



Premorbid risk factors influencing labour market attachment after mild traumatic brain injury

Graff, Heidi Jeannet; Siersma, Volkert Dirk; Møller, Anne; Kragstrup, Jakob; Andersen, Lars L.; Egerod, Ingrid Eugenie; Rytter, Hana Malá

Published in:
BMJ Open

Publication date:
2019

Document version
Publisher's PDF, also known as Version of record

Document license:
[CC BY-NC](#)

Citation for published version (APA):
Graff, H. J., Siersma, V. D., Møller, A., Kragstrup, J., Andersen, L. L., Egerod, I. E., & Rytter, H. M. (2019). Premorbid risk factors influencing labour market attachment after mild traumatic brain injury: a national register study with long-term follow-up. *BMJ Open*, 9, [e027297].

BMJ Open Premorbid risk factors influencing labour market attachment after mild traumatic brain injury: a national register study with long-term follow-up

Heidi Jeannet Graff,¹ Volkert Siersma,² Anne Møller,^{3,4} Jakob Kragstrup,⁵ Lars L Andersen,⁶ Ingrid Egerod,⁷ Hana Malá Rytter^{8,9}

To cite: Graff HJ, Siersma V, Møller A, *et al*. Premorbid risk factors influencing labour market attachment after mild traumatic brain injury: a national register study with long-term follow-up. *BMJ Open* 2019;**9**:e027297. doi:10.1136/bmjopen-2018-027297

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2018-027297>).

Received 15 October 2018
Revised 15 January 2019
Accepted 6 March 2019



► <http://dx.doi.org/10.1136/bmjopen-2018-026104>



© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Heidi Jeannet Graff;
heidi.graff@supermail.dk

ABSTRACT

Objectives Some patients with mild traumatic brain injury (mTBI) experience persistent postconcussive symptoms, influencing the ability to work. This study assessed associations between mTBI and labour market attachment (up to 5 years postinjury) in patients with different premorbid characteristics.

Design and setting Danish national cohort study with 5-year register follow-up.

Participants We included hospital admitted patients between 18 and 60 years diagnosed with mTBI (International Classification of Diseases, version 10 diagnosis S06.0) (n=19 732). For each patient, one control was selected matched on age, gender and municipality (n=18 640).

Primary outcome measure Primary outcome was 'not attending ordinary work', and premorbid risk factors were cohabitation status, education, ethnicity, gender, age and comorbidities.

Results The odds of not attending ordinary work increased from 6 months to 5 years. The highest increased odds (approximately twice as high for patients) of not attending ordinary work at 5 years were found in the highest educational group (OR 2.15, 95% CI 1.78 to 2.59), for patients of non-Danish origin (OR 1.98, 95% CI 1.52 to 2.57), for patients between 30 and 39 years (OR 1.93, 95% CI 1.68 to 1.23) and for patients with somatic comorbidities (OR 1.81, 95% CI 1.38 to 2.37). Contrary to expectations, we did not find higher odds in patients with psychiatric diagnoses (OR 1.12, 95% CI 0.76 to 1.60).

Conclusions Important premorbid characteristics for lower labour market participation after mTBI were higher education, non-Danish origin, age 30–39 years and having somatic comorbidities. Demographic and health-related variables should be considered when assessing patients with mTBI at risk of long-term sickness absence.

Trial registration number NCT03214432; Results.

INTRODUCTION

The incidence of hospital-treated mild traumatic brain injury (mTBI) is estimated to range from 100 to 300 cases per 100 000 people worldwide, most pronounced in the youngest, oldest and male part of the

Strength and limitations of this study

- The use of national registers prevented loss to follow-up.
- The study had access to a substantial amount of data, including covariates, labour market data and potential predictors.
- The study did not have access to patient records which increased the risk of misclassification.
- The registers did not allow access to clinical information such as injury severity.

population.^{1–3} mTBI negatively influences health, function, life satisfaction and ability to work.^{1–3} The majority of patients experience postconcussive symptoms⁴ defined as self-reported somatic, affective and cognitive symptoms,⁵ such as nausea, vomiting, headache, irritability, concentration difficulties, memory problems, fatigue, visual disturbance, sensitivity to noise, depression and anxiety.^{5,6} They are most common during the first days and weeks, typically resolving within 3 months.^{7–9} For a subgroup of ~15%–30%, the symptoms are persistent¹⁰ and may last for years.¹¹

The aetiology of persistent postconcussive symptoms is not completely understood, and existing research suggests a multifactorial interaction between demographics, injury-related and psychological risk factors affecting outcome.^{4,12} Injury-related factors such as loss of consciousness, amnesia,^{13,14} previous neurological injuries and pre-existing physical limitations^{3,8} have been emphasised as predictive of the development of immediate postconcussive symptoms, but other studies have not consistently found clinical associations.^{15,16} Additionally, persistent symptoms appear not to be specific to individuals with mTBI since non-brain injured controls also meet diagnostic criteria for postconcussive symptoms.¹⁷ Consequently, premorbid

demographics and psychological factors have been discussed intensively, since these factors have shown to be the most robust prognostic factors.¹² A multivariable prognostic model for mTBI demonstrated premorbid mental health, female sex, younger age and postinjury neuropsychological functioning as well as anxiety being the most strong independent prognostic factors for symptomatic outcomes.¹² Ponsford *et al*¹⁴ and Cnossen *et al*¹⁸ also found female gender, educational level, prior traumatic brain injury and premorbid psychiatric disorders including anxiety, depression, sleeping disorders and bipolar disorders to be the strongest predictors of post-concussive symptoms. Additionally, it has been suggested that patients suffering most are those being unmarried,⁸ living alone, having more than one comorbidity, multiple traumatic brain injuries (TBIs) and being of non-white ethnic group.¹⁹

Labour market attachment may change after mTBI and this constitutes a huge societal burden due to work disability and productivity loss.^{20 21} Most individuals acquiring mTBI return to work within 6 months post-injury,²¹ but a subgroup of individuals does not return to work^{14 22 23} and may receive social transfer payments 2 years postinjury.²¹ Studies have considered several important risk factors in the 'return to work process' after mTBI. A systematic review highlights premorbid factors, such as high education as associated with quicker return to work.²⁴ Additionally, younger age has been shown to predict a quicker return to work.²¹ Stulemeijer *et al* found that no premorbid physical problems, low levels of post-concussive symptoms and posttraumatic stress (PTS) early after injury, high education, absence of symptoms on admission, no extracranial injuries and low levels of pain were predictive of low levels of postconcussive symptoms and full return to work at 6 months.²⁵ Other studies showed inconsistent results, and premorbid factors such as age, sex, emotional problems, physical comorbidities and prior head injury were not being predictive of full return to work.²¹ Postinjury psychological distress has been found to predict incomplete return to work.²⁶ Moreover, psychological factors such as cognitive appraisal and coping strategies seem to influence the development of persistent postconcussive symptoms affecting labour market attachment.²⁷

Risk factors of labour market attachment after mTBI have not been as thoroughly investigated as risk factors of postconcussive symptoms. Current studies often have methodologically shortcomings being based on self-reported data and restricted to short follow-up periods. Large national register-based studies are lacking, primarily because such registers are only available in few countries. In Denmark, we have access to high-quality registers of labour market attachment and health. Most studies include a wide range of both premorbid and postmorbid potential risk factors and have not separately focused on premorbid risk factors.^{20 21 25 26} Assessment of premorbid risk factors is important during recovery to help clinicians identify patients at risk of long-term work disability and

to target the most appropriate treatment and prevention. Additionally, premorbid risk factors are present in the general population, which allows us to compare the effects on labour market attachment between patients with mTBI and the general population. We therefore aimed to assess associations between mTBI and labour market attachment (up to 5 years postinjury) in patients with different premorbid characteristics related to cohabitation status, education, ethnicity, gender, age and comorbidities.

METHODS

Study design and participants

This study was a longitudinal nationwide register-based cohort study with 5 years of follow-up on labour market attachment in patients diagnosed with mTBI from 1 January 2008 to 31 December 2012. The study used the same cohort and data as in a yet unpublished study of Graff HJ *et al*, entitled: Labour market attachment after mild traumatic brain injury: nationwide cohort study with 5 year register follow-up in Denmark (Graff, submitted for publication). Various national administrative registers were used to identify patients with mTBI, matching controls, potential confounders and outcome variables. The unique personal identification number, the central personal registry number (CPR number)²⁸ assigned to all individuals with a permanent residence in Denmark were used to link the registers.²⁹

Patients between 18 and 60 years were extracted from the Danish National Patient Register (DNPR) during 1 January 2003 – 31 December 2007.³⁰ Denmark has a universal healthcare system with equal access to healthcare services,³¹ hence, the DNPR contains somatic and psychiatric administrative data, diagnoses, treatments and examinations for all hospitals in Denmark, adhering to the International Classification of Diseases, version 10 (ICD-10).³⁰ Patients were hospital admitted, emergency or outpatient treated and diagnosed with concussion (ICD-10 diagnosis S06.0) as primary diagnosis. Patients were included at the first concussion diagnosis appearing in the DNPR during the inclusion period. Additionally, patients had to be available for the labour market at the index date, defined as gainfully employed or receiving unemployment benefits but actively job seeking.³²

Exclusion criteria were major neurological injuries, such as spinal cord and column injuries,³³ TBIs including concussions³⁴ 5 years before the index date (1 January 1998–31 December 2002). Additionally, we excluded patients who had major neurological injuries as secondary diagnosis to the concussion of interest during the inclusion period. Patients who had stayed outside of Denmark 5 years before and during the inclusion period (1998–2007) were excluded.

For each patient, one control was randomly extracted from the population register matched on age, gender and municipality. The controls without a concussion diagnosis were extracted during 1 January 2003–31 December

2007 and were excluded according to the same criteria as patients.

OUTCOME VARIABLES

Not attending ordinary work

Data on 'not attending ordinary work' measured a week before 6 months and 5 years were derived from the Danish Register for Evaluation of Marginalization (DREAM) for the calendar years 2008–2012. DREAM contains all social transfer payments granted by the municipality including sickness absence benefits, unemployment benefits, government education, integration benefits, transitional allowance, light duties, social security benefits, vocational rehabilitation, flex job, unemployment benefits (flex job), early retirement, disability pension or death. The municipally granted social transfer payment is registered with a code once a week in DREAM.^{29 32 35} During the period of the study, every employee in Denmark was entitled to sickness benefits for the first 30 days (employment period). Sick leave spells lasting >4 consecutive weeks were compensated by the Danish municipalities.³⁶ Sick-listed individuals could receive sickness benefits for a maximum of 12 months.³⁷ Patients with a permanently reduced working capacity could receive a 'flex job' with modified working conditions and individuals not being able to return to gainful occupation, could after an extensive assessment be granted disability pension.^{38 39} These benefits are registered in DREAM.

Not attending ordinary work was defined according to the Danish Reform of the Sickness Benefit Scheme, the Disability Pension and Flex-job Scheme,^{37–39} and dichotomised into receiving any social transfer payment in any given week during follow-up versus not receiving any social transfer payment in DREAM. If no code was given in DREAM, it was assumed that the patient was gainfully employed or self-supporting.

Risk factors

Premorbid variables included in the study were gender, age, cohabitation status, education, ethnicity, comorbidities and psychological factors. Data on gender and age were extracted from the Danish Civil Registration System (CRS),⁴⁰ which is a register providing individual information on vital status, migration and personal information such as citizenship. Cohabitation status was derived from the Danish Family Relations Database, which utilises data from the CRS.^{40 41} Cohabitation status was categorised into 'married or cohabiting couple' and 'single'. The highest attained educational level was derived from educational registers and measured the week before the index date.⁴² Education was consolidated into: low education (primary education), medium education (lower and upper secondary education, postsecondary–non-tertiary education) and high education (short cycle tertiary education, bachelor, master, doctoral or equivalent). Data on ethnic origin were extracted from the CRS and categorised into: Danish born or not Danish

born. Premorbid comorbidities and psychiatric diagnoses were extracted from the DNPR.³⁰ Comorbidities were included in the analysis as 19 indicators of chronic diseases defined as in Charlson comorbidity index.^{43 44} Psychiatric diagnoses were included as diagnoses 5 years before the index date (1998–2002).⁴⁵ Preinjury income was measured as personal gross income including revenue and social transfer income at the index date. These data were obtained from the income statistics register.⁴⁶ Income categories reflected the quartiles in the present cohort and were included to describe the study population. All data were provided by Statistics Denmark.²⁹

Statistical analysis

Baseline characteristics were described with total numbers and percentages and differences between groups were assessed with χ^2 tests.

The increased tendency for patients with mTBI of not attending ordinary work at 6 months and 5 years, respectively, was assessed as the ratio of the odds of not attending ordinary work for patients with mTBI and their matching controls for every subgroup. These ORs and their corresponding 95% CIs were estimated in multivariable logistic regression models where the correlation inherent to the matching was adjusted for with generalised estimating equations: the estimates for mTBI were adjusted for ethnicity, municipality, calendar year, seasonal variation, comorbidities, psychiatric illness, age and gender. The influence of each of the premorbid variables: cohabitation status, education, ethnicity, gender, age, comorbidities and psychiatric illness, was assessed individually by adding the corresponding interaction to the base model and was presented by a p value for the test of this interaction and separate ORs for each of the categories of the premorbid variable. A $p < 0.05$ was considered statistically significant. All statistical analyses were performed with SAS V.9.4.

Patient and public involvement

Since this study had a national register-based design containing deidentified individual data, it was not possible to involve patients in the study design, development of the research question, conduct of the study and dissemination of the results.

RESULTS

In total, 19 732 patients with mTBI and 18 640 controls were included. Table 1 indicates socioeconomic difference between patients with mTBI and controls regarding educational level and income. Additionally, more patients with mTBI were married and had more somatic and psychiatric comorbidities compared with controls (table 1). In some cases, it was not possible to find a matching control (see figure 1).

Table 1 Social and preinjury health characteristics of patients with mTBI and controls

	Controls (n=18 640)	mTBI (n=19 732)	Total (n=38 372)	Missing	P value*
Age, years, n (%)					0.8461
18–29	8187 (43.92)	8734 (44.26)	16 921 (44.10)	0	
30–39	4118 (22.09)	4290 (21.74)	8408 (21.91)		
40–49	3458 (18.55)	3653 (18.51)	7111 (18.53)		
50–60	2877 (15.43)	3055 (15.48)	5932 (15.46)		
Gender, n (%)					0.5839
Male	11 266 (60.44)	11 872 (60.17)	23 138 (60.30)	0	
Female	7374 (39.56)	7860 (39.83)	15 234 (39.70)		
Education, n (%)					<0.0001
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, Kr†), n (%)					<0.0001
<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 (%)					<0.0001
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 (%)					<0.0001
No comorbidities	17 863 (95.83)	18 580 (94.16)	36 443 (94.97)	0	
One comorbidity	577 (3.10)	842 (4.27)	1419 (3.70)	0	
Two comorbidities	154 (0.83)	210 (1.06)	364 (0.95)	0	
Three comorbidities	46 (0.25)	100 (0.51)	146 (0.38)	0	
Psychiatric diagnosis, n (%)					<0.0001
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)		

*P value from a Pearson's χ^2 test.

†Currency exchange rate of May 2018: 1€=7.44834 Kr.

CCI, Charlson comorbidity index; mTBI, mild traumatic brain injury.

Premorbid risk factors of not attending ordinary work

We examined the increased prevalence of not attending ordinary work at 6 months and 5 years for subgroups of patients and controls. The logistic regression model was used to examine the influence of mTBI on not attending ordinary work in of each of the subgroups (table 2).

While single patients with mTBI were more affected on employment status in the short-term (OR 1.38, 95% CI 1.30 to 1.46), patients with mTBI with a partner were marginally more long-term affected (OR 1.64, 95% CI 1.48 to 1.81). A clear inverse educational gradient was observed, where both in the short-run and long-run

(OR 1.51, 95% CI 1.31 to 1.74) (OR 2.15, 95% CI 1.78 to 2.59) higher educated patients with mTBI were most affected on their ability to work. Patients with mTBI with a non-Danish origin were long-term affected on employment status (OR 1.98, 95% CI 1.52 to 2.57), which also was the case with women (OR 1.62, 95% CI 1.48 to 1.77). We observed a short-term gradient related to age, most pronounced among the oldest-age group (50–60 years) (OR 1.54, 95% CI 1.37 to 1.73). However, patients with mTBI between 30 and 39 years were more long-term affected on employment status (OR 1.93, 95% CI 1.68 to 1.23). Patients with mTBI with comorbidities were both

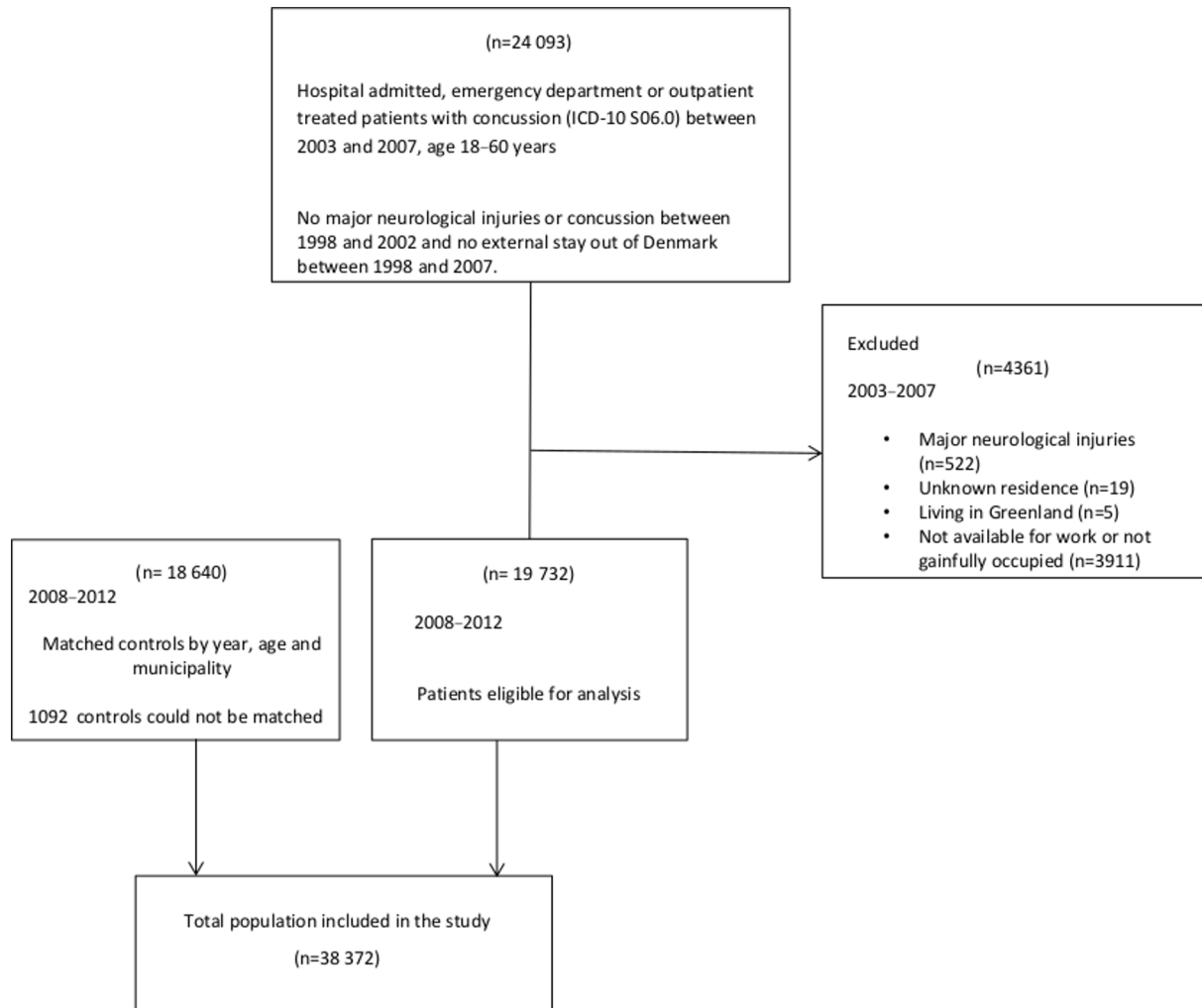


Figure 1 Inclusion of the study population. ICD-10, International Classification of Diseases, version 10.

short-term and long-term affected (OR 1.81, 95% CI 1.38 to 2.37). Conversely, patients with mTBI without psychiatric comorbidities were more affected on employment status at 5 years postinjury (OR 1.56, 95% CI 1.46 to 1.65) (table 2).

DISCUSSION

This national register-based cohort study examined the prevalence of not attending ordinary work and premorbid risk factors in a large cohort of patients with mTBI up to 5 years postinjury. Our results provide evidence that several premorbid risk factors influence labour market attachment.

Table 1 shows that people with low educational level have a higher incidence of mTBI. Against expectations, we found an inversed educational gradient after trauma. However, the highest educational group seems the most affected by mTBI in that their excess odds of not attending ordinary work were the highest compared with the other two educational groups. The OR is a relative measure with the advantage that it is independent of the prevalence of the outcome so that ORs of subgroups can be directly compared. However, it may be hard to get a

feel of the effect sizes. For instance, the percentage of not attending ordinary work is lower the higher the education. Hence, a given OR denotes a higher percentage point difference between mTBI and controls the lower the education, that is, the higher the baseline probability of not attending ordinary work.

Our results are not consistent with previous studies, showing higher education predicting quicker return to work.^{25 26} Education is a strong predictor of adult occupation and level of income which determines socioeconomic position.⁴⁷ These variables have consistently been related to health status and ability to work.^{48 49} Highly educated individuals are more likely to have flexible occupations and a high degree of autonomy in their work schedule and are more likely to have cooperative employers.⁴⁹ Friedland and Dawson found that patients with mTBI had significantly higher return to work rates if they had a job with a high degree of independence and decision-making, such as being a student, homemaker, professional or manager.⁵⁰ These professions have been found to have a higher return to work rate compared with lower skilled and manual workers.⁵¹ However, high-education occupations may also be characterised by a high

Table 2 The effects of mTBI on labour market attachment in subgroups of premorbid characteristics: demographics, comorbidities and psychological illness, up to 5 years postinjury

	Controls (n=18 640)*	mTBI (n=19 732)*	Crude OR (95% CI)	P value	Adjusted OR (95% CI)†	P value
Age (years)						
18–29						
6 months	3420 (41.80)	3647 (41.76)	1.16 (1.10 to 1.23)	<0.0001	1.19 (1.12 to 1.26)	<0.0001
5 years	3160 (38.62)	3870 (44.31)	1.47 (1.36 to 1.59)	<0.0001	1.56 (1.43 to 1.71)	<0.0001
30–39						
6 months	798 (19.33)	1471 (34.29)	1.23 (1.13 to 1.35)	<0.0001	1.31 (1.18 to 1.46)	<0.0001
5 years	666 (16.13)	1562 (36.41)	1.68 (1.50 to 1.89)	<0.0001	1.93 (1.68 to 2.23)	<0.0001
40–49						
6 months	462 (13.38)	1192 (32.63)	1.15 (1.03 to 1.28)	0.0123	1.26 (1.11 to 1.42)	0.0003
5 years	577 (16.71)	1406 (38.49)	1.14 (1.00 to 1.30)	0.0492	1.27 (1.10 to 1.48)	0.0014
50–60						
6 months	427 (14.85)	979 (32.05)	1.41 (1.28 to 1.56)	<0.0001	1.54 (1.37 to 1.73)	<0.0001
5 years	1117 (38.84)	1582 (51.78)	0.89 (0.78 to 1.02)	0.0902	0.93 (0.80 to 1.08)	0.3541
Gender						
Male						
6 months	2536 (22.51)	4034 (33.98)	1.24 (1.18 to 1.30)	<0.0001	1.30 (1.22 to 1.37)	<0.0001
5 years	2860 (25.39)	4735 (39.88)	1.36 (1.28 to 1.46)	<0.0001	1.48 (1.36 to 1.60)	<0.0001
Female						
6 months	2571 (34.87)	3255 (41.41)	1.25 (1.18 to 1.32)	<0.0001	1.31 (1.23 to 1.40)	<0.0001
5 years	2660 (36.07)	3685 (46.88)	1.48 (1.37 to 1.60)	<0.0001	1.62 (1.48 to 1.77)	<0.0001
Education						
Low education						
6 months	2524 (36.31)	3899 (43.56)	1.19 (1.12 to 1.26)	<0.0001	1.21 (1.13 to 1.29)	<0.0001
5 years	2968 (42.69)	4648 (51.93)	1.27 (1.18 to 1.37)	<0.0001	1.32 (1.20 to 1.43)	<0.0001
Medium education						
6 months	1978 (24.78)	2511 (33.64)	1.33 (1.25 to 1.40)	<0.0001	1.41 (1.32 to 1.51)	<0.0001
5 years	1947 (24.39)	2731 (36.59)	1.54 (1.42 to 1.68)	<0.0001	1.70 (1.54 to 1.88)	<0.0001
High education						
6 months	519 (14.97)	678 (22.73)	1.40 (1.24 to 1.57)	<0.0001	1.51 (1.31 to 1.74)	<0.0001
5 years	494 (14.25)	813 (27.25)	1.87 (1.60 to 2.19)	<0.0001	2.15 (1.78 to 2.59)	<0.0001
Cohabitation status						
Single						
6 months	2006 (35.24)	3607 (44.80)	1.32 (1.25 to 1.38)	<0.0001	1.38 (1.30 to 1.46)	<0.0001
5 years	1973 (34.66)	4037 (50.14)	1.44 (1.35 to 1.54)	<0.0001	1.54 (1.43 to 1.66)	<0.0001
Married or cohabiting couple						
6 months	3095 (24.01)	3672 (31.48)	1.17 (1.10 to 1.24)	<0.0001	1.21 (1.13 to 1.30)	<0.0001
5 years	3532 (27.39)	4376 (37.51)	1.49 (1.37 to 1.62)	<0.0001	1.64 (1.48 to 1.81)	<0.0001
Ethnicity						
Danish born						
6 months	4730 (26.79)	6767 (36.17)	1.24 (1.19 to 1.29)	<0.0001	1.30 (1.24 to 1.36)	<0.0001
5 years	5146 (29.14)	7825 (41.82)	1.40 (1.33 to 1.47)	<0.0001	1.52 (1.43 to 1.62)	<0.0001
Not Danish born						
6 months	371 (40.06)	512 (50.84)	1.30 (1.12 to 1.52)	0.0008	1.34 (1.11 to 1.61)	0.0024

Continued

Table 2 Continued

	Controls (n=18 640)*	mTBI (n=19 732)*	Crude OR (95% CI)	P value	Adjusted OR (95% CI)†	P value
5 years	359 (38.77)	588 (58.39)	1.86 (1.51 to 2.31)	<0.0001	1.98 (1.52 to 2.57)	<0.0001
Comorbidities						
No comorbidity						
6 months	4832 (27.05)	6750 (36.33)	1.24 (1.19 to 1.29)	<0.0001	1.29 (1.24 to 1.35)	<0.0001
5 years	5205 (29.14)	7758 (41.75)	1.40 (1.33 to 1.48)	<0.0001	1.52 (1.43 to 1.62)	<0.0001
>1 comorbidity						
6 months	275 (35.39)	315 (40.54)	1.31 (1.13 to 1.51)	0.0004	1.38 (1.15 to 1.66)	0.0006
5 years	539 (46.79)	662 (57.47)	1.61 (1.30 to 2.00)	<0.0001	1.81 (1.38 to 2.37)	<0.0001
Psychiatric diagnosis‡						
No diagnosis						
6 months	4981 (27.15)	6561 (35.39)	1.26 (1.21 to 1.30)	<0.0001	1.31 (1.26 to 1.37)	<0.0001
5 years	5368 (29.26)	7600 (40.99)	1.43 (1.36 to 1.51)	<0.0001	1.56 (1.46 to 1.65)	<0.0001
>1 diagnosis						
6 months	126 (42.71)	728 (61.07)	1.14 (0.90 to 1.43)	0.2780	1.16 (0.89 to 1.51)	0.2868
5 years	152 (51.53)	820 (68.79)	1.12 (0.83 to 1.51)	0.4496	1.12 (0.79 to 1.60)	0.5266

*Top row indicates total numbers of included patients and controls in the study. Column numbers and percentages indicate each subgroup experiencing the outcome.

†ORs adjusted for ethnicity, municipality, calendar year, seasonal variation, comorbidities, psychiatric illness, age and gender of not attending ordinary work for patients with mTBI in comparison to the control group.

‡Psychiatric diagnosis in secondary care 5 years prior to the index date (1 January 1998–31 December 2002).

mTBI, mild traumatic brain injury.

workload, increased demand for adaptability and have tasks demanding cognitive and emotional abilities, which can be challenging for patients with mTBI who are affected regarding cognitive functions.⁵² This emphasises the importance of considering young and highly educated individuals as a particularly vulnerable group at risk of long-term sickness absence after mTBI.

Our study also found that age influenced attachment to the labour market. At 5 years, we found a lower labour market attachment in working-age adults between 30 and 39 years, followed by adults between 18 and 29 years. A possible explanation is that adults between 20 and 40 years of age represent groups of fully or nearly fully trained individuals who are in the process of establishing professional careers as well as anchoring themselves privately, including getting married and having children. This period of life is therefore producing high demands from both the family and professional perspective, leading to adverse outcomes post-mTBI. Besides that, there may be competing inner psychological demands from the person with mTBI regarding one's own expectations.

Kristman *et al* found that individuals between 20 and 29 years were quicker off social transfer payments than older individuals.⁵³ However, several other studies have shown individuals >40 years to have poorer outcome.⁵⁴ Conversely, we found that individuals between 50 and 60 years were less affected on ability to work at 5 years post-injury. In the Danish welfare system, certain conditions

are required for voluntary withdrawal from the labour market (early retirement) before retirement age for individuals who had paid for such a scheme. The scheme requires availability for the labour market (excluding sickness absence) and fulfilling the minimum requirements for income, possibly creating an incentive to maintain an attachment to the labour market.⁵⁵

Regarding ethnic origin, we found that the odds were only slightly higher at 6 months. However, at 5-year follow-up, they were almost two times higher compared with those of Danish origin. Some studies have focused on outcomes in ethnic minorities after mTBI,^{56 57} but only a few on employment.⁵⁸ The studies conducted are primarily from USA, which can be difficult to use as a frame of reference to a Danish labour market setting. Studies on the general population show mixed results.⁵⁹ However, the evidence generally points to decreased health, more sick leave spells and higher risk of disability pension and early retirement among ethnic minorities.^{60 61} Our study adds further support to these findings.

Although patients had more comorbidities compared with the general population, we found that the prevalence of comorbidities was small, which can be explained by approximately two-thirds of the included patients being <50 years. The higher prevalence of comorbidities compared with the general population is also reported in a previous study Danish study.⁶²

The odds of not attending ordinary work for patients with somatic comorbidities were increased both at 6

months and 5 years compared with those without comorbidities. These results are in agreement with previous research showing that comorbidities predict health-related quality of life¹⁹ and higher use of general practice services years before the mTBI, indicating higher comorbidity burden.⁶² Also, comorbidities have been associated with the risk of long-term sickness absence in the general population.⁶³ Our results showed that the prevalence of not attending ordinary work due to chronic somatic diseases increased during follow-up, which is expected as comorbidities increase by age and affect work ability.⁶⁴

This study found that cohabitation status increased the odds of not attending ordinary work at 6 months for those being single. However, the odds were larger for those being married and cohabiting couple at 5 years. Additionally, we found only slightly elevated odds of not attending ordinary work in women at 5-year follow-up compared with men. A systematic review found female gender to be one of the strongest prognostic factors for various symptomatic outcomes.¹² Corrigan *et al* also demonstrated an interaction between gender, age and marital status, showing that women were more likely to be unemployed than men, decreased employment was most evident for married women and better employment outcomes were seen with increasing age.⁶⁵ Other studies report patients being unmarried are more likely to be unemployed postinjury.⁶⁶

Gender effects in outcomes after mTBI have been extensively discussed especially in terms of predictors of prolonged recovery.¹² However, given the small gender effects demonstrated in this study, the results are contrasting to what has previously been published. One possible explanation is that Denmark has a very low level of gender inequality in general, also in terms of labour market possibilities.

Finally, extensive research on persistent postconcussive symptoms after mTBI has previously demonstrated that preinjury depression, anxiety and neuroticism are significant predictors.⁶⁷ This study found that absence of psychiatric diagnoses predicted not attending ordinary work, and that the odds did not increase from 6 months to 5 years. For patients with psychiatric diseases, mTBI did not affect labour market attachment. This was unexpected, since psychiatric diseases often affect labour market attachment.⁶⁴ These results were also in contrast to increasing odds in patients with physiological comorbidities, which we also demonstrated in this study. However, it also needs to be remembered that this study evaluated the presence of psychiatric disease not as a predictor of worsened outcome, but as a factor that may increase the effect of mTBI on labour market attachment.

Strengths and weaknesses

This is, to our knowledge, the first large national register-based epidemiological study exclusively focusing on premorbid demographics, comorbidities and psychological factors predicting labour market attachment after mTBI. The use of register data rendered 5 years complete

follow-up possible. The inclusion of a large study population with matching controls increased the statistical power and ensured representativeness. The extraction of data from national registers prevented recall bias and selection bias due to non-response. The DNPR was used to extract the study population and potential confounders using ICD-10 codes. The DNPR has previously been used to examine hospital-treated populations; however, some studies point at variation in data validity for DNPR.⁶⁸ The DNPR did not allow access to clinical information, such as injury severity, and we could not use case definitions for mTBI.⁶⁹ A study showed that the most frequently used ICD-9 code 850 for concussion only classify limited number of mTBI cases and also detect severe and moderate cases.⁷⁰ This limitation could lead to misclassification and could also be the case for the ICD-10 diagnosis S06.0. However, this has not been examined. Most Danish emergency departments classify patients with concussion on similar criteria, and the population can therefore be considered homogeneous.^{62,71} DREAM on social transfer payments is considered a complete register valid for data analyses of public health research³⁵ which allowed us to do long-term follow-up on labour outcomes.

Conclusions and implications

The impact of mTBI on attending ordinary work 6 months and 5 years after trauma was different between various risk factors. Especially sensitive groups are those with high education, between 30 and 39 years, non-Danish origin, individuals with somatic comorbidities, single status (at 6 months) and married and cohabiting status (5 years). No evidence of difference in impact was found for women and the presence of psychiatric diagnoses.

The study demonstrates the importance of taking demographic and health-related variables into account when assessing patients with mTBI at risk for long-term sickness absence. Relatively little attention has been paid to the aspects of educational gradient and age gap on labour market attachment, and the mechanisms which lead to this inversed social gradient. This should be studied further in the future in relation to mTBI. We recommend that patients with mTBI are supported in reintegrating into the labour market, so long-term exclusion from the workforce is prevented. National guidelines are recommended to ensure a comprehensive and coordinated standardisation of public services which to date only exist for patients with more severe head injuries.

Author affiliations

¹Department of Anaesthesia, Centre of Head and Orthopaedics, University Hospital Rigshospitalet, Copenhagen, Denmark

²Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Copenhagen, Denmark

³Department of Occupational Medicine and Social Medicine, Copenhagen University Hospital Holbaek, Holbaek, Denmark

⁴Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Copenhagen, Denmark

⁵Department of Public Health, The Research Unit for General Practice and Section of General Practice, University of Copenhagen, Copenhagen, Denmark

⁶Musculoskeletal disorders and physical workload, National Research Centre for the Working Environment, Copenhagen, Denmark

⁷Department of intensive care, Centre for Cancer and Organ Diseases, University Hospital Rigshospitalet, Copenhagen, Denmark

⁸Department of Psychology, Faculty of Social Science, University of Copenhagen, Copenhagen, Denmark

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

Contributors All authors participated in the study design, interpretation of the data and revising it critically. HJG obtained the funding, drafted the protocol and manuscript. HJG and VS performed the statistical analyses. AM, LA, JK, IE and HMR participated in the study design and conceptualisation. All authors approved the final manuscript.

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's Foundation (20-000054).

Competing interests None declared.

Patient consent for publication Not required.

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 5 July 2017 (ClinicalTrials.gov Identifier: NCT03214432).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

- McMahon P, Hricik A, Yue JK, *et al*. Symptomatology and functional outcome in mild traumatic brain injury: results from the prospective TRACK-TBI study. *J Neurotrauma* 2014;31:26–33.
- 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;43:28–60.
- Thornhill S, Teasdale GM, Murray GD, *et al*. Disability in young people and adults one year after head injury: prospective cohort study. *BMJ* 2000;320:1631–5.
- 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.
- Ryan LM, Warden DL. Post concussion syndrome. *Int Rev Psychiatry* 2003;15:310–6.
- Iverson GL. Outcome from mild traumatic brain injury. *Curr Opin Psychiatry* 2005;18:301–17.
- Carroll L, Cassidy JD, Peloso P, *et al*. Prognosis for mild traumatic brain injury: results of the who collaborating centre task force on mild traumatic brain injury. *J Rehabil Med* 2004;36:84–105.
- 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.
- Rutherford WH, Merrett JD, McDonald JR. Symptoms at one year following concussion from minor head injuries. *Injury* 1979;10:225–30.
- Mittenberg W, Canary EM, Condit D, *et al*. Treatment of post-concussion syndrome following mild head injury. *J Clin Exp Neuropsychol* 2001;23:829–36.
- King NS, Kirwilliam S. Permanent post-concussion symptoms after mild head injury. *Brain Inj* 2011;25:462–70.
- Silverberg ND, Gardner AJ, Brubacher JR, *et al*. Systematic review of multivariable prognostic models for mild traumatic brain injury. *J Neurotrauma* 2015;32:517–26.
- Bazarian JJ, Wong T, Harris M, *et al*. Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. *Brain Inj* 1999;13:173–89.
- 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.
- Ponsford J, Cameron P, Fitzgerald M, *et al*. Predictors of postconcussive symptoms 3 months after mild traumatic brain injury. *Neuropsychology* 2012;26:304–13.
- Mearns S, Shores EA, Taylor AJ, *et al*. The prospective course of postconcussion syndrome: the role of mild traumatic brain injury. *Neuropsychology* 2011;25:454–65.
- Wäljas M, Iverson GL, Lange RT, *et al*. A prospective biopsychosocial study of the persistent post-concussion symptoms following mild traumatic brain injury. *J Neurotrauma* 2015;32:534–47.
- Crossen MC, Winkler EA, Yue JK, *et al*. Development of a Prediction Model for Post-Concussive Symptoms following Mild Traumatic Brain Injury: A TRACK-TBI Pilot Study. *J Neurotrauma* 2017;34:2396–409.
- Theadom A, Parag V, Dowell T, *et al*. Persistent problems 1 year after mild traumatic brain injury: a longitudinal population study in New Zealand. *Br J Gen Pract* 2016;66:e16–e23.
- Silverberg ND, Panenka WJ, Iverson GL. Work Productivity Loss After Mild Traumatic Brain Injury. *Arch Phys Med Rehabil* 2018;99:250–6.
- 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–S209.
- Nolin P, Heroux L. Relations among sociodemographic, neurologic, clinical, and neuropsychologic variables, and vocational status following mild traumatic brain injury: a follow-up study. *J Head Trauma Rehabil* 2006;21:514–26.
- Theadom A, Barker-Collo S, Jones K, *et al*. Work Limitations 4 Years After Mild Traumatic Brain Injury: A Cohort Study. *Arch Phys Med Rehabil* 2017;98:1560–6.
- Donker-Cools BHPM, Wind H, Frings-Dresen MHW. Prognostic factors of return to work after traumatic or non-traumatic acquired brain injury. *Disabil Rehabil* 2016;38:733–41.
- Stulemeijer M, van der Werf S, Borm GF, *et al*. Early prediction of favourable recovery 6 months after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2008;79:936–42.
- de Koning ME, Scheenen ME, van der Horn HJ, *et al*. Prediction of work resumption and sustainability up to 1 year after mild traumatic brain injury. *Neurology* 2017;89:1908–14.
- Scheenen ME, Visser-Keizer AC, van der Naalt J, *et al*. Description of an early cognitive behavioral intervention (UPFRONT-intervention) following mild traumatic brain injury to prevent persistent complaints and facilitate return to work. *Clin Rehabil* 2017;31:1019–29.
- Schmidt M, Pedersen L, Sørensen HT. The Danish civil registration system as a tool in epidemiology. *Eur J Epidemiol* 2014;29:541–9.
- Thygesen LC, Daasnes C, Thaulow I, *et al*. Introduction to Danish (nationwide) registers on health and social issues: structure, access, legislation, and archiving. *Scand J Public Health* 2011;39:12–16.
- Lynge E, Sandegaard JL, Rebolj M. The Danish national patient register. *Scand J Public Health* 2011;39:30–3.
- Magnussen J, Vrangbaek K, Saltman RB. *Health Care System, Recent reforms and current policy challenges*, 2009:1–21.
- Danish Agency for Labour Market and Recruitment. Styrelsen for Arbejdsmarked og Rekruttering. DREAM version 41. 2018. <https://www.dst.dk/-/media/Kontorer/13-Forskning-og-Metode/DREAM-koder-version-41.docx?la=da> (accessed 18 sep 2018).
- Noonan VK, Thorogood NP, Fingas M, *et al*. The validity of administrative data to classify patients with spinal column and cord injuries. *J Neurotrauma* 2013;30:173–80.
- Engberg AW, Teasdale TW. [Epidemiology and treatment of head injuries in Denmark 1994–2002, illustrated with hospital statistics]. *Ugeskr Laeger* 2007;169:199–203.
- Hjollund NH, Larsen FB, Andersen JH. Register-based follow-up of social benefits and other transfer payments: accuracy and degree of completeness in a Danish interdepartmental administrative database compared with a population-based survey. *Scand J Public Health* 2007;35:497–502.
- Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om sygedagpenge. 2010/1 LSF 68. <http://www.retsinformation.dk/eli/ft/201012L00068> (Accessed 3 Jan 2019).
- Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om sygedagpenge LBK nr 653 af 26/06/2012 Historisk. <https://www.retsinformation.dk/Forms/R0710.aspx?id=142423#fs6> (accessed 3 Jan 2019).
- Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse af lov om en aktiv beskæftigelsesindsats. LBK nr 685 af 29/06/2005 Historisk. <https://www.retsinformation.dk/Forms/R0710.aspx?id=30223> (Accessed 3 Jan 2019).

39. 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).
40. Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011;39:22–5.
41. Danmarks Statistik [Statistics Denmark]. Households, Families and Children. Secondary Households, Families and Children. 2017. <http://www.dst.dk/en/Statistik/dokumentation/documentationofstatistics/households-families-and-children> (Accessed 19 Sep 2018).
42. Jensen VM, Rasmussen AW. Danish education registers. *Scand J Public Health* 2011;39:91–4.
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.
45. Pedersen P, Lund T, Lindholdt L, et al. Labour market trajectories following sickness absence due to self-reported all cause morbidity—a longitudinal study. *BMC Public Health* 2016;16:337.
46. Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments. *Scand J Public Health* 2011;39:103–5.
47. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60:7–12.
48. Huijts T, Eikemo TA, Skalická V. Income-related health inequalities in the Nordic countries: examining the role of education, occupational class, and age. *Soc Sci Med* 2010;71:1964–72.
49. Diderichsen F, Andersen I, Manuel C, et al. Health inequality—determinants and policies. *Scand J Public Health* 2012;40:12–105.
50. Friedland JF, Dawson DR. Function after motor vehicle accidents: a prospective study of mild head injury and posttraumatic stress. *J Nerv Ment Dis* 2001;189:426–34.
51. Walker WC, Marwitz JH, Kreutzer JS, et al. Occupational categories and return to work after traumatic brain injury: a multicenter study. *Arch Phys Med Rehabil* 2006;87:1576–82.
52. Carroll LJ, Cassidy JD, Cancelliere C, et al. Systematic review of the prognosis after mild traumatic brain injury in adults: cognitive, psychiatric, and mortality outcomes: results of the international collaboration on mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014;95:S152–S173.
53. Kristman VL, Cote P, Hogg-Johnson S, et al. The Burden of work disability Associated with Mild Traumatic Brain Injury in Ontario Compensated Workers: A Prospective Cohort Study—!2009-11-16~!2010-02-21~!2010-03-16~!. *The Open Occupational Health & Safety Journal* 2010;2:1–8.
54. King N. Permanent post concussion symptoms after mild head injury: a systematic review of age and gender factors. *NeuroRehabilitation* 2014;34:741–8.
55. Beskæftigelsesministeriet [The Ministry of Employment]. Bekendtgørelse om fleksibel efterløn. BEK nr 1576 af 17/12/2013 Historisk. <https://www.retsinformation.dk/forms/R0710.aspx?id=160737> (accessed 03 Jan 2019).
56. Hoffman JM, Dikmen S, Temkin N, et al. Development of posttraumatic stress disorder after mild traumatic brain injury. *Arch Phys Med Rehabil* 2012;93:287–92.
57. Greenspan AI, Stringer AY, Phillips VL, et al. Symptoms of post-traumatic stress: intrusion and avoidance 6 and 12 months after TBI. *Brain Inj* 2006;20:733–42.
58. Sander AM, Pappadis MR, Davis LC, et al. Relationship of race/ethnicity and income to community integration following traumatic brain injury: investigation in a non-rehabilitation trauma sample. *NeuroRehabilitation* 2009;24:15–27.
59. Carneiro IG, Rasmussen CD, Jørgensen MB, et al. The association between health and sickness absence among Danish and non-Western immigrant cleaners in Denmark. *Int Arch Occup Environ Health* 2013;86:397–405.
60. Edén L, Ejlertsson G, Lamberger B, et al. Immigration and socio-economy as predictors of early retirement pensions. *Scand J Soc Med* 1994;22:187–93.
61. Nilsson M. Differences and similarities in work absence behavior, empirical evidence from micro data. Thesis for the degree of Doctor of Philosophy, Växjö University, Sweden 2005. 2005. <http://www.diva-portal.org/smash/get/diva2:206939/FULLTEXT01.pdf> (Accessed 19 Sep 2018).
62. 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.
63. Sundstrup E, Jakobsen MD, Mortensen OS, et al. Joint association of multimorbidity and work ability with risk of long-term sickness absence: a prospective cohort study with register follow-up. *Scand J Work Environ Health* 2017;43:146–54.
64. Ármannsdóttir B, Mårdbý AC, Haukenes I, et al. Cumulative incidence of sickness absence and disease burden among the newly sick-listed, a cross-sectional population-based study. *BMC Public Health* 2013;13:329.
65. Corrigan JD, Lineberry LA, Komaroff E, et al. Employment after traumatic brain injury: differences between men and women. *Arch Phys Med Rehabil* 2007;88:1400–9.
66. Kreutzer JS, Marwitz JH, Walker W, et al. Moderating factors in return to work and job stability after traumatic brain injury. *J Head Trauma Rehabil* 2003;18:128–38.
67. Broshek DK, De Marco AP, Freeman JR. A review of post-concussion syndrome and psychological factors associated with concussion. *Brain Inj* 2015;29:228–37.
68. Schmidt M, Schmidt SA, Sandegaard JL, et al. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol* 2015;7:449–90.
69. Carroll L, 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;36:113–25.
70. Tate RL, McDonald S, Lulham JM. Incidence of hospital-treated traumatic brain injury in an Australian community. *Aust N Z J Public Health* 1998;22:419–23.
71. Undén J, Ingebrigtsen T, Romner B. Scandinavian guidelines for initial management of minimal, mild and moderate head injuries in adults: an evidence and consensus-based update. *BMC Med* 2013;11:50.