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Occupational Outcomes Following Mild Traumatic Brain Injury in Canadian Military Personnel Deployed in Support of the Mission in Afghanistan: A Retrospective Cohort Study

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ABSTRACT

Objective: Deployment-related mild traumatic brain injury (MTBI) occurs in an important minority of military personnel but its long-term impacts are unclear. This study explores the impact of deployment-related MTBI on continued fitness-for-duty, with the ultimate intent of identifying potential targets for intervention to attenuate its effects.

Participants: Consisted of 16193 CAF personnel who deployed in support of the mission in Afghanistan and completed an Enhanced Post-deployment Screening (EPDS) questionnaire over the period January 2009 – July 2012.

Primary Outcome: The primary outcome was development of permanent medical unfitness defined as a "career-limiting medical employment limitation" (CL-MEL). The secondary outcome was the diagnostic categories recorded for each individual at the time a CL-MEL was established

Design: This study used a retrospective cohort design. Linked administrative and health data provided the primary outcome and the diagnoses responsible for it. Survival analysis was used to estimate the risk of CL-MEL's and Cox regression provided adjusted hazard ratios (aHRs) for the association between CL-MEL and MTBI, accounting for key covariates and confounders. Final diagnoses associated with CL-MEL's were identified.

Results: Over a median follow-up period of 3.42 years, 6.57% of the study population developed CL-MEL. MTBI was independently associated with CL-MEL (aHR = 1.65, 95% confidence interval = 1.35-2.03). Mental disorders and musculoskeletal conditions were

the primary diagnoses associated with CL-MEL (identified as the primary diagnosis in 55.4% and 25.9%, respectively), and a neurologic condition was only documented in 5.8% of those with MTBI who developed CL-MEL.

Conclusion: Deployment-related MTBI was associated with adverse occupational outcome but mental disorders and musculoskeletal conditions primarily drove subsequent disability. These findings support a diagnostic and treatment approach focusing on these co-morbidities as the most promising strategy to minimize the burden of disability in MTBI-exposed military personnel.

Strengths and limitations of this study:

- MTBI was assessed through self-reports, raising the possibility of recall bias and reporting errors.
- We were only able to control for mental health problems, PCS and musculoskeletal pain reported at the time of screening, which took place several years, on average, before the outcome. It is possible that problems reported at that time had resolved or, conversely, that subsequent problems in those areas had developed at the time medical fitness problems were identified.
- The large sample size allowed us to control for a broad range of covariates and potential confounders.
- The length of follow up exceeds that in many other published studies on the topic.

INTRODUCTION

Mild traumatic brain injury (MBTI) is reported by up to a quarter of military personnel who deployed to the conflicts in SW Asia.[1] By definition, MTBI is associated with changes in mental status (e.g., loss of consciousness, or being dazed or confused) at the moment of injury. Transient symptoms such as headache, irritability, and problems concentrating typically occur acutely and resolve spontaneously in most individuals days to weeks after the injury. However, some individuals continue to complain of persistent post-concussive symptoms (PCS).[2]

Estimates of the prevalence of persistent PCS vary. Approximately one-quarter of CAF personnel with a deployment-related MTBI reported three or more PCS six months after their return from deployment,[3] a fraction similar to or below those reported in US military personnel (up to 33%)[4] but above those seen in civilian accident victims (up to 15%) and in those with sport-related concussions.[5;6]

The pathophysiology of these persistent PCS remains unclear, but they have strong conceptual and empirical links with mental disorders and other psychosocial factors.[5] In recent combat operational settings, blast is one of the most common mechanisms of MTBI. Consequently, MTBI often co-occurs with psychological injury and other serious physical injuries, complicating the clinical picture.[7] Regardless, persistent PCS are associated with impairments in well-being and functioning.[8;9] Conceptually, their impacts could be especially strong under the demands of military service. However, while studies on the incidence and prevalence

of deployment-related MTBI in military personnel abound,[3;4;10] studies on functional outcomes are sparse.[11]

This paucity of research on long-term functional impacts of deployment-related MTBI stands in stark contrast to the profusion of dire predictions of the impact of this "signature injury" of the conflicts in SW Asia.[1;12] To address these concerns, the US Departments of Defence and of Veterans Affairs have ramped up efforts to diagnose MTBI and to provide cognitive rehabilitation and other MTBI-specific services in those with persistent symptoms.[13] The approach of the CAF has been different, focusing instead diagnosis and treatment of co-morbid mental disorders and a symptom-specific approach for those with persistent, unexplained symptoms.[14]

This paper explores one important long-term impact of deployment-related MTBI, specifically its effect on continued fitness for military service. It uses self-report data on MTBI, mental health symptoms, musculoskeletal pain, and PCS collected during post-deployment mental health screening, linked with subsequent administrative data on occupational impairments. It two main objectives were to:

1. Determine whether those who self-reported MTBI at the time of post-deployment screening were more likely to be disabled compared to those without MTBI after controlling for co-morbid mental and physical conditions as well as other potential confounders;
2. Determine the primary diagnoses to which disability was attributable in those with deployment related MTBI.

METHODS

Context: Canada's Mission in Afghanistan: The Canadian Armed Forces (CAF) has deployed more than 40,000 personnel in support of their combat and peace support mission in Afghanistan. More than 150 deaths occurred, most related to injuries from improvised explosive devices.

Study Design: This was a retrospective longitudinal cohort study that integrated administrative and medical data in a cohort of CAF personnel.

Respondents: Respondents were 16193 CAF personnel who deployed in support of the mission in Afghanistan and completed an Enhanced Post-deployment Screening (EPDS) questionnaire over the period January 2009 – July 2012. CAF policy requires an EPDS 90 to 180 days after return for personnel deployed for 60 days or more. Participants had deployed largely for six to eight months to Kandahar Province (Afghanistan) or in the Persian Gulf region, where they fulfilled a broad range of combat, peacekeeping, operational support, administrative and other roles. Participants were screened a median of 136 days after return from deployment (interquartile range: 100–178 days). Compliance with EPDS is at least 76%.[15]

Data Collection: Data on MTBI, mental health problems, PCS, musculoskeletal pain, and combat exposure were extracted from the EPDS database. Data on sociodemographic and military characteristics, disability, and the diagnoses driving disability were obtained from administrative databases (extract date:

October 17, 2013). Data linkages were based on service number, a unique CAF-specific personal identifier.

Covariates of Interest and Potential Confounders:

Mild traumatic brain injury: MTBI was assessed using the first two questions of the Brief Traumatic Brain Injury Screening Tool.[16] The first item assesses injury during the deployment from the following mechanisms: fragment, bullet, vehicular, fall, blast, or any other mechanism. The second item assesses symptoms of altered mental status *immediately* after the injury. The screen is considered positive in those with injury associated with being dazed, confused, or seeing stars, having loss of consciousness, or having post-traumatic amnesia. This criterion is 80% sensitive and 93% specific for clinician-diagnosed deployment-related MTBI.[17] To keep the focus of the study on *mild* TBI, subjects reporting loss of consciousness of greater than 20 minutes (N = 40) were excluded, leaving 16153 in the final data set.

Post-concussive symptoms (PCS): Seven post-concussive symptoms were assessed at the time of post-deployment screening: (headache, dizziness, memory problems, fatigue, difficulty concentrating, insomnia and irritability), using items and thresholds described in detail elsewhere. A PCS case was defined as having three or more of these symptoms. This definition is modelled after the World Health Organization ICD-10 definition for post-concussion syndrome and is commonly used other studies exploring the relationship between MTBI, post-concussive symptoms and mental health problems.[4;18]

Common mental health problems (MHP's): Common MHP's were assessed as described elsewhere using instruments that did not include physical symptoms that overlap with those defined in the ICD-10 definition of PCS, such as feeling tired, trouble concentrating, sleep problems, and irritability. Specifically, depression was assessed with the 2-item PHQ-2[19] with a cut-off point of 4 or greater.[20] Post-traumatic stress disorder (PTSD) was assessed using the 2-item PCL-2 with a cut-off of 6 points or greater[21;22]. Panic disorder was assessed using the PHQ, with a modified algorithm that did not require the presence of four or more symptoms during the most recent panic attack.[23]

Back and Joint Pain: These were assessed using two items from the PHQ physical symptom inventory (recall period = 4 weeks; response categories = "not at all," "bothered a little," and "bothered a lot"). The aggregate outcome of "back or joint pain" included those who reported being "bothered a lot" on one or both of these items.

Combat exposure: A modified, 30-item version of the scale developed by Walter Reed Army Institute for Research (US) was used to measure the extent of combat exposure.[24] Each item was a yes/no question regarding having experienced specific potentially traumatic experiences while deployed, and the scale score was simply the sum of positive responses (range 0 to 30, $\alpha = 0.91$). For analysis purposes, the scale score was divided into tertiles, determined with respect to a larger reference population of CAF personnel undergoing post-deployment screening after a number of different military operations since 2009.

Sociodemographic and military characteristics: These potential confounders were assessed using items developed for the EPDS questionnaire: Sex, age, language (English or French), marital status, rank, component (Regular vs. Reserve Force), element (Army, Navy, or Air Force), years of military service, number of previous deployments, deployment length, and timing of screening relative to return from deployment. Missing data were filled in where possible using administrative data sources.

Occupational Outcomes:

Occupational Fitness in the CAF: The CAF's "Universality of Service" doctrine ensures operational readiness by requiring all personnel to be able to perform certain common military tasks and to be deployable to any environment with little or no medical support. Individuals persistently in violation of Universality of Service will be medically released.

Significant and persistent medical employment limitations (MEL's) assigned by a treating physician are reviewed and coded by physicians in the CAF's Medical Standards Section, who link MEL's to one primary and up to two secondary diagnostic categories (e.g., mental disorders, cardiovascular disorder) that are driving the MEL's. There is no specific diagnostic category for TBI; those with TBI-related MEL's are captured in the category of neurological conditions.

Outcome Definitions:

The *primary outcome* was defined as the development of "career-limiting medical employment limitations" (CL-MEL), meaning MEL's that reliably result in a medical release from

service. This outcome was used instead of a medical discharge from service because there is an unpredictable delay of up to several years between the recognition of CL-MEL's and ultimate discharge. Consultation with physicians in the Medical Standards Section identified certain patterns of medical employment limitations encoded in administrative data that reliably lead to a breach of Universality of Service.

The *secondary outcome* was the diagnostic categories recorded in the Medical Standard's Database for each individual at the time a CL-MEL was established.

Statistical Analysis:

The data were analyzed using SAS for Windows, version 9.3. The chained equations multiple imputation method was implemented to account for missing data.[25] Overall, less than 1% of the analyzed data had missing values.

Time to event analysis was used to account for differing periods of follow-up and censoring. Kaplan-Meier curves were used to generate event probabilities. Zero-time was defined as the return date from the first Afghanistan-related deployment. Event-time was the date of the medical exam associated with the first persistent CL-MEL designation. Individuals were censored at the earlier of military service discharge date or database extraction date.

Cox regression modeled the association of injury status with CL-MEL risk. The proportional hazards assumption was examined using Schoenfeld residual plots and with an assessment of the

significance of changes in the injury status hazard ratio as the logarithm of follow-up time increased.[26] We used 4 models to estimate the unadjusted and adjusted hazard ratio's for injury status. Model 1 estimated the unadjusted risk; model 2 estimated the adjusted risk controlling for socio-demographic and military characteristics. In addition to these factors, model 3 adjusted for mental disorders and persistent PCS while model 4 additionally adjusted for severe back or joint pain.

The rank, years of military service, number of previous deployments, and duration of last deployment variables were measured with respect to the first deployment return date. Injury status, presence of a mental disorder, PCS, and severe back or joint pain variables were measured with respect to the EPDS date.

RESULTS

Study Cohort Characteristics: The cohort consisted largely of male, non-commissioned Army personnel under the age of 40 years, who were in the Regular Force (Table 1). MTBI was reported in 5.22% and other non-MTBI injuries were documented in 16.76%. Symptoms of major depression, PTSD, and panic disorder were reported at post-deployment screening in 3.67%, 5.70%, and 1.94% respectively, while any of the three mental health problems was reported in 8.80%. Bothersome back or joint pain was reported by 17.83%. Finally, three or more PCS were present at the time of EPDS in 8.69%.

Table 1: Demographic, military characteristic and type of diagnosis of the study cohort (N=16,153)

		Count	%
Sex	Male	14641	90.67
	Female	1507	9.33
	Total	16148	
Age	24 years or less	3134	19.42
	25 to 35 years	7075	43.84
	35 to 44 years	4049	25.09
	45 years or more	1882	11.66
	Total	16140	
Rank	Officer	2331	14.45
	Senior NCM	2863	17.75
	Junior NCM	10940	67.81
	Total	16134	
Component	Reserve Force	2339	14.48
	Regular Force	13812	85.52
	Total	16151	
Element	Land	12824	79.54
	Sea	959	5.95
	Air	2340	14.51
	Total	16123	
Years of military service	5 years or less	5236	32.42
	6 to 15 years	6240	38.64
	16 years or more	4675	28.95
	Total	16151	
Previous deployments	None	7516	46.96
	1 or 2	5025	31.40
	3 or more	3464	21.64
	Total	16005	
Deployment length	Less than 180 days	2284	14.16
	180 or more days	13853	85.84
	Total	16137	
Combat exposure	1st tertile	4535	28.41
	2nd tertile	6397	40.08
	3rd tertile	5029	31.51
	Total	15961	
MTBI	No injury	12602	78.02
	Other injury	2708	16.76
	MTBI	843	5.22
	Total	16153	
MHP*	No MHP	14058	91.20
	MHP	1356	8.80
	Total	15414	
3 or more PCs	No	14712	91.31
	Yes	1401	8.69
	Total	16113	

* Any mental disorder defined as any of the following: major depression (PHQ-2), PTSD (2-item PCL) or panic disorder.

Career-Limiting MEL's: 6.57% had a CL-MEL recorded over a median follow up time of 3.42 years (IQR: 2.71-4.29 years). At five years of follow up those who self-reported a deployment-related MTBI had a probability of CL-MEL of 26.1% (95% CI: 21.6-31.5) compared to 17.2% (95% CI: 14.9 - 19.8) in those with other injuries and 8.0% (95% CI: 7.2-8.9) for those with no injuries (Figure 1 and Table 2).

Table 2. Probability of career-limiting medical employment limitations (95% CI) by injury status at year of follow-up

	Stratum		
Years of Follow-up	MTBI	Other Injury	No injury
1	1.72(1.00-2.95)	1.31(0.93-1.84)	0.74(0.60-0.91)
2	6.72(5.14-8.78)	4.17(3.45-5.03)	2.08(1.84-2.36)
3	13.13(10.78-15.93)	7.93(6.86-9.14)	4.23(3.85-4.65)
4	19.10(16.00-22.72)	13.27(11.70-15.03)	6.21(5.68-6.78)
5	26.13(21.57-31.45)	17.24(14.96-19.83)	8.02(7.18-8.96)

Diagnostic Categories Driving MEL's: While those reporting MTBI had an elevated risk of adverse occupational outcome, clinicians seldom attributed CL-MEL's to a neurological condition: Of those reporting deployment-related MTBI who developed CL-MEL, 5.8% had a neurological condition identified as a primary or secondary contributing diagnosis (Table 3) and only 4.3% had a neurological condition identified as the primary contributing diagnosis (data not shown). Instead, mental disorders (64.8%) and musculoskeletal conditions (51.1%) were the predominant diagnoses recorded for CL-MEL (identified also as the

primary diagnosis in 55.4% and 25.9%, respectively, (data not shown).

Table 3. Primary or secondary diagnosis categories by injury status in personnel with career-limiting medical employment limitations.

Diagnosis category	Injury Status							
	MTBI (N=139)		Non-MTBI Injury (N=284)		No Injury (N=637)		Overall (N=1060)	
	No. CL-MEL	% (95% CI)	No. CL-MEL	% (95% CI)	No. CL-MEL	% (95% CI)	No. CL-MEL	% (95% CI)
Mental health and behavioral	90	64.8 (56.8-72.7)	164	57.8 (52.0-63.5)	305	48.0 (44.1-51.8)	559	52.8 (49.8-55.8)
MSK system and connective tissue	71	51.1 (42.8-59.4)	139	48.9 (43.1-54.8)	205	32.3 (28.6-35.9)	415	39.2 (36.2-42.1)
Skin and subcutaneous tissue	8	5.8 (1.9-9.6)	33	11.6 (7.9-15.4)	94	14.8 (12.0-17.5)	135	12.8 (10.7-14.8)
Ear and mastoid process	15	10.8 (5.6-16.0)	23	8.1 (4.9-11.3)	60	9.4 (7.2-11.7)	98	9.3 (7.5-11.0)
Eye and adnexa	8	5.8 (1.9-9.6)	24	8.5 (5.2-11.7)	65	10.2 (7.9-12.6)	97	9.2 (7.4-10.9)
Nervous system	**8**	**5.8 (1.9-9.6)**	5	1.8 (0.2-3.3)	15	2.4 (1.8-3.5)	28	2.6 (1.7-3.6)

Given the potential difficulty in attributing disability to MTBI, mental disorders, and musculoskeletal conditions in military personnel exposed to both psychological and physical trauma, 4 regression models were created in order to examine changes in the injury status hazard ratio as additional covariates, including proxies for psychological and physical injury (Table 4).

Table 4. Cox Proportional Hazards Models showing the risk of career-limiting medical employment limitations with demographic and military characteristics, injury status, mental health problems and persistent post-concussive symptoms

Variable	**Model 1**[1] aHR(95%CI)	**Model 2**[2] aHR(95%CI)	**Model 3**[3] aHR(95%CI)	**Model 4**[4] aHR(95%CI)
Age				
≤24	--	1.00	1.00	1.00
25-34		**1.33(1.07-1.66)**	**1.25(1.00-1.55)**	1.24(0.996-1.55)
35-44		**1.81(1.37-2.39)**	**1.63(1.23-2.15)**	**1.57(1.19-2.07)**
≥45		**2.88(2.10-3.97)**	**2.62(1.90-3.62)**	**2.48(1.80-3.43)**

Sex				
Male	--	1.00	1.00	1.00
Female		**1.43(1.17-1.76)**	1.14(0.93-1.39)	1.13(0.92-1.39)
Rank				
Officer	--	1.00	1.00	1.00
Senior NCM		**1.79(1.38-2.32)**	**1.60(1.23-2.07)**	**1.54(1.19-2.00)**
Junior NCM		**2.55(2.01-3.25)**	**2.18(1.72-2.78)**	**2.09(1.65-2.66)**
Component				
Reserve Force	**--**	1.00	1.00	1.00
Regular Force		**2.43(1.90-3.11)**	**2.21(1.73-2.84)**	**2.19(1.71-2.81)**
Element	--			
Land		1.00	1.00	1.00
Sea		1.04(0.80-1.35)	1.00(0.77-1.30)	1.01(0.78-1.31)
Air		1.00(0.83-1.21)	1.07(0.88-1.29)	1.05(0.87-1.27)
Years of Service	**--**			
≤5		1.00	1.00	1.00
6-14		**1.24(1.03-1.49)**	1.13(0.93-1.35)	1.09(0.90-1.31)
>=15		**1.86(1.40-2.47)**	**1.64(1.24-2.17)**	**1.58(1.19-2.09)**
Number of previous deployments	--			
0		1.00	1.00	1.00
1 or 2		0.90(0.78-1.05)	0.96(0.83-1.11)	0.96(0.83-1.11)
≥3		0.84(0.68-1.03)	0.90(0.73-1.12)	0.91(0.74-1.12)
Duration of last deployment	--			
≤180 days		1.00	1.00	1.00
>181 days		0.94(0.79-1.12)	0.96(0.81-1.14)	0.97(0.82-1.16)
Combat exposure†	--			
1st tertile		1.00	1.00	1.00
2nd tertile		**1.44(1.20-1.72)**	**1.25(1.05-1.50)**	**1.23(1.03-1.47)**
3rd tertile		**2.06(1.69-2.51)**	**1.52(1.24-1.85)**	**1.49(1.22-1.82)**
Injury Status				
Uninjured	1.00	1.00	1.00	1.00
Non-MTBI injury	**2.05(1.78-2.35)**	**1.78(1.54-2.05)**	**1.56(1.35-1.81)**	**1.42(1.22-1.65)**
MTBI injury	**3.17(2.64-3.81)**	**2.67(2.20-3.25)**	**1.83(1.49-2.24)**	**1.65(1.35-2.03)**
Any mental disorder*	**--**	**--**		
No			1.00	1.00
Yes			**2.70(2.28-3.21)**	**2.55(2.15-3.02)**
3 or more PCS	--	**--**		
No			1.00	1.00
Yes			**2.05(1.72-2.44)**	**1.87(1.57-2.23)**
Severe back or joint pain	--	**--**	--	
No				1.00
Yes				**1.63(1.42-1.87)**

[1]Model1: unadjusted
[2]Model2: Model1 adjusted for socio-demographic and military characteristics
[3]Model3: Model2 adjusted for mental disorders and PCS
[4]Model4: Model3 adjusted for severe back or joint pain (based on PHQ-15)
†The following item cut-off was used for the combat exposure tertile categories: less than 3 items (1st tertile), 3 to 10 items (2nd tertile), more than 10 items (3rd tertile)
*Any mental disorder defined as any of the following: major depression (PHQ-2), PTSD (2-item PCL) or panic disorder.

Model 1 shows the unadjusted risk of CL-MEL for those with a history of MTBI (HR, 3.17 [95% CI, 2.64-3.81]) was significantly higher than for non-MTBI Injury (HR, 2.05[95% CI, 1.78-2.35]),

relative to the uninjured. The risk of CL-MEL for those with a history of MTBI had decreased in the final model (Model 4), but remained modestly elevated (aHR, 1.65 [95% CI, 1.35-2.03]). The presence of any mental disorder (aHR, 2.55 [95% CI, 2.15-3.02]), 3 or more PCS (aHR, 1.87 [95% CI, 1.57-2.23]) and musculoskeletal pain (aHR, 1.63 [95% CI, 1.42-1.87]) also had an increased risk of CL-MEL's.

Given the residual effect of 3 or more PCS on outcome, a post-hoc analysis was conducted to determine whether 3 or more PCS was mediating the association between MTBI and CL-MEL using SAS MEDIATE macro.[27] This revealed that PCS only mediated 3.65% [95% CI: 0.22-7.09%]) of the relationship between MTBI and CL-MEL's.

Combat exposure, age 35 years or more, being of senior or junior non-commissioned rank, and having more than 15 years of military service also showed increased risk of CL-MEL's (Table 4). Sex, element (Army, Navy, Air Force), number of previous deployments and duration of last deployment were not associated with CL-MEL's.

DISCUSSION

Summary of Key Findings:

The ultimate objective of this paper was to determine the effect of deployment-related MTBI on subsequent disability defined by the development of career-limiting medical employment limitations (CL-MEL's). MTBI was indeed associated with a substantial absolute and relative risk of this outcome (26.1% within five years after return from deployment), well above the

corresponding risk in the uninjured (8.0%). Those with non-MTBI injuries had an intermediate risk (17.2%).

However, only 5.8% of those with MTBI who developed CL-MEL had a neurological condition identified as a diagnosis contributing to their CL-MEL designation. Instead, mental disorders and musculoskeletal conditions predominated.

We further explored the association of MTBI with CL-MEL using Cox regression. MTBI remained associated with the development of CL-MEL's, even after adjustment for potential confounders, including mental health problems, post-concussive symptoms and musculoskeletal pain reported at the time of post-deployment screening (adjusted HR for MTBI vs no injury = 1.65 [95% CI 1.35-2.03]). Finally, the effect of deployment-related MTBI on occupational fitness was at most minimally mediated by post-concussive symptoms.

Comparison with Other Findings:

To the best of our knowledge this is the first study to systematically examine the effect of deployment-related MTBI on disability, specifically the development of medical employment limitations that are incompatible with continued military service.

The only similar military study examined the extent to which musculoskeletal disorders impacted subsequent determinations of lack of medical fitness in a large cohort of US Army personnel.[28] Coherent with our findings, those authors identified a mental disorder (specifically post-traumatic stress disorder) and a

musculoskeletal condition (low back pain) as the two leading causes of lack of medical fitness. However, MTBI was identified as the third most common cause in that study, but the actual prevalence of MTBI is not reported, precluding any comparison with our study. Military studies of MTBI more than 6 months after deployment show a variety of adverse health effects, but none have explored occupational outcomes.[29;30]

The comparative civilian literature on occupational impacts of MTBI is also limited. The Worker's Compensation Board of the Province of British Columbia in Canada found that 15% of MTBI claimants were on short term disability for > 10 weeks.[31] A recent systematic review also reported that most workers with MTBI returned to work within 3 to 6 months after injury and that MTBI did not appear to be a significant risk factor for long term work disability.[32] Our own finding of a high absolute risk of persistent occupational impairments after deployment-related TBI may relate to differences in patterns of co-morbidity (notably, the high risk of psychological trauma and non-TBI injuries in those with deployment-related MTBI) in our population or to the stringent occupational fitness requirements for military personnel relative to civilians.

Limitations and Strengths:

We acknowledge the difficulty in attributing disability to MTBI as opposed to commonly co-morbid conditions with overlapping symptoms such as mental disorders. Although we captured the clinician-indicated primary medical condition that contributed to the adverse occupational outcome and had

covariates that measured psychological and physical injury as well as persisting PCS, we were not able to measure the changing nature of these variables with follow-up time.

All primary covariates of interest were assessed by self-report at the time of non-anonymous, post-deployment screening. This raises several limitations: First, the lack of anonymity could potentially lead to under-reporting of mental health problems. Second, MTBI was assessed through self-reports, raising the possibility of recall bias and reporting errors. Current military case definitions for MTBI include those who were only dazed/confused or saw stars, which can lead to misclassification when head trauma coincides with psychological trauma in a combat setting.[33] Finally, we were only able to control for mental health problems, PCS and musculoskeletal pain reported at the time of screening, which took place several years, on average, before the outcome. It is possible that problems reported at that time had resolved or, conversely, that subsequent problems in those areas had developed at the time medical fitness problems were identified.

Our definition of PCS is also an important limitation: Universally accepted research criteria for establishing post-concussive syndrome do not currently exist. The definition employed in this study was based on ICD-10 and has been used in other military studies,[4;18] but civilian research has shown that it is less specific than others.[34] We strove to mitigate that potential effect by excluding anxiety and depression (present in the ICD-10 criteria) from our operational definition of PCS.

Furthermore, depression and PTSD were evaluated using the PHQ-2 and PCL-2 scales that excluded symptoms considered for assessment of PCS.

The structure of the questionnaire precluded any determination of the nature of other injuries at the time of EPDS. These were likely musculoskeletal in nature given findings from injury surveillance on military operations.[35]

Although debate continues about the long-term effects of repeated MTBI, we did not have the ability to control for the potential effect of this in this study.[36;37]

Finally, the results of this study are rooted in the CAF's unique occupational fitness standards and hence not directly generalizable to other military organizations or employers in other sectors.

This study's primary strength is that it explores an important but under-researched issue: the occupational impact of deployment-related MTBI in a military population. The large sample size allowed us to control for a broad range of covariates and potential confounders. The length of follow up exceeds that in many other published studies on the topic. Finally, time-to-event analysis allowed for efficient use of the data.

Implications:

Military personnel who report deployment-related MTBI are at significantly increased risk for adverse occupational outcomes. However, medical unfitness was largely driven by mental and musculoskeletal disorders and to a far lesser extent by neurologic diagnoses. The pathogenesis of poor health in some

individuals following MTBI remains poorly understood and is undoubtedly multifactorial in nature.[38] Consequently, there is no consensus about how to mitigate adverse health outcomes in those with MTBI.

Given this challenge, military and veteran organizations in the US have increased their detection of MTBI through screening and outreach and have implemented MTBI-specific treatments such as cognitive rehabilitation.[13;39] Civilian guidelines have instead argued for a symptom based approach in light of the multifactorial nature of persistent PCS.[40] This approach emphasizes detection and treatment of mental disorders when present. The Canadian Armed Forces formally endorsed this approach in 2008.[14]

The findings of the present study suggest that military attrition following deployment related MTBI may best be mitigated by focussing on assessment and maximal treatment of mental disorders and musculoskeletal problems. Our observation that neurologic diagnosis were an infrequent cause of medical unfitness in those with MTBI and that PCS only weakly mediated the association of MTBI with adverse occupational outcome casts some doubt as to the potential benefit of the routine use of cognitive rehabilitation therapy given the lack of rigorously controlled studies in this context.[41]

Additional research on outcome after MTBI is needed. Collecting information on the specific musculoskeletal problems driving disability in this population would provide useful context and might identify specific disorders for prevention and

control efforts. Similarly, information on the timing of mental disorder onset might ultimately lead to interventions to facilitate early disclosure of symptoms and subsequent initiation of treatment.

Conclusion:

The past decade has seen growing concern about the long-term impacts of deployment-related MTBI in military personnel. This study provides a clearer picture as to the extent of that risk. Adverse occupational outcomes in those with deployment-related MTBI were primarily driven by musculoskeletal conditions and mental disorders and to a far lesser extent by a neurological diagnosis. These findings support a more holistic diagnostic and treatment approach focusing on these co-morbidities as the most promising strategy to minimize the burden of disability in MTBI-exposed military personnel.

Methodological refinements in future observational studies of outcome after MTBI will address some of the limitations of the present study. However, the question as to the optimal approach for treatment and rehabilitation of those with deployment-related MTBI will only be addressed definitively through carefully-designed intervention trials.

Contributors: All authors contributed substantially to the study. The primary author (BG) was responsible for the design, implementation, and analysis of the manuscript. The second author (CR) managed the data acquisition and collection and conducted the statistical analyses. The third author (MZ) contributed to the design, and implementation of the study. The fourth author (DB) contributed to the development of the statistical analytic approach. All authors contributed to the interpretation of the study results as well as the writing of the manuscript. All authors have read and agree with the manuscript's final content.

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Parts of this work have previously been presented at the Canadian

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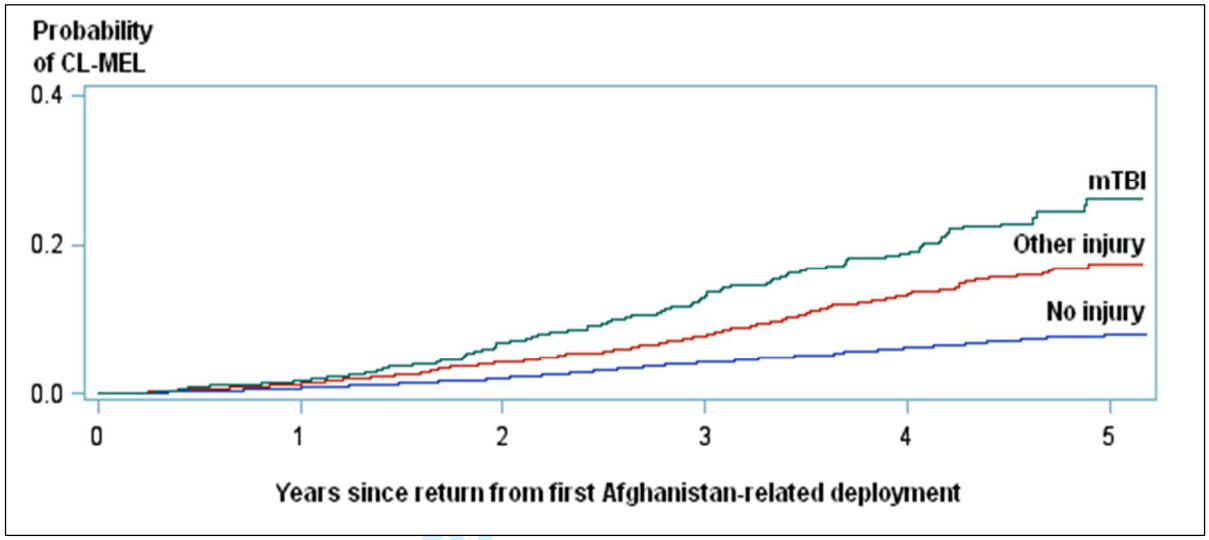
Figure 1. Kaplan-Meier estimates of the probability of a career-limiting medical employment limitation (CL-MEL) by type of injury.



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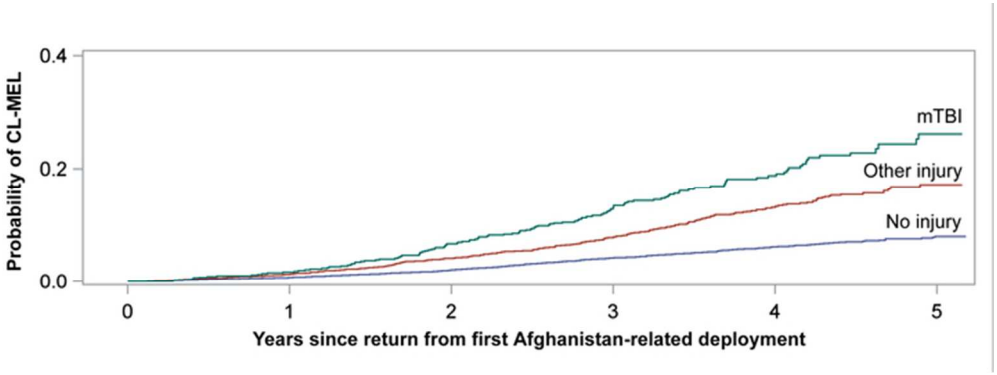

Figure 1. Kaplan-Meier estimates of the probability of a career-limiting medical employment limitation (CL-MEL) by type of injury.
61x22mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6-7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8 (sources of data) 8-12 (details of methods)
Bias	9	Describe any efforts to address potential sources of bias	12
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12-14
		(*b*) Describe any methods used to examine subgroups and interactions	16
		(*c*) Explain how missing data were addressed	12
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Only baseline (page 2)
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	12
		(c) Summarise follow-up time (eg, average and total amount)	14
Outcome data	15*	Report numbers of outcome events or summary measures over time	14
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15.29
		(*b*) Report category boundaries when continuous variables were categorized	29
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations			16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	29

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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

BMJ Open

Occupational Outcomes Following Mild Traumatic Brain Injury in Canadian Military Personnel Deployed in Support of the Mission in Afghanistan: A Retrospective Cohort Study

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Running Head: Military Occupational Outcomes and Mild Traumatic Brain Injury

Occupational Outcomes Following Mild Traumatic Brain Injury in Canadian Military Personnel Deployed in Support of the Mission in Afghanistan: A Retrospective Cohort Study

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ABSTRACT

Objective: Deployment-related mild traumatic brain injury (MTBI) occurs in a significant number of military personnel but its long-term impacts are unclear. This study explores the impact of deployment-related MTBI on continued fitness-for-duty, with the ultimate intent of identifying potential targets for intervention to attenuate its effects.

Participants: Consisted of 16193 CAF personnel who deployed in support of the mission in Afghanistan and completed an Enhanced Post-deployment Screening (EPDS) questionnaire over the period January 2009 – July 2012.

Primary Outcome: The primary outcome was development of permanent medical unfitness defined as a "Career-limiting Medical Condition" (CL-MC). The secondary outcome was the diagnostic categories recorded for each individual at the time a CL-MC was established

Design: This study used a retrospective cohort design. Linked administrative and health data provided the primary outcome and the diagnoses responsible for it. Survival analysis was used to estimate the risk of a CL-MC and Cox regression provided adjusted hazard ratios (aHRs) for the association between a CL-MC and MTBI, accounting for key covariates and confounders. Diagnostic categories associated with CL-MC's were identified.

Results: Over a median follow-up period of 3.42 years, 6.57% of the study population developed a CL-MC. MTBI was independently associated with CL-MC's (aHR = 1.65, 95% confidence interval =

1.35-2.03). Mental disorders and musculoskeletal conditions were the primary diagnoses associated with CL-MC's (identified as the primary diagnosis in 55.4% and 25.9%, respectively), and a neurologic condition was only documented in 5.8% of those with MTBI who developed a CL-MC

Conclusion: Deployment-related MTBI was associated with adverse occupational outcome but mental disorders and musculoskeletal conditions primarily drove subsequent medical unfitness. These findings support a diagnostic and treatment approach focusing on these co-morbidities as the most promising strategy to minimize the burden of disability in MTBI-exposed military personnel.

Strengths and limitations of this study:

- MTBI was assessed through self-reports, raising the possibility of recall bias and reporting errors.
- We were only able to control for mental health problems, PCS and musculoskeletal pain reported at the time of screening, which took place several years, on average, before the outcome. It is possible that problems reported at that time had resolved or, conversely, that subsequent problems in those areas had developed at the time medical fitness problems were identified.
- The large sample size allowed us to control for a broad range of covariates and potential confounders.
- The length of follow up exceeds that in many other published studies on the topic.

INTRODUCTION

Mild traumatic brain injury (MBTI) is reported by up to a quarter of military personnel who deployed to the conflicts in SW Asia.[1] By definition, MTBI is associated with changes in mental status (e.g., loss of consciousness, or being dazed or confused) at the moment of injury. Transient symptoms such as headache, irritability, and problems concentrating typically occur acutely and resolve spontaneously in most individuals days to weeks after the injury. However, in some individuals these same symptoms remain beyond three months and are referred to as persistent post-concussive symptoms (PCS).[2]

Estimates of the prevalence of persistent PCS vary. Approximately one-quarter of CAF personnel with a deployment-related MTBI reported three or more PCS six months after their return from deployment,[3] a fraction similar to or below those reported in US military personnel (up to 33%)[4] but above those seen in civilian accident victims (up to 15%) and in those with sport-related concussions.[5;6]

The pathophysiology of these persistent PCS remains unclear, but they have strong conceptual and empirical links with mental disorders and other psychosocial factors.[5] In recent combat operational settings, blast is one of the most common mechanisms of MTBI.[7;8] Consequently, MTBI often co-occurs with psychological injury and other serious physical injuries, complicating the clinical picture.[9] Regardless, persistent PCS are associated with impairments in well-being and functioning.[10;11] Conceptually, their

impacts could be especially strong under the demands of military service. However, while studies on the incidence and prevalence of deployment-related MTBI in military personnel abound,[3;4;12] studies on functional outcomes are sparse.[8]

This paucity of research on long-term functional impacts of deployment-related MTBI stands in stark contrast to the profusion of dire predictions of the impact of this "signature injury" of the conflicts in SW Asia.[1;13] To address these concerns, the US Departments of Defence and of Veterans Affairs have ramped up efforts to diagnose MTBI and to provide cognitive rehabilitation and other MTBI-specific services in those with persistent symptoms.[14] The approach of the CAF has been different, focusing instead diagnosis and treatment of co-morbid mental disorders and a symptom-specific approach for those with persistent, unexplained symptoms.[15]

This paper explores one important long-term impact of deployment-related MTBI, specifically its effect on continued fitness for military service. It uses self-report data on MTBI, mental health symptoms, musculoskeletal pain, and PCS collected during post-deployment mental health screening, linked with subsequent administrative data on occupational impairments. It two main objectives were to:

1. Determine whether those who self-reported MTBI at the time of post-deployment screening were more likely to be medically unfit compared to those without MTBI after controlling for co-morbid mental and physical conditions as well as other potential confounders;

2. Determine the primary diagnoses to which medical unfitness was attributable in those with deployment related MTBI.

METHODS

Context: Canada's Mission in Afghanistan: The Canadian Armed Forces (CAF) has deployed more than 40,000 personnel in support of their combat and peace support mission in Afghanistan. More than 150 deaths occurred, most related to injuries from improvised explosive devices.

Study Design: This was a retrospective longitudinal cohort study that integrated administrative and medical data in a cohort of CAF personnel.

Respondents: Respondents were 16193 CAF personnel who deployed in support of the mission in Afghanistan and completed an Enhanced Post-deployment Screening (EPDS) questionnaire over the period January 2009 – July 2012. CAF policy requires an EPDS 90 to 180 days after return for personnel deployed for 60 days or more. Participants had deployed largely for six to eight months to Kandahar Province (Afghanistan) or in the Persian Gulf region, where they fulfilled a broad range of combat, peacekeeping, operational support, administrative and other roles. Participants were screened a median of 136 days after return from deployment (interquartile range: 100–178 days). Compliance with EPDS is at least 76%.[16]

Data Collection: Data on MTBI, mental health problems, PCS, musculoskeletal pain, and combat exposure were extracted from the EPDS database. Data on sociodemographic and military

characteristics, disability, and the diagnoses driving disability were obtained from administrative databases (extract date: October 17, 2013). Data linkages were based on service number, a unique CAF-specific personal identifier.

Covariates of Interest and Potential Confounders:

Mild traumatic brain injury: MTBI was assessed using the first two questions of the Brief Traumatic Brain Injury Screening Tool.[17] The first item assesses injury during the deployment from the following mechanisms: fragment, bullet, vehicular, fall, blast, or any other mechanism. The second item assesses symptoms of altered mental status *immediately* after the injury. The screen is considered positive in those with injury associated with being dazed, confused, or seeing stars, having loss of consciousness, or having post-traumatic amnesia. This criterion is 80% sensitive and 93% specific for clinician-diagnosed deployment-related MTBI.[18] To keep the focus of the study on *mild* TBI, subjects reporting loss of consciousness of greater than 20 minutes (N = 40) were excluded, leaving 16153 in the final data set.

Post-concussive symptoms (PCS): Seven post-concussive symptoms were assessed at the time of post-deployment screening: (headache, dizziness, memory problems, fatigue, difficulty concentrating, insomnia and irritability), using items and thresholds described in detail elsewhere. A PCS case was defined as having three or more of these symptoms. This definition is modelled after the World Health Organization ICD-10 definition for post-concussion syndrome and is commonly used other studies

exploring the relationship between MTBI, post-concussive symptoms and mental health problems.[4;19]

Common mental health problems (MHP's): Common MHP's were assessed as described elsewhere using instruments that did not include physical symptoms that overlap with those defined in the ICD-10 definition of PCS, such as feeling tired, trouble concentrating, sleep problems, and irritability. Specifically, depression was assessed with the 2-item PHQ-2[20] with a cut-off point of 4 or greater.[21] Post-traumatic stress disorder (PTSD) was assessed using the 2-item PCL-2 with a cut-off of 6 points or greater[22;23]. Panic disorder was assessed using the PHQ, with a modified algorithm that did not require the presence of four or more symptoms during the most recent panic attack.[24]

Back and Joint Pain: These were assessed using two items from the PHQ physical symptom inventory (recall period = 4 weeks; response categories = "not at all," "bothered a little," and "bothered a lot"). The aggregate outcome of "back or joint pain" included those who reported being "bothered a lot" on one or both of these items.

Combat exposure: A modified, 30-item version of the scale developed by Walter Reed Army Institute for Research (US) was used to measure the extent of combat exposure.[25] Each item was a yes/no question regarding having experienced specific potentially traumatic experiences while deployed, and the scale score was simply the sum of positive responses (range 0 to 30, $\alpha = 0.91$). For analysis purposes, the scale score was divided into tertiles, determined with respect to a larger reference population of CAF

personnel undergoing post-deployment screening after a number of different military operations since 2009.

Sociodemographic and military characteristics: These potential confounders were assessed using items developed for the EPDS questionnaire: Sex, age, language (English or French), marital status, rank, component (Regular vs. Reserve Force), element (Army, Navy, or Air Force), years of military service, number of previous deployments, deployment length, and timing of screening relative to return from deployment. Missing data were filled in where possible using administrative data sources.

Occupational Outcomes:

Occupational Fitness in the CAF: Military service is both physically and psychologically demanding. The medical fitness requirements for service are commensurately stringent and vary with the tasks specific to different military occupations. However, like all militaries, there is a common set of core essential tasks that all individuals must be capable of performing in order to serve in uniform in the Canadian Armed Forces. In addition, all military personnel need to be able to deploy to any location with little or no medical support. [26]

Upon enrollment every member undergoes a thorough medical examination and is assigned a medical category. This medical category is a numeric profile that summarizes to chain of command key information about a member's employability within their given military trade. The factors included in a medical category are:

visual acuity, colour vision, hearing, geographical factor, occupational factor and air factor.[27]

For most disorders, the “Geographical” and “Occupational” factor codes drive retention decisions. The geographical factor captures an individual’s need for medical care that might be unavailable at potential work locations (e.g. during deployment). The occupational factor captures an individual’s capacity to perform required job functions under the physical and mental stress associated with operational conditions. The codes for the geographical and occupational factors can range from 1 to 6; higher grades represent more severe limitations.

When a CAF member is ill or becomes injured they are required to be assessed by a CAF medical officer (a physician) all of whom are experienced in the practice of occupational medicine. A thorough medical assessment, diagnosis and treatment plan is developed. The medical officer also has a responsibility to inform the chain of command as to any health related employment limitations that impact the member’s ability to perform expected tasks and duties safely. This information is expressed in the form of written Medical Employment Limitations (MELs).

These temporary MELs will result in a temporary change to one or more medical category factors while waiting for a medical condition to ameliorate. If the medical condition has plateaued and/or is not expected to significantly improve in the

foreseeable future a Permanent Medical Category change is assigned.

Throughout the process described, individual base/unit military medical physicians do all determinations of MELs and medical category changes. However, all permanent medical category changes are required to undergo a centralized review. This review is conducted by the Medical Standards Section in the Canadian Forces Health Services Group Headquarters in Ottawa for a final determination. The purpose of this centralized review is to ensure consistency in the application of MEL's and medical categories.

CAF member's with permanent medical category changes as a result of health conditions undergo a separate review by a career board who then determine if the individual can remain in their current occupation. If they cannot perform the essential tasks required of all military members, and/or are deemed to be unable to deploy to any location with little or no medical support, they will ultimately be medically released.

Outcome Definitions:

The *primary outcome* was defined as the development of a "career-limiting medical conditions(CL-MC), meaning a permanent medical category that reliably results in a medical release from service.[28] This outcome was used instead of a medical discharge from service because there is an unpredictable delay of up to several years between the recognition of CL-MC and ultimate

discharge. Consultation with physicians in the Medical Standards Section identified certain patterns of category changes, primarily based on the geographic and occupational factors, encoded in administrative data that reliably result in medical release.[28]

The *secondary outcome* was the diagnostic category recorded in the Medical Standard's Database for each individual at the time a CL-MC was established. This includes one primary and up to two secondary diagnostic categories (e.g., mental disorders, cardiovascular disorder) that are driving the CL-MC. There is no specific diagnostic category for TBI; those with TBI are captured in the category of neurological conditions.

Statistical Analysis:

The data were analyzed using SAS for Windows, version 9.3. The chained equations multiple imputation method was implemented to account for missing data.[29] Overall, less than 1% of the analyzed data had missing values.

Time to event analysis was used to account for differing periods of follow-up and censoring. Kaplan-Meier curves were used to generate event probabilities. Zero-time was defined as the return date from the first Afghanistan-related deployment. Event-time was the date of the medical exam associated with the first persistent CL-MC designation. Individuals were censored at the earlier of military service discharge date or database extraction date.

Cox regression modeled the association of injury status with CL-MC risk. The proportional hazards assumption was examined using Schoenfeld residual plots and with an assessment of the significance of changes in the injury status hazard ratio as the logarithm of follow-up time increased.[30] We used 4 models to estimate the unadjusted and adjusted hazard ratio's for injury status. Model 1 estimated the unadjusted risk; model 2 estimated the adjusted risk controlling for socio-demographic and military characteristics. In addition to these factors, model 3 adjusted for mental disorders and persistent PCS while model 4 additionally adjusted for severe back or joint pain.

The rank, years of military service, number of previous deployments, and duration of last deployment variables were measured with respect to the first deployment return date. Injury status, presence of a mental disorder, PCS, and severe back or joint pain variables were measured with respect to the EPDS date.

RESULTS

Study Cohort Characteristics: The cohort consisted largely of male, non-commissioned Army personnel under the age of 40 years, who were in the Regular Force (Table 1). MTBI was reported in 5.22% and other non-MTBI injuries were documented in 16.76%. Symptoms of major depression, PTSD, and panic disorder were reported at post-deployment screening in 3.67%, 5.70%, and 1.94% respectively, while any of the three mental health problems was reported in 8.80%. Bothersome back or joint pain was reported by

17.83%. Finally, three or more PCS were present at the time of EPDS in 8.69%.

Table 1: Demographic, military characteristic and type of diagnosis of the study cohort (N=16,153)

		Count	%
Sex	Male	14641	90.67
	Female	1507	9.33
	Total	16148	
Age	24 years or less	3134	19.42
	25 to 35 years	7075	43.84
	35 to 44 years	4049	25.09
	45 years or more	1882	11.66
	Total	16140	
Rank	Officer	2331	14.45
	Senior NCM	2863	17.75
	Junior NCM	10940	67.81
	Total	16134	
Component	Reserve Force	2339	14.48
	Regular Force	13812	85.52
	Total	16151	
Element	Land	12824	79.54
	Sea	959	5.95
	Air	2340	14.51
	Total	16123	
Years of military service	5 years or less	5236	32.42
	6 to 15 years	6240	38.64
	16 years or more	4675	28.95
	Total	16151	
Previous deployments	None	7516	46.96
	1 or 2	5025	31.40
	3 or more	3464	21.64
	Total	16005	
Deployment length	Less than 180 days	2284	14.16
	180 or more days	13853	85.84
	Total	16137	
Combat exposure	1st tertile	4535	28.41
	2nd tertile	6397	40.08
	3rd tertile	5029	31.51
	Total	15961	
MTBI	No injury	12602	78.02
	Other injury	2708	16.76
	MTBI	843	5.22
	Total	16153	
MHP*	No MHP	14058	91.20
	MHP	1356	8.80
	Total	15414	
3 or more PCs	No	14712	91.31
	Yes	1401	8.69
	Total	16113	

* Any mental disorder defined as any of the following: major

depression (PHQ-2), PTSD (2-item PCL) or panic disorder.

Career-Limiting Medical Conditions: 6.57% had a CL-MC recorded over a median follow up time of 3.42 years (IQR: 2.71-4.29 years). At five years of follow up those who self-reported a deployment-related MTBI had a probability of CL-MC of 26.1% (95% CI: 21.6-31.5) compared to 17.2% (95% CI: 14.9 - 19.8) in those with other injuries and 8.0% (95% CI: 7.2-8.9) for those with no injuries (Figure 1 and Table 2).

Table 2. Probability of Career-limiting Medical Conditions (95% CI) by injury status at year of follow-up

	Stratum		
Years of Follow-up	MTBI	Other Injury	No injury
1	1.72(1.00-2.95)	1.31(0.93-1.84)	0.74(0.60-0.91)
2	6.72(5.14-8.78)	4.17(3.45-5.03)	2.08(1.84-2.36)
3	13.13(10.78-15.93)	7.93(6.86-9.14)	4.23(3.85-4.65)
4	19.10(16.00-22.72)	13.27(11.70-15.03)	6.21(5.68-6.78)
5	26.13(21.57-31.45)	17.24(14.96-19.83)	8.02(7.18-8.96)

Diagnostic Categories Driving Career-limiting Medical Conditions: While those reporting MTBI had an elevated risk of adverse occupational outcome, clinicians seldom attributed a CL-MC to a neurological condition: Of those reporting deployment-related MTBI who developed a CL-MC, 5.8% had a neurological condition identified as a primary or secondary contributing diagnosis (Table 3) and only 4.3% had a neurological condition identified as the primary contributing diagnosis (data not shown). Instead, mental disorders (64.8%) and musculoskeletal conditions (51.1%) were the predominant diagnoses recorded for

CL-MC's (identified also as the primary diagnosis in 55.4% and 25.9%, respectively, (data not shown).

Table 3. Primary or secondary diagnosis categories by injury status in personnel with Career-limiting Medical Conditions.

Diagnosis category	Injury Status							
	MTBI (N=139)		Non-MTBI Injury (N=284)		No Injury (N=637)		Overall (N=1060)	
	No. CL-MC	% (95% CI)	No. CL-MC	% (95% CI)	No. CL-MC	% (95% CI)	No. CL-MC	% (95% CI)
Mental health and behavioral	90	64.8 (56.8-72.7)	164	57.8 (52.0-63.5)	305	48.0 (44.1-51.8)	559	52.8 (49.8-55.8)
MSK system and connective tissue	71	51.1 (42.8-59.4)	139	48.9 (43.1-54.8)	205	32.3 (28.6-35.9)	415	39.2 (36.2-42.1)
Skin and subcutaneous tissue	8	5.8 (1.9-9.6)	33	11.6 (7.9-15.4)	94	14.8 (12.0-17.5)	135	12.8 (10.7-14.8)
Ear and mastoid process	15	10.8 (5.6-16.0)	23	8.1 (4.9-11.3)	60	9.4 (7.2-11.7)	98	9.3 (7.5-11.0)
Eye and adnexa	8	5.8 (1.9-9.6)	24	8.5 (5.2-11.7)	65	10.2 (7.9-12.6)	97	9.2 (7.4-10.9)
Nervous system	**8**	**5.8 (1.9-9.6)**	5	1.8 (0.2-3.3)	15	2.4 (1.8-3.5)	28	2.6 (1.7-3.6)

Given the potential difficulty in attributing disability to MTBI, mental disorders, and musculoskeletal conditions in military personnel exposed to both psychological and physical trauma, 4 regression models were created in order to examine changes in the injury status hazard ratio as additional covariates, including proxies for psychological and physical injury (Table 4).

Table 4. Cox Proportional Hazards Models showing the risk of Career-limiting Medical Conditions with demographic and military characteristics, injury status, mental health problems and persistent post-concussive symptoms

Variable	**Model 1**[1] aHR(95%CI)	**Model 2**[2] aHR(95%CI)	**Model 3**[3] aHR(95%CI)	**Model 4**[4] aHR(95%CI)
Age				
≤24	--	1.00	1.00	1.00
25-34		**1.33(1.07-1.66)**	**1.25(1.00-1.55)**	1.24(0.996-1.55)
35-44		**1.81(1.37-2.39)**	**1.63(1.23-2.15)**	**1.57(1.19-2.07)**
≥45		**2.88(2.10-3.97)**	**2.62(1.90-3.62)**	**2.48(1.80-3.43)**
Sex				
Male	--	1.00	1.00	1.00

Female		**1.43(1.17-1.76)**	1.14(0.93-1.39)	1.13(0.92-1.39)
Rank				
Officer	--	1.00	1.00	1.00
Senior NCM		**1.79(1.38-2.32)**	**1.60(1.23-2.07)**	**1.54(1.19-2.00)**
Junior NCM		**2.55(2.01-3.25)**	**2.18(1.72-2.78)**	**2.09(1.65-2.66)**
Component				
Reserve Force	**--**	1.00	1.00	1.00
Regular Force		**2.43(1.90-3.11)**	**2.21(1.73-2.84)**	**2.19(1.71-2.81)**
Element	--			
Land		1.00	1.00	1.00
Sea		1.04(0.80-1.35)	1.00(0.77-1.30)	1.01(0.78-1.31)
Air		1.00(0.83-1.21)	1.07(0.88-1.29)	1.05(0.87-1.27)
Years of Service	**--**			
≤5		1.00	1.00	1.00
6-14		**1.24(1.03-1.49)**	1.13(0.93-1.35)	1.09(0.90-1.31)
>=15		**1.86(1.40-2.47)**	**1.64(1.24-2.17)**	**1.58(1.19-2.09)**
Number of previous deployments	--			
0		1.00	1.00	1.00
1 or 2		0.90(0.78-1.05)	0.96(0.83-1.11)	0.96(0.83-1.11)
≥3		0.84(0.68-1.03)	0.90(0.73-1.12)	0.91(0.74-1.12)
Duration of last deployment	--			
≤180 days		1.00	1.00	1.00
>181 days		0.94(0.79-1.12)	0.96(0.81-1.14)	0.97(0.82-1.16)
Combat exposure†	--			
1st tertile		1.00	1.00	1.00
2nd tertile		**1.44(1.20-1.72)**	**1.25(1.05-1.50)**	**1.23(1.03-1.47)**
3rd tertile		**2.06(1.69-2.51)**	**1.52(1.24-1.85)**	**1.49(1.22-1.82)**
Injury Status				
Uninjured	1.00	1.00	1.00	1.00
Non-MTBI injury	**2.05(1.78-2.35)**	**1.78(1.54-2.05)**	**1.56(1.35-1.81)**	**1.42(1.22-1.65)**
MTBI injury	**3.17(2.64-3.81)**	**2.67(2.20-3.25)**	**1.83(1.49-2.24)**	**1.65(1.35-2.03)**
Any mental disorder*	**--**	**--**		
No			1.00	1.00
Yes			**2.70(2.28-3.21)**	**2.55(2.15-3.02)**
3 or more PCS	--	**--**		
No			1.00	1.00
Yes			**2.05(1.72-2.44)**	**1.87(1.57-2.23)**
Severe back or joint pain	--	**--**	--	
No				1.00
Yes				**1.63(1.42-1.87)**

[1]Model1: unadjusted
[2]Model2: Model1 adjusted for socio-demographic and military characteristics
[3]Model3: Model2 adjusted for mental disorders and PCS
[4]Model4: Model3 adjusted for severe back or joint pain (based on PHQ-15)
†The following item cut-off was used for the combat exposure tertile categories: less than 3 items (1st tertile), 3 to 10 items (2nd tertile), more than 10 items (3rd tertile)
*Any mental disorder defined as any of the following: major depression (PHQ-2), PTSD (2-item PCL) or panic disorder.

Model 1 shows the unadjusted risk of a CL-MC for those with a history of MTBI (HR, 3.17 [95% CI, 2.64-3.81]) was significantly higher than for non-MTBI Injury (HR, 2.05[95% CI,

1.78-2.35]), relative to the uninjured. The risk of a CL-MC for those with a history of MTBI had decreased in the final model (Model 4), but remained modestly elevated (aHR, 1.65 [95% CI, 1.35-2.03]). The presence of any mental disorder (aHR, 2.55 [95% CI, 2.15-3.02]), 3 or more PCS (aHR, 1.87 [95% CI, 1.57-2.23]) and musculoskeletal pain (aHR, 1.63 [95% CI, 1.42-1.87]) also had an increased risk of CL-MC.

Given the residual effect of 3 or more PCS on outcome, a post-hoc analysis was conducted to determine whether 3 or more PCS was mediating the association between MTBI and CL-MC's using SAS MEDIATE macro.[31] This revealed that PCS only mediated 3.65% [95% CI: 0.22-7.09%]) of the relationship between MTBI and CL-MC's.

Combat exposure, age 35 years or more, being of senior or junior non-commissioned rank, and having more than 15 years of military service also showed increased risk of CL-MC's (Table 4). Sex, element (Army, Navy, Air Force), number of previous deployments and duration of last deployment were not associated with CL-MC.

DISCUSSION

Summary of Key Findings:

The ultimate objective of this paper was to determine the effect of deployment-related MTBI on subsequent medical unfitness defined by the development of a career-limiting medical condition (CL-MC). MTBI was indeed associated with a substantial absolute and relative risk of this outcome (26.1% within five years after return from deployment), well above the corresponding risk in the

uninjured (8.0%). Those with non-MTBI injuries had an intermediate risk (17.2%).

However, only 5.8% of those with MTBI who developed a CL-MC had a neurological condition identified as a diagnosis contributing to their CL-MC designation. Instead, mental disorders and musculoskeletal conditions predominated.

We further explored the association of MTBI with CL-MC's using Cox regression. MTBI remained associated with the development of a CL-MC, even after adjustment for potential confounders, including mental health problems, post-concussive symptoms and musculoskeletal pain reported at the time of post-deployment screening (adjusted HR for MTBI vs no injury = 1.65 [95% CI 1.35-2.03]). Finally, the effect of deployment-related MTBI on medical fitness was at most minimally mediated by post-concussive symptoms.

Comparison with Other Findings:

To the best of our knowledge this is the first study to systematically examine the effect of deployment-related MTBI on disability, specifically the development of career-limiting medical conditions that are incompatible with continued military service.

The only similar military study examined the extent to which musculoskeletal disorders impacted subsequent determinations of lack of medical fitness in a large cohort of US Army personnel.[32] Coherent with our findings, those authors identified a mental disorder (specifically post-traumatic stress disorder) and a

musculoskeletal condition (low back pain) as the two leading causes of lack of medical fitness. However, MTBI was identified as the third most common cause in that study, but the actual prevalence of MTBI is not reported, precluding any comparison with our study. Military studies of MTBI more than 6 months after deployment show a variety of adverse health effects, but none have explored occupational outcomes.[8;33;34]

The comparative civilian literature on occupational impacts of MTBI is also limited. The Worker's Compensation Board of the Province of British Columbia in Canada found that 15% of MTBI claimants were on short term disability for > 10 weeks.[34] A recent systematic review also reported that most workers with MTBI returned to work within 3 to 6 months after injury and that MTBI did not appear to be a significant risk factor for long term work disability.[35] Our own finding of a high absolute risk of persistent occupational impairments after deployment-related TBI may relate to differences in patterns of co-morbidity (notably, the high risk of psychological trauma and non-TBI injuries in those with deployment-related MTBI) in our population or to the stringent occupational fitness requirements for military personnel relative to civilians.

Limitations and Strengths:

We acknowledge the difficulty in attributing disability to MTBI as opposed to commonly co-morbid conditions with overlapping symptoms such as mental disorders. Although we captured the clinician-indicated primary medical condition that contributed to the adverse occupational outcome and had

covariates that measured psychological and physical injury as well as persisting PCS, we were not able to measure the changing nature of these variables with follow-up time.

All primary covariates of interest were assessed by self-report at the time of non-anonymous, post-deployment screening. This raises several limitations: First, the lack of anonymity could potentially lead to under-reporting of mental health problems. Second, MTBI was assessed through self-reports using the Brief Traumatic Brain Injury Screen used by the US. Recently, the sensitivity and specificity of this tool has been criticised.[18] In addition, the fact that it relies on self-report (as do most) assessments of MTBI raises the possibility of recall bias and reporting errors. Current military case definitions for MTBI include those who were only dazed/confused or saw stars, which can lead to misclassification when head trauma coincides with psychological trauma in a combat setting.[36] This will continue to be a challenge until such time as reliable objective diagnostic tests for MTBI are developed. Finally, we were only able to control for mental health problems, PCS and musculoskeletal pain reported at the time of screening, which took place several years, on average, before the outcome. It is possible that problems reported at that time had resolved or, conversely, that subsequent problems in those areas had developed at the time medical fitness problems were identified.

Our definition of PCS is also an important limitation: Universally accepted research criteria for establishing post-concussive syndrome do not currently exist. The definition

employed in this study was based on ICD-10 and has been used in other military studies,[4;19] but civilian research has shown that it is less specific than others.[37] We strove to mitigate that potential effect by excluding anxiety and depression (present in the ICD-10 criteria) from our operational definition of PCS. Furthermore, depression and PTSD were evaluated using the PHQ-2 and PCL-2 scales that excluded symptoms considered for assessment of PCS.

The structure of the questionnaire precluded any determination of the nature of other injuries at the time of EPDS. These were likely musculoskeletal in nature given findings from injury surveillance on military operations.[38]

Although debate continues about the long-term effects of repeated MTBI, we did not have the ability to control for its potential effect in this study.[39;40] It is therefore possible that much of the effect of MTBI on occupational impairment was due to multiple MTBI. Had this been the case, we would however have expected that the comprehensive assessment performed on all military personnel who are at risk of release on medical grounds should have uncovered this and be reflected in the estimates of neurologic disorders as a driver of disability.

Finally, the results of this study are rooted in the CAF's unique occupational fitness standards and hence not directly generalizable to other military organizations or employers in other sectors.

This study's primary strength is that it explores an important but under-researched issue: the occupational impact of

deployment-related MTBI in a military population. The large sample size allowed us to control for a broad range of covariates and potential confounders. The length of follow up exceeds that in many other published studies on the topic. Finally, time-to-event analysis allowed for efficient use of the data.

Implications:

Military personnel who report deployment-related MTBI are at significantly increased risk for adverse occupational outcomes. However, medical unfitness was largely driven by mental and musculoskeletal disorders and to a far lesser extent by neurologic diagnoses. The pathogenesis of poor health in some individuals following MTBI remains poorly understood and is undoubtedly multifactorial in nature.[41] Consequently, there is no consensus about how to mitigate adverse health outcomes in those with MTBI.

Given this challenge, military and veteran organizations in the US have increased their detection of MTBI through screening and outreach and have implemented MTBI-specific treatments such as cognitive rehabilitation.[14;42] Civilian guidelines have instead argued for a symptom based approach in light of the multifactorial nature of persistent PCS.[43] This approach emphasizes detection and treatment of mental disorders when present. The Canadian Armed Forces formally endorsed this approach in 2008.[15]

The findings of the present study suggest that military attrition following deployment related MTBI may best be mitigated by focussing on assessment and maximal treatment of mental

disorders and musculoskeletal problems. Our observation that neurologic diagnosis were an infrequent cause of medical unfitness in those with MTBI and that PCS only weakly mediated the association of MTBI with adverse occupational outcome casts some doubt as to the potential benefit of the routine use of cognitive rehabilitation therapy given the lack of rigorously controlled studies in this context.[44]

Additional research on outcome after MTBI is needed. Collecting information on the specific musculoskeletal problems driving disability in this population would provide useful context and might identify specific disorders for prevention and control efforts. Similarly, information on the timing of mental disorder onset might ultimately lead to interventions to facilitate early disclosure of symptoms and subsequent initiation of treatment.

Conclusion:

The past decade has seen growing concern about the long-term impacts of deployment-related MTBI in military personnel. This study provides a clearer picture as to the extent of that risk. Adverse occupational outcomes in those with deployment-related MTBI were primarily driven by musculoskeletal conditions and mental disorders and to a far lesser extent by a neurological diagnosis. These findings support a more holistic diagnostic and treatment approach focusing on these co-morbidities as the most promising strategy to minimize the burden of disability in MTBI-exposed military personnel.

Methodological refinements in future observational studies of outcome after MTBI will address some of the limitations of the present study. However, the question as to the optimal approach for treatment and rehabilitation of those with deployment-related MTBI will only be addressed definitively through carefully-designed intervention trials.

Contributors: All authors contributed substantially to the study. The primary author (BG) was responsible for the design, implementation, and analysis of the manuscript. The second author (CR) managed the data acquisition and collection and conducted the statistical analyses. The third author (MZ) contributed to the design, and implementation of the study. The fourth author (DB) contributed to the development of the statistical analytic approach. All authors contributed to the interpretation of the study results as well as the writing of the manuscript. All authors have read and agree with the manuscript's final content.

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Figure 1. Kaplan-Meier estimates of the probability of Career-limiting Medical Conditions (CL-MC) by type of injury.

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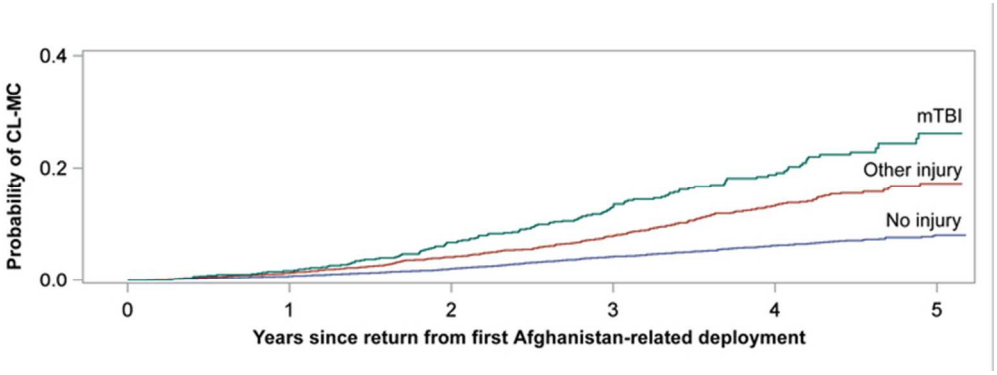

Figure 1. Kaplan-Meier estimates of the probability of Career-limiting Medical Conditions (CL-MC) by type of injury.
61x22mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6-7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8 (sources of data) 8-12 (details of methods)
Bias	9	Describe any efforts to address potential sources of bias	12
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12-14
		(*b*) Describe any methods used to examine subgroups and interactions	16
		(*c*) Explain how missing data were addressed	12
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Only baseline (page 2)
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	12
		(c) Summarise follow-up time (eg, average and total amount)	14
Outcome data	15*	Report numbers of outcome events or summary measures over time	14
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15.29
		(*b*) Report category boundaries when continuous variables were categorized	29
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations			16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	29

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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