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Title:

"The effect of socioeconomic deprivation on 12 month Traumatic Brain Injury (TBI) outcome"

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Abstract

Objectives:

To assess the impact of social deprivation on Traumatic Brain Injury (TBI) global outcome, measured at 12 months post injury.

Design:

The study was a prospective observational study conducted using consecutive admissions with TBI.

Subjects:

1322 consecutive adult patients with TBI were recruited into the study between 2010 and 2015. A total number of 1191 completed the 12 month follow up period.

Methods:

All patients were assessed by the TBI rehabilitation team at both six weeks and 12 months following TBI. Details of the injury and demographic data was collated at six weeks. This included age, gender, medical comorbidities, ZIP Code and GCS. Social deprivation was measured by the Indices of Multiple Deprivation (IMD) Score. The outcome measure used was the Extended Glasgow Outcome Score (GOSE) at 12 months. Univariate analyses were followed by a Multi-Ordinal Regression to evaluate predictor variables.

Results:

With regard to the representation of IMD deciles, the study population approximated to the general Sheffield population ($p=0.139$). Within the univariate analyses, statistically significant relationships were noted between IMD and GOSE ($p=<0.001$). There was no relationship noted between IMD and GCS at the time of injury ($p=0.409$), or medical co-morbidity ($p=0.682$). The Ordinal Regression revealed a significant relationship between worse GOSE and IMD ($p=0.002$), age ($p=0.001$), GCS ($p<0.001$), alcohol intoxication ($p<0.001$) and Medical Comorbidity ($p=0.041$).

Conclusions:

Increasing social deprivation is associated with poorer global TBI outcomes at 12 months. Furthermore, age, TBI severity and Pre-existing Medical comorbidity are all associated with a poorer TBI outcome at 12 months. This highlights the importance of social deprivation in determining TBI outcome.

Introduction

Traumatic Brain Injury (TBI) is a cause of major morbidity and mortality worldwide. It is associated with severe sequelae which have a detrimental impact upon an individual's quality of life. Moreover, TBI carries a large health economic burden worldwide, with an estimated expenditure of $76 billion per year in the United States of America (USA).[1] The cause of the elevated expenditure is multifactorial. A significant proportion of this expenditure is attributed to the acute cost secondary to the increasing incidence of TBI, 790 per 100,000 per year with 235 per 100,000 requiring hospitalisation.[2,3] However, the long-term healthcare costs associated with TBI rehabilitation accounts for the majority of the expense post-TBI.[2, 3] Numerous factors are associated with an increased long term expenditure including; increased TBI severity, increased duration of Post-Traumatic Amnesia (PTA), initial post injury hypotension and an increased number of TBI sequelae.[4,5] The underpinning feature between these factors is the association with poorer TBI outcomes, leading to an increased healthcare burden and elevated associated costs. Furthermore, various patient demographic factors have been associated with with poor TBI outcomes these include: increasing age, male gender and lower educational status have been associated with poor TBI outcomes.[6,7, 8]

Socio-Economic Status (SES) is known to have a profound impact on an individual's health. It is widely accepted that a lower SES is associated with poorer healthcare outcomes following numerous significant healthcare events such as Myocardial Infarction (MI).[9, 10] Within the context of TBI there are conflicting findings regarding the impact of SES on long-term outcome. Existing literature focusses mainly upon the association between SES and TBI mortality, which has produced varying results.[9,11,12] Further research has demonstrated that increased social deprivation has been identified as an independent risk factor for TBI, particularly in young adult males.[13,14,15,16] Additionally, it has been demonstrated in both adult and paediatric populations that reduced SES correlates with poorer global TBI outcomes.[17,18,19,20] In addition to specific TBI sequelae including anxiety and reduced cognitive ability. [21, 22, 23] However, other studies have concluded that SES has no impact upon outcomes following TBI.[24] Due to differences in study design and methodology, with particular reference to measuring SES, the pre-exisiting literature regarding the impact of SES is limited. SES is a multifaceted concept which

The aim of this prospective observational study was to assess the relationship, if any, between SES and global TBI outcomes at one year post-TBI. Secondary analyses were conducted to assess the relationship between SES and other patient factors including; age, gender, and TBI aetiology.

Methods

This prospective observational study was completed within the specialist neurorehabilitation service of the Sheffield Teaching Hospitals (STH) Trust. All patients admitted to the STH Trust, between 2010 and 2015, due to TBI were screened for inclusion into the Sheffield Brain Injury after Trauma (SHEFBIT) cohort within 24 hours of admission.

All patients over the age of 18, with a formal diagnosis of TBI made using the Common Data Elements criteria were eligible for inclusion in this study.[25] Paediatric patients were excluded as they receive both acute and follow up care at a different site within the STH Trust. The SHEFBIT population is representative of all adult patients with TBI with regard to; patient demographics, TBI aetiology, and TBI severity.

The initial assessment was conducted at six weeks post injury. During the primary assessment, patient demographic factors including: age, gender, and ethnicity were recorded. Furthermore, key injury factors such as the admission Glasgow Coma Scale (GCS) score and TBI severity were recorded in addition to a review of imaging. Furthermore, the underlying TBI aetiology was recorded using the Trauma Audit and Research Network Classification (TARN).[26] The TARN Classification classifies TBI aetiology as; Fall, Road Traffic Collision (RTC), Assault, Sports Injuries or Other (falls from greater than 2m etc).[26] A record of alcohol intoxication at the time of injury was extracted from the medical records. Additional assessments were conducted including an assessment of medical comorbidity using the Cumulative Illness Rating Scale (CIRS); with a score of >10 establishing significant medical comorbidity. The threshold of >10 as a marker of significant medical comorbidity has been widely validated for use within medical research.[27] A history of a formally diagnosed psychiatric disorder was recorded. All patients within the SHEFBIT cohort underwent a CT scan at the time of their injury. CT scans were assessed used the "overall appearance" system. This is a validated tool which grades CT abnormalities after TBI as; normal, mild focal injury (one cerebral lobe), moderate injury (two adjacent cerebral lobes) and severe (diffuse) injury.[28]

Socio-economic Status (SES) was assessed using the English Indices of Multiple Deprivation (IMD) 2015 Score, a validated tool for measuring SES.[29] The IMD score is derived from population and census data linked to an individual's postal code (ZIP Code). The postal code of study participants was recorded at the time of the injury, it was not updated if the patients moved during the 12 month follow up. The IMD score represents a composite score of societal measures regarding: income, employment, access to healthcare and education, and crime rates associated to each area arranged according to the postal code. All postal codes are grouped into Lower Super Output Areas (LSOAs).[29] LSOA's are small geographically defined areas across England containing a group of individuals. The LSOA's are grouped to produce an overall score of deprivation from each of the competitive measures which gives the IMD raw score. From the IMD raw score deciles are produced where decile 1 is the most deprived and decile 10 is the least.[29] In this study the IMD raw score was used as the measure of socio-economic status.

At 12 months the follow up a structured clinical interview was used to formulate an Extended Glasgow Outcome Score (GOSE). The GOSE is the primary method of assessing global outcome following TBI.[29] The GOSE enables classification of patient outcome following TBI into eight categories: Death, Vegetative State, Severe Disability (Upper and Lower), Moderate Disability (Upper and Lower) and Good Recovery (Upper and Lower).[30] Whilst GOSE provides a global assessment of TBI outcome, it has been demonstrated to correlate with other the assessments of specific TBI sequelae including depression.[31]

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) 24. To facilitate the formation of the final multi-variate analysis, primary univariate analyses were conducted between both patient demographics (age, gender, ethnicity and IMD raw Score), injury characteristics (GCS, TBI severity and aetiology) and the GOSE score to establish baseline correlations. The final method of assessment within this study was conducted using an Multi-Ordinal Regression (OR) analysis with GOSE score as the dependent variable. Analyses were conducted between IMD raw score and other variables including; significant pre-existing medical co-morbidity, age and gender. An independent t-test was conducted to assess the representation of IMD deciles within the study population compared to the population data of Sheffield region.

This study was completed within the STH under the ethical approval of both the Sheffield Hospital Trust (ref: STH16208) and the University of Sheffield Ethics Committee (ref:008315).

Results

A total of 1322 participants were recruited between August 2010 and April 2015, shown in Figure 1. A total 132 individuals were lost to follow up prior to final assessment by 12 months, resulting in a final study population size of 1191. The median age within the final cohort was 45.54 years. The majority of patients were male (68.43%) and identified as “White British” (92.40%). Full patient demographics are shown in Table 1. The study population was representative of all TBI aetiologies with reference to the TARN classification: 35.48% were classified as Falls, 27.84% as RTC, 17.78% as Assault, 6.05% as Sports Injuries and 12.86% as Other. The majority of cases were mild TBI (49.87%), with moderate (33.92%) and severe TBI (16.20%) accounting for fewer cases (Table 1). A substantial proportion (38.50%) of the study participants belong to the the first and second deciles (most deprived) according to IMD score. The full distribution of the IMD deciles is displayed in Table 2. The key outcome measurement was the GOSE score at 12 months post TBI, the spread of GOSE score is shown in Table 3.

An Independent t-test demonstrated that the study population was not significantly different from the Sheffield population (p=0.139) with regard to the representation of IMD deciles. The proportion of individuals from each of the IMD deciles reflects that of the wider Sheffield population as demonstrated in Figure 2.

Within the univariate analyses; increasing IMD raw score (more deprived) (p=<0.001), increasing age (p=<0.001), and lower GCS (p=<0.001) all demonstrated statistically significant rela-

tionships with poorer GOSE score at 12 months post-injury. There was no significant relationship found between IMD raw score and GCS at the point of injury (p=0.401). There was no significant relationship between the participants lost to follow up and the IMD raw score (0.492). IMD raw score had a statistically significant relationship with Age (p=<0.001) with a Pearson's R value of (0.119). The univariate analyses are displayed in Table 4.

A Multi-Ordinal Regression (OR) with GOSE as the dependent variable was conducted. IMD raw score (p=<0.002), GCS at the point of injury (p=<0.001), age (p=0.001), psychiatric history (p=<0.001), medical comorbidity (p=0.041), alcohol intoxication (p=<0.001) and CT scan abnormality (p=0.003) all demonstrated statistically significant relationships with GOSE score at 12 months (Table 5a, Table 5b). Gender (p=0.288), Ethnicity (p=0.831) and Initial Employment status (p=0.081) did not demonstrate significant relationships with GOSE score at 12 months (Table 5a, Table 5b).

Both increasing IMD raw score (more deprived) (odds ratio=0.99) and age (odds ratio=0.99) had an inverse relationship to GOSE score. Conversely increasing GCS at admission is associated with an improved GOSE score at 12 months (odds ratio=1.26). Other protective factors found were the absence of a formal psychiatric diagnosis and the absence of alcohol intoxication at the time of injury.

With regard to the Pseudo R-Squared value for the OR analysis, The Nagelkerke value was 0.344. The Nagelkerke value demonstrates that the OR model used correctly predicts 34.4% of the pseudo-variants included within the model when predicting GOSE score at 12 months.The final model was statistically significant (p=<0.001), -2 Log Likelihood Value (3639.946) Chi-Squared value (482.082).

Discussion

The aim of this prospective study was to assess the impact of SES upon global TBI outcomes at 12 months. A total of 1191 patients completed the 12 month observational study with only 132 patients (10.74%) lost to follow up.

Within the previous literature it has been shown that there is an increased incidence of TBI in individuals with a lower SES.[13,14,15,16,32] However, the differences in study methodology leads to difficulty in producing adequate comparisons between different populations. Within this study 39.13% of study participants were found to be in the lowest two IMD deciles (most deprived), compared to 16.28% in the highest two deciles (least deprived). This is in keeping with the findings of the pre-existing literature with regard to the increased incidence of TBI in areas of increased social deprivation.[33] However, as demonstrated by the independent t-test (p=0.139), the study population was not significantly different from the population within the wider Sheffield region. Therefore, the over representation of the lower IMD deciles within this study was not elevated beyond the norm compared to the Sheffield population. It should be noted that according to data from the United Kingdom Office of National Statistics, Sheffield has a relatively deprived population compared to England as a whole; 37% of the LSOAs in Sheffield fall into the 20% most deprived in the country.[32] The over representation of the lowest two deciles (most deprived) within the study is understandable and mimics that of the Sheffield

population. The proportion of individuals in the study population from the lowest two IMD deciles, is not significantly different from the Sheffield population. Therefore the incidence of TBI in Sheffield may differ compared to more affluent regions within England.

Within the univariate analyses GOSE had a statistically significant relationship with age (p=<0.001), admission GCS (p=<0.001) and IMD raw score (p=<0.001). The findings with regard to age and GCS were anticipated and correlate well with the findings of the pre-existing literature.[34,35]

Further univariate analyses were conducted to assess the relationship between IMD Raw Score and key patient demographics including pre-existing medical comorbidity (p=0.682), age (p=<0.001) and GCS at the time of injury (p=0.492). Full univariate analyses available in Table 4. It is widely accepted that increasing age, significant medical comorbidity and lower GCS at the time of the injury are all associated with poorer TBI outcomes.[34,35,36] This reflects the results of this study. The assessments of these relationships were vital as they demonstrate that there was no difference in the severity of injury sustained with regard to SES. Furthermore, as there was no significant difference between IMD decile and significant medical comorbidity, the baseline medical state of the patients was not significantly different. This is important as increased medical comorbidity is associated with worse TBI outcomes.[37] Moreover, the weakly positive relationship between increasing age and improved SES demonstrates that on average, patients with lower SES were younger. This hypothetically should be a protective factor because, as discussed above, increasing age is associated with poorer TBI outcome.[34] The assessment of the relationship between SES and age, medical comorbidity and TBI severity was important as it demonstrated that these factors, known to be detrimental to TBI outcome, were not the cause of the disparity in TBI outcome between those of higher and lower SES.

The results of the multiordinal analysis demonstrated that; age (p=<0.001), admission GCS (p=<0.001), IMD Raw Score (p=0.002), Medical Comorbidity (p=0.041), Psychiatric History (p=<0.001) and Alcohol Intoxication at the time of injury (p=<0.001) all were independent predictors of poor global TBI outcome. Within the model, gender (p=0.288), employment at the time of injury (p=0.081), and ethnicity (p=0.831) all did not have a significant impact upon global TBI outcome (Table 5a, 5b). Previous literature on the impact of alcohol intoxication at the time of injury on global TBI outcome shows that whilst alcohol intoxication is associated with a longer period of PTA or loss of consciousness post-TBI, this does not impact the global outcome.[38] With regard to ethnicity, studies in the USA have demonstrated that ethnicity can affect TBI outcomes. However, in that study, health insurance status was the key factor impacting outcomes.[39] Therefore the impact of ethnicity in UK populations may not demonstrate the same relationship, as demonstrated in this study, due to universal access to healthcare. It has been acknowledged that a history of a formal psychiatric disorder is associated with persistent post-TBI symptoms.[40,41]

The results of this study clearly demonstrate that lower SES is associated with poorer global TBI outcomes at 12 months (p=0.002). The previous literature on SES has produced conflicting results regarding the impact on TBI outcomes. The cause of this disparity may be differences in study methodology with particular reference to assessing SES, as a variety of methods are

used these include; population-based tools (e.g IMD Score, Townsend Deprivation Index), occupational prestige, family income or educational attainment.[18,19,21]

A number of studies have demonstrated that lower SES is associated with poor physical and mental health outcomes in both paediatric and adult populations.[17,18,19,21,23] The pre-existing literature demonstrates an increased incidence of post-TBI sequelae including anxiety, in addition to poorer performance on global outcomes and disability scoring scales.[21,23] Furthermore, within paediatric populations lower SES has been associated with poor behavioural performance, increased social dysfunction and reduced cognitive outcome following TBI.[17,20,22] With regard to mortality, similar conflicting results are reported between studies using varied methods of measuring SES.[9,11] However, where population based measures of SES are used (i.e IMD Score), it has been reported that lower SES has no impact upon TBI mortality.[11,12]

Aside from the size of the study cohort other key strengths of this study include the low attrition rate (10.74%) and the representative TBI patient population. The SHEFBIT study population is wholly representative of hospitalised TBI with regard to aetiology and injury severity as it is not limited to severe TBI or specific patient populations i.e military personnel. This includes appropriate representation of mild, moderate and severe TBI in sufficient numbers to make inferences about the subgroups in a clinically relevant setting. Moreover, there is good representation from each of the IMD deciles, particularly when compared with the Sheffield population. All cases were prospectively recruited within the same specialist neurorehabilitation clinic facilitating appropriate continuity of care for all patients. The assessments were conducted by a single observer using a structured clinical interview, to minimise the risk of inter-observer bias. As explained later, the IMD is a particularly strong measure of SES compared to other tools.

The English Indices of Multiple Deprivation 2015 provides a composite measure of SES which is widely validated and used within medical research.[37,42,43] However, as the score is formed according to the population data linked to a postal code (ZIP Code) and LSOA rather than individualised characteristics i.e the overall historical educational attainment of an area rather than an individuals personal educational level, there may be an under or overestimate of SES on a case by case basis. It may, therefore, incorporate a degree of *ecological fallacy*, whereby within a set of statistical data, assumptions on the characteristics of an individual are derived from the group to which that individual belongs. Therefore, an IMD value may underestimate the unique SES of an affluent person living in a more deprived area and vice versa. Furthermore, an individual may move and subsequently their IMD score would change according to their postal code (ZIP Code) whilst their individual characteristics do not change.[35,42,43] Despite these limitations, the use of IMD is validated for use within medical research and across population data it provides a much greater insight into SES compared to one dimensional measures, which include health insurance status, occupation or educational attainment, which are used commonly within the literature. For example the use of an individual's occupation may be ambiguous due to the patients description of their job such as the term "engineer" can be a phrase taken to mean chartered engineer or a car mechanic. Furthermore, the use of educational attainment alone may result in difficulties comparing individuals from different age groups due to changes in societal norms regarding school leaving age etc. One-dimensional measures of

SES may limit the extent to which deprivation is manifest within studies. The English Indices of Deprivation (IMD) Score score has been validated for comparison with other similar measures of SES, allowing comparisons to be made between different study populations which reduces the limitations of cultural differences between different countries or healthcare systems.[29] Therefore, the use of IMD score within this study as the measure of SES produces the most meaningful and tangible results.

This prospective observational study aimed to assess the relationship between SES and global TBI outcome at 12 months. The results of this study demonstrate that a lower SES is associated with a poorer TBI outcomes. An avenue of future work would be to assess potential contributing factors to TBI outcome including engagement with the allied health professional rehabilitation programmes including physiotherapy and occupational therapy. Moreover, as this study suggests a disparity in a healthcare outcomes secondary to socioeconomic deprivation, this may warrant targeted intervention to improve neurorehabilitation efficacy in more deprived populations.

Conclusion

Within this large, prospective observational cohort social deprivation had a statistically significant relationship ($p=<0.002$) with poorer TBI outcomes at 12 months measured using the GOSE scale. Furthermore, the representation of SES within this study mirrored that of the wider Sheffield population indicating that the incidence of TBI was not increased according to increased social deprivation.

Declaration of Interest

The authors report no declarations of interest.

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Table 1. Patient Demographics

	Number of Patients (n)	Percentage of Patients (%)
Total Number of Patients	1191	100
Median Age (Years)	45.54	
Average Length of Stay (Days)	9.57 (SD 18.46)	
Gender		
a. Male	815	68.43

b. Female	376	31.57
Ethnicity		
a. White British	1101	92.40
b. Non-White British	90	7.60
TBI Aetiology		
a. Fall	418	35.10
b. Road Traffic Collision	328	27.54
c. Assault	215	18.05
d. Sport	76	6.38
e. Other	154	12.93
TBI Severity		
a. Mild	594	49.87
b. Moderate	404	33.92
c. Severe	193	16.20
Significant Medical Comorbidities		
a. Yes	851	71.45
b. No	340	28.55
Intoxicated at time of Injury		
a. Yes	299	25.10
b. No	892	74.90
Median Admission GCS	13	

Table 3. Glasgow Outcome Scale Extended (GOSE) at 12 Months Post-TBI

GOSE Score	Number of Patients (n)	Percentage of Cases (%)
Dead	61	5.12
Vegetative State	0	0.00
Severe Lower	11	0.92
Severe Upper	127	10.66
Moderate Lower	262	22.00
Moderate Upper	216	18.14

Good Lower	214	17.97
Good Upper	299	25.10

Table 2. Distribution of Indices of Multiple Deprivation Score (IMD) in Study Participants.

IMD decile	Number of Patients (n)	Percentage of Cases (%)	Percentage in Sheffield Population (%)
1	303	25.44	22.00
2	163	13.69	9.10
3	116	9.74	14.20
4	63	5.29	8.30
5	95	7.98	7.60
6	92	7.72	6.40
7	95	7.98	6.00
8	70	5.88	8.70
9	87	7.30	7.70
10	107	8.98	9.90

Table 4. Univariate Analyses

Univariate Analyses vs Indices of Multiple Deprivation					
Variable	**Value**	**df**	**SE**	**Approximate Tb**	**p-Value**
Medical Comorbidity	6.57	9			0.682
GCS	0.024		0.029	0.841	0.401
GOSE	0.104		0.030	3.613	**<0.001**
Age	0.119		0.032	3.787	**<0.001**
Univariate Analyses vs Extended Glasgow Outcome Scale					
Variable	**Value**	**df**	**SE**	**Approximate Tb**	**p-Value**
Age	-0.152		0.038	-4.306	**<0.001**
Medical Comorbidity	54.57	6			**<0.001**
GCS	0.358		0.024	13.218	**<0.001**

GCS = Glasgow Coma Score
GOSE = Extended Glasgow Outcome Score
*Emboldened results indicate p-value <0.05

Table 5a. Ordinal Regression of GOSE at 12 months Post-TBI; Continuous and Binary Variables

Variable	Estimate	S.E	Odds Ratio	Confidence Interval (95%)		p-Value
Age at Injury	-0.013	0.004	0.99	**0.98**	**0.99**	**0.001**
GCS on Admission	0.231	0.023	1.26	**1.20**	**1.32**	**<0.001**
IMD Raw Score	-0.009	0.003	0.99	**0.98**	**0.99**	**0.002**

Gender (Male)	0.127	0.12	1.13	0.89	1.44	0.288
Ethnicity (Non-White)	0.044	0.208	1.04	0.70	1.57	0.831
Psychiatric History	1.03	0.143	2.80	**2.12**	**3.71**	**<0.001**
Alcohol Intoxication	0.612	0.139	1.84	**1.40**	**2.42**	**<0.001**
Medical Comorbidity	0.293	0.143	1.34	**1.01**	**1.78**	**0.041**

IMD = English Indices of Multiple Deprivation
GCS = Glasgow Coma Score
GOSE = Extended Glasgow Outcome Score
*Emboldened results indicate p-value <0.05

Table 5b. Ordinal Regression of GOSE at 12 months Post-TBI; Categorical Variables						
Variable	**Estimate**	**S.E**	**Odds Ratio**	**Confidence Interval (95%)**		**p-Value**
Initial Employment						
i. Unemployed	0.343	0.197	1.41	0.95	2.07	0.081
ii. Employed	-0.038	0.226	0.96	0.62	1.50	0.866
iii. Retired	0a					
TBI Aetiology						
i. Fall	0.6	0.181	1.82	**1.28**	**2.60**	**0.001**
ii. Road Traffic Collision	0.429	0.174	1.54	**1.09**	**2.16**	**0.014**
iii. Sport	0.787	0.266	2.20	**1.30**	**3.70**	**0.003**
iv. Other	0.22	0.205	1.25	0.83	1.86	0.283

v. Assault	0a					
CT Scan Findings						
i. No Findings	0.741	0.253	2.10	**1.28**	**3.44**	**0.003**
ii. Mild Injury	1.10	0.247	3.01	**1.86**	**4.88**	**<0.001**
iii. Moderate Injury	0.468	0.226	1.60	**1.03**	**2.48**	**0.038**
iv. Severe Injury	0a					

*Emboldened results indicate p-value <0.05
Oa indicates the reference category

Figure 1. Study Participants over the 12 month Observational Period

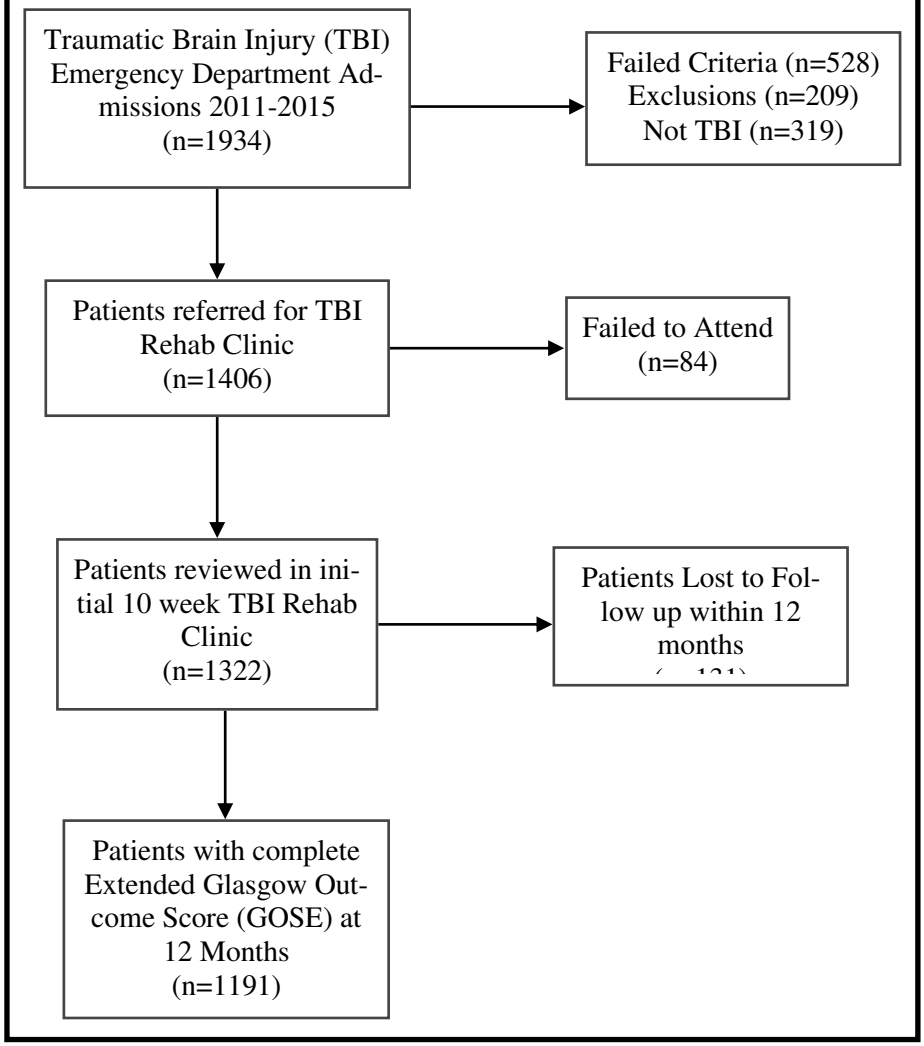

Figure 2. Distribution of Indices of Multiple Deprivation (IMD) Score in Study Participants compared to the Sheffield Population.