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Association Between Traumatic Brain Injury and Risk of Suicide

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Supplemental content

IMPORTANCE Traumatic brain injuries (TBIs) can have serious long-term consequences, including psychiatric disorders. However, few studies have assessed the association between TBI and risk of suicide.

OBJECTIVE To examine the association between TBI and subsequent suicide.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study using nationwide registers covering 7 418 391 individuals (≥10 years) living in Denmark (1980-2014) with 164 265 624 person-years' follow-up; 567 823 (7.6%) had a medical contact for TBI. Data were analyzed using Poisson regression adjusted for relevant covariates, including fractures not involving the skull, psychiatric diagnoses, and deliberate self-harm.

EXPOSURE Medical contacts for TBI recorded in the National Patient Register (1977-2014) as mild TBI (concussion), skull fracture without documented TBI, and severe TBI (head injuries with evidence of structural brain injury).

MAIN OUTCOMES AND MEASURES Suicide recorded in the Danish Cause of Death register until December 31, 2014.

RESULTS Of 34 529 individuals who died by suicide (mean age, 52 years [SD, 18 years]; 32.7% women; absolute rate 21 per 100 000 person-years [95% CI, 20.8-21.2]), 3536 (10.2%) had medical contact: 2701 with mild TBI, 174 with skull fracture without documented TBI, and 661 with severe TBI. The absolute suicide rate was 41 per 100 000 person-years (95% CI, 39.2-41.9) among those with TBI vs 20 per 100 000 person-years (95% CI, 19.7-20.1) among those with no diagnosis of TBI. The adjusted incidence rate ratio (IRR) was 1.90 (95% CI, 1.83-1.97). Compared with those without TBI, severe TBI (absolute rate, 50.8 per 100 000 person-years; 95% CI, 46.9-54.6) was associated with an IRR of 2.38 (95% CI, 2.20-2.58), whereas mild TBI (absolute rate, 38.6 per 100 000 person-years; 95% CI, 37.1-40.0), and skull fracture without documented TBI (absolute rate, 42.4 per 100 000 person-years; 95% CI, 36.1-48.7) had an IRR of 1.81 (95% CI, 1.74-1.88) and an IRR of 2.01 (95% CI, 1.73-2.34), respectively. Suicide risk was associated with number of medical contacts for TBI compared with those with no TBI contacts: 1 TBI contact, absolute rate, 34.3 per 100 000 person-years (95% CI, 33.0-35.7; IRR, 1.75; 95% CI, 1.68-1.83); 2 TBI contacts, absolute rate, 59.8 per 100 000 person-years (95% CI, 55.1-64.6; IRR, 2.31; 95% CI, 2.13-2.51); and 3 or more TBI contacts, absolute rate, 90.6 per 100 000 person-years (95% CI, 82.3-98.9; IRR, 2.59; 95% CI, 2.35-2.85; all $P < .001$ for the IRR's). Compared with the general population, temporal proximity since the last medical contact for TBI was associated with risk of suicide ($P<.001$), with an IRR of 3.67 (95% CI, 3.33-4.04) within the first 6 months and an incidence IRR of 1.76 (95% CI, 1.67-1.86) after 7 years.

CONCLUSIONS AND RELEVANCE In this nationwide registry-based retrospective cohort study individuals with medical contact for TBI, compared with the general population without TBI, had increased suicide risk.

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Individuals with a history of traumatic brain injury (TBI) have been shown to have higher rates of nonfatal deliberate self-harm, suicide, and all-cause mortality than members of the general population.[1-3] Individuals with TBI may experience significant physical, cognitive, and emotional symptoms that place them at higher risk of suicide.[4] A recent systematic review[3] supported this premise by reporting an association of increased risk of suicide among TBI survivors compared with individuals with no TBI. However, most previous studies examining the relation of TBI and completed suicide have been limited by methodological shortcomings, such as small sample sizes, in particular very low numbers of suicide cases with TBI (maximum of 105 cases in studies that also included a control population).[5-12] These factors have compromised more detailed analyses, for instance with respect to severity, timely relation, and control of confounding variables. Several studies[2,13] have used standardized mortality rate (SMR) calculations based on governmental released age- and sex-mortality rates to estimate the risk of suicide associated with TBI. These estimates have varied widely, with reported SMRs ranging from 0.82 to more than 4, and they have lacked appropriate confounding control.[2,7,8,10,14] Recently, a Swedish register-based study reported a 3-fold higher risk of suicide in patients with TBI than in the age- and sex-matched general population; however, this estimate was not adjusted for important risk factors related to both TBI and suicide, such as preexisting psychiatric illness and nonfatal deliberate self-harm.[15]

The primary objective of this retrospective cohort study was to examine the association between TBI and subsequent suicide.

Key Points

Question What is the association between medical contact for traumatic brain injury (TBI) and risk of suicide?

Findings In this registry-based retrospective cohort study from Denmark that included 34 529 deaths by suicide over 35 years, individuals with medical contact for traumatic brain injury, compared with the general population without traumatic brain injury, had an increased risk of suicide, incident rate ratio of 1.90.

Meaning Traumatic brain injury may be associated with increased risk of suicide.

Methods

An anonymized data set was used for research purposes, and the project was approved by the Danish Data Protection Agency (journal number 2012-58-0004). Hence according to Danish legislation, informed consent from participants was not required.

Study Population

All individuals who were alive and living in Denmark during the study period were included in our analyses. In total, the cohort comprised 7 418 390 individuals aged 10 years or older from January 1, 1980, who were followed up until their dates of death or emigration from Denmark or December 31, 2014, whichever came first. By using the unique personal identification number assigned to each person in Denmark, linkage of data between various national registries was possible. We retrieved data from the Danish Civil Registration System,[16] the Database for Integrated Labour Market Research,[17] the National Hospital Register,[18] the Psychiatric Central Research Register,[19] and the Cause of Death Register.[20] All registers have full national coverage and contain continuously updated administrative data on all residents living in Denmark. Diagnoses in the National Hospital Register[18] and the Psychiatric Central Research Register[19] were recorded according to the diagnostic system of the *International Classification of Diseases, Eighth Revision* (*ICD-8*) until January 1, 1994; after that, *ICD-10* codes were used. Private psychiatric hospital treatment does not exist in Denmark; however, about 1% of somatic hospital beds are located in private hospitals.[21]

Measures

Exposure Variables

Traumatic brain injury was recorded in the National Patient Register, which covers 3 different forms of medical contacts. Since 1977, TBI was recorded for inpatient treatment and from 1995, contacts on outpatient visits and visits to emergency units were included in the registers. If a patient was registered twice within a month for a TBI, this was considered to be a recording of the same event. Traumatic brain injury was categorized into the following types: (1) mild TBI (defined as concussion), (2) skull fracture without documented TBI, and (3) severe TBI (head injuries with evidence of structural brain injury) (see the *ICD*-codes in eTable 1 in the Supplement). This categorization is based on the definition given by the American Congress of Rehabilitation Medicine and has been used in prior population-based studies of TBI.[22,23] In the analyses of TBI severity, these categories were mutually exclusive and individuals were categorized according to severity, ranging from mild TBI through skull fracture without documented TBI to severe TBI.

To assess the association between TBI and suicide in greater depth, we included the following covariates: *number of medical contacts for likely distinct TBI events* (0, 1, 2 or ≥3), *accumulated number of days in hospital treatment for TBI* (<1, same day discharge; 1; 2; 3; 4; 5; 6-14; and ≥15 days), *age at first TBI* (0-10, >11-15, >16-20, >21-40, >41-60, and ≥61 years), and *time since last medical contact for TBI* (0-6 months, >6-12 months, >1-2 years, >2-3 years, >3-4 years, >4-5 years, >5-6 years, >6-7 years, ≥7 years since discharge).

Outcome

From the Cause of Death Register,[20] we retrieved the outcome measure on death by suicide (*ICD-8* codes E950-E959 or *ICD-10* codes X60-X84, Y87).

Important Covariates

We also obtained diagnoses of fractures not involving the skull or spine (non-central nervous system [CNS]-related

fractures), to explore if fractures that occur to the head vs other fractures were associated with a higher risk of suicide and to adjust for this indicator of other injuries. From the National Patient Register, diagnoses of epilepsy were also included because people with epilepsy might have a higher frequency of TBI and psychiatric disorders.[24-26] In addition, estimates were adjusted for long-term physical diseases using the Charlson comorbidity index[27] (eTable 1 in the Supplement).

Psychiatric illness and nonfatal deliberate self-harm are associated with suicide,[28] so data on contacts for these issues were retrieved from the Psychiatric Central Research Register,[19] including all diagnoses given during hospital contact to inpatients since 1969 while outpatient and emergency department contacts were added in 1995 (eTable 1 in the Supplement). Contacts due to deliberate self-harm were identified using *ICD-8* codes 950-959 or *ICD-10* codes X60-X84 or when the reason for contact was indicated as deliberate self-harm using both somatic and psychiatric hospital registries. In addition, patient contacts at a psychiatric hospital where a diagnosis of injury or poisoning (*ICD-10* codes S51, S55, S59, S61, S65, S69, T36-T50, or T52-T60) had been recorded and no record of a substance misuse disorder existed (*ICD-10* codes F11-F19) were considered to be deliberate self-harm.

The Danish Civil Registration System[16] and the Database for Integrated Labour Market Research[17] include data on sex, age, and marital status (never married, married or registered partnership, divorced, widowed, or unknown), cohabitation status (cohabitation, no cohabitation), educational level (elementary school, vocational training, high school, university degree, ongoing or missing), and socioeconomic status (working, unemployed, disability pension, early retirement, student, and other or missing).

Statistical Analysis

Incidence rate ratios (IRRs) were estimated using adjusted Poisson regression models and time-varying variables (all variables were time-varying except for sex) using SAS (SAS Institute Inc; version 9.4). This method approximates Cox regression.[29] All incidence IRRs provided in the Tables represents results of between group tests of difference. First, our primary outcome was to estimate the risk of suicide among individuals diagnosed and discharged alive with TBI relative to individuals without head injuries. The basic model was adjusted for sex, age, and calendar period. In the fully adjusted models, we further adjusted for marital status, cohabitation status, socioeconomic status, other injuries, epilepsy, the Charlson comorbidity index (0, 1, 2, 3, 4, 5, or ≥6 chronic disorders),[18,27] "pre-TBI psychiatric disorders," ie, psychiatric disorders diagnosed before any medical contact for TBI, and equivalently "pre-TBI deliberate self-harm." Second, in a range of fully adjusted models, we examined how suicide was associated with different measures of TBI, such as (1) TBI severity, (2) number of TBI contacts, (3) days in treatment for TBI, (4) age at first TBI, (5) injury type, and (6) time since last TBI. We also tested the following covariates for trend: number of medical contacts for likely distinct TBI events, accumulated number of days in hospital treatment for TBI, and time since last medical contact for TBI. Test of trend was 2-sided and performed with the Cochran-Armitage test.

No adjustment was carried out for post-TBI psychiatric disorders and post-TBI deliberate self-harm because these potentially may act as mediators between TBI and suicide. To explore this further, we estimated incidence IRRs of the risk of suicide associated with before and after TBI psychiatric diagnosis and deliberate self-harm, respectively, in analyses confined to patients with TBI. In addition, multiplicative interaction analyses were carried out between TBI and pre-TBI psychiatric disorders and pre-TBI deliberate self-harm, respectively. In eTables 2 and 3 in the Supplement, the results of test of interaction terms are provided in the footnotes.

We also tested the overall association between TBI and suicide in a sub-cohort of individuals 18 years or more old born after 1962 to validate the association among individuals with full register follow-up as well as in a subcohort excluding those who received a TBI diagnosis in a deliberate self-harm episode.

Overall, the level of statistical significance was $P < .05$, and tests were 2-sided. To minimize type I errors due to multiple testing, all presented P values are Bonferroni corrected with a factor 53 equal to the total number of carried out tests, and statistically significant estimates (with a $P < .00095$ after Bonferroni correction) were noted in the Tables.

Results

Of the 7 418 391 living residents of Denmark during the 1980-2014 follow-up period (observed for a total of 164 265 624 person-years; **Table 1**), 567 823 had received a diagnosis of TBI (mean age at first TBI, 34.3 years [SD, 23.6 years], 41% women). Of the total population, 423 502 individuals (5.7%) were diagnosed with a mild TBI, 24 221 (0.3%) with skull fracture, and 120 100 (1.6%) with severe TBI. In all, 34 529 individuals died by suicide, mean age of 52 years (23 238 men; 11 291 women) and an overall absolute rate of 21.0 per 100 000 person-years (95% CI, 20.8-21.2). Among the 34 529 suicides, 3536 (10.2%) had previously been diagnosed with TBI (2578 men; 958 women), including 2701 with mild TBI, 174 with skull fracture without documented TBI, and 661 with severe TBI (**Table 2**).

The absolute rate of suicide in individuals with hospital contact for TBI was 40.6 per 100 000 person-years (95% CI, 39.2-41.9) compared with 19.9 per 100 000 person-years (95% CI, 19.7-20.1) in those with no hospital contact for TBI, for a difference of 20.7 per 100 000 person-years (95% CI, 19.3-22.1). The IRR was 2.64 (95% CI, 2.55-2.74) in the model adjusted for sex, age, and calendar period and was 1.90 (95% CI, 1.83-1.97) in the fully adjusted model. Furthermore, the fully adjusted analyses showed an increased risk of suicide by TBI severity: the absolute rate for mild TBI was 38.6 per 100 000 person-years (95% CI, 37.1-40.0) with an IRR

Table 1. Suicides Among Individuals With or Without a Traumatic Brain Injury Diagnosis

Characteristics	No Traumatic Brain Injury[a]				Traumatic Brain Injury[a]			
	No. of Suicides	No. of Individuals	Person-Years	Suicide Rate per 100 000 Person-Years (95% CI)	No. of Suicides	No. of Individuals	Person-Years	Suicide Rate per 100 000 Person-Years (95% CI)
Total sample	30 993	6 850 568	155 547 816	19.9 (19.7-20.1)	3536	567 823	8 717 809	40.6 (39.2-41.9)
Female	10 333	3 370 464	79 907 964	12.9 (12.7-13.2)	958	331 283	3 486 838	27.5 (25.7-29.2)
Male	20 660	3 480 104	75 639 853	27.3 (26.9-27.7)	2578	236 540	5 230 971	49.3 (47.4-51.2)
Marital Status								
Never married	8460	2 328 003	57 351 734	14.8 (14.4-15.1)	1456	228 386	4 457 070	32.7 (31.0-34.3)
Married or regular partnership	13 034	2 848 577	73 329 800	17.8 (17.5-18.1)	1024	195 165	2 847 597	36.0 (33.8-38.2)
Divorced	5221	656 993	12 176 573	42.9 (41.7-44.0)	790	82 468	970 905	81.4 (75.7-87.0)
Widowed or unknown	4278	1 016 995	12 689 709	33.7 (32.7-34.7)	266	61 804	442 236	60.1 (52.9-67.4)
Cohabitation Status								
Yes	13 953	3 904 296	102 773 420	13.6 (13.4-13.8)	1147	288 794	4 817 192	23.8 (22.4-25.2)
No	17 040	2 946 272	52 774 396	32.3 (31.8-32.8)	2389	279 029	3 900 617	61.2 (58.8-63.7)
Educational Level								
Elementary school	24 233	5 345 816	118 697 403	20.4 (20.2-20.7)	2596	424 383	6 523 481	39.8 (38.3-41.3)
Vocational training	3103	548 530	14 968 305	20.7 (20.0-21.5)	487	55 272	969 136	50.3 (45.8-54.7)
High school	2229	467 674	11 967 172	18.6 (17.9-19.4)	299	47 206	701 234	42.6 (37.8-47.5)
University degree	320	113 164	2 661 425	12.0 (10.7-13.3)	31	10 498	171 930	18.0 (11.7-24.4)
Ongoing or missing	1108	375 384	7 253 512	15.3 (14.4-16.2)	123	30 464	352 027	34.9 (28.8-41.1)
Socioeconomic Status								
Working	3773	2 449 108	51 962 417	7.3 (7.0-7.5)	567	237 166	3 801 017	14.9 (13.7-16.1)
Unemployed	600	212 607	4 014 386	14.9 (13.8-16.1)	181	36 348	475 051	38.1 (32.6-43.7)
Disability pension	2041	273 905	4 660 465	43.8 (41.9-45.7)	526	53 097	662 876	79.4 (72.6-86.1)
Early retirement or retired	3742	1 619 246	19 371 870	19.3 (18.7-19.9)	309	110 191	871 680	35.4 (31.5-39.4)
Student or others	285	930 841	10 705 503	2.7 (2.4-3.0)	42	67 704	777 115	5.4 (3.8-7.0)
Missing	20 552	1 364 861	64 833 174	31.7 (31.3-32.1)	1911	63 317	2 130 070	89.7 (85.7-93.7)
Fractures Not Involving the Skull or Spine								
No	26 745	5 183 808	136 820 949	19.5 (19.3-19.8)	2162	320 362	5 939 942	36.4 (34.9-37.9)
Yes	4248	1 666 760	18 726 867	22.7 (22.0-23.4)	1374	247 461	2 777 866	49.5 (46.8-52.1)
Epilepsy								
No	30 328	6 713 439	153 830 167	19.7 (19.5-19.9)	3202	532 540	8 319 191	38.5 (37.2-39.8)
Yes	665	137 129	1 717 649	38.7 (35.8-41.7)	334	35 283	398 617	83.8 (74.8-92.8)
Charlson Comorbidity Index (Chronic Disorders)[27]								
None	24 414	4 677 403	137 457 373	17.8 (17.5-18.0)	2712	392 059	7 419 233	36.6 (35.2-37.9)
1	3687	948 414	10 685 147	34.5 (33.4-35.6)	517	87 791	825 380	62.6 (57.2-68.0)
2	1953	723 416	5 350 422	36.5 (34.9-38.1)	181	47 923	311 049	58.2 (49.7-66.7)
3	533	264 371	1 288 325	41.4 (37.9-44.9)	72	20 993	97 234	74.0 (56.9-91.2)
4 disorders	150	872 651	328 499	45.7 (38.4-53.0)	15	7999	29 616	50.6 (25.0-76.3)
5	136	97 830	278 561	48.8 (40.6-57.0)	14	6140	18 242	76.7 (36.5-117.0)
≥6	120	51 869	159 489	75.2 (61.8-88.7)	25	4918	17 054	146.6 (89.1-204.1)
Pretraumatic Brain Injury Psychiatric Disorder								
No	20 220	6 182 893	147 203 422	13.7 (13.5-13.9)	2693	520 418	8 219 174	32.8 (31.5-34.0)
Yes	10 773	667 675	8 344 394	129.1 (126.7-131.5)	843	47 405	498 634	169.1 (157.6-180.5)
Pretraumatic Brain Injury Deliberate Self-harm								
No	24 976	6 742 863	153 672 792	16.3 (16.1-16.5)	3066	552 882	8 534 233	35.9 (34.7-37.2)
Yes	6017	107 705	1 875 024	320.9 (312.8-329.0)	470	14 941	183 576	256.0 (232.9-279.2)

[a] Mean age (SD) at the last observation for individuals with no traumatic brain injury was 52.7 (23.6) years; for individuals with it, 49.3 (21.7) years.

Table 2. Risk of Suicide by Medical Contact for Traumatic Brain Injury

	No Medical Contacts for Traumatic Brain Injury	Medical Contacts for Traumatic Brain Injury	Mild Traumatic Brain Injury	Skull Fracture	Severe Traumatic Brain Injury
No. of suicides	30 993	3536	2701	174	661
Individuals	6 850 568	567 823	423 502	24 221	120 100
Person-years	155 547 816	8 717 809	7 005 537	410 166	1 302 105
Rate per 100 000 Person-Years (95% CI)					
Suicide	19.9 (19.7-20.1)	40.6 (39.2-41.9)	38.6 (37.1-40.0)	42.4 (36.1-48.7)	50.8 (46.9-54.6)
Difference	1 [Reference]	20.7 (19.3-22.1)	18.7 (17.2-20.2)	22.5 (16.2-28.8)	30.9 (27.0-34.8)
Incidence Rate Ratio Variable Adjustment (95% CI)					
Basic model[a]	1 [Reference]	2.64 (2.55-2.74)[c]	2.53 (2.43-2.63)[c]	2.42 (2.09-2.81)[c]	3.35 (3.10-3.62)[c]
Fully adjusted[b]	1 [Reference]	1.90 (1.83-1.97)[c]	1.81 (1.74-1.88)[c]	2.01 (1.73-2.34)[c]	2.38 (2.20-2.58)[c]

[a] Sex, age, and calendar period.

[b] Sex, age, calendar period, educational level, cohabitation status, socioeconomic status, marital status, fractures not involving the skull or the spine, epilepsy, Charlson comorbidity index, pretraumatic brain injury psychiatric diagnosis, and pretraumatic brain injury deliberate self-harm.

[c] $P < .001$ after adjustment for multiple comparisons.

of 1.81 (95% CI, 1.74-1.88); 42.4 per 100 000 person-years, skull fracture (95% CI, 36.1-48.7) with an IRR of 2.01 (95% CI, 1.73-2.34, $P < .001$), and 50.8 per 100 000 person-years, severe TBI (95% CI, 46.9-54.6) with an IRR of 2.38 (95% CI, 2.20-2.58, $P < .001$) compared with individuals with no medical contact for TBI (Table 2). Individuals with a severe TBI also had a higher risk of suicide than individuals with a mild TBI (between-group difference IRR, 1.32; 95% CI, 1.21-1.44; $P < .001$) but not significantly different compared with those who had a skull fracture (IRR, 1.18; 95% CI, 1.00-1.40; $P = .048$). There was no significant difference in suicide risk between those with a mild TBI and a skull fracture (IRR, 1.11; 95% CI, 0.96-1.30; $P = .17$).

A higher suicide rate was noted with increasing number of medical contacts for likely distinct TBI events (test for trend, $P < .001$); compared with those with no TBI contact, 1 contact was associated with an IRR of 1.75 (95% CI, 1.68-1.83, $P < .001$) whereas 2 contacts had an IRR of 2.31 (95% CI, 2.13-2.51), and 3 or more contacts had an IRR of 2.59 (95% CI, 2.35-2.85), ie, not significantly different from 2 contacts ($P \geq .99$) (**Figure**, A). Moreover, a higher suicide frequency was noted relative to increasing number of days in treatment for TBI (test for trend, $P < .001$). As seen in Figure, B, the IRR for individuals hospitalized at least 1 day was 1.78 (95% CI, 1.69-1.88), whereas IRRs of more than 2 were noted for those whose treatment had lasted at least 3 days compared with individuals with no medical contact for TBI (see eTable 4 in the Supplement). Temporal proximity since last medical contact for TBI was associated with risk of suicide (test for trend, $P < .001$), with an IRR of 3.67 (95% CI, 3.33-4.04) the first 6 months and 1.76 (95% CI, 1.67-1.86) after 7 years compared with the background population. The risk of suicide with in the first 6 months after the TBI incident was also significantly higher (test of between group difference IRR, 2.10 (95% CI, 1.89-2.34; $P < .001$) compared with more than 7 years after a TBI.

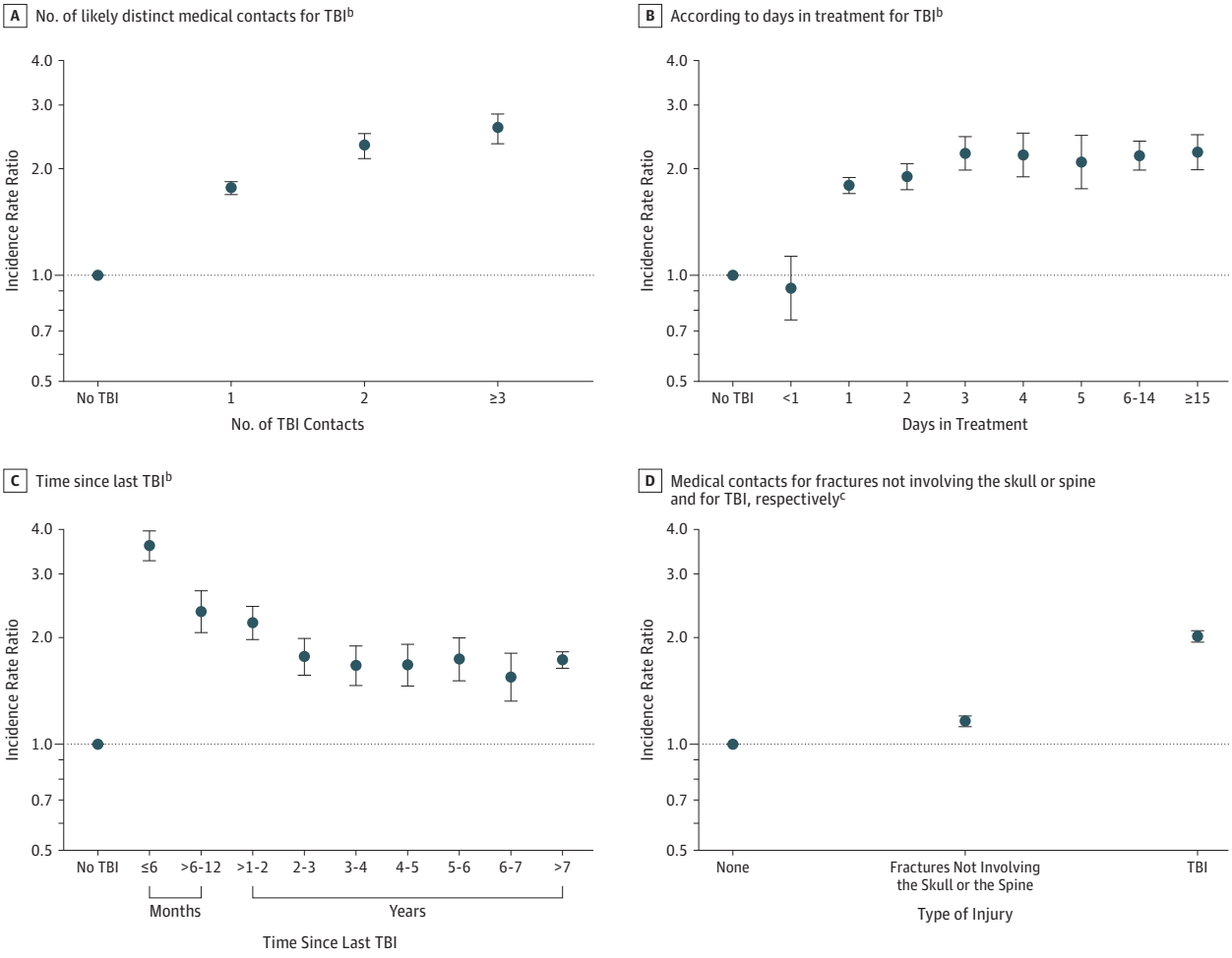
In Figure, D, the results presented were not adjusted for non-CNS-related fractures, and it shows that those with TBI had an IRR of 2.00 (95% CI, 1.93-2.08; $P < .001$) for suicide after a medical contact for TBI but also that those with fractures not involving the skull or spine had a higher rate of suicide with an IRR of 1.15 (95% CI, 1.12-1.19) than did the background population. Compared with individuals with a non-CNS-related fracture, those with a TBI had a significantly higher risk of suicide (IRR, 1.73; 95% CI, 1.66-1.81; $P < .001$).

The fully adjusted analyses showed that suicide rates were significantly elevated for all age groups of first TBI compared with individuals without TBI (**Table 3**). Those who had a first medical contact and were between the ages of 16 and 20 years had the highest suicide risk (IRR, 3.01; 95% CI, 2.74-3.30) compared with individuals with no TBI and also were at significantly higher risk of suicide than those experiencing TBI in all other age-groups (test of between group difference IRR, 1.65; 95% CI, 1.50-1.82; $P < .001$).

Individuals who were diagnosed with a psychological illness after their TBI had a higher risk of suicide (IRR, 4.90; 95% CI, 4.55-5.29; $P < .001$) than did those with TBI only, as were those who had engaged in deliberate self-harm after experiencing their TBI (IRR, 7.54; 95% CI, 6.91-8.22; $P < .001$; **Table 4**). Likewise, individuals who had been diagnosed with a psychological illness before their TBI had a higher risk of suicide (IRR, 2.32; 95% CI, 2.10-2.55; $P < .001$) than did those with TBI only, as were those who had engaged in deliberate self-harm before experiencing their TBI (IRR, 2.85; 95% CI, 2.53-3.19; $P < .001$). Analyses of interaction showed a negative association between TBI and prior psychiatric diagnosis or prior deliberate self-harm, thus among individuals who had both preexisting psychological illnesses or had engaged in self-harm prior to their experiencing a TBI were at lower risk of suicide than those who had psychological illness or had engaged in deliberate self-harm but who did not experience a TBI ($P < .001$ for interaction terms; eTable 2 and eTable 3 in the Supplement).

The sensitivity analyses including only individuals with full register follow-up born after 1962 supported the overall association between TBI and suicide in the younger population, with a slightly higher association between TBI and suicide (IRR, 2.42; 95% CI, 2.25-2.59; eTable 5 in the Supplement). The association between TBI and suicide in analyses

Figure. Incidence of Suicide Among Denmark Residents After Traumatic Brain Injury (TBI), 1980-2014[a]



[a] See eTable 2 for complete data estimates. Error bars indicate 95% CIs.

[b] Adjusted for sex, age, and calendar period, educational level, cohabitation status, marital status, socioeconomic status, fractures not involving the skull or the spine, epilepsy, Charlson comorbidity index, and psychiatric illness prior to traumatic brain injury (TBI) and prior to TBI-deliberate self-harm. Less than 1 day indicates same-day discharge.

[c] Adjusted for all characteristics listed in footnote *b* except fractures not involving the skull or the spine.

excluding individuals who received a TBI diagnosis as a result of a deliberate self-harm episode yielded an IRR of 1.88 (95% CI, 1.81-1.95).

Discussion

In this registry-based, retrospective, cohort study involving all Denmark residents, those with medical contact for TBI compared with the general population without TBI had an increased risk of suicide. Additional analyses revealed that the risk of suicide was higher for individuals with severe TBI, numerous medical contacts, and longer hospital stays. Analysis further showed that these individuals were at highest risk in the first 6 months after discharge. The association between TBI and suicide is likely to be partly mediated by post-TBI psychiatric symptoms because the risk of suicide among those who developed a psychiatric diagnosis or engaged in deliberate self-harm after a TBI diagnosis was higher than among individuals with only a TBI diagnosis. Traumatic brain injury constitutes a major public health problem with many serious consequences; furthermore, medical contact due to TBI had occurred prior to 10.2% of suicides. The absolute suicide rate in Denmark was 21 per 100 000 person-years in the 1980-2014 period, but it was almost twice as high among individuals with TBI, 41 per 100 000 person-years.

This study reports a lower difference between those with TBI and the general population than what has been reported in other studies, which in most cases have described this relative difference (although expressed as odds ratios, hazard rates, or in SMRs) to be somewhat higher than 2-fold.[2,10,11,13-15] Some of the previously reported estimates were only adjusted for sex and age, although a few were also adjusted for race, income, or marital status, and these resemble the basic adjusted findings in this study (Table 2), for which an incidence RR of 2.64 (95% CI, 2.55-2.74) was obtained. Only 2 previous studies[11,12]

Table 3. Number of Suicides Associated With Age at First Medical Contact for Traumatic Brain Injury (TBI)

	No. of Individuals With No Medical Contact for TBI	Age at First Medical Contact for TBI, y					
		0-10	11-15	16-20	21-40	41-60	≥61
No. of suicides	30 993	170	169	468	1482	854	393
Individuals	6 850 568	106 737	56 279	69 925	141 149	93 615	100 118
Person-years	155 547 816	1 787 170	1 123 237	1 347 030	2 483 594	1 280 048	696 731
Suicide rate per 100 000 person-years (95% CI)							
Age-standardized reference-group of no TBI[a]		16.9 (16.6-17.1)	16.9 (16.6-17.1)	16.9 (16.6-17.1)	22.0 (21.7-22.2)	27.0 (26.7-27.4)	29.1 (28.6-29.6)
Age of first TBI categories[a]		19.8 (19.5-20.1)	17.5 (17.2-17.7)	18.8 (18.5-19.0)	52.6 (52.2-53.0)	65.6 (65.0-66.1)	69.4 (68.5-70.2)
Rate difference per 100 000 person-years (95% CI)	1 [Reference]	2.9 (2.6-3.3)	0.6 (0.3-0.9)	1.9 (1.6-2.2)	30.7 (30.2-31.1)	38.6 (37.9-39.2)	40.3 (39.3-41.3)
Incidence rate ratio (95% CI) after adjustment[b]	1 [Reference]	1.61 (1.38-1.88)[c]	1.88 (1.62-2.20)[c]	3.01 (2.74-3.30)[c]	2.21 (2.10-2.34)[c]	1.56 (1.46-1.68)[c]	1.37 (1.24-1.51)[c]

[a] Age-standardized suicide rates.

[b] Adjusted for sex, age, calendar period, educational level, cohabitation status, marital status, socioeconomic status, fractures not involving the skull or the spine, epilepsy, Charlson comorbidity index, pretraumatic brain injury psychiatric diagnosis, and pretraumatic brain injury deliberate self-harm.

[c] $P < .001$ after adjustment for multiple comparisons.

Table 4. Suicide Rates Ratios According to Timing of First Psychiatric Diagnosis and Deliberate Self-harming With a Traumatic Brain Injury (TBI) Diagnosis

	Individuals With TBI				Individuals With TBI, but No Pre-TBI Psychiatric Diagnosis or Pre-TBI Deliberate Self-harm			
	Pre-TBI Psychiatric Diagnosis		Pre-TBI Deliberate Self-harm		Post-TBI Psychiatric Diagnosis		Post-TBI Deliberate Self-harm	
	No	Yes	No	Yes	No	Yes	No	Yes
No. of suicides	2693	843	3066	470	1630	1063	2257	809
Individuals	520 418	47 405	552 882	14 941	447 914	72 504	534 721	18 161
Person-years	8 219 175	498 634	8 534 233	183 576	7 482 034	737 141	8 272 011	262 222
Rate per 100 000 Person-Years								
Suicide	32.8 (31.5-34.0)	169.1 (157.6-180.5)	35.9 (34.7-37.2)	256.0 (232.9-279.2)	21.8 (20.7-22.8)	144.2 (135.5-152.9)	27.3 (26.2-28.4)	308.5 (287.3-329.8)
Difference	1 [Reference]	136.3 (124.8-147.8)	1 [Reference]	220.1 (196.9-243.3)	1 [Reference]	122.4 (113.6-131.2)	1 [Reference]	281.2 (259.9-302.5)
Incidence Rate Ratio Variable Adjustment								
Basic model[a]	1 [Reference]	4.92 (4.55-5.33)[b]	1 [Reference]	7.51 (6.81-8.28)[b]	1 [Reference]	7.22 (6.68-7.80)[b]	1 [Reference]	11.50 (10.6-12.5)[b]
Fully adjusted[c,d,e]	1 [Reference]	2.32 (2.10-2.55)[b]	1 [Reference]	2.85 (2.53-3.19)[b]	1 [Reference]	4.90 (4.55-5.29)[b]	1 [Reference]	7.54 (6.91-8.22)[b]

[a] Adjusted for sex, age, and calendar period.

[b] $P < .001$ after adjustment for multiple comparisons.

[c] Adjusted for sex, age, calendar period, educational level, cohabitation status, socioeconomic status, marital status, fractures not involving the skull or the spine, epilepsy, and Charlson comorbidity index.

[d] Analysis in which the psychiatric diagnosis is the dependent variable is also adjusted for deliberate self-harm.

[e] Analysis in which deliberate self-harm is the dependent variable is also adjusted for psychiatric diagnosis.

have reported estimates that were adjusted for pre-TBI psychiatric diagnoses; however, both studies were based on selected subgroups, ie, children[11] and military veterans (90% male population)[12] and were limited by small numbers of TBI-related suicide cases. As such no other studies, to our knowledge, have previously provided adjusted estimates for important confounders, such as pre-TBI psychiatric diagnosis, epilepsy, other fractures, a range of somatic comorbidity, and pre-TBI deliberate self-harm, which decreases the association between TBI and suicide. Still, a significantly higher suicide rate after medical contact for TBI was found. Furthermore, some findings in our study affirmed those reported in previous studies, such as suicide risk being associated with the number of medical contacts for TBI,[6,9] an increased rate with increased TBI severity,[2] and a higher suicide rate among individuals who experience a first TBI in young adulthood.[2,11] Moreover, the risk of suicide was substantially higher after TBI than after non–CNS-related fractures, indicating that the association between TBI and suicide was not merely due to injury proneness. Furthermore, the interaction analyses indicating that in individuals with a pre-TBI history of either a psychiatric diagnosis or an engagement of deliberate self-harm, a TBI was associated with a lower risk of suicide than among those who only had a psychiatric diagnosis or engaged in deliberate self-harm. This seems paradoxical and might be due to increased medical attention after the TBI or possible TBI induced initiative apathy among those who in addition to a psychiatric history or deliberate self-harm experience a TBI, reducing suicide events that otherwise would have occurred.

Traumatic brain injury is a major public health problem that has many serious consequences, including suicide. The high prevalence of TBI globally emphasizes the importance for preventing TBI in order to ameliorate its sequelae, such as increased suicide risk, which can be prevented resulting in saved lives. Falls or road traffic accidents[30] account for the largest share of TBIs. Helmet use has a protective effect, especially falls related to bicycling[31,32] and falls that occur at work.[33]

This study has several strengths. First, this is a large-scale cohort study that included 7 418 391 individuals, 34 529 suicides, and 35 years of follow-up. It compared individual-level data in the analyses that were adjusted for time-varying important and well-known risk factors of suicide. Second, it included only suicide death as an outcome, not including uncertain deaths like in other previous studies,[15] and classification of suicide in the Danish Cause of Death Register has recently been found to be very reliable.[34]

Limitations

This study also has several limitations. First, before 1995 medical outpatient contacts were not registered; thus, mild TBI incidents were treated in medical outpatient settings before 1995 and were not counted as individuals with TBIs, which may bias the estimates in a conservative direction. Second, no information on what treatment patients with TBIs received was available, which would have been useful to estimate whether different treatment regimens or subsequent follow-up would have reduced the suicide risk. Third, this study analyzed the number of medical contacts without further distinction among the 3 subtypes of medical encounter (hospitalization, emergency department, or outpatient); however, we evaluated the days in treatment as a measure of severity. Fourth, some individuals may not seek medical treatment after experiencing a mild TBI or for mild psychiatric disorders or for deliberate self-harm, consequently this would be unregistered and result in misclassification that bias estimates. Nevertheless, the risk of suicide was more increased after severe TBI than after mild TBI and also increased with the severity of the TBI when measured by the length of hospitalization for TBI, which might be a more accurate measure of TBI severity. Fifth, the National Patient Register has registered inpatient contacts since 1977; therefore, some individuals may have entered the study cohort with a pre-1977 incident of TBI, which may result in an underestimation of the risk estimate particularly in the elderly. Nevertheless, sensitivity analyses including only individuals with lifetime full registry data follow-up support the overall results.

Conclusions

In this nationwide registry-based retrospective cohort study, individuals with medical contact for TBI, compared with the general population without TBI, had an increased risk of suicide.

ARTICLE INFORMATION

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