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Labour market attachment after mild traumatic brain injury: Nationwide cohort study with 5-year register follow-up

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ABSTRACT

Objectives: Sickness absence after mild traumatic brain injury (mTBI) is frequent. Although most patients return to work the first couple of months post-injury, for some patients sickness absence becomes prolonged due to post-concussive symptoms. Our objective was to examine labour market attachment following mTBI up to 5 years post-injury.

Design and setting: Nationwide cohort study with register follow-up.

Participants: Patients between 18-60 years with mTBI (ICD-10 diagnosis S06.0) were extracted from the Danish National Patient Register (n=19 732). Controls were matched on sex, age and municipality (n=18 640). Exclusion criteria were: major neurological injuries at the index date and 5 years before trauma, moving address outside Denmark, unknown residence, residence in Greenland, and not being available for employment.

Primary and secondary outcome measures: Primary outcome was "not attending ordinary work". Secondary outcomes were health-related benefits, limited attachment to the labour market, permanent lack of attachment to the labour market and death. Data were extracted from the DREAM register.

Results: 5 years after diagnosis, 43% of patients were not attending ordinary work. The odds increased from 6 months (OR 1.30, 95% CI 1.24-1.36) to 5 years (OR 1.54, 95% CI 1.45-1.63). The odds of health-related benefits were 32% (OR 1.32, 95% CI 1.22-1.42) at 6 months and 22% (OR 1.22, 95% CI 1.12-1.33) at 5 years. Limited attachment to the labour market showed increased odds at 5 years (OR 1.38, 95% CI 1.27-1.51) and the odds of permanent lack of attachment to the labour market were higher for patients compared to controls, (OR 2.59, 95% CI 2.30-2.92). Death was more than two times higher at 5 years post-injury (OR 2.62, 95% CI 2.10-3.26).

Conclusions:

43% of patients with mTBI were not attending ordinary work 5 years post-trauma. Prevention and treatment of persisting post-concussive symptoms should be considered.

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ARTICLE SUMMARY

Strengths and limitations of this study

- This was a nationwide cohort study with register-based follow-up including nearly 20 000 patients with mild traumatic brain injury (mTBI).
- The data were extracted from high-quality Danish national registers.
- This study estimated the prevalence and odds (OR) of not attending ordinary work, health-related benefits and death in patients with mTBI up to 5 years post-injury.
- This study had no access to patient records, with the inherent risk of misclassification.

INTRODUCTION

Mild traumatic brain injury (mTBI), also known as "concussion", is a common neurological disease defined as an acute brain injury resulting from mechanical energy to the head from external physical force, typically classified with a Glasgow Coma Scale score of 13-15 post-injury.[1]

Approximately 70-90% of all TBIs fall into the category of mTBI.[2-4] The incidence of hospital and emergency treated patients is 50-300 cases per 100 000 people in the US, Scandinavia and Australia[4 5] and more frequent among young people and men.[4] However, these numbers probably fall short as studies also show numbers more than 700 cases per 100 000 people per year.[4]

Numerous studies have examined post-concussive symptoms in adults showing symptoms like dizziness, fatigue, sensory and emotional disturbances, insomnia, posttraumatic headache, as well as memory and concentration difficulties[6-8] leading to long-term sickness and absence from work. Post-concussive symptoms result in an increased use of general practice services the first year post-injury, as reported by a Danish study.[9] In up to 15% of patients with mTBI, post-concussive symptoms are persistent (>12 months post-injury).[10, 11] Additionally, several risk factors are associated with persisting symptomatology, such as female gender, premorbid physical or psychiatric comorbidities, injury-related conditions, such as duration of post traumatic amnesia, history of previous head injury, psychological distress, and drug and alcohol abuse.[8, 12, 13]

There is substantial evidence that most patients return to work within the first couple of months after mTBI, but a small proportion of patients is unable to return to work due to disability.[14, 15] A systematic review by Cancelliere et al. found that most patients (>75%) had returned to work after six months and 5% were on social transfer payments two years post-injury.[16]

Return to work (RTW) has been conceptualized as being a dynamic process with different related outcomes of labour market attachment or time off work, but also outcomes related to the process of return to work such as psychological functioning, job satisfaction or work stress.[17, 18]

RTW after mTBI has been suggested to depend on multiple factors such as injury related factors,[16] premorbid demographics such as younger age,[14] work place related factors such as support,[19] influence on work planning[20] and patient characteristics such as psychosocial status.[21] The studies on which these conclusions are based have methodological differences and limitations in study design which complicate evaluation of evidence regarding the magnitude of the problem. They have small sample sizes, are not representative,[6] are often based on self-reported data, have short follow-up and considerable dropout which can lead to attrition bias.[15] The present analysis overcomes these challenges by using Danish nationwide administrative data to examine a larger, representative sample and to perform long-term follow up. This study is concerned with patients with mTBI who are not able to return to work. We examined a comprehensive range of post-injury transitions in the labour market aiming at analysing attachment to the labour market up to five years after mTBI using a portfolio of outcomes, including a variation of social transfer payments and data on permanent lack of attachment to the labour market and death.

METHODS

The data used in the present analyses is obtained by using the possibility to link several Danish national administrative registers. These registers are available for research purposes, through the unique personal identification number (CPR number) assigned to all Danish citizens at birth or immigration, provided by the Danish Civil Registration System (CRS) operating the Population register.[22]

Study population

The study was designed as a nationwide population-based cohort study of all mTBI cases in Denmark in the five-year inclusion period 1st of January 2003 – 31st of December 2007. These cases were identified in the Danish National Patient Register (DNPR) which contains the information on

all in- and outpatient contacts in Danish secondary care.[23] Notably, it codes each contact with International Classification of Diseases, version 10 (ICD-10) diagnosis codes. The mTBI patients were included in the cohort on their index date, the date of their first entry in the DNPR in the inclusion period with concussion (ICD-10 code S06.0) as primary diagnosis. The included patients with mTBI had to be working-age adults between 18-60 years of age available for the labour market on the index date; the upper limit was set because individuals in Denmark older than 60 years are entitled to early retirement, if they have paid for such a scheme.[24] Availability for the labour market was defined as gainful employment or receiving unemployment benefits, but actively job seeking (see Figure 1). Furthermore, they were not hospital treated or diagnosed with other major neurological injuries such as spinal cord and column injuries[25] and TBI (including concussion)[5] in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period[5, 26] since previous brain injury and neurological problems are found to be associated with prolonged symptoms.[27] Finally, patients were not included if they had lived outside of Denmark at any time during the inclusion period and the five-year period before.

For each mTBI case in the cohort, a control was randomly selected from the Population register. The population of controls had similar inclusion criteria as the cases, but they had no diagnosis of concussion during the inclusion period 1st of January 2003 – 31st of December 2007. The control was matched to the case on sex, municipality, age (year of birth ± 0.5 years, expanded to 1 and 2 years in case of no initial match) and available for the labour market on the corresponding case's index date (see Figure 1).

Insert Figure 1

Availability for the labour market was assessed from the Danish Register for Evaluation of Marginalization (DREAM), a national database containing weekly information on all individuals

who have received any social public transfer payments.[28] Patients and their matching controls were excluded from the cohort if there were any major neurological injuries[5, 25] as secondary diagnoses at the index date, they were unavailable for the labour market, they had unknown residence or were inhabitants of Greenland.

Outcome measures

The outcomes of the present analyses were assessments of variations in attachment to the labour market evaluated in the DREAM database the week before the case's index date, and at 6 months, 12 months, 2 years and 5 years after the case's index date (Figure 1).

Not attending ordinary work

1. "Not attending ordinary work" was the primary outcome and was indicated by any entry in DREAM, i.e. receiving any social transfer payment, such as unemployment benefits unrelated to the subject's health condition, sickness absence benefits, social benefits granted, short and long-term sickness or death. If there was no DREAM entry, it was assumed that the subject was gainfully employed or self-supporting at that time (Figure 1).

The set of secondary outcomes are defined increasingly narrower than the primary outcome and focus on attachment to the labour market due to health conditions. At the time of the current study, employers in Denmark were obliged to finance sickness benefits for the first 30 days. Sickness benefits lasting more than four consecutive weeks were to be compensated by the Danish municipalities.[29] Sick-listed individuals could receive sickness benefits for a maximum of one year. If individuals were not able to return to ordinary work due to long-term limited work capacity, a partial return to work at lower capacity was possible with a "flex job". If the sick-listed individual

was not able to return to work at all, the municipality could grant disability pension after an extensive assessment.[30, 31] The grading of the outcomes is illustrated in Figure 1.

Health-related benefits

2. Health-related benefits were indicated by DREAM entries given for short- or long-term restrictions in attachment to the labour market due to health conditions (excluding unemployment benefits unrelated to the subject's health condition). These were sickness absence benefits, vocational rehabilitation, flex job, unemployment benefits specifically granted citizens on flex job, social security benefits, light duties, disability pension and death.

Limited attachment to the labour market

3. Social transfer payments due to limited attachment to the labour market were indicated by DREAM entries given for reduced work capacity and thereby long-term restrictions in attachment to the labour market due to health conditions (excluding sickness absence benefits compared to secondary outcome 2). These were vocational rehabilitation, flex job, unemployment benefits specifically granted citizens on flex job, social security benefits, light duties, disability pension and death.

Permanent lack of attachment to the labour market

4. Permanent lack of attachment to the labour market was indicated by DREAM entries given for permanent withdrawal from the labour market due to health conditions. These were disability pension and death.

Death

5. Death was indicated by the DREAM entry for death.

Potential confounders

Sex, age and municipality at the index date were obtained from the Population register linked to the DNPR. The municipality information was categorized into the five regions reflecting Denmark's reform of local government structure from 2007.[32] From the index date calendar year and season were derived. Calendar year was included in the model as a previous study found increasing odds of returning to work during the study period.[33] The reason could be a change in diagnostic practice and the Danish sickness benefit Act becoming more effective over the years. Seasonal variation was considered a confounder, as a previous study suggested that TBI is associated with season-specific activities and most pronounced during fall and winter.[34] Information on income was taken as personal gross income including revenue and social transfer income and was obtained from the Income Statistics Register.[35] Income was divided into four income groups: <100 000, 100 000-200 000, 200 000-300 000, >300 000 DKK roughly reflecting the quartiles in the present cohort. Information on the highest attained educational level was obtained from the Danish Education Register[36] and was categorized into three educational groups: low education (basic schooling), medium education (high school, trade and craft educations) and high education (short education, medium length education, bachelor's degree, university degrees and Ph.D.). Information on cohabitation status and ethnic origin was obtained from the Danish Family Relations Database[22, 37] and was categorized into married or cohabiting couple and single, and as Danish born and not Danish born respectively. Pre-injury illness burden was measured by Charlson comorbidity index (CCI), a weighted sum of 19 indicators for selected diagnoses.[38, 39] For the present CCI evaluation, a diagnosis was indicated for an individual when a corresponding ICD-10 code was encountered in

the DNPR in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period. Psychiatric diagnoses are not incorporated in CCI but are possible confounders related to both labour market attachment and an increased risk of TBI.[40, 41] Hence, information on psychiatric diagnoses separately from CCI was obtained from the DNPR over the same five-year period.

Statistical analysis

The distribution of the baseline covariates at the index date, and the outcomes at the index date and the follow-up time points were reported as numbers and percentages separately for mTBI patients and their matched controls. Raw comparisons of the baseline covariates between the mTBI patients and their controls are done by Chi-squared tests.

The difference in tendency of some degree of decreased attachment to the labour market, between patients with mTBI and their controls, at each of the index date and the four follow-up time points, was assessed by odds ratios (OR) and corresponding 95% confidence intervals (95%CI) from a multivariable logistic regression model; an OR>1 implied higher odds for the mTBI group. The model was parameterized so that the assessments at the four follow-up time points were adjusted for differences already present at the index date, i.e. pre-injury differences. Hence, the assessment at the index date can be viewed as an assessment of the employment aspect of a social gradient in mTBI incidence; the assessments at the follow-up time points report on the short- and long-term differences in attachment attributable to mTBI. Results are reported both unadjusted and adjusted for the potential confounders: age, gender, municipality, seasonal variation, calendar year, education, income, cohabitation status, ethnicity, pre-injury comorbidities and pre-injury psychiatric diagnosis. Inference was done by generalized estimating equations to adjust for repeated measurement and matching.

Subjects with missing values in one of the covariates were omitted from analyses where these covariates were included. P-values below 0.05 were considered statistically significant. SAS version 9.4 was used for statistical analysis.

Patient and public involvement

Patients and the public were not involved in the design and the conduct of the study

RESULTS

Baseline characteristics of the population

19 732 patients with mTBI were eligible for the cohort and 18 640 matching controls were included in the study. In some cases, notably with patients from small municipalities, it was not possible to find a matching control, see Figure 2. Furthermore, there was a weak tendency in patients with mTBI to have lower socio-economic status (education, income) and higher prevalence of pre-injury diseases (CCI, psychiatric diseases) compared to their matched controls (Table 1).

Insert Figure 2 (flow-chart)

Table 1. Social and pre-injury health characteristics of patients with mTBI and controls					
	Controls (n=18 640)	**mTBI** (n=19 732)	**Total** (n=38 372)	**Missing**	**p-value**[1]
Age, *n(%)*					0.8461
18-29 years	8187 (43.92)	8734 (44.26)	16 921 (44.10)	0	
30-39 years	4118 (22.09)	4290 (21.74)	8408 (21.91)		
40-49 years	3458 (18.55)	3653 (18.51)	7111 (18.53)		
50-60 years	2877 (15.43)	3055 (15.48)	5932 (15.46)		
Gender, *n(%)*					0.5839
Men	11 266 (60.44)	11 872 (60.17)	23 138 (60.30)	0	
Women	7374 (39.56)	7860 (39.83)	15 234 (39.70)		
Education, *n(%)*					<.0001
Low education	6942 (37.73)	8951 (46.14)	15 893 (42.05)	574	
Medium education	7992 (43.43)	7464 (38.48)	15 456 (40.89)		
High education	3466 (18.84)	2983 (15.38)	6449 (17.06)		
Income (Danish kroner, DKK[2]**),** *n(%)*					<.0001
<100.000	4144 (22.27)	4482 (22.72)	8626 (22.50)	40	
100.000-200.000	4152 (22.31)	5697 (28.89)	9849 (25.69)		
200.000-300.000	5325 (28.62)	5418 (27.47)	10 743 (28.03)		
>300.000	4988 (26.80)	4126 (20.92)	9114 (23.78)		
Cohabitation status, *n(%)*					<.0001
Married or cohabiting couple	5701 (30.68)	8051 (40.83)	13 752 (35.90)	70	
Single	12 884 (69.32)	11 666 (59.17)	24 550 (64.10)		
Ethnic origin, *n(%)*					0.5772
Danish born	17 659 (95.02)	18 710 (94.89)	36 369 (94.95)	70	
Born abroad	926 (4.98)	1007 (5.11)	1933 (5.05)		
CCI (categorical), *n(%)*					<.0001
No comorbidities	17 863 (95.83)	18 580 (94.16)	36 443 (94.97)	0	
1 comorbidity	577 (3.10)	842 (4.27)	1419 (3.70)	0	
2 comorbidities	154 (0.83)	210 (1.06)	364 (0.95)	0	
3 comorbidities	46 (0.25)	100 (0.51)	146 (0.38)	0	
Psychiatric diagnosis, *n(%)*					<.0001
No diagnosis	18 345 (98.42)	18 540 (93.96)	36 885 (96.12)	0	
≥1 diagnosis	295 (1.58)	1192 (6.04)	1487 (3.88)		

[1] P-value from a Pearson´s chi-squared test

[2] Currency exchange rate of May 2018: 1 EUR = 7.44834 DKK

Analysis of attachment to labour market

Table 2 shows the prevalence for each outcome for patients and controls during 5 years of follow-up, reported at the index date, at 6 and 12 months and 2 and 5 years

Table 2. Prevalence of labour market attachment and death in patients with mTBI and controls at 6 and 12 months and 2 and 5 years post-injury

		Controls (n=18 640)[1]	**mTBI** (n=19 732)[1]	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**[2]	**p-value**
Not attending ordinary work							
	Index date, n(%)	5040 (27.04)	6247 (31.66)	1.25 (1.20-1.30)	<.0001	1.01 (0.97-1.06)	0.5406
	6 months, n(%)	5107 (27.40)	7289 (36.94)	1.24 (1.20-1.29)	<.0001	1.30 (1.25-1.36)	<.0001
	12 months, n(%)	4898 (26.28)	7149 (36.23)	1.28 (1.22-1.33)	<.0001	1.35 (1.28-1.42)	<.0001
	2 years, n(%)	4793 (25.71)	7297 (36.98)	1.36 (1.29-1.42)	<.0001	1.46 (1.38-1.54)	<.0001
	5 years, n(%)	5520 (29.61)	8420 (42.67)	1.42 (1.35-1.49)	<.0001	1.54 (1.45-1.64)	<.0001
Health-related benefits							
	Index date, n(%)	795 (4.27)	2230 (11.30)	2.85 (2.62-3.10)	<.0001	2.07 (1.90-2.25)	<.0001
	6 months, n(%)	1120 (6.01)	3600 (18.24)	1.21 (1.13-1.29)	<.0001	1.32 (1.22-1.42)	<.0001
	12 months, n(%)	1197 (6.42)	3584 (18.16)	1.12 (1.04-1.20)	0.0020	1.22 (1.13-1.32)	<.0001
	2 years, n(%)	1336 (7.17)	3790 (19.21)	1.07 (0.99-1.15)	0.0968	1.17 (1.08-1.27)	0.0002
	5 years, n(%)	1676 (8.99)	4649 (23.56)	1.08 (1.00-1.17)	0.0528	1.22 (1.12-1.33)	<.0001
Limited attachment to the labour market							
	Index date, n(%)	795 (4.27)	2230 (11.30)	2.86 (2.64-3.11)	<.0001	1.93 (1.76-2.10)	<.0001
	6 months, n(%)	816 (4.38)	2326 (11.79)	1.01 (0.95-1.08)	0.8162	1.02 (0.96-1.09)	0.5123
	12 months, n(%)	846 (4.54)	2388 (12.10)	1.00 (0.94-1.07)	0.9858	1.03 (0.96-1.11)	0.3815
	2 years, n(%)	884 (4.74)	2784 (14.11)	1.14 (1.06-1.23)	0.0005	1.23 (1.13-1.33)	<.0001
	5 years, n(%)	1192 (6.39)	3787 (19.19)	1.20 (1.11-1.30)	<.0001	1.39 (1.27-1.51)	<.0001
Permanent lack of attachment to the labour market							
	Index date, n(%)	0 (0)	0 (0)	.	.	.	.
	6 months, n(%)	33 (0.18)	82 (0.42)	3.40 (2.36-4.90)	<.0001	1.90 (1.36-2.66)	0.0002
	12 months, n(%)	58 (0.31)	173 (1.88)	3.63 (2.77-4.75)	<.0001	2.14 (1.66 -2.77)	<.0001
	2 years, n(%)	117 (0.63)	424 (2.15)	4.20 (3.49-5.05)	<.0001	2.61 (2.17-3.14)	<.0001
	5 years, n(%)	299 (1.60)	1068 (5.41)	3.67 (3.28-4.11)	<.0001	2.59 (2.30-2.92)	<.0001
Death							
	Index date, n(%)	0 (0)	0 (0)	.	.	.	.
	6 months, n(%)	5 (0.03)	59 (0.30)	11.46 (4.38-29.94)	<.0001	6.37 (2.71-14.96)	<.0001
	12 months, n(%)	12 (0.06)	100 (0.51)	8.03 (4.29-15.05)	<.0001	4.67 (2.59-8.40)	<.0001
	2 years, n(%)	26 (0.14)	207 (1.05)	7.67 (5.01-11.75)	<.0001	4.72 (3.12-7.13)	<.0001
	5 years, n(%)	118 (0.63)	477 (2.42)	3.91 (3.17-4.82)	<.0001	2.62 (2.11-3.26)	<.0001

[1]Prevalence expressed as the total number and percentage of patients and controls experiencing the outcome

[2] Generalized estimating equation model with odds ratio of the outcome event in patients compared to controls adjusted for age, gender, municipality, seasonal variation, calendar year, education, income, cohabitation status, ethnicity, comorbidities and pre-injury psychiatric diagnosis

Primary outcome

Not attending ordinary work

For the primary outcome, we found that patients compared to controls had an overall higher increase of not attending ordinary work from the index date (32%, 27%) to 5 years post-injury (43%, 30%) (Table 2). Compared to the secondary outcomes, the prevalence was higher for not attending ordinary work which included social transfer payments that were not health related. For the unadjusted model, there were 25% higher odds of not attending ordinary work (OR 1.25, 95% CI 1.19-1.30) for patients compared to controls at the index date. However, for the adjusted model, no differences were seen between groups at the index date. During the 5 year of follow-up, the odds of not attending ordinary work increased, and at 5 years the odds were 54% higher (OR 1.54, 95% CI 1.45-1.63) among patients with mTBI (Table 2) compared to controls.

Secondary outcomes

Health-related benefits

The overall prevalence of health-related benefits was significantly higher for patients (11%) compared to controls (4%) at the index date, and the difference between groups continued during follow-up. The odds of health-related benefits were more than two times higher (OR 2.07, 95% CI 1.90-2.25) at the index date even after adjustment for potential socio-economic confounders and the odds of health-related benefits continued to stay elevated during follow-up. Table 2.

Limited attachment to the labour market

For social transfer payments related to limited attachment to the labour market, the prevalence was also higher for patients (11%) compared to controls (4%) at the index date and slightly increased during follow-up. The adjusted OR was almost two times higher at the index date for patients

compared to controls (OR 1.92, 95% CI 1.76-2.10). However, the long-term effect of mTBI on limited attachment to the labour market was most pronounced at 2 years and 5 years.

Permanent lack of attachment to the labour market

During follow-up, a higher prevalence of permanent lack of attachment to the labour market was seen in patients compared to controls, which increased from 6 months to 5 years. At 6 months the adjusted odds for permanent lack of attachment to the labour market was almost two times higher for patients (OR 1.90, 95% CI 1.36-2.66) and the long-term perspective continued showing large effect.

Death

The prevalence of death was higher among patients showing an increase from 0.30% at 6 months to 2.42% at 5 years. The adjusted odds for death for patients with mTBI was six-fold increased at 6 months follow-up (OR 6.37 95% CI 2.71-14.95) and the long-term effects continued to be large but diminishing during follow-up.

DISCUSSION

This nationwide register-based study examined the consequences of mTBI on short and long-term labour market attachment in a large cohort of working-age patients with mTBI up to 5 years post-injury compared to matched controls of the general population. The proportion of approximately 20 000 included patients in this study are difficult to compare to previous studies, since these mostly report incidence rates.[4] However, a Danish study included 10 000 patients in 1994 and 2002[5], and another Danish register-based study included approximately 90 000 patients during a 13-year follow-up period.[9]

We found that the attachment to the labour market varied between patients and controls at the date of injury. The odds of not attending ordinary work indicating any social transfer payment was increased by 25% and remained higher for patients during the 5 years of follow-up (of about 40%). A social gradient in not attending ordinary work at the index date could be suspected, as patients had a significantly lower educational level, income and more comorbidities compared to controls (see Table 1). Our findings agree with a Danish register-based cohort study[9] demonstrating that individuals with mTBI had a higher use of general practice even 5 years before mTBI. However, when we controlled for socio-economic factors, comorbidities and psychiatric diagnoses, there was no difference in the odds of not attending ordinary work between the two groups in our sample at index date. Yet, the adjusted odds of not attending ordinary work remained increased by 30-50% during the 5 years follow-up. This strongly supports that mTBI is the incident leading to not returning to work.

For the secondary outcomes, we saw the prevalence of sick listed decreased during follow-up, while the prevalence of limited and finally permanent lack of attachment to the labour market increased as expected. The proportion of individuals receiving health-related benefits at the index date was also higher for patients compared to controls, and the risk was more than two times higher for patients even after controlling for possible confounders. This may indicate increased morbidity in patients with mTBI prior to the trauma as seen in another Danish study[9], and variations in health seeking behavior which result in health-related social transfer payments. However, at 6 months the odds diminished to 30% and were further decreased during the follow-up around 16-20%. Comparing our results to other studies, Stulemeijer et al. found a 76% full RTW rate at 6 months,[42] De Koning et al. found a complete RTW rate of 77% at 12 months[43] and Losoi et al. also found that 97% had fully RTW by 12 months after mTBI.[6] These findings are slightly higher than those reported in this study. However, previous investigations are not directly comparable because there is a lack of

consistency in definitions of labour market attachment and RTW measures. RTW is increasingly regarded as an evolving process consisting of different phases such as off work, work reentry, retention and advancement and measures in each phase.[44] Additionally, differences between countries in registration of social transfer payments, political legislation and socioeconomic differences can complicate comparison.[16]

Theadom et al. found in a cohort study with 4 years of follow-up that work productivity was reduced by 15.5% among patients with mTBI, who had to make job changes in order to continue working.[45] Our study found a long-term prevalence of 19% and increased odds of almost 40% of limited attachment to the labour market indicating long-term employment restrictions due to health conditions. These results indicate that most patients return to work after mTBI, but a small proportion of patients suffer long-term consequences related to mTBI, preventing them from fully re-integrating into the labour market. Since a previous study indicates an association between increasing length of sickness absence and increasing risk of disability pension,[46] these patients are in a particular risk of transitioning from temporary to permanent social benefits, meaning an exit from the labour market. For permanent lack of attachment to the labour market, the prevalence in our study was higher for patients even though there were significantly fewer events especially at 6 and 12 months and 2 years, indicating that it takes time to qualify for disability pension in Denmark. The odds of permanent lack of attachment to the labour market were still more than twice as high in the short as well as the long-term among patients with mTBI, even when controlled for potential confounders.

Finally, the prevalence of death was higher in patients compared to controls. The odds of death were more than 6 times higher for patients and continued to stay significantly higher during follow-up. This is a surprising result. However, Selassie et al. found an in-hospital all-cause mortality rate after mTBI of 1.4%[47] and Pentland et al. found similar results at 0.45% in a cohort with 21 years of

follow up,[48] agreeing with the result found in the present study. Additionally, a Danish study found an increased risk of suicide among patients with mTBI[49]. Although not the aim of the present study, future research may benefit from exploring the risk factors in excess mortality in patients with mTBI.

Strengths and limitations

This study applied a register-based design which prevented information bias in the collection of labour market data and confounding factors. The DREAM register enabled us to estimate point prevalence during 5 years of follow-up and to examine much more diverse labour market outcome measures which is infrequent in TBI research.[16] Furthermore, the sensitivity and specificity of the DREAM register is considered high.[50] Finally, the use of national register data has made it possible to include a large sample size and a matching control group which increased the statistical power. We also adjusted for a wide range of pre-injury potential confounders. However, residual confounding cannot be ruled out. The patients in this study were extracted from the DNPR. Consequently, we did not have access to patient records, which hindered us to apply the operational case definition for mTBI suggested by WHO.[1] Even though the DNPR is considered to be the most comprehensive register of its kind[23], its validity and consistency with clinical diagnoses are widely discussed, especially regarding clinical diagnoses and inaccurate coding leading to misclassification. The ICD-9 code (850) for concussion has in several studies been reported as the most frequently used for classification of mTBI[1, 51] but has also shown lack of sensitivity and specificity.[1] This could also be expected to be the case for ICD-10. Additionally, a large proportion of the mTBI patients are not treated at the hospital, some are treated in primary care settings, and some refrain from counselling a physician,[52] which can lead to low incidence rates and selection bias, limiting the generalizability of the results.[53]

Implications

According to previous studies, a small proportion of patients with mTBI may suffer from persistent post-concussive symptoms for months and years after injury, preventing them from returning to previous work.[13, 41, 54] This study showed that patients with mTBI have a higher prevalence of receiving social transfer benefits compared to the general population post-injury. This represents a substantial cost for the society as a whole. In Denmark there are no national guidelines for the treatment and rehabilitation of patients with mTBI. This is in contrast to the guidelines developed for patients suffering more severe forms of TBI. We assume that the treatment trajectory in mTBI patients is therefore lengthy and inefficient, as it is highly dependent on referrals from general practitioners, insurance companies and the municipalities. Moreover, the offered services are highly variable and poorly coordinated. Our data suggest that from a societal perspective, also the treatment of patients with mTBI needs a comprehensive and coordinated approach, including the identification of patients at risk of developing persistent post-concussive symptoms and initiation of a treatment plan in a timely fashion. Future research should therefore focus on examining the contributory causes as to why patients with mTBI do not return to work.

CONCLUSIONS

Most patients returned to work after mTBI. However, a small proportion of patients with mTBI received social transfer payments related to health and work disability to a higher extend than the general population up to 5 years post-injury, even when controlling for possible socio-economic and health related confounders. Additionally, the prevalence of death was increased during follow-up. Initiatives that prevent the progression of persistent post-concussive symptoms should be considered to reduce lack of attachment to the labour market in this patient group in the future.

ETHICS APPROVAL

The study was approved by the Danish Data Protection Agency (Datatilsynet) no. (05179- RH-2016-389). The study protocol was registered on clinicaltrial.gov on July 5, 2017 (ClinicalTrials.gov Identifier: NCT03214432).

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Competing interest statement

None declared

Patient consent

Not required

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Contributors

All authors participated in the study design, interpretation of the data, revising it critically and the final approval of the manuscript to be published. HJG obtained the funding, drafted the protocol and manuscript and collaborated with VS on performing the statistical analyses. AM, LA, JK, IE and HMR participated in the study design and conceptualization.

Data sharing statement

No additional data are available

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Figure 1. Description of unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1) and the secondary outcomes (2-5) in terms of the social transfer payments and other social conditions that are included in each.

Figure 2. Inclusion of the study population

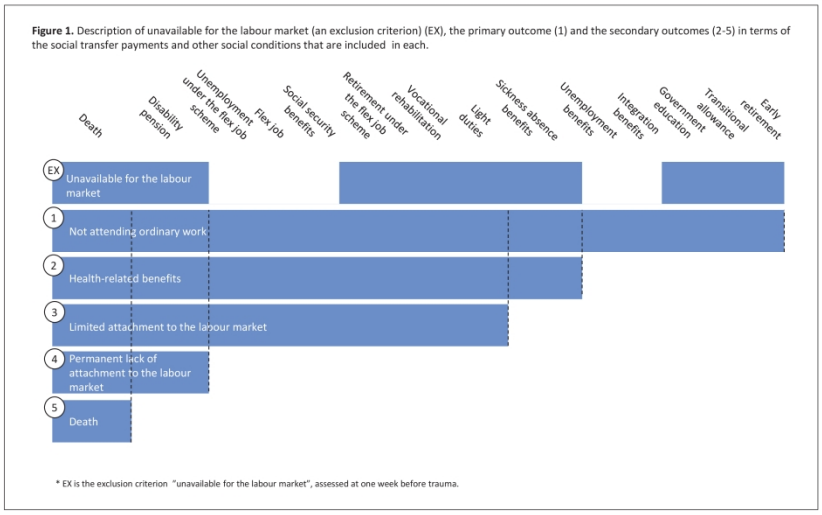

Figure 1. Description of unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1) and the secondary outcomes (2-5) in terms of the social transfer payments and other social conditions that are included in each.

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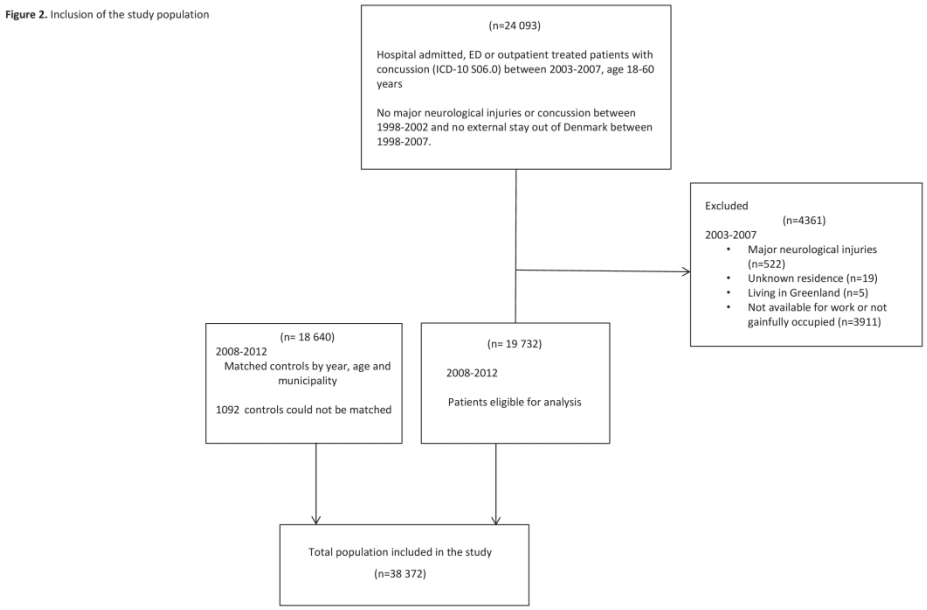

Figure 2. Inclusion of the study population

297x209mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	3, 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-11
Bias	9	Describe any efforts to address potential sources of bias	7, 20
Study size	10	Explain how the study size was arrived at	7, 8, 13
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11, 12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12, 13
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13-14
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13-15
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	15-17

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	15-17
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	17-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Labour market attachment after mild traumatic brain injury: Nationwide cohort study with 5-year register follow-up in Denmark

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Labour market attachment after mild traumatic brain injury: Nationwide cohort study with 5-year register follow-up in Denmark

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ABSTRACT

Objectives: Sickness absence after mild traumatic brain injury (mTBI) is frequent due to post-concussive symptoms. We examined labour market attachment following mTBI up to 5 years post-injury.

Design and setting: Nationwide cohort study with register follow-up.

Participants: Patients between 18-60 years with mTBI (ICD-10 diagnosis S06.0) were extracted from the Danish National Patient Register (n=19 732). Controls were matched on sex, age and municipality (n=18 640). Patients with spinal cord and column injuries, TBI and concussions five-years pre-injury or as secondary diagnosis to the concussion in the inclusion period were excluded.

Primary and secondary outcome measures: Data were extracted from the DREAM register. Primary outcome was "not attending ordinary work" defined as receiving any social transfer payment. Secondary outcomes were health-related benefits, limited attachment to the labour market, permanent lack of attachment to the labour market and death.

Results: 5 years after diagnosis, 43% of patients were not attending ordinary work. The odds increased from 6 months (OR 1.30, 95% CI 1.24-1.36) to 5 years (OR 1.54, 95% CI 1.45-1.63). The odds of health-related benefits were 32% (OR 1.32, 95% CI 1.22-1.42) at 6 months and 22% (OR 1.22, 95% CI 1.12-1.33) at 5 years. Limited attachment to the labour market showed increased odds at 5 years (OR 1.38, 95% CI 1.27-1.51) and the odds of permanent lack of attachment to the labour market were higher for patients compared to controls, (OR 2.59, 95% CI 2.30-2.92). Death was more than two times higher at 5 years post-injury (OR 2.62, 95% CI 2.10-3.26).

Conclusions:

43% of concussed patients were not attending ordinary work 5 years post-injury and received health and social transfer benefits. We conclude that mTBI has a long-term impact on labour market attachment. Prevention and treatment of persisting post-concussive symptoms should be considered.

ClinicalTrials.gov Identifier: NCT03214432

ARTICLE SUMMARY

Strengths and limitations of this study

- This was a nationwide cohort study with register-based follow-up including nearly 20 000 patients with mild traumatic brain injury (mTBI).
- The data were extracted from high-quality Danish national registers.
- This study estimated the prevalence and odds (OR) of not attending ordinary work, health-related benefits and death in patients with mTBI up to 5 years post-injury.
- This study had no access to patient records, with the inherent risk of misclassification.

INTRODUCTION

Mild traumatic brain injury (mTBI) is a common neurological disease defined as an acute brain injury resulting from mechanical energy to the head from external physical force, typically classified with a Glasgow Coma Scale score of 13-15 post-injury. [1] Concussion (commotio cerebri) represents an entity, that is grouped under mTBI, although the pathophysiology behind may be dissimilar and heterogeneous. The differentiation remains elusive due to the usual absence of objective findings on conventional imaging. The clinical diagnosis of concussion is based on short-lasting alteration of consciousness and presence of posttraumatic amnesia and confusion.[2, 3] Despite recent efforts to improve the clinical diagnostic process,[4, 5] accurate diagnosis of mTBI is still a challenge due to frequent confounding factors.

Approximately 70-90% of all TBIs fall into the category of mTBI.[6-8] The incidence of hospital and emergency treated patients is 50-300 cases per 100 000 people in the US, Scandinavia and Australia[8, 9] and more frequent among young people and men.[8] However, these numbers probably fall short as studies also show numbers more than 700 cases per 100 000 people per year.[8]

Numerous studies have examined post-concussive symptoms in adults showing symptoms like dizziness, fatigue, insomnia, posttraumatic headache and memory and concentration difficulties[10-12] leading to long-term sickness and absence from work. Post-concussive symptoms result in an increased use of general practice services the first year post-injury, as reported by a Danish study.[13] In 15% of patients with mTBI, post-concussive symptoms are persistent (>12 months post-injury).[14, 15] Additionally, several risk factors are associated with persisting symptomatology, such as female gender, premorbid physical or psychiatric comorbidities, injury-related conditions, previous head injury, psychological distress, and drug and alcohol abuse.[12, 16, 17]

Most patients return to work within the first couple of months after mTBI, but a small proportion of patients is unable to return to work due to disability.[18, 19] Cancelliere et al. found that

most patients (>75%) had returned to work after six months and 5% were on social transfer payments two years post-injury.[20]

Return to work (RTW) has been conceptualized as being a dynamic process with different related outcomes of labour market attachment or time off work, but also outcomes related to the process of return to work such as psychological functioning and job satisfaction.[21, 22] RTW after mTBI has been suggested to depend on multiple factors such as injury related factors,[20] premorbid demographics such as younger age,[18] work place related factors such as support,[23] and influence on work planning[24] and patient characteristics such as psychosocial status.[25] These studies have methodological limitations in study design which complicate evaluation of evidence regarding the magnitude of the problem. They have small sample sizes, are not representative,[10] are based on self-reported data and have short follow-up and considerable dropout leading to attrition bias.[19] The present analysis overcomes these challenges by using Danish nationwide administrative data to examine a larger, representative sample and to perform long-term follow up. This study is concerned with labour market attachment in hospital treated patients receiving the diagnosis concussion (commotio cerebri) as the only brain injury diagnosis.

We examined a comprehensive range of post-injury transitions in the labour market aiming at analysing attachment to the labour market up to five years after mTBI using a portfolio of outcomes, including a variation of social transfer payments and data on permanent lack of attachment to the labour market and death.

METHODS

The data used in the present analyses is obtained by linking several Danish national registers through the unique personal identification number (CPR number) assigned to all Danish citizens at birth or immigration, provided by the Danish Civil Registration System (CRS).[26]

Study population

The study was a nationwide population-based cohort study of all mTBI cases in Denmark in the five-year inclusion period 1st of January 2003 – 31st of December 2007. Cases were identified in the Danish National Patient Register (DNPR) which contains information on all in- and outpatient contacts in Danish secondary care.[27] Notably, it codes each contact with International Classification of Diseases, version 10 (ICD-10) diagnosis codes. Patients with mTBI were included in the cohort on their index date, the date of their first entry in the DNPR in the inclusion period with concussion (ICD-10 code S06.0) as primary diagnosis, excluding patients with diagnosis (primary or secondary) of cerebral oedema, diffuse and focal brain injury, subdural, epidural and subarachnoid haemorrhage, crushing injury and fracture of head, neck, skull, face and facial bones, and injuries of brain and cranial nerves in the inclusion period.[9] Included patients with mTBI were working-age adults between 18-60 years available for the labour market on the index date; the upper limit was set because individuals in Denmark older than 60 years are entitled to early retirement, if they have paid for such a scheme.[28] Availability for the labour market was defined as gainful employment or receiving unemployment benefits, but actively job seeking (see Figure 1). Furthermore, they were not hospital treated or diagnosed with other major neurological injuries such as spinal cord and column injuries[29] and traumatic brain injury (TBI) (including concussion)[9] in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period[9, 30] since previous brain injury and neurological problems are found to be associated with prolonged symptoms.[31] Finally,

patients were not included if they had lived outside of Denmark at any time during the inclusion period and the five-year period before.

For each mTBI case in the cohort, a control was randomly selected from the Population register. Controls had similar inclusion criteria as the cases, but they had no diagnosis of concussion during the inclusion period 1st of January 2003 – 31st of December 2007.

The control was matched to the case on sex, municipality and age (year of birth ± 0.5 years, expanded to 1 and 2 years in case of no initial match) (see Figure 1). The same exclusion criteria were applied for the selection of controls.

Insert Figure 1

Availability for the labour market was assessed from the Danish Register for Evaluation of Marginalization (DREAM), containing weekly information on all individuals receiving any social public transfer payments.[32] Patients and their matching controls were excluded from the cohort if there were any major neurological injuries[9, 29] as secondary diagnoses at the index date, they were unavailable for the labour market, they had unknown residence or were inhabitants of Greenland.

Outcome measures

The outcomes of the present analyses were assessments of variations in attachment to the labour market evaluated in the DREAM database (Figure 1) the week before the case's index date, and at 6 months, 12 months, 2 years and 5 years after the case's index date (Figure 1).

Not attending ordinary work

1. "Not attending ordinary work" was the primary outcome and was indicated by any entry in DREAM, i.e. receiving any social transfer payment, such as unemployment benefits unrelated to the subject's health condition, sickness absence benefits, social benefits granted, short and long-term

sickness or death. If there was no DREAM entry, it was assumed that the subject was gainfully employed or self-supporting at that time (Figure 1).

The set of secondary outcomes are defined increasingly narrower than the primary outcome and focus on attachment to the labour market due to health conditions. At the time of the current study, employers in Denmark were obliged to finance sickness benefits for the first 30 days. Sickness benefits lasting more than four consecutive weeks were to be compensated by the Danish municipalities.[33] Sick-listed individuals could receive sickness benefits for a maximum of one year[34]. If individuals were not able to return to ordinary work due to long-term limited work capacity, a partial return to work at lower capacity was possible with a "flex job". If the sick-listed individual was not able to return to work at all, the municipality could grant disability pension.[35, 36] The grading of the outcomes is illustrated in Figure 1.

Health-related benefits

2. Health-related benefits were indicated by DREAM entries given for short- or long-term restrictions in attachment to the labour market due to health conditions (excluding unemployment benefits unrelated to the subject's health condition). These were sickness absence benefits, vocational rehabilitation, flex job, unemployment benefits specifically granted to citizens on flex job, social security benefits, light duties, disability pension and death.

Limited attachment to the labour market

3. Social transfer payments due to limited attachment to the labour market were indicated by DREAM entries given for reduced work capacity and thereby long-term restrictions in attachment to the labour market due to health conditions (excluding sickness absence benefits compared to

secondary outcome 2). These were vocational rehabilitation, flex job, unemployment benefits specifically granted to citizens on flex job, social security benefits, light duties, disability pension and death.

Permanent lack of attachment to the labour market

4. Permanent lack of attachment to the labour market was indicated by DREAM entries given for permanent withdrawal from the labour market due to health conditions. These were disability pension and death.

Death

5. Death was indicated by the DREAM entry for death.

Potential confounders

Sex, age and municipality at the index date were obtained from the Population register linked to the DNPR. The municipality information was categorized into five regions reflecting Denmark's reform of local government structure from 2007.[37] From the index date calendar year and season were derived. Calendar year was included in the model as a previous study found increasing odds of returning to work during the study period.[38] The reason could be a change in diagnostic practice and the Danish sickness benefit Act becoming more effective over the years. Seasonal variation was considered a confounder, as a previous study suggested that TBI is associated with season-specific activities and most pronounced during fall and winter.[39] Pre-injury income was measured at the index date and taken as personal gross income including revenue and social transfer income and was obtained from the Income Statistics Register.[40] Income was divided into four income groups: <100 000, 100 000-200 000, 200 000-300 000, >300 000 DKK roughly reflecting the quartiles in

the present cohort. Information on the highest attained educational level was obtained from the Danish Education Register[41] and was categorized into three educational groups: low education (primary education), medium education (lower and upper secondary education, post-secondary–non-tertiary education) and high education (short cycle tertiary education, bachelor, master, doctoral or equivalent). Information on cohabitation status and ethnic origin was obtained from the Danish Family Relations Database[26, 42] and was categorized into married or cohabiting couple and single, and as Danish born and not Danish born respectively. Pre-injury illness burden was measured by Charlson comorbidity index (CCI), a weighted sum of 19 indicators for selected diagnoses.[43, 44] For the present CCI evaluation, a diagnosis was indicated for an individual when a corresponding ICD-10 code was encountered in the DNPR in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period. Psychiatric diagnoses are not incorporated in CCI but are possible confounders related to both labour market attachment and an increased risk of TBI.[45, 46] Hence, information on psychiatric diagnoses separately from CCI was obtained from the DNPR over the same five-year period.

Statistical analysis

Baseline covariates at the index date, and the outcomes at the index date and the follow-up time points were reported as numbers and percentages separately for mTBI patients and their matched controls. Raw comparisons of the baseline covariates between the mTBI patients and their controls are done by Chi-squared tests.

The difference in tendency of some degree of decreased attachment to the labour market, between patients with mTBI and their controls, at each of the index date and the four follow-up time points, was assessed by odds ratios (OR) and corresponding 95% confidence intervals (95%CI) from a multivariable logistic regression model; an OR>1 implied higher odds for the mTBI group. The model was parameterized so that the assessments at the four follow-up time points were adjusted for

differences already present at the index date, i.e. pre-injury differences. Hence, the assessment at the index date can be viewed as an assessment of the employment aspect of a social gradient in mTBI incidence; the assessments at the follow-up time points report on the short- and long-term differences in attachment attributable to mTBI. Results are reported both unadjusted and adjusted for the potential confounders: age, gender, municipality, seasonal variation, calendar year, education, income, cohabitation status, ethnicity, pre-injury comorbidities and pre-injury psychiatric diagnosis. Inference was done by generalized estimating equations to adjust for repeated measurement and matching.

Subjects with missing values in one of the covariates were omitted from analyses where these covariates were included. P-values below 0.05 were considered statistically significant. SAS version 9.4 was used for statistical analysis.

Patient and public involvement

Patients and the public were not involved in the design and the conduct of the study.

RESULTS

Baseline characteristics of the population

19 732 patients with mTBI were eligible for the cohort and 18 640 matching controls were included in the study. In some cases, notably with patients from small municipalities, it was not possible to find a matching control, see Figure 2. Overall, the cohort was characterized by a weak tendency in patients with mTBI to have lower education, lower income, being married or cohabiting, and having a higher prevalence of pre-injury diseases (both somatic diseases as captured by CCI and psychiatric diseases) compared to their matched controls (Table 1).

Insert Figure 2 (flow-chart)

Table 1. Social and pre-injury health characteristics of patients with mTBI and controls					
	Controls (n=18 640)	**mTBI** (n=19 732)	**Total** (n=38 372)	**Missing**	**p-value**[1]
Age, *n(%)*					0.8461
18-29 years	8187 (43.92)	8734 (44.26)	16 921 (44.10)	0	
30-39 years	4118 (22.09)	4290 (21.74)	8408 (21.91)		
40-49 years	3458 (18.55)	3653 (18.51)	7111 (18.53)		
50-60 years	2877 (15.43)	3055 (15.48)	5932 (15.46)		
Gender, *n(%)*					0.5839
Men	11 266 (60.44)	11 872 (60.17)	23 138 (60.30)	0	
Women	7374 (39.56)	7860 (39.83)	15 234 (39.70)		
Education, *n(%)*					<.0001
Low education	6942 (37.73)	8951 (46.14)	15 893 (42.05)	574	
Medium education	7992 (43.43)	7464 (38.48)	15 456 (40.89)		
High education	3466 (18.84)	2983 (15.38)	6449 (17.06)		
Income (Danish kroner, DKK[2]**),** *n(%)*					<.0001
<100.000	4144 (22.27)	4482 (22.72)	8626 (22.50)	40	
100.000-200.000	4152 (22.31)	5697 (28.89)	9849 (25.69)		
200.000-300.000	5325 (28.62)	5418 (27.47)	10 743 (28.03)		
>300.000	4988 (26.80)	4126 (20.92)	9114 (23.78)		
Cohabitation status, *n(%)*					<.0001
Married or cohabiting couple	5701 (30.68)	8051 (40.83)	13 752 (35.90)	70	
Single	12 884 (69.32)	11 666 (59.17)	24 550 (64.10)		
Ethnic origin, *n(%)*					0.5772
Danish born	17 659 (95.02)	18 710 (94.89)	36 369 (94.95)	70	
Born abroad	926 (4.98)	1007 (5.11)	1933 (5.05)		
CCI (categorical), *n(%)*					<.0001
No comorbidities	17 863 (95.83)	18 580 (94.16)	36 443 (94.97)	0	
1 comorbidity	577 (3.10)	842 (4.27)	1419 (3.70)	0	
2 comorbidities	154 (0.83)	210 (1.06)	364 (0.95)	0	
3 comorbidities	46 (0.25)	100 (0.51)	146 (0.38)	0	
Psychiatric diagnosis, *n(%)*					<.0001
No diagnosis	18 345 (98.42)	18 540 (93.96)	36 885 (96.12)	0	
≥1 diagnosis	295 (1.58)	1192 (6.04)	1487 (3.88)		

[1] P-value from a Pearson´s chi-squared test

[2] Currency exchange rate of May 2018: 1 EUR = 7.44834 DKK

Analysis of attachment to labour market

Table 2 shows the prevalence for each outcome for patients and controls during 5 years of follow-up.

Table 2. Prevalence of labour market attachment and death in patients with mTBI and controls at 6 and 12 months and 2 and 5 years post-injury

		Controls (n=18 640)[1]	**mTBI** (n=19 732)[1]	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**[2]	**p-value**
Not attending ordinary work							
	Index date, n(%)	5040 (27.04)	6247 (31.66)	1.25 (1.20-1.30)	<.0001	1.01 (0.97-1.06)	0.5406
	6 months, n(%)	5107 (27.40)	7289 (36.94)	1.24 (1.20-1.29)	<.0001	1.30 (1.25-1.36)	<.0001
	12 months, n(%)	4898 (26.28)	7149 (36.23)	1.28 (1.22-1.33)	<.0001	1.35 (1.28-1.42)	<.0001
	2 years, n(%)	4793 (25.71)	7297 (36.98)	1.36 (1.29-1.42)	<.0001	1.46 (1.38-1.54)	<.0001
	5 years, n(%)	5520 (29.61)	8420 (42.67)	1.42 (1.35-1.49)	<.0001	1.54 (1.45-1.64)	<.0001
Health-related benefits							
	Index date, n(%)	795 (4.27)	2230 (11.30)	2.85 (2.62-3.10)	<.0001	2.07 (1.90-2.25)	<.0001
	6 months, n(%)	1120 (6.01)	3600 (18.24)	1.21 (1.13-1.29)	<.0001	1.32 (1.22-1.42)	<.0001
	12 months, n(%)	1197 (6.42)	3584 (18.16)	1.12 (1.04-1.20)	0.0020	1.22 (1.13-1.32)	<.0001
	2 years, n(%)	1336 (7.17)	3790 (19.21)	1.07 (0.99-1.15)	0.0968	1.17 (1.08-1.27)	0.0002
	5 years, n(%)	1676 (8.99)	4649 (23.56)	1.08 (1.00-1.17)	0.0528	1.22 (1.12-1.33)	<.0001
Limited attachment to the labour market							
	Index date, n(%)	795 (4.27)	2230 (11.30)	2.86 (2.64-3.11)	<.0001	1.93 (1.76-2.10)	<.0001
	6 months, n(%)	816 (4.38)	2326 (11.79)	1.01 (0.95-1.08)	0.8162	1.02 (0.96-1.09)	0.5123
	12 months, n(%)	846 (4.54)	2388 (12.10)	1.00 (0.94-1.07)	0.9858	1.03 (0.96-1.11)	0.3815
	2 years, n(%)	884 (4.74)	2784 (14.11)	1.14 (1.06-1.23)	0.0005	1.23 (1.13-1.33)	<.0001
	5 years, n(%)	1192 (6.39)	3787 (19.19)	1.20 (1.11-1.30)	<.0001	1.39 (1.27-1.51)	<.0001
Permanent lack of attachment to the labour market							
	Index date, n(%)	0 (0)	0 (0)	.	.	.	.
	6 months, n(%)	33 (0.18)	82 (0.42)	3.40 (2.36-4.90)	<.0001	1.90 (1.36-2.66)	0.0002
	12 months, n(%)	58 (0.31)	173 (1.88)	3.63 (2.77-4.75)	<.0001	2.14 (1.66 -2.77)	<.0001
	2 years, n(%)	117 (0.63)	424 (2.15)	4.20 (3.49-5.05)	<.0001	2.61 (2.17-3.14)	<.0001
	5 years, n(%)	299 (1.60)	1068 (5.41)	3.67 (3.28-4.11)	<.0001	2.59 (2.30-2.92)	<.0001
Death							
	Index date, n(%)	0 (0)	0 (0)	.	.	.	.
	6 months, n(%)	5 (0.03)	59 (0.30)	11.46 (4.38-29.94)	<.0001	6.37 (2.71-14.96)	<.0001
	12 months, n(%)	12 (0.06)	100 (0.51)	8.03 (4.29-15.05)	<.0001	4.67 (2.59-8.40)	<.0001
	2 years, n(%)	26 (0.14)	207 (1.05)	7.67 (5.01-11.75)	<.0001	4.72 (3.12-7.13)	<.0001
	5 years, n(%)	118 (0.63)	477 (2.42)	3.91 (3.17-4.82)	<.0001	2.62 (2.11-3.26)	<.0001

[1]Prevalence expressed as the total number and percentage of patients and controls experiencing the outcome

[2] Generalized estimating equation model with odds ratio of the outcome event in patients compared to controls adjusted for age, gender, municipality, seasonal variation, calendar year, education, income, cohabitation status, ethnicity, comorbidities and pre-injury psychiatric diagnosis

Primary outcome

Not attending ordinary work

It can be seen from table 2 and figure 3 that patients compared to controls had an overall higher increase of not attending ordinary work from the index date (32%, 27%) to 5 years post-injury (43%, 30%) (Table 2) (Figure 3). Compared to the secondary outcomes, the prevalence was higher for not attending ordinary work which included social transfer payments that were not health related. For the unadjusted model, there were 25% higher odds of not attending ordinary work (OR 1.25, 95% CI 1.19-1.30) for patients compared to controls at the index date. However, for the adjusted model, no differences were seen between groups at the index date. During the 5 year of follow-up, the odds of not attending ordinary work increased, and at 5 years the odds were 54% higher (OR 1.54, 95% CI 1.45-1.63) among patients with mTBI (Table 2) (Figure 3) compared to controls.

Insert Figure 3

Secondary outcomes

Health-related benefits

The overall prevalence of health-related benefits was significantly higher for patients (11%) compared to controls (4%) at the index date, and the difference between groups continued during follow-up. The odds of health-related benefits were more than two times higher (OR 2.07, 95% CI 1.90-2.25) at the index date even after adjustment for potential socio-economic confounders and the odds of health-related benefits continued to stay elevated during follow-up. Table 2.

Limited attachment to the labour market

For social transfer payments related to limited attachment to the labour market, the prevalence was also higher for patients (11%) compared to controls (4%) at the index date and slightly increased during follow-up. The adjusted OR was almost two times higher at the index date for patients compared to controls (OR 1.92, 95% CI 1.76-2.10). However, the long-term effect of mTBI on limited attachment to the labour market was most pronounced at 2 years and 5 years.

Permanent lack of attachment to the labour market

During follow-up, a higher prevalence of permanent lack of attachment to the labour market was seen in patients compared to controls, which increased from 6 months to 5 years. At 6 months the adjusted odds for permanent lack of attachment to the labour market was almost two times higher for patients (OR 1.90, 95% CI 1.36-2.66) and the long-term perspective continued showing large effect.

Death

The prevalence of death was higher among patients showing an increase from 0.30% at 6 months to 2.42% at 5 years. The adjusted odds for death for patients with mTBI was six-fold increased at 6 months follow-up (OR 6.37 95% CI 2.71-14.95) and the long-term effects continued to be large but diminishing during follow-up.

DISCUSSION

We examined short and long-term labour market attachment in a large cohort of working-age patients with mTBI up to 5 years post-injury compared to the general population. The proportion of approximately 20 000 included patients in this study are difficult to compare to previous studies, since these mostly report incidence rates.[8] However, a Danish study included 10 000 patients in

1994 and 2002,[9] and another Danish register-based study included approximately 90 000 patients during a 13-year follow-up period.[13]

We found that attachment to the labour market varied between patients and controls at the date of injury. The odds of not attending ordinary work was increased by 25% and remained higher for patients during the 5 years of follow-up (of about 40%). A social gradient in not attending ordinary work at the index date could be suspected, as patients had a significantly lower educational level, income and more comorbidities compared to controls (see Table 1). Our findings agree with a Danish register-based cohort study[13] demonstrating that individuals with mTBI had a higher use of general practice even 5 years before mTBI. However, when we controlled for socio-economic factors, comorbidities and psychiatric diagnoses, there were no difference in the odds of not attending ordinary work between the two groups in our sample at index date. Yet, the adjusted odds of not attending ordinary work remained increased by 30-50% during the 5 years follow-up. This strongly supports that mTBI is the incident leading to not returning to work.

For the secondary outcomes, the prevalence of sick listed decreased during follow-up, while the prevalence of limited and permanent lack of attachment to the labour market increased as expected. The proportion of individuals receiving health-related benefits at the index date was also higher for patients compared to controls, and the risk was more than two times higher for patients even after controlling for possible confounders. This may indicate increased morbidity in patients with mTBI prior to the trauma as seen in another Danish study[13], and variations in health seeking behavior which result in health-related social transfer payments. However, at 6 months the odds diminished to 30% and were further decreased during follow-up to 16-20%. Stulemeijer et al. found a 76% full RTW rate at 6 months,[47] De Koning et al. found a complete RTW rate of 77% at 12 months[48] and Losoi et al. also found that 97% had fully RTW by 12 months after mTBI.[10] These findings are slightly higher than those reported in this study. However, previous investigations are

not directly comparable because there is a lack of consistency in definitions of labour market attachment and RTW measures. RTW is increasingly regarded as an evolving process consisting of different phases such as off work, work reentry, retention and advancement.[49] Additionally, differences between countries in registration of social transfer payments, political legislation and socioeconomic differences can complicate comparison.[20]

Theadom et al. found that work productivity was reduced by 15.5% among patients with mTBI, who had to make job changes to continue working.[50] Our study found a long-term prevalence of 19% and increased odds of almost 40% of limited attachment to the labour market indicating long-term employment restrictions due to health conditions. These results indicate that most patients return to work after mTBI, but a small proportion of patients suffer long-term consequences related to mTBI, preventing them from fully re-integrating into the labour market. Since a previous study indicates an association between increasing length of sickness absence and increasing risk of disability pension,[51] these patients are in risk of transitioning from temporary to permanent social benefits, meaning an exit from the labour market. For permanent lack of attachment to the labour market, the prevalence in our study was higher for patients even though there were significantly fewer events especially at 6 and 12 months and 2 years, indicating that it takes time to qualify for disability pension in Denmark. The odds of permanent lack of attachment to the labour market were still more than twice as high in the short as well as the long-term among patients with mTBI, even when controlled for potential confounders.

Finally, the prevalence of death was higher in patients compared to controls. The odds of death were more than 6 times higher for patients and subsequently declined during follow-up. This is a surprising result assumed to be predicted by a set of different factors (socio-economic indicators, comorbidities etc.) than those predicting labour market attachment. Selassie et al. found an in-hospital all-cause mortality rate after mTBI of 1.4%[52] and Pentland et al. found similar results at

0.45% in a cohort with 21 years of follow up,[53] agreeing with the result found in the present study. Additionally, a Danish study found an increased risk of suicide among patients with mTBI[54]. Although not the aim of the present study, future research may benefit from exploring the risk factors in excess mortality in patients with mTBI.

Strengths and limitations

This study applied a register-based design preventing information bias in the collection of data. The DREAM register enabled us to estimate point prevalence during 5 years of follow-up and to examine much more diverse labour market outcomes which is infrequent in TBI research.[20] Furthermore, the sensitivity and specificity of the DREAM register is considered high.[55] Finally, the use of national register data has made it possible to include a large sample size and a matching control group which increased the statistical power. We also adjusted for a wide range of pre-injury potential confounders. However, residual confounding such as injury mechanism and psychological effects affecting outcome cannot be ruled out. Patients were extracted from the DNPR. Consequently, we did not have access to patient records, which hindered us to apply the operational case definition for mTBI suggested by WHO.[4] Even though the DNPR is considered the most comprehensive register of its kind,[27] its validity and consistency with clinical diagnoses are widely discussed, especially regarding clinical diagnoses and inaccurate coding leading to misclassification. The ICD-9 code (850) for concussion has in several studies been reported as frequently used for the classification of mTBI[4, 56] but has also shown lack of sensitivity and specificity.[4] This could also be expected to be the case for ICD-10. Additionally, a large proportion of patients with mTBI are not treated at the hospital, some are treated in primary care settings, and some refrain from counselling a physician,[57] which can lead to low incidence rates and selection bias, limiting the generalizability of the results.[58]

Implications

A small proportion of patients with mTBI may suffer from persistent post-concussive symptoms for months and years after injury, preventing returning to previous work.[17, 46, 59] This study showed that patients with mTBI have a higher prevalence of receiving social transfer payments compared to the general population post-injury. In Denmark there are no national guidelines for the treatment and rehabilitation of patients with mTBI. This is in contrast to the guidelines developed for patients suffering more severe forms of TBI. We therefore assume that the treatment trajectory in patients with mTBI is lengthy and inefficient, as it is highly dependent on referrals from general practitioners, insurance companies and the municipalities. Our data suggest that patients with mTBI needs a comprehensive and coordinated approach, including the identification of patients at risk of developing persistent post-concussive symptoms and initiation of a treatment plan in a timely fashion. Future research should focus on examining the contributory causes as to why patients with mTBI do not return to work.

CONCLUSIONS

Most patients returned to work after mTBI. However, a small proportion of patients with mTBI received social transfer payments related to health and work disability to a higher extent than the general population at 5 years post-injury. Additionally, the prevalence of death was increased during follow-up. Initiatives that identify and prevent the progression of persistent post-concussive symptoms should be considered to reduce lack of attachment to the labour market in this patient group.

ETHICS APPROVAL

The study was approved by the Danish Data Protection Agency (Datatilsynet) no. (05179- RH-2016-389). The study protocol was registered on clinicaltrial.gov on July 5, 2017 (ClinicalTrials.gov Identifier: NCT03214432).

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Competing interest statement

None declared

Patient consent

Not required

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Contributors

All authors participated in the study design, interpretation of the data, revising it critically and the final approval of the manuscript to be published. HJG obtained the funding, drafted the protocol and manuscript and collaborated with VS on performing the statistical analyses. AM, LA, JK, IE and HMR participated in the study design and conceptualization.

Data sharing statement

No additional data are available

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Figure 1. Description of social transfer payments as part of the Danish welfare system. Categories describe unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1) and the secondary outcomes (2-5) in terms of the different social transfer payments and other social conditions (first row) that are included in each.

Figure 2. Inclusion of the study population

Figure 3. Prevalence and adjusted odds of not attending ordinary work at the index date and up to 5 years after concussion

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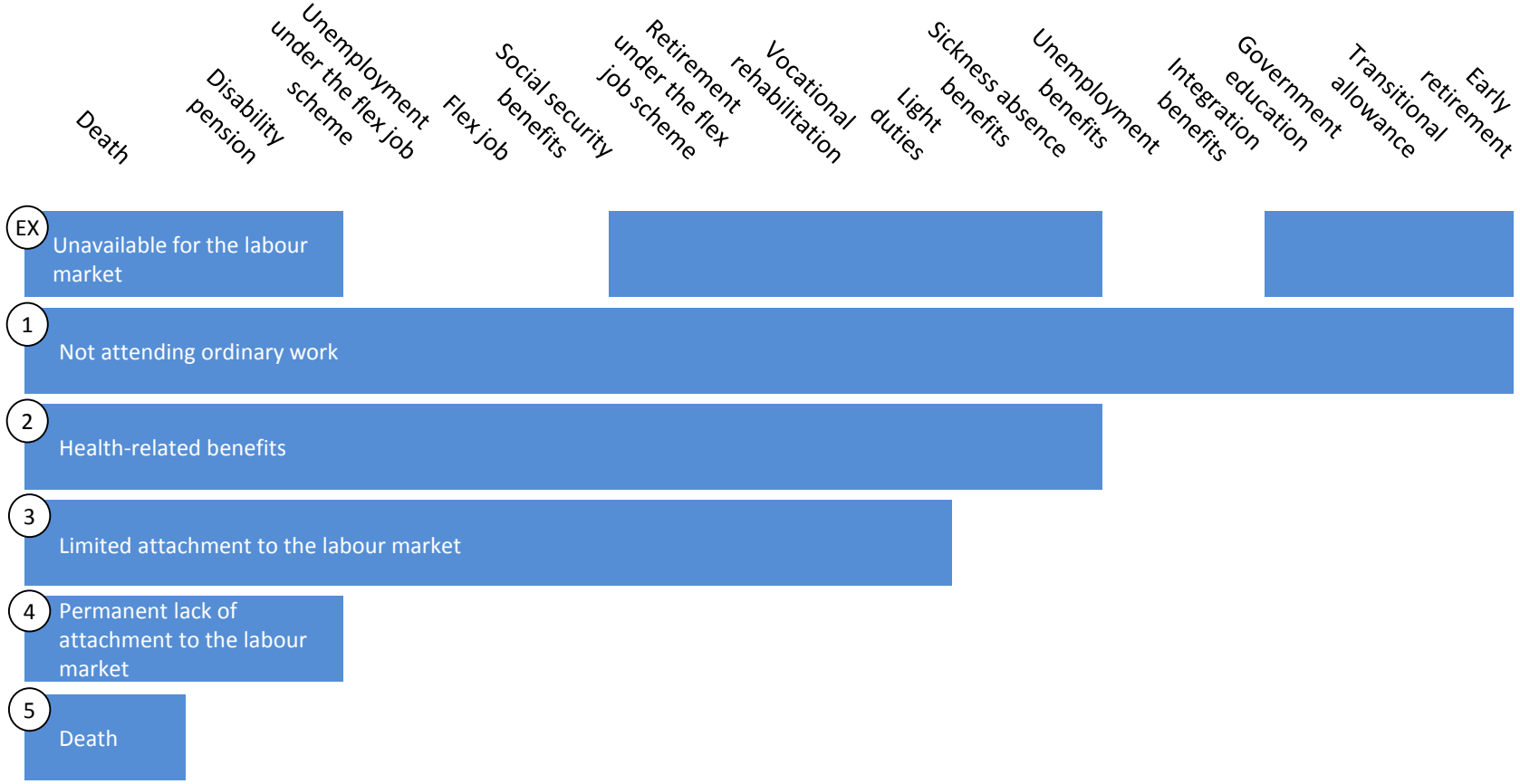
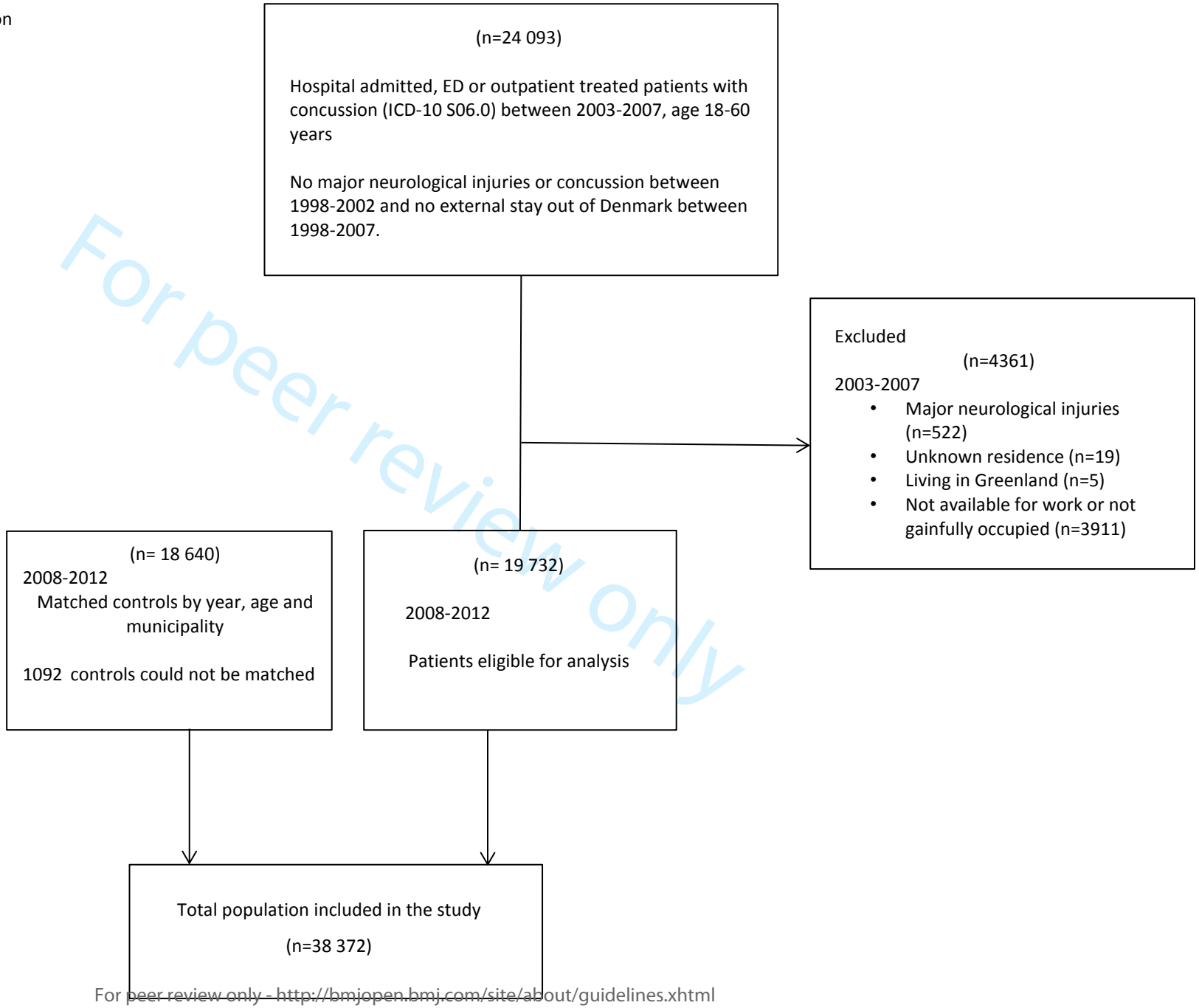


* EX is the exclusion criterion "unavailable for the labour market", assessed at one week before trauma.

Figure 2. Inclusion of the study population



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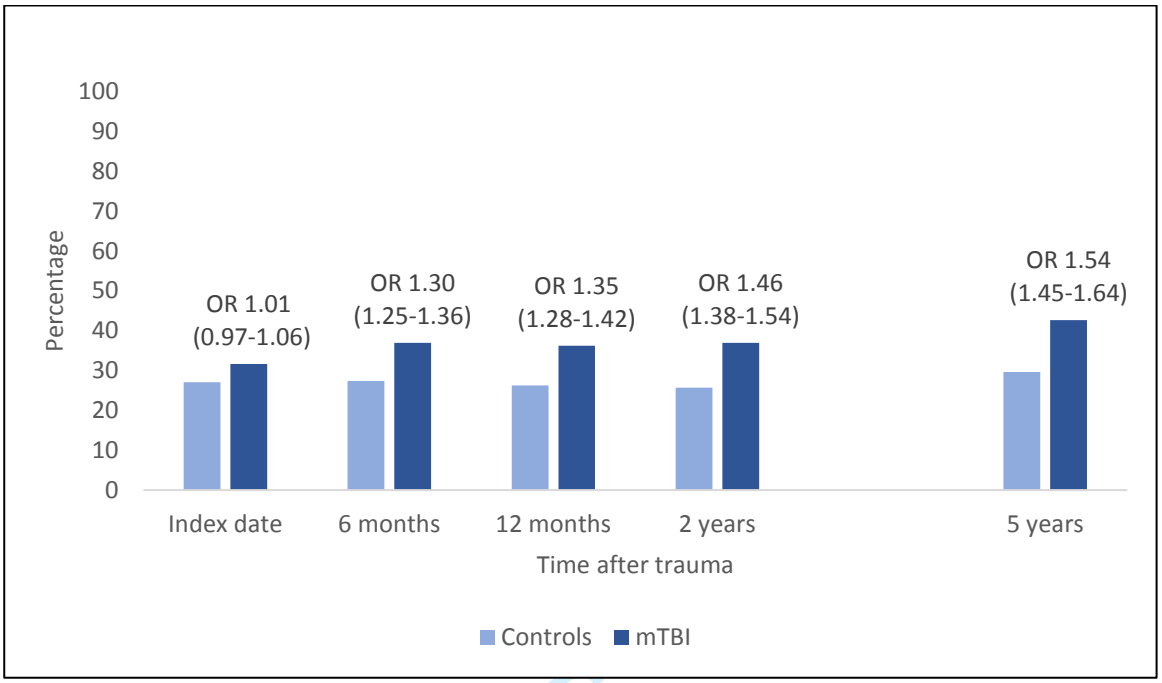

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	3, 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-11
Bias	9	Describe any efforts to address potential sources of bias	7, 20
Study size	10	Explain how the study size was arrived at	7, 8, 13
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11, 12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12, 13
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13-14
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13-15
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	15-17

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	15-17
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	17-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Labour market attachment after mild traumatic brain injury: Nationwide cohort study with 5-year register follow-up in Denmark

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Labour market attachment after mild traumatic brain injury: Nationwide cohort study with 5-year register follow-up in Denmark

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ABSTRACT

Objectives: Sickness absence after mild traumatic brain injury (mTBI) is frequent due to post-concussive symptoms. We examined labour market attachment following mTBI up to 5 years post-injury.

Design and setting: Nationwide cohort study with register follow-up.

Participants: Patients between 18-60 years with mTBI (ICD-10 diagnosis S06.0) were extracted from the Danish National Patient Register (n=19 732). Controls were matched on sex, age and municipality (n=18 640). Patients with spinal cord and column injuries, TBI and concussions five-years pre-injury or as secondary diagnosis to the concussion in the inclusion period were excluded.

Primary and secondary outcome measures: Data were extracted from the DREAM register. Primary outcome was "not attending ordinary work" defined as receiving any social transfer payment. Secondary outcomes were health-related benefits, limited attachment to the labour market, permanent lack of attachment to the labour market and death.

Results: 5 years after diagnosis, 43% of patients were not attending ordinary work. The odds increased from 6 months (OR 1.30, 95% CI 1.24-1.36) to 5 years (OR 1.54, 95% CI 1.45-1.63). The odds of health-related benefits were 32% (OR 1.32, 95% CI 1.22-1.42) at 6 months and 22% (OR 1.22, 95% CI 1.12-1.33) at 5 years. Limited attachment to the labour market showed increased odds at 5 years (OR 1.38, 95% CI 1.27-1.51) and the odds of permanent lack of attachment to the labour market were higher for patients compared to controls, (OR 2.59, 95% CI 2.30-2.92). Death was more than two times higher at 5 years post-injury (OR 2.62, 95% CI 2.10-3.26).

Conclusions:

43% of concussed patients were not attending ordinary work 5 years post-injury and received health and social transfer benefits. We conclude that mTBI has a long-term impact on labour market attachment. Prevention and treatment of persisting post-concussive symptoms should be considered.

ClinicalTrials.gov Identifier: NCT03214432

ARTICLE SUMMARY

Strengths and limitations of this study

- This was a nationwide cohort study with register-based follow-up including nearly 20 000 patients with mild traumatic brain injury (mTBI).
- The data were extracted from high-quality Danish national registers.
- This study estimated the prevalence and odds (OR) of not attending ordinary work, health-related benefits and death in patients with mTBI up to 5 years post-injury.
- This study had no access to patient records, with the inherent risk of misclassification.

INTRODUCTION

Mild traumatic brain injury (mTBI) is a common neurological disease defined as an acute brain injury resulting from mechanical energy to the head from external physical force. Operational criteria include at least one of following: confusion or disorientation, loss of consciousness, post-traumatic amnesia (<24 hours), transient neurological abnormalities, absence of intracranial lesions not requiring surgery and Glasgow Coma Scale score of 13-15 post-injury. [1] Concussion (commotio cerebri) represents an entity, that is grouped under mTBI, although the pathophysiology behind may be dissimilar and heterogeneous. The differentiation remains elusive due to the usual absence of objective findings on conventional imaging. The clinical diagnosis of concussion is based on short-lasting alteration of consciousness and presence of posttraumatic amnesia and confusion.[2, 3] Despite recent efforts to improve the clinical diagnostic process,[4, 5] accurate diagnosis of mTBI is still a challenge due to frequent confounding factors.

Approximately 70-90% of all TBIs fall into the category of mTBI.[6-8] The incidence of hospital and emergency treated patients is 50-300 cases per 100 000 people in the US, Scandinavia and Australia[8, 9] and more frequent among young people and men.[8] However, these numbers probably fall short as studies also show numbers more than 700 cases per 100 000 people per year.[8]

Numerous studies have examined post-concussive symptoms in adults showing symptoms like dizziness, fatigue, insomnia, posttraumatic headache and memory and concentration difficulties[10-12] leading to long-term sickness and absence from work. Post-concussive symptoms result in an increased use of general practice services the first year post-injury, as reported by a Danish study.[13] In 15% of patients with mTBI, post-concussive symptoms are persistent (>12 months post-injury).[14, 15] Additionally, several risk factors are associated with persisting symptomatology, such as female gender, premorbid physical or psychiatric comorbidities, injury-related conditions, previous head injury, psychological distress, and drug and alcohol abuse.[12, 16, 17]

Most patients return to work within the first couple of months after mTBI, but a small proportion of patients is unable to return to work due to disability.[18, 19] Cancelliere et al. found that most patients (>75%) had returned to work after six months and 5% were on social transfer payments two years post-injury.[20]

Return to work (RTW) has been conceptualized as being a dynamic process with different related outcomes of labour market attachment or time off work, but also outcomes related to the process of return to work such as psychological functioning and job satisfaction.[21, 22] RTW after mTBI has been suggested to depend on multiple factors such as injury related factors,[20] premorbid demographics such as younger age,[18] work place related factors such as support,[23] and influence on work planning[24] and patient characteristics such as psychosocial status.[25] These studies have methodological limitations in study design which complicate evaluation of evidence regarding the magnitude of the problem. They have small sample sizes, are not representative,[10] are based on self-reported data and have short follow-up and considerable dropout leading to attrition bias.[19] The present analysis overcomes these challenges by using Danish nationwide administrative data to examine a larger, representative sample and to perform long-term follow up. This study is concerned with labour market attachment in hospital treated patients receiving the diagnosis concussion (commotio cerebri) as the only brain injury diagnosis.

We examined a comprehensive range of post-injury transitions in the labour market aiming at analysing attachment to the labour market up to five years after mTBI using a portfolio of outcomes, including a variation of social transfer payments and data on permanent lack of attachment to the labour market and death.

METHODS

The data used in the present analyses is obtained by linking several Danish national registers through the unique personal identification number (CPR number) assigned to all Danish citizens at birth or immigration, provided by the Danish Civil Registration System (CRS).[26]

Study population

The study was a nationwide population-based cohort study of all mTBI cases in Denmark in the five-year inclusion period 1st of January 2003 – 31st of December 2007. Cases were identified in the Danish National Patient Register (DNPR) which contains information on all in- and outpatient contacts in Danish secondary care.[27] Notably, it codes each contact with International Classification of Diseases, version 10 (ICD-10) diagnosis codes. Patients with mTBI were included in the cohort based on their index date, the date of their first entry in the DNPR in the inclusion period with concussion (ICD-10 code S06.0) as primary diagnosis, excluding patients with diagnosis (primary or secondary) of cerebral oedema, diffuse and focal brain injury, subdural, epidural and subarachnoid haemorrhage, crushing injury and fracture of head, neck, skull, face and facial bones, and injuries of brain and cranial nerves in the inclusion period.[9] Included patients with mTBI were working-age adults between 18-60 years available for the labour market on the index date; the upper limit was set because individuals in Denmark older than 60 years are entitled to early retirement, if they have paid for such a scheme.[28] Availability for the labour market was defined as gainful employment or receiving unemployment benefits, but actively job seeking (see Figure 1). Furthermore, they were not hospital treated or diagnosed with other major neurological injuries such as spinal cord and column injuries[29] and traumatic brain injury (TBI) (including concussion)[9] in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period[9, 30] since previous brain injury and neurological problems are found to be associated with prolonged

symptoms.[31] Finally, patients were not included if they had lived outside of Denmark at any time during the inclusion period and the five-year period before.

For each mTBI case in the cohort, a control was randomly selected from the Population register. Controls had similar inclusion criteria as the cases, but they had no diagnosis of concussion during the inclusion period 1st of January 2003 – 31st of December 2007.

The control was matched to the case on sex, municipality and age (year of birth ± 0.5 years, expanded to 1 and 2 years in case of no initial match) (see Figure 1). The same exclusion criteria were applied for the selection of controls.

Insert Figure 1

Availability for the labour market was assessed from the Danish Register for Evaluation of Marginalization (DREAM), containing weekly information on all individuals receiving any social public transfer payments.[32] Patients and their matching controls were excluded from the cohort if there were any major neurological injuries[9, 29] as secondary diagnoses at the index date, they were unavailable for the labour market, they had unknown residence or were inhabitants of Greenland.

Outcome measures

The outcomes of the present analyses were assessments of variations in attachment to the labour market evaluated in the DREAM database (Figure 1) the week before the case's index date, and at 6 months, 12 months, 2 years and 5 years after the case's index date (Figure 1).

Not attending ordinary work

1. "Not attending ordinary work" was the primary outcome and was indicated by any entry in DREAM, i.e. receiving any social transfer payment, such as unemployment benefits unrelated to the subject's health condition, sickness absence benefits, social benefits granted, short and long-term

sickness or death. If there was no DREAM entry, it was assumed that the subject was gainfully employed or self-supporting at that time (Figure 1).

The set of secondary outcomes are defined increasingly narrower than the primary outcome and focus on attachment to the labour market due to health conditions. At the time of the current study, employers in Denmark were obliged to finance sickness benefits for the first 30 days. Sickness benefits lasting more than four consecutive weeks were to be compensated by the Danish municipalities.[33] Sick-listed individuals could receive sickness benefits for a maximum of one year[34]. If individuals were not able to return to ordinary work due to long-term limited work capacity, a partial return to work at lower capacity was possible with a "flex job". If the sick-listed individual was not able to return to work at all, the municipality could grant disability pension.[35, 36] The grading of the outcomes is illustrated in Figure 1.

Health-related benefits

2. Health-related benefits were indicated by DREAM entries given for short- or long-term restrictions in attachment to the labour market due to health conditions (excluding unemployment benefits unrelated to the subject's health condition). These were sickness absence benefits, vocational rehabilitation, flex job, unemployment benefits specifically granted to citizens on flex job, social security benefits, light duties, disability pension and death.

Limited attachment to the labour market

3. Social transfer payments due to limited attachment to the labour market were indicated by DREAM entries given for reduced work capacity and thereby long-term restrictions in attachment to the labour market due to health conditions (excluding sickness absence benefits compared to

secondary outcome 2). These were vocational rehabilitation, flex job, unemployment benefits specifically granted to citizens on flex job, social security benefits, light duties, disability pension and death.

Permanent lack of attachment to the labour market

4. Permanent lack of attachment to the labour market was indicated by DREAM entries given for permanent withdrawal from the labour market due to health conditions. These were disability pension and death.

Death

5. Death was indicated by the DREAM entry for death.

Potential confounders

Sex, age and municipality at the index date were obtained from the Population register linked to the DNPR. The municipality information was categorized into five regions reflecting Denmark's reform of local government structure from 2007.[37] From the index date calendar year and season were derived. Calendar year was included in the model as a previous study found increasing odds of returning to work during the study period.[38] The reason could be a change in diagnostic practice and the Danish sickness benefit Act becoming more effective over the years. Seasonal variation was considered a confounder, as a previous study suggested that TBI is associated with season-specific activities and most pronounced during fall and winter.[39] Pre-injury income was measured at the index date and taken as personal gross income including revenue and social transfer income and was obtained from the Income Statistics Register.[40] Income was divided into four income groups: <100 000, 100 000-200 000, 200 000-300 000, >300 000 DKK roughly reflecting the quartiles in

the present cohort. Information on the highest attained educational level was obtained from the Danish Education Register[41] and was categorized into three educational groups: low education (primary education), medium education (lower and upper secondary education, post-secondary–non-tertiary education) and high education (short cycle tertiary education, bachelor, master, doctoral or equivalent). Information on cohabitation status and ethnic origin was obtained from the Danish Family Relations Database[26, 42] and was categorized into married or cohabiting couple and single, and as Danish born and not Danish born respectively. Pre-injury illness burden was measured by Charlson comorbidity index (CCI), a weighted sum of 19 indicators for selected diagnoses.[43, 44] For the present CCI evaluation, a diagnosis was indicated for an individual when a corresponding ICD-10 code was encountered in the DNPR in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period. Psychiatric diagnoses are not incorporated in CCI but are possible confounders related to both labour market attachment and an increased risk of TBI.[45, 46] Hence, information on psychiatric diagnoses separately from CCI was obtained from the DNPR (any ICD-10 Classification of Mental and Behavioural Disorders indicated as F diagnosis) over the same five-year period.

Statistical analysis

Baseline covariates at the index date, and the outcomes at the index date and the follow-up time points were reported as numbers and percentages separately for mTBI patients and their matched controls. Raw comparisons of the baseline covariates between the mTBI patients and their controls are done by Chi-squared tests.

The difference in tendency of some degree of decreased attachment to the labour market, between patients with mTBI and their controls, at each of the index date and the four follow-up time points, was assessed by odds ratios (OR) and corresponding 95% confidence intervals (95%CI) from a multivariable logistic regression model; an OR>1 implied higher odds for the mTBI group. The

model was parameterized so that the assessments at the four follow-up time points were adjusted for differences already present at the index date, i.e. pre-injury differences. Hence, the assessment at the index date can be viewed as an assessment of the employment aspect of a social gradient in mTBI incidence; the assessments at the follow-up time points report on the short- and long-term differences in attachment attributable to mTBI. Results are reported both unadjusted and adjusted for the potential confounders: age, gender, municipality, seasonal variation, calendar year, education, income, cohabitation status, ethnicity, pre-injury comorbidities and pre-injury psychiatric diagnosis. Inference was done by generalized estimating equations to adjust for repeated measurement and matching.

Subjects with missing values in one of the covariates were omitted from analyses where these covariates were included. P-values below 0.05 were considered statistically significant. SAS version 9.4 was used for statistical analysis.

Patient and public involvement

Patients and the public were not involved in the design and the conduct of the study.

RESULTS

Baseline characteristics of the population

19 732 patients with mTBI were eligible for the cohort and 18 640 matching controls were included in the study. In some cases, notably with patients from small municipalities, it was not possible to find a matching control, see Figure 2. Overall, the cohort was characterized by a weak tendency in patients with mTBI to have lower education, lower income, being married or cohabiting, and having a higher prevalence of pre-injury diseases (both somatic diseases as captured by CCI and psychiatric diseases) compared to their matched controls (Table 1).

Insert Figure 2 (flow-chart)

Table 1. Social and pre-injury health characteristics of patients with mTBI and controls

	Controls (n=18 640)	**mTBI** (n=19 732)	**Total** (n=38 372)	**Missing**	**p-value**[1]
Age, *n(%)*					0.8461
18-29 years	8187 (43.92)	8734 (44.26)	16 921 (44.10)	0	
30-39 years	4118 (22.09)	4290 (21.74)	8408 (21.91)		
40-49 years	3458 (18.55)	3653 (18.51)	7111 (18.53)		
50-60 years	2877 (15.43)	3055 (15.48)	5932 (15.46)		
Gender, *n(%)*					0.5839
Men	11 266 (60.44)	11 872 (60.17)	23 138 (60.30)	0	
Women	7374 (39.56)	7860 (39.83)	15 234 (39.70)		
Education, *n(%)*					<.0001
Low education	6942 (37.73)	8951 (46.14)	15 893 (42.05)	574	
Medium education	7992 (43.43)	7464 (38.48)	15 456 (40.89)		
High education	3466 (18.84)	2983 (15.38)	6449 (17.06)		
Income (Danish kroner, DKK[2]**),** *n(%)*					<.0001
<100.000	4144 (22.27)	4482 (22.72)	8626 (22.50)	40	
100.000-200.000	4152 (22.31)	5697 (28.89)	9849 (25.69)		
200.000-300.000	5325 (28.62)	5418 (27.47)	10 743 (28.03)		
>300.000	4988 (26.80)	4126 (20.92)	9114 (23.78)		
Cohabitation status, *n(%)*					<.0001
Married or cohabiting couple	5701 (30.68)	8051 (40.83)	13 752 (35.90)	70	
Single	12 884 (69.32)	11 666 (59.17)	24 550 (64.10)		
Ethnic origin, *n(%)*					0.5772
Danish born	17 659 (95.02)	18 710 (94.89)	36 369 (94.95)	70	
Born abroad	926 (4.98)	1007 (5.11)	1933 (5.05)		
CCI (categorical), *n(%)*					<.0001
No comorbidities	17 863 (95.83)	18 580 (94.16)	36 443 (94.97)	0	
1 comorbidity	577 (3.10)	842 (4.27)	1419 (3.70)	0	
2 comorbidities	154 (0.83)	210 (1.06)	364 (0.95)	0	
≥3 comorbidities	46 (0.25)	100 (0.51)	146 (0.38)	0	
Psychiatric diagnosis, *n(%)*					<.0001
No diagnosis	18 345 (98.42)	18 540 (93.96)	36 885 (96.12)	0	
≥1 diagnosis	295 (1.58)	1192 (6.04)	1487 (3.88)		

[1] P-value from a Pearson´s chi-squared test

[2] Currency exchange rate of May 2018: 1 EUR = 7.44834 DKK

Analysis of attachment to labour market

Table 2 shows the prevalence for each outcome for patients and controls during 5 years of follow-up.

Table 2. Prevalence of labour market attachment and death in patients with mTBI and controls at 6 and 12 months and 2 and 5 years post-injury

		Controls (n=18 640)[1]	**mTBI** (n=19 732)[1]	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**[2]	**p-value**
Not attending ordinary work							
	Index date, n(%)	5040 (27.04)	6247 (31.66)	1.25 (1.20-1.30)	<.0001	1.01 (0.97-1.06)	0.5406
	6 months, n(%)	5107 (27.40)	7289 (36.94)	1.24 (1.20-1.29)	<.0001	1.30 (1.25-1.36)	<.0001
	12 months, n(%)	4898 (26.28)	7149 (36.23)	1.28 (1.22-1.33)	<.0001	1.35 (1.28-1.42)	<.0001
	2 years, n(%)	4793 (25.71)	7297 (36.98)	1.36 (1.29-1.42)	<.0001	1.46 (1.38-1.54)	<.0001
	5 years, n(%)	5520 (29.61)	8420 (42.67)	1.42 (1.35-1.49)	<.0001	1.54 (1.45-1.64)	<.0001
Health-related benefits							
	Index date, n(%)	795 (4.27)	2230 (11.30)	2.85 (2.62-3.10)	<.0001	2.07 (1.90-2.25)	<.0001
	6 months, n(%)	1120 (6.01)	3600 (18.24)	1.21 (1.13-1.29)	<.0001	1.32 (1.22-1.42)	<.0001
	12 months, n(%)	1197 (6.42)	3584 (18.16)	1.12 (1.04-1.20)	0.0020	1.22 (1.13-1.32)	<.0001
	2 years, n(%)	1336 (7.17)	3790 (19.21)	1.07 (0.99-1.15)	0.0968	1.17 (1.08-1.27)	0.0002
	5 years, n(%)	1676 (8.99)	4649 (23.56)	1.08 (1.00-1.17)	0.0528	1.22 (1.12-1.33)	<.0001
Limited attachment to the labour market							
	Index date, n(%)	795 (4.27)	2230 (11.30)	2.86 (2.64-3.11)	<.0001	1.93 (1.76-2.10)	<.0001
	6 months, n(%)	816 (4.38)	2326 (11.79)	1.01 (0.95-1.08)	0.8162	1.02 (0.96-1.09)	0.5123
	12 months, n(%)	846 (4.54)	2388 (12.10)	1.00 (0.94-1.07)	0.9858	1.03 (0.96-1.11)	0.3815
	2 years, n(%)	884 (4.74)	2784 (14.11)	1.14 (1.06-1.23)	0.0005	1.23 (1.13-1.33)	<.0001
	5 years, n(%)	1192 (6.39)	3787 (19.19)	1.20 (1.11-1.30)	<.0001	1.39 (1.27-1.51)	<.0001
Permanent lack of attachment to the labour market							
	Index date, n(%)	0 (0)	0 (0)	.	.	.	.
	6 months, n(%)	33 (0.18)	82 (0.42)	3.40 (2.36-4.90)	<.0001	1.90 (1.36-2.66)	0.0002
	12 months, n(%)	58 (0.31)	173 (1.88)	3.63 (2.77-4.75)	<.0001	2.14 (1.66 -2.77)	<.0001
	2 years, n(%)	117 (0.63)	424 (2.15)	4.20 (3.49-5.05)	<.0001	2.61 (2.17-3.14)	<.0001
	5 years, n(%)	299 (1.60)	1068 (5.41)	3.67 (3.28-4.11)	<.0001	2.59 (2.30-2.92)	<.0001
Death							
	Index date, n(%)	0 (0)	0 (0)	.	.	.	.
	6 months, n(%)	5 (0.03)	59 (0.30)	11.46 (4.38-29.94)	<.0001	6.37 (2.71-14.96)	<.0001
	12 months, n(%)	12 (0.06)	100 (0.51)	8.03 (4.29-15.05)	<.0001	4.67 (2.59-8.40)	<.0001
	2 years, n(%)	26 (0.14)	207 (1.05)	7.67 (5.01-11.75)	<.0001	4.72 (3.12-7.13)	<.0001
	5 years, n(%)	118 (0.63)	477 (2.42)	3.91 (3.17-4.82)	<.0001	2.62 (2.11-3.26)	<.0001

[1]Prevalence expressed as the total number and percentage of patients and controls experiencing the outcome

[2] Generalized estimating equation model with odds ratio of the outcome event in patients compared to controls adjusted for age, gender, municipality, seasonal variation, calendar year, education, income, cohabitation status, ethnicity, comorbidities and pre-injury psychiatric diagnosis

Primary outcome

Not attending ordinary work

It can be seen from table 2 and figure 3 that patients compared to controls had an overall higher increase of not attending ordinary work from the index date (32%, 27%) to 5 years post-injury (43%, 30%) (Table 2) (Figure 3). Compared to the secondary outcomes, the prevalence was higher for not attending ordinary work which included social transfer payments that were not health related. For the unadjusted model, there were 25% higher odds of not attending ordinary work (OR 1.25, 95% CI 1.19-1.30) for patients compared to controls at the index date. However, for the adjusted model, no differences were seen between groups at the index date. During the 5 year of follow-up, the odds of not attending ordinary work increased, and at 5 years the odds were 54% higher (OR 1.54, 95% CI 1.45-1.63) among patients with mTBI (Table 2) (Figure 3) compared to controls.

Insert Figure 3

Secondary outcomes

Health-related benefits

The overall prevalence of health-related benefits was significantly higher for patients (11%) compared to controls (4%) at the index date, and the difference between groups continued during follow-up. The odds of health-related benefits were more than two times higher (OR 2.07, 95% CI 1.90-2.25) at the index date even after adjustment for potential socio-economic confounders and the odds of health-related benefits continued to stay elevated during follow-up. Table 2.

Limited attachment to the labour market

For social transfer payments related to limited attachment to the labour market, the prevalence was also higher for patients (11%) compared to controls (4%) at the index date and slightly increased during follow-up. The adjusted OR was almost two times higher at the index date for patients compared to controls (OR 1.92, 95% CI 1.76-2.10). However, the long-term effect of mTBI on limited attachment to the labour market was most pronounced at 2 years and 5 years.

Permanent lack of attachment to the labour market

During follow-up, a higher prevalence of permanent lack of attachment to the labour market was seen in patients compared to controls, which increased from 6 months to 5 years. At 6 months the adjusted odds for permanent lack of attachment to the labour market was almost two times higher for patients (OR 1.90, 95% CI 1.36-2.66) and the long-term perspective continued showing large effect.

Death

The prevalence of death was higher among patients showing an increase from 0.30% at 6 months to 2.42% at 5 years. The adjusted odds for death for patients with mTBI was six-fold increased at 6 months follow-up (OR 6.37 95% CI 2.71-14.95) and the long-term effects continued to be large but diminishing during follow-up.

DISCUSSION

We examined short and long-term labour market attachment in a large cohort of working-age patients with mTBI up to 5 years post-injury compared to the general population. The proportion of approximately 20 000 included patients in this study are difficult to compare to previous studies, since these mostly report incidence rates.[8] However, a Danish study included 10 000 patients in

1994 and 2002,[9] and another Danish register-based study included approximately 90 000 patients during a 13-year follow-up period.[13]

We found that attachment to the labour market varied between patients and controls at the date of injury. The odds of not attending ordinary work was increased by 25% and remained higher for patients during the 5 years of follow-up (of about 40%). A social gradient in not attending ordinary work at the index date could be suspected, as patients had a significantly lower educational level, income and more comorbidities compared to controls (see Table 1). Our findings agree with a Danish register-based cohort study[13] demonstrating that individuals with mTBI had a higher use of general practice even 5 years before mTBI. However, when we controlled for socio-economic factors, comorbidities and psychiatric diagnoses, there were no difference in the odds of not attending ordinary work between the two groups in our sample at index date. Yet, the adjusted odds of not attending ordinary work remained increased by 30-50% during the 5 years follow-up. This strongly supports that mTBI is the incident leading to not returning to work.

For the secondary outcomes, the prevalence of sick listed decreased during follow-up, while the prevalence of limited and permanent lack of attachment to the labour market increased as expected. The proportion of individuals receiving health-related benefits at the index date was also higher for patients compared to controls, and the risk was more than two times higher for patients even after controlling for possible confounders. This may indicate increased morbidity in patients with mTBI prior to the trauma as seen in another Danish study[13], and variations in health seeking behavior which result in health-related social transfer payments. However, at 6 months the odds diminished to 30% and were further decreased during follow-up to 16-20%. Stulemeijer et al. found a 76% full RTW rate at 6 months,[47] De Koning et al. found a complete RTW rate of 77% at 12 months[48] and Losoi et al. also found that 97% had fully RTW by 12 months after mTBI.[10] These findings are slightly higher than those reported in this study. However, previous investigations are

not directly comparable because there is a lack of consistency in definitions of labour market attachment and RTW measures. RTW is increasingly regarded as an evolving process consisting of different phases such as off work, work reentry, retention and advancement.[49] Additionally, differences between countries in registration of social transfer payments, political legislation and socioeconomic differences can complicate comparison.[20]

Theadom et al. found that work productivity was reduced by 15.5% among patients with mTBI, who had to make job changes to continue working.[50] Our study found a long-term prevalence of 19% and increased odds of almost 40% of limited attachment to the labour market indicating long-term employment restrictions due to health conditions. These results indicate that most patients return to work after mTBI, but a small proportion of patients suffer long-term consequences related to mTBI, preventing them from fully re-integrating into the labour market. Since a previous study indicates an association between increasing length of sickness absence and increasing risk of disability pension,[51] these patients are at risk of transitioning from temporary to permanent social benefits, meaning an exit from the labour market. For permanent lack of attachment to the labour market, the prevalence in our study was higher for patients even though there were significantly fewer events especially at 6 and 12 months and 2 years, indicating that it takes time to qualify for disability pension in Denmark. The odds of permanent lack of attachment to the labour market were still more than twice as high in the short as well as the long-term among patients with mTBI, even when controlled for potential confounders.

Finally, the prevalence of death was higher in patients compared to controls. The odds of death were more than 6 times higher for patients and subsequently declined during follow-up. This is a surprising result assumed to be predicted by a set of different factors (socio-economic indicators, comorbidities etc.) than those predicting labour market attachment. Selassie et al. found an in-hospital all-cause mortality rate after mTBI of 1.4%[52] and Pentland et al. found similar results at

0.45% in a cohort with 21 years of follow up,[53] agreeing with the result found in the present study. Additionally, a Danish study found an increased risk of suicide among patients with mTBI[54]. Although not the aim of the present study, future research may benefit from exploring the risk factors in excess mortality in patients with mTBI.

Strengths and limitations

This study applied a register-based design preventing information bias in the collection of data. The DREAM register enabled us to estimate point prevalence during 5 years of follow-up and to examine much more diverse labour market outcomes which is infrequent in TBI research.[20] Furthermore, the sensitivity and specificity of the DREAM register is considered high.[55] Finally, the use of national register data has made it possible to include a large sample size and a matching control group which increased the statistical power. We also adjusted for a wide range of pre-injury potential confounders. However, residual confounding such as injury mechanism and psychological effects affecting outcome cannot be ruled out. Patients were extracted from the DNPR. Consequently, we did not have access to patient records, which hindered us to apply the operational case definition for mTBI suggested by WHO.[4] Even though the DNPR is considered the most comprehensive register of its kind,[27] its validity and consistency with clinical diagnoses are widely discussed, especially regarding clinical diagnoses and inaccurate coding leading to misclassification. The ICD-9 code (850) for concussion has in several studies been reported as frequently used for the classification of mTBI[4, 56] but has also shown lack of sensitivity and specificity.[4] This could also be expected to be the case for ICD-10. Additionally, a large proportion of patients with mTBI are not treated at the hospital, some are treated in primary care settings, and some refrain from consulting a physician,[57] which can lead to low incidence rates and selection bias, limiting the generalizability of the results.[58]

Implications

A small proportion of patients with mTBI may suffer from persistent post-concussive symptoms for months and years after injury, preventing returning to previous work.[17, 46, 59] This study showed that patients with mTBI have a higher prevalence of receiving social transfer payments compared to the general population post-injury. In Denmark there are no national guidelines for the treatment and rehabilitation of patients with mTBI. This is in contrast to the guidelines developed for patients suffering more severe forms of TBI. We therefore assume that the treatment trajectory in patients with mTBI is lengthy and inefficient, as it is highly dependent on referrals from general practitioners, insurance companies and the municipalities. Our data suggest that patients with mTBI needs a comprehensive and coordinated approach, including the identification of patients at risk of developing persistent post-concussive symptoms and initiation of a treatment plan in a timely fashion. Future research should focus on examining the contributory causes as to why patients with mTBI do not return to work.

CONCLUSIONS

Most patients returned to work after mTBI. However, a small proportion of patients with mTBI received social transfer payments related to health and work disability to a higher extent than the general population at 5 years post-injury. Additionally, the prevalence of death was increased during follow-up. Initiatives that identify and prevent the progression of persistent post-concussive symptoms should be considered to reduce lack of attachment to the labour market in this patient group.

ETHICS APPROVAL

The study was approved by the Danish Data Protection Agency (Datatilsynet) no. (05179- RH-2016-389). The study protocol was registered on clinicaltrial.gov on July 5, 2017 (ClinicalTrials.gov Identifier: NCT03214432).

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Competing interest statement

None declared

Patient consent

Not required

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Contributors

All authors participated in the study design, interpretation of the data, revising it critically and the final approval of the manuscript to be published. HJG obtained the funding, drafted the protocol and manuscript and collaborated with VS on performing the statistical analyses. AM, LA, JK, IE and HMR participated in the study design and conceptualization.

Data sharing statement

No additional data are available

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Figure 1. Description of social transfer payments as part of the Danish welfare system. Categories describe unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1) and the secondary outcomes (2-5) in terms of the different social transfer payments and other social conditions (first row) that are included in each.

Figure 2. Inclusion of the study population

Figure 3. Prevalence and adjusted odds of not attending ordinary work at the index date and up to 5 years after concussion

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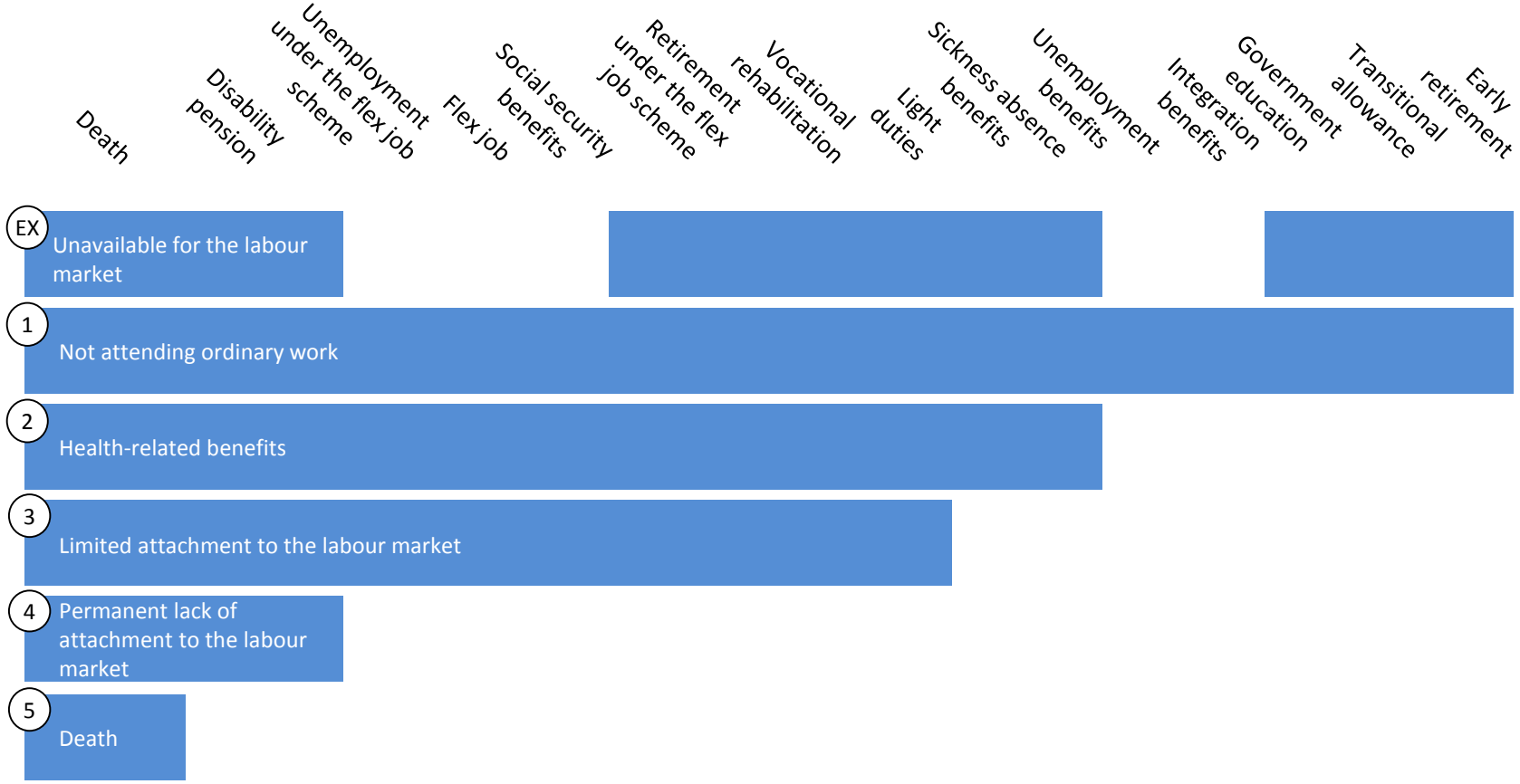
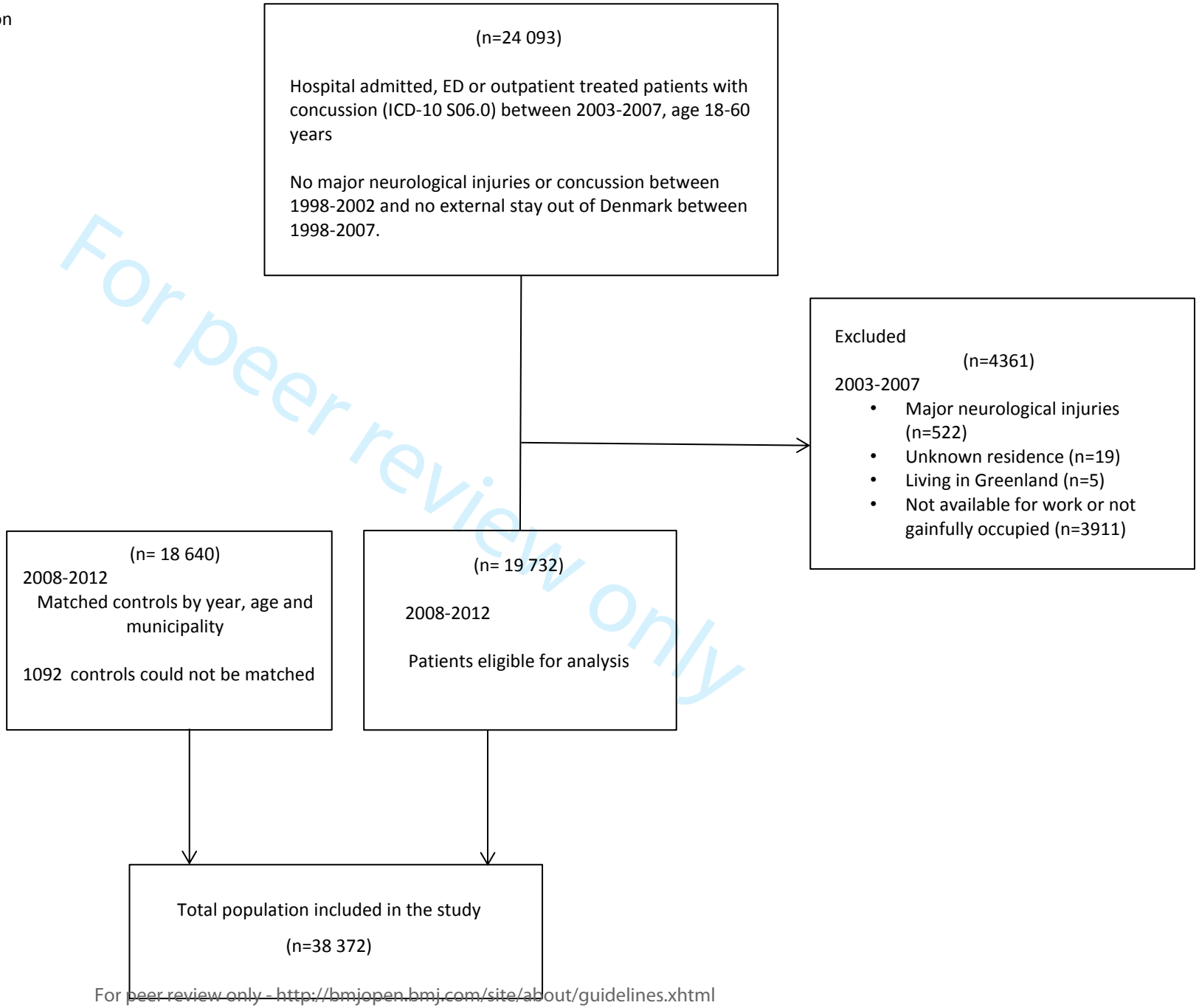


* EX is the exclusion criterion "unavailable for the labour market", assessed at one week before trauma.

Figure 2. Inclusion of the study population



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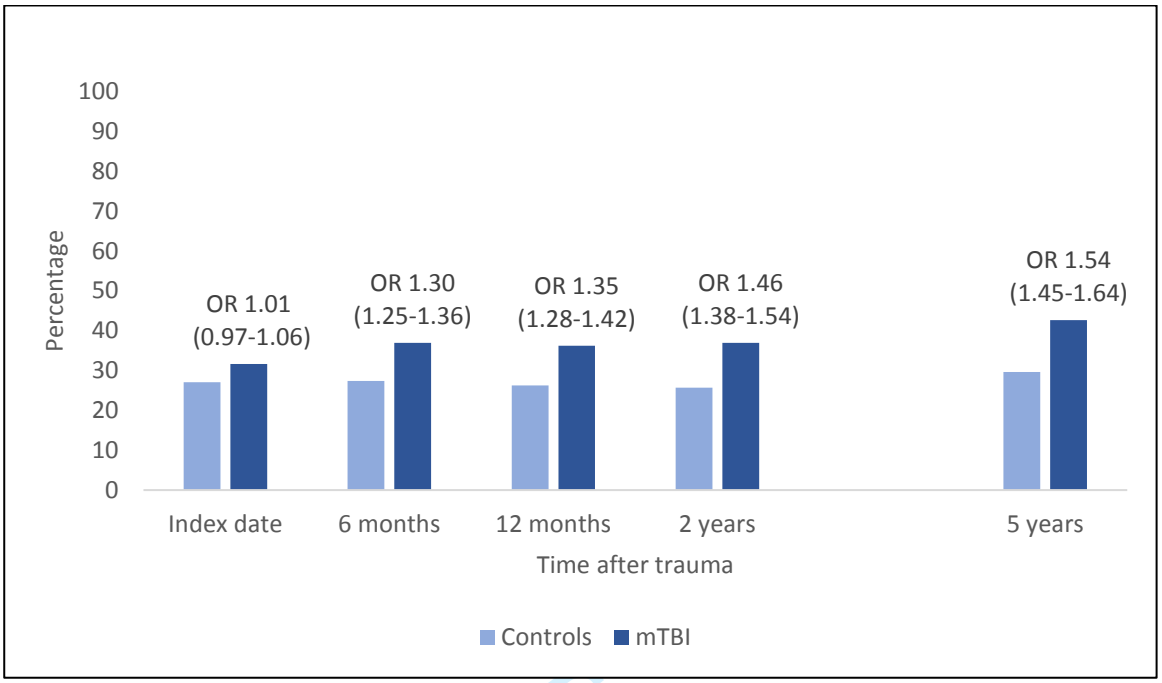

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	3, 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-11
Bias	9	Describe any efforts to address potential sources of bias	7, 20
Study size	10	Explain how the study size was arrived at	7, 8, 13
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11, 12
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12, 13
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	13-14
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13-15
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	15-17

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	15-17
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	17-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.