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Original article

Absence from work in the 12 months following mild traumatic brain injury in Europe: a CENTER-TBI cohort study

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ABSTRACT

Background: Most of the prior research on absence from work after a mild traumatic brain injury (mTBI) was of a small sample size and had a limited number of follow-up assessments.
Objectives: Therefore, this study investigated the prevalence of absence from work, trajectories, and associated factors in the 12 months following mTBI in Europe.
Methods: Data from a European cohort (CENTER-TBI) were used. Absence from work was assessed at 2 weeks, 3 months, 6 months, and 12 months after mTBI. Associated factors included sociodemographic factors, current psychoactive substance use, pre-injury medical history, injury-related factors, medical care, complications, and discharge, and 2-week follow-up questionnaires. Inferential analyses relied on generalized estimating equations.
Results: This study included 1080 adults with mTBI who were working at the time of the injury (median [IQR] age, 46.0 [23.0] years; 69 % men). Absence from work decreased from 32 % at 2 weeks to 20 % at 12 months after the injury ($P < 0.001$). Around 76 % of adults returned to work within the first 3 months, whereas > 43 % of those absent from work at 3 months remained absent at 12 months. The 3 factors with the strongest association with absence from work were admission to hospital wards (OR = 2.57) or intensive care units (OR = 4.76), the presence of a pre-injury psychiatric disorder (OR = 2.55), and older age (OR = 1.61).
Conclusions: One-fifth of workers with mTBI were absent from work 12 months after the injury. Early identification of those at particular risk for not returning to work should be a clinical priority.
Study registration: NCT02210221 (https://clinicaltrials.gov/).

Introduction

Mild traumatic brain injury (mTBI) is defined as a TBI with a Glasgow Coma Scale (GCS) score of ≥ 13 half an hour after the injury and a post-traumatic amnesia duration of < 24 h [1]. Worldwide, there are about 69 million new cases of TBI each year, and 56 million of them are of mild severity [2]. Delayed diagnosis, persistent symptoms, and impaired mental health may have deleterious effects on the working ability of adults with mTBI.

In previous years, multiple studies have investigated absence from work in the working-age mTBI population [3–13]. For example, a study

Abbreviations: AIS, Abbreviated Injury Scale; CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CI, confidence interval; GAD-7, Generalized Anxiety Disorder-7; GCS, Glasgow Coma Scale; GOSE, Glasgow Outcome Scale–Extended; IQR, interquartile range; ISS, Injury Severity Score; LASSO, least absolute shrinkage and selection operator; MICE, multiple imputation by chained equation; mTBI, mild traumatic brain injury; OR, odds ratio; PCL-5, Post-traumatic Stress Disorder Checklist for DSM-5; PHQ-9, Patient Health Questionnaire-9; QOLIBRI, Quality of Life after Brain Injury; RPQ, Rivermead Post-concussion Symptoms Questionnaire; SD, standard deviation; SF-12, 12-item Short-Form Health Survey.

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[#] Details on the CENTER-TBI Participants and Investigators are provided under the Acknowledgments section.

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of 435 mTBI individuals presenting to emergency departments of trauma centers in the United States revealed that the prevalence of absence from work was 59 % at 2 weeks and 17 % at 12 months after the injury [10]. Although the previous body of scientific literature is of interest, it displays several limitations that should be acknowledged at this point. Most studies included fewer than 200 participants [3,4,7,9,11–13], which may have impacted the generalizability of the findings. Moreover, all, except 1 study, were conducted in a single country [3–7,9–13]. Given that employment and health policies vary by country, results in 1 country may not be extrapolated to another country. In addition, research has frequently included only 1 or 2 follow-up assessments [4,5,8,9,12,13], and hence, it was not possible to investigate detailed trajectories of absence from work following the injury. In this context, more data on work status and its correlates following an mTBI are urgently needed.

Therefore, this study aimed to investigate the prevalence of absence from work, its trajectories, and its associated factors in the 12 months following mTBI in Europe. With the premise that most adults would return to work within the first few months after the injury, we hypothesized that the prevalence of absence from work would gradually decrease in the year following the mTBI. An additional hypothesis was that certain demographic factors (eg, age), health behaviors (eg, alcohol misuse), medical conditions (eg, pre-injury psychiatric disorder), and injury-related factors (eg, baseline GCS) would be statistically associated with absence from work. Although the same dataset has already been used in the literature focusing on all TBIs [14,15] and mTBI [8], it is worth noting that the previous mTBI study focused on a single follow-up assessment (ie, 6 months post-injury), which limits the possibility of studying trajectories and conducting detailed longitudinal analyses.

Material and methods

Study design

This study relied on data from the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) dataset [16]. The CENTER-TBI dataset included 4509 individuals living in Europe and Israel (18 countries) with mild, moderate, or severe TBI [17]. Data were collected between 2014 and 2017. Adults included in the CENTER-TBI study had to be referred to one of the participating centers within 24 h of the TBI, with an indication to undergo a head computed tomography scan. After being referred to a participating center, there were 3 possible care pathways: direct discharge from the emergency room, admission to hospital wards, and admission to intensive care units. The minimum follow-up was 6 months and lasted for up to 24 months. Data collection relied on medical records and personal interviews. An electronic form was used by research personnel at each participating center to collect the data, which was de-identified before being stored on a secure database [17].

Regulatory and ethical considerations

Ethics approval for the CENTER-TBI study was obtained from each participating center [17]. Informed consent was mandatory in line with local and national requirements. Details on the ethical approval at each participating center are available online [18]. The study was registered at https://clinicaltrials.gov/ under the number NCT02210221.

Study participants

The analysis included only participants with a baseline-derived GCS score of ≥ 13, who were working at the time of the injury, and had available follow-up data on absence from work. The baseline-derived GCS score was preferred over the GCS score assessed at the accident scene, as this score was frequently missing (ie, 40 % of the data was missing). The baseline-derived GCS, which was centrally computed, corresponds to the post-stabilization GCS score; if this score was missing, the closest

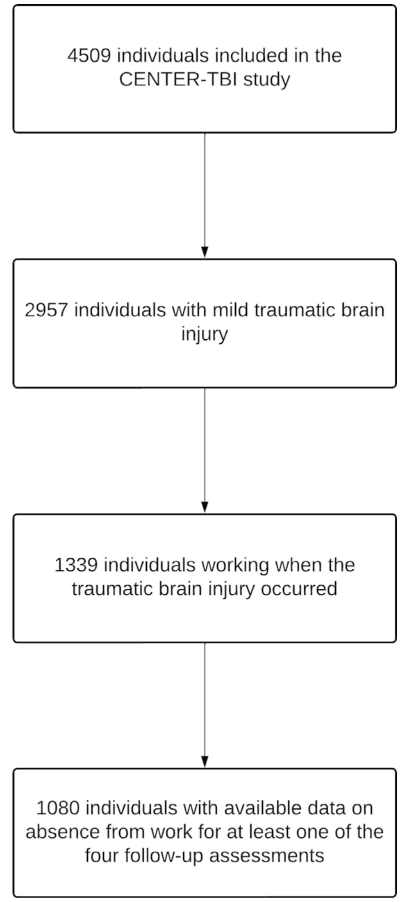

Fig. 1. Flowchart of study participants. Abbreviation: CENTER-TBI Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury.

pre-hospital, non-missing GCS score was used. Adults were considered actively working if they reported working ≥ 35 h per week, working 20−34 h per week, working < 20 h per week, or having special employment/sheltered employment. Considering this definition, full-time students were excluded from this research. The flow chart of the study participants is displayed in Fig. 1. The study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (Supplementary Table 1).

Absence from work (dependent variable)

Absence from work was assessed within the year following mTBI. There were 4 assessments at 2 weeks, 3 months, 6 months, and 12 months after the injury. Only absence from work was assessed at these follow-ups in the present research. Not all participants were seen at each of these assessments; however, every participant had at least 1 follow-up assessment regarding their absence from work. Adults were considered absent from work if they reported being unable to work, being retired, or actively seeking employment. The reason for retirement was not documented. In contrast, adults were considered to have returned to work if they returned to the previous job at the same level or hours, returned to the previous job at a reduced level or hours, returned to the previous job at an increased level or hours from pre-injury, changed job/had a different work, or had special employment/sheltered employment.

Factors associated with 12-month absence from work

Factors assessed at the time of injury, or 2 weeks after the injury, included sociodemographic factors, current psychoactive substance use, pre-injury medical history, injury-related factors, medical care, complications and discharge, and 2-week follow-up questionnaires.

Sociodemographic factors

Sociodemographic factors included age, sex, marital status, years of education, occupational category, and European region.

Current psychoactive substance use

Psychoactive substances included tobacco, alcohol misuse (> 2 units per day), and cannabis, the use of these substances being assessed in the 3 months preceding mTBI. For alcohol misuse, the definition relied on the cutoff frequently chosen in Europe [19].

Pre-injury medical history

Pre-injury medical history included the number of chronic physical conditions, a psychiatric disorder, and a previous TBI. Fourteen chronic physical conditions were assessed; the list of these conditions has been detailed elsewhere [20].

Injury-related factors

Injury-related factors were the geographical area of the accident, injury intention, baseline-derived GCS score, and Injury Severity Score (ISS). The ISS corresponds to the sum of the squares of the 3 body regions displaying the highest Abbreviated Injury Scale (AIS) score; ISS scores range from 0 to 75 [21].

Medical care, complications, and discharge

Medical care, complications, and discharge-related factors included stratum (ie, direct discharge from the emergency room, admission to hospital wards, or admission to intensive care units), intracranial surgery, extracranial surgery, intracranial complication, extracranial complication, and GCS at discharge.

Two-week follow-up questionnaires

Several questionnaires were undertaken at the 2-week assessment. Not all individuals participated in the 2-week follow-up. These questionnaires were the Generalized Anxiety Disorder-7 (GAD-7), the Glasgow Outcome Scale−Extended (GOSE), the Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5), the Patient Health Questionnaire-9 (PHQ-9), the Quality of Life after Brain Injury (QOLIBRI), the Rivermead Post-concussion Symptoms Questionnaire (RPQ), the 12-item Short-Form Health Survey (SF-12) mental component, and the SF-12 physical component. The GAD-7 ranges from 0 to 21, and higher scores indicate higher generalized anxiety disorder symptoms [22]. A cutoff of 10 is used to identify moderate-to-severe generalized anxiety disorder symptoms. The GOSE is a measure of disability and recovery after TBI, which ranges from 1 (death) to 8 (upper good recovery) [23]. The PCL-5 measures post-traumatic stress disorder symptoms; the score ranges from 0 to 80, and an increased score corresponds to more severe symptoms [24]. A cutoff around 31−33 is suggestive of post-traumatic stress disorder [25]. The PHQ-9 is a scale aimed at assessing depression (0−27 score; a higher score indicates more depressive symptoms) [26]. A cutoff of 10 is used to define major depression. Regarding the QOLIBRI, this questionnaire assesses the disease-specific quality of life, and the score ranges from 0 to 100, with decreasing scores indicating decreasing quality of life [27]. The RPQ measures post-concussion symptoms, and the score range is 0−64 (higher scores indicate more severe symptoms) [28]. Finally, the SF-12 evaluates generic health-related quality of life, with a mental and a physical component, ranging from 0 (poorest quality of life) to 100 (best quality of life) [29]. Although these variables were also assessed later in the follow-up, the present research focused on the 2-week assessment only to strengthen the potential causality between these variables and the 12-month absence from work, this causality being interpreted cautiously given the observational nature of the study.

Statistical analysis

Missing data

The proportion of missing data ranged from 0 % for age, sex, European region, baseline-derived GCS score, and stratum to 82 % for the SF-12 (mental and physical components; Table 1). There were 99 % of mTBI adults working at the time of the injury who had at least 1 missing value in the independent variables. The median (interquartile range [IQR]) number of missing data per individual in the independent variables was 8 (2). Missing data were imputed using multiple imputation by chained equation (MICE). As previous research has indicated, the number of imputations should equal the proportion of incomplete cases [30], 99 datasets were imputed.

Descriptive analysis

The characteristics of individuals with mTBI at the injury and 2 weeks after the injury were described before and after multiple imputation. Categorical variables were described using N (%), and continuous variables were described using median (IQR). For the GAD-7, PCL-5, and PHQ-9 questionnaires, the proportion of participants with scores equal to or higher than 10 for the GAD-7, 32 for the PCL-5, and 10 for the PHQ-9 was estimated. Furthermore, the prevalence of absence from work was analyzed at 2 weeks, 3 months, 6 months, and 12 months after the injury. The change in the prevalence of absence from work was studied using a generalized estimating equation, which relied on the binomial family with a logit link function, with absence from work as the dependent variable and time as the independent variable. Trajectories of absence from work within the year of mTBI were also descriptively analyzed. The same 4 follow-ups were used. For each follow-up except the 2-week follow-up, 4 trajectories were studied using proportions: proportion of participants not working among those not working at the previous follow-up, proportion of participants working among those not working at the previous follow-up, proportion of participants not working among those working at the previous follow-up, and proportion of participants working among those working at the previous follow-up. The different working categories were detailed at each evaluation. The descriptive analyses focusing on the absence from work and its trajectories during the 12 months following the mTBI were repeated in people without any intracranial surgery during the hospitalization (if any) and any intracranial complication at discharge. These sensitivity analyses were motivated by the fact that the definition of mTBI sometimes includes normal structural brain imaging [31].

Inferential analysis

The associations between time since the TBI, the characteristics of the mTBI population at the injury and 2 weeks after the injury (ie, the independent variables), and absence from work in the 12 months following the injury (ie, the dependent variable) were studied using generalized estimating equations relying on the binomial family with a logit link function. The first regression analysis was unadjusted, and each association was analyzed separately. Due to the presence of > 20 independent variables, it was not feasible to include all variables in the adjusted analysis. The selection of the variables relied on the least absolute shrinkage and selection operator (LASSO). The LASSO regression was performed on the 99 imputed datasets. An independent variable was included in the final model only if it had been selected in at least half of the imputed datasets. After this selection, sex, years of education, current tobacco use, current alcohol misuse, the GAD-7, the PHQ-9, and the RPQ were excluded from the analysis. All numerical variables were scaled to allow comparisons of their respective estimates. For the occupational category, due to the small size of the “None” category, it was merged with the “Other” category. For the region of Central and Eastern Europe, which included a small number of participants, a merger was made with Southern Europe. Given that the data assessed at 2 weeks had > 65 % missing data, and although these missing data were imputed, 2 adjusted analyses were conducted: 1 model excluded the 2-

Table 1
Characteristics of the mild traumatic brain injury population before and after multiple imputation ($N = 1080$).

Characteristics	Category	Before multiple imputation	Missing data (N [%])	After multiple imputation
Sociodemographic factors				
Age (in years)	Median (IQR)	46.0 (23.0)	0 (0)	46.0 (23.0)
Sex	Female	336 (31)	0 (0)	336 (31)
	Male	744 (69)		744 (69)
Marital status	Married or living together	625 (60)	34 (3)	644 (60)
	Never married, separated, divorced, or widowed	421 (40)		436 (40)
Years of education	Median (IQR)	14.0 (5.0)	110 (10)	14.2 (5.0)
Occupational category	Manager or professional	249 (23)	6 (1)	250 (23)
	Technician, supervisor, or associate professional	162 (15)		162 (15)
	Clerk or sales	116 (11)		117 (11)
	Skilled manual worker	171 (16)		172 (16)
	Manual worker	198 (18)		199 (18)
	Other	177 (16)		178 (16)
	None	1 (< 1)		1 (< 1)
European region	Central and Eastern Europe	19 (2)	0 (0)	19 (2)
	Northern Europe	315 (29)		315 (29)
	Southern Europe	247 (23)		247 (23)
	Western Europe	499 (46)		499 (46)
Current psychoactive substance use				
Tobacco	No	717 (71)	65 (6)	759 (70)
	Yes	298 (29)		321 (30)
Alcohol (misuse)	No	652 (64)	64 (6)	694 (64)
	Yes	364 (36)		386 (36)
Cannabis	No	967 (96)	68 (6)	1030 (95)
	Yes	45 (4)		50 (5)
Pre-injury medical history				
Number of chronic physical conditions	Median (IQR)	1.0 (1.0)	1 (< 1)	1.0 (1.0)
Psychiatric disorder	No	967 (90)	11 (1)	976 (90)
	Yes	102 (10)		104 (10)
Previous traumatic brain injury	No	928 (89)	39 (4)	961 (89)
	Yes	113 (11)		119 (11)
Injury-related factors				
Geographical area of injury	Rural	215 (21)	45 (4)	228 (21)
	Urban	820 (79)		852 (79)
Injury intention	Intentional	58 (5)	2 (< 1)	58 (5)
	Undetermined	21 (2)		21 (2)
	Unintentional	999 (93)		1001 (93)
Baseline-derived GCS score	Median (IQR)	15.0 (0.0)	0 (0)	15.0 (0.0)
Injury Severity Score	Median (IQR)	10.0 (13.0)	6 (< 1)	10.0 (13.0)
Medical care, complications, and discharge				
Stratum	Direct discharge from the emergency room	334 (31)	0 (0)	334 (31)
	Admission to hospital wards	475 (44)		475 (44)
	Admission to intensive care units	271 (25)		271 (25)
Intracranial surgery	No	687 (90)	320 (30)	798 (74)
	Yes	73 (10)		282 (26)
Extracranial surgery	No	620 (82)	320 (30)	796 (74)
	Yes	140 (18)		284 (26)
Intracranial complication	No	697 (95)	350 (32)	771 (71)
	Yes	33 (5)		309 (29)
Extracranial complication	No	669 (92)	350 (32)	780 (72)
	Yes	61 (8)		300 (28)
GCS at discharge	Median (IQR)	15.0 (0.0)	465 (33)	15.0 (0.0)
Two-week follow-up questionnaires				
GAD-7[a]	Median (IQR)	2.0 (6.0)	723 (67)	2.7 (6.7)
GOSE	Median (IQR)	7.0 (3.0)	809 (75)	6.0 (2.2)
PCL-5[b]	Median (IQR)	9.0 (16.0)	724 (67)	9.9 (17.4)
PHQ-9[c]	Median (IQR)	5.0 (9.0)	724 (67)	5.4 (8.3)
QOLIBRI	Median (IQR)	71.0 (29.0)	710 (66)	67.4 (31.5)
RPQ	Median (IQR)	6.0 (17.0)	716 (66)	7.2 (17.0)
SF-12 – mental component	Median (IQR)	47.4 (15.8)	888 (82)	46.4 (15.9)
SF-12 – physical component	Median (IQR)	44.9 (17.5)	888 (82)	40.5 (18.4)

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; GCS, Glasgow Coma Scale; GOSE, Glasgow Outcome Scale–Extended; IQR, interquartile range; ISS, Injury Severity Score; PCL-5, Post-traumatic Stress Disorder Checklist for DSM-5; PHQ-9, Patient Health Questionnaire-9; QOLIBRI, Quality of Life after Brain Injury; RPQ, Rivermead Post-concussion Symptoms Questionnaire; SF-12, 12-item Short-Form Health Survey.
Data are N (%) unless otherwise specified.
Given that the prevalence of participants with at least one missing data point was 99 %, 99 datasets were imputed using chained equations. Figures displayed in the table are pooled over the 99 imputed datasets.

[a] 14 % and 17 % of adults had a GAD-7 score higher than or equal to 10 before and after multiple imputation, which indicates moderate-to-severe generalized anxiety disorder symptoms.

[b] 11 % and 14 % of adults had a PCL-5 score higher than or equal to 32 before and after multiple imputation, suggesting the presence of post-traumatic stress disorder.

[c] 26 % and 28 % of adults had a PHQ-9 score higher than or equal to 10 before and after multiple imputation, which defines major depression.

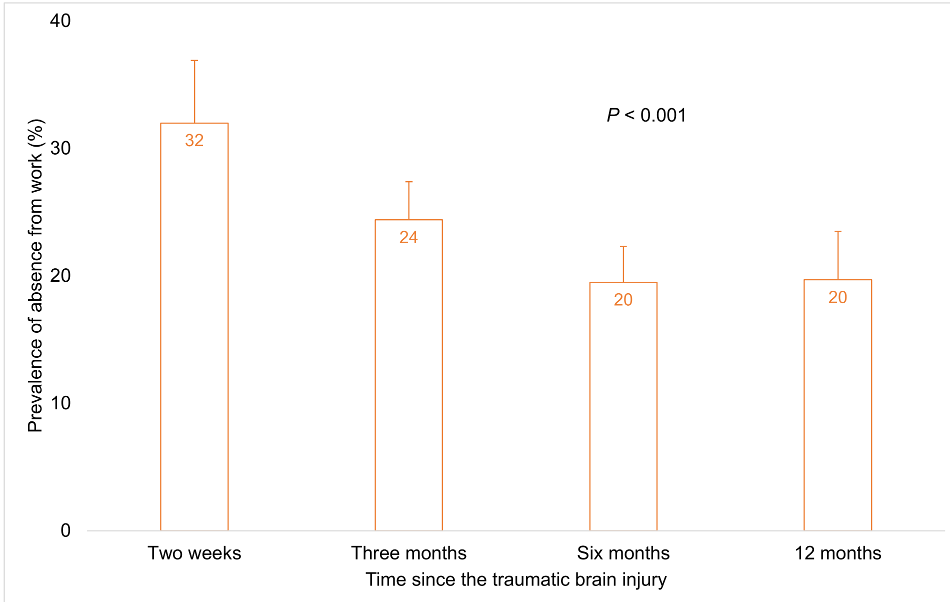

Fig. 2. Prevalence of absence from work in adults with mild traumatic brain injury in the year following the injury in Europe. The upper bar corresponds to the upper limit of the 95 % confidence interval. There were 64 %, 16 %, 18 %, and 53 % of missing data for absence from work at 2 weeks, 3 months, 6 months, and 12 months, respectively. The *P* value was obtained using a generalized estimating equation, which relied on the binomial family with a logit link function, with absence from work as the dependent variable and time as the numerical independent variable.

week follow-up questionnaires, and 1 model included them. This inferential analysis was repeated in the population of mTBI adults without any intracranial surgery during the hospitalization (if any) and any intracranial complication at discharge. The results of the generalized estimating equations were pooled over the 99 imputed datasets and displayed using odds ratios (ORs) and CIs. *P* values < 0.050 were considered statistically significant. The statistical analysis was conducted using R version 4.4.2 [32].

Results

Characteristics of the population

A total of 1080 individuals were included in the present study. The characteristics of the population are displayed in Table 1. The median (IQR) age was 46.0 (23.0) years; 69 % of the participants were male. The prevalence of pre-injury psychiatric disorders was 10 %. The median (IQR) baseline-derived GCS score was 15.0 (0.0), while the median (IQR) ISS was 10.0 (13.0). The most frequent stratum was the admission to hospital wards (ie, 44 %). At 2 weeks, 17 % of the population displayed moderate-to-severe generalized anxiety disorder symptoms (ie, a GAD-7 score higher or equal to 10), 14 % had possible post-traumatic stress disorder (ie, a PCL-5 score higher or equal to 32), and 28 % showed major depression (ie, a PHQ-9 score higher or equal to 10).

Trajectories of absence from work in the year following mild traumatic brain injury

Participants with data at 2 weeks numbered 388, at 3 months, 905, at 6 months, 882, and at 12 months, 512. The prevalence of absence from work in the year following mTBI is shown in Fig. 2. The proportion of individuals absent from work was 32 % at 2 weeks and decreased to 20 % at 12 months ($P < 0.001$). For mTBI adults without intracranial surgery during hospitalization (if any) and any intracranial complication at discharge, the prevalence of absence from work was 51 % at 2 weeks and 17 % at 12 months ($P < 0.001$; Supplementary Figure 1). Fig. 3 further displays trajectories of absence from work in the year following mTBI. Among people absent from work at 2 weeks, most (ie, 70 %) returned to work at 3 months, while 99 % of those already working at 2 weeks continued working at 3 months. Overall, 76 % of the population returned to work within the first 3 months. The trajectory of people absent from work changed between 3 and 6 months. At the 3-month follow-up, 62 % of those not working remained absent from work at the 6-month follow-up. Most people who worked at 3 months continued working at 6 months (ie, 96 %). The trajectories observed between 3 and 6 months persisted between 6 and 12 months. Overall, 43 % of those not working at 3 months were absent from work at 12 months. These trajectories were corroborated in the mTBI population without intracranial surgery and any intracranial complication (Supplementary Figure 2). The only exception is that, as already mentioned, most adults (ie, 51 %) were absent from work at 2 weeks.

Factors associated with 12-month absence from work in people with mild traumatic brain injury

Table 2 shows the association between time since the TBI, the characteristics of participants (ie, the independent variables), and absence from work in the 12 months following traumatic brain injury (ie, the dependent variable). The adjusted analysis, not including 2-week follow-up questionnaires, revealed that absence from work was statistically associated with time since the TBI (2 weeks: reference; 3 months: OR = 0.25, 95 % CI = 0.18–0.35; 6 months: OR = 0.16, 95 % CI = 0.11–0.23; and 12 months: OR = 0.11, 95 % CI = 0.07–0.16), age (in years; per one-standard deviation [SD] increase: OR = 1.61, 95 % CI = 1.41–1.83), skilled manual occupation (managerial or professional occupation: reference; OR = 1.48, 95 % CI = 1.06–2.07), manual occupation (OR = 1.53, 95 % CI = 1.11–2.12), the number of chronic physical conditions (per one-SD increase: OR = 1.14, 95 % CI = 1.02–1.27), a pre-injury psychiatric disorder (OR = 2.41, 95 % CI = 1.72–3.39), the baseline-derived GCS score (per one-SD increase: OR = 0.81, 95 % CI = 0.73–0.89), the ISS (per one-SD increase: OR = 1.52, 95 % CI = 1.31–1.77), and stratum (direct discharge from the emergency room: reference; admission to hospital wards: OR = 2.64, 95 % CI = 1.40–4.99; admission to intensive care units: OR = 4.57, 95 % CI = 2.32–9.02). The adjusted analysis, including 2-week follow-up questionnaires, corroborated most of these findings.

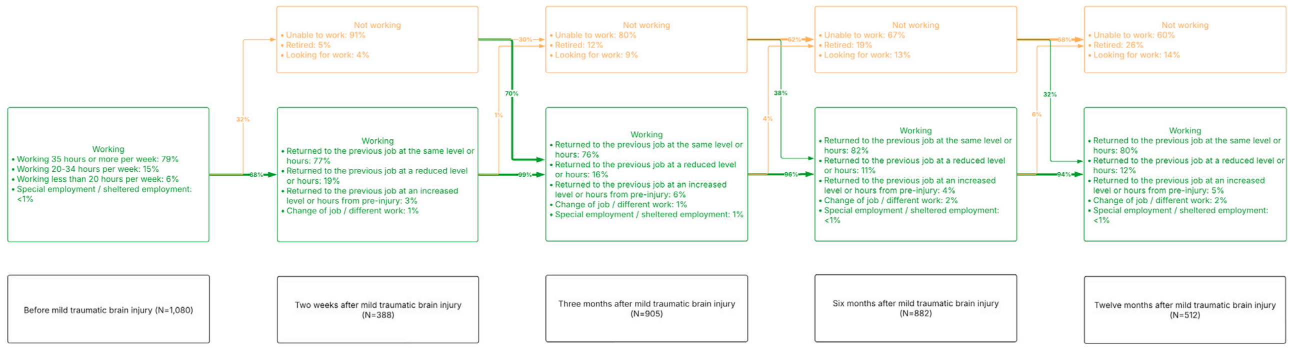

Fig. 3. Trajectories of absence from work in the year following mild traumatic brain injury in Europe.

Table 2
Association between time since the traumatic brain injury, the characteristics of adults, and absence from work in the 12 months following mild traumatic brain injury (generalized estimating equations).

		Unadjusted analysis			Adjusted analysis (without 2-week follow-up questionnaires)			Adjusted analysis (with 2-week follow-up questionnaires)		
Characteristics	Category	Odds ratio	95 % confidence interval	*P* value	Odds ratio	95 % confidence interval	*P* value	Odds ratio	95 % confidence interval	*P* value
Time since the traumatic brain injury	Two weeks	Reference			Reference			Reference		
	Three months	**0.69**	**0.53−0.89**	**0.005**	**0.25**	**0.18−0.35**	**< 0.001**	**0.24**	**0.17−0.34**	**< 0.001**
	Six months	**0.52**	**0.39−0.68**	**< 0.001**	**0.16**	**0.11−0.23**	**< 0.001**	**0.15**	**0.11−0.22**	**< 0.001**
	Twelve months	**0.52**	**0.39−0.71**	**< 0.001**	**0.11**	**0.07−0.16**	**< 0.001**	**0.10**	**0.07−0.16**	**< 0.001**
Sociodemographic factors										
Age (in years)	Per one-SD increase	**1.40**	**1.27−1.55**	**< 0.001**	**1.61**	**1.41−1.83**	**< 0.001**	**1.61**	**1.40−1.85**	**< 0.001**
Sex	Female	Reference			Not included			Not included		
	Male	1.04	0.85−1.26	0.726						
Marital status	Married or living together	Reference			Reference			Reference		
	Never married, separated, divorced, or widowed	1.04	0.86−1.26	0.695	1.21	0.95−1.53	0.122	1.16	0.91−1.49	0.236
Occupational category	Manager or professional	Reference			Reference			Reference		
	Technician, supervisor, or associate professional	0.91	0.66−1.24	0.544	0.92	0.65−1.30	0.641	0.93	0.65−1.33	0.698
	Clerk or salesperson	1.20	0.86−1.68	0.285	1.06	0.72−1.57	0.765	1.03	0.69−1.54	0.874
	Skilled manual worker	**1.49**	**1.12−1.99**	**0.007**	**1.48**	**1.06−2.07**	**0.023**	**1.59**	**1.12−2.25**	**0.010**
	Manual worker	**1.52**	**1.16−2.00**	**0.003**	**1.53**	**1.11−2.12**	**0.010**	**1.59**	**1.13−2.24**	**0.007**
	Other / None	0.89	0.66−1.20	0.436	0.83	0.59−1.16	0.267	0.84	0.59−1.19	0.323
Years of education	Per one-SD increase	**0.88**	**0.79−0.97**	**0.012**	Not included			Not included		
European region	Central and Eastern Europe / Southern Europe	1.12	0.90−1.40	0.323	1.09	0.84−1.43	0.515	1.11	0.82−1.50	0.485
	Northern Europe	0.89	0.72−1.11	0.295	0.91	0.71−1.18	0.481	0.95	0.72−1.24	0.693
	Western Europe	Reference			Reference			Reference		
Current psychoactive substance use										
Tobacco	No	Reference			Not included			Not included		
	Yes	1.14	0.93−1.41	0.212						
Alcohol (misuse)	No	Reference			Not included			Not included		
	Yes	1.09	0.89−1.33	0.398						
Cannabis	No	Reference			Reference			Reference		
	Yes	1.09	0.67−1.77	0.728	1.29	0.76−2.21	0.345	1.49	0.81−2.75	0.201
Pre-injury medical history										
Number of chronic physical conditions	Per one-SD increase	**1.27**	**1.17−1.39**	**< 0.001**	**1.14**	**1.02−1.27**	**0.017**	1.11	0.99−1.25	0.075
Psychiatric disorder	No	Reference			Reference			Reference		
	Yes	**2.29**	**1.75- 3.00**	**< 0.001**	**2.41**	**1.72−3.39**	**< 0.001**	**2.55**	**1.69−3.84**	**< 0.001**
Previous traumatic brain injury	No	Reference			Reference			Reference		
	Yes	0.87	0.65−1.17	0.363	0.97	0.68−1.38	0.859	0.86	0.60−1.25	0.430
Injury-related factors										
Geographical area of injury	Rural	Reference			Reference			Reference		
	Urban	0.97	0.77−1.22	0.800	1.26	0.96−1.65	0.102	1.31	0.97−1.77	0.082
Injury intention	Intentional	Reference			Reference			Reference		
	Undetermined	**2.36**	**1.14−4.86**	**0.020**	1.88	0.83−4.26	0.133	2.01	0.80−5.08	0.138
	Unintentional	1.37	0.87−2.16	0.176	1.13	0.68−1.88	0.638	1.12	0.65−1.96	0.679
Baseline-derived GCS score	Per one-SD increase	**0.70**	**0.64−0.75**	**< 0.001**	**0.81**	**0.73−0.89**	**< 0.001**	**0.81**	**0.72−0.91**	**< 0.001**
ISS	Per one-SD increase	**1.82**	**1.66−1.99**	**< 0.001**	**1.52**	**1.31−1.77**	**< 0.001**	**1.40**	**1.17−1.68**	**< 0.001**

(*continued*)

Table 2 (*Continued*)

Characteristics	Category	Unadjusted analysis			Adjusted analysis (without 2-week follow-up questionnaires)			Adjusted analysis (with 2-week follow-up questionnaires)		
		Odds ratio	95 % confidence interval	*P* value	Odds ratio	95 % confidence interval	*P* value	Odds ratio	95 % confidence interval	*P* value
Medical care, complications, and discharge										
Stratum	Admission to hospital wards	**1.43**	**1.12−1.82**	**0.004**	**2.64**	**1.40−4.99**	**0.003**	**2.57**	**1.35−4.89**	**0.004**
	Admission to intensive care units	**3.97**	**3.09−5.08**	**< 0.001**	**4.57**	**2.32−9.02**	**< 0.001**	**4.76**	**2.36−9.59**	**< 0.001**
	Direct discharge from the emergency room	Reference			Reference			Reference		
Intracranial surgery	No	Reference			Reference			Reference		
	Yes	0.79	0.56−1.12	0.184	0.88	0.53−1.46	0.628	0.96	0.58−1.58	0.874
Extracranial surgery	No	Reference			Reference			Reference		
	Yes	**1.58**	**1.07−2.34**	**0.022**	1.39	0.96−2.00	0.079	**1.45**	**1.01−2.08**	**0.047**
Intracranial complication	No	Reference			Reference			Reference		
	Yes	**0.63**	**0.49−0.82**	**< 0.001**	1.03	0.53−2.00	0.932	1.18	0.61−2.30	0.623
Extracranial complication	No	Reference			Reference			Reference		
	Yes	1.03	0.75−1.42	0.862	1.41	0.91−2.18	0.122	1.28	0.82−1.99	0.277
GCS at discharge	Per one-SD increase	0.97	0.82−1.15	0.708	1.02	0.89−1.17	0.796	1.01	0.88−1.17	0.850
Two-week follow-up questionnaires										
GAD-7	Per one-SD increase	**1.35**	**1.13−1.60**	**< 0.001**	Not included			Not included		
GOSE	Per one-SD increase	**0.66**	**0.53−0.82**	**< 0.001**				**0.74**	**0.57−0.97**	**0.031**
PCL-5	Per one-SD increase	**1.31**	**1.12−1.54**	**< 0.001**				0.96	0.78−1.19	0.724
PHQ-9	Per one-SD increase	**1.37**	**1.14−1.64**	**< 0.001**				Not included		
QOLIBRI	Per one-SD increase	**0.69**	**0.56−0.85**	**< 0.001**				0.93	0.71−1.22	0.601
RPQ	Per one-SD increase	**1.25**	**1.04−1.50**	**0.019**				Not included		
SF-12 − mental component	Per one-SD increase	0.83	0.64−1.08	0.169				0.96	0.76−1.22	0.760
SF-12 − physical component	Per one-SD increase	**0.69**	**0.54−0.88**	**0.003**				0.95	0.72−1.24	0.685

Abbreviations: GAD-7, Generalized Anxiety Disorder-7; GOSE, Glasgow Outcome Scale−Extended; ISS, Injury Severity Score; LASSO, least absolute shrinkage and selection operator; mTBI, mild traumatic brain injury; PCL-5, Post-traumatic Stress Disorder Checklist for DSM-5; PHQ-9, Patient Health Questionnaire-9; QOLIBRI, Quality of Life after Brain Injury; RPQ, Rivermead Post-concussion Symptoms Questionnaire; SD, standard deviation; SF-12, 12-item Short-Form Health Survey.
Statistically significant results are displayed in bold.
Unadjusted and adjusted generalized estimating equations, relying on the binomial family with a logit link function, were conducted on each imputed dataset, and the results were pooled across the 99 datasets. The dependent variable was absence from work within the 12 months following mTBI. Absence from work was assessed at 2 weeks, 3 months, 6 months, and 12 months. Regarding the independent variables, there was a small number of participants in the occupational category "None," and this category was, therefore, merged with the category "Other". Moreover, the region was recoded as a three-category variable, given the small sample size for the category "Central and Eastern Europe" (ie, the category "Central and Eastern Europe" was merged with the category "Southern Europe"). Additionally, given the relatively small population size (ie, 1080 adults) and the presence of more than 25 independent variables, it was decided to select a subset of independent variables for inclusion in the adjusted generalized estimating equations. After applying LASSO regression, the following variables were excluded from the analysis: sex, years of education, current tobacco use, current alcohol misuse, the two-week GAD-7, the two-week PHQ-9, and the two-week RPQ. Moreover, given that two-week follow-up questionnaires had > 65 % missing data, a first adjusted model was conducted without these variables. The second adjusted model included the following variables: GOSE, PCL-5, QOLIBRI, SF-12 (mental component), and SF-12 (physical component). Finally, all numerical variables were standardized.

However, the association was no longer statistically significant for the number of chronic physical conditions (per one-SD increase: OR = 1.11, 95 % CI = 0.99−1.25), while extracranial surgery (OR = 1.45, 95 % CI = 1.01−2.08) and the GOSE (per one-SD increase: OR = 0.74, 95 % CI = 0.57−0.97) were statistically associated with the absence from work. Results were similar in participants with mTBI who had not undergone intracranial surgery during their hospitalization (if any) and did not display any intracranial complications at discharge (Supplementary Table 2). Minor changes were observed, such as a lack of statistically significant association for the stratum and the GOSE, and a statistically significant relationship for the number of chronic physical conditions in the sensitivity analyses, including the 2-week questionnaires.

Discussion

Main findings

This European study of 1080 adults with mTBI revealed that the absence from work significantly decreased from 32 % at 2 weeks to 20 % at 12 months after the injury. Two trajectories were identified within the 12 months following the mTBI. During the first 3 months, most participants returned to work, even those who were not working 2 weeks after the injury. In contrast, most people absent from work at 3 months continued to be absent from work at 6 months, and the same pattern was observed between 6 and 12 months. Several variables were statistically associated with the absence from work in the 12 months following the mTBI: time since the injury (ie, the odds of absence decreased with time), older age, manual occupation, the presence of a pre-injury psychiatric disorder, a lower baseline-derived GCS score, a higher ISS score, admission to hospital wards or intensive care units (compared with direct discharge from the emergency room), extracranial surgery, and a lower GOSE score. Relatively similar results were obtained in the sensitivity analyses focusing on adults without intracranial surgery during hospitalization and any intracranial complication at discharge. To the best of the authors' knowledge, this research is one of the first multi-country studies on this topic, while it is also one of the first studies to investigate detailed trajectories of absence from work following a mTBI.

Interpretation of the findings

Before going further, it should be acknowledged that 69 % of this mTBI population was either admitted to hospital wards or intensive care units after multiple imputation of missing data, and a substantial proportion of the sample had intracranial surgery. These care pathways and healthcare utilization are uncommon in people with mTBI, which raises questions about the generalizability of the present results. The fact that the proportion of people undergoing surgery (either intracranial or extracranial surgery) and those with complications (either intracranial or extracranial) was higher after than before the multiple imputation of missing data likely reflects the fact that the missingness of the data was related to the severity of the underlying TBI, a pattern already reported in the literature [33].

A critical finding of the study is that 20 % of adults with mTBI were absent from work 12 months after the injury. This result aligns with some of the previous research published on the topic. For example, a cohort of 152 adults with mTBI from the United States found that the absence from work was 22 % at 3 months and 21 % at 6 months [9]. The present study not only corroborates these results but also shows that absence from work is common in the 12 months following mTBI in a European population. This body of research further shows that most adults with mTBI who return to work do so within the first 3 months, while those absent from work at 3 months are less likely to return to work later. Although figures and trajectories were similar in the mTBI population without intracranial surgery or intracranial complications, the 2-week absence from work was 51 % in this sample. This result may seem counterintuitive, as people with intracranial abnormalities were excluded from this analysis. That said, the 2-week follow-up is an early assessment that may not accurately depict absence from work following mTBI. The 3-month absence from work was comparable between the overall population (ie, 24 %) and the population without intracranial surgery or intracranial complications (ie, 28 %).

The generalized estimating equations corroborate the above findings, as time since mTBI was associated with decreased odds of absence from work. Moreover, in line with a previous study [3], older participants were more likely to be absent from work than their younger counterparts. Older adults with mTBI may face substantial barriers to returning to work early. These barriers may involve persistent symptoms and delayed referral to rehabilitation. Additional barriers include issues with the organization and the psychosocial work environment, such as a lack of knowledge in the workplace on how to handle complex and non-linear return-to-work processes. These circumstances may lead to deficient employer engagement, insufficient workplace accommodations, and a lack of co-worker support [34]. Interestingly, a manual occupation was associated with a higher likelihood of a 12-month absence from work compared with a non-manual occupation. Other research has identified a similar pattern, suggesting that balance and fine motor skill impairments, as well as a less accommodating workplace environment, could compromise the return to work in manual workers [35,36].

Regarding behavioral factors, there was no statistically significant relationship between current alcohol misuse and the 12-month absence from work. Although this lack of statistical significance may be surprising, similar research findings have been obtained on alcohol misuse and the 12-month absence from work [3–13], as well as in terms of overall recovery following a mild-to-moderate traumatic brain injury [37]. However, this prior body of research investigated alcohol consumption and not specifically alcohol misuse, which warrants caution when interpreting the absence of a significant relationship in the present study.

In terms of the pre-injury medical history, the presence of a pre-injury psychiatric disorder increased the odds of absence from work in the year following mTBI. This result should be cautiously interpreted, as psychiatric disorders did not significantly affect the return to work after mTBI in a previous sample of 103 adults [38]. Nonetheless, the lack of statistically significant findings in this prior study could be partially explained by its relatively small sample size. People with psychiatric disorders may experience more difficulties in coping with mTBI than those without these disorders. Based on data obtained outside the field of mTBI (ie, stroke), there is evidence that emotion-focused coping strategies play a substantial role in the return to work after a significant health event [39]. In people with psychiatric disorders, such strategies focusing on emotions might be altered, potentially impairing a successful return to work. Moreover, anxiety and depression are risk factors for increased cognitive impairments and functional difficulties after a TBI [40]. Adults with mTBI and anxiety and depression may have persistent difficulties in using coping strategies that rely on solving problems. In addition, psychiatric disorders and TBI share some genetic and epigenetic vulnerability [41,42]. In terms of epigenetic vulnerability, there is some preliminary evidence obtained in a rat model showing that the deleterious effects of mTBI on post-traumatic stress disorder are potentially mediated via an alteration of the methylation of the hippocampal DNA [42]. mTBI could also be a trigger for an increase in the intensity of psychiatric symptoms in people with a pre-injury mental health disorder. In the present sample, it should be noted that 17 % of participants had moderate-to-severe generalized anxiety disorder symptoms, while 28 % had major depression.

Furthermore, the baseline-derived GCS score, the ISS score, being hospitalized in hospital wards or intensive care units (compared with direct discharge from the emergency room), and extracranial surgery were positively and statistically associated with absence from work. Similarly, another research identified multiple bodily injuries and intracranial abnormalities, which can be viewed as indirect markers of the injury severity, as risk factors for delayed return to work after mTBI [3]. More severe mTBI may be associated with longer disability and a persisting need for specialized rehabilitation, and such trends may favor the absence from work. Finally, there was an inverse relationship between the 2-week GOSE score and 12-month absence from work. This finding, which is in line with the literature [43], highlights the fact that disability following mTBI may undermine the return to work.

Clinical and public health implications and directions for future research

Older age, a manual occupation, the presence of a pre-injury psychiatric disorder, several injury-related factors, and a post-injury disability were identified as positively associated with higher odds of absence from work after a mTBI. From a clinical perspective, these identifiers may help clinicians distinguish individuals with mTBI at an increased risk for not returning to work. Older workers may be followed more regularly after mTBI to identify early barriers to returning to work and facilitate such a return. In terms of occupational category, it is essential to mitigate the deleterious effects of the complex interplay between persisting symptoms and insufficient occupational support on the return to work among manual workers. Early intervention vocational rehabilitation [44] and coordinated, personalized programs [45] could help mitigate these deleterious effects. Such interventions could be implemented in both inpatient and outpatient settings, depending on the individual's clinical profile, occupational background, and objectives [46]. Regarding the presence of a pre-injury psychiatric disorder, the psychological and psychiatric management of people with mTBI is critical, and those with impaired mental health should be referred to mental health specialists to discuss the introduction of supportive interventions and the initiation of a dedicated follow-up. Beyond the factors above associated with returning to work, clinicians could also attempt to characterize the coping strategies used by adults with mTBI who did return to work after the injury. These coping strategies (eg, emotion- and problem-focused strategies) may vary within the mTBI population [39], highlighting the need for personalized and tailored interventions (eg, cognitive training, neuropsychological training, and psychotherapy) [47,48]. From a public health perspective, the fact that 20 % of adults with mTBI were absent from work at 12 months from the injury calls for the implementation of measures aiming at favoring a gradual return to work in this population when symptoms are no longer disabling. These measures align with recent recommendations from experts, which suggest improving care pathways for people with mTBI to better structure their follow-up [49]. For future research, it is crucial to corroborate these findings in other cohorts of mTBI adults. At the same time, there is a need for further studies based on data collected more than a year after the injury.

Limitations

The study findings should be interpreted in the light of several limitations. First, a substantial proportion of missing data on absence from work was present at each follow-up assessment, and although some analyses relied on generalized estimating equations, these missing data may have impacted the results. The rate of missing data was also particularly high for 2-week questionnaires, and this rate may have affected the results of the generalized estimating equations that included questionnaires assessed at 2 weeks. Second, having more data on the occupational environment (eg, detailed job types, physical job demands, and work-related stress) and occupational status would have enabled more detailed analyses. More specifically, the reason for retirement was undocumented. Given that retirement may be unrelated to the injury in some cases, absence from work in people with mTBI may have been overestimated. Moreover, some adults may be outside the workforce for reasons unrelated to the mTBI (eg, job loss due to economic reasons). Third, data collection relied on medical records and personal interviews, and some of the independent variables were likely self-reported (eg, a previous traumatic brain injury), potentially introducing recall and social desirability biases. At the same time, psychoactive substance use (eg, alcohol misuse) was assessed in the last 3 months. In terms of pre-injury psychiatric disorders, as these conditions are associated with stigma [50], their presence may have been underreported. Moreover, there was no data on the specific type of psychiatric disorder. Fourth, mTBI does not usually require hospitalization and is often managed in outpatient settings. The present sample, which was observed in level-1 trauma centers and hospitalized in almost 70 % of cases (ie, 44 % in hospital wards and 25 % in intensive care units), may not accurately represent the population with mTBI. Fifth, although the definition of mTBI requires information on post-traumatic amnesia, such amnesia and its duration were not recorded.

Conclusions

The present study of 1080 workers with mTBI from Europe showed that the absence from work decreased in the year following the injury, reaching 20 % at 12 months post-injury. Older age, a manual occupation, the presence of a pre-injury psychiatric disorder, several injury-related factors, and a lower 2-week GOSE score were positively and statistically associated with higher odds of absence from work within the 12 months following mTBI. Further studies are warranted to corroborate the present results in other regions of the world. At the same time, additional data are needed on the absence from work for > 12 months after mTBI.

Data and code statement

The CENTER-TBI data are accessible to interested researchers after sending a proposal on the online platform (https://www.center-tbi.eu/). The code used for this study is available from the corresponding author upon reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Louis Jacob: Formal analysis, Investigation, Methodology, Supervision, Visualization, Writing – original draft, Writing – review & editing. **John Castro:** Formal analysis, Methodology, Visualization, Writing – review & editing. **Camille Heslot:** Visualization, Writing – review & editing. **Nada Andelic:** Visualization, Writing – review & editing. **Olli Tenovuo:** Visualization, Writing – review & editing. **Philippe Azouvi:** Investigation, Methodology, Supervision, Visualization, Writing – review & editing.

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Supplementary materials

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