

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-026104
Article Type:	Research
Date Submitted by the Author:	17-Aug-2018
Complete List of Authors:	<p>Graff, Heidi; University Hospital Rigshospitalet, Department of Anaesthesia, 4231, Centre of Head and Orthopaedics</p> <p>Siersma, Volkert; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Denmark</p> <p>Møller, Anne; Copenhagen University Hospital Holbæk, Department of Occupational Medicine; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Denmark</p> <p>Kragstrup, Jakob; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice</p> <p>Andersen, Lars; National Research Centre for the Working Environment; Aalborg University, Sport Sciences, Department of Health Science and Technology</p> <p>Egerod, Ingrid; University of Copenhagen, Intensive Care Unit, Rigshospitalet</p> <p>Malá, Hana; University of Copenhagen, Department of Psychology; University Hospital Bispebjerg-Frederiksberg, Department of Neurology</p>
Keywords:	Labour market attachment, Mild traumatic brain injury, Sickness absence, Post-concussive symptoms, Unemployment

SCHOLARONE™
Manuscripts

1
2
3
4 **Labour market attachment after mild traumatic brain injury:**
5 **Nationwide cohort study with 5-year register follow-up**
6
7
8

9 Heidi Jeannet Graff, MSc in Public Health^{1,2}

10 Volkert Siersma, Statistician³

11 Anne Møller, Ph.D., Assistant professor^{3,4}

12 Jakob Kragstrup, Professor³

13 Lars Louis Andersen, Professor^{5,6}

14 Ingrid Egerod, Professor⁷

15 Hana Malá, Associate Professor^{8,9}

16
17
18
19
20
21
22
23 **Affiliations:**

24
25
26 ¹ Department of Anaesthesia, Centre of Head and Orthopaedics, University Hospital Rigshospitalet,
27
28 Copenhagen, Denmark

29
30
31 ² Trauma Center and Acute Admission, Centre of Head and Orthopaedics, University Hospital
32
33 Rigshospitalet, Copenhagen, Denmark

34
35
36 ³ Department of Public Health, The Research Unit for General Practice and Section of General Practice,
37
38 University of Copenhagen, Denmark

39
40
41 ⁴ Department of Occupational Medicine, Copenhagen University Hospital Holbæk, Denmark

42
43
44 ⁵ National Research Centre for the Working Environment, Copenhagen, Denmark

45
46
47 ⁶ Sport Sciences, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark

48
49
50 ⁷ Intensive Care Unit, Rigshospitalet, University of Copenhagen, Denmark

51
52
53 ⁸ Department of Psychology, University of Copenhagen, Denmark

54
55
56 ⁹ Department of Neurology, University Hospital Bispebjerg-Frederiksberg, Copenhagen, Denmark

1
2
3
4 **Corresponding author:**
5

6 Heidi Jeannet Graff, University Hospital Rigshospitalet, Department of Anaesthesia, Blegdamsvej 9, 2100
7
8 Copenhagen, Denmark.
9

10
11 Phone: +45 40688504
12

13 Email: heidi.jeannet.graff@regionh.dk
14
15

16 **Word count:** 3928
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

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).

1
2
3
4 **Conclusions:**

5
6 43% of patients with mTBI were not attending ordinary work 5 years post-trauma. Prevention and
7
8 treatment of persisting post-concussive symptoms should be considered.
9

10
11
12
13 ClinicalTrials.gov Identifier: NCT03214432
14
15

16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

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 difficulties⁶⁻⁸ 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}

1
2
3
4 RTW after mTBI has been suggested to depend on multiple factors such as injury related factors,¹⁶
5 premorbid demographics such as younger age,¹⁴ work place related factors such as support,¹⁹
6 influence on work planning²⁰ and patient characteristics such as psychosocial status.²¹ The studies
7
8 on which these conclusions are based have methodological differences and limitations in study
9
10 design which complicate evaluation of evidence regarding the magnitude of the problem. They have
11
12 small sample sizes, are not representative,⁶ are often based on self-reported data, have short follow-
13
14 up and considerable dropout which can lead to attrition bias.¹⁵ The present analysis overcomes these
15
16 challenges by using Danish nationwide administrative data to examine a larger, representative
17
18 sample and to perform long-term follow up. This study is concerned with patients with mTBI who
19
20 are not able to return to work. We examined a comprehensive range of post-injury transitions in the
21
22 labour market aiming at analysing attachment to the labour market up to five years after mTBI
23
24 using a portfolio of outcomes, including a variation of social transfer payments and data on
25
26 permanent lack of attachment to the labour market and death.
27
28
29
30
31

32 **METHODS**

33
34 The data used in the present analyses is obtained by using the possibility to link several Danish
35
36 national administrative registers. These registers are available for research purposes, through the
37
38 unique personal identification number (CPR number) assigned to all Danish citizens at birth or
39
40 immigration, provided by the Danish Civil Registration System (CRS) operating the Population
41
42 register.²²
43
44
45
46
47

48 **Study population**

49
50 The study was designed as a nationwide population-based cohort study of all mTBI cases in
51
52 Denmark in the five-year inclusion period 1st of January 2003 – 31st of December 2007. These cases
53
54 were identified in the Danish National Patient Register (DNPR) which contains the information on
55
56
57
58
59
60

1
2
3
4 all in- and outpatient contacts in Danish secondary care.²³ Notably, it codes each contact with
5
6 International Classification of Diseases, version 10 (ICD-10) diagnosis codes. The mTBI patients
7
8 were included in the cohort on their index date, the date of their first entry in the DNPR in the
9
10 inclusion period with concussion (ICD-10 code S06.0) as primary diagnosis. The included patients
11
12 with mTBI had to be working-age adults between 18-60 years of age available for the labour market
13
14 on the index date; the upper limit was set because individuals in Denmark older than 60 years are
15
16 entitled to early retirement, if they have paid for such a scheme.²⁴ Availability for the labour market
17
18 was defined as gainful employment or receiving unemployment benefits, but actively job seeking
19
20 (see Figure 1). Furthermore, they were not hospital treated or diagnosed with other major
21
22 neurological injuries such as spinal cord and column injuries²⁵ and TBI (including concussion)⁵ in
23
24 the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion period^{5, 26}
25
26 since previous brain injury and neurological problems are found to be associated with prolonged
27
28 symptoms.²⁷ Finally, patients were not included if they had lived outside of Denmark at any time
29
30 during the inclusion period and the five-year period before.
31
32
33

34 For each mTBI case in the cohort, a control was randomly selected from the Population
35
36 register. The population of controls had similar inclusion criteria as the cases, but they had no
37
38 diagnosis of concussion during the inclusion period 1st of January 2003 – 31st of December 2007.
39
40 The control was matched to the case on sex, municipality, age (year of birth \pm 0.5 years, expanded
41
42 to 1 and 2 years in case of no initial match) and available for the labour market on the
43
44 corresponding case's index date (see Figure 1).
45
46
47
48

49 Insert Figure 1
50
51

52 Availability for the labour market was assessed from the Danish Register for Evaluation of
53
54 Marginalization (DREAM), a national database containing weekly information on all individuals
55
56
57
58
59
60

1
2
3
4 who have received any social public transfer payments.²⁸ Patients and their matching controls were
5
6 excluded from the cohort if there were any major neurological injuries^{5, 25} as secondary diagnoses at
7
8 the index date, they were unavailable for the labour market, they had unknown residence or were
9
10 inhabitants of Greenland.

14 **Outcome measures**

15
16 The outcomes of the present analyses were assessments of variations in attachment to the labour
17
18 market evaluated in the DREAM database the week before the case's index date, and at 6 months,
19
20 12 months, 2 years and 5 years after the case's index date (Figure 1).

24 Not attending ordinary work

25
26
27 1. "Not attending ordinary work" was the primary outcome and was indicated by any entry in
28
29 DREAM, i.e. receiving any social transfer payment, such as unemployment benefits unrelated to the
30
31 subject's health condition, sickness absence benefits, social benefits granted, short and long-term
32
33 sickness or death. If there was no DREAM entry, it was assumed that the subject was gainfully
34
35 employed or self-supporting at that time (Figure 1).

36
37
38
39
40 The set of secondary outcomes are defined increasingly narrower than the primary outcome and
41
42 focus on attachment to the labour market due to health conditions. At the time of the current study,
43
44 employers in Denmark were obliged to finance sickness benefits for the first 30 days. Sickness
45
46 benefits lasting more than four consecutive weeks were to be compensated by the Danish
47
48 municipalities.²⁹ Sick-listed individuals could receive sickness benefits for a maximum of one year.
49
50 If individuals were not able to return to ordinary work due to long-term limited work capacity, a
51
52 partial return to work at lower capacity was possible with a "flex job". If the sick-listed individual
53
54
55
56
57
58
59
60

1
2
3
4 was not able to return to work at all, the municipality could grant disability pension after an
5 extensive assessment.^{30, 31} The grading of the outcomes is illustrated in Figure 1.
6
7
8
9

10 Health-related benefits

11
12 2. Health-related benefits were indicated by DREAM entries given for short- or long-term
13 restrictions in attachment to the labour market due to health conditions (excluding unemployment
14 benefits unrelated to the subject's health condition). These were sickness absence benefits,
15 vocational rehabilitation, flex job, unemployment benefits specifically granted citizens on flex job,
16 social security benefits, light duties, disability pension and death.
17
18
19
20
21
22
23
24

25 Limited attachment to the labour market

26
27 3. Social transfer payments due to limited attachment to the labour market were indicated by
28 DREAM entries given for reduced work capacity and thereby long-term restrictions in attachment
29 to the labour market due to health conditions (excluding sickness absence benefits compared to
30 secondary outcome 2). These were vocational rehabilitation, flex job, unemployment benefits
31 specifically granted citizens on flex job, social security benefits, light duties, disability pension and
32 death.
33
34
35
36
37
38
39
40
41
42

43 Permanent lack of attachment to the labour market

44
45 4. Permanent lack of attachment to the labour market was indicated by DREAM entries given for
46 permanent withdrawal from the labour market due to health conditions. These were disability
47 pension and death.
48
49
50
51
52
53
54
55
56
57
58
59
60

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 Register³⁶ 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

1
2
3
4 the DNPR in the five-year period 1st of January 1998 – 31st of December 2002 before the inclusion
5
6 period. Psychiatric diagnoses are not incorporated in CCI but are possible confounders related to
7
8 both labour market attachment and an increased risk of TBI.^{40, 41} Hence, information on psychiatric
9
10 diagnoses separately from CCI was obtained from the DNPR over the same five-year period.
11
12
13

14 **Statistical analysis**

15
16 The distribution of the baseline covariates at the index date, and the outcomes at the index date and
17
18 the follow-up time points were reported as numbers and percentages separately for mTBI patients
19
20 and their matched controls. Raw comparisons of the baseline covariates between the mTBI patients
21
22 and their controls are done by Chi-squared tests.
23

24
25 The difference in tendency of some degree of decreased attachment to the labour market, between
26
27 patients with mTBI and their controls, at each of the index date and the four follow-up time points,
28
29 was assessed by odds ratios (OR) and corresponding 95% confidence intervals (95%CI) from a
30
31 multivariable logistic regression model; an OR>1 implied higher odds for the mTBI group. The
32
33 model was parameterized so that the assessments at the four follow-up time points were adjusted for
34
35 differences already present at the index date, i.e. pre-injury differences. Hence, the assessment at
36
37 the index date can be viewed as an assessment of the employment aspect of a social gradient in
38
39 mTBI incidence; the assessments at the follow-up time points report on the short- and long-term
40
41 differences in attachment attributable to mTBI. Results are reported both unadjusted and adjusted
42
43 for the potential confounders: age, gender, municipality, seasonal variation, calendar year,
44
45 education, income, cohabitation status, ethnicity, pre-injury comorbidities and pre-injury psychiatric
46
47 diagnosis. Inference was done by generalized estimating equations to adjust for repeated
48
49 measurement and matching.
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 Subjects with missing values in one of the covariates were omitted from analyses where these
5 covariates were included. P-values below 0.05 were considered statistically significant. SAS version
6
7
8 9.4 was used for statistical analysis.
9

12 **Patient and public involvement**

14 Patients and the public were not involved in the design and the conduct of the study
15
16

18 **RESULTS**

20 **Baseline characteristics of the population**

22 19 732 patients with mTBI were eligible for the cohort and 18 640 matching controls were included
23
24 in the study. In some cases, notably with patients from small municipalities, it was not possible to
25
26 find a matching control, see Figure 2. Furthermore, there was a weak tendency in patients with
27
28 mTBI to have lower socio-economic status (education, income) and higher prevalence of pre-injury
29
30 diseases (CCI, psychiatric diseases) compared to their matched controls (Table 1).
31
32
33

34
35 Insert Figure 2 (flow-chart)
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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-value¹
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, DKK²), 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

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

²Generalized 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

1
2
3
4 compared to controls (OR 1.92, 95% CI 1.76-2.10). However, the long-term effect of mTBI on
5
6 limited attachment to the labour market was most pronounced at 2 years and 5 years.
7
8

9 10 *Permanent lack of attachment to the labour market*

11
12 During follow-up, a higher prevalence of permanent lack of attachment to the labour market was
13
14 seen in patients compared to controls, which increased from 6 months to 5 years. At 6 months the
15
16 adjusted odds for permanent lack of attachment to the labour market was almost two times higher
17
18 for patients (OR 1.90, 95% CI 1.36-2.66) and the long-term perspective continued showing large
19
20 effect.
21
22

23 24 25 *Death*

26
27 The prevalence of death was higher among patients showing an increase from 0.30% at 6 months to
28
29 2.42% at 5 years. The adjusted odds for death for patients with mTBI was six-fold increased at 6
30
31 months follow-up (OR 6.37 95% CI 2.71-14.95) and the long-term effects continued to be large but
32
33 diminishing during follow-up.
34
35

36 37 **DISCUSSION**

38
39 This nationwide register-based study examined the consequences of mTBI on short and long-term
40
41 labour market attachment in a large cohort of working-age patients with mTBI up to 5 years post-
42
43 injury compared to matched controls of the general population. The proportion of approximately 20
44
45 000 included patients in this study are difficult to compare to previous studies, since these mostly
46
47 report incidence rates.⁴ However, a Danish study included 10 000 patients in 1994 and 2002⁵, and
48
49 another Danish register-based study included approximately 90 000 patients during a 13-year
50
51 follow-up period.⁹
52
53
54
55
56
57
58
59
60

1
2
3
4 We found that the attachment to the labour market varied between patients and controls at the
5 date of injury. The odds of not attending ordinary work indicating any social transfer payment was
6 increased by 25% and remained higher for patients during the 5 years of follow-up (of about 40%).
7
8 A social gradient in not attending ordinary work at the index date could be suspected, as patients
9
10 had a significantly lower educational level, income and more comorbidities compared to controls
11
12 (see Table 1). Our findings agree with a Danish register-based cohort study⁹ demonstrating that
13
14 individuals with mTBI had a higher use of general practice even 5 years before mTBI. However,
15
16 when we controlled for socio-economic factors, comorbidities and psychiatric diagnoses, there was
17
18 no difference in the odds of not attending ordinary work between the two groups in our sample at
19
20 index date. Yet, the adjusted odds of not attending ordinary work remained increased by 30-50%
21
22 during the 5 years follow-up. This strongly supports that mTBI is the incident leading to not
23
24 returning to work.
25
26
27
28

29 For the secondary outcomes, we saw the prevalence of sick listed decreased during follow-up, while
30
31 the prevalence of limited and finally permanent lack of attachment to the labour market increased as
32
33 expected. The proportion of individuals receiving health-related benefits at the index date was also
34
35 higher for patients compared to controls, and the risk was more than two times higher for patients
36
37 even after controlling for possible confounders. This may indicate increased morbidity in patients
38
39 with mTBI prior to the trauma as seen in another Danish study⁹, and variations in health seeking
40
41 behavior which result in health-related social transfer payments. However, at 6 months the odds
42
43 diminished to 30% and were further decreased during the follow-up around 16-20%. Comparing our
44
45 results to other studies, Stulemeijer et al. found a 76% full RTW rate at 6 months,⁴² De Koning et
46
47 al. found a complete RTW rate of 77% at 12 months⁴³ and Losoi et al. also found that 97% had fully
48
49 RTW by 12 months after mTBI.⁶ These findings are slightly higher than those reported in this
50
51 study. However, previous investigations are not directly comparable because there is a lack of
52
53
54
55
56
57
58
59
60

1
2
3
4 consistency in definitions of labour market attachment and RTW measures. RTW is increasingly
5
6 regarded as an evolving process consisting of different phases such as off work, work reentry,
7
8 retention and advancement and measures in each phase.⁴⁴ Additionally, differences between
9
10 countries in registration of social transfer payments, political legislation and socioeconomic
11
12 differences can complicate comparison.¹⁶
13

14
15 Theadom et al. found in a cohort study with 4 years of follow-up that work productivity was
16
17 reduced by 15.5% among patients with mTBI, who had to make job changes in order to continue
18
19 working.⁴⁵ Our study found a long-term prevalence of 19% and increased odds of almost 40% of
20
21 limited attachment to the labour market indicating long-term employment restrictions due to health
22
23 conditions. These results indicate that most patients return to work after mTBI, but a small
24
25 proportion of patients suffer long-term consequences related to mTBI, preventing them from fully
26
27 re-integrating into the labour market. Since a previous study indicates an association between
28
29 increasing length of sickness absence and increasing risk of disability pension,⁴⁶ these patients are
30
31 in a particular risk of transitioning from temporary to permanent social benefits, meaning an exit
32
33 from the labour market. For permanent lack of attachment to the labour market, the prevalence in
34
35 our study was higher for patients even though there were significantly fewer events especially at 6
36
37 and 12 months and 2 years, indicating that it takes time to qualify for disability pension in
38
39 Denmark. The odds of permanent lack of attachment to the labour market were still more than twice
40
41 as high in the short as well as the long-term among patients with mTBI, even when controlled for
42
43 potential confounders.
44
45

46
47 Finally, the prevalence of death was higher in patients compared to controls. The odds of death
48
49 were more than 6 times higher for patients and continued to stay significantly higher during follow-
50
51 up. This is a surprising result. However, Selassie et al. found an in-hospital all-cause mortality rate
52
53 after mTBI of 1.4%⁴⁷ and Pentland et al. found similar results at 0.45% in a cohort with 21 years of
54
55
56
57
58
59
60

1
2
3
4 follow up,⁴⁸ agreeing with the result found in the present study. Additionally, a Danish study found
5 an increased risk of suicide among patients with mTBI⁴⁹. Although not the aim of the present study,
6
7 future research may benefit from exploring the risk factors in excess mortality in patients with
8
9
10 mTBI.
11
12
13

14 **Strengths and limitations**

15
16 This study applied a register-based design which prevented information bias in the collection of
17 labour market data and confounding factors. The DREAM register enabled us to estimate point
18 prevalence during 5 years of follow-up and to examine much more diverse labour market outcome
19 measures which is infrequent in TBI research.¹⁶ Furthermore, the sensitivity and specificity of the
20 DREAM register is considered high.⁵⁰ Finally, the use of national register data has made it possible
21 to include a large sample size and a matching control group which increased the statistical power.
22
23 We also adjusted for a wide range of pre-injury potential confounders. However, residual
24 confounding cannot be ruled out. The patients in this study were extracted from the DNPR.
25
26 Consequently, we did not have access to patient records, which hindered us to apply the operational
27 case definition for mTBI suggested by WHO.¹ Even though the DNPR is considered to be the most
28 comprehensive register of its kind²³, its validity and consistency with clinical diagnoses are widely
29 discussed, especially regarding clinical diagnoses and inaccurate coding leading to
30 misclassification. The ICD-9 code (850) for concussion has in several studies been reported as the
31 most frequently used for classification of mTBI^{1,51} but has also shown lack of sensitivity and
32 specificity.¹ This could also be expected to be the case for ICD-10. Additionally, a large proportion
33 of the mTBI patients are not treated at the hospital, some are treated in primary care settings, and
34 some refrain from counselling a physician,⁵² which can lead to low incidence rates and selection
35 bias, limiting the generalizability of the results.⁵³
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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 clinicaltrials.gov on July 5, 2017 (ClinicalTrials.gov Identifier: NCT03214432).

Acknowledgements

Competing interest statement

None declared

Patient consent

Not required

Funding

This work was supported by the Research Foundation, Rigshospitalet (E-22260-03) (E-23473-01), the Danish Health Foundation (Helsefonden) (16-B-0050) and the Aase and Ejnar Danielsen Foundation (20-000054).

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.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Data sharing statement

No additional data are available

For peer review only

REFERENCES

1. Carroll LJ, Cassidy JD, Holm L, et al. Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004;(43 Suppl):113-25.
2. Levin HS, Diaz-Arrastia RR. Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *Lancet Neurol* 2015;14:506-17.
3. van der Naalt J, Timmerman ME, de Koning ME, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. *Lancet Neurol* 2017;16:532-40.
4. Cassidy JD, Carroll LJ, Peloso PM, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004;(43 Suppl):28-60.
5. Engberg AW, Teasdale TW. Epidemiology and treatment of head injuries in Denmark 1994-2002, illustrated with hospital statistics. *Ugeskr Laeger* 2007;169:199-203.
6. Losoi H, Silverberg ND, Waljas M, et al. Recovery from Mild Traumatic Brain Injury in Previously Healthy Adults. *J Neurotrauma* 2016;33:766-76.
7. Dumke HA. Posttraumatic Headache and Its Impact on Return to Work After Mild Traumatic Brain Injury. *J Head Trauma Rehabil* 2017;32:E55-E65.
8. Ponsford J, Willmott C, Rothwell A, et al. Factors influencing outcome following mild traumatic brain injury in adults. *J Int Neuropsychol Soc* 2000;6:568-79.
9. Galili SF, Bech BH, Vestergaard C, et al. Use of general practice before and after mild traumatic brain injury: a nationwide population-based cohort study in Denmark. *BMJ Open* 2017;7:e017735.

10. Rutherford WH, Merrett JD, McDonald JR. Symptoms at one year following concussion from minor head injuries. *Injury* 1979;10:225-30.
11. Rees PM. Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil* 2003;84:1885-94.
12. Edna TH, Cappelen J. Late post-concussional symptoms in traumatic head injury. An analysis of frequency and risk factors. *Acta Neurochir (Wien)* 1987;86:12-7.
13. Ponsford J, Cameron P, Fitzgerald M, et al. Predictors of postconcussive symptoms 3 months after mild traumatic brain injury. *Neuropsychology* 2012;26:304-13.
14. Vicki L, Kristman PC, Sheilah Hogg-Johnson, David Cassidy, et al. The Burden of Work Disability Associated with Mild Traumatic Brain Injury in Ontario Compensated Workers: A Prospective Cohort Study. *The Open Occupational Health & Safety Journal* 2010;2:1-8.
15. Waljas M, Iverson GL, Lange RT, et al. Return to work following mild traumatic brain injury. *J Head Trauma Rehabil* 2014;29:443-50.
16. Cancelliere C, Kristman VL, Cassidy JD, et al. Systematic review of return to work after mild traumatic brain injury: results of the International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S201-9.
17. Pransky G, Gatchel R, Linton SJ, et al. Improving return to work research. *J Occup Rehabil* 2005;15:453-7.
18. Young AE, Wasiak R, Roessler RT, et al. Return-to-work outcomes following work disability: stakeholder motivations, interests and concerns. *J Occup Rehabil* 2005;15:543-56.
19. Sveen U, Soberg HL, Ostensjo S. Biographical disruption, adjustment and reconstruction of everyday occupations and work participation after mild traumatic brain injury. A focus group study. *Disabil Rehabil* 2016;38:2296-304.

- 1
2
3
4 20. Friedland JF, Dawson DR. Function after motor vehicle accidents: a prospective study of
5 mild head injury and posttraumatic stress. *J Nerv Ment Dis* 2001;189:426-34.
6
7
8 21. Mani K, Cater B, Hudlikar A. Cognition and return to work after mild/moderate traumatic
9 brain injury: A systematic review. *Work* 2017;58:51-62.
10
11
12 22. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011;39:22-5.
13
14 23. Lyng E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public*
15 *Health* 2011;39:30-3.
16
17
18 24. Beskæftigelsesministeriet. Bekendtgørelse om efterlønsbevis, udskydelsesreglen og skattefri
19 præmie m.v. BEK nr 4 af 02/01/2017 Gældende.
20
21 <https://www.retsinformation.dk/forms/R0710.aspx?id=186130>. (accessed 8 aug 2018)
22
23 25. Noonan VK, Thorogood NP, Fingas M, et al. The validity of administrative data to classify
24 patients with spinal column and cord injuries. *J Neurotrauma* 2013;30:173-80.
25
26
27 26. National Center for Injury Prevention and Control. Report to Congress on Mild Traumatic
28 Brain Injury in the United States: Steps to prevent a Serious Public Health Problem. 2003.
29
30 <https://www.cdc.gov/traumaticbraininjury/pdf/mtbireport-a.pdf>. (accessed 8 aug 2018)
31
32
33 27. Cassidy JD, Cancelliere C, Carroll LJ, et al. Systematic review of self-reported prognosis in
34 adults after mild traumatic brain injury: results of the International Collaboration on Mild
35 Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S132-51.
36
37
38 28. Arbejdsmarkedsstyrelsen. DREAM version 41. 2018. [https://www.dst.dk/-](https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da)
39 [/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da](https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da).
40
41 (accessed 8 aug 2018)
42
43 29. Beskæftigelsesministeriet. Bekendtgørelse af lov om sygedagpenge. LBK nr 871 af
44 28/06/2013 (Historisk). <https://www.retsinformation.dk/forms/R0710.aspx?id=152326>
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 30. Beskæftigelsesministeriet. Lov om ændring af lov om en aktiv beskæftigelsesindsats, lov om
5 aktiv socialpolitik, lov om fleksydelse, lov om betaling for uddannelse i forbindelse med
6 visse tilbud efter lov om en aktiv beskæftigelsesindsats m.m. og ligningsloven. LOV nr 565
7 af 09/06/2006 Gældende. <https://www.retsinformation.dk/forms/r0710.aspx?id=30748>
8
9
10
11
12 31. Beskæftigelsesministeriet DMOE. Bekendtgørelse af lov om højeste, mellemste, forhøjet
13 almindelig og almindelig førtidspension m.v. LBK nr 1209 af 17/11/2017 Gældende.
14 <https://www.retsinformation.dk/eli/lta/2017/1209>
15
16
17
18 32. Ministry for Economic Affairs and the Interior. Structural reform 2007.
19 <http://english.oim.dk/responsibilities-of-the-ministry/economics-of-municipalities-and->
20 [regions/structural-reform/](http://english.oim.dk/responsibilities-of-the-ministry/economics-of-municipalities-and-).
21
22
23
24
25 33. Hannerz H, Mortensen OS, Poulsen OM, et al. Time trend analysis of return to work after
26 stroke in Denmark 1996-2006. *Int J Occup Med Environ Health* 2012;25:200-4.
27
28
29 34. Rao DP, McFaull S, Thompson W, et al. Trends in self-reported traumatic brain injury
30 among Canadians, 2005-2014: a repeated cross-sectional analysis. *CMAJ Open*
31 2017;5:E301-E07.
32
33
34
35 35. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments.
36 *Scand J Public Health* 2011;39:103-5.
37
38
39
40 36. Jensen VM, Rasmussen AW. Danish Education Registers. *Scand J Public Health*
41 2011;39:91-4.
42
43
44
45 37. Statistics Denmark. Households, Families and Children. Secondary Households, Families
46 and Children 2017.
47 <http://www.dst.dk/en/Statistik/dokumentation/documentationofstatistics/households-->
48 [families-and-children.](http://www.dst.dk/en/Statistik/dokumentation/documentationofstatistics/households--)
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 38. Thygesen SK, Christiansen CF, Christensen S, et al. The predictive value of ICD-10
5 diagnostic coding used to assess Charlson comorbidity index conditions in the population-
6 based Danish National Registry of Patients. *BMC Med Res Methodol* 2011;11:83.
7
8
9
10 39. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic
11 comorbidity in longitudinal studies: development and validation. *J Chronic Dis*
12 1987;40:373-83.
13
14
15
16 40. Pedersen P, Lund T, Lindholdt L, et al. Labour market trajectories following sickness
17 absence due to self-reported all cause morbidity-a longitudinal study. *BMC Public Health*
18 2016;16:337.
19
20
21
22
23 41. Carroll LJ, Cassidy JD, Cancelliere C, et al. Systematic review of the prognosis after mild
24 traumatic brain injury in adults: cognitive, psychiatric, and mortality outcomes: results of the
25 International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med*
26 *Rehabil* 2014;95:S152-73.
27
28
29
30
31
32 42. Stulemeijer M, van der Werf S, Borm GF, et al. Early prediction of favourable recovery 6
33 months after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2008;79:936-42.
34
35
36 43. de Koning ME, Scheenen ME, van der Horn HJ, et al. Prediction of work resumption and
37 sustainability up to 1 year after mild traumatic brain injury. *Neurology* 2017;89:1908-14.
38
39
40
41 44. Steenstra IA, Lee H, de Vroome EM, et al. Comparing current definitions of return to work:
42 a measurement approach. *J Occup Rehabil* 2012;22:394-400.
43
44
45 45. Theadom A, Barker-Collo S, Jones K, et al. Work Limitations 4 Years After Mild Traumatic
46 Brain Injury: A Cohort Study. *Arch Phys Med Rehabil* 2017;98:1560-66.
47
48
49 46. Lund T, Kivimaki M, Labriola M, et al. Using administrative sickness absence data as a
50 marker of future disability pension: the prospective DREAM study of Danish private sector
51 employees. *Occup Environ Med* 2008;65:28-31.
52
53
54
55
56
57
58
59
60

- 1
2
3
4 47. Selassie AW, Fakhry SM, Ford DW. Population-based study of the risk of in-hospital death
5 after traumatic brain injury: the role of sepsis. *J Trauma* 2011;71:1226-34.
6
7
8 48. Pentland B, Hutton LS, Jones PA. Late mortality after head injury. *J Neurol Neurosurg*
9 *Psychiatry* 2005;76:395-400.
10
11
12 49. Madsen T, Erlangsen A, Orlovskaya S, et al. Association Between Traumatic Brain Injury and
13 Risk of Suicide. *JAMA*. 2018;320:580–588.
14
15
16 50. Stapelfeldt CM, Jensen C, Andersen NT, et al. Validation of sick leave measures: self-
17 reported sick leave and sickness benefit data from a Danish national register compared to
18 multiple workplace-registered sick leave spells in a Danish municipality. *BMC Public*
19 *Health* 2012;12:661.
20
21
22
23
24
25 51. Chen AY, Colantonio A. Defining neurotrauma in administrative data using the
26 International Classification of Diseases Tenth Revision. *Emerg Themes Epidemiol* 2011;8:4.
27
28
29 52. Mannix R, O'Brien MJ, Meehan WP, 3rd. The epidemiology of outpatient visits for minor
30 head injury: 2005 to 2009. *Neurosurgery* 2013;73:129-34
31
32
33
34 53. Kristman VL, Borg J, Godbolt AK, et al. Methodological issues and research
35 recommendations for prognosis after mild traumatic brain injury: results of the International
36 Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil*
37 2014;95:S265-77.
38
39
40
41
42 54. van der Naalt J, van Zomeren AH, Sluiter WJ, et al. One year outcome in mild to moderate
43 head injury: the predictive value of acute injury characteristics related to complaints and
44 return to work. *J Neurol Neurosurg Psychiatry* 1999;66:207-13.
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 Figure 1. Description of unavailable for the labour market (an exclusion criterion) (EX), the primary
5
6 outcome (1) and the secondary outcomes (2-5) in terms of the social transfer payments and other
7
8 social conditions that are included in each.
9

10
11 Figure 2. Inclusion of the study population
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

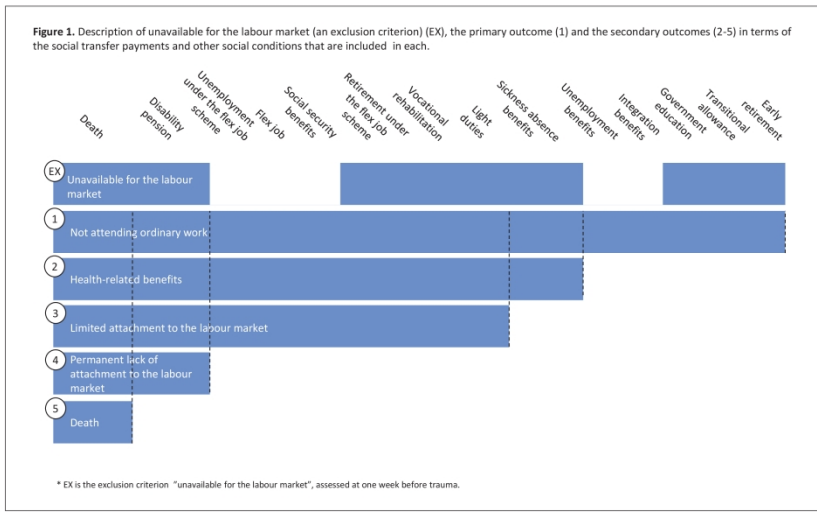


Figure 1. Description of unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1) and the secondary outcomes (2-5) in terms of the social transfer payments and other social conditions that are included in each.

297x209mm (300 x 300 DPI)

Figure 2. Inclusion of the study population

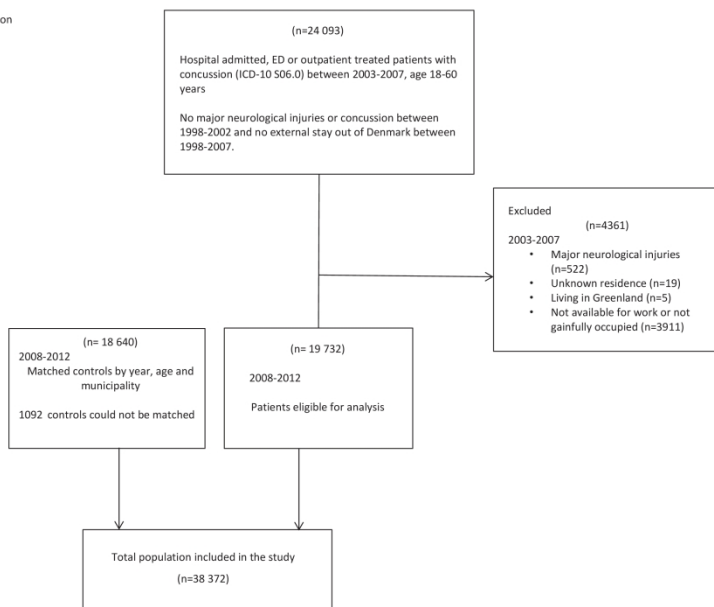


Figure 2. Inclusion of the study population

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 (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3 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 (b) For matched studies, give matching criteria and number of exposed and unexposed	7-9
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 (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	12, 13
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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	13- 14
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	13- 15
Outcome data	15*	Report numbers of outcome events or summary measures over time	15- 17

1	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	15-17
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
4				
5				
6				
7				
8	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
9				
10	Discussion			
11				
12	Key results	18	Summarise key results with reference to study objectives	17-20
13				
14	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
15				
16	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
17				
18	Generalisability	21	Discuss the generalisability (external validity) of the study results	20
19				
20	Other information			
21	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
22				
23				

*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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-026104.R1
Article Type:	Research
Date Submitted by the Author:	16-Jan-2019
Complete List of Authors:	Graff, Heidi; University Hospital Rigshospitalet, Department of Anaesthesia, 4231, Centre of Head and Orthopaedics Siersma, Volkert; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Denmark Møller, Anne; Copenhagen University Hospital Holbæk, Department of Occupational Medicine; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Denmark Kragstrup, Jakob; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice Andersen, Lars; National Research Centre for the Working Environment; Aalborg University, Sport Sciences, Department of Health Science and Technology Egerod, Ingrid; University of Copenhagen, Intensive Care Unit, Rigshospitalet Malá, Hana; University of Copenhagen, Department of Psychology; University Hospital Bispebjerg-Frederiksberg, Department of Neurology
Primary Subject Heading:	Neurology
Secondary Subject Heading:	Epidemiology, Neurology, Occupational and environmental medicine, Public health
Keywords:	Labour market attachment, Mild traumatic brain injury, Sickness absence, Post-concussive symptoms, Unemployment

SCHOLARONE™
Manuscripts

1
2
3
4 **Labour market attachment after mild traumatic brain injury:**
5
6 **Nationwide cohort study with 5-year register follow-up in Denmark**
7
8
9

10 Heidi Jeannet Graff, MSc in Public Health^{1,2}

11 Volkert Siersma, Statistician³

12 Anne Møller, Assistant professor^{3,4}

13 Jakob Kragstrup, Professor³

14 Lars Louis Andersen, Professor^{5,6}

15 Ingrid Egerod, Professor⁷

16 Hana Malá Rytter, Associate Professor^{8,9}

17
18
19
20
21
22
23
24
25
26 **Affiliations:**
27

28
29 ¹Department of Anaesthesia, Centre of Head and Orthopaedics, Rigshospitalet, Copenhagen
30 University Hospital, Denmark
31

32
33
34 ²Trauma Center and Acute Admission, Centre of Head and Orthopaedics, Rigshospitalet,
35 Copenhagen University Hospital, Denmark
36

37
38
39 ³Department of Public Health, The Research Unit for General Practice and Section of General
40 Practice, University of Copenhagen, Denmark
41

42
43
44 ⁴Department of Occupational Medicine, Copenhagen University Hospital Holbæk, Denmark
45

46
47
48 ⁵National Research Centre for the Working Environment, Copenhagen, Denmark
49

50
51
52 ⁶Sport Sciences, Department of Health Science and Technology, Aalborg University, Aalborg,
53 Denmark
54

55
56
57 ⁷Intensive Care Unit, Rigshospitalet, Copenhagen University Hospital, Denmark
58
59
60

1
2
3
4⁸Department of Psychology, University of Copenhagen, Denmark
5
6

7⁹Department of Neurology, University Hospital Bispebjerg-Frederiksberg, Copenhagen, Denmark
8
9

10
11 **Corresponding author:**
12

13
14 Heidi Jeannet Graff, University Hospital Rigshospitalet, Department of Anaesthesia, Blegdamsvej
15
16 9, 2100 Copenhagen, Denmark.
17

18
19 Phone: +45 40688504
20

21 Email: heidi.jeannet.graff@regionh.dk
22
23

24
25 **Word count: 3993**
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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).

1
2
3
4 **Conclusions:**
5

6 43% of concussed patients were not attending ordinary work 5 years post-injury and received health
7 and social transfer benefits. We conclude that mTBI has a long-term impact on labour market
8 attachment. Prevention and treatment of persisting post-concussive symptoms should be considered.
9
10
11
12
13
14
15

16 ClinicalTrials.gov Identifier: NCT03214432
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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 difficulties¹⁰⁻¹² 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

1
2
3
4 most patients (>75%) had returned to work after six months and 5% were on social transfer
5
6 payments two years post-injury.²⁰
7

8
9 Return to work (RTW) has been conceptualized as being a dynamic process with different
10 related outcomes of labour market attachment or time off work, but also outcomes related to the
11 process of return to work such as psychological functioning and job satisfaction.^{21, 22} RTW after
12 mTBI has been suggested to depend on multiple factors such as injury related factors,²⁰ premorbid
13 demographics such as younger age,¹⁸ work place related factors such as support,²³ and influence on
14 work planning²⁴ and patient characteristics such as psychosocial status.²⁵ These studies have
15 methodological limitations in study design which complicate evaluation of evidence regarding the
16 magnitude of the problem. They have small sample sizes, are not representative,¹⁰ are based on self-
17 reported data and have short follow-up and considerable dropout leading to attrition bias.¹⁹ The
18 present analysis overcomes these challenges by using Danish nationwide administrative data to
19 examine a larger, representative sample and to perform long-term follow up. This study is
20 concerned with labour market attachment in hospital treated patients receiving the diagnosis
21 concussion (commotio cerebri) as the only brain injury diagnosis.
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37

38
39 We examined a comprehensive range of post-injury transitions in the labour market aiming at
40 analysing attachment to the labour market up to five years after mTBI using a portfolio of
41 outcomes, including a variation of social transfer payments and data on permanent lack of
42 attachment to the labour market and death.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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 injuries²⁹ 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,

1
2
3
4 patients were not included if they had lived outside of Denmark at any time during the inclusion
5
6 period and the five-year period before.
7

8
9 For each mTBI case in the cohort, a control was randomly selected from the Population
10
11 register. Controls had similar inclusion criteria as the cases, but they had no diagnosis of concussion
12
13 during the inclusion period 1st of January 2003 – 31st of December 2007.
14

15
16 The control was matched to the case on sex, municipality and age (year of birth \pm 0.5 years,
17
18 expanded to 1 and 2 years in case of no initial match) (see Figure 1). The same exclusion criteria
19
20 were applied for the selection of controls.
21
22

23
24
25 Insert Figure 1
26

27
28 Availability for the labour market was assessed from the Danish Register for Evaluation of
29
30 Marginalization (DREAM), containing weekly information on all individuals receiving any social
31
32 public transfer payments.³² Patients and their matching controls were excluded from the cohort if
33
34 there were any major neurological injuries^{9, 29} as secondary diagnoses at the index date, they were
35
36 unavailable for the labour market, they had unknown residence or were inhabitants of Greenland.
37
38

39 40 41 **Outcome measures**

42
43
44 The outcomes of the present analyses were assessments of variations in attachment to the labour
45
46 market evaluated in the DREAM database (Figure 1) the week before the case's index date, and at 6
47
48 months, 12 months, 2 years and 5 years after the case's index date (Figure 1).
49

50 51 **Not attending ordinary work**

52
53 1. "Not attending ordinary work" was the primary outcome and was indicated by any entry in
54
55 DREAM, i.e. receiving any social transfer payment, such as unemployment benefits unrelated to the
56
57 subject's health condition, sickness absence benefits, social benefits granted, short and long-term
58
59
60

1
2
3
4 sickness or death. If there was no DREAM entry, it was assumed that the subject was gainfully
5
6 employed or self-supporting at that time (Figure 1).
7
8
9

10
11 The set of secondary outcomes are defined increasingly narrower than the primary outcome and
12
13 focus on attachment to the labour market due to health conditions. At the time of the current study,
14
15 employers in Denmark were obliged to finance sickness benefits for the first 30 days. Sickness
16
17 benefits lasting more than four consecutive weeks were to be compensated by the Danish
18
19 municipalities.³³ Sick-listed individuals could receive sickness benefits for a maximum of one
20
21 year³⁴. If individuals were not able to return to ordinary work due to long-term limited work
22
23 capacity, a partial return to work at lower capacity was possible with a “flex job”. If the sick-listed
24
25 individual was not able to return to work at all, the municipality could grant disability pension.^{35, 36}
26
27
28
29 The grading of the outcomes is illustrated in Figure 1.
30
31
32
33

34 Health-related benefits

35
36 2. Health-related benefits were indicated by DREAM entries given for short- or long-term
37
38 restrictions in attachment to the labour market due to health conditions (excluding unemployment
39
40 benefits unrelated to the subject’s health condition). These were sickness absence benefits,
41
42 vocational rehabilitation, flex job, unemployment benefits specifically granted to citizens on flex
43
44 job, social security benefits, light duties, disability pension and death.
45
46
47
48
49

50 Limited attachment to the labour market

51
52 3. Social transfer payments due to limited attachment to the labour market were indicated by
53
54 DREAM entries given for reduced work capacity and thereby long-term restrictions in attachment
55
56 to the labour market due to health conditions (excluding sickness absence benefits compared to
57
58
59
60

1
2
3
4 secondary outcome 2). These were vocational rehabilitation, flex job, unemployment benefits
5
6 specifically granted to citizens on flex job, social security benefits, light duties, disability pension
7
8 and death.
9

10
11
12
13 Permanent lack of attachment to the labour market

14
15
16 4. Permanent lack of attachment to the labour market was indicated by DREAM entries given for
17
18 permanent withdrawal from the labour market due to health conditions. These were disability
19
20 pension and death.
21
22

23
24
25 Death

26
27 5. Death was indicated by the DREAM entry for death.
28
29
30
31

32 **Potential confounders**

33
34 Sex, age and municipality at the index date were obtained from the Population register linked to the
35
36 DNPR. The municipality information was categorized into five regions reflecting Denmark's
37
38 reform of local government structure from 2007.³⁷ From the index date calendar year and season
39
40 were derived. Calendar year was included in the model as a previous study found increasing odds of
41
42 returning to work during the study period.³⁸ The reason could be a change in diagnostic practice and
43
44 the Danish sickness benefit Act becoming more effective over the years. Seasonal variation was
45
46 considered a confounder, as a previous study suggested that TBI is associated with season-specific
47
48 activities and most pronounced during fall and winter.³⁹ Pre-injury income was measured at the
49
50 index date and taken as personal gross income including revenue and social transfer income and
51
52 was obtained from the Income Statistics Register.⁴⁰ Income was divided into four income groups:
53
54 <100 000, 100 000-200 000, 200 000-300 000, >300 000 DKK roughly reflecting the quartiles in
55
56
57
58
59
60

1
2
3
4 the present cohort. Information on the highest attained educational level was obtained from the
5
6 Danish Education Register⁴¹ and was categorized into three educational groups: low education
7
8 (primary education), medium education (lower and upper secondary education, post-secondary–
9
10 non-tertiary education) and high education (short cycle tertiary education, bachelor, master, doctoral
11
12 or equivalent). Information on cohabitation status and ethnic origin was obtained from the Danish
13
14 Family Relations Database^{26, 42} and was categorized into married or cohabiting couple and single,
15
16 and as Danish born and not Danish born respectively. Pre-injury illness burden was measured by
17
18 Charlson comorbidity index (CCI), a weighted sum of 19 indicators for selected diagnoses.^{43, 44} For
19
20 the present CCI evaluation, a diagnosis was indicated for an individual when a corresponding ICD-
21
22 10 code was encountered in the DNPR in the five-year period 1st of January 1998 – 31st of
23
24 December 2002 before the inclusion period. Psychiatric diagnoses are not incorporated in CCI but
25
26 are possible confounders related to both labour market attachment and an increased risk of TBI.^{45, 46}
27
28 Hence, information on psychiatric diagnoses separately from CCI was obtained from the DNPR
29
30 over the same five-year period.
31
32
33
34
35
36
37

38 **Statistical analysis**

39
40 Baseline covariates at the index date, and the outcomes at the index date and the follow-up time
41
42 points were reported as numbers and percentages separately for mTBI patients and their matched
43
44 controls. Raw comparisons of the baseline covariates between the mTBI patients and their controls
45
46 are done by Chi-squared tests.
47
48

49 The difference in tendency of some degree of decreased attachment to the labour market, between
50
51 patients with mTBI and their controls, at each of the index date and the four follow-up time points,
52
53 was assessed by odds ratios (OR) and corresponding 95% confidence intervals (95%CI) from a
54
55 multivariable logistic regression model; an OR>1 implied higher odds for the mTBI group. The
56
57 model was parameterized so that the assessments at the four follow-up time points were adjusted for
58
59
60

1
2
3
4 differences already present at the index date, i.e. pre-injury differences. Hence, the assessment at
5
6 the index date can be viewed as an assessment of the employment aspect of a social gradient in
7
8 mTBI incidence; the assessments at the follow-up time points report on the short- and long-term
9
10 differences in attachment attributable to mTBI. Results are reported both unadjusted and adjusted
11
12 for the potential confounders: age, gender, municipality, seasonal variation, calendar year,
13
14 education, income, cohabitation status, ethnicity, pre-injury comorbidities and pre-injury psychiatric
15
16 diagnosis. Inference was done by generalized estimating equations to adjust for repeated
17
18 measurement and matching.
19
20
21
22
23 Subjects with missing values in one of the covariates were omitted from analyses where these
24
25 covariates were included. P-values below 0.05 were considered statistically significant. SAS version
26
27 9.4 was used for statistical analysis.
28
29
30
31

32 **Patient and public involvement**

33
34 Patients and the public were not involved in the design and the conduct of the study.
35
36
37

38 **RESULTS**

39 **Baseline characteristics of the population**

40
41
42 19 732 patients with mTBI were eligible for the cohort and 18 640 matching controls were included
43
44 in the study. In some cases, notably with patients from small municipalities, it was not possible to
45
46 find a matching control, see Figure 2. Overall, the cohort was characterized by a weak tendency in
47
48 patients with mTBI to have lower education, lower income, being married or cohabiting, and having
49
50 a higher prevalence of pre-injury diseases (both somatic diseases as captured by CCI and
51
52 psychiatric diseases) compared to their matched controls (Table 1).
53
54
55
56
57

58 Insert Figure 2 (flow-chart)
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

	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, DKK²), 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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Analysis of attachment to labour market

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

For peer review only

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

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

²Generalized 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

1
2
3
4 1994 and 2002,⁹ and another Danish register-based study included approximately 90 000 patients
5
6 during a 13-year follow-up period.¹³
7

8
9 We found that attachment to the labour market varied between patients and controls at the
10 date of injury. The odds of not attending ordinary work was increased by 25% and remained higher
11 for patients during the 5 years of follow-up (of about 40%). A social gradient in not attending
12 ordinary work at the index date could be suspected, as patients had a significantly lower educational
13 level, income and more comorbidities compared to controls (see Table 1). Our findings agree with a
14 Danish register-based cohort study¹³ demonstrating that individuals with mTBI had a higher use of
15 general practice even 5 years before mTBI. However, when we controlled for socio-economic
16 factors, comorbidities and psychiatric diagnoses, there were no difference in the odds of not
17 attending ordinary work between the two groups in our sample at index date. Yet, the adjusted odds
18 of not attending ordinary work remained increased by 30-50% during the 5 years follow-up. This
19 strongly supports that mTBI is the incident leading to not returning to work.
20
21
22
23
24
25
26
27
28
29
30
31
32
33

34 For the secondary outcomes, the prevalence of sick listed decreased during follow-up, while
35 the prevalence of limited and permanent lack of attachment to the labour market increased as
36 expected. The proportion of individuals receiving health-related benefits at the index date was also
37 higher for patients compared to controls, and the risk was more than two times higher for patients
38 even after controlling for possible confounders. This may indicate increased morbidity in patients
39 with mTBI prior to the trauma as seen in another Danish study¹³, and variations in health seeking
40 behavior which result in health-related social transfer payments. However, at 6 months the odds
41 diminished to 30% and were further decreased during follow-up to 16-20%. Stulemeijer et al. found
42 a 76% full RTW rate at 6 months,⁴⁷ De Koning et al. found a complete RTW rate of 77% at 12
43 months⁴⁸ and Losoi et al. also found that 97% had fully RTW by 12 months after mTBI.¹⁰ These
44 findings are slightly higher than those reported in this study. However, previous investigations are
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 not directly comparable because there is a lack of consistency in definitions of labour market
5 attachment and RTW measures. RTW is increasingly regarded as an evolving process consisting of
6 different phases such as off work, work reentry, retention and advancement.⁴⁹ Additionally,
7 differences between countries in registration of social transfer payments, political legislation and
8 socioeconomic differences can complicate comparison.²⁰

9
10
11
12
13
14
15
16 Theadom et al. found that work productivity was reduced by 15.5% among patients with
17 mTBI, who had to make job changes to continue working.⁵⁰ Our study found a long-term
18 prevalence of 19% and increased odds of almost 40% of limited attachment to the labour market
19 indicating long-term employment restrictions due to health conditions. These results indicate that
20 most patients return to work after mTBI, but a small proportion of patients suffer long-term
21 consequences related to mTBI, preventing them from fully re-integrating into the labour market.
22 Since a previous study indicates an association between increasing length of sickness absence and
23 increasing risk of disability pension,⁵¹ these patients are in risk of transitioning from temporary to
24 permanent social benefits, meaning an exit from the labour market. For permanent lack of
25 attachment to the labour market, the prevalence in our study was higher for patients even though
26 there were significantly fewer events especially at 6 and 12 months and 2 years, indicating that it
27 takes time to qualify for disability pension in Denmark. The odds of permanent lack of attachment
28 to the labour market were still more than twice as high in the short as well as the long-term among
29 patients with mTBI, even when controlled for potential confounders.

30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48 Finally, the prevalence of death was higher in patients compared to controls. The odds of death
49 were more than 6 times higher for patients and subsequently declined during follow-up. This is a
50 surprising result assumed to be predicted by a set of different factors (socio-economic indicators,
51 comorbidities etc.) than those predicting labour market attachment. Selassie et al. found an in-
52 hospital all-cause mortality rate after mTBI of 1.4%⁵² and Pentland et al. found similar results at
53
54
55
56
57
58
59
60

1
2
3
4 0.45% in a cohort with 21 years of follow up,⁵³ agreeing with the result found in the present study.

5
6 Additionally, a Danish study found an increased risk of suicide among patients with mTBI⁵⁴.

7
8 Although not the aim of the present study, future research may benefit from exploring the risk
9
10 factors in excess mortality in patients with mTBI.
11
12
13
14

15 16 **Strengths and limitations**

17
18 This study applied a register-based design preventing information bias in the collection of data. The
19
20 DREAM register enabled us to estimate point prevalence during 5 years of follow-up and to
21
22 examine much more diverse labour market outcomes which is infrequent in TBI research.²⁰

23
24 Furthermore, the sensitivity and specificity of the DREAM register is considered high.⁵⁵ Finally, the
25
26 use of national register data has made it possible to include a large sample size and a matching
27
28 control group which increased the statistical power. We also adjusted for a wide range of pre-injury
29
30 potential confounders. However, residual confounding such as injury mechanism and psychological
31
32 effects affecting outcome cannot be ruled out. Patients were extracted from the DNPR.
33
34

35
36 Consequently, we did not have access to patient records, which hindered us to apply the operational
37
38 case definition for mTBI suggested by WHO.⁴ Even though the DNPR is considered the most
39
40 comprehensive register of its kind,²⁷ its validity and consistency with clinical diagnoses are widely
41
42 discussed, especially regarding clinical diagnoses and inaccurate coding leading to
43
44 misclassification. The ICD-9 code (850) for concussion has in several studies been reported as
45
46 frequently used for the classification of mTBI^{4, 56} but has also shown lack of sensitivity and
47
48 specificity.⁴ This could also be expected to be the case for ICD-10. Additionally, a large proportion
49
50 of patients with mTBI are not treated at the hospital, some are treated in primary care settings, and
51
52 some refrain from counselling a physician,⁵⁷ which can lead to low incidence rates and selection
53
54 bias, limiting the generalizability of the results.⁵⁸
55
56
57
58
59
60

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.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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).

Acknowledgements

Competing interest statement

None declared

Patient consent

Not required

Funding

This work was supported by the Research Foundation, Rigshospitalet (E-22260-03) (E-23473-01), the Danish Health Foundation (Helsefonden) (16-B-0050) and the Aase and Ejnar Danielsen Foundation (20-000054).

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.

1
2
3
4 **Data sharing statement**
5

6 No additional data are available
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

REFERENCES

1. Carroll LJ, Cassidy JD, Holm L, et al. Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004;(43 Suppl):113-25.
2. The American Congress of Rehabilitation Medicine (ACRM). Definition of mild traumatic brain injury. *J Head Trauma Rehabil* 1993;8:86-87.
https://acrm.org/wpcontent/uploads/pdf/TBIDef_English_10-10.pdf
(accessed 05 jan. 2019).
3. Katz DI, Cohen SI, Alexander MP, Handbook of Clinical Neurology, Vol. 127 (3rd series) Traumatic Brain Injury, Part I, J. Grafman and A.M. Salazar, Editors, 2015: 129-242.
4. McCrory P, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med* 2013;47:250–258.
5. Uden L, Calcagnile O, Uden J, et al. Validation of the Scandinavian guidelines for initial management of minimal, mild and moderate traumatic brain injury in adults. *BMC Med* 2015;13:292.
6. Levin HS, Diaz-Arrastia RR. Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *Lancet Neurol* 2015;14:506-17.
7. van der Naalt J, Timmerman ME, de Koning ME, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. *Lancet Neurol* 2017;16:532-40.
8. Cassidy JD, Carroll LJ, Peloso PM, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004;(43 Suppl):28-60.

- 1
2
3
4 9. Engberg AW, Teasdale TW. Epidemiology and treatment of head injuries in Denmark 1994-
5 2002, illustrated with hospital statistics. *Ugeskr Laeger* 2007;169:199-203.
6
7
- 8
9 10. Losoi H, Silverberg ND, Waljas M, et al. Recovery from Mild Traumatic Brain Injury in
10 Previously Healthy Adults. *J Neurotrauma* 2016;33:766-76.
11
12
- 13 11. Dumke HA. Posttraumatic Headache and Its Impact on Return to Work After Mild
14 Traumatic Brain Injury. *J Head Trauma Rehabil* 2017;32:E55-E65.
15
16
- 17 12. Ponsford J, Willmott C, Rothwell A, et al. Factors influencing outcome following mild
18 traumatic brain injury in adults. *J Int Neuropsychol Soc* 2000;6:568-79.
19
20
- 21 13. Galili SF, Bech BH, Vestergaard C, et al. Use of general practice before and after mild
22 traumatic brain injury: a nationwide population-based cohort study in Denmark. *BMJ Open*
23 2017;7:e017735.
24
25
- 26 14. Rutherford WH, Merrett JD, McDonald JR. Symptoms at one year following concussion
27 from minor head injuries. *Injury* 1979;10:225-30.
28
29
- 30 15. Rees PM. Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil*
31 2003;84:1885-94.
32
33
- 34 16. Edna TH, Cappelen J. Late post-concussional symptoms in traumatic head injury. An
35 analysis of frequency and risk factors. *Acta Neurochir (Wien)* 1987;86:12-7.
36
37
- 38 17. Ponsford J, Cameron P, Fitzgerald M, et al. Predictors of postconcussive symptoms 3
39 months after mild traumatic brain injury. *Neuropsychology* 2012;26:304-13.
40
41
- 42 18. Vicki L. Kristman PC, Sheilah Hogg-Johnson, David Cassidy, et al. The Burden of Work
43 Disability Associated with Mild Traumatic Brain Injury in Ontario Compensated Workers:
44 A Prospective Cohort Study. *The Open Occupational Health & Safety Journal* 2010;2:1-8.
45
46
- 47 19. Waljas M, Iverson GL, Lange RT, et al. Return to work following mild traumatic brain
48 injury. *J Head Trauma Rehabil* 2014;29:443-50.
49
50
51
52
53
54
55
56
57
58
59
60

- 1
- 2
- 3
- 4 20. Cancelliere C, Kristman VL, Cassidy JD, et al. Systematic review of return to work after
- 5 mild traumatic brain injury: results of the International Collaboration on Mild Traumatic
- 6 Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S201-9.
- 7
- 8
- 9
- 10
- 11 21. Pransky G, Gatchel R, Linton SJ, et al. Improving return to work research. *J Occup Rehabil*
- 12 2005;15:453-7.
- 13
- 14
- 15
- 16 22. Young AE, Wasiak R, Roessler RT, et al. Return-to-work outcomes following work
- 17 disability: stakeholder motivations, interests and concerns. *J Occup Rehabil* 2005;15:543-
- 18 56.
- 19
- 20
- 21
- 22
- 23 23. Sveen U, Soberg HL, Ostensjo S. Biographical disruption, adjustment and reconstruction of
- 24 everyday occupations and work participation after mild traumatic brain injury. A focus
- 25 group study. *Disabil Rehabil* 2016;38:2296-304.
- 26
- 27
- 28
- 29
- 30 24. Friedland JF, Dawson DR. Function after motor vehicle accidents: a prospective study of
- 31 mild head injury and posttraumatic stress. *J Nerv Ment Dis* 2001;189:426-34.
- 32
- 33
- 34 25. Mani K, Cater B, Hudlikar A. Cognition and return to work after mild/moderate traumatic
- 35 brain injury: A systematic review. *Work* 2017;58:51-62.
- 36
- 37
- 38
- 39 26. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011;39:22-5.
- 40
- 41 27. Lyng E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public*
- 42 *Health* 2011;39:30-3.
- 43
- 44
- 45 28. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse om
- 46 efterlønsbevis, udskydelsesreglen og skattefri præmie m.v. BEK nr 4 af 02/01/2017
- 47 Gældende. <https://www.retsinformation.dk/forms/R0710.aspx?id=186130>. (accessed 8 aug
- 48 2018)
- 49
- 50
- 51
- 52
- 53
- 54
- 55 29. Noonan VK, Thorogood NP, Fingas M, et al. The validity of administrative data to classify
- 56 patients with spinal column and cord injuries. *J Neurotrauma* 2013;30:173-80.
- 57
- 58
- 59
- 60

- 1
2
3
4 30. National Center for Injury Prevention and Control. Report to Congress on Mild Traumatic
5 Brain Injury in the United States: Steps to prevent a Serious Public Health Problem. 2003.
6
7 <https://www.cdc.gov/traumaticbraininjury/pdf/mtbireport-a.pdf>. (accessed 8 aug 2018)
8
9
- 10
11 31. Cassidy JD, Cancelliere C, Carroll LJ, et al. Systematic review of self-reported prognosis in
12 adults after mild traumatic brain injury: results of the International Collaboration on Mild
13 Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S132-51.
14
15
- 16 32. Styrelsen for Arbejdsmarked og Rekruttering [Danish Agency for Labour Market and
17 Recruitment] . DREAM version 41. 2018. [https://www.dst.dk/-/media/Kontorer/13-](https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da)
18 [Forskning-og-Metode/DREAM-koder-version-41.docx?la=da](https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da). (accessed 8 aug 2018)
19
20
21
22
23
24
- 25 33. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om
26 sygedagpenge. 2010/1 LSF 68. <http://www.retsinformation.dk/eli/ft/201012L00068>.
27
28 (accessed 03 jan. 2019).
29
30
31
- 32 34. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om
33 sygedagpenge. LBK nr 653 af 26/06/2012 Historisk.
34
35 <https://www.retsinformation.dk/Forms/R0710.aspx?id=142423#Afs6>. (accessed 03 jan.
36
37
38
39
40
41
42
43
44
45
46
47
- 48 35. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om en
49 aktiv beskæftigelsesindsats. LBK nr 685 af 29/06/2005 Historisk.
50
51 <https://www.retsinformation.dk/Forms/R0710.aspx?id=30223>. (accessed 03 jan. 2019).
52
53
54
55
56
57
58
59
60
36. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om social
pension. LBK nr 783 af 09/07/2012.
<https://www.retsinformation.dk/Forms/R0710.aspx?id=142132>. (accessed 03 jan. 2019).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

37. Ministry for Economic Affairs and the Interior. Structural reform 2007.
<http://english.oim.dk/responsibilities-of-the-ministry/economics-of-municipalities-and-regions/structural-reform/>.
38. Hannerz H, Mortensen OS, Poulsen OM, et al. Time trend analysis of return to work after stroke in Denmark 1996-2006. *Int J Occup Med Environ Health* 2012;25:200-4.
39. Rao DP, McFaul S, Thompson W, et al. Trends in self-reported traumatic brain injury among Canadians, 2005-2014: a repeated cross-sectional analysis. *CMAJ Open* 2017;5:E301-E07.
40. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments. *Scand J Public Health* 2011;39:103-5.
41. Jensen VM, Rasmussen AW. Danish Education Registers. *Scand J Public Health* 2011;39:91-4.
42. Statistics Denmark. Households, Families and Children. Secondary Households, Families and Children 2017.
<http://www.dst.dk/en/Statistik/dokumentation/documentationofstatistics/households--families-and-children>.
43. Thygesen SK, Christiansen CF, Christensen S, et al. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. *BMC Med Res Methodol* 2011;11:83.
44. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-83.

- 1
2
3
4 45. Pedersen P, Lund T, Lindholdt L, et al. Labour market trajectories following sickness
5 absence due to self-reported all cause morbidity-a longitudinal study. *BMC Public Health*
6 2016;16:337.
7
8
9
10
11 46. Carroll LJ, Cassidy JD, Cancelliere C, et al. Systematic review of the prognosis after mild
12 traumatic brain injury in adults: cognitive, psychiatric, and mortality outcomes: results of the
13 International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med*
14 *Rehabil* 2014;95:S152-73.
15
16
17
18
19
20 47. Stulemeijer M, van der Werf S, Borm GF, et al. Early prediction of favourable recovery 6
21 months after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2008;79:936-42.
22
23
24 48. de Koning ME, Scheenen ME, van der Horn HJ, et al. Prediction of work resumption and
25 sustainability up to 1 year after mild traumatic brain injury. *Neurology* 2017;89:1908-14.
26
27
28
29 49. Steenstra IA, Lee H, de Vroome EM, et al. Comparing current definitions of return to work:
30 a measurement approach. *J Occup Rehabil* 2012;22:394-400.
31
32
33 50. Theadom A, Barker-Collo S, Jones K, et al. Work Limitations 4 Years After Mild Traumatic
34 Brain Injury: A Cohort Study. *Arch Phys Med Rehabil* 2017;98:1560-66.
35
36
37
38 51. Lund T, Kivimaki M, Labriola M, et al. Using administrative sickness absence data as a
39 marker of future disability pension: the prospective DREAM study of Danish private sector
40 employees. *Occup Environ Med* 2008;65:28-31.
41
42
43
44 52. Selassie AW, Fakhry SM, Ford DW. Population-based study of the risk of in-hospital death
45 after traumatic brain injury: the role of sepsis. *J Trauma* 2011;71:1226-34.
46
47
48
49 53. Pentland B, Hutton LS, Jones PA. Late mortality after head injury. *J Neurol Neurosurg*
50 *Psychiatry* 2005;76:395-400.
51
52
53
54 54. Madsen T, Erlangsen A, Orlovska S, et al. Association Between Traumatic Brain Injury and
55 Risk of Suicide. *JAMA*. 2018;320:580-588.
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

55. Stapelfeldt CM, Jensen C, Andersen NT, et al. Validation of sick leave measures: self-reported sick leave and sickness benefit data from a Danish national register compared to multiple workplace-registered sick leave spells in a Danish municipality. *BMC Public Health* 2012;12:661.
56. Chen AY, Colantonio A. Defining neurotrauma in administrative data using the International Classification of Diseases Tenth Revision. *Emerg Themes Epidemiol* 2011;8:4.
57. Mannix R, O'Brien MJ, Meehan WP, 3rd. The epidemiology of outpatient visits for minor head injury: 2005 to 2009. *Neurosurgery* 2013;73:129-34
58. Kristman VL, Borg J, Godbolt AK, et al. Methodological issues and research recommendations for prognosis after mild traumatic brain injury: results of the International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S265-77.
59. van der Naalt J, van Zomeren AH, Sluiter WJ, et al. One year outcome in mild to moderate head injury: the predictive value of acute injury characteristics related to complaints and return to work. *J Neurol Neurosurg Psychiatry* 1999;66:207-13.

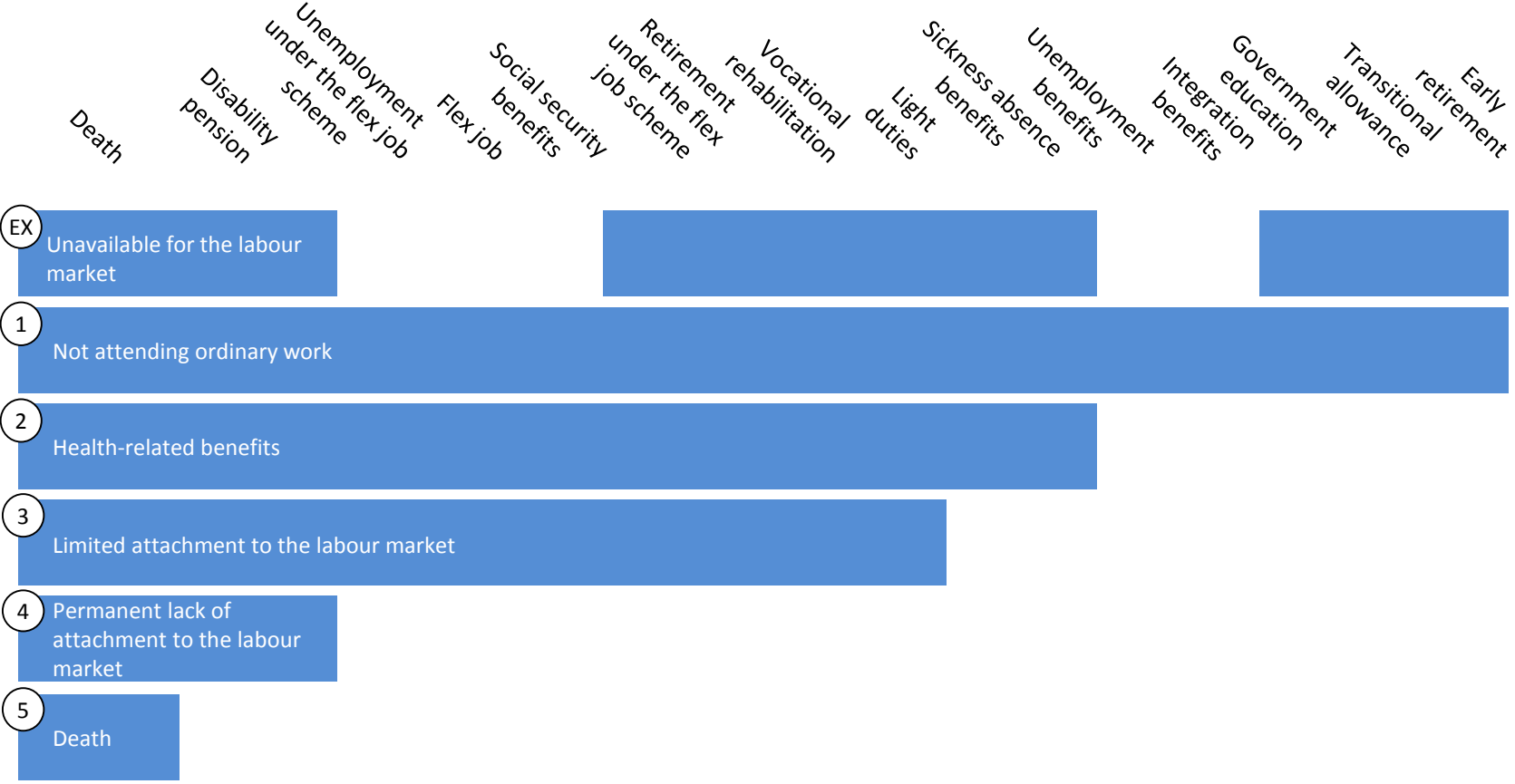
1
2
3
4 Figure 1. Description of social transfer payments as part of the Danish welfare system. Categories
5 describe unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1)
6
7 and the secondary outcomes (2-5) in terms of the different social transfer payments and other social
8
9 conditions (first row) that are included in each.
10
11
12

13
14 Figure 2. Inclusion of the study population
15
16

17 Figure 3. Prevalence and adjusted odds of not attending ordinary work at the index date and up to 5
18
19 years after concussion
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

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.



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

Figure 2. Inclusion of the study population

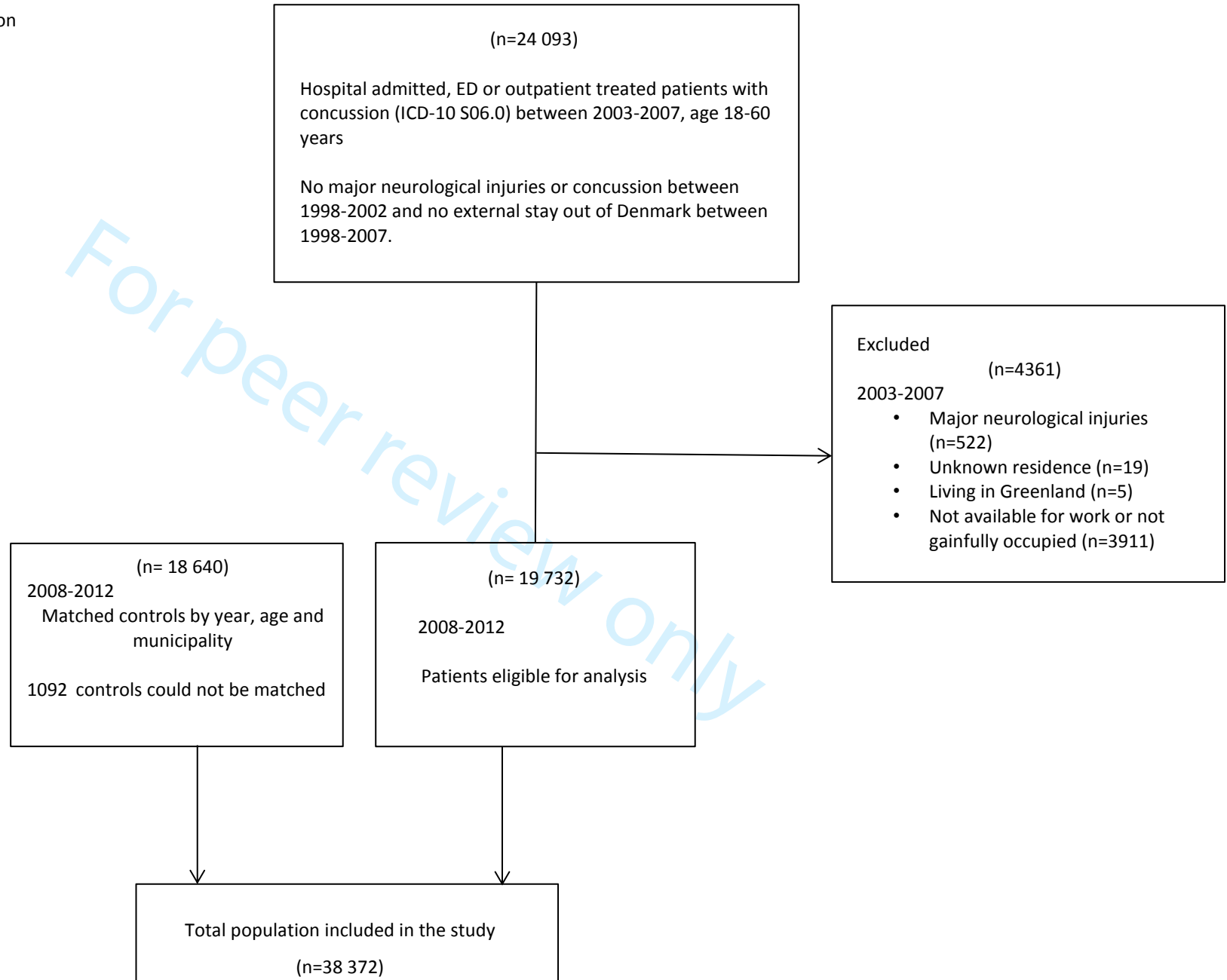
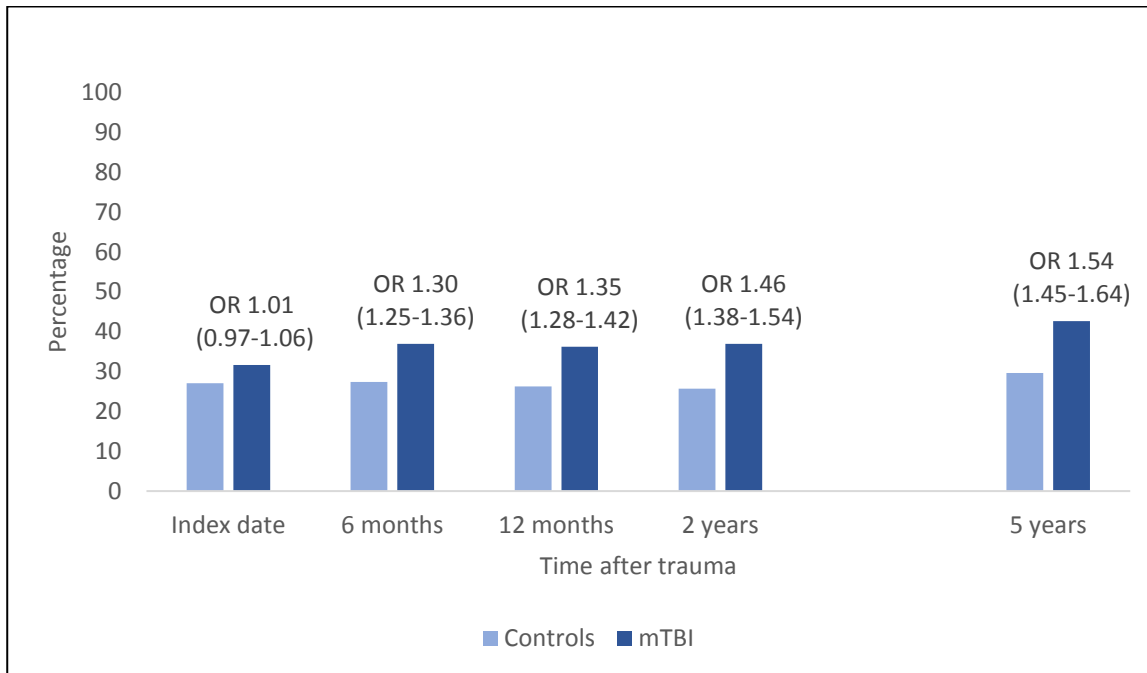


Figure 3. Prevalence and adjusted odds of not attending ordinary work at the index date and up to 5 years after concussion



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 (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3 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 (b) For matched studies, give matching criteria and number of exposed and unexposed	7-9
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 (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	12, 13
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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	13- 14
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	13- 15
Outcome data	15*	Report numbers of outcome events or summary measures over time	15- 17

1	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	15-17
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
4				
5				
6				
7				
8	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
9				
10	Discussion			
11				
12	Key results	18	Summarise key results with reference to study objectives	17-20
13				
14	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
15				
16	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
17				
18	Generalisability	21	Discuss the generalisability (external validity) of the study results	20
19				
20	Other information			
21	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
22				
23				

*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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-026104.R2
Article Type:	Research
Date Submitted by the Author:	12-Mar-2019
Complete List of Authors:	<p>Graff, Heidi; University Hospital Rigshospitalet, Department of Anaesthesia, 4231, Centre of Head and Orthopaedics</p> <p>Siersma, Volkert; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Denmark</p> <p>Møller, Anne; Copenhagen University Hospital Holbæk, Department of Occupational Medicine; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Denmark</p> <p>Kragstrup, Jakob; University of Copenhagen, Department of Public Health, The Research Unit for General Practice and Section of General Practice</p> <p>Andersen, Lars; National Research Centre for the Working Environment; Aalborg University, Sport Sciences, Department of Health Science and Technology</p> <p>Egerod, Ingrid; University of Copenhagen, Intensive Care Unit, Rigshospitalet</p> <p>Malá, Hana; University of Copenhagen, Department of Psychology; University Hospital Bispebjerg-Frederiksberg, Department of Neurology</p>
Primary Subject Heading:	Neurology
Secondary Subject Heading:	Epidemiology, Neurology, Occupational and environmental medicine, Public health
Keywords:	Labour market attachment, Mild traumatic brain injury, Sickness absence, Post-concussive symptoms, Unemployment

SCHOLARONE™
Manuscripts

1
2
3
4 **Labour market attachment after mild traumatic brain injury:**
5
6 **Nationwide cohort study with 5-year register follow-up in Denmark**
7
8
9

10 Heidi Jeannet Graff, MSc in Public Health^{1,2}

11 Volkert Siersma, Statistician³

12 Anne Møller, Assistant professor^{3,4}

13 Jakob Kragstrup, Professor³

14 Lars Louis Andersen, Professor^{5,6}

15 Ingrid Egerod, Professor⁷

16 Hana Malá Rytter, Associate Professor^{8,9}

17
18
19
20
21
22
23
24
25
26 **Affiliations:**

27
28
29 ¹Department of Anaesthesia, Centre of Head and Orthopaedics, Rigshospitalet, Copenhagen
30 University Hospital, Denmark

31
32
33
34
35 ²Trauma Center and Acute Admission, Centre of Head and Orthopaedics, Rigshospitalet,
36 Copenhagen University Hospital, Denmark

37
38
39
40
41 ³Department of Public Health, The Research Unit for General Practice and Section of General
42 Practice, University of Copenhagen, Denmark

43
44
45
46 ⁴Department of Occupational Medicine, Copenhagen University Hospital Holbæk, Denmark

47
48
49 ⁵National Research Centre for the Working Environment, Copenhagen, Denmark

50
51
52
53
54 ⁶Sport Sciences, Department of Health Science and Technology, Aalborg University, Aalborg,
55 Denmark

56
57
58
59
60 ⁷Intensive Care Unit, Rigshospitalet, Copenhagen University Hospital, Denmark

1
2
3
4⁸Department of Psychology, University of Copenhagen, Denmark
5
6

7⁹Department of Neurology, University Hospital Bispebjerg-Frederiksberg, Copenhagen, Denmark
8
9

10
11 **Corresponding author:**
12

13
14 Heidi Jeannet Graff, University Hospital Rigshospitalet, Department of Anaesthesia, Blegdamsvej
15
16 9, 2100 Copenhagen, Denmark.
17

18
19 Phone: +45 40688504
20

21 Email: heidi.jeannet.graff@regionh.dk
22
23

24
25 **Word count:** 4026
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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).

1
2
3
4 **Conclusions:**
5

6 43% of concussed patients were not attending ordinary work 5 years post-injury and received health
7 and social transfer benefits. We conclude that mTBI has a long-term impact on labour market
8 attachment. Prevention and treatment of persisting post-concussive symptoms should be considered.
9
10
11
12
13
14
15

16 ClinicalTrials.gov Identifier: NCT03214432
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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 difficulties¹⁰⁻¹² 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}

1
2
3
4 Most patients return to work within the first couple of months after mTBI, but a small
5
6 proportion of patients is unable to return to work due to disability.^{18, 19} Cancelliere et al. found that
7
8 most patients (>75%) had returned to work after six months and 5% were on social transfer
9
10 payments two years post-injury.²⁰
11
12

13 Return to work (RTW) has been conceptualized as being a dynamic process with different
14
15 related outcomes of labour market attachment or time off work, but also outcomes related to the
16
17 process of return to work such as psychological functioning and job satisfaction.^{21, 22} RTW after
18
19 mTBI has been suggested to depend on multiple factors such as injury related factors,²⁰ premorbid
20
21 demographics such as younger age,¹⁸ work place related factors such as support,²³ and influence on
22
23 work planning²⁴ and patient characteristics such as psychosocial status.²⁵ These studies have
24
25 methodological limitations in study design which complicate evaluation of evidence regarding the
26
27 magnitude of the problem. They have small sample sizes, are not representative,¹⁰ are based on self-
28
29 reported data and have short follow-up and considerable dropout leading to attrition bias.¹⁹ The
30
31 present analysis overcomes these challenges by using Danish nationwide administrative data to
32
33 examine a larger, representative sample and to perform long-term follow up. This study is
34
35 concerned with labour market attachment in hospital treated patients receiving the diagnosis
36
37 concussion (commotio cerebri) as the only brain injury diagnosis.
38
39
40
41
42

43 We examined a comprehensive range of post-injury transitions in the labour market aiming at
44
45 analysing attachment to the labour market up to five years after mTBI using a portfolio of
46
47 outcomes, including a variation of social transfer payments and data on permanent lack of
48
49 attachment to the labour market and death.
50
51
52
53
54
55
56
57
58
59
60

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 injuries²⁹ 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

1
2
3
4 symptoms.³¹ Finally, patients were not included if they had lived outside of Denmark at any time
5
6 during the inclusion period and the five-year period before.
7

8
9 For each mTBI case in the cohort, a control was randomly selected from the Population
10
11 register. Controls had similar inclusion criteria as the cases, but they had no diagnosis of concussion
12
13 during the inclusion period 1st of January 2003 – 31st of December 2007.
14

15
16 The control was matched to the case on sex, municipality and age (year of birth \pm 0.5 years,
17
18 expanded to 1 and 2 years in case of no initial match) (see Figure 1). The same exclusion criteria
19
20 were applied for the selection of controls.
21
22

23
24
25 Insert Figure 1
26

27
28 Availability for the labour market was assessed from the Danish Register for Evaluation of
29
30 Marginalization (DREAM), containing weekly information on all individuals receiving any social
31
32 public transfer payments.³² Patients and their matching controls were excluded from the cohort if
33
34 there were any major neurological injuries^{9, 29} as secondary diagnoses at the index date, they were
35
36 unavailable for the labour market, they had unknown residence or were inhabitants of Greenland.
37
38

39 40 41 **Outcome measures**

42
43
44 The outcomes of the present analyses were assessments of variations in attachment to the labour
45
46 market evaluated in the DREAM database (Figure 1) the week before the case's index date, and at 6
47
48 months, 12 months, 2 years and 5 years after the case's index date (Figure 1).
49

50 51 **Not attending ordinary work**

52
53 1. "Not attending ordinary work" was the primary outcome and was indicated by any entry in
54
55 DREAM, i.e. receiving any social transfer payment, such as unemployment benefits unrelated to the
56
57 subject's health condition, sickness absence benefits, social benefits granted, short and long-term
58
59
60

1
2
3
4 sickness or death. If there was no DREAM entry, it was assumed that the subject was gainfully
5
6 employed or self-supporting at that time (Figure 1).
7
8
9

10
11 The set of secondary outcomes are defined increasingly narrower than the primary outcome and
12
13 focus on attachment to the labour market due to health conditions. At the time of the current study,
14
15 employers in Denmark were obliged to finance sickness benefits for the first 30 days. Sickness
16
17 benefits lasting more than four consecutive weeks were to be compensated by the Danish
18
19 municipalities.³³ Sick-listed individuals could receive sickness benefits for a maximum of one
20
21 year³⁴. If individuals were not able to return to ordinary work due to long-term limited work
22
23 capacity, a partial return to work at lower capacity was possible with a “flex job”. If the sick-listed
24
25 individual was not able to return to work at all, the municipality could grant disability pension.^{35, 36}
26
27
28
29 The grading of the outcomes is illustrated in Figure 1.
30
31
32
33

34 Health-related benefits

35
36 2. Health-related benefits were indicated by DREAM entries given for short- or long-term
37
38 restrictions in attachment to the labour market due to health conditions (excluding unemployment
39
40 benefits unrelated to the subject’s health condition). These were sickness absence benefits,
41
42 vocational rehabilitation, flex job, unemployment benefits specifically granted to citizens on flex
43
44 job, social security benefits, light duties, disability pension and death.
45
46
47
48
49

50 Limited attachment to the labour market

51
52 3. Social transfer payments due to limited attachment to the labour market were indicated by
53
54 DREAM entries given for reduced work capacity and thereby long-term restrictions in attachment
55
56 to the labour market due to health conditions (excluding sickness absence benefits compared to
57
58
59
60

1
2
3
4 secondary outcome 2). These were vocational rehabilitation, flex job, unemployment benefits
5
6 specifically granted to citizens on flex job, social security benefits, light duties, disability pension
7
8 and death.
9

10
11
12
13 Permanent lack of attachment to the labour market

14
15
16 4. Permanent lack of attachment to the labour market was indicated by DREAM entries given for
17
18 permanent withdrawal from the labour market due to health conditions. These were disability
19
20 pension and death.
21
22

23
24
25 Death

26
27 5. Death was indicated by the DREAM entry for death.
28
29
30
31

32 **Potential confounders**

33
34 Sex, age and municipality at the index date were obtained from the Population register linked to the
35
36 DNPR. The municipality information was categorized into five regions reflecting Denmark's
37
38 reform of local government structure from 2007.³⁷ From the index date calendar year and season
39
40 were derived. Calendar year was included in the model as a previous study found increasing odds of
41
42 returning to work during the study period.³⁸ The reason could be a change in diagnostic practice and
43
44 the Danish sickness benefit Act becoming more effective over the years. Seasonal variation was
45
46 considered a confounder, as a previous study suggested that TBI is associated with season-specific
47
48 activities and most pronounced during fall and winter.³⁹ Pre-injury income was measured at the
49
50 index date and taken as personal gross income including revenue and social transfer income and
51
52 was obtained from the Income Statistics Register.⁴⁰ Income was divided into four income groups:
53
54 <100 000, 100 000-200 000, 200 000-300 000, >300 000 DKK roughly reflecting the quartiles in
55
56
57
58
59
60

1
2
3
4 the present cohort. Information on the highest attained educational level was obtained from the
5
6 Danish Education Register⁴¹ and was categorized into three educational groups: low education
7
8 (primary education), medium education (lower and upper secondary education, post-secondary–
9
10 non-tertiary education) and high education (short cycle tertiary education, bachelor, master, doctoral
11
12 or equivalent). Information on cohabitation status and ethnic origin was obtained from the Danish
13
14 Family Relations Database^{26, 42} and was categorized into married or cohabiting couple and single,
15
16 and as Danish born and not Danish born respectively. Pre-injury illness burden was measured by
17
18 Charlson comorbidity index (CCI), a weighted sum of 19 indicators for selected diagnoses.^{43, 44} For
19
20 the present CCI evaluation, a diagnosis was indicated for an individual when a corresponding ICD-
21
22 10 code was encountered in the DNPR in the five-year period 1st of January 1998 – 31st of
23
24 December 2002 before the inclusion period. Psychiatric diagnoses are not incorporated in CCI but
25
26 are possible confounders related to both labour market attachment and an increased risk of TBI.^{45, 46}
27
28 Hence, information on psychiatric diagnoses separately from CCI was obtained from the DNPR
29
30 (any ICD-10 Classification of Mental and Behavioural Disorders indicated as F diagnosis) over the
31
32 same five-year period.
33
34
35
36
37
38
39

40 **Statistical analysis**

41
42 Baseline covariates at the index date, and the outcomes at the index date and the follow-up time
43
44 points were reported as numbers and percentages separately for mTBI patients and their matched
45
46 controls. Raw comparisons of the baseline covariates between the mTBI patients and their controls
47
48 are done by Chi-squared tests.
49

50
51 The difference in tendency of some degree of decreased attachment to the labour market, between
52
53 patients with mTBI and their controls, at each of the index date and the four follow-up time points,
54
55 was assessed by odds ratios (OR) and corresponding 95% confidence intervals (95%CI) from a
56
57 multivariable logistic regression model; an OR>1 implied higher odds for the mTBI group. The
58
59
60

1
2
3
4 model was parameterized so that the assessments at the four follow-up time points were adjusted for
5
6 differences already present at the index date, i.e. pre-injury differences. Hence, the assessment at
7
8 the index date can be viewed as an assessment of the employment aspect of a social gradient in
9
10 mTBI incidence; the assessments at the follow-up time points report on the short- and long-term
11
12 differences in attachment attributable to mTBI. Results are reported both unadjusted and adjusted
13
14 for the potential confounders: age, gender, municipality, seasonal variation, calendar year,
15
16 education, income, cohabitation status, ethnicity, pre-injury comorbidities and pre-injury psychiatric
17
18 diagnosis. Inference was done by generalized estimating equations to adjust for repeated
19
20 measurement and matching.
21
22
23

24
25 Subjects with missing values in one of the covariates were omitted from analyses where these
26
27 covariates were included. P-values below 0.05 were considered statistically significant. SAS version
28
29 9.4 was used for statistical analysis.
30
31
32

33 34 **Patient and public involvement**

35
36 Patients and the public were not involved in the design and the conduct of the study.
37
38
39

40 41 **RESULTS**

42 43 **Baseline characteristics of the population**

44
45 19 732 patients with mTBI were eligible for the cohort and 18 640 matching controls were included
46
47 in the study. In some cases, notably with patients from small municipalities, it was not possible to
48
49 find a matching control, see Figure 2. Overall, the cohort was characterized by a weak tendency in
50
51 patients with mTBI to have lower education, lower income, being married or cohabiting, and having
52
53 a higher prevalence of pre-injury diseases (both somatic diseases as captured by CCI and
54
55 psychiatric diseases) compared to their matched controls (Table 1).
56
57
58
59
60

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-value¹
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, DKK²), 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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Analysis of attachment to labour market

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

For peer review only

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

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

²Generalized 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

1
2
3
4 1994 and 2002,⁹ and another Danish register-based study included approximately 90 000 patients
5
6 during a 13-year follow-up period.¹³
7

8
9 We found that attachment to the labour market varied between patients and controls at the
10
11 date of injury. The odds of not attending ordinary work was increased by 25% and remained higher
12
13 for patients during the 5 years of follow-up (of about 40%). A social gradient in not attending
14
15 ordinary work at the index date could be suspected, as patients had a significantly lower educational
16
17 level, income and more comorbidities compared to controls (see Table 1). Our findings agree with a
18
19 Danish register-based cohort study¹³ demonstrating that individuals with mTBI had a higher use of
20
21 general practice even 5 years before mTBI. However, when we controlled for socio-economic
22
23 factors, comorbidities and psychiatric diagnoses, there were no difference in the odds of not
24
25 attending ordinary work between the two groups in our sample at index date. Yet, the adjusted odds
26
27 of not attending ordinary work remained increased by 30-50% during the 5 years follow-up. This
28
29 strongly supports that mTBI is the incident leading to not returning to work.
30
31
32
33

34 For the secondary outcomes, the prevalence of sick listed decreased during follow-up, while
35
36 the prevalence of limited and permanent lack of attachment to the labour market increased as
37
38 expected. The proportion of individuals receiving health-related benefits at the index date was also
39
40 higher for patients compared to controls, and the risk was more than two times higher for patients
41
42 even after controlling for possible confounders. This may indicate increased morbidity in patients
43
44 with mTBI prior to the trauma as seen in another Danish study¹³, and variations in health seeking
45
46 behavior which result in health-related social transfer payments. However, at 6 months the odds
47
48 diminished to 30% and were further decreased during follow-up to 16-20%. Stulemeijer et al. found
49
50 a 76% full RTW rate at 6 months,⁴⁷ De Koning et al. found a complete RTW rate of 77% at 12
51
52 months⁴⁸ and Losoi et al. also found that 97% had fully RTW by 12 months after mTBI.¹⁰ These
53
54 findings are slightly higher than those reported in this study. However, previous investigations are
55
56
57
58
59
60

1
2
3
4 not directly comparable because there is a lack of consistency in definitions of labour market
5 attachment and RTW measures. RTW is increasingly regarded as an evolving process consisting of
6 different phases such as off work, work reentry, retention and advancement.⁴⁹ Additionally,
7 differences between countries in registration of social transfer payments, political legislation and
8 socioeconomic differences can complicate comparison.²⁰

9
10
11
12
13
14
15
16 Theadom et al. found that work productivity was reduced by 15.5% among patients with
17 mTBI, who had to make job changes to continue working.⁵⁰ Our study found a long-term
18 prevalence of 19% and increased odds of almost 40% of limited attachment to the labour market
19 indicating long-term employment restrictions due to health conditions. These results indicate that
20 most patients return to work after mTBI, but a small proportion of patients suffer long-term
21 consequences related to mTBI, preventing them from fully re-integrating into the labour market.
22 Since a previous study indicates an association between increasing length of sickness absence and
23 increasing risk of disability pension,⁵¹ these patients are at risk of transitioning from temporary to
24 permanent social benefits, meaning an exit from the labour market. For permanent lack of
25 attachment to the labour market, the prevalence in our study was higher for patients even though
26 there were significantly fewer events especially at 6 and 12 months and 2 years, indicating that it
27 takes time to qualify for disability pension in Denmark. The odds of permanent lack of attachment
28 to the labour market were still more than twice as high in the short as well as the long-term among
29 patients with mTBI, even when controlled for potential confounders.

30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48 Finally, the prevalence of death was higher in patients compared to controls. The odds of death
49 were more than 6 times higher for patients and subsequently declined during follow-up. This is a
50 surprising result assumed to be predicted by a set of different factors (socio-economic indicators,
51 comorbidities etc.) than those predicting labour market attachment. Selassie et al. found an in-
52 hospital all-cause mortality rate after mTBI of 1.4%⁵² and Pentland et al. found similar results at
53
54
55
56
57
58
59
60

1
2
3
4 0.45% in a cohort with 21 years of follow up,⁵³ agreeing with the result found in the present study.

5
6 Additionally, a Danish study found an increased risk of suicide among patients with mTBI⁵⁴.

7
8 Although not the aim of the present study, future research may benefit from exploring the risk
9
10 factors in excess mortality in patients with mTBI.
11
12
13
14

15 16 **Strengths and limitations**

17
18 This study applied a register-based design preventing information bias in the collection of data. The
19
20 DREAM register enabled us to estimate point prevalence during 5 years of follow-up and to
21
22 examine much more diverse labour market outcomes which is infrequent in TBI research.²⁰
23

24
25 Furthermore, the sensitivity and specificity of the DREAM register is considered high.⁵⁵ Finally, the
26
27 use of national register data has made it possible to include a large sample size and a matching
28
29 control group which increased the statistical power. We also adjusted for a wide range of pre-injury
30
31 potential confounders. However, residual confounding such as injury mechanism and psychological
32
33 effects affecting outcome cannot be ruled out. Patients were extracted from the DNPR.
34

35
36 Consequently, we did not have access to patient records, which hindered us to apply the operational
37
38 case definition for mTBI suggested by WHO.⁴ Even though the DNPR is considered the most
39
40 comprehensive register of its kind,²⁷ its validity and consistency with clinical diagnoses are widely
41
42 discussed, especially regarding clinical diagnoses and inaccurate coding leading to
43
44 misclassification. The ICD-9 code (850) for concussion has in several studies been reported as
45
46 frequently used for the classification of mTBI^{4, 56} but has also shown lack of sensitivity and
47
48 specificity.⁴ This could also be expected to be the case for ICD-10. Additionally, a large proportion
49
50 of patients with mTBI are not treated at the hospital, some are treated in primary care settings, and
51
52 some refrain from consulting a physician,⁵⁷ which can lead to low incidence rates and selection
53
54 bias, limiting the generalizability of the results.⁵⁸
55
56
57
58
59
60

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.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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).

Acknowledgements

Competing interest statement

None declared

Patient consent

Not required

Funding

This work was supported by the Research Foundation, Rigshospitalet (E-22260-03) (E-23473-01), the Danish Health Foundation (Helsefonden) (16-B-0050) and the Aase and Ejnar Danielsen Foundation (20-000054).

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.

1
2
3
4 **Data sharing statement**
5

6 No additional data are available
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

REFERENCES

1. Carroll LJ, Cassidy JD, Holm L, et al. Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004;(43 Suppl):113-25.
2. The American Congress of Rehabilitation Medicine (ACRM). Definition of mild traumatic brain injury. *J Head Trauma Rehabil* 1993;8:86-87.
https://acrm.org/wpcontent/uploads/pdf/TBIDef_English_10-10.pdf
(accessed 05 jan. 2019).
3. Katz DI, Cohen SI, Alexander MP, Handbook of Clinical Neurology, Vol. 127 (3rd series) Traumatic Brain Injury, Part I, J. Grafman and A.M. Salazar, Editors, 2015: 129-242.
4. McCrory P, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med* 2013;47:250–258.
5. Uden L, Calcagnile O, Uden J, et al. Validation of the Scandinavian guidelines for initial management of minimal, mild and moderate traumatic brain injury in adults. *BMC Med* 2015;13:292.
6. Levin HS, Diaz-Arrastia RR. Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *Lancet Neurol* 2015;14:506-17.
7. van der Naalt J, Timmerman ME, de Koning ME, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. *Lancet Neurol* 2017;16:532-40.
8. Cassidy JD, Carroll LJ, Peloso PM, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004;(43 Suppl):28-60.

- 1
2
3
4 9. Engberg AW, Teasdale TW. Epidemiology and treatment of head injuries in Denmark 1994-
5 2002, illustrated with hospital statistics. *Ugeskr Laeger* 2007;169:199-203.
6
7
- 8
9 10. Losoi H, Silverberg ND, Waljas M, et al. Recovery from Mild Traumatic Brain Injury in
10 Previously Healthy Adults. *J Neurotrauma* 2016;33:766-76.
11
12
- 13 11. Dumke HA. Posttraumatic Headache and Its Impact on Return to Work After Mild
14 Traumatic Brain Injury. *J Head Trauma Rehabil* 2017;32:E55-E65.
15
16
- 17 12. Ponsford J, Willmott C, Rothwell A, et al. Factors influencing outcome following mild
18 traumatic brain injury in adults. *J Int Neuropsychol Soc* 2000;6:568-79.
19
20
- 21 13. Galili SF, Bech BH, Vestergaard C, et al. Use of general practice before and after mild
22 traumatic brain injury: a nationwide population-based cohort study in Denmark. *BMJ Open*
23 2017;7:e017735.
24
25
- 26 14. Rutherford WH, Merrett JD, McDonald JR. Symptoms at one year following concussion
27 from minor head injuries. *Injury* 1979;10:225-30.
28
29
- 30 15. Rees PM. Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil*
31 2003;84:1885-94.
32
33
- 34 16. Edna TH, Cappelen J. Late post-concussional symptoms in traumatic head injury. An
35 analysis of frequency and risk factors. *Acta Neurochir (Wien)* 1987;86:12-7.
36
37
- 38 17. Ponsford J, Cameron P, Fitzgerald M, et al. Predictors of postconcussive symptoms 3
39 months after mild traumatic brain injury. *Neuropsychology* 2012;26:304-13.
40
41
- 42 18. Vicki L. Kristman PC, Sheilah Hogg-Johnson, David Cassidy, et al. The Burden of Work
43 Disability Associated with Mild Traumatic Brain Injury in Ontario Compensated Workers:
44 A Prospective Cohort Study. *The Open Occupational Health & Safety Journal* 2010;2:1-8.
45
46
- 47 19. Waljas M, Iverson GL, Lange RT, et al. Return to work following mild traumatic brain
48 injury. *J Head Trauma Rehabil* 2014;29:443-50.
49
50
51
52
53
54
55
56
57
58
59
60

- 1
- 2
- 3
- 4 20. Cancelliere C, Kristman VL, Cassidy JD, et al. Systematic review of return to work after
- 5 mild traumatic brain injury: results of the International Collaboration on Mild Traumatic
- 6 Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S201-9.
- 7
- 8
- 9
- 10
- 11 21. Pransky G, Gatchel R, Linton SJ, et al. Improving return to work research. *J Occup Rehabil*
- 12 2005;15:453-7.
- 13
- 14
- 15
- 16 22. Young AE, Wasiak R, Roessler RT, et al. Return-to-work outcomes following work
- 17 disability: stakeholder motivations, interests and concerns. *J Occup Rehabil* 2005;15:543-
- 18 56.
- 19
- 20
- 21
- 22
- 23 23. Sveen U, Soberg HL, Ostensjo S. Biographical disruption, adjustment and reconstruction of
- 24 everyday occupations and work participation after mild traumatic brain injury. A focus
- 25 group study. *Disabil Rehabil* 2016;38:2296-304.
- 26
- 27
- 28
- 29
- 30 24. Friedland JF, Dawson DR. Function after motor vehicle accidents: a prospective study of
- 31 mild head injury and posttraumatic stress. *J Nerv Ment Dis* 2001;189:426-34.
- 32
- 33
- 34 25. Mani K, Cater B, Hudlikar A. Cognition and return to work after mild/moderate traumatic
- 35 brain injury: A systematic review. *Work* 2017;58:51-62.
- 36
- 37
- 38
- 39 26. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011;39:22-5.
- 40
- 41 27. Lyngge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public*
- 42 *Health* 2011;39:30-3.
- 43
- 44
- 45 28. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse om
- 46 efterlønsbevis, udskydelsesreglen og skattefri præmie m.v. BEK nr 4 af 02/01/2017
- 47 Gældende. <https://www.retsinformation.dk/forms/R0710.aspx?id=186130>. (accessed 8 aug
- 48 2018)
- 49
- 50
- 51
- 52
- 53
- 54
- 55 29. Noonan VK, Thorogood NP, Fingas M, et al. The validity of administrative data to classify
- 56 patients with spinal column and cord injuries. *J Neurotrauma* 2013;30:173-80.
- 57
- 58
- 59
- 60

- 1
2
3
4 30. National Center for Injury Prevention and Control. Report to Congress on Mild Traumatic
5 Brain Injury in the United States: Steps to prevent a Serious Public Health Problem. 2003.
6
7 <https://www.cdc.gov/traumaticbraininjury/pdf/mtbireport-a.pdf>. (accessed 8 aug 2018)
8
9
- 10
11 31. Cassidy JD, Cancelliere C, Carroll LJ, et al. Systematic review of self-reported prognosis in
12 adults after mild traumatic brain injury: results of the International Collaboration on Mild
13 Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S132-51.
14
15
- 16 32. Styrelsen for Arbejdsmarked og Rekruttering [Danish Agency for Labour Market and
17 Recruitment] . DREAM version 41. 2018. [https://www.dst.dk/-/media/Kontorer/13-](https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da)
18 [Forskning-og-Metode/DREAM-koder-version-41.docx?la=da](https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da). (accessed 8 aug 2018)
19
20
21
22
23
24
- 25 33. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om
26 sygedagpenge. 2010/1 LSF 68. <http://www.retsinformation.dk/eli/ft/201012L00068>.
27
28 (accessed 03 jan. 2019).
29
30
- 31 34. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om
32 sygedagpenge. LBK nr 653 af 26/06/2012 Historisk.
33
34 <https://www.retsinformation.dk/Forms/R0710.aspx?id=142423#Afs6>. (accessed 03 jan.
35 2019).
36
37
38
39
- 40 35. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om en
41 aktiv beskæftigelsesindsats. LBK nr 685 af 29/06/2005 Historisk.
42
43 <https://www.retsinformation.dk/Forms/R0710.aspx?id=30223>. (accessed 03 jan. 2019).
44
45
46
47
- 48 36. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om social
49 pension. LBK nr 783 af 09/07/2012.
50
51 <https://www.retsinformation.dk/Forms/R0710.aspx?id=142132>. (accessed 03 jan. 2019).
52
53
54
55
56
57
58
59
60

- 1
2
3
4 37. Ministry for Economic Affairs and the Interior. Structural reform 2007.
5
6 <http://english.oim.dk/responsibilities-of-the-ministry/economics-of-municipalities-and->
7
8 [regions/structural-reform/](http://english.oim.dk/responsibilities-of-the-ministry/economics-of-municipalities-and-).
9
10
11 38. Hannerz H, Mortensen OS, Poulsen OM, et al. Time trend analysis of return to work after
12
13 stroke in Denmark 1996-2006. *Int J Occup Med Environ Health* 2012;25:200-4.
14
15 39. Rao DP, McFaul S, Thompson W, et al. Trends in self-reported traumatic brain injury
16
17 among Canadians, 2005-2014: a repeated cross-sectional analysis. *CMAJ Open*
18
19 2017;5:E301-E07.
20
21
22 40. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments.
23
24 *Scand J Public Health* 2011;39:103-5.
25
26 41. Jensen VM, Rasmussen AW. Danish Education Registers. *Scand J Public Health*
27
28 2011;39:91-4.
29
30
31 42. Statistics Denmark. Households, Families and Children. Secondary Households, Families
32
33 and Children 2017.
34
35 <http://www.dst.dk/en/Statistik/dokumentation/documentationofstatistics/households-->
36
37 [families-and-children.](http://www.dst.dk/en/Statistik/dokumentation/documentationofstatistics/households--)
38
39
40 43. Thygesen SK, Christiansen CF, Christensen S, et al. The predictive value of ICD-10
41
42 diagnostic coding used to assess Charlson comorbidity index conditions in the population-
43
44 based Danish National Registry of Patients. *BMC Med Res Methodol* 2011;11:83.
45
46
47 44. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic
48
49 comorbidity in longitudinal studies: development and validation. *J Chronic Dis*
50
51 1987;40:373-83.
52
53
54
55
56
57
58
59
60

- 1
2
3
4 45. Pedersen P, Lund T, Lindholdt L, et al. Labour market trajectories following sickness
5 absence due to self-reported all cause morbidity-a longitudinal study. *BMC Public Health*
6 2016;16:337.
7
8
- 9
10
11 46. Carroll LJ, Cassidy JD, Cancelliere C, et al. Systematic review of the prognosis after mild
12 traumatic brain injury in adults: cognitive, psychiatric, and mortality outcomes: results of the
13 International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med*
14 *Rehabil* 2014;95:S152-73.
15
16
- 17
18
19 47. Stulemeijer M, van der Werf S, Borm GF, et al. Early prediction of favourable recovery 6
20 months after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2008;79:936-42.
21
22
- 23
24
25 48. de Koning ME, Scheenen ME, van der Horn HJ, et al. Prediction of work resumption and
26 sustainability up to 1 year after mild traumatic brain injury. *Neurology* 2017;89:1908-14.
27
28
- 29
30
31 49. Steenstra IA, Lee H, de Vroome EM, et al. Comparing current definitions of return to work:
32 a measurement approach. *J Occup Rehabil* 2012;22:394-400.
33
34
- 35
36
37 50. Theadom A, Barker-Collo S, Jones K, et al. Work Limitations 4 Years After Mild Traumatic
38 Brain Injury: A Cohort Study. *Arch Phys Med Rehabil* 2017;98:1560-66.
39
40
- 41
42
43 51. Lund T, Kivimaki M, Labriola M, et al. Using administrative sickness absence data as a
44 marker of future disability pension: the prospective DREAM study of Danish private sector
45 employees. *Occup Environ Med* 2008;65:28-31.
46
47
- 48
49
50 52. Selassie AW, Fakhry SM, Ford DW. Population-based study of the risk of in-hospital death
51 after traumatic brain injury: the role of sepsis. *J Trauma* 2011;71:1226-34.
52
53
- 54
55
56 53. Pentland B, Hutton LS, Jones PA. Late mortality after head injury. *J Neurol Neurosurg*
57 *Psychiatry* 2005;76:395-400.
58
59
- 60
54. Madsen T, Erlangsen A, Orlovskaya S, et al. Association Between Traumatic Brain Injury and
Risk of Suicide. *JAMA*. 2018;320:580-588.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

55. Stapelfeldt CM, Jensen C, Andersen NT, et al. Validation of sick leave measures: self-reported sick leave and sickness benefit data from a Danish national register compared to multiple workplace-registered sick leave spells in a Danish municipality. *BMC Public Health* 2012;12:661.
56. Chen AY, Colantonio A. Defining neurotrauma in administrative data using the International Classification of Diseases Tenth Revision. *Emerg Themes Epidemiol* 2011;8:4.
57. Mannix R, O'Brien MJ, Meehan WP, 3rd. The epidemiology of outpatient visits for minor head injury: 2005 to 2009. *Neurosurgery* 2013;73:129-34
58. Kristman VL, Borg J, Godbolt AK, et al. Methodological issues and research recommendations for prognosis after mild traumatic brain injury: results of the International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S265-77.
59. van der Naalt J, van Zomeren AH, Sluiter WJ, et al. One year outcome in mild to moderate head injury: the predictive value of acute injury characteristics related to complaints and return to work. *J Neurol Neurosurg Psychiatry* 1999;66:207-13.

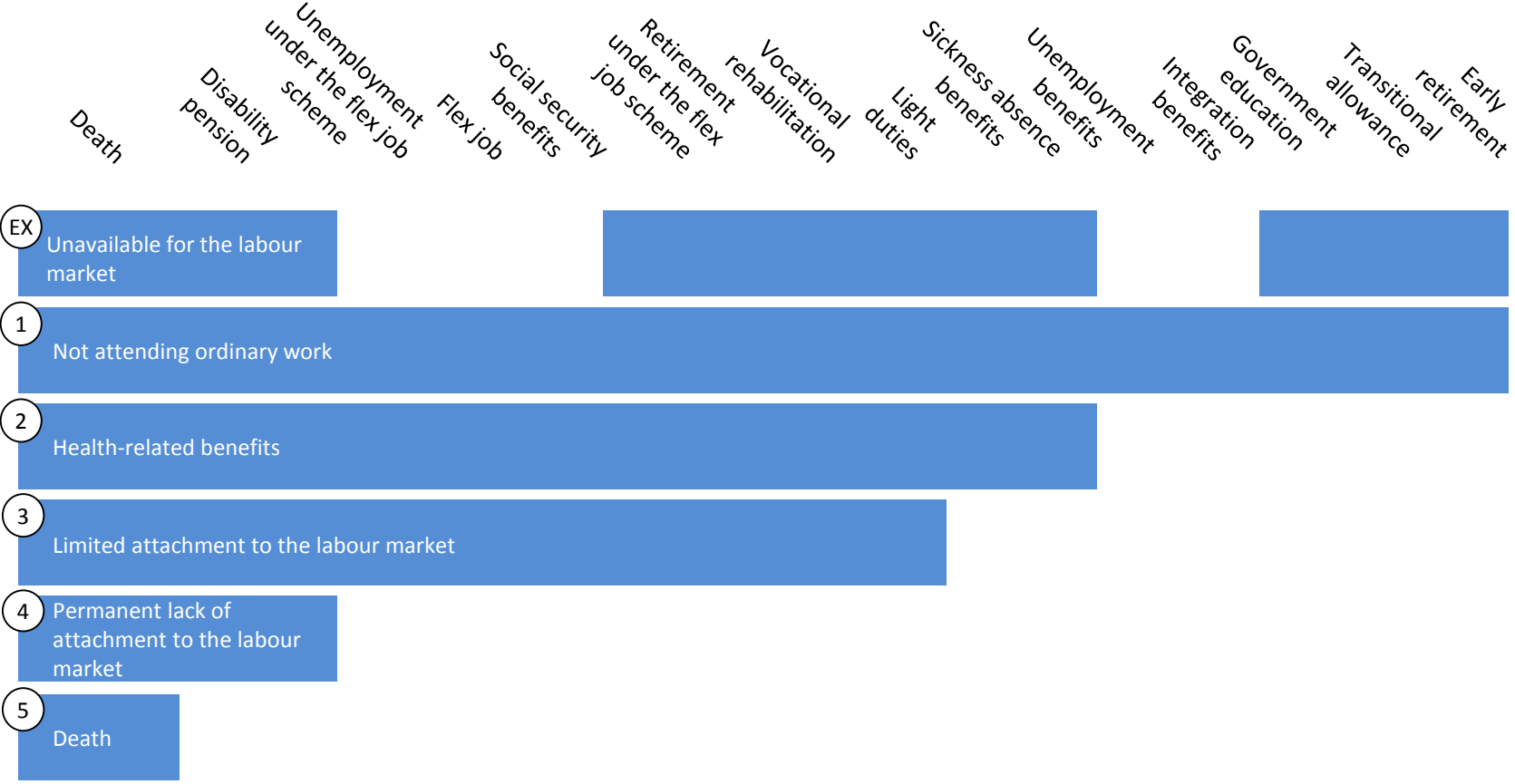
1
2
3
4 Figure 1. Description of social transfer payments as part of the Danish welfare system. Categories
5 describe unavailable for the labour market (an exclusion criterion) (EX), the primary outcome (1)
6
7 and the secondary outcomes (2-5) in terms of the different social transfer payments and other social
8
9 conditions (first row) that are included in each.
10
11
12

13
14 Figure 2. Inclusion of the study population
15
16

17 Figure 3. Prevalence and adjusted odds of not attending ordinary work at the index date and up to 5
18
19 years after concussion
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

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.



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

Figure 2. Inclusion of the study population

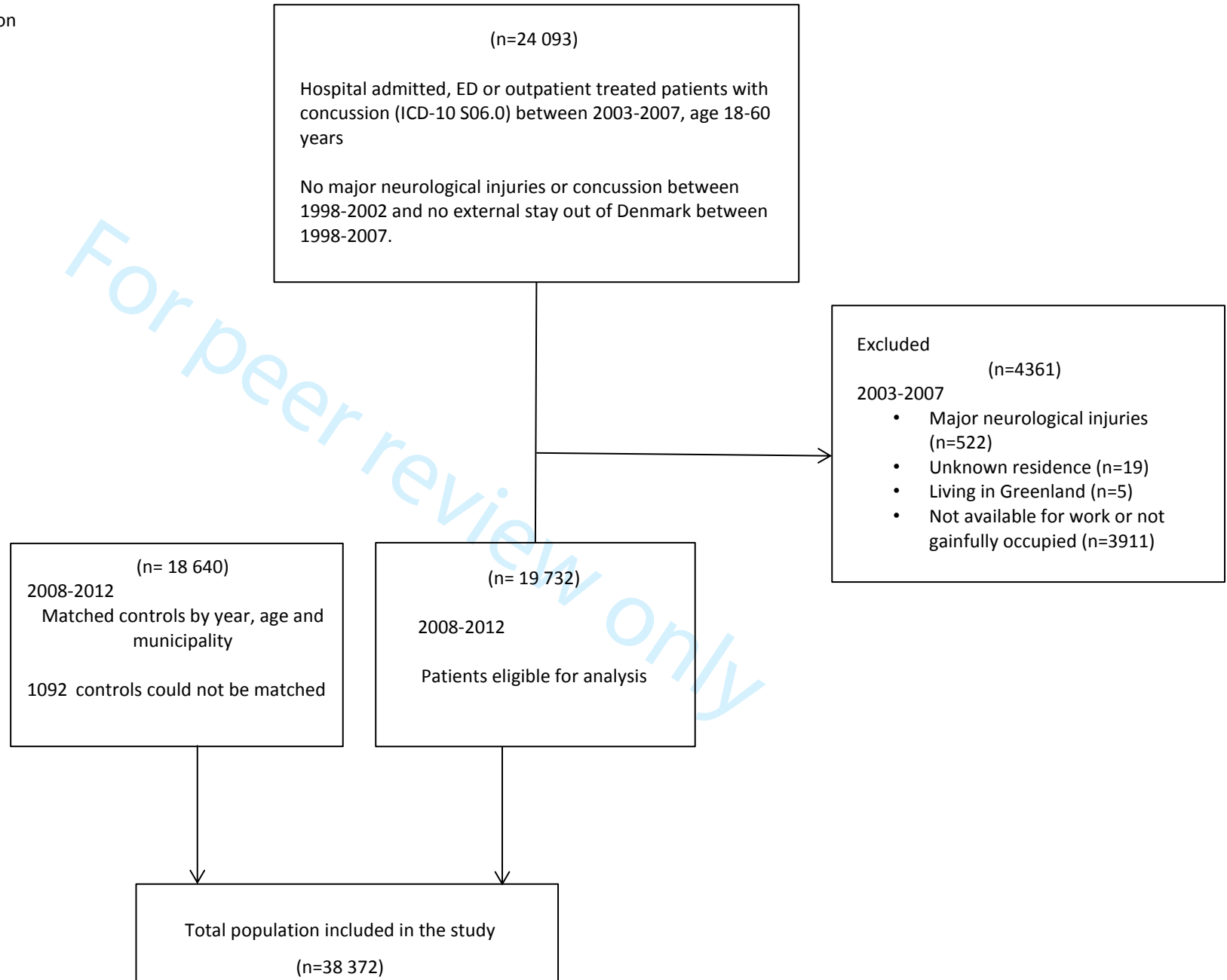
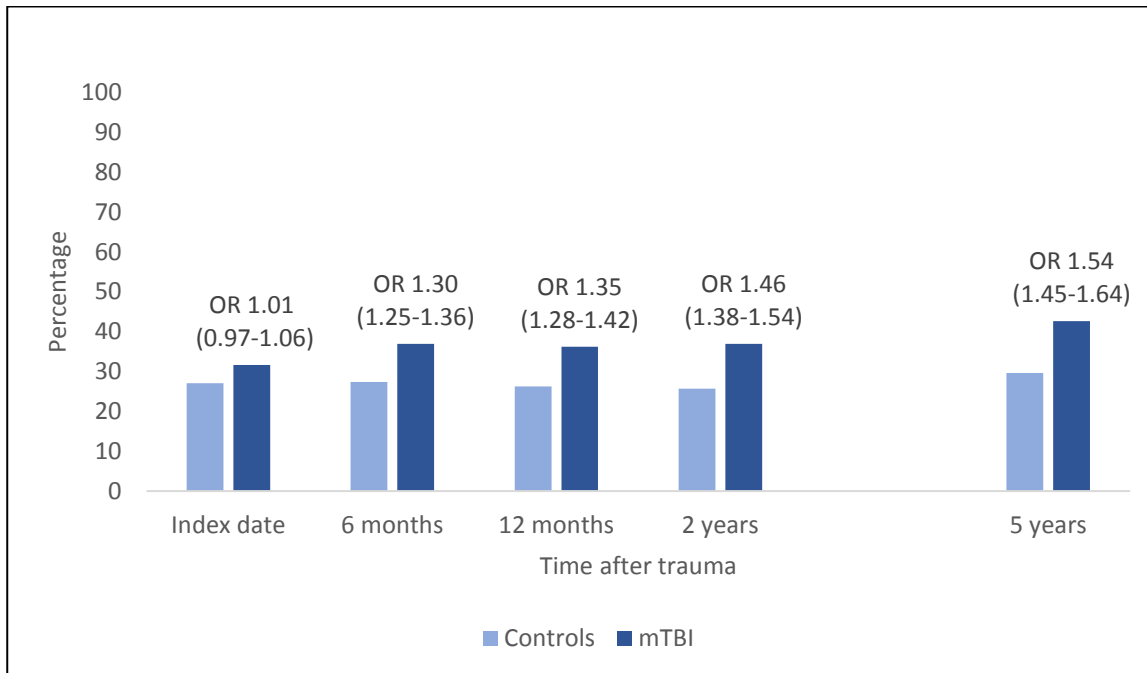


Figure 3. Prevalence and adjusted odds of not attending ordinary work at the index date and up to 5 years after concussion



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 (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3 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 (b) For matched studies, give matching criteria and number of exposed and unexposed	7-9
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 (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	12, 13
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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	13- 14
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	13- 15
Outcome data	15*	Report numbers of outcome events or summary measures over time	15- 17

1	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	15-17
2			(b) Report category boundaries when continuous variables were categorized	
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
4				
5				
6				
7				
8	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
9				
10	Discussion			
11				
12	Key results	18	Summarise key results with reference to study objectives	17-20
13				
14	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
15				
16	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
17				
18	Generalisability	21	Discuss the generalisability (external validity) of the study results	20
19				
20	Other information			
21	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
22				
23				

*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>.