

Supplementary Online Content

Fralick M, Sy E, Hassan A, Burke MJ, Mostofsky E, Karsies T. Association of concussion with the risk of suicide: a systematic review and meta-analysis. *JAMA Neurol*. Published online November 12, 2018. doi: 0.1001/jamaneurol.2018.3487

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Systematic Review Search strategy, Analysis – further details, and PROSPERO Details.

Systematic Review Search strategy

All search terms were identified following consultation with a librarian with expertise in systematic review and with clinicians who are content experts in the field. The databases below were searched until May 1, 2017.

PubMed (MEDLINE)

1. Suicide [MeSH]
2. suicid* [tiab]
3. self kill* [tiab]
4. Brain concussion [MeSH]
5. Brain injuries [MeSH]
6. concuss* [tiab]
7. brain injur* [tiab]
8. brain traum* [tiab]
9. cortical contusion* [tiab]
10. commotio cerebri [tiab]

PubMed Search

- Search (#1 or #2 or #3) AND search (#4 or #5 or #6 or #7 or #8 or #9 or #10)
- Filters: Humans; English; French; Italian

EMBASE

1. Suicid*:ab,ti OR 'suicidal behavior'/exp OR (self NEXT/1 kill*):ab,ti
2. 'Brain injury'/exp OR concus*:ab,ti OR (brain NEXT/1 traum*):ab,ti OR (brain NEXT/1 injur*):ab,ti

EMBASE Search

- 1&2
- Filters: Humans; English; French; Italian

PsycINFO

[DE "head injuries" OR TI concuss* OR AB concuss*] AND [(DE "suicide" OR DE "Assisted Suicide" OR DE "Attempted suicide" OR DE "suicidal ideation" OR TI suicide* OR AB suicide*)]

Limiters: English, French, Italian, Human

PILOTS

SU.EXACT("completed suicide") OR (SU.EXACT("deaths by suicide") OR (Self-kill*) OR (Suicid* OR Su.exact("deaths by suicide"))) AND concuss*

Google Scholar

1. With all of the words: concussion, suicide
 - a. Titles and abstracts reviewed for the first 10 pages of results
 - b. 3 full manuscripts reviewed, 0 articles included
2. With all of the words: suicide & With the exact phrase: "traumatic brain injury"
 - a. Titles and abstracts reviewed for the first 10 pages of results
 - b. 3 full manuscripts reviewed, 1 article included

Annual Academy of Neurology Conference

1. Annual Academy of Neurology (2012, 2013, 2014, 2015, 2016)
 - a. Search words: concussion, suicide, traumatic brain injury
 - b. We did not identify any additional relevant studies

Analysis – Further Details

Reporting of suicide attempt versus ideation

For the study by Bryant et al., they defined “suicidality” using a score which include prior ideation as well as attempt. Since it included both ideation and possibly attempt, we provide the point-estimate in our table of suicidal ideation.

Number of concussion/mild TBI

When the number of concussion or mild TBI were not provided in the manuscript, we contacted the paper’s corresponding author. In the case of the study by Richard et al., the number of mild TBI could not be determined in the manuscript. Dr. Richard verified that the number of mild TBI was 5,314.

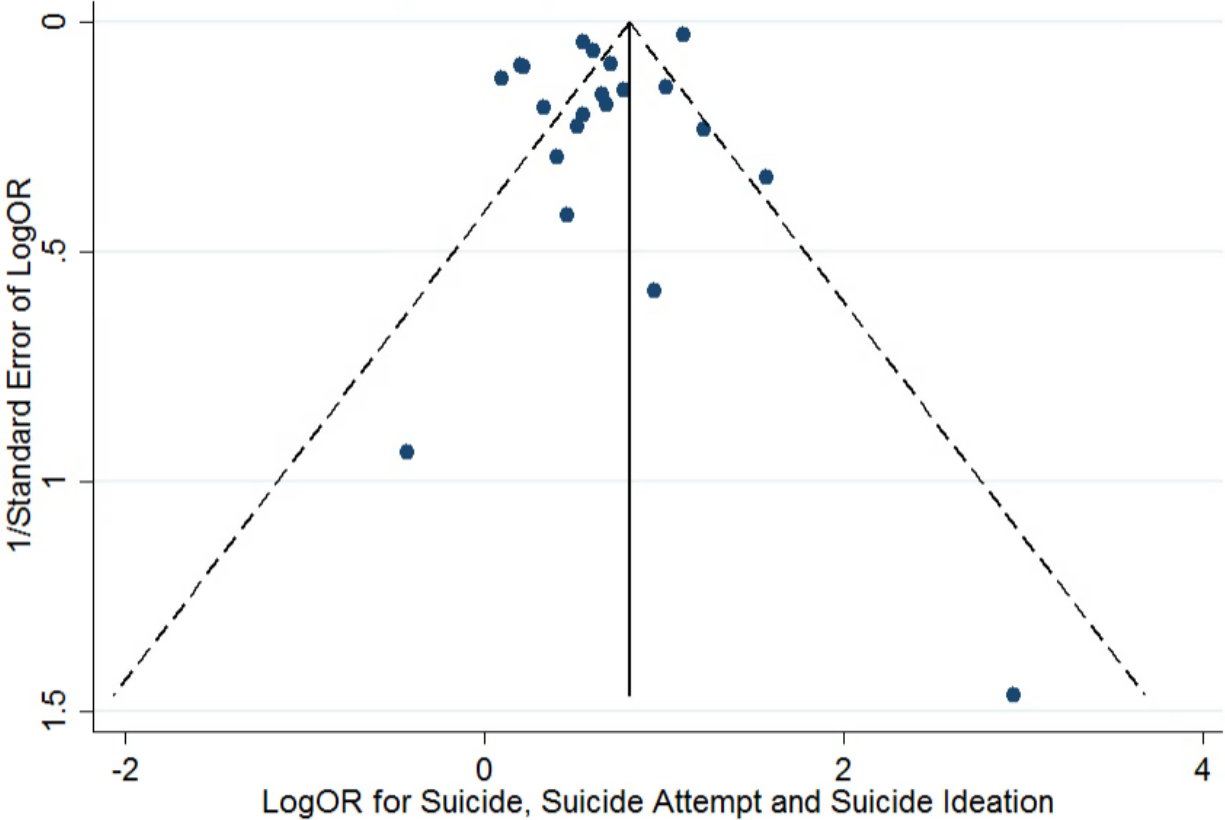
Relative risk calculation

For the study by Schneider et al., there were 0 suicide attempts in the non-TBI group, so we used a continuity correction of 0.5 added to each cell and calculated an unadjusted risk ratio. Ilie et al. reported separate estimates for recent TBI and past TBI, so we calculated a combined estimate using a random-effects model. They also provided odds ratios for patients with hazardous drinking, but we did not include these in our combined estimate. Vanderploeg et al. reported separate estimates for the risk of suicidal ideation among deployed and non-deployed military personnel, so we calculated a combined estimate using a random-effects model.

PROSPERO Details

Our study was registered on PROSPERO (CRD: 42016049388) *a priori*. We intended to perform a secondary analysis assessing the risk of suicide attempt stratified by the number of prior concussions. We did not pursue this analysis because too few studies reported number of concussion. More than >90% of the studies presented a history of concussion as a binary variable (yes/no). In addition, we planned to perform other subgroup analyses (e.g., stratified by presence of comorbid psychiatric disease, restricted by method of concussion diagnosis), but these were not possible due to a lack of statistical power and limited available data (e.g., few studies provided details on comorbid psychiatric disease).

eFigure. Funnel plot assessment for risk of publication bias using effect estimates from all included studies.



Dotted lines represent pseudo 95% CI.

eTable 1. Results of the critical appraisal using the Newcastle-Ottawa Scale

Study	Study Design	Selection		Comparability		Exposure		Total Score		
		Case Definition Adequate?	Cases Representative?	Selection of Controls	Definition of Controls	Based on Design or Analysis	Ascertainment of Exposure		Same method for Cases and Controls	Non-response Rate
Barnes, 2012	Case Control	-	+	-	+	+	-	+	+	5
Skopp, 2012	Case Control	+	+	+	+	++	-	+	-	7

Study	Study Design	Selection		Comparability		Outcome		Total Score		
		Exposed Cohort Representative?	Selection of Non-Exposed Cohort	Ascertainment of Exposure	Outcome not present at study start?	Based on Design or Analysis	Assessment of Outcome		Timing of Follow-up	Adequate Follow-up
Brenner, 2011	Retrospective Cohort	+	+	-	+	++	+	-	-	6
Bryan, 2013	Retrospective Cohort	-	+	+	-	++	-	-	-	4
Bryant, 2016	Prospective Cohort	+	+	+	-	++	+	+	-	7
Fazel, 2014	Retrospective Cohort	+	+	-	+	++	+	+	-	7
Fralick, 2016	Retrospective Cohort	+	+	-	+	-	+	+	+	6
Oquendo, 2004	Retrospective Cohort	-	+	-	-	-	-	+	+	3
Richard, 2015	Retrospective Cohort	+	+	-	+	+	+	+	-	6
Schneider, 2016	Retrospective Cohort	-	+	-	-	-	+	-	-	2
Stein, 2015	Prospective Cohort	+	+	-	+	+	-	+	+	6
Teasdale, 2001	Retrospective Cohort	+	-	-	+	-	+	+	-	4

Study	Study Design	Selection		Comparability		Outcome		Total Score	
		Representative Sample?	Sample Size Adequate	Non-Respondents	Ascertainment of Exposure	Based on Design or Analysis	Assessment of Outcome		Statistical Test
Ilie, 2014	Cross-Sectional	+	+	+	-	+	+	+	6
Vanderploeg, 2015	Cross-Sectional	+	+	-	-	+	+	+	5
Mackelprang, 2014	Cross-Sectional	+	+	-	-	+	-	+	4
Ilie, 2016	Cross-sectional	+	+	+	+	++	+	+	8
Topolovec-Vranic, 2017	Cross-sectional	+	+	-	-	+	++	+	6

eTable 2. Additional characteristics of included studies

A. Suicide					
Study	Suicides among individuals with concussion	Individuals with concussion or mild TBI (% male, average age)	Suicides among individuals without TBI	Individuals without concussion or any traumatic brain injury	Approximating absolute risk of suicide following concussion
Teasdale, 2001	N=750	N=126,114 (60%, 25)	Data not available	Data not available	0.59% of patients with concussion died from suicide, median time from concussion to suicide was 3.6 years. The maximum duration of follow-up was 15 years
Brenner, 2011	N=33	N=12,159 (90%, 58) ^A	N = 11,279	N = 7,800,846 (a random sample of 389053 were used for the analysis)	0.27% of patients died from suicide, median duration of follow-up unknown
Skopp, 2012	N=97	N=420 (Cases N=97, Controls = 323) (96%, 98% < 40) ^B	Not applicable	N=8,221 (Cases N=1,635, Controls N=6,586)	Case-control study and thus absolute risk could not be accurately calculated.
Fazel, 2014	N=1,664	N=333,118 (69%, 19) ^C	N = 5,962	N = 3,331,180	0.50% of patients with concussion died from suicide over a median follow-up of 4-years
Richard, 2015	N=31 ^D	N=5,314 (57%, 8)	N=390	N=113,582	0.49% of patients with concussion died from suicide over a median follow-up of 12.3-years.
Fralick, 2016	N=667	N=235,110 (52%, 41)	N= 3,934	N=2,397,192	0.28% of patients with concussion died from suicide over a median follow-up of 9.3 years

Legend: TBI = traumatic brain injury. Age is in years.

^A Numbers reflect patients included in the study including those without concussion.

^B All patients who died by suicide, average age was not provided.

^C All TBI patients. The age is for age at time of TBI.

^D There were 26 concussions, but the authors included 5 other TBI and that is the number (i.e., 31) they used to calculate their effect size. For our estimate of approximating the absolute rate of suicide following concussions we used the number of concussions only.

eReferences.

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