | 106(22.6) | 87(18.6) | 77(16.5) | 112(23.9) | -0.014, $p = 0.629$ |
| No | 776 (58.7) | 28(3.9) | 4(0.6) | 68(9.5) | 159(22.2) | 132(18.4) | 137(19.1) | 189(26.4) | |
| Nursing Hme | 28 (2.1) | 8(36.4) | 1(4.5) | 7(31.8) | 2(9.1) | 1(4.5) | 2(9.1) | 1(4.5) | |

(RHFUQ) and Rivermead Post-Concussion Symptoms Score(RPCS) also showed improvement over the time period (Table 5). However these scores still represent a considerable level of impairment and participation restriction even at one year. The RHFUQ dropped from 15.1(SD10.7) to 11.1 (SD 9.5) and the RPCS dropped from

18.7(SD12.6) to 14.6 (SD 11.3) at one year. ($p < 0.001$)

Anxiety and depression scores on the HADS remained high although had dropped from 10 weeks. Using the established cut-off score of > 8, 48.1% demonstrated clinically significant levels of depression and 48.9% for anxiety at 10 weeks. This dropped to 36.8% and 36.5%

Table 2
Injury features and association with GOSE at 1 yr. Correlation with Kendall- τ for ordinal data, Kruskal-Wallis for nominal variables (> 2 categories) and Mann-Whitney for binary variables, *significance for $p < 0.05$.

| Variable | Number at 10wks | GOSE at 1 yr | | | | | | | Correlation with GOSE (Mann-Whitney, Kendall- τ , Kruskal Wallis), p-value |
|-----------------------------|-----------------|--------------|--------------|--------------|----------------|----------------|------------|------------|---|
| | | Dead | Severe Lower | Severe Upper | Moderate Lower | Moderate Upper | Good Lower | Good Upper | |
| Severity | | | | | | | | | |
| Mild($GCS > 12$) | 651 (49.2) | 20(3.3) | 1(0.2) | 38(6.3) | 88(14.7) | 109(18.2) | 129(21.5) | 215(35.8) | -0.352, $p < 0.001^*$ |
| Moderate ($8 < GCS < 13$) | 448 (33.9) | 29(7.1) | 3(0.7) | 43(10.5) | 116(28.4) | 75(18.4) | 67(16.4) | 75(18.4) | |
| Severe($GCS < 9$) | 223 (16.9) | 11(5.5) | 7(3.5) | 50(25.1) | 63(31.7) | 36(18.1) | 20(10.1) | 12(6.0) | |
| Aetiology | | | | | | | | | |
| Fall | 469 (35.5) | 49(11.6) | 5(1.2) | 46(10.9) | 65(15.4) | 72(17.0) | 79(18.7) | 107(25.3) | 0.014, $p = 0.627$ |
| RTC | 368 (27.8) | 5(1.5) | 3(0.9) | 33(9.9) | 76(22.7) | 67(20.0) | 61(18.2) | 90(26.9) | |
| Assault | 235 (17.8) | 1(0.5) | 1(0.5) | 21(9.8) | 81(37.7) | 35(16.3) | 35(16.3) | 41(19.1) | |
| Sport | 80 (6.1) | 0(0) | 1(1.3) | 5(6.5) | 9(11.7) | 12(15.6) | 13(16.9) | 37(48.1) | |
| Other | 170 (12.9) | 5(3.2) | 1(0.6) | 26(16.6) | 36(22.9) | 34(21.7) | 28(17.8) | 27(17.2) | |
| Alco Intox | | | | | | | | | |
| Yes | 325 (24.6) | 7(2.3) | 1(0.3) | 42(13.9) | 113(37.3) | 55(18.2) | 43(14.2) | 42(13.9) | 108483, $p < 0.001^*$ |
| No | 997 (75.4) | 53(5.9) | 10(1.1) | 89(9.8) | 154(17.0) | 165(18.3) | 173(19.1) | 260(28.8) | |
| Psych Hx | | | | | | | | | |
| Yes | 255(19.3) | 12(5.1) | 1(0.4) | 65(27.4) | 89(37.6) | 30(12.7) | 25(10.5) | 15(6.3) | 64208, $p < 0.001^*$ |
| No | 1067(80.7) | 48(4.9) | 10(1) | 66(6.8) | 178(18.4) | 190(19.6) | 191(19.7) | 287(29.6) | |
| CT Lesions | | | | | | | | | |
| NAD | 506 (38.3) | 14(3) | 1(0.2) | 32(6.8) | 71(15) | 79(16.7) | 103(21.8) | 172(36.4) | -0.350, $p < 0.001^*$ |
| Mild | 253 (19.1) | 8(3.6) | 0(0) | 14(6.3) | 40(17.9) | 45(20.1) | 50(22.3) | 67(29.9) | |
| Moderate | 475 (35.9) | 31(7.3) | 7(1.6) | 63(14.8) | 122(28.7) | 81(19.1) | 60(14.1) | 61(14.4) | |
| Diffuse | 88 (6.7) | 7(8.1) | 3(3.5) | 22(25.6) | 34(39.5) | 15(17.4) | 3(3.5) | 2(2.3) | |

Table 3
changes in GOSE at 10 weeks and 1 year.

| GOSE 10wks | GOSE 1 yr (% from GOSE 10wks) | | | | | | | Total GOSE 10wks (%) |
|----------------------------|-------------------------------|--------------|--------------|----------------|----------------|------------|------------|----------------------|
| | Dead | Severe Lower | Severe Upper | Moderate Lower | Moderate Upper | Good Lower | Good Upper | |
| VS | 0(0) | 2(100) | 0(0) | 0(0) | 0(0) | 0(0) | 0(0) | 2 (0.2) |
| Severe Lower | 4(13.8) | 5(17.2) | 14(48.3) | 6(20.7) | 0(0) | 0(0) | 0(0) | 29 (2.4) |
| Severe Upper | 17(7.0) | 3(1.2) | 94(38.7) | 105(43.2) | 13(5.3) | 10(4.1) | 1(0.4) | 243(20.1) |
| Moderate Lower | 20(5.5) | 1(0.3) | 18(5) | 126(34.7) | 119(32.8) | 59(16.3) | 20(5.5) | 363(30.1) |
| Moderate Upper | 9(3.4) | 0(0) | 4(1.5) | 24(9) | 73(27.3) | 98(36.7) | 59(22.1) | 267(22.1) |
| Good Lower | 6(3.6) | 0(0) | 1(0.6) | 3(1.8) | 11(6.6) | 43(25.7) | 103(61.7) | 167(13.8) |
| Good Upper | 4(2.9) | 0(0) | 0(0) | 3(2.2) | 4(2.9) | 6(4.4) | 119(87.5) | 136(11.3) |
| Total GOSE 1 yr (%) | 60(5) | 11(0.9) | 131(10.9) | 267(22.1) | 220(18.2) | 216(17.9) | 302(25) | 1207 |

respectively after 1 year. While this was a statistically significant drop ($p < 0.001$) for both domains, this still represents a high level of emotional distress. If a further cut off score ≥ 11 is used to represent very severe cases, the corresponding figures for depression and anxiety were 32.7% and 36.8% at 10 weeks and reduced to 21.8% and 25.3% at one year.

4. Discussion

This is the largest prospective single centre study that we are aware of, using face to face interviews. There were 1322 cases with data at 10 weeks and 1207 successfully followed up at one year with a follow-up proportion of 91.3% which represents very successful retention rate. TBI studies are notorious for their high attrition rate with as many as 70% lost by six months.[9] This leads to systematic bias in most TBI studies. This was overcome by chasing patient follow-up. While any recruited population is prone to biased selection or institutional effects, we have tried to recruit a cohort that is largely representative of adults admitted with TBI and of relevance to all clinicians working in the field.

Over the course of a year, while there were substantial improvements in many patients, there was still a considerable degree of remaining disability even in those with mild TBI (MTBI) or a normal CT scan. At the same time many individuals with severe TBI (STBI) showed marked improvements with several reaching a full or Good Recovery group status. This highlights the difficulty in predicting outcome based

purely on TBI severity.

Research in TBI is often confounded by the many ways of defining and hence measuring TBI outcome. We have used a number of indicators across various domains of function, participation restriction and activity limitation which are consistent with the ICF (International Classification of Functioning).[8] The primary outcome measure was GOSE which is recognised as the most common TBI outcome measure. [31,32] This is a composite measure of overall global function, including as it does, elements of physical impairment, activity limitation and participation restriction. The GOSE can be considered a “real life” outcome measure. While some have considered the GOSE relatively insensitive to change, particularly in MTBI,[40] this was not our experience in this study. There was considerable movement across levels although 37% retained the same status as at 10 weeks. Indeed 11.4% showed a drop in their functional status on the GOSE indicating the delayed or ongoing effects of TBI which may reach their maximal effect sometime after the injury. This is often true of behavioural sequelae.⁷

Other studies have reported that long term outcomes often show little improvement with similar levels of disability up to 7 years after injury.[41–43] Others have shown a plateauing of recovery after 2 years.[44–46] The largest multicentre report of GOSE found deterioration in scores after 5 years [47] or even 10 years.[48] We intend to continue follow up to ascertain the nature of long-term change beyond 1 year.

The proportion who experienced good recovery increased from

Table 4

return to work and association with variables of interest; Correlation with Kendall- τ for ordinal data, Kruskal-Wallis for nominal variables (> 2 categories) and Mann-Whitney for binary variables, *significance for $p < 0.05$.

| Variable | Number at 1 yr | Return to Work | | | Correlation with GOSE (Mann-Whitney, Kendall- τ , Kruskal Wallis), p-value |
|-----------------------|-----------------------|----------------|-----------|-----------|---|
| | | Full | Partial | None | |
| Severity | Mild (580) | 345(59.5) | 149(25.7) | 86(14.8) | -0.284, $p < 0.001^*$ |
| | Moderate(379) | 147(38.8) | 123(32.5) | 109(28.8) | |
| | Severe(188) | 34(18.1) | 55(29.3) | 99(52.7) | |
| Gender | Male(790) | 348(44) | 237(30) | 205(25.9) | 160987, $p = 0.108$ |
| | Female(357) | 178(49.9) | 90(25.2) | 89(24.9) | |
| Aetiology | Fall(374) | 189(50.5) | 105(28.1) | 80(21.4) | 20.23, $p < 0.001^*$ |
| | RTC(330) | 151(45.7) | 89(27.0) | 90(27.3) | |
| | Assault(214) | 76(35.5) | 79(36.9) | 59(27.6) | |
| | Sport(77) | 50(64.9) | 13(16.9) | 14(18.2) | |
| | Other(152) | 60(39.5) | 41(27.0) | 51(33.6) | |
| NS-SEC | Professional(91) | 46(56.8) | 21(25.9) | 14(17.3) | 13.08, $p < 0.001^*$ |
| | Lower Manager(177) | 89(50.3) | 54(30.5) | 34(19.2) | |
| | Intermediate(99) | 45(45.5) | 31(31.3) | 23(23.2) | |
| | Small Employer(80) | 31(38.7) | 28(35) | 21(26.3) | |
| | Lower Supervisor(191) | 90(47.1) | 49(25.7) | 52(27.2) | |
| | Semi-routine(261) | 108(41.4) | 68(26.1) | 85(32.6) | |
| | Routine(147) | 63(42.9) | 43(29.3) | 41(27.9) | |
| | Never worked(57) | 18(31.6) | 17(29.8) | 22(38.6) | |
| Student(54) | 36(66.7) | 16(29.4) | 2(3.7) | | |
| Pre-injury Employment | Employed(806) | 380(47.1) | 237(29.4) | 189(23.4) | 29.19, $p < 0.001^*$ |
| | Unemployed(167) | 44(26.3) | 52(31.1) | 71(42.5) | |
| | Retired(174) | 101(58.0) | 39(22.4) | 34(19.5) | |

Table 5
outcome questionnaires at 10 weeks and 1 yr. Comparison with Wilcoxon Signed Ranks Test. RHFUQ Rivermead Head Injury Follow-up Questionnaire, RPCS Rivermead Post-concussion Score, HADS Hospital Anxiety and Depression Scale, GOSE Extended Glasgow Outcome Scale.

| Variable | Mean value(SD) at 10 weeks | Mean value(SD) at 1 yr | Wilcoxon Signed Ranks, z-score, p- value |
|-----------------------|-------------------------------|---------------------------|--|
| RHFUQ | 14.9(10.6) | 11.1(9.5) | -15.18, p < 0.001 |
| RPCS | 18.8(12.5) | 14.6(11.3) | -11.94, p < 0.001 |
| HADS-A | 8.14(5.40) | 6.36(5.27) | -12.68, p < 0.001 |
| HADS-D | 7.48(5.20) | 5.89(5.16) | -11.95, p < 0.001 |
| GOSE (excl deaths) | 5.57(1.34) | 6.23(1.40) | -18.83, p < 0.001 |

25.1% to 42.9% by one year. In the same time 4.5% (60) of the cohort had died. Given that almost 50% of individuals sustained MTBI, the relatively small proportion who managed the highest recovery was perhaps disappointing. The short mean length of stay also reflects the relatively "mild" nature of injury. This low overall proportion, highlights the repercussions for individuals, families and for society as more than half of individuals even with MTBI, exhibit considerable change to their previous level of function.

An important finding was that no individuals from the lowest outcome group (SL) at 10 weeks, moved into the good recovery group, either lower or upper. Only one individual moved from the second lowest outcome at 10 weeks (SU) into the best group (GU) and 4.1% moved into the GL outcome. It is therefore very unlikely that anyone in the Severe Disability group at 10 weeks, is going to show good recovery after 1 year.

In terms of demographic or injury features that were associated with GOSE, we found that GCS, age, CT scan abnormality, socioeconomic class, pre-injury employment, past psychiatric or medical illness and alcohol intoxication all showed an association with outcome.

While other studies have also found associations with TBI severity, [4,14,49] negative associations have also been shown.[5,41,50] Increasing TBI severity affects self-awareness or the ability to judge one's own limitations or impairment. It is suggested that those with severe injury, may over-rate their recovery and report fewer problems [51] which may explain some of the disparity between studies.

The relationship between age and worse outcome, has been noted previously.[23,43] After many decades of improving mortality rates in TBI, the relative stagnation in mortality rates in recent years has been attributed to the ageing population pyramid and the increased proportion of TBI in the elderly.[1]

Association with CT findings has only been shown after STBI[52] and in general, CT modelling provides poor predictions of outcome[53] Classification systems for CT scans such as the Marshall system, are focussed mainly on STBI and the need for neurosurgical intervention. [52,54] They are poor across the whole TBI spectrum, most of which are MTBI. Our use of the "overall appearance" method allows description across the full TBI spectrum and is the first report that we are aware of that shows a clear association of CT abnormality and one year global outcome across a mixed TBI group. The development of a true predictive model based on CT scans remains a "holy grail" in TBI management but probably requires the development and availability of better radiological methods.

It was equally important in this study, to note the features that did not show an association with outcome e.g gender, ethnicity, injury aetiology and social isolation. Other studies however, have reported a link with such features.[55,56]

The poor outcome for many individuals was also clearly reflected in the other main outcome measure which was return to work(RTW). This was assessed as the capacity to work including voluntary or unpaid work and was compared against the previous capacity to work for those

who were unemployed or retired. This could therefore be equally applied to those who were retired as it considered the capacity to work in terms of a return to previous physical and cognitive levels.

RTW is one of the most important contributors to successful rehabilitation and reintegration [57,58] It was therefore disappointing that in this group, a large proportion of individuals did not return to work fully, with 25% managing no work whatsoever. The outcome was related to injury severity as well as to employment status prior to injury. It was also interesting that there was an association with socio-economic class(SEC) as derived from employment type and professional group.[29] Interestingly, others have found an inverse link with SEC. [59]

Our results are broadly within the limits of previous studies although much of the literature is focussed on highly selective populations of STBI or young individuals. Furthermore, studies differ in their definition of "return to work"; some consider even a partial return as a successful outcome. The rate of unemployment can be as high as 61% in the large TBIMS cohort [58] and generally studies in STBI show less likelihood of RTW.[6,22,60] A systematic review reported an overall rate of 41% employed. [61] Relationships to TBI severity, age and previous disability have been demonstrated previously. [3,22,38,49,58,60,62] In a study of mild-moderate TBI, everyone returned to work although a quarter were part-time. [5] No one else has found comparable rates of return. It has also been shown that RTW can fluctuate considerably with time and it is likely to be a dynamic variable.[63] It is therefore important to continue to follow this cohort in order to document further changes or fluctuations in employment status.

Outcome was also measured in the form of a symptom checklist (Rivermead Post Concussion Score) and a measure of participation restriction(Rivermead Head Injury Follow-up Questionnaire). These showed improvement over a year but still represented quite high levels of disability. In many cases, the highest levels of symptoms were often reported in those with MTBI and normal CT scans; we have noted the higher levels of depression in those with normal CTs compared to mild scan abnormality.[64] It has been shown that up to 25% of individuals have long term disability and symptoms after MTBI and have been described as the "miserable minority".[65] Interventions aimed at support of this group are a pressing requirement in TBI care. It has also been found that those with the best outcome can sometimes report the most unmet need requiring intervention.[43] It has even been reported that scores on RPCS can increase after one year although this was not our experience.[50] Similar results were also shown with measure of psychosocial distress in the form of the HADS. Both anxiety and depression scores reduced over one year but still represented a very high level of these conditions at one year (> 40%). Even at the higher cut-off value on the test, the levels of severe depression and anxiety were > 20%.[64]

We have successfully shown the ability of a dedicated Service to identify and survey most adult admissions with TBI and to successfully follow up patients with minimal loss. This is an impressive achievement in itself. This is likely to be the most comprehensive means of case capture with active seeking out of cases rather than waiting for referrals or examination of databases and medical coding. The service was set up to coordinate the care of TBI admissions, provide support to the individuals and their family, to detect post-injury complications and to address specific problems by means of appropriate follow-up. In terms of the numbers of TBI cases that one would expect in the regional population(400,000), it would seem that the majority of these have been identified by the pathway and followed up at clinic. Again this is an impressive feat. A similar service also in the UK reported a likely follow-up rate of only 3% of likely TBIs[68] and a multicentre study of STBI, identified only 1/3 of likely cases[69] There is clearly considerable unrecognised or unmet need and the recognition of this is an important step in informing purchasers and health providers.[4,47]

Recent research in a number of Scandinavian centres has

demonstrated the use of a “continuous chain” of rehabilitation to improve TBI outcomes and shows clear benefit for dedicated rehabilitation pathways.[17,43,45] These studies also report that a very high proportion of individuals (upto 80%) are receiving ongoing rehabilitation even after one year. This perhaps reflects the success of universal health care coverage and provision in such countries. Unfortunately such provision is much less frequent in the UK despite a similar health care system based on need rather than payment.

Comparison of our results to other literature is important but there is considerable variation across studies making it difficult to draw parallels.

Many studies focus on moderate-severe TBI and the proportion identified with Good Recovery at one year ranges from 1.3% [70] up to 74%.[23,42–45,60,66,67,71–73] Even in a pure STBI group, 46% can show GR.[16] Others have found little change in GOSE after 5–7 years.[41,43,47,57] Even in pure STBI studies, using a dichotomised outcome of good/bad, studies show a wide range of good outcome between 7–64%.[16,22,60,66,69] Our findings suggest that even many with MTBI have poor outcome but that injury severity was strongly associated to global outcome. Studies show a number of other associations with injury or demographic features but there is no consistent agreement between studies and it is difficult to make any conclusions as to the features that predict outcome.[2,60,66]

Such results highlight the fact that prediction of long term outcome is very difficult. Predictive TBI models have largely focussed on acute prognosis and the need for neurosurgery, or on mortality[73,74] but these show poor correlation at one year with GOSE [60] The problem with long term modelling is that psychological and social factors will become more significant than initial injury features over time.[6,43,50] In general, attempts to model outcome in the long term have had mixed results with a low proportion of variance attributable to the model even for GCS or CT abnormality.[16,23,66] It is hoped that data from this cohort can also be modelled and we hope to report this shortly without dichotomising the outcome and hence oversimplifying outcome into good and bad.[74] Such results may provide helpful but realistic information for patients, relatives and for service development, leading to better guidelines [75].

There are a number of particular strengths of this study. This includes the large number of prospective TBI admissions followed from the date of injury onwards. While all study populations are prone to some form of recruitment bias, this population had minimal exclusions and therefore better represents the true spectrum of adult TBI including elderly patients. Some studies look at very select groups e.g. medicolegal cases or only RTC. [49,60] The use of GOSE allows for a consideration of previous disability or work status and measures change since injury which is useful for elderly or those with medical comorbidity. The assessment and consistency of a dedicated brain injury clinic and the ability to chase up and encourage clinic follow-up were undoubted strengths given the attrition in many other studies. The use of patient-reported outcome with community based individuals is another strength. The use of a single observer to assess GOSE removes inter-observer variation although does introduce risk of a systematic bias. A range of outcomes was measured and covers a number of ICF domains. [8]

A number of weaknesses should also be noted. This is a single centre study and the results from one regional population may not be applicable to all other groups. The GOSE has been criticised as relatively insensitive to change and does not differentiate between disability caused by TBI or other injury from trauma. The observer for outcome was not blinded and could be biased. We have not recorded a quality of life measurement nor assessed cognitive function.

In conclusion, we have shown that a specialised rehabilitation service can systematically organise TBI follow-up with minimal losses. Most centres do not arrange routine TBI follow-up. In the context of increasing health costs and economic austerity, it is important to show the value of follow-up. It is known that collaborative effects can

decrease care costs and improve outcomes;[19] it is imperative for accredited programmes to show their value. It is clear from this study, that many individuals continue to suffer poor outcome after TBI and are unable to return to their pre-injury lives. This affects global function, work, levels of psychosocial distress, participation and symptoms. Such loss causes considerable suffering in society and should be the target for intervention by TBI Services.

Declaration of Competing Interest

The authors have no conflicts of interest; no funding was received for this project

References

- [1] B. Roozenbeek, A.I. Maas, D.K. Menon, Changing patterns in the epidemiology of traumatic brain injury, *Nat. Rev. Neurol.* 9 (2013) 231–236.
- [2] J.D. Corrigan, A.W. Selassie, J.A. Orman, The epidemiology of traumatic brain injury, *J. Head Trauma Rehab.* 25 (2010) 72–80.
- [3] L.J. Jacobsson, M. Westerberg, J. Lexell, Health-related quality-of-life and life satisfaction 6–15 years after traumatic brain injuries in northern Sweden, *Brain Inj.* 24 (2010) 1075–1086.
- [4] S.S. Dikmen, J.E. Machamer, J.M. Powell, N.R. Temkin, Outcome 3 to 5 years after moderate to severe traumatic brain injury, *Arch. Phys. Med. Rehabil.* 84 (2003) 1449–1457.
- [5] J. Van der Naalt, A.H. Van Zomeren, W.J. Sluiter, J.M. Minderhoud, One year outcome in mild to moderate head injury: the predictive value of acute injury characteristics related to work complaints and return to work, *J. Neurol. Neurosurg. Psychiatry* 66 (1999) 207–213.
- [6] J.H. Olver, J.L. Ponsford, C. Curran, Outcomes following traumatic brain injury: a comparison between 2 and 5 years after injury, *Brain Inj.* 10 (1996) 841–848.
- [7] M. Rosenthal, B.K. Christensen, T.P. Ross, Depression following traumatic brain injury, *Arch. Phys. Med. Rehabil.* 79 (1998) 90–103.
- [8] G. Stucki, T. Ewert, A. Cieza, Value and application of the ICF in rehabilitation medicine, *Disabil. Rehabil.* 24 (2002) 932–938.
- [9] J.D. Corrigan, J.A. Bogner, J.W. Mysiw, D. Clinchot, L. Fugate, Systematic bias in outcome studies of persons with traumatic brain injury, *Arch. Phys. Med. Rehabil.* 78 (1997) 132–137.
- [10] D. Mellick, K.A. Gerhart, G.G. Whiteneck, Understanding outcomes based on the post-acute hospitalization pathways followed by persons with traumatic brain injury, *Brain Inj.* 17 (2003) 55–71.
- [11] A. Sörbo, B. Rydenhag, K.S. Sunnerhagen, M. Blomqvist, S. Svensson, I. Emanuelson, Outcome after severe brain damage, what makes the difference? *Brain Inj.* 19 (2005) 493–503.
- [12] R. Singh, G. Venkateshwara, J. Kirkland, J. Batterley, S. Bruce, Clinical pathways in head injury: improving the quality of care with early rehabilitation, *Disabil. Rehabil.* 34 (2012) 439–442.
- [13] L. Turner-Stokes, A. Pick, A. Nair, P.B. Disler, D.T. Wade, Multi-disciplinary rehabilitation for acquired brain injury in adults of working age, *Cochrane Database Syst. Rev.* 12 (2015) CD004170.
- [14] A.W. Engberg, A. Liebach, A. Nordenbo, Centralized rehabilitation after severe traumatic brain injury—a population-based study, *Acta Neurol. Scand.* 113 (2006) 178–184.
- [15] F. Khan, L. Turner-Stokes, L. Ng, T. Kilpatrick, Multidisciplinary rehabilitation for adults with multiple sclerosis, *Cochrane Database Syst. Rev.* 2 (2007) CD006036.
- [16] M. Stenberg, L.O. Koskinen, R. Levi, B.M. Stålnacke, Severe traumatic brain injuries in Northern Sweden: a prospective 2-year study, *J. Rehabil. Med.* 45 (2013) 792–800.
- [17] N. Andelic, E. Bautz-Holter, P. Ronning, K. Olafsen, S. Sigurdardottir, A.K. Schanke, U. Sveen, S. Tornas, M. Sandhaug, C. Roe, Does an early onset and continuous chain of rehabilitation improve the long-term functional outcome of patients with severe traumatic brain injury? *J. Neurotrauma* 29 (2012) 66–74.
- [18] R. Singh, G. Venkateshwara, J. Batterley, S. Bruce, Early rehabilitation in head injury; can we improve the outcomes? *Arch. Trauma Res.* 2 (2013) 103–107.
- [19] L. Turner-Stokes, Evidence for the effectiveness of multi-disciplinary rehabilitation following acquired brain injury: a synthesis of two systematic approaches, *J. Rehabil. Med.* 40 (2008) 691–701.
- [20] D.N. Cope, K. Hall, Head injury rehabilitation: benefit of early intervention, *Arch. Phys. Med. Rehabil.* 63 (1982) 433–437.
- [21] C. Paniak, G. Toller-Lobe, S. Reynolds, A. Melnyk, J. Nagy, A randomized trial of two treatments for mild traumatic brain injury: 1 year follow-up, *Brain Inj.* 14 (2000) 219–226.
- [22] N. Andelic, S. Sigurdardottir, A.K. Schanke, L. Sandvik, U. Sveen, C. Roe, Disability, physical health and mental health 1 year after traumatic brain injury, *Disabil. Rehabil.* 32 (2010) 1122–1131.
- [23] R. Raj, S. Bendel, M. Reinikainen, R. Kivisaari, J. Siironen, M. Lång, et al., Hyperoxemia and long-term outcome after traumatic brain injury, *Crit Care* 17 (2013) R177.
- [24] Head Injury Triage, Assessment, Investigation and Early Management of Head Injury in Children, Young People and Adults Issued: January, NICE clinical guideline 176, 2014, guidance.nice.org.uk/cg176.

- [25] D.K. Menon, K. Schwab, D.W. Wright, A.I. Maas, Position statement: definition of traumatic brain injury, *Arch. Phys. Med. Rehabil.* 91 (2010) 1637–1640.
- [26] F. Lecky, M. Woodford, D.W. Yates, Trends in trauma care in England and Wales 1989–97. UK Trauma Audit and Research Network, *Lancet* 355 (2000) 1771–1775.
- [27] J.M. Wardlaw, V.J. Easton, P. Statham, Which CT features help predict outcome after head injury? *J. Neurol. Neurosurg. Psychiatry.* 72 (2002) 188–192.
- [28] T. Chandola, C. Jenkinson, The new UK National Statistics Socio-Economic Classification (NS-SEC); investigating social class differences in self-reported health status, *Hawaii J. Med. Public Health* 22 (2000) 182–190.
- [29] J.T. Wilson, L.E. Pettigrew, G.M. Teasdale, Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use, *J. Neurotrauma* 15 (1998) 573–585.
- [30] E.A. Wilde, G.G. Whiteneck, J. Bogner, T. Bushnik, D.X. Cifu, S. Dikmen, L. French, J.T. Giacino, T. Hart, J.F. Malec, S.R. Millis, T.A. Novack, M. Sherer, D.S. Tulsky, R.D. Vanderploeg, N. von Steinbuechel, Recommendations for the use of common outcome measures in traumatic brain injury research, *Arch. Phys. Med. Rehabil.* 91 (2010) 1650–1660.
- [31] B. Jennett, J. Snoeck, M.R. Bond, Disability after severe head injury: observations on the use of Glasgow Outcome Scale, *J. Neurol. Neurosurg. Psych.* 44 (1981) 285–293.
- [32] J.T. Wilson, P. Edwards, H. Fiddes, E. Stewart, G.M. Teasdale, Reliability of postal questionnaires for the glasgow outcome scale, *J. Neurotrauma* 19 (2002) 999–1005.
- [33] N. Brooks, L. Campsie, C. Symington, The five year outcome of severe blunt head injury: a relative's view, *J. Neurol. Neurosurg. Psychiatry* 49 (1986) 764–770.
- [34] T.L. Massagli, F. Rivara, Association between injury indices and outcome after severe traumatic brain injury in children, *Arch. Phys. Med. Rehabil.* 77 (1996) 125–132.
- [35] S. Crawford, F. Wenden, D.T. Wade, The Rivermead head injury follow-up questionnaire. A study of a new rating scale and other measures to evaluate outcomes after head injury, *J. Neurol. Neurosurg. Psychiatry* 60 (1996) 510–514.
- [36] N. King, Emotional, neuropsychological, and organic factors: their use in the prediction of persisting postconcussion symptoms after moderate and mild head injuries, *J. Neurol. Neurosurg. Psychiatry* 61 (1996) 75–81.
- [37] A. Zigmond, R.P. Snaith, The hospital anxiety and depression scale, *Acta Psych. Scand.* 67 (1983) 361–370.
- [38] J. Dahm, D. Wong, J. Ponsford, Validity of the Depression Anxiety Stress Scales in assessing depression and anxiety following traumatic brain injury, *J. Affect. Disord.* 151 (2013) 392–396.
- [39] N. Dawkins, M.E. Cloherty, F. Gracey, J.J. Evans, The factor structure of the Hospital Anxiety and Depression Scale in acquired brain injury, *Brain Inj.* 20 (2006) 125–139.
- [40] S. Sigurdardottir, N. Andelic, C. Roe, A.K. Schanke, Depressive symptoms and psychological distress during the first five years after traumatic brain injury: relationship with psychosocial stressors, fatigue and pain, *J. Rehabil. Med.* 45 (2013) 808–814.
- [41] L. Whitnall, T.M. McMillan, G.D. Murray, G.M. Teasdale, Disability in young people and adults after head injury: 5-7 year follow up of a prospective cohort study, *J. Neurol. Neurosurg. Psychiatry* 77 (2006) 640–645.
- [42] S. Thornhill, G.M. Teasdale, G.D. Murray, J. McEwen, C.W. Roy, K.I. Penny, Disability in young people and adults one year after head injury: prospective cohort study, *BMJ* 320 (2000) 1631–1635.
- [43] M.V. Forslund, C. Roe, J.C. Arango-Lasprilla, S. Sigurdardottir, N. Andelic, Impact of personal and environmental factors on employment outcome two years after moderate-to-severe traumatic brain injury, *J. Rehabil. Med.* 45 (2013) 801–807.
- [44] L. Ruttan, K. Martin, A. Liu, B. Colella, R.E. Green, Long-term cognitive outcome in moderate to severe traumatic brain injury: a meta-analysis examining timed and untimed tests at 1 and 4.5 or more years after injury, *Arch. Phys. Med. Rehabil.* 89 (2008) S69–S76.
- [45] M. Sandhaug, N. Andelic, B. Langhammer, A. Mygland, Functional level during the first 2 years after moderate and severe traumatic brain injury, *Brain Inj.* 29 (2015) 1431–1438.
- [46] K.M. Jaffe, N.L. Polissar, G.C. Fay, S. Liao, Recovery trends over three years following pediatric traumatic brain injury, *Arch. Phys. Med. Rehabil.* 76 (1995) 17–26.
- [47] J.D. Corrigan, J.P. Cuthbert, C. Harrison-Felix, G.G. Whiteneck, J.M. Bell, A.C. Miller, V.G. Coronado, C.R. Pretz, US population estimates of health and social outcomes 5 years after rehabilitation for traumatic brain injury, *J. Head Trauma Rehabil.* 29 (2014) E1–9.
- [48] C.R. Pretz, K. Dams-O'Connor, Longitudinal description of the Glasgow Outcome Scale-Extended for individuals in the traumatic brain injury model systems national database: a National Institute on Disability and Rehabilitation Research traumatic brain injury model systems study, *Arch. Phys. Med. Rehabil.* 94 (2013) 2486–2493.
- [49] R.L. Wood, N.A. Rutterford, Psychosocial adjustment 17 years after severe brain injury, *J. Neurol. Neurosurg. Psychiatry* 77 (2006) 71–73.
- [50] H.L. Soberg, C. Roe, A. Anke, J.C. Arango-Lasprilla, T. Skandsen, U. Sveen, N. von Steinbuechel, N. Andelic, Health related quality of life 12 months after severe traumatic brain injury: a prospective nationwide cohort study, *J. Rehabil. Med.* 45 (2013) 785–791.
- [51] M. Sherer, P. Bergloff, E. Levin, W.M. High, K.E. Oden, T. Nick, Impaired awareness and employment outcome after traumatic brain injury, *J. Head Trauma Rehabil.* 13 (1998) 52–61.
- [52] A.I. Maas, C.W. Hukkelhoven, L.F. Marshall, E.W. Steyerberg, Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors, *Neurosurgery* 57 (2005) 1173–1182.
- [53] M. Stenberg, L.D. Koskinen, P. Jonasson, R. Levi, B.M. Stålnacke, Computed tomography and clinical outcome in patients with severe traumatic brain injury, *Brain Inj.* 31 (2017) 351–358.
- [54] L.F. Marshall, S.B. Marshall, M.R. Klauber, Clark MvB, H.M. Eisenberg, J.A. Jane, T.G. Luerssen, A. Marmarou, M.A. Foulkes, A new classification of head injury based on computerized tomography, *J. Neurosurg.* 75 (1991) S14–20.
- [55] E. Farace, W.M. Alves, Do women fare worse: a meta-analysis of gender differences in traumatic brain injury outcome, *J. Neurosurg.* 93 (2000) 539–545.
- [56] D.B. Huang, R. Spiga, H. Koo, Use of the Zung depression scale in patients with traumatic brain injury: 1 year post-injury, *Brain Inj.* 19 (2005) 903–908.
- [57] J.D. Corrigan, J.A. Bogner, W.J. Mysiw, D. Clinchot, L. Fugate, Life satisfaction following traumatic brain injury, *J. Head Trauma Rehabil.* 16 (2001) 543–555.
- [58] J.P. Cuthbert, C. Harrison-Felix, J.D. Corrigan, J.M. Bell, C. Miller, Unemployment in the United States after traumatic brain injury for working-age individuals: prevalence and associated factors 2 years postinjury, *J. Head Trauma Rehabil.* 30 (2015) 160–174.
- [59] S. Sigurdardottir, N. Andelic, C. Roe, T. Jerstad, A.K. Schanke, Post-concussion symptoms after traumatic brain injury at 3 and 12 months post-injury: a prospective study, *Brain Inj.* 23 (2009) 489–497.
- [60] K. Draper, J. Ponsford, M. Schonberger, Psychosocial and emotional outcomes 10 years following traumatic brain injury, *J. Head Trauma Rehabil.* 22 (2007) 278–287.
- [61] A. Willemse-van Son, G.M. Ribbers, A.P. Verhagen, H.J. Stam, Prognostic factors of long-term functioning and productivity after traumatic brain injury: a systematic review of prospective cohort studies, *Clin. Rehabil.* 21 (2007) 1024–1037.
- [62] J.L. Ponsford, J.H. Olver, C. Curran, A profile of outcome: two years after traumatic brain injury, *Brain Inj.* 9 (1995) 1–10.
- [63] J.S. Kreutzer, J.H. Marwitz, W. Walker, et al., Moderating factors in return to work and job stability after traumatic brain injury, *J. Head Trauma Rehabil.* 18 (2003) 128–138.
- [64] R. Singh, S. Mason, F. Lecky, J. Dawson, Prevalence of depression after TBI in a prospective cohort: the SHEFBIT study, *Brain Inj.* 32 (2018) 84–90.
- [65] (a) T.M. McMillan, G.M. Teasdale, E. Stewart, Disability in young people and adults after head injury: 12-14 year follow-up of a prospective cohort, *J. Neurol. Neurosurg. Psych.* 83 (2012) 1086–1091; (b) R.M. Ruff, L. Camenzuli, Miserable minority: emotional risk factors that influence the outcome of a mild TBI, *Brain Inj.* 10 (1996) 551–565.
- [66] A.K. Godbolt, M. Stenberg, M. Lindgren, T. Ulfarsson, M. Lannsjö, B.M. Stålnacke, J. Borg, Associations between care pathways and outcome 1 year after severe traumatic brain injury, *J. Head Trauma Rehabil.* 30 (2015) E41–51.
- [67] W.C. Walker, J.S. Ketchum 3rd, J.H. Marwitz, S.A. Kolakowsky-Hayner, D.K. McClish, T. Bushnik, Global Outcome and Late Seizures After Penetrating Versus Closed Traumatic Brain Injury: A NIDRR TBI Model Systems Study, *J. Head Trauma Rehabil.* 30 (2015) 231–240.
- [68] H. Seeley, J. Pickard, J. Allanson, P. Hutchinson, The epidemiology of a specialist neurorehabilitation clinic: implications for clinical practice and regional service development, *Brain Inj.* 28 (2014) 1559–1567.
- [69] C. Jourdan, V. Bosserelle, S. Azerad, et al., Predictive factors for 1-year outcome of a cohort of patients with severe traumatic brain injury (TBI): results from the Paris-TBI study, *Brain Inj.* 27 (2013) 1000–1007.
- [70] S.T. Siponkoski, L. Wilson, N. von Steinbuechel, J. Sarajuuri, S. Koskinen, Quality of life after traumatic brain injury: Finnish experience of the QOLIBRI in residential rehabilitation, *J. Rehabil. Med.* 45 (2013) 835–842.
- [71] M.E. de Koning, J.M. Spikman, A. Coers, M.C. Schönherr, J. van der Naalt, Pathways of care the first year after moderate and severe traumatic brain injury—discharge destinations and outpatient follow-up, *Brain Inj.* 29 (2015) 423–429.
- [72] I. Asikainen, M. Kaste, S. Sarna, Predicting late outcome for patients with traumatic brain injury referred to a rehabilitation programme: a study of 508 Finnish patients 5 years or more after injury, *Brain Inj.* 12 (1998) 95–107.
- [73] (a) C.A. Hawley, S. Joseph, Predictors of positive growth after traumatic brain injury: a longitudinal study, *Brain Inj.* 22 (2008) 427–435; (b) MRC CRASH Trial Collaborators, P. Perel, M. Arango, T. Clayton, P. Edwards, E. Komolafe, S. Pocock, I. Roberts, H. Shakur, E. Steyerberg, S. Yuthakasemsunt, Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients, *BMJ* 336 (2008) 425–429.
- [74] A.I. Maas, G.D. Murray, B. Roozenbeek, H.F. Lingsma, I. Butcher, G.S. McHugh, J. Weir, J. Lu, E.W. Steyerberg, International Mission on Prognosis Analysis of Clinical Trials in Traumatic Brain Injury (IMPACT) Study Group. Advancing care for traumatic brain injury: findings from the IMPACT studies and perspectives on future research, *Lancet Neurol.* 12 (2013) 1200–1210.
- [75] A. Scerrati, S. De Rosa, L. Mongardi, M.A. Cavallo, G. Trapella, P. De Bonis, Standard of care, controversies, and innovations in the medical treatment of severe traumatic brain injury, *J. Neurosurg.* 62 (2018) 574–583.