

RESEARCH ARTICLE

Selecting patients for early interdisciplinary rehabilitation during neurointensive care after moderate to severe traumatic brain injury

Kristin Alvsåker^{1,2}  | Rolf Hanao³ | Theresa M. Olasveengen^{4,5}

¹Postoperative and Intensive Care Department, Oslo University Hospital, Oslo, Norway

²Department of Physical medicine and Rehabilitation, Oslo University Hospital, Oslo, Norway

³Neurosurgical Department, Oslo University Hospital, Oslo, Norway

⁴Department of Anaesthesia and Intensive Care, Oslo University Hospital, Oslo, Norway

⁵Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Correspondence

Kristin Alvsåker, Postoperative and Intensive Care Department, Oslo University Hospital, Postboks 4950 Nydalen, Oslo 0424, Norway.
Email: uxkral@ous-hf.no

Abstract

Background: Early interdisciplinary rehabilitation (EIR) in neurointensive care is a limited resource reserved for patients with moderate to severe traumatic brain injury (TBI) believed to profit from treatment. We evaluated how key parameters related to injury severity and patient characteristics were predictive of receiving EIR, and whether these parameters changed over time.

Methods: Among 1003 adult patients with moderate to severe TBI admitted over 72 h to neurointensive care unit during four time periods between 2005 and 2020, EIR was given to 578 and standard care to 425 patients. Ten selection criteria thought to best represent injury severity and patient benefit were evaluated (Glasgow Coma Scale, Head Abbreviated Injury Scale, New-Injury-Severity-Scale, intracranial pressure monitoring, neurosurgery, age, employment, Charlson Comorbidity Index, severe psychiatric disease, and chronic substance abuse).

Results: In multivariate regression analysis, patients who were employed (adjOR 1.99 [95% CI 1.41, 2.80]), had no/mild comorbidity (adjOR 3.15 [95% CI 1.72, 5.79]), needed neurosurgery, had increasing injury severity and were admitted by increasing time period were more likely to receive EIR, whereas receiving EIR was less likely with increasing age (adjOR 0.97 [95% CI 0.96, 0.98]) and chronic substance abuse. Overall predictive ability of the model was 71%. Median age and comorbidity increased while employment decreased from 2005 to 2020, indicating patient selection became less restrictive with time.

Conclusion: Injury severity and need for neurosurgery remain important predictors for receiving EIR, but the importance of age, employment, and comorbidity have changed over time. Moderate prediction accuracy using current clinical criteria suggest unrecognized factors are important for patient selection.

KEYWORDS

interdisciplinary rehabilitation, neurointensive care unit, selection criteria, traumatic brain injury

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Editorial Comment

In this Norwegian regional study of selection for early interdisciplinary rehabilitation after severe traumatic brain injury, authors identified several independent risk factors that were associated with admission for such rehabilitation during 2005–2020. These included (but were not restricted to) having undergone neurosurgery, a higher New Injury Severity Score, not having chronic substance abuse, having fewer comorbidities, and being younger. The study highlights variables that are associated with selection for highly specialized neurorehabilitation, and which may thus indirectly be perceived by clinicians to predict the rehabilitation potential of the patients.

1 | INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide.¹ The high morbidity and mortality of TBI are linked to the severity of the injury, and the mortality is skewed towards more severe TBI.² Age and preexisting medical conditions also influence outcome.^{3–6} The elderly often have a less physiological reserve capacity making them more prone to poor prognosis even after a less severe TBI.^{2,3,7}

Whether early mobilization in ICU for patients with severe TBI is beneficial or harmful, is still not clear.⁸ Coordinated rehabilitation efforts from several disciplines in ICU, called early interdisciplinary rehabilitation (EIR), have been supported by limited evidence for increased functional outcome in patients with severe TBI in a continuous chain of rehabilitation compared to a broken chain.^{9,10} Despite the uncertainties about the effectiveness of these rehabilitation strategies, various rehabilitation programs are widely implemented during neurointensive care.¹¹ Further, ICU capacity is limited, EIR is resource demanding,¹² and little is known about patient selection.¹³ The selection of patients for EIR in the ICU is complex and influenced by the severity of brain injury, the patients' potential to benefit from treatment, and the availability of resources for EIR at the time.

Patient outcomes are a result of patient characteristics on admission, quality of care and random events.¹⁴ By increasing our knowledge about the patient and injury characteristics associated with receiving EIR and how these may have varied with time, we will get a better understanding of how to improve the quality of care by providing the right treatments to the right patients. Specifically, the aims of the study were to (1) evaluate how key parameters related to injury severity and patient characteristics were predictive of receiving EIR and (2) assess how these parameters may have changed over time.

2 | METHODS

This article adhere to the STROBE guidelines for reports of cohort studies.¹⁵

2.1 | Study design

We conducted a retrospective observational cohort study comparing patients who received EIR (exposed group) to patients who received

standard of care (SC) (control group) after moderate to severe TBI. The patients were recruited from the “Early Interdisciplinary Rehabilitation after Traumatic Brain Injury registry,” established in 2005.

The registry is approved by the local data protection officer, (Approval 19/11590) for the purpose of monitoring quality and improving quality of care, and requirement of informed consent is waived. Cohorts exposed and not exposed to EIR within the TBI population were identified. The project was approved by the advisory board and local data protection office November 12, 2020 (Approval 2020/24438).

2.2 | Study setting

Patients with moderate to severe TBI from the South East region of Norway are admitted to Oslo University Hospital (OUH) for neuroprotective care in neuro-ICU or general surgical ICU. Neuroprotective treatment include neurosurgery and deep sedation, mechanical ventilation, treatment of fever and tracheostomy when prolonged weaning from ventilator is expected.^{16,17} EIR was established in 2005¹⁸ and is given after the patients have survived the immediate neurointensive care and are being weaned from organ support.

Capacity for EIR has increased during the observation period. In 2005, the EIR-team was staffed to treat two patients in the neuro-ICU. After receiving EIR the patients were discharged directly to specialized rehabilitation at a regional rehabilitation hospital. The capacity increased to three patients in 2010, and the patients were increasingly transferred to an intermediate rehabilitation section at Department of Physical medicine and Rehabilitation before further discharge to the rehabilitation hospital. From 2010 patients aged 16–17 years have been admitted to pediatric ICU instead of neuro-ICU and have therefore not been included in the registry. Since 2014, patients over 70 years and those who died in ICU have been included in the registry (Figure 1).

2.3 | Participants

Eligible patients were identified from the EIR-registry, and included if they were (1) admitted between October 10, 2005 and December 31 2020, (2) diagnosed with TBI (ICD-10 diagnoses S06.1-09) occurring within 72 h of hospital admission, (3) aged between 16 and

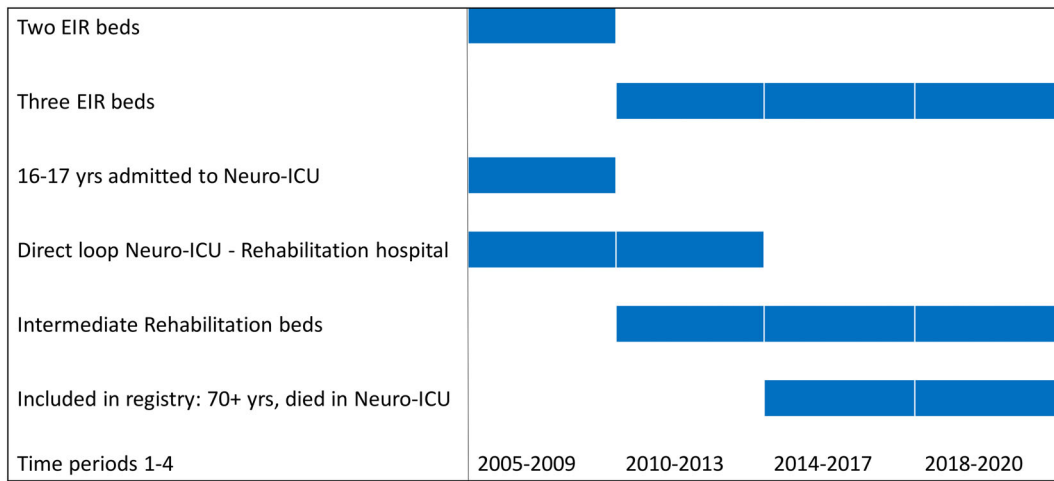
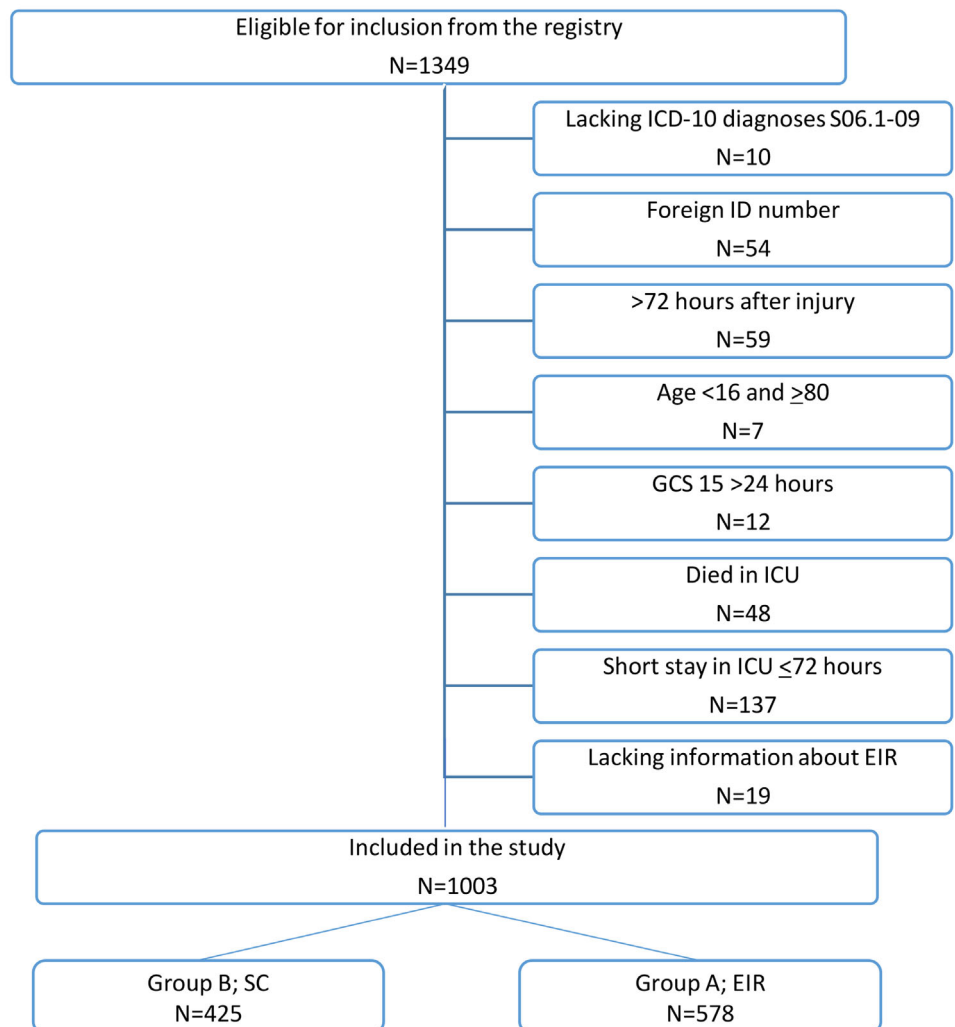


FIGURE 1 Factors influencing the enrollment of patients in the “Early Interdisciplinary rehabilitation after traumatic brain injury” registry at OUH.

FIGURE 2 Patient flowchart illustrating the inclusion and exclusion criteria for this study.



79, (4) had lowest unsedated Glasgow Coma Score (GCS) 3–14 within the first 24 h after injury, (5) survived to ICU discharge, (6) had ICU length of stay >72 h. Patients with incomplete hospital records

(unable to determine exposure to EIR) were excluded. If GCS was 15 before intubation and the patient thereafter deteriorated neurologically within 24 h, a patient with GCS 15 was accepted (Figure 2).

Patients characteristics in excluded patients with a short stay in ICU (24–72 h) are shown in Supplemental Material 1 (Table S1).

2.4 | Description of early interdisciplinary rehabilitation (exposure)

Early interdisciplinary rehabilitation consisted of three elements: (1) guiding and training in activity daily living,¹⁹ (2) physiotherapy focused on positioning, transfers, mobilization of the patient to sitting or standing,²⁰ and (3) stimulation of swallowing and eating/drinking²¹ in a protective environment. The therapeutic efforts were coordinated and individually adjusted by a physiotherapist and occupational therapist. The rehabilitation physician was responsible for the profile of the program and the intensive care nurses for monitoring the patients' vital parameters during the therapeutic sessions. EIR was normally given twice a day with a duration of 45–60 min in each session and started after short-acting opioid infusions (most commonly fentanyl) were discontinued.²²

The control group received SC, which consisted of intensive nurse care 1:1 or the combination of intensive nurse care and physiotherapy. The physiotherapy consisted of passive and individually adjusted active movements of joints, respiratory physiotherapy, and gradually mobilization to sitting on the edge of the bed or standing with support. Physiotherapy was normally given once a day with a duration of 30 min.

2.5 | Selection criteria for EIR

The daily ICU treatment team consisting of a neurosurgeon, anaesthesiologist, and rehabilitation physician used local clinical guidelines to select patients for EIR. Selection criteria included patients (1) being admitted to the neurointensive care unit >72 h after having suffered brain injury sufficient to cause disturbance of consciousness and neurological deficits, (2) believed to have potential benefit from treatment (physiological reserve capacity and compliance), and (3) prioritized for EIR with the resources in ICU available at the time. This is in accordance with Patients' Rights Act in Norway.^{23,24}

Reduced physiological reserve comes with increasing age. Cardio-pulmonary and disease related deconditioning has been shown to lead to poor outcome after surgery due to lack of ability to cope with the surgical stress response.^{25,26} Reduced preinjury compliance associated with psychotic symptoms or addictive behavior in patients with moderate TBI, where recovery to his or hers habitual condition is expected, other types of treatment in the aftermath may be needed.^{27,28}

The following 10 injury and patient factors were selected from the registry to reflect these domains; 5 injury related variables: lowest Glasgow Coma Score (GCS) in 24 h after injury,²⁹ Head Abbreviated Injury Scale (AIS),³⁰ New Injury Severity Score (NISS),³¹ intracranial pressure (ICP) monitoring, and neurosurgery, and 5 patient related variables: age, Charlson Comorbidity Index (CCI),³² employment,

severe psychiatric disease and chronic substance abuse.³³ There were important changes in both EIR capacity and registry practice over time. Capacity increased from two to three ICU beds and intermediate rehabilitation beds became available from time period 2, and the registry started to systematically include patients >70 years from period 3. The time periods were therefore also considered important of EIR selection.

2.6 | Data collection

Available sociodemographic data were gender, age, and employment (employed, students or pupils in high school versus not employed, disabled, or retired). Chronic substance abuse was defined as lasting more than 3 months and severe psychiatric disorder defined as bipolar disease or schizophrenia. Comorbidity is measured by CCI.³⁴ Injury severity related data included lowest GCS within 24 h, cause of injury (transport, fall, violence, other/unknown), Head AIS version 1998 and NISS. Head AIS and NISS were collected from the Oslo University Hospital Trauma Registry.³⁵ Neurosurgical treatment was defined as ICP monitoring, and neurosurgery (craniotomy, placement of external ventricular or lumbar drain or hemicraniectomy).

Discharge from ICU and OUH was categorized as (a) discharge to specialized rehabilitation (regional rehabilitation hospital or rehabilitation ward), (b) other wards at the hospital, (c) local hospital, (d) general rehabilitation, (e) nursing home, (f) home, or (g) died prior to hospital discharge.

Time periods were categorized as (1) 2005–2009, (2) 2010–2013, (3) 2014–2017, and (4) 2018–2020.

2.7 | Statistical analyses

First, sociodemographic and injury related characteristics were described using common descriptive statistics. The differences between EIR and SC groups were presented as percentages for categorical variables and 95% confidence interval (CI) for continuous variables. Second, we analyzed the associations between EIR and the 10 a priori variables believed to best represent patient and injury characteristics used in the clinical decision making for EIR using univariate logistic regression for continuous variables and bivariate logistic regression for categorical variables with EIR as the dependent variable. We also included “Time periods” as a variable since there were important changes in both capacity and registry practice over time. Values were reported as odds ratios (OR) with 95% CI. The threshold level of significance was adjusted by using Bonferroni's correction for multiple comparisons (corrected *p*-value <.0045).³⁶

Third, we used multivariate logistic regression analyses to build a prediction model for factors associated with receiving EIR. All 10 injury and patient factors were tested for multicollinearity. When variables were found to be co-dependent (i.e., NISS and Head AIS), the most predictive variable was selected for the multivariate logistic regression analysis. Hosmer and Lemeshow goodness-of-fit test was used with a

TABLE 1 Patient characteristics of the study population.

	SC, n = 425	EIR, n = 578	Total, n = 1003
Pre-injury variables			
Male n (%)	326 (77)	433 (75)	759 (76)
Age, median (95% CI)	55 (51, 57)	41 (38, 43)	47 (45, 49)
Age, n (%)			
<40	100 (24)	276 (48)	376 (38)
40–49	74 (17)	98 (17)	172 (17)
50–59	87 (21)	104 (18)	191 (19)
≥60	164 (39)	100 (17)	264 (26)
Employed ^a	146 (36)	379 (66)	525 (54)
Any substance abuse ^b	211 (50)	256 (45)	467 (47)
Chronic substance abuse ^c n (%)	152 (36)	124 (22)	276 (28)
Severe psychiatric disease ^d , n (%)	24 (6)	17 (3)	41 (4)
CCI n (%)			
0	243 (57)	452 (78)	695 (69)
1	84 (20)	69 (12)	153 (15)
2	40 (9)	39 (7)	79 (8)
>3	58 (14)	18 (3)	76 (8)
Injury related variables			
Cause of injury n (%)			
Transport	141 (33)	243 (42)	384 (38)
Falls	237 (56)	244 (42)	481 (48)
Violence	18 (4)	44 (8)	62 (6)
Other, unknown	29 (7)	47 (8)	76 (8)
GCS, median (CI 95%)	8 (7, 9)	7 (7, 8)	7 (7, 8)
Head AIS, n (%)			
2	2 (0.5)	0	2 (0.2)
3	46 (11)	27 (5)	73 (7)
4	144 (34)	148 (26)	292 (29)
5	233 (55)	403 (70)	636 (63)
NISS, median (CI 95%)	43 (43, 48)	50 (50, 50)	50 (48, 50)
ICP monitoring, n (%)	336 (79)	538 (93)	874 (87)
Neurosurgery ^e , n (%)	185 (44)	354 (61)	539 (54)
Anesthesiological variables			
Tube, n (%)	393 (92)	564 (98)	957 (95)
Tracheostomy, n (%)	228 (54)	451 (78)	679 (68)
Ventilator at discharge from OUS, n (%)	187 (44)	99 (17)	286 (29)
LOS at ventilator, median (CI 95%)	10 (9, 11)	17 (16, 18)	14 (13, 15)
LOS at ICU, median (CI 95%)	11 (10, 12)	21 (20, 21)	16 (16, 17)
Discharge place from ICU, n (%)			

(Continues)

TABLE 1 (Continued)

	SC, n = 425	EIR, n = 578	Total, n = 1003
Specialized rehabilitation ^f	64 (15)	353 (61)	417 (42)
Other wards at the hospital	89 (21)	65 (11)	154 (15)
Local hospital	272 (64)	160 (28)	432 (43)
Discharge place from OUH, n (%)			
Specialized rehabilitation ^f	62 (15)	374 (65)	436 (44)
Local hospitals	324 (76)	186 (32)	510 (51)
General rehabilitation	2 (0.5)	3 (0.5)	5 (0.5)
Nursing home	8 (2)	5 (1)	13 (1)
Home	26 (6)	7 (1)	33 (3)
Died prior to hospital discharge	3 (0.7)	3 (0.5)	6 (0.6)
Time periods			
2005–2009	130 (31)	138 (24)	268 (27)
2010–2013	100 (23)	149 (26)	249 (25)
2014–2017	122 (29)	156 (27)	278 (28)
2018–2020	73 (17)	135 (23)	208 (21)

Note: Admission date were calculated as 1 day.

Abbreviations: 95% CI, 95% confidence interval; CCI, Charlson Comorbidity Index; GCS, Glasgow Coma Scale (range 3–15); Head AIS, Head Abbreviated Injury Scale; ICP monitoring, intracranial pressure monitoring; LOS, length of stay; Neuro-ICU, neuro-intensive care unit; NISS, New Injury Severity Score; OUH, Oslo University Hospital.

^aMissing n = 24. Employed included employed, students, part-time employed or employed on sickleave.

^bMissing n = 8.

^cMissing n = 6. Chronic substance was defined as substance abuse lasting over 3 months.

^dSevere psychiatric disease included bipolar disease or schizophrenia.

^eNeurosurgery included craniotomy, CSF drainage or hemicraniectomy.

^fSpecialized rehabilitation included regional rehabilitation hospital or rehabilitation ward.

statistically non-significant result ($p > .05$). Sensitivity and specificity of the model were presented in percentages. Fourth, trend analyses of the selection criteria variables were presented graphically with mean (standard error) values for each year, and analyzed using linear regression. The slope and intercept were reported in the form of the equation that defined the best-fit line. Statistical and graphical packages IBM SPSS, version 26 and GraphPad Prism 9.3.1 were used for analysis.

3 | RESULTS

The EIR-registry included 1349 patients from 2005 through 2020, and 1003 of these patients met the inclusion criteria for this study. The most common reasons for exclusion were length of ICU

TABLE 2 Univariate regression analyses of the selection criteria variables for receiving early interdisciplinary rehabilitation in ICU.

	Odds ratio (95% CI)	p-value
Patient related factors		
Age	0.96 (0.96, 0.97)	<.001
Employed ^a	3.48 (2.67, 4.54)	<.001
CCI <3	4.92 (2.85, 8.48)	<.001
Chronic substance abuse ^b	0.48 (0.36, 0.64)	<.001
Severe psychiatric disease ^c	0.51 (0.27, 0.96)	.032
Injury related factors		
GCS	0.95 (0.92, 0.98)	.004
Head AIS	1.73 (1.41, 2.11)	<.001
NISS	1.03 (1.02, 1.04)	<.001
ICP monitoring	3.56 (2.40, 5.30)	<.001
Neurosurgery ^d	2.05 (1.60, 2.64)	<.001
Time periods 1–4 ^e	1.16 (1.03, 1.30)	.013

Note: Corrected *p*-value threshold for multiple comparisons: $p < .05/11 = <0.0045$.

Abbreviations: 95% CI, 95% confidence interval; CCI, Charlson Comorbidity Index; GCS, Glasgow Coma Scale (range 3–15); Head AIS, Head Abbreviated Injury Scale; ICP monitoring, intracranial pressure monitoring; NISS, New Injury Severity Score.

^aMissing *n* = 24. Employed included employed, students, part-time employed or employed on sickleave.

^bMissing *n* = 6. Chronic substance was defined as substance abuse lasting over 3 months.

^cSevere psychiatric disease included bipolar disease or schizophrenia.

^dNeurosurgery included craniotomy, CSF drainage or hemicraniectomy.

^eTime periods 1–4 included the years (1) 2005–2009, (2) 2010–2013, (3) 2014–2017, and (4) 2018–2020.

admission <72 h (*n* = 137), admission >72 h after injury (*n* = 59), foreign nationals (*n* = 54) and patients who died in ICU (*n* = 48). A complete overview of included and excluded TBI patients can be found in Figure 2. Patient and injury characteristics for the entire cohort, as well as for the EIR and SC groups are presented in Table 1.

3.1 | Selection criteria predictors for receiving EIR

Univariate analysis of the 10 a priori selection criteria are presented in Table 2. For the patient related factors; lower comorbidity (CCI <3) and employment were associated with higher likelihood for receiving EIR, while higher age and chronic substance abuse were associated with lower likelihood of receiving EIR. Severe psychiatric disease was not significantly associated with EIR after adjusting for multiple analysis. For the injury related factors; ICP monitoring, neurosurgery, lower GCS score, higher AIS and NISS scores where all significantly associated with higher likelihood of receiving EIR.

The final regression model predicting EIR was based on seven variables. In adjusted analysis, patients who were employed (adjOR 1.99 [95% CI 1.41, 2.80]) and had lower comorbidity (CCI <3) (adjOR 3.15 [95% CI 1.72, 5.79]) were much more likely to receive EIR,

whereas receiving EIR was less likely with increasing age (adjOR 0.97 [95% CI 0.96, 0.98]) and chronic substance abuse (adjOR 0.55 [95% CI 0.39, 0.78]). Increasing injury severity (adjOR 1.02 [1.01, 1.03]), need of neurosurgery (adjOR 2.64 [95% CI 1.95, 3.57]) and being admitted by increasing time period (adjOR 1.39 [95% CI 1.20, 1.59]) were associated with higher likelihood for receiving EIR. The sensitivity of the model indicated 80% of patients receiving EIR would be predicted by the seven of the 10 selection criteria variables. The specificity of the model was lower, indicating only 58% of the patients receiving SC would be predicted by the model. Overall predictive ability of the model was 71% (Table 3).

3.2 | Changes in patient selection with time

Age and comorbidity (CCI) increased and rate of employment decreased with time for both groups, with the SC group remaining almost 10 years older on average compared to the EIR group (intercept $p < .001$). The increase in comorbidity (CCI) was more pronounced for the SC group compared to the EIR group (slope $p = .0268$), while age increased at similar rates for both groups (slope $p = .3695$). Severe psychiatric disease is relatively uncommon in both groups, but remained more common in the SC group (intercept $p = .0255$). Proportion of patients with chronic drug use fluctuated in both groups—although the downward slope for the SC groups was significantly different from the slight upward slope for the EIR group (slope $p = .028$). Initial GCS, Head AIS, and NISS scores all increased with time (similar slopes) for both groups, with GCS remaining lower and Head AIS and NISS remaining higher for the EIR group compared to the SC group (intercepts $p \leq .001$). There was no obvious increase in proportion of patients who received neurosurgery with time, and the proportion remained higher for the EIR group throughout the observation period (intercept $p < .001$). There was a marked decrease in proportion of ICP monitored patients in the SC group during the study period ($p = .001$) (Figure 3).

4 | DISCUSSION

Patients receiving EIR were significantly different from those receiving SC in that they were younger and healthier, and had more severe injuries. This suggests that there is a true selection when assigning EIR, and that treating clinicians largely select patients believed to benefit most. Although the patient and injury characteristics included in our local clinical guidance for EIR were predictive in our regression model, the model had moderate prediction accuracy indicating important unexplained variation in patient selection.

The moderate prediction accuracy would indicate that there are other, unmeasured factors in play for EIR selection. These might be important patient related factors not captured in our registry, but could also be related to limitations in capacity where eligible patient might not receive EIR during surge periods and holidays, whereas patients less likely to benefit, receive EIR when capacity is high.

TABLE 3 Multivariate logistic regression analyses of factors associated with receiving early interdisciplinary rehabilitation in ICU in 974 patients.

Predictors	Category	n	Coefficient	AdjOR (95% CI)	p-value
Age	Continuous	974	-0.033	0.968 (0.958, 0.978)	<.001
Employed ^a	1 Yes	522	0.687	1.988 (1.413, 2.797)	<.001
	0 No	452			
CCI <3	1 Yes	899	1.148	3.153 (1.716, 5.793)	<.001
	0 No	75			
Chronic substance abuse ^b	1 Yes	269	-0.596	0.551 (0.389, 0.781)	<.001
	0 No	705			
NISS	Continuous	974	0.020	1.020 (1.009, 1.032)	<.001
Neurosurgery ^c	1 Yes	524	0.971	2.641 (1.953, 3.571)	<.001
	0 No	450			
Time periods 1-4 ^d	Continuous	974	0.326	1.385 (1.204, 1.594)	<.001

Note: Corrected p-value threshold for multiple comparisons: $p < .05/11 = <0.0045$. Hosmer and Lemeshow goodness-of-fit test $p = .854$, $p > .05$. The sensitivity of the model was 79.5% indicating that 80% of the patients receiving EIR was predicted by the model to fall in the EIR group. The specificity of the model was 58% indicating that 58% of the patients receiving SC was predicted by the model to fall into the SC group. Over all predictive ability of the model was 70.6% = 71%.

Abbreviations: 95% CI, 95% confidence interval; CCI, Charlson Comorbidity Index; NISS, New Injury Severity Score.

^aMissing $n = 24$. Employed included employed, students, part-time employed or employed on sickleave.

^bMissing $n = 6$. Chronic substance was defined as substance abuse lasting over 3 months.

^cNeurosurgery included craniotomy, CSF drainage or hemicraniectomy.

^dTime periods 1-4 included the years (1) 2005-2009, (2) 2010-2013, (3) 2014-2017, and (4) 2018-2020.

Selection criteria for EIR in the ICU has not been extensively studied. A recent study from our institution explored predictors for direct pathways to specialized rehabilitation from acute settings in all TBI patients (mild to severe) admitted to our hospital, and similar to our study found injury severity and age to be important predictors of being transferred to specialized rehabilitation.³⁷ In addition to overlapping rehabilitation selection criteria, having received EIR is likely a strong predictor for admission to specialized rehabilitation upon hospital discharge in itself.

Physiological reserve capacity is often referred to as "rehabilitation potential." This is an important factor in the decisions made by the interdisciplinary team regarding which level of Neurointensive care treatment and rehabilitation the patients will receive.¹² While patients with higher physiological reserve capacity (younger age, work ability and few comorbidities) generally received EIR in our study, an unexpectedly high proportion that would seemingly meet criteria for EIR did not. Twenty-eight percent employed individuals did not receive EIR, indicating there might be other stronger predictors for EIR selection. As very few patients in our cohort died on ward or were discharged to a nursing home both with and without EIR, it is unlikely that EIR was withheld by the treatment team due to injury severity or futility.

The importance of patient factors such as age, employment, and comorbidity decreased over time in our cohort. Increased capacity for EIR in our ICU and inclusion of patients over 70 years in the registry from 2014 likely contributes to this trend. However, when all patients over 70 years are removed from the cohort, the population has still become 5 years older between 2005 and 2020. Increase in age in

both groups may also in part be explained by previously described epidemiological changes to the TBI population the last decade with higher proportions of falls in older age categories and lower percentages of traffic accidents in younger patients.³⁸ With fewer younger, healthier patients in the ICU, older, more frail patients with lower priority might have had greater access to EIR. On one hand, elderly TBI patients are known to have more comorbidities, less physiological reserve and have increased risk of secondary brain injuries due to hypoxia and hypotension, and hence a lower threshold to triage to specialized centers has been suggested.⁷ However, with limited EIR resources, the increased risk and frailty in the elderly needs to be weighed against diminished brain reserve with less plasticity and neural repair limiting the effectiveness of rehabilitation.³⁹

Our study has several limitations. First, changes in EIR capacity and administrative practices for enrollment of patients in our registry are important limitations in the study. Second, registry data based on the medical records are unlikely to capture all nuances of the patient assessments that result in EIR versus standard care decision making. Third, the observational study design limits causal inference as it is unlikely that we have captured all confounders. Fourth, 29 eligible patients were excluded from the univariate and multivariate analysis due to missing data for one or more variables (Tables 2 and 3), and it is conceivable that the missing data on employment or psychiatric disease is not randomly missing, potentially influencing the results.

Moderate overall prediction accuracy indicate that the selection process to some degree matched the intention of the selection criteria. There are however important gaps in our knowledge related to

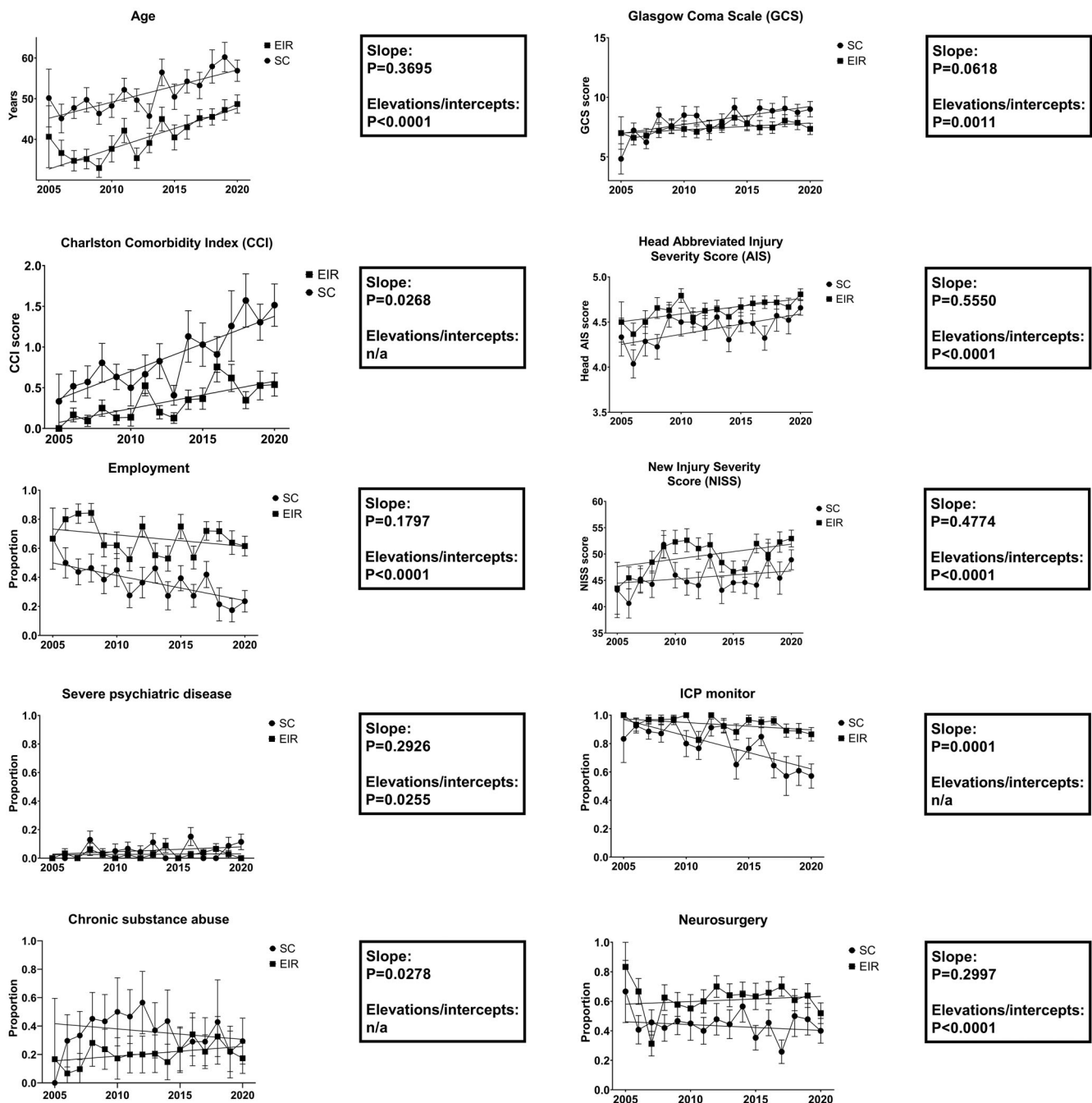


FIGURE 3 Changes in the 10 selection criteria variables in the study population during the time period October 10, 2005–December 31, 2020.

patient- and non-patient factors influencing the selection of patients in EIR. Future studies are needed to improve our understanding of how patients are selected for EIR, both in our everyday clinical practice and when conducting clinical trials in the TBI population.

5 | CONCLUSIONS

Injury severity and neurosurgery remain important predictors for receiving EIR, but EIR is increasingly being offered to unemployed and

older patients with more comorbidity. Moderate prediction accuracy using current clinical criteria suggest unrecognized factors are important for patient selection.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Data analyses were performed by Kristin Alvsåker and Theresa M. Olasveengen. Kristin Alvsåker drafted the manuscript. Kristin Alvsåker, Theresa M. Olasveengen, and Rolf Hanoa edited the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Kristin Alvsåker  <https://orcid.org/0000-0002-4421-8824>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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